

Posters

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Endocrinology

PO-Endo 01.01

Functional ovarian cysts and age at menarche in a population of high school girls

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Objective: Functional cyst includes follicular, corpus luteum, and theca-lutein types, all of which are benign and usually self-limited. They are rather should be considered a variation of a normal physiologic process. The aim of this study is to examine the correlation between the functional cyst and the menarche age.

Materials and methods: We retrospectively reviewed charts of 50 Medicine girls University of Alexandroupolis and 6 teenagers from Hospital Kastoria, aged (17–24) years old with non inflammatory benign ovarian masses from January 1999 to December 2006. Operations were performed because of pain or ultrasound suspected features. The patients who were not operated were kept under observation and had ultrasound tests monthly, receiving orale contraceptive to facilitate resolution of the cyst. We evaluated the current age at menarche and functional ovarian cysts among Medicine girls.

Results: The ovarian cysts were unilateral and simple, with the size varying between 3 and 5 cm in 45 cases and more than 5 cm in 11 cases. In 4 cases were found size less than 3 cm. Ovarian cysts with size more than 4 cm were in 75% with late menarche (>14 years) and in 70% of them associated with menstrual cycle abnormalities. Among 56 young women 5 (8.9%) were initially qualified for the operation. The main indication for surgery was the presence of the ovarian mass. The diagnoses of the presence of ovarian mass were the follows: acute abdominal pain and recurrent abdominal pain despite conservative treatment, abdominal distension, menstrual bleeding. Hormonal treatment was given in 39 cases, whereas in 8 cases only follow up sonography was performed.

Conclusions: In this study population there is a correlation between late menarche and increased size of functional ovarian cysts. Prospective multicenter studies are necessary in order to clarify this finding.

PO-Endo 01.02

Surgical treatment of ovarian masses in teenagers. A fifteen year report

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Objective: One of the major problems in adolescent gynaecology is the presence of an ovarian tumour Ovarian neoplasms constitute 1–2% of all childhood and adolescent malignancies, and represent the most common gynaecological tumour (60–70%) during this period of a woman's life. In this report we analysed cases from a Greek population for: Preoperative and Intraoperative tumor evaluation, operative treatment, staging, follow-up and pregnancy rate.

Materials and methods: The purpose of this retrospective study was to determine the frequency, clinical aspects and surgical management of ovarian masses in fifty-two adolescent patients, in whom surgery was deemed necessary, between the years 1991–2006 We considered age, symptoms, ultrasound investigations, CA 125 levels, family history, operative treatment, surgical complications tumour size, histopathological examinations, pregnancy rate and follow up.

Results: Ovarian lesions in teenagers include a broad array of pathologic diagnoses that have variable and non-specific presenting symptoms. The majority of operated women 39 (75.5%) were under 17 years of age. The mean age was 16.635 ± 5 SD years (range min 14–max 19 years). The most common presenting complaint was abdominal pain in 34 (65.4%). Forty seven patients (90.4%) had benign lesions, two (3.8%) had borderline tumours and three patients had malignant lesions (5.8%). Most of the patients who wished to conceive subsequently did so.

Conclusions: For benign ovarian disorders the operation should be designed to optimize future fertility while in patients with malignancy, complete staging and resection of the lesion should be the first concern.

PO-Endo 01.03

Reconstructive surgical management of cryptomenorrhea due to complex uterovaginal malformations with duplicate uterus and complete vaginal agenesis

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Objective: The coincidence of obstructed duplicate uterus with functioning endometrium and complete vaginal agenesis is a very rare condition. We present the surgical reconstructive options.

Materials and methods: Three adolescent girls, aged 15–18 years with primary amenorrhea, cyclic abdominal pain, echo-free pelvic mass and complete vaginal agenesis by normal external genitalia were operated in our clinic. A combinative vaginal and laparoscopic approach was followed to reconstruct a neovagina by human amniotic membranes, establish the uterovaginal continuity, restore free cervical passage and perform pelvic adhesiolysis. We evaluated the operative, anatomical and functional results over a 6-months-follow-up period. **Results:** Mean neovaginal length was 10 cm (range: 9–12 cm) and a width allowing the easy introduction of two fingers. In all patients the uterovaginal continuity could successfully be restored; in one patient a two-step surgical approach had to be followed to fully establish cervical passage. Satisfactory anatomical and functional results could be achieved, with no operative morbidity. Two girls had a uterus bicornis unicollis, but no metroplasty or hemihysterectomy had to be

performed. Regular menstruation resumed with normal ultrasound findings in the follow-up. One patient engaged in sexual activities 2 months after surgery, while the other two continued intermittently using a vaginal dilator to prevent contraction of the neovagina.

Conclusions: In rare cases of obstructed functioning uterus due to a complete vaginal agenesis, a combinative laparoscopic and vaginal surgical approach may effectively restore anatomy and function, by an overall minimal operative morbidity. Especially processed human amniotic membranes provide excellent results in neovaginal reconstruction.

PO-Endo 01.04

Differential basal and postprandial insulin in patients with PCOS

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Objective: Insulin resistance is characterized by inadequately high glucose levels in relation to the corresponding insulin concentrations. It is found in subjects with overweight and obesity and also in patients with PCOS. This study employed a standardized test meal for a more physiologic test situation than offered by the oral glucose tolerance test. Whether or not there are differences under everyday conditions between the basal and postprandial state in PCOS patients is as yet unknown.

Materials and methods: 32 non-diabetic PCOS-women from the LIPCOS study and 64 BMI—and age-matched normocyclic controls were given a standardized test meal (260 kcal, 62% carb, 32% fat, 6% protein) for submaximal stimulation of insulin and glucose which were determined at baseline and at 60, 120 and 180 min postprandially.

Results: Basal and postprandial insulin levels were quite similar in PCOS-patients and controls (C). However, glucose levels at baseline were significantly elevated in PCOS-patients (92.8 ± 1.7 (PCOS) vs. 84.7 ± 1.2 mg/dl (C); $p < 0.001$). By contrast, postprandial glucose levels were no longer different.

Conclusions: These data demonstrate that in the fasting state PCOS patients have greater insulin resistance than weight- and age-matched controls. Interestingly, insulin resistance is not different between PCOS and normocyclic women in the postprandial state, suggesting that mechanisms of action for insulin metabolism might differ between the fasting and postprandial state that remain to be elucidated.

PO-Endo 01.05

Bilateral Leydig cell hyperplasia of the ovary in a postmenopausal woman: a case report

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Objective: Leydig cell tumors and hyperplasia of the ovary are usually benign neoplastic diseases. Rarely, they may cause hyperandrogenism with associated clinical features. It is a rare finding in the postmenopausal woman, especially a bilateral occurrence is unusual. In the literature, only a handful of cases of bilateral Leydig cell tumor/hyperplasia of the ovary are described.

Materials and methods: We report upon a case of a 73-year-old woman, who presented in our alopecia ambulance with a testosterone level of 2.8 ng/ml (0.03–0.6 ng/ml) and normal tumor marker levels of CEA and CA 125. Ultrasound revealed normal sized, right-sided slightly polycystic ovaries. Further, the patient was pharmacological treated for Morbus Osler, bronchial asthma, and hypertension. No association of hyperandrogenism with the patient's medication list was detected. Bilateral laparoscopic adnexectomy was performed and histopathological examination revealed bilateral Leydig cell hyperplasia. Hyperandrogenism with hirsutism and alopecia resolved completely after surgical treatment.

Conclusions: Taken together, this case of bilateral Leydig cell hyperplasia of the ovary represents a rare cause of virilisation in postmenopausal patients. It should be considered in a setting of hyperandrogenism and virilisation.

PO-Endo 01.06

Epidermal growth factor in follicular fluids of polycystic ovaries

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Objective: Epidermal growth factor (EGF) is a potent inhibitor of the FSH stimulated estradiol secretion by inhibiting the aromatase in human granulosa cells. EGF might act as a paracrine intraovarian factor and hence impair the maturation of follicles in the polycystic ovarian syndrome (PCOS).

Materials and methods: 27 IVF patients were examined in the three groups: women without signs of PCOS with normal ovaries ($n = 9$), ovulatory women with the sonographic appearance of polycystic ovaries (PCO) ($n = 10$) and anovulatory women with classical PCOS ($n = 8$). EGF concentrations were determined in serum and in the follicular fluid by ELISA.

Results: The mean serum concentration of EGF is significantly higher compared to the follicular fluid (median 274.9 pg/ml vs. 1.9 pg/ml, $p < 0.05$). However, no differences were detected in the EGF serum levels of all the three groups. The EGF levels in the follicular fluid of women with polycystic ovaries (PCO and PCOS) is significantly higher compared to normal women (median 2.2 pg/ml vs. 2.0 pg/ml vs. 0.7 pg/ml, $p = 0.031$). The EGF concentrations in the follicular fluid did not differ between polycystic ovaries with or without classical signs of PCOS ($p = 0.791$).

Conclusions: EGF concentrations in follicular fluids of polycystic ovaries were higher than in normal ovaries. EGF possibly contributed to the pathogenesis of PCOS by impairing the maturation of follicles through the inhibition of aromatase activity in human granulosa cells.

PO-Endo 01.07

Homocysteine augments aromatase (CYP19) expression in human luteinized granulosa cells

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Objective: 5, 10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme of homocysteine metabolism. A C → T mutation at

position 677 of the MTHFR cDNA (677C > T) produces a thermolabile form of the enzyme with significantly reduced enzymic activity. We have shown previously that the MTHFR 677C > T mutation strongly affects the ovarian response to recombinant FSH during controlled hyperstimulation. As this genetic variation is associated with increased plasma homocysteine (hcy) levels, we investigated whether hcy may influence the gene expression of CYP11, CYP19, and StAR which are important enzymes involved in the steroid metabolism of human granulosa cells (GC).

Materials and methods: Immortalized HGL5 cells were cultured for a total of 5 days in M-199 medium supplemented with 10% fetal calf serum and 0, 25, 100, or 200 μ M D/L-hcy. Total RNA was extracted and reverse transcribed to cDNA. Gene expression was determined by real-time PCR. The calculation of relative expression ratios was carried out with the Relative Expression Software Tool (REST) version 2008.

Results: Exposure of HGL5 GC to hcy significantly enhanced the expression of CYP19 mRNA in a dose-dependent manner. Incubation with 25 μ M D/L-hcy increased CYP19 mRNA expression 4.29-fold (CI 95%: 2.05–10.99; $p < 0.001$), 100 μ M D/L-hcy 8.04-fold (CI 95%: 1.76–43.85; $p < 0.05$) and 200 μ M D/L-hcy 10.58-fold (CI 95%: 1.76–79.66; $p < 0.0001$). In contrast, there was no significant effect on CYP11 and StAR expression.

Conclusions: The present study demonstrates that hcy specifically augments CYP19 mRNA expression in human luteinized granulosa cells, suggesting an interference of hcy with specific steps of steroid metabolism in human GC. This might be one mechanism by which the MTHFR 677C > T mutation affects ovarian responsiveness in controlled ovarian hyperstimulation cycles.

PO-Endo 01.08

Two heterozygote mutations of DHH gene in one patient with complete XY gonadal dysgenesis and polyneuropathy: treatment and outcome case report

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Objective: We report about the complex diagnosis and treatment modalities of a patient with rare sexual differentiation disorder caused by two heterozygous mutations (mutation in exon 1.1 het. c.83 8/insCCGGG and exon 2 het. c.554C > G [S185W]) reported for the first time in the DHH (desert hedgehog) gene with a 46 XY male karyotype.

Materials and methods: A 24 year old patient was admitted for gonadectomy of streak gonads after emergency surgery for impalement injury caused by cohabitation trial. The patient with previously diagnosed XY gonadal dysgenesis and symptoms of polyneuropathy particularly in lower limbs (status post removal of several distal phalanges), has been neglecting the diagnosis for 5 years. She presented a primarily juvenile external genital with a 2 cm wide and 7 cm long vagina and accompanying epithelial atrophy. A gonadectomy with removal of two streak gonads was performed. A local substitution of estradiol and systemic substitution of estradiol was begun.

Results: Sertoli type epithelial cells and leydig-like cells were detected within the streak gonads. In the removed streak gonads no evidence of neoplasia has been found. The patient was diagnosed with uterine aplasia and lacking prostate gland. Five months after treatment initiation, cohabitation is possible. The patient still suffers from

a polyneuropathy, especially in the distal parts of lower limbs. Sural nerve motoric compound action potential (MCAP) was bilaterally not detectable and tibial nerve MCAP was extremely reduced.

Conclusions: The described mutations demonstrate a very rare combination of gonadal dysgenesis and polyneuropathy. In this rare case of 46XY male karyotype, female phenotype and complete gonadal dysgenesis with juvenile external gonads and polyneuropathy, a multidisciplinary approach from gynaecologists, neurologists, genetics and psychologists can aid the patient in creating an acceptable sexual and psychosocial consciousness.

PO-Endo 01.09

Characterization of adult stem cells in endometrial biopsies obtained during routine diagnostics

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Objective: Human endometrium displays a highly regenerative capacity possibly owed to adult stem cell activity. It is hypothesized that disorders of the endometrium such as endometriosis and endometrial carcinoma are associated with a disorder of stem cell function. As a limiting factor of experimental studies to date only uteri from hysterectomies were used to assess stem cell activity. We conducted this study to characterize stem cells of the superficial layers of the stratum superficial, accessible by diagnostic endometrial biopsy in a routine clinical setting. We wanted to show that minimal invasive endometrial biopsies are an eligible tool to obtain multi-potent stem cells to enable studies in larger patient populations.

Materials and methods: 36 patients underwent routine endometrial biopsy during diagnostics prior to infertility therapy. Endometrial stroma cells were isolated by immunodepletion and the expression of stem cell markers was analyzed by quantitative real time PCR and FACS analysis. Differentiation potential and cloning efficiency of serially passaged cell clones were studied in vitro.

Results: Endometrial stroma cell clones derived from endometrial biopsies displayed characteristic properties of stem cells including clonality, long time cultivation, multipotent differentiation potential and expression of the stem cell markers CD 146, CD73, Msi-1, Notch-1 and Sox-2.

Conclusions: Adult stem cells can be obtained from endometrial biopsies in a routine diagnostic setting. These findings will stimulate and accelerate stem cell based studies to develop innovative diagnostic and therapeutic concepts of endometrial disorders in large patient populations. Furthermore these results let appear the endometrium as a promising source for induced pluripotent stem cell generation (iPS).

PO-Endo 01.10

Pharmacodynamic effects of chlormadinone acetate (CMA) on prostaglandin biosynthesis in human endometrium

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Objective: Dysmenorrhoea is associated with significantly reduced quality of life. In a clinical study a reduction of dysmenorrhoeic symptoms was observed in women using oral contraceptives containing CMA. Our working hypothesis is that CMA exerts its

beneficial effect by a stronger reduction of prostaglandin biosynthesis compared to other synthetic progestins. The aim of our study is to investigate the impact of CMA on cyclooxygenase-2 (COX-2) and the phospholipase A₂ inhibitor annexin-1 in human endometrial explants and a human endometrial stromal cell line.

Materials and methods: Human endometrial explants and the immortalized Yale human endometrial stromal cell line (YHES, ATCC) were used as model. The explants were obtained by aspiration curettage using a Pipelle (Laboratoire C.C.D). RT-qPCR assays (Universal Probe Library, Roche) were used on a LightCycler 480 instrument to analyze COX-2-mRNA levels by treatment with interleukin-1 β (IL-1 β), CMA \pm IL-1 β and dexamethasone \pm IL-1 β (10⁻⁶ M each) within 6 h of culture for endometrial explants, 5 h of culture for YHES.

Results: COX-2-mRNA was down-regulated in endometrial explants after 4 and 6 h of culture. The effects were more distinctive in the proliferative phase than in the secretory phase. Analog effects were observed for the production of PGF_{2 α} . However, there was a high interindividual variation in expression levels. Similar effects of CMA and dexamethasone were observed in YHES after 5 h of culture compared to IL-1 β stimulated samples. No significant effects on annexin-1-mRNA levels were found.

Conclusions: Our findings indicate that CMA exerts dexamethasone-like glucocorticoidal effects in human endometrium and interacts with the arachidonic acid cascade by reducing COX-2-mRNA expression. This mechanism of action may explain the beneficial effect of CMA in dysmenorrhoea.

PO-Endo 01.11

Stimulation of estrogen- and progesterone-receptor in human granulosa cells

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Objective: Luteinizing hormone (LH) is a triggering signal molecule for ovulation and responsible for numerous mechanisms in the ovary. During the follicular phase, FSH induces granulosa cells (GCs) to produce and express more LH-receptors. Therefore GCs are adequate target cells for LH. The aim of our study was to determinate the effect of different doses of LH on estrogen and progesterone receptors in human GCs.

Materials and methods: Human GCs were obtained from patients undergoing controlled ovarian hyperstimulation for in-vitro-fertilization with or without ICSI. After seven days of cultivation 10, 100 or 1000 mU/ml LH was substituted. The expression of both estrogen (ER-alpha and ER-beta) and both progesterone (PR-A and PR-B) receptors were analysed on mRNA-level by RT-PCR (TaqMan-PCR) and on protein-level by immunocytochemistry. The mRNA-isolation was performed after 2 h of stimulation. For immunocytochemistry GCs were cultivated for another 48 h. Unstimulated controls were always included.

Results: Addition of 100 mU/ml and 1000 mU/ml LH lead to a significant higher expression of ER-beta and PR-A on mRNA-level analysed by RT-PCR (TaqMan-PCR) and protein level analysed by immunocytochemistry. LH did not affect ER-alpha and PR-B expression significantly.

Conclusions: LH is known to be essential for ovulation and stimulates progesterone production in the corpus luteum. Results of our study suggest that LH mediates ER-beta and PR-A expression in human GCs. Therefore ER-beta and PR-A seem to be involved in ovulation and maintenance of the corpus luteum.

PO-Endo 01.12

Successful pregnancy after laparoscopic uterosacropexy in a young woman with total uterine prolapse

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Objective: Need for fertility preserving prolapse surgery in a 37 year old woman.

Materials and methods: In September of 2005 a healthy 37-year old woman had a spontaneous delivery of a 3590 g child. In May 2006 she frequented our urogynecological unit because of a symptomatic descensus uteri et vaginae III^o (dyspareunia, restriction of sports activities and worse influence of quality of live in general). Hysterectomy and anterior and posterior repair was recommended to the patient e.m. But the woman's wish was to preserve their fertility. In the case of uncompleted family planning a uterus preserving approach was necessary. After urodynamic examination (no marked stress incontinence was found) we decided with the couple to perform a minimal invasive uterosacropexy. We performed standard laparoscopy. The retroperitoneal space on the right side of the rectum between cervix, cul de sac and sacrum os was opened. The right ureter was identifying and pushed laterally. Two sutures through the longitudinal anterior ligament and the cervix was supplied. A small polypropylene mesh was fixed on the cervix with the two sutures. From vaginally the uterus was pushed up and the mesh was fixed corresponding on the longitudinal anterior sacrum ligament. The peritoneum was closed to prevent any delay associated with the use of the mesh. Postoperatively a minimal descensus was the result. The patient had no complaints and was delivered after 6 days.

Results: The patient became pregnant spontaneously 6 months later. In July 2007 the patient had a primary, uncomplicated caesarean section (wish of the patient to prevent a secondary prolapse) in the 38th week of pregnancy. A mature boy with a weight of 3605 g was born.

Conclusions: This case report is an example of laparoscopic uterosacropexy as a successful minimal invasive approach to preserve fertility in young women with total uterine prolapse.

Perinatal medicine

PO-Geb 01.01

What expectations do pregnant women have of modern obstetric departments?

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Objective: Unlike institutions of other specialities, obstetric departments are not only considered by their medical standard. Therefore, the aim of this survey was to evaluate the needs and expectations that pregnant women have for an ideal delivery.

Materials and methods: 566 pregnant women from all three hospitals in Mannheim, Germany, were included. The questionnaire comprised a general part including personal details and a special section with 34 questions on prenatal, sub part, and postnatal aspects.

Results: Presentation of the obstetric department by brochures, internet website, and labour ward tours was rated high. Besides, respondents considered introducing their clinical chart during pregnancy to be important, rather than attending antenatal classes. Also of great

importance was the possibility to get to know the obstetric staff before delivery. For the respondents it was relevant that a single midwife attended during labour. Friendliness of the personnel and state-of-the-art medicine were considered to be very important. The presentation of the labour ward regarding ambience, colours and light was more important than the modernity or the offer of alternative medicine. A 24 h in-house consultant, attendance of a physician during second stage of labour, as well as a neonatal intensive care unit were also rated high. Most pregnant women preferred on ward lactation counselling. On the maternity ward, quality and variety of food and ambience were rated high. The respondents appreciated the opportunity to have the second routine examination of the neonate at the obstetric department. During puerperium, most women desired care by a midwife.

Conclusions: According to this comprehensive survey, there are three key-factors for an ideal delivery and the choice of the obstetric department: safety, friendliness of the staff and a good standard of comfort. Obstetric units should give pregnant women the opportunity to get acquainted with the hospital and the staff ahead of birth.

PO-Geb 01.02

Preterm premature rupture of the membranes-PPROM

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Objective: The preterm premature rupture of the membranes (PPROM) is defined as rupture of the amniotic membranes prior to 37 weeks of gestation. PPROM occurs in approximately 3% of all pregnancies and is responsible for a third of all preterm births. In 0.6–0.7% of all pregnancies PPROM occurs at or before 26 weeks of gestation and is associated with high perinatal morbidity and mortality. Previous preterm delivery, history of or current cervical incompetence, cerclage, history of PPROM and tobacco use could be identified as risk factors for PPROM at 14–24 weeks. The purpose of this study was to identify risk factors for PPROM prior to 28 weeks of gestation in pregnant women treated at the Department of Obstetrics and Gynecology at the University Hospital Vienna.

Materials and methods: This retrospective study included all patients ($n = 56$) with PPROM prior to 29 weeks of gestation during the years 2007–2009. Statistical analysis is going to be performed using SPSS version 16.

Results: The evaluation of all data is still in progress and the results are going to be presented at the congress.

Conclusions: This study gives an epidemiological overview of the number of cases of PPROM during the years of 2007–2009 at the department of obstetrics and gynecology at the university clinic Vienna and defines the possible risk factors leading to PPROM.

PO-Geb 01.03

Anticipation and decision making criteria of pregnant women in marketing of obstetric

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Objective: The last three decades have been marked with copious attempts to reduce health care related financial costs. The field of obstetrics has been hit especially hard, particularly in conjunction with regressive birth rates. The aim of this work was to elucidate

which informational resources and which ultimate decision making criteria play a role for women who are choosing a birthing location. **Materials and methods:** From December 2008–April 2009, 183 women were reviewed post partum at the Jena University Hospital. 108 questionnaires were returned fully completed. The battery of questions encompasses informational resources and decision making criteria helpful in choosing a birthing location. In this work, several parameters concerning satisfaction, as well as anticipation, of the women were evaluated.

Results: Pregnant women and women in childbed are a very well-informed and demanding audience. The most important resources are the internet, tours through the clinic and individual guidance by the gynaecologist or midwife. The most important determinants in the decision making process were identified by the respondents as: good reputation of the physicians and regional proximity of the clinic to the respondent's residence. Alternative methods of delivery were not named as items of interest. Individual counselling for breast feeding has a high priority and aids in identifying the most fitting clinic. Pregnant women highly value the 24-h presence of a doctor, modern and readily available equipment and the integration of a level 1 perinatal center in the clinic. Aspects of satisfaction and anticipation of the respondents were also ascertained in the questionnaire. The women expectations were predominantly either met or exceeded.

Conclusions: The better evaluation of anticipation and decision making criteria of pregnant women can aid in optimizing the public representation of an obstetrics clinic, while unearthing potential areas of development.

PO-Geb 01.04

Antepartum third trimester bleeding: etiology and characteristics

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Objective: The aim of the present study was to correlate third trimester hemorrhage with certain demographic and intrapartum factors. **Materials and methods:** In a ten retrospective study from 01.01.2000 to 31.12.2007 150 cases of pregnant women who presented with third trimester uterine bleeding were evaluated. The etiology of the hemorrhage was investigated and characteristics of the two major pathologies (abruption placenta and placenta previa) were compared to each other. Characteristics included in the analysis were maternal age, religion (Christians–Muslims), hypertensive disorders in pregnancy, nicotine and alcohol abuse, previous cesarean section, induced abortions, parity, gestational age at hemorrhage, management of the hemorrhage (conservative—need for emergency cesarean section), need for transfusion. Statistical analysis was performed by use of the SPSS 10 statistical package.

Results: Placenta previa was the most common pathology in the third trimester hemorrhage. Advanced maternal age, hypertensive disorders in pregnancy, smoking, and need for transfusion were significantly higher in the group of abruption placenta. Muslims presented a high prevalence of abruption placenta ($p < 0.01$). History of previous cesarean section, induced abortions and conservative management of the hemorrhage were strongly correlated to placenta previa ($p < 0.01$). **Conclusions:** Evaluation of pregnancy characters might be indicative for the etiology of the third trimester bleeding and should be taken into account in order to eliminate perinatal complications.

PO-Geb 01.05**Severe hypertriglyceridemia in a case of a 31 year old pregnant female after necrotizing pancreatitis***Stephanie Gawlik¹, Christof Sohn¹, Bettina Schlehe¹¹Universitätsfrauenklinik, Gynäkologie und Geburtshilfe, Heidelberg, Germany

Objective: We report a case of severe hypertriglyceridemia and its management in a pregnancy 2009 after having suffered from necrotizing pancreatitis in 1997.

Materials and methods: A 31 year old primigravida was admitted to the hospital at 31 weeks of gestation. The patient had suffered from acute pancreatitis in 1997 with admission to the intensive care unit.

Results: In her case the necrotizing pancreatitis was managed surgically by open laparotomy. In her first pregnancy she presented with extremely high levels of plasma triglycerides. With conservative care including the use of gemfibrozil and heparin, the situation remained stable until the 35th week of gestation. With still rising levels the pregnancy was terminated in the 36th week of gestation by caesarean section and a healthy newborn was delivered.

Conclusions: Severe Hypertriglyceridemia in pregnancy threatens maternal and fetal prognosis. A familiarity with the potential life threatening complications including thrombosis, emboly and intra-uterine fetal death is necessary for its clinical management. In patients with a different clinical background it can cause pancreatitis which is a potentially life-threatening condition. The timing and route of delivery should be individualized.

PO-Geb 01.06**Cardiovascular predictors in gestational diabetes***Tanja Groten¹, Wilgard Hunger-Battefeld², Ekkehardt Schleußner¹¹Jena University Hospital, Friedrich-Schiller University of Jena, Department of Obstetrics, Jena, Germany, ²Jena University Hospital, Friedrich-Schiller University of Jena, Department of Internal Medicine III, Jena, Germany

Objective: Gestational diabetes (GDM) and diabetes type II (DM2) both evolving insulin resistance are related diseases. Additionally, DM2 is associated with elevated cardiovascular morbidity and mortality. Besides the high blood glucose itself the underlying pathophysiology causing DM2 affects endothelial and vessel health. We asked the question whether in pregnant women with GDM predictive markers like insulin resistance (HOMA-index), blood lipids, Lp(a), hsCRP (as a predictor of systemic inflammation) and elevated blood pressure are present and valid to unmask lifelong health risk.

Materials and methods: All women presenting for 75 g-oral-glucose-tolerance testing at the University hospital of Jena in 2009 ($n = 191$) were examined. Starving antecubital vein blood was taken in all 189 patients (95 healthy and 94 patients with GDM) to determine the levels of insulin, C-peptide, blood lipids, Lp(a), HbA1c, hsCRP and blood count.

Results: Compared to controls women with GDM were older (33 ± 6 vs. 30 ± 5 years, $p < 0.001$), presented with higher pregravid BMI (28 ± 7 vs. 24 ± 5 kg/m², $p < 0.001$), had higher levels of HbA1c (5.5 ± 0.5 vs. $5.1 \pm 0.2\%$, $p < 0.001$), insulin (18 ± 15 vs. 9 ± 4 mU/l), c-peptide (2.9 ± 1.5 vs. 1.9 ± 0.7) and HOMA-Index (3.1 vs. 1.5) ($p < 0.001$, for all parameters). Additionally, in patients with GDM the hsCRP was significantly elevated (5.0 vs. 2.9 , $p < 0.001$) and systolic (120 ± 14 vs. 112 ± 11 mmHg; $p < 0.001$) and diastolic (74 ± 11 vs. 69 ± 9 , $p < 0.001$) blood pressure were increased. There was no difference in blood lipids, Lp(a) and uric acid between the groups.

Conclusions: Besides impaired glucose tolerance patients with GDM display a range of cardiovascular risk factors (BMI, hsCRP, RR, insulin resistance). Thus the diagnosis of GDM during pregnancy reveals individuals at risk to develop cardiovascular diseases later in

life. Therefore the responsibility of the attending gynecologist essentially comprises preventive care including counseling (life style) and possibly also medication (Metformin, Glitazone GLP-1-analoga or DPPIV-Inhibitors might be beneficial).

PO-Geb 01.07**Polymorphism of the epoxide hydrolase 1 (EPXH1): impact on the severity of hypertensive pregnancy disorders***Tanja Groten¹, Ekkehardt Schleußner¹, F. O. Danso², Robert Zeillinger³¹Jena University Hospital, Friedrich-Schiller University of Jena, Department of Obstetrics, Jena, Germany, ²University of Science and Technology Kumasi, Department of Obstetrics and Gynecology, Kumasi, Ghana, ³University of Vienna, Austria, Department of Obstetrics and Gynecology, Wien, Austria

Objective: With an incidence of 3–7% in all pregnant women preeclampsia is still the leading cause of fetal and maternal mortality. Clinical studies have documented a familiar tendency to develop preeclampsia. Additionally, patients with impaired endothelial health are at higher risk. Thus we studied genetic polymorphism of endothelial health related genes in women with and without preeclampsia.

Materials and methods: 241 African and 279 Caucasian women were recruited in a two hospital-based case-control study for genetic testing of the polymorphisms Epoxide Hydrolase 1 (EPXH1) (codon 113, Tyr/His), Endothelial Nitric Oxide Synthase (codon 298, Glu/Asp), Angiotensinogen (codon 235, Met/Thr) and the Estrogen Receptor 1 polymorphism in intron 1 at position -401 T/C.

Results: From the 241 African women, 95 developed preeclampsia including 19 evolving eclampsia. From the 279 Caucasian women 81 had preeclampsia including 28 developing a HELLP (hemolysis, elevated liver enzymes and low platelets)-syndrome. There was no difference in polymorphism distribution between cases and controls. However we could show statistically significant association of the EPHX polymorphism encoding Histidin with the severe courses of the disease. 85% His/His, 5% His/Tyr, 0% Tyr/Tyr in African women with eclampsia vs 67% His/His, 25% His/Tyr und 5% Tyr/Tyr in those with preeclampsia alone ($p = 0.026$) and 61% His/His, 36% His/Tyr, 3,6% Tyr/Tyr in Caucasian women developing a HELLP-syndrome vs 44% His/His, 40% His/Tyr und 17% Tyr/Tyr in preeclampsia alone ($p = 0.045$).

Conclusions: EPXH plays an important role in both activation and detoxification of exogenous chemicals. The 113 Tyr/His exchange leads to decreased enzymatic activity interfering the capability of detoxification especially in endothelial cells which is believed to be part of the pathomechanism of preeclampsia. Our data implicate the genetic background to impact on the course of the disease and alter the capability of the maternal organism to deal with the pregnancy derived agents causing preeclampsia.

PO-Geb 01.08**Clinical experience in treatment of severe postpartum anemia with ferric carboxymaltose***Maria Günthner-Biller¹, Julia Knabl¹, Bernd Kost¹, Barbara Schiessl², Franz Kainer¹¹Ludwig-Maximilians-Universität, Obstetrics and Gynecology, Munich, Germany, ²Universität Aachen, Obstetrics and Gynecology, Aachen, Germany

Objective: Postpartum anemia is a common obstetric problem—up to 30% of pregnant women suffer from iron deficiency anemia. This

situation is worsened by considerable blood loss during childbirth. Blood loss stimulates erythropoiesis, which, to be successful, requires the presence of mobilizable iron reserves. Anemia due to iron deficiency contributes to several postpartum morbidities such as lethargy, lactation failure, cognitive impairment, and postpartum depression. Most women are treated with oral iron supplements to replenish the depleted iron stores, however, the utility of oral iron is limited by gastrointestinal complaints and patient nonadherence. Intravenous iron also has limitations due to irritation at the injection site and limited absorption rate.

Materials and methods: To meet this clinical challenge we established a protocol at the department of Obstetrics and Gynecology at the Ludwig-Maximilians-University for the treatment of severe postpartum anemia with intravenous ferric carboxymaltose. All patients with a blood loss of greater 1000 cc or a postpartum hemoglobin level below 8 g/dl were treated with ferric carboxymaltose according to the manufacturer's guidelines.

Results: Since June 2008 we have treated 48 patients with severe postpartum anemia. Median predelivery Hb was 9.5 g/dl, median blood loss 1950 cc. Median hemoglobin level before treatment were 5.8 g/dl and have risen 2–3 weeks after treatment to 10.6 g/dl. Additionally patients reported significantly improved quality of life with no side effects.

Conclusions: Ferric carboxymaltose is a new, very effective and safe drug for treating severe postpartum anemia.

PO-Geb 01.09

Correlation between transperineal sonography and open magnetic resonance imaging to determine head station in pregnant women at term

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Objective: During labor the transperineal sonography is becoming an established method to evaluation of labor progress and success rate for a ventouse. Otherwise, the ischial spines, the maternal landmark in vaginal examination, cannot be visualized by ultrasound, but with magnetic resonance imaging (MRI). The aim of this study was to examine the correlation between the station of the presenting part at term measured by transperineal ultrasound and open MRI.

Materials and methods: 31 pregnant women at term (>37 weeks of gestation), who were not in labor, underwent an open MRI. The ischial spines were located in a parasagittal plane and the corresponding interspinal level was identified in a midsagittal plane. The distance between the presenting part above the interspinal level was scaled. Immediately after MRI, without changing the supine position, a transperineal ultrasound using a Voluson 730 expert machine was performed. The angle of progression formed between a line placed through the midline of the symphysis pubis, and a second line drawn from the inferior apex of the symphysis tangentially to the fetal skull was measured by ultrasound and MRI.

Results: Angle of progression measured by ultrasound (mean 77,75° STD 8.2) and MRI (mean 79,48° STD 6.5) correlated significantly ($p < 0.001$; Intraclass Correlation 0.89 (95% CI: 0.78–0.94). A linear regression was found between the angle of progression in transperineal sonography and the distance from the presenting part to the ischial spine line in MRI ($p < 0.001$; $r^2 = 0.39$). An angle of about 120° would be corresponded with engagement (station 0).

Conclusions: Transperineal ultrasound brings objectivity to the assessment of fetal station. The angle of progression measured by transperineal sonography and MRI correlated well.

PO-Geb 01.10

Three-dimensional perineal ultrasound: correlation of persisting pelvic floor disorders and hiatal measurements immediately after the first delivery

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Objective: Morphologic changes of the female pelvic floor can be visualized by three-dimensional perineal ultrasound. This study aims to compare biometrical measurements of the levator ani muscle immediately after the first delivery and two years thereafter and to correlate the sonographic findings to clinical and anamnestic parameters.

Materials and methods: In this prospective observational study 130 primiparae were recruited two days after their first delivery. A 3D-perineal ultrasound was performed with standardized setting two days and 18–24 months after delivery. Biometric measurements of the levator muscle were assessed at rest and at valsalva in axial and sagittal planes. In the follow-up examination after two years an additional vaginal examination was performed. Obstetric parameters were obtained from the clinical file. A questionnaire enquired anamnestic data such as urinary incontinence.

Results: Levator hiatus distension at valsalva was wider after spontaneous and vaginal-operative delivery compared to cesarean section ($p < 0.001$ immediately after delivery, $p < 0.05$ two years after delivery) or in case of clinically relevant vaginal descensus ($p < 0.01$). A correlation between fetal head circumference and hiatal distension could only be proved immediately after delivery ($p < 0.05$) but not after two years. There was no coherence between unilateral levator avulsion and clinical evidence of vaginal descensus or urinary incontinence. Over-all prevalence for urinary stress-incontinence after two years was 10%, most of the cases after vaginal delivery. Urinary stress incontinence is significantly correlated to hiatus distension at valsalva at short- and at mid-term ($p < 0.01$ respectively $p < 0.05$).

Conclusions: The widest distension of levator hiatus can be detected after spontaneous or vaginal-operative delivery compared to cesarean section. This finding even persists two years after the first delivery. This study does not prove a predictive value of early post-partum perineal ultrasonography for the incidence of mid-term pelvic-floor dysfunction.

PO-Geb 01.11

Management of a complete thrombosis of the right leg and pelvic veins with pulmonary embolism in 35 weeks of pregnancy: a case report

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We describe the diagnosis and the peripartum management of a complete thrombosis of the right leg and pelvic veins with pulmonary embolism in pregnancy. The 2nd-grav, 0-para presented in 34 + 5 weeks of pregnancy with severe pain in the right groin since 2 days to exclude a hernia. In addition she suffered from dyspnoea

and dry cough. A thrombosis with pulmonary embolism was diagnosed. Under treatment with 3 l of oxygen and anticoagulation she was in stable condition. Aim was the prolongation of pregnancy for 3 weeks to reduce the risk of embolism during delivery. Because of contractions and suspicious CTG the delivery was carried out six days later by cesarian with block of the right vs. iliaca com. by balloon catheter. Thrombectomy was performed in the same session.

PO-Geb 01.12

The pivotal role of protein inhibitors of activated STATs (PIAS) in regulating trophoblastic functions

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Objective: Signal Transducer and Activator of Transcription 3 (STAT3) is an intracellular signaling molecule which, in trophoblastic cells, can be phosphorylated at its tyr705 (p-STAT3 tyr705) residue by Leukemia Inhibitory Factor (LIF) receptor binding. This phosphorylation correlates with invasiveness. Protein inhibitors of activated STATs (PIAS) antagonize STAT function by interfering with STAT DNA-binding and are, therefore, expected to regulate trophoblast invasion.

Materials and methods: We have analyzed PIAS1, PIAS3, STAT1, STAT3, Janus Kinase 1 (JAK1) and SOCS3 spontaneous expression in the following qualitatively different trophoblastic cell lines by gel electrophoresis and Western blotting: JEG-3 (choriocarcinoma), ACH-3P (hybrid of JEG-3 and 1st trimester trophoblast), AC1-M59 (hybrid of JEG-3 and 3rd trimester trophoblast), HTR8/SVneo (extravillous trophoblast) and a murine prolactin producing cell line. Freshly isolated 1st and 3rd trimester trophoblast cells have been analyzed for PIAS1 and PIAS3 expression. For intracellular localization immunoperoxidase staining of p-STAT3 tyr705 has been performed on HTR8/SVneo and JEG-3 cells.

Results: All analyzed cell lines express PIAS1, but JEG-3, ACH-3P, AC1-M59 as well as 1st and 3rd trimester trophoblast do not express detectable PIAS3. The same PIAS3 negative cell lines express significantly less STAT3-alpha/-beta and SOCS3, but significantly more STAT1 and JAK1. 1st and 3rd trimester trophoblast do not express PIAS3. Nuclear appearance of pSTAT3 is more pronounced in PIAS3 negative JEG-3 cells than in PIAS3 positive HTR8/SVneo cells.

Conclusions: The presence or absence of PIAS3 correlates positively or negatively with a variety of intracellular molecules, which underlines its leading role in controlling cellular functions.

PO-Geb 01.13

Association between birth weight and second trimester 3D placental volumetry, intraplacental vascularization and amniotic fluid cytokines

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Objective: The placenta is of utmost importance for fetal growth and well-being. Defective placentation and impaired placental circulation may result in anomalies of fetal growth. Growth factors and cytokines in the amniotic fluid may reflect changes in placental function and fetal growth. Therefore, it was our aim to investigate whether 3D placental volume parameters, intraplacental circulation and different amniotic fluid parameters are associated with birth weight.

Materials and methods: At the University Hospital of Erlangen 210 patients with singleton pregnancy and gestational age between 15 + 0 and 17 + 6 weeks were included in our study. Fetal biometry with regard to biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL) was routinely performed. Placental volume and vascularization were assessed by 3D ultrasound and 3D power Doppler. Placental volume (PV), four placental ratios (PR1 = PV/BPD; PR2 = PV/HC; PR3 = PV/AC; PR4 = PV/FL) and vascularization indices (VI, FI, VFI) were calculated. Visfatin, leptin, endoglin, VEGF and PIGF were measured in the amniotic fluid.

Results: While in linear regression analysis both PV, the four placental ratios, VI and VFI had a significant influence on birth weight only FI significantly predicted birth weight below the 10th percentile in logistic regression. Leptin and Visfatin in the amniotic fluid were significantly associated with birth weight and VEGF with PV/FI in linear regression analysis.

Conclusions: Second trimester placental volume and vascularization parameters correlate with birth weight. Additionally leptin and visfatin in the amniotic fluid have influence on fetal development. Therefore, placental volumetry and vascularization show potential for identifying fetal growth anomalies.

PO-Geb 01.14

Fetal anemia in consequence of massive fetomaternal transfusion syndrome

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Objective: Fetomaternal transfusion syndrome is the leakage of fetal erythrocytes into the maternal circulation. Massive loss of red blood cells can lead to fetal anemia and in consequence to fetal death. Typical symptoms of this rare event are reduced fetal movements, sinusoidal heart rate patterns in the cardiotocography, fetal hydrops and other sonographic fetal anemia-related findings like an increased systolic velocity in the middle cerebral artery.

Materials and methods: We present a case of severe fetomaternal transfusion syndrome that was diagnosed during the 28th week of pregnancy. The patient felt a decrease in fetal movements, the fetal heart trace showed a silent pattern and sonographic evaluation showed a discrete fetal hydrops as well as an increased velocity in the middle cerebral artery ($V_{max} >95$ centile). In suspicion of a life-threatening fetal anemia, an emergency caesarean section was performed. The premature infant was born with a significantly reduced hemoglobin of 1.6 g/dl, was treated immediately by neonatal blood transfusion and transferred to neonatal intensive care unit. Maternal blood analysis showed a massive fetomaternal bleeding with 4.9% fetal erythrocytes in the maternal blood circulation. The pathological examination of the placenta showed an expanded intervillous hematoma and inclusion of necrotic chorionic villi was found, so that fetal anemia in consequence of both, fetomaternal transfusion and fetoplacental bleeding was diagnosed.

PO-Geb 01.15**The influence of obstetric and neonatal factors on the counts of CD34+ and CD133+ cells in the collected cord blood in order to optimize the cord blood donor selection**

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Objective: This study was designed to investigate the influence of obstetric and neonatal factors on the counts of CD34+ and CD133+ cells in the cord blood to optimize the cord blood donor selection.

Materials and methods: There have been two methods used to separate the cells from cord blood: The sucrose gradient separation procedure, the isolation and magnetic separation by MACS. Lastly, flow cytometry was used to measure data.

Results: 115 cord blood units were assessed in this study. There were increased number of cells with vaginal delivery versus Cesarean section; secondary Cesarean section delivery compared to primary; by smokers then the non-smokers; by the births starting from the 38 week of pregnancy than the ones between 34 and 37 week of birth and by boys than girls. The cell counts were lower by the normal pH levels compared to the cell count that were higher by pH levels lower than 7.21 and higher than 7.31.

Conclusions: The cell count seems to be higher by normal deliveries than Cesarean sections, by secondary sections then primary sections, by on time deliveries then premature ones although they did not reach statistical significance. The increased stress levels and uterine contractions cause high blood pressure, release of adrenaline, higher heart rate and a faster circulation. This can explain the higher levels of cells found in umbilical cord units. The same explanation can be also made for the high levels found by the secondary Cesarean section deliveries, normal births and on time deliveries. A general suggestion as a guidance cannot be made according to the results found by the older studies and this study. Although the results show that the levels of the cells found can vary, it must have been focused not on the quantity, but the quality of the cells.

PO-Geb 01.16**Models of midwifery care in Germany**

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Objective: Midwifery models of care are well researched in English-speaking countries. In Germany, midwives attend all births by law. Midwifery is often defined in terms of midwives' employment relation: employed (*angestellt*) or freelance (*freiberuflich*). This dichotomy and international literature incite the question of whether these terms leave German midwifery care models unexplained. This study aims to determine what models of care occur in which birth locations.

Materials and methods: A cross-sectional survey of midwives who attended births in the Hannover region during 2009 was administered ($n = 211$). The main outcome measures were practice locations, employment patterns, scope of services, and midwifery attitudes.

Results: The preliminary response rate is 30.1%. 89.1% of midwives provided intrapartum care primarily in clinics, 5.2% in birth centres and 5.7% in clients' homes. Most midwives (93.3%) found mobility,

choice, trust, and natural birth to be "very" or "somewhat important." Knowing women before labour was important for more freelance (93.8%) than employed midwives (45.9%). Most midwives provided additional services, often postnatal care (65.8%) and lactation consulting (59.5%). Additional care was mostly freelance (89.7%). 73.8% of midwives offered additional services in locations where they attended births, 60.9% in further locations. Compared to employed midwives, more freelance midwives provided pre-, intra- and postnatal care to the same women "almost always" or "often" (2.7% employed, 100% freelance) and knew their clients more often (30.8% versus 100%).

Conclusions: Employment relations do not equate models of care. Many midwives provide services in several relations. The most common combination is employed shift-work with additional freelance services. Some midwives offer the equivalent of one-to-one and caseload models of care. Midwives' attitudes about investigated aspects of midwifery were similar across employment relations and location. Future research should consider whether women in Germany desire continuity of midwifery care.

PO-Geb 01.17**Cardiac disease in pregnant women: maternal and fetal outcomes**

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Objective: The physiological changes of pregnancy can result in cardiovascular complications in women with Congenital Heart Disease (CHD), which may have negative implications for mother and fetus.

Materials and methods: Retrospective case-control study. Comparison: delivery population with CHD ↔ without CHD. Patients followed in cooperation with a tertiary care center for CHD by same clinical and obstetrical team. Data collected by record review, including maternal characteristics, Functional Class (FC), mode of delivery, obstetric and neonatal outcome. Statistics SPSS.

Results: Between January 1995 and December 2009, pregnancies of 72 women with CHD and of 72 controls (age 29.5 ± 5.4 years) followed. No maternal/fetal deaths occurred. CHD included complex heart disease (25.0%), left and right sided heart obstruction (18.1% and 23%), posttricuspid shunts and pretricuspid shunts (8.3% and 11.1%) and others (12.5%). Caesarean section rate was significantly higher in patients with CHD (52.4% vs. 29.2%). In subgroup with CHD c-section rate rises to 72.2%. Depending on Functional class I and II, the c-section rate was 28% vs. 68%. In class III were only three women, two needed a c-section. Length of hospital stay was 2 days longer (median) in CHD group. Postpartal intensive care treatment was necessary in 15.3% of cases, in subgroup with complex heart failure it was 50%. Adverse neonatal outcomes were in women with CHD significantly higher compared to the controls and included small-for-gestational-age birth weight (27.2% vs. 8.5%), IUGR (6.9% vs. 4.2%), premature birth (12.5% vs. 7.0%). No significant difference in respiratory distress syndrome. 2 babies out of the CHD group showed cardiac anomalies, 3 in the control group.

Conclusions: Pregnant women with CHD are often at particular risk for cardiac complications during pregnancy. Potential difficulties and complications associated with CHD can be successfully managed by a team approach including experienced congenital cardiologists and obstetricians.

PO-Geb 01.18**Labor induction with prostaglandins: is BMI a relevant parameter?**

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Objective: Labor induction is a procedure in obstetrics with increasing frequency. Often prostaglandins (PG) are used. There are several compounds which are administered in different ways. However in a considerable proportion of cases the procedure is not successful. Are there factors apart from parity, which influence the success of this measure?

Materials and methods: We conducted a retrospective study in a series of 143 women with first pregnancy who underwent labor induction with Dinoprost application locally. Success was defined as delivery within 48 h either vaginal delivery or caesarean section. After dividing the entire group by the medians of age, gestational week, increases of weight during pregnancy and BMI in either two subgroups data were analyzed with chi square test or Fisher's exact test. Body mass index (BMI) is defined as weight (kg) divided by square of height (m).

Results: Overall labor induction by PG was successful in 63% applying the definition above. Neither age nor gestational age or increase of weight during pregnancy seemed to have any influence on the procedure. But for BMI we found a negative correlation. In the vaginal delivery group this correlation was highly significant.

Conclusions: In future labor induction by PG will play an important role in obstetrics as proportion of obesity, gestational diabetes and other causes are growing at least caused by increasing age of pregnant women. It will be more often necessary to induce labor before the expected birth date to avoid threat for the fetus. Even the sample size is small the result of our study could be reason to check the hypothesis in a prospective study.

PO-Geb 01.19**Kristeller Manoeuvre-objective data on a practice widespread in obstetrics**

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Objective: Among the manoeuvres used in the second stage of labor uterine fundal pressure is one of the most controversial. Fundal pressure involves application of manual pressure to the uppermost part of the uterus directed towards the birth canal in an attempt to assist spontaneous vaginal delivery and to avoid prolonged second stage or the need for operative procedures. Estimations concerning its prevalence range up to 5% of all deliveries. No confirmed benefit of this technique has been documented yet and some potentially life-threatening adverse events such as rib fractures or uterine rupture on the maternal side as well as neonatal central nervous system or brachial plexus injuries have been described in this context.

Materials and methods: The aim of this study is to examine the effect of the external pressure on the intra-uterine milieu. The pressure produced by the Kristeller Manoeuvre is quantified by an inflatable ballon fixed to the practitioners forearm and is displayed in a pressure curve in mm H₂O-units. Pressure alterations in the uterus during the manoeuvre are likewise measured by a common intra-uterine sensor-tip catheter.

Results: We present data of the Kristeller Manoeuvre on 5 pregnant women concerning obstetrical outcome of mother and child. Besides

the description of the duration of second stage of labor and possible complications we focus on the differences between the external pressure applied by the manoeuvre and the pressure measured simultaneously in the uterus.

Conclusions: The role of fundal pressure during labor remains poorly evaluated and controversial. Recent studies showed that its application was ineffective in shortening the second stage of labor. Because of the associated risks and the questionable clinical benefit exact quantification of the effects of this manoeuvre in relation to the intra-uterine pressure changes is of paramount importance.

PO-Geb 01.20**High-dose intravenous iron treatment in pregnancy and puerperium: safety and efficacy**

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Objective: Oral iron showed to be insufficient when it is about to treat severe iron deficiency anemia. Parenteral iron preparations available till now were superior to oral iron but could only be administered in a limited dosage because of the risk of adverse reactions. Ferric carboxymaltose (FCM, Ferinject[®]) is a new formulation for intravenous iron treatment making possible the application of a large amount of iron combined with a very low incidence of adverse reactions. Till now no data are available for the direct comparison of the previous used preparation Ferric-hydroxide-saccharate (FHS, Venofer[®]) and FCM.

Materials and methods: In the pregnancy group a total of 52 women between 20 and 39 weeks of gestation were treated either with FCM (15 mg/kg bodyweight, max. 1000 mg i.v.) or FHS (2 × 200 mg i.v., in part repeatedly) 204 women in childbed were treated in the same period of time identically to the pregnancy group. Indication for treatment was a clinically relevant anemia. In both groups the increase in hemoglobin level, the ferritin level and the incidence of adverse reactions were recorded and compared.

Results: The pregnancy groups were statistically comparable regarding gestational and maternal age, ferritin levels, pre- and posttherapeutic hemoglobin levels. 2 patients (8.3%) presented mild and transient adverse events after administration of FCM, 5 patients (17.9%) after FHS. Corresponding results for the postpartum group were found regarding the same parameters. 5 patients (4.9%) presented mild and transient adverse events after FCM-administration. 6 patients (5.9%) after FHS administration.

Conclusions: Treatment with FCM is well tolerated. Both substances share a similar safety profile. FCM treatment mostly requires only a single administration; the risk for adverse events is decreased by 50% compared to treatment with FHS which requires at least two administrations cycles. FCM provides a better patient's comfort and a better cost-effectiveness.

PO-Geb 01.21**Tissue elastography of uterine cervix: prediction of successful labor induction?**

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Objective: The process of connective tissue remodelling in the cervix leading to delivery occurs in three stages: softening, ripening and

dilation. The Bishop score has proven to be suitable for predicting onset and progress of labor as well as successful labor induction followed by spontaneous vaginal delivery. However, its specificity in patients with low scores is unsatisfactory. Many studies have confirmed the value of sonographic measurement of cervical length for predicting imminent spontaneous delivery in preterm and term births. None the less, there is a disagreement on its effectiveness in predicting a successful labor induction. Ultrasound elastography is a new tool for imaging and estimation of tissue elasticity, whose usefulness in obstetrics has not been investigated yet. Goal of the study is to evaluate the feasibility and reproducibility of cervical elastography measurement (strain and displacement) in late weeks of gestation. Intra- and interobserver variability was also evaluated.

Materials and methods: Prospective pilot study assessing cervical elastographic pattern in patients undergoing labour induction for medical indications and in post term pregnancies. Ultrasound was performed using a 9 MHz vaginal probe (Aplio XG ultrasound system, Toshiba Medical Systems). Raw data were collected under standardized conditions and analyzed depending on different pattern of measurement (for example localization, dimension and form of region of interest).

Results: Cervical elastography in late weeks of gestation is feasible. Different patterns of measurement influenced elastographic analysis. Preliminary results will be extensively discussed.

Conclusions: Ultrasound elastography is a new tool for imaging and estimation of cervical elasticity modifications during pregnancy. Further studies are needed to evaluate its clinical value for prediction of a successful labor induction.

PO-Geb 01.22

Does fetal sex of twin pairs affect pregnancy outcome?

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Objective: It is proposed that the gender of twin fetuses influences the pregnancy and fetal outcome. The objective of this retrospective investigation was to evaluate the impact of fetal gender on preterm birth and further pregnancy outcome.

Materials and methods: Our analysis is based on data raised over 7 years covering 342 twin pairs at the department for gynecology and obstetrics of the university hospital of Schleswig-Holstein, Campus Kiel. As arbitrate parameters the rate of preterm birth, the average age of pregnancy, the reason for delivery, the APGAR-Score, the fetal blood sampling rate and the mortality rate were evaluated. Also regarding the condition of the amniae the hitherto pronounced relationship between pregnancy outcome and fetal sex of twin pairs were scrutinized.

Results: In twin pregnancies with one or two male fetuses the preterm birth rate was higher (delivery ≤ 28 weeks: 13.5% vs 7.1%, $p = 0.01$) and the APGAR-Score lower (APGAR 5 min: 8.8 vs 9.1, $p = 0.03$), as was the rate of vaginal birth (29.8% vs 38.4%, $p = 0.02$). These findings showed to be independent from the condition of the amniae and were found in comparable peculiarity in mono or dichordial twin-pregnancies. The fetal gender did not affect the reason for delivery, the fetal blood sampling rate and the mortality rate.

Conclusions: Male fetal sex is a risk factor for preterm birth and a poor outcome in the perinatal period.

PO-Geb 01.23

Neonatal and maternal outcomes by gestational diabetes mellitus and impaired glucose tolerance: a retrospective analysis of our 6-years experience

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Objective: To evaluate the management and outcomes of pregnancies affected by gestational diabetes mellitus (GDM) and impaired glucose tolerance (IGT).

Materials and methods: We retrospectively analysed the pregnancy course of 124 women affected by IGT, 130 affected by GDM and 674 women with a negative glucose challenge test, who delivered in our Obstetrics Clinic between 2000 and 2006. Data was analysed by R(version 2.9.2) considering significant $p < 0.05$. Also a multivariate analysis was performed.

Results: Mean age at delivery was 33.7 years (± 4.8). In the 32.63% of cases the diagnosis was made after the 28th gestational week, while in two cases with a history of previous GDM it was made before the 10th gestational week. The glycate haemoglobin was higher than 6.5% in 1.43% of IGT and 5.41% of GDM. 19.33% of GDM and 4.5% of IGT needed insulin therapy. Birth traumatic lesions were significantly more prevalent among newborns of women with GDM than of healthy women (3.36% vs. 1.93%, $p < 0.05$). Among women with IGT there was a higher incidence of macrosomia, and the sole case of intrauterine death. By multivariate analysis, both GDM and IGT resulted independent risk factors for respiratory distress syndrome (RDS). Among the 59 patients with GDM who completed the post-partum follow up, 13.5% reported a persistent IGT and 6.7% a diabetes mellitus type 2.

Conclusions: GDM and IGT are independent risk factors for RDS, and women with IGT seem to have worse pregnancy outcomes compared with controls or women with GDM. By gestational disorders of the glucose metabolism, it is important to make women aware of their gestational risks, as also of the possible persistence of a glucose dysmetabolism in the post-partum.

PO-Geb 01.24

Prenatal presentation of chromosomal aberration del 7 (q32)

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Objective: About 10% of all chromosomal aberrations are structural. We want to demonstrate the prenatal symptoms of the deletion of a part of the terminal end of the long arm of chromosome 7 (del 7(q32 \rightarrow qter). There are 32 cases described in literature. They were all diagnosed postnatally. Due to a 100% severe mental retardation in surviving children, this chromosomal aberration is of clinical relevance.

Materials and methods: We present 2 cases with the prenatal diagnosis of chromosomal aberration del 7(q32). Case 1 was a 26 year old woman, VG IIP, which was referred at 22 weeks of gestation due to a suspected microcephaly. After finding and counseling the diagnosis, the parents decided for termination of pregnancy. Case 2 was 36 year old woman, IIIG IIP, referred at 27 weeks of gestation due to IUGR for further examination.

Results: As common symptoms the fetuses demonstrated IUGR and severe microcephaly. Furthermore we found cerebral midline defects (corpus-callosum-agenesis and holoprosencephaly) in both fetuses. In addition renal anomalies were diagnosed (bilateral hydronephrosis and right sided renal agenesis). Further symptoms which were only revealed in one fetus were median cleft lip and palate, periventricular VSD and agenesis of os sacrum. Postnatal symptoms were coloboma and deep asymmetric insertion of the ears.

Conclusions: As common symptoms in both affected fetuses we found IUGR, microcephaly, cerebral midline defects and renal anomalies. The cerebral anomalies can be explained by the holoprosencephaly-gene SHH involved in the affected chromosomal region. Due to the high number of deleted genes (>50) there is a wide variation of additional symptoms in our cases and in literature. In case of prenatal diagnosis of chromosomal aberration del 7 (q32) the parents has to be counseled about a bad prognosis.

PO-Geb 01.25

Case report: massive respiratory dysfunction as sign of fulminant postpartum dilatative cardiomyopathy

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Objective: Referral of a 35 year-old gravida 3, para 2 at 40 + 3 weeks with regular labor and progressive respiratory dysfunction: coughing with putrid, bloody mucus, tachycardia, orthopnea, decreased peripheral O₂-saturation and need of oxygenation. Anamnesis revealed symptoms of a pulmonary infect. An antibiotic therapy was immediately initiated. About an hour after arrival the patient's respiratory situation deteriorated rapidly despite oxygenation by mask. Decision to perform a secondary caesarean section was made; upon arrival in the operating room the patient's O₂-saturation had dropped below 80%, requiring emergency caesarean section. A healthy infant was delivered while the surgical intervention was uncomplicated. Postsurgically, the patient was referred to the intensive care unit, still being intubated. Over the next days further investigations revealed a pulmonary embolism and pathological cardiomegaly, while laboratory results showed an increase in pro-BNP. Further diagnostics showed massive left ventricular failure (ejection fraction 15%; NYHA IV). Cardiac biopsy was performed, resulting in diagnosis of postpartum dilatative cardiomyopathy (PPCM). Despite medication with bromocriptine and levosimendan, cardiac function continued to decrease, requiring surgical intervention and implantation of an intracorporal, left-ventricular assist device (HeartMateII®). Following surgery, cardiac function progressively improved and stabilized. The patient was discharged 5 weeks postpartum in stabilized health and will continue to be closely cardiologically monitored as an out-patient. As of now, it is unclear how long the cardiac-assist device will be left with the patient and what kind of further therapy is needed after explantation.

Conclusions: Postpartum dilatative cardiomyopathy (PPCM) is a rare condition in pregnant women and the cause is still unknown. PPCM should be considered as a differential diagnosis if otherwise healthy pregnant women present with an acute respiratory dysfunction.

PO-Geb 01.26

Serum levels of free β-HCG and PAPP-A measured by electrochemiluminescence immunoassay: influence on diagnostic performance of first trimester screening

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Objective: Trisomy 21 is the most frequent aneuploidy. Risk-calculation combining maternal age, free β-HCG, PAPP-A and nuchal translucency leads to detection rates of 85–90% with a false positive rate of 5%.

Materials and methods: Levels of free β-HCG and PAPP-A were measured retrospectively in serum samples of 191 patients with euploid fetuses taken at time of first trimester screening using three different analysis systems: MODULAR ANALYTICS <E170> with Elecsys test, KRYPTOR and IMMULITE 2000. Methods were compared by applying Pasing-Bablock regression analysis and Bland-Altman plot. Risk of trisomy 21 was calculated by Palomaki algorithm. A risk of 1 in 300 or more was considered to be high.

Results: The Elecsys tests showed excellent linear correlations with the other two methods and featured best specificity (92% versus 88.5% by KRYPTOR and 80.6% by IMMULITE 2000) and lowest false positive rates (7.9% versus 11.5% by KRYPTOR and 19.4% by IMMULITE 2000).

Conclusions: The new Elecsys tests improve the performance of first trimester screening.

PO-Geb 01.27

Seroprevalence of Chlamydia trachomatis in Lagos prepregnancy class population 1997 to 2009

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Objective: There is a little information on the incidence and prevalence of Chlamydia trachomatis infection in Lagos/Nigeria. The risk of infection in sero-positive women has been found to produce tubal factor, spontaneous abortion and spontaneous infection of membrane even in developed countries. The aim of the study is to determine the seroprevalence of Chlamydia trachomatis antibody in prepregnancy class population of men and women. Setting: A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos. This is a cross sectional study of men and women attending the prepregnancy class facilities in the centre.

Materials and methods: Between June 1997 and December 2009, the seroprevalence of Chlamydia trachomatis was determined in this study in 2,450 men and women. A total of 729 Chlamydia trachomatis IgG sero-positive, were screened for IgM seropositivity using ELISA kits.

Results: A total of 407 (55.3%) males out of 736, 866 (50.5%) females out of 1,714 were found to be susceptible to Chlamydia trachomatis. The infection seropositivity rate related to prior infection was 44.7% (329) males and 49.5% (848) in females. Chlamydia trachomatis IgM seropositivity was found in 34.6% (75) out of 217 males and 41.2% (211) out of 512 females.

Conclusions: This prevalence of Chlamydia antibody in prepregnancy class population of men and women shows high susceptibility and

reinfection or active infection rates leading to high risk of transmission among couples.

PO-Geb 01.28

Prenatal diagnosis of fetal pulmonary malformations

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Objective: Congenital pulmonary airway malformation is a rare, but the most common developmental anomaly of the respiratory tract (suggested incidence 1:8300–35000 live births) with a variable prognosis depended on the size of the malformation and the presence of fetal hydrops.

Materials and methods: A 38-year-old primiparous woman was incidentally diagnosed for congenital pulmonary airway malformation at 19 weeks of gestation during second trimester screening. Ultrasound showed macrocystic malformation of the left lung with polyhydramnios and marked mediastinal shift causing cardiac dextroposition and appearance of a hypoplastic right lung. No other associated anomalies were seen. Despite the suggested poor prognosis the patient decided to continue the pregnancy. She presented at 26 gestational weeks with preterm contractions and rupture of membranes. Due to funis presentation and fetal bradycardia, cesarean section was performed (Apgar score 4/6/8; 700 g). The preterm infant had a severe respiratory distress syndrome, the prenatal diagnose was confirmed. After nine days puncture of a large pulmonary cyst was performed, followed by partial resection of the left lower pulmonary lobe at the age of four months. After 1 year the infant showed a good development without severe impairment of pulmonary function.

Conclusions: Prenatal diagnosis of congenital pulmonary airway malformations has increased due to routine ultrasound examination. Poor prognostic signs include large lesions, bilateral lung involvement, polyhydramnios and mediastinal shift, resulting in cardiac compression, fetal hydrops and pulmonary hypoplasia. There are no reliable prenatal criteria for determining fetal or neonatal outcome. In cases of fetal hydrops thoraco-amniotic drainage or open fetal surgery might be an option. For postnatal symptomatic patients surgical resection is the definitive treatment, it may also be performed to prevent recurrent infection and malignant transformation.

PO-Geb 01.29

Stimulation of umbilical cord blood cells with gram-positive lysates from vaginal swabs: a model system to investigate immunomodulatory effects of clinically relevant gram-positive bacteria on the fetal innate immune system

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Preterm birth is one of the major causes for neonatal morbidity and mortality. An increasing number of studies strongly indicated, that ascending genital tract infections originating from perturbation of the vaginal microflora represent a major pathway to preterm labor and delivery. The aim of the study was to investigate and compare the

immunomodulatory effects of different clinically relevant gram-positive bacteria Streptococcus, Staphylococcus and Enterococcus isolates on the innate immune system of the fetus. Gram-positive bacteria include various molecular patterns, e.g. lipoteichoic acids, peptidoglycans, lipoproteins, lipopeptides but also CpG motif-containing nucleic acids revealing strong immunomodulatory properties on the innate and adaptive immune system of adults. Therefore, bacterial strains from Streptococcus, Staphylococcus and Enterococcus were isolated from vaginal swabs of pregnant women and cultured in LB medium. These were used to stimulate freshly prepared umbilical cord blood cells. Pam, different PGs and CpG were additionally tested as well as the gram-negative LPS of *E. coli* partly serving as negative respectively positive controls. The immunomodulatory effects were determined by analysis of preselected marker cyto- and chemokines from the supernatants of stimulated cells measured by ELISA or Luminex technology. The analysis of preselected marker (pro-, anti-inflammatory, TH1- or TH2)- cytokines and chemokines from the supernatants of the stimulated cells provided valuable insight in the capacity of these bacteria to activate and modulate the fetal immune system and thus contributed to a rational estimation of the importance of these pathogens in pregnancy complications. A kind of ranking in cytokine-release of the different examined gram-positive bacteria could be found which means there might be considered more or less aggressive gram-positive bacteria concerning prematurity.

PO-Geb 01.30

Peripartum cardiomyopathie-report of 2 cases

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Objective: Peripartum cardiomyopathy (PPCM) is a rare disorder in which left heart failure occurs in the peripartum period in previously healthy women. The incidence ranges from 1 in 1,300 to 1 in 15,000 pregnancies. The aetiology of PPCM remains unknown. We would like to present two case reports to examine risk factors, treatment modalities and prognosis.

Materials and methods: Two case reports of women presenting PPCM after caesarean section. Klinikum Darmstadt, perinatal centre level 1; 2009/2010.

Results: CASE 1: 32-year-old healthy woman, gravida VI, para I, 28th week of pregnancy, admitted to our hospital because of preterm contractions and rupture of the membranes. Tokolysis and rds prevention were started immediately. After three days of treatment the patient developed a global cardiac decompensation with pleural effusion. At the same time labour was progressing. After emergency delivery, the woman was transferred to intensive care.

Postoperative examinations showed an insufficiency of the valves. The woman was treated successfully with pharmacologic heart failure therapy. CASE 2: 30-year-old woman, gravida IV, para 0, 28th week of pregnancy was admitted to hospital because of severe pre-eclampsia. She had no history of heart disease, exposure to cardiotoxic agents or family history of heart muscle disease. Severe hypertension and dyspnoea were leading to initiate further cardiac examination. Transthoracic echocardiography showed pulmonary hypertension and cardiomegaly. Even being treated with extended antihypertensive therapy medical condition was getting worse and doppler sonography exhibited a fetal undersupply. After caesarean section, intensive-care medicine was necessary to cure the patient.

Conclusions: Diagnosis of PPCM is based upon the clinical presentation of heart failure and may occur as normal adaptation to pregnancy. Tokolysis and preeclampsia should be considered as risk factors. Early diagnosis and proper interdisciplinary management are the corner stones for a better outcome of these patients.

PO-Geb 01.31**Gastroschisis: sonographic findings, perinatal management and postnatal outcome**

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Objective: Gastroschisis is a defect in the fetal abdominal wall occurring mostly in younger women with increasing prevalence worldwide. In a retrospective longitudinal study we evaluated the perinatal management and outcome as well as the association between extraabdominal bowel dilatation and bowel necrosis.

Materials and methods: We investigated prenatal ultrasound and medical records of all fetuses with gastroschisis that were diagnosed from 1999 to 2009 at the Department of Obstetrics and Gynecology of the University of Würzburg. The incidence of intrauterine death or abortion, perinatal death and bowel resection were evaluated. The children were followed up for growth and morbidity until the age of 1 year.

Results: A total of 32 cases was evaluated, which all were diagnosed by prenatal ultrasound at a mean gestational age of 23 weeks (12–26 weeks). 29 children were delivered by primary caesarean section at mean 35 weeks of gestation (33–37 weeks). There was one intrauterine death, in two women a termination of pregnancy was performed. The mean birth weight was 2360 g (1470–3700 g). We observed a bowel dilatation of more than 17 mm in 79.3% of cases and of more than 20 mm in 58.6% of cases. Increased echogenicity of bowel was observed in 7 cases and rigid bowel in 4 cases. In 9 patients a bowel resection was necessary. In 26 patients a primary closure of the abdominal wall was possible. 2 children died within the first months postpartum. We could not observe any correlation between bowel dilatation, bowel echogenicity or rigidity and adverse perinatal outcome like bowel resection or postnatal death.

Conclusions: The data suggest that fetuses with isolated gastroschisis have a good prognosis. Fetuses with bowel dilatation are not at increased risk for adverse perinatal outcome.

PO-Geb 01.32**Low maternal serum cholesterol concentration is associated with severe intrauterine growth restriction**

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Objective: Placental cholesterol supply is essential for fetal development. The group of low density lipoproteins (LDL) account substantially for placental cholesterol uptake (in order to support the fetal growth). This is reflected in a two-fold increase of maternal serum LDL-bound cholesterol concentration at the end of the pregnancy. A low LDL-bound cholesterol concentration has been suggested to play a role in the pathogenesis of intrauterine growth restriction (IUGR). However, there are inconsistent publications so far. We hypothesized that maternal cholesterol in pregnancies complicated by IUGR is lower compared to normal controls.

Materials and methods: Maternal serum of 26 IUGR pregnancies and 26 gestational age matched controls (CN) were analysed. Total cholesterol, low density and high density lipoprotein-bound cholesterol, and triglyceride concentration was measured once between 25 and 34 weeks of gestation. Statistical estimates were performed by student's *t* test.

Results: Mean gestational age at sampling was 28.2 weeks in both groups. Mean gestational age at delivery was 29.5 weeks for IUGR and 39.1 weeks for CN. The mean birth weight percentile was 4.5 for the IUGR and 42.0 for the CN group. Serum concentrations of LDL-cholesterol and total cholesterol were significantly reduced in pregnancies complicated by IUGR (LDL: IUGR mean 100 mg/dl, STD ± 29,1; CN mean 152 mg/dl, STD ± 39,8; *p* < 0.0001; total cholesterol: IUGR mean 214 mg/dl, STD ± 34,7; CN mean 260 mg/dl, STD ± 49,5; *p* < 0.001).

Conclusions: Our results show a lower maternal LDL and total cholesterol concentration in IUGR pregnancies. This data contribute to the hypothesis of a decreased cholesterol supply to the fetus in IUGR.

PO-Geb 01.33**Perinatal outcome of fetuses with prenatal diagnosis of single umbilical artery**

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Objective: The congenital vascular anomaly “Single Umbilical Artery” (SUA) is recognized as a marker for further fetal malformations, chromosomal abnormalities and/ or poor perinatal outcome (e.g. preterm labor, low birthweight). In an unselected population the prevalence of SUA is to be rated between 0.2–2% of fetuses. The purpose of this study is to examine the perinatal results in patients following the prenatal diagnosis of SUA.

Materials and methods: 38 fetuses with SUA were included in this study. Prenatal diagnostics and pregnancy management were performed in the Departments of Obstetrics and Gynecology at Munich University Hospital Grosshadern and at Kiel University Hospital between 2001 and 2009. The examinations were performed by experienced obstetricians. Data concerning the course of pregnancy, delivery and fetal outcome were analyzed and correlated to the specific prenatal findings.

Results: Mean birth weight was 2777 g (985–4950 g) while mean gestational age at delivery was 258 days (199–281). 34% (13/38) were born premature while 8% (3/ 38) prior to 35 weeks. Mean pH-value was 7.27 (7.10–7.40). In 21% (8/ 38) arterial pH was below 7.20. Congenital heart defects were diagnosed in 13% (5/38) e.g. ASD, VSD, TGA, PFO. One fetus was diagnosed with anal atresia. Overall 16% (6/38) of newborns suffered from congenital malformations. Two of the newborns (5%) died within the first 2 weeks of life.

Conclusions: The high and in literature until now strongly varying incidence (15–61%) of congenital anomalies and abnormal karyotypes as well as further obstetrical complications associated with SUA, justify detailed pre- and postnatal examination of affected fetuses by means of high qualified obstetrical ultrasound, fetal echocardiography and invasive prenatal testing. A risk adapted pregnancy surveillance and delivery as well as sophisticated neonatal care is mandatory to offer best possible perinatal management.

PO-Geb 01.34**Gestational diabetes, comparison of the management and neonatal outcome over the time of a decade**Sara Fill Malfertheiner¹, *Kerstin Wollschlaeger¹, Serban-Dan Costa¹¹Medical Faculty, Otto-von-Guericke University Magdeburg,

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Objective: Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy, its prevalence ranges from 1% to 20% of all pregnancies. GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The diagnosis of GDM is important because it impacts maternal health care during and after pregnancy. In this study we compare changes in pregnancy outcome of GDM and the neonatal outcome in the course of 10 years.

Materials and methods: We have analyzed a study population of 305 pregnant women with GDM or diabetes mellitus typ 1 (DM typ 1). In our study we compare all patients who had delivered in our department and were diagnosed with GDM/DM typ 1 in the years 1995–1998 with those of the years 2005–2006. The analyzed variables are age, gravida, para, gestational age, mode of delivery, time of delivery, and neonatal parameters (sex, birth weight/length, head circumference, Apgar-scores and ph in arterial umbilical cord blood).

Results: In the 4 years from 1995–1998, 63 patients were diagnosed for GDM/DM1 (1.37% of the overall birth rate), in the years 2005–2006 it were 10.14% ($n = 242$) of the overall birth rate. From 1995 to 1998, 57.14% of the women with GDM were under diet control, 42.86% received insulin. In 2005–2006, 57% diagnosed for GDM were treated with insulin. Regarding birth weight, birth length and head circumference there was significant difference between the two groups. Newborns from the 1995 to 1998 had lower Apgar-scores at 1 and 5 min, and lower arterial umbilical cord blood pH.

Conclusions: We presume that the main reason for the drastic increase of GDM in only 10 years is a better awareness and diagnostic testing. Our results regarding the neonatal outcome emphasize how important the diagnosis and treatment of GDM is.

PO-Geb 01.35**Effect of passive CMV-isoimmunization in pregnancies with seroconversion***Idil Birgit Kabartas¹, Verena Julia Stinshoff¹, Olivia Chow¹,Angelika Larbig¹, Markus Gonser¹¹HSK-Wiesbaden, Department of Obstetrics and Prenatal Medicine, Wiesbaden, Germany

Objective: Congenital CMV infection is affecting approximately 1% of all neonates and is associated with significant neurological sequels in almost half of them. In pregnancies with primary CMV infection a reduction of transplacental virus transmission from 40% to 16% under treatment with CMV hyperimmune globulin (HIg) (100 IE/kg BW) was reported by G. Nigro (Nigro G. et al., N Engl J Med 2005; 353:1350–1362). The aim of this study is to examine the outcome of treatment with a higher dosage of CMV-HIg in order to prevent transplacental virus transmission. Furthermore, the patients were observed with regard to adverse effects.

Materials and methods: Seven pregnancies with a primary CMV infection were treated with CMV-HIg (200 IE/kg BW, Biotest Pharma, Dreieich, Germany). Anomaly scans were performed before and after treatment and neonatal outcome was observed prospectively, including urinary PCR-analysis in the first 3 days.

Results: The iv. CMV-HIg administration was tolerated well by all 7 patients. There were no adverse effects such as allergic or general

reactions. No signs of congenital CMV infection were detected during pregnancy or postpartum during the follow up period. Urinary PCR was negative in all 7 newborns.

Conclusions: Preventive treatment of primary CMV infection in pregnancy with CMV-HIg is safe and seems to be effective in our small study.

PO-Geb 01.36**A case of multiple thrombotic thrombocytopenic purpura relapses in pregnancy***Karlien Rommens¹, Alexander Puhl¹, Helmut Schinzel², Heinz Kölbl¹¹Universitätsmedizin, Klinik und Poliklinik für Geburtshilfe undFrauenkrankheiten, Mainz, Germany, ²Universitätsmedizin,

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Objective: Thrombotic thrombocytopenic purpura (TTP) is a rare but severe multisystem disorder. It has for a long time been a pathology that was difficult and frustrating to treat with a infaust prognosis. Since the introduction of plasma manipulation techniques, particularly plasma-exchange (PE), these patients have benefited greatly.

Materials and methods: In our case report we introduce a 24 year old pregnant woman whose life probably depended on plasma-exchange techniques several times during her pregnancy and after the birth of her son. The followup of this woman was possible by regularly blood counts because she was a clinically stable patient, known with a history of TTP-relapses. But there is still discussion about the most adequate tests of diagnosing TTP in pregnant women to differ from hemolysis, elevated liver enzymes and low platelets syndrome (HELLP).

Conclusions: Both pathologies have parallels in clinical signs and laboratory testings but need a different therapy. The deficiency of ADAMTS-13 activity is suggested to possibly be a prognostic factor of TTP-relapses in pregnancies and could be the best indicator to start therapy. On the other hand, the costs make it not attractive as a prognostic test. A literature study shows that, because of the rarity of the disease there is a need of international cooperative trials to give us more information on still unanswered questions.

PO-Geb 01.37**Fetal cardiac decompensation induced by aortic and pulmonary valve stenosis: slightly increased nuchal translucency as first sonographic marker for severe congenital heart disease in early pregnancy***Julia Aigner¹, Frauke Kleinsorge¹, Michael Elsässer¹,Bettina Schlehe¹, Christof Sohn¹, Alexander Scharf¹¹University of Heidelberg, Gynecology and Obstetrics, Heidelberg, Germany

Objective: A 25-years old primigravida has been seen in the 13 + 1 week of gestation for measuring nuchal translucency. The sonographic scan showed an increased nuchal translucency of 3.6 mm, furthermore a reversed enddiastolic flow in the ductus venosus. The objective of this case report was to show the association of slightly increased nuchal translucency and reversed enddiastolic flow in the ductus venosus with severe congenital heart disease.

Materials and methods: Amniocentesis was performed and showed a normal result. The malformation scan in the 21st gestational week revealed a ventricular septal defect but no other sonoanatomic noticeable problems. A second heart scan was performed in the 28th week, thereby aortic and pulmonary valve stenosis could be detected additionally increased fetal growth restriction. In the 34th week ascites and pleural effusions were apparent, furthermore left and

right ventricular hypertrophy as a sign of beginning cardiac decompensation. The fetal weight gain was low (estimated weight 1800 g). The therapeutic options in this stage of pregnancy (Caesarean section and cardiologic treatment versus “watch and wait”) were heavily discussed with pediatrics and gynecologists. Due to the expected poor fetal outcome the parents decided for conservative management.

Results: The patient presented in 36th week with regular contractions. Caesarean section was performed. Postpartal echocardiography confirmed the suspicion of an aortic and pulmonary valve stenosis, combined with an extended ventricular septal defect. The pediatricians reopened the pulmonary valve. Unfortunately valvuloplasty of the aortic valve was not possible. Two days later pediatricians had to note cardiac arrest. Cardiopulmonary reanimation was done unfortunately not successful.

Conclusions: Only slightly increased nuchal translucency and reversed enddiastolic flow in the ductus venosus showed in this case an association with a severe congenital heart disease and infaust prognosis of the newborn.

PO-Geb 01.38

Angiogenic factors as routine aid in diagnosis in cases with suspected preeclampsia: first clinical experience

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Objective: The diagnosis of preeclampsia is in daily clinical work not always easy and trivial. Not all women with hypertension and other signs and symptoms of preeclampsia really have or develop preeclampsia. Angiogenic factors like sFlt1, PlGF and the sFlt1/PlGF ratio are now available on automated laboratory platforms. Measurement of these factors is able to provide additional information regarding the precise diagnosis of preeclampsia.

Materials and methods: In a retrospective, single centre case-control study, we analyzed 30 cases with “suspicion of preeclampsia”. In addition to the standard investigations (blood pressure, proteinuria) and laboratory parameters, sFlt1/PlGF ratio was measured using the des Elecsys[®]-System (Roche).

Results: Preeclampsia was confirmed in twelve cases (40%) with a sFlt1/PlGF ratio >85 as cut off. In 18 cases (60%) preeclampsia could be reliably excluded by a sFlt1/PlGF ratio <85 at the time point of the measurement.

Conclusions: In the clinical situation “suspicion of preeclampsia”, the determination of the sFlt1/PlGF ratio provides a valuable additional information. The reliable exclusion of preeclampsia and angiogenic factor-tailored down-step management in hypertensive pregnancies is also able to save costs.

PO-Geb 01.39

Adrenal pseudocysts in pregnancy: a case-report

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Objective: Adrenal pseudocysts are rare entities and are more rarely diagnosed in pregnancy. There are only a few case reports on this subject in literature.

Materials and methods: The patient is a 28 year old woman, gravida 1, at 17 weeks of gestation. The patient presented an inappropriate abdominal growth for the gestational week with no clinical symptoms. A cystical tumor larger than 25 cm, which filled almost the whole abdomen, was diagnosed through ultrasound during a screening examination. With the suspicion of an ovarian process a laparotomy was then performed in a peripheral hospital. The uterus and the adnexa were without pathological findings and, because of the retroperitoneal location and the unclear origin of the tumor, the operation was terminated. After the patient was transferred to our clinic we performed a relaparotomy. Preoperative tumor markers and routine lab test were normal, the MRI described a 18 × 25 cm big multilocular mass, with clear delimitation and with unclear organ of origin, which compressed the V. cava inferior. The operative site presented a 25 cm firm elastic tumor located in the retroperitoneal space and filling almost the whole abdomen. The left kidney was displaced far to the right. The upper abdomen and pelvis were without pathological findings, the peritoneum was smooth. The 4620 g heavy cyst was removed in toto without difficulty. The patient had an uncomplicated postoperative evolution, so she was discharged on the 7th postoperative day. The histology described an adrenal pseudocyst and parts of an adrenal gland. In order to prevent a transient adrenal failure we started oral substitution therapy with corticoids which could be completely tapered afterwards. The pregnancy proceeded uneventfully, the patient delivered at term a healthy 3100 g girl.

Conclusions: Adrenal pseudocysts can be treated by surgical excision during pregnancy, without posing a risk to the mother or the child. A good pregnancy outcome is, as reported in the case above, absolutely possible.

PO-Geb 01.40

Anti-Muellerian hormone during pregnancy

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Objective: To study serum Anti-Mullerian hormone concentration throughout pregnancy and puerperium. **Setting:** A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos. **Study and design:** A cross-sectional study.

Materials and methods: Anti-Mullerian Hormone was measured in maternal blood. In a total of 92, during the first, second, third trimester, puerperium and in normal non pregnant women using Elisa kits.

Results: During the first, second, third trimester and prepregnancy the Anti-Mullerian Hormone levels were 1.9 + 0.48, 2.1 + 0.58, 1.89 + 0.7 and 2.08 + 0.49 ng/ml respectively.

Conclusions: Our result shows that during pregnancy there are no much significant changes in Anti-Mullerian Hormone levels in Nigeria.

PO-Geb 01.41

Placenta praevia, 8 years after trachelectomy: a case report

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Radical vaginal trachelectomy (RVT) was first reported over 14 years ago as a fertility-preserving treatment for early-stage cervical cancer. Combined with laparoscopic bilateral pelvic and parametran

lymphonodectomy the treatment is an oncologically safe procedure for very carefully selected young patients with the desire of fertility conservation. Pregnancy following RVT is associated with a variety of adverse pregnancy outcomes including second-trimester loss, preterm delivery and very rare improper attachment of the placenta. Closely monitoring a pregnancy after radical vaginal trachelectomy is a very important and often a challenging job to the responsible physician. This is a report of a 38 year old patient, who underwent radical vaginal trachelectomy at the age of 30. 8 years later the Patient underwent ovarial stimulation and became pregnant using an IVF protocol. First semester screening and second trimenon scan showed no abnormalities concerning the fetus. At 23 + 5 weeks the patient presented with severe vaginal bleeding and the placenta praevia was first diagnosed. The parametrical area was highly vasculated and beginning signs of infiltration of the placenta into the myometrium in terms of a placenta increta could not be ruled out. Due to repeated vaginal bleeding we administered betamethasone to accelerate fetal lung maturity. At time of the abstract we target a delivery between 28+ and 32+ weeks by caesarian section balancing the risk of premature delivery versus bleeding and abruption of the placenta.

PO-Geb 01.42

Paroxetine exposure during pregnancy: increased risk of congenital malformations?

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Objective: Selective serotonin reuptake inhibitors like paroxetine are used to treat major depression, anxiety and obsessive-compulsive disorder during the childbearing years. In late 2005 the U.S. Food and Drug Administration recommended to avoid paroxetine in pregnancy because of an increased risk of cardiovascular malformations. Since that time there is an ongoing controversial debate about the safety of paroxetine during pregnancy.

Materials and methods: In a prospective follow-up study we collected data of pregnancy outcomes after medication with paroxetine ($n = 222$) between 1990 and 2009. Our national Teratology Information Service (TIS) was contacted by physicians and patients after exposure to paroxetine in the first trimester. We compared the results with a control group ($n = 733$) of our TIS in the same interval, which was not or not severely exposed.

Results: Both samples did not differ in gestational age at first contact (median: paroxetine group 50 days vs control group 51 days). After exposure to paroxetine 20 patients ($20/222 = 9.0\%$) preferred termination of pregnancy. The incidence of elective terminations of pregnancy was much higher ($p < 0.001$) after medication with paroxetine than in the control group ($19/733 = 2.6\%$). The other 202 documented pregnancies ended with spontaneous abortion in 23 cases and live births in 179 cases. The abortion rate ($23/202 = 11.4\%$) did not differ significantly from the control group ($81/714 = 11.3\%$). Four congenital anomalies were reported after intrauterine exposure to paroxetine: clubfeet after exposure throughout pregnancy (40 mg/day), large naevus flammeus after maternal medication up to wk 7 (100 mg/day), spastic torticollis after medication up to wk 12 (20 mg/day), unilateral renal agenesis (10 mg/day, long term medication). The rate of congenital anomalies was not increased after application of paroxetine in early pregnancy ($4/179 = 2.2\%$ vs $25/633 = 3.9\%$; relative risk 0.56; 95% confidence interval 0.17, 1.67).

Conclusions: Our prospective controlled follow-up study does not support the assumption of a teratogenic effect of paroxetine.

PO-Geb 01.43

Spontaneous fracture in pregnancy with known PNH: a case report

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Objective: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare form of hemolytic anaemia, resulting from the clonal expansion of hematopoietic stem cells that have somatic mutations in the X-linked gene PIG-A. It is characterised clinically by haemolytic anaemia, bone marrow failure and thromboembolic events in unusual locations, which are the leading cause of mortality in PNH. Since 2007 there has been a new disease modifying treatment with eculizumab, a humanised monoclonal antibody that inhibits complement factor C5.

Materials and methods: A 30 year old woman 33 weeks pregnant was referred to our hospital because of lower back pain in the ileosacral area on the left side since three days that started while she was vacuum cleaning. There was no history of prior trauma. The patient had been diagnosed with PNH in 1999. She had dysphagia and anaemia which required PRBC transfusions but had no known thromboembolic events. The patient has been treated with eculizumab since 2008. So far she had been doing well with her pregnancy, her haemoglobin has remained stable around 8–10 g/dl and her platelets around 90–120 G/l. Physical examination showed normal neurological status, there was normal development of the fetus, no costophrenic angle tenderness. An MRI showed a hypodense area in the left sided sacral bone consistent with fracture. There was no sign of a venous thrombosis on the MRI and the D-dimers were low making a thromboembolic event as a cause of the pain unlikely. Medical induction of labour is planned for 38 weeks of pregnancy.

Conclusions: A Medline search revealed about 100 reported cases of pregnancy in women with PNH, in only 11 of which eculizumab treatment was reported. In none of the cases spontaneous fractures have been reported. In our opinion this rare case should prompt us for further investigation.

PO-Geb 01.44

Allergen induced cytokine release in human placenta: a possible role in fetal programming of allergies?

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Background: Previous animal experiments indicated the transmissibility of general allergic diathesis from the mother to the fetus. All major cell types known to be involved in allergic processes, including dendritic cells, T cells, B cells and mast cells are present in the decidua. Thus, allergen induced mediator release may prime the fetus for easier sensitization in later life.

Objective: To analyse differences in cytokine production from placental tissue of atopic and healthy mothers after contact with a relevant allergen.

Materials and methods: We developed a one sided placenta perfusion model with an internal standard to perfuse two separate cotyledons from the same placenta simultaneously with apple allergen-containing medium (mal d 1) and allergen-free medium for 5 h. Hence, each control cotyledon provides the respective baseline values for quantitative analysis of allergen induced mediator release. Outflow samples were collected and analyzed for immune mediator release. Histamine concentration was determined spectrophotofluorometrically after extraction and derivatization with *o*-phthalaldehyde. The cytokines IL-2, IL-4, IL-6, IL-10, TNF- α and IFN- γ were analyzed by using a cytometric multiplex bead array.

Results: After application of relevant allergens in perfusion medium, a significant time-dependent release of TNF- α and IL-6 was detectable in placenta of mothers suffering from apple allergy compared to those from healthy mothers. The expression of the other interleukins and histamine was not remarkably altered.

Conclusions: Allergens can induce allergy related effects, which may disturb the immunological balance at the fetomaternal interface and might prime the developing fetal immune system for facilitated later susceptibility for allergic sensitizations.

PO-Geb 01.45

Pregnancy with maternal TGA (transposition of great arteries) and NYHA II–III°

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Objective: Pregnancies with maternal congenital heart defects (CHDs) are very heterogeneous requiring interdisciplinary cooperation. The congenital TGA counts as a severe cyanotic vitium, which even after surgical correction during infancy need lifelong cardiologic medical care. Doctors are increasingly confronted with the desires of patients to have children whereas obstetricians are hardly able to refer to any cases due to few available data. We report of a 29-year-old 2nd gravida/nullipara at 24 + 2 weeks of gestation (WOG) and congenital TGA with surgical intervention during infancy (balloon-atrio-septostomie, atrial reversal after Senning). She presents with tricuspid insufficiency I°, ventricular extra systole, sinus bradycardia, NYHA II–III°. Fetal development was in line with time (690 g), no malformations, pathologic Doppler ultrasonography of umbilica (Resistance Index RI > 95th percentile)- and both uterine arteries (RI > 95th percentile), tricuspid and mitral insufficiency I° and minimal aortic insufficiency. Maternal echocardiography: borderline enlarged system ventricle with global hypokinetic contractions, reduced ejection fraction (0.37), hypertrophic interventricular septum, insufficiency of anatomic tricuspid- and functional mitral valve, minimal aortic valve insufficiency. Pathologic increased doppler-sonography of the uterine artery is associated with an increased risk for pre-eclampsia. By this particular patient and preexisting cardiac damage increased blood pressure can lead to cardiac arrest. Admittance at 26 WOG, control of echocardiography, brain natriuretic peptide and clinical symptoms. Regular fetal growth- and Doppler control, cardiotocogram and induction of lung development were performed. Scheduled cesarean in spinal anesthesia and endocarditic prophylaxis was planned and performed at 32 WOG with birth of a healthy newborn developed right for time. Post cesarean course normal. Discharge in unchanged cardiologic status.

Conclusions: Pregnancies in women with congenital heart defects require an early interdisciplinary surveillance of heart function. Date of delivery by cesarean depends of the heart function.

PO-Geb 01.46

Bloom syndrome and pregnancy: a case report

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The Bloom syndrome is a rare, autosomal recessive disorder characterized by a pre- and postnatal proportionate growth deficiency, characteristic dermatologic lesions and a strong predisposition to a

wide range of cancers. Male patients are infertile, whereas in female patients fertility is generally reduced. Up to now there have only been five reported cases of pregnancies in Bloom Syndrome patients. This case is a clinical Report of a 25 year old woman with Bloom Syndrome, initially diagnosed at the age of 13. After three miscarriages, in the fourth pregnancy she was successfully treated for preterm labor at 32 weeks, as well as gestational diabetes. At 36 weeks she was delivered of a healthy male infant by cesarean section, following a therapy resistant pyelonephritis.

PO-Geb 01.47

Screening for partner abuse during pregnancy in a German Maternity Hospital

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Objective: Domestic violence (DV) is a serious health problem, which is known to be associated with adverse pregnancy outcomes, such as preterm birth. Hence, diverse professional health bodies recommend routine screening during pregnancy. In Germany a large cohort study has shown that one in four women has been suffering from partner abuse. However, data in pregnancy are lacking in Germany. This has led us to conduct a prospective cohort study.

Materials and methods: 585 pregnant women attending the antenatal clinics in a large German teaching hospital were approached. 111 women agreed to participate in an interview conducted in a separate room by a trained person. A standardized questionnaire was used; socio-demographic data were assessed.

Results: Of 111 pregnant women questioned, 31 (27.9%) admitted to physical and/or psychological violence by a partner during pregnancy. Most women screened thought that routine screening should be part of antenatal care in Germany.

Conclusions: Screening for DV in pregnancy should be part of routine antenatal care in Germany. Specific guidelines are needed.

PO-Geb 01.48

Management of pregnancy in a patient with anal and total uterine prolapse after congenital bladder extrophy: a case report

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Objective: Management of bladder extrophy is a challenge for clinicians. Pregnancy in patients with bladder extrophy is rare due to associated malformations.

Materials and methods: We present the case of a 35 year old G3 P0 A2 who was first seen at our site at 14 + 1 weeks of gestation [wg] after in vitro fertilisation [ivf]. She presented with congenital bladder extrophy, pelvic malformation with partially missing pubic bones, anal and total uterine prolapse, PAI-I-polymorphism and impaired glucose tolerance. **Results:** We present our management of this high risk setting which was marked by minor infectious complications, pelvic pain syndrome, second degree pyelectasy and non severe prolapse of ileum conduit. Also maternal and fetal outcome are reported.

Conclusions: In this high risk setting intensified pregnancy monitoring led to delivery of a healthy premature boy. Serious maternal complications did not occur. Treatment of urogenital infections was

adamant. Pessary treatment was not necessary and could have possibly led to further complications.

PO-Geb 01.49

Cerclage and cervical occlusion for prevention of preterm birth: a nine year single institution review

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Objective: To compare the outcomes of prophylactic, therapeutic and emergency cerclage ± cervical occlusion (CO).

Materials and methods: A retrospective study was performed including data of 186 singleton pregnancies who received a prophylactic ($n = 78$), therapeutic ($n = 64$) or emergency ($n = 44$) cerclage ± CO and delivered at University Hospital of Zurich in 2000–08. Outcomes observed were as follows: Pregnancy loss before 24 weeks, prolongation of pregnancy, preterm delivery before 28 or 34 weeks, presence of preterm prelabour rupture of membranes (PPROM), clinical chorioamnionitis necessitating delivery and neonatal survival.

Results: Mean gestational age at time of prophylactic, therapeutic and emergency cerclage ± CO was 16.6 ± 3.4 weeks, 21.0 ± 4.2 weeks and 23.0 ± 3.6 weeks, respectively. Pregnancy loss rate before 24 weeks was 0, 6 and 23% in the prophylactic, therapeutic and emergency cerclage ± CO group, respectively. Mean prolongation of pregnancy was 20.7 ± 5 weeks, 14.7 ± 6 weeks and 7.4 ± 6.1 weeks after prophylactic, therapeutic and emergency cerclage ± CO, respectively. Four%, 14% and 48% of patients delivered <28 weeks, 10, 27 and 61% of patients delivered <34 weeks and 73, 63 and 32% of patients delivered at term after prophylactic, therapeutic and emergency cerclage ± CO, respectively. PPRM and clinical chorioamnionitis complicated 14, 19 and 34%, and 6, 3 and 39% of pregnancies after prophylactic, therapeutic and emergency cerclage ± CO, respectively. Neonatal survival rate was 100, 91 and 64% after prophylactic, therapeutic and emergency cerclage ± CO respectively.

Conclusions: The presented data suggest that cerclage ± CO can prolong pregnancy and increase the change of viable pregnancy outcome. The presence of bulging membranes seems to be associated with higher rates of PPRM and chorioamnionitis as well as shorter prolongation of pregnancy.

PO-Geb 01.50

Seroprevalence of toxoplasmosis in Lagos prepregnancy class population 1997 to 2009

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Objective: There is a little information on the incidence and prevalence of Toxoplasmosis infection in Lagos/Nigeria. The risk of congenital infection in sero-positive pregnant women has been found to produce congenital abnormalities and spontaneous abortion even in developed countries. The aim of the study is to determine the seroprevalence of Toxoplasmosis antibody in prepregnancy class population of men and women. **Setting:** A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos. **Study and design:** This is a cross sectional study of men and women attending the prepregnancy class facilities in the centre.

Materials and methods: Between June 1997 and December 2009, the seroprevalence of Toxoplasmosis was determined in this study in 2,273 men and women. A total of 803 Toxoplasmosis IgG seropositive, were screened for IgM seropositivity using ELISA kits.

Results: A total of 344 (52.4%) males out of 656, 796 (49.2%) females out of 1,617 were found to be susceptible to Toxoplasmosis. The infection seropositivity rate related to prior infection was 47.6% (312) males and 50.8% (821) in females. CMV IgM seropositivity was found in 17.6% (40) out of 227 males and 22% (127) out of 576 females.

Conclusions: This prevalence of Toxoplasmosis antibody in prepregnancy class population of men and women shows high susceptibility and reinfection or active infection rates leading to high risk of transmission among couples.

PO-Geb 01.51

Is ectopic pregnancy really increased in ART?

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Objective: Assisted reproductive techniques (ART) have been considered a risk factor for ectopic pregnancy (EP). We have studied the incidence of EP in 76,077 ART cycles. Furthermore, the recurrence of EP has been estimated after a subsequent spontaneous pregnancy in 15%; we analysed if ART increases the risk of recurrence in this subgroup.

Materials and methods: Between the years 2000 and 2008, 633 EPs were diagnosed after ART at our Institution. Retrospective analysis was performed, calculating the incidence of EP in relation to the total number of gestations after ART. For patients with a history of EP, we calculated the recurrence rate after ART.

Results: The general incidence of EP was 2.24% per pregnancy after ART. For different techniques the incidence was: 2.61% with general IVF (3.2% after IVF only, and 2.50% after ICSI), and 2.08% after thawed-embryo transfer which is not significantly different from the incidence after fresh embryo transfer. Age at stimulation onset did not predict the risk of EP. With different stimulation protocols, EP-incidence was higher if clomifen citrate ($p = 0.006$) or an antagonist protocol ($p = 0.008$) were used, as compared to the long protocol with GnRH-analogs. The number of days with stimulation, total gonadotropin doses, estradiol peak and number of oocytes retrieved did not significantly differ in women with EP as compared to intrauterine gestations after IVF. In the group of patients with at least one previous EP, the recurrence rate per pregnancy after ART was 8.26%. According to the treatment, the recurrence rate per gestation was: 11.5% after IVF; 4.9% after thawed-embryo transfer; 17.5% after IUI; and 14.3% after timed intercourse.

Conclusions: In our series the incidence of EP after ART was not increased when compared to the 2% for the general population. What's more, the recurrence of EP was not increased after ART.

PO-Geb 01.52

Management of large, persistent adnexal masses in pregnancy

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Objective: In an era of routine prenatal ultrasound, diagnoses of adnexal masses during pregnancy are not uncommon; 0.2–2% of total pregnancies are estimated to be complicated by an adnexal mass,

approximately 1–6% of these masses are malignant. Ultrasound examination is the primary modality used to detect and evaluate ovarian masses in pregnancy. If sonography is inconclusive, magnetic resonance imaging (MRI) is the preferred additional modality for imaging the pelvis and to assess the risk of malignancy.

Materials and methods: We performed a review of cases which were seen at our department in a period between 2005 and 2010. We included all suspected adnexal masses with a maximal diameter of 7 cm or more diagnosed in ultrasound examinations during pregnancy. Masses which showed spontaneous remission over pregnancy were excluded from this review. In every case, expert-ultrasound examination was performed. All cases were histopathological clarified.

Results: 18 cases were included to this study. In 8 (44.4%) cases, additional MRI diagnostic was performed. 5 (27.7%) patients had to undergo surgical intervention during pregnancy because of acute indication or suspected malignancy. One pregnancy had to be interrupted in the 13th gestational week out of medical indication. The other 12 masses were monitored at close intervals over pregnancy; surgical therapy was performed during caesarean section or surgical intervention after spontaneous delivery. In total, the interventions delivered histopathological results of 2N ovarii, 3 borderline ovarian tumors, 1 dysgerminoma of the ovary and 12 benign masses.

Conclusions: The management of huge adnexal masses during pregnancy can be challenging for the patient and the clinician and involves the evaluation of sometimes competing maternal and fetal risks and benefits. Potential malignancy clearly has an influence on the decision for intervention versus expectant management. In these reviewed cases, correct classification of the masses by expert-ultrasound and additional MRI-examination was possible in most of the included cases.

PO-Geb 01.53

Severe H1N1-infection during pregnancy: a case report

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H1N1 is known to induce fulminant courses in youths and young adults. We report the case of a 24 year old patient (4th gravid, 2nd para) encountered for fever up to 38°C during 20th week of a so far uncomplicated pregnancy. Ultrasound examination and urine testing was inconspicuous. The throat complaints relieved during the antibiotic therapy. In the next days the patient developed dyspnoea and rising cyanosis. The patient had to be intubated on the 5th day because of decreasing oxygen saturation. Coincidentally a progressive pancytopenia and increasing inflammatory activity was recorded. Echocardiography, blood cultures, and bronchial lavage brought no pathological findings. The cranial, thoracic, and abdominal computer tomography showed the ARDS and hepatomegalie but no other pathological findings. Recent HIV, CMV, HSV, classical influenza, and parainfluenza-infections were excluded. A H1N1-infection was confirmed by PCR on the 6th day. The antiviral therapy was changed from Zanamivir to Oseltamivir. Extracorporeal membrane oxygenation became necessary because of insufficient oxygen saturation by mechanical ventilation. At this time pregnancy seemed to be unimpaired. Suddenly a spontaneous expulsion of the fetus occurred on the 7th day (weight 460 g, no anomalies detectable). No curettage post abortem was necessary. As a result of the antiviral therapy

H1N1-DNA was not detectable at day 16. Despite all affords the respiratory situation could not be improved significantly. Additionally the patient developed a multiorgan failure during the time course and died on the 28th day of treatment. The recent case illustrates a very dangerous and impressive course of a H1N1-infection.

PO-Geb 01.54

Adnexal torsion after ovariopexie in pregnancy

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Objective: Adnexal torsion is a rare event of emergency in pregnancy, because it is usually associated with functional cysts or tumours of the ovary. We report an ovarian torsion in the second trimester of pregnancy, after a history of previous multiples torsions without pregnancy and a status after ovariopexie.

Materials and methods: Case presentation: A 27 year old woman presented in the 19th week of her first pregnancy with severe pain in her left lower back pain irradiating into the right leg. She reported intermittent nausea and vomiting without fever or other abdominal or urinary symptoms. She had been treated for polycystic ovaries for 3 years with three laparoscopies within the last 14 months for ovarian torsion and an ovariopexie at the last operation. After analgetic treatment the pain resolved after a few hours, as it did in another two times of clinical admissions. At any time blood values were normal. The abdominal sonography showed a normally developed pregnancy without an adnexal mass or free fluid. Due to the recurrent pain and the previous history, laparoscopy was performed in the 20th week and revealed an haemorrhagic torsted ovary without signs of infection. An ovariectomy was performed. Histology proofed the diagnosis. Post-operative recovery was uneventful with a normally ongoing pregnancy. **Results:** Because of the pregnancy diagnosis was made with a delay of about 10 days. This was due to the limited possibilities of diagnostic methods and the untypical presentation of symptoms. However, the removal of the left ovary could be performed without further harm to the patient or the fetus.

Conclusions: Adnexal torsion in pregnancy is an emergency with high potential risks for patient and pregnancy. It should be considered in the differential diagnosis of acute lower abdominal or back pain, since it can present with untypical symptoms. Risk factors should be evaluated.

PO-Geb 01.55

The routine measurement of the sFlt1/PlGF ratio allows differential diagnosis of hypertensive pregnancy disorders and a prediction of pregnancy outcome

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Objective: We have shown previously that automated measurement of sFlt1 and PIGF is a reliable tool in the assessment of preeclampsia (PE). The sFlt1/PIGF ratio (ratio) is superior over the single measurement of sFlt1 or PIGF in PE diagnosis. The aim of this study was to characterize the ratio in different types of hypertensive pregnancy disorders. Secondly, we wanted to prove whether the ratio helps to identify women at risk for immediate delivery.

Materials and methods: In a multicenter case control trial we investigated 126 patients with PE/HELLP, 35 with pregnancy induced hypertension (PIH), 45 with chronic hypertension (cHTN) and 328 controls. sFlt1 and PIGF were measured in serum samples on an automated Elecsys platform. To evaluate the ratio in the course of pregnancy, different timeframes (24–27 +6, 28–33 +6, >34 weeks) were investigated. Hazard Ratios adjusted for gestational age for preeclamptic women in the upper quartile of the ratio were calculated. **Results:** PE patients showed a higher ratio compared to controls, whereas the ratio was the higher the earlier pregnancy was complicated by PE (668 ± 104 vs. 3.38 ± 0.61 for 24–27 + 6 weeks; 436 ± 63.9 vs. 11.0 ± 3.72 for 28–33 + 6 weeks; 143 ± 18.1 vs. 29.5 ± 5.63 for >34 weeks). However, patients with cHTN and PIH had a significantly lower ratio than patients with PE/HELLP ($p < 0.001$). Overall, a ratio >422 was associated with a 3.5 higher risk of immediate delivery (95% Confidence Interval: 1.98–6.19). Pregnancy was significantly prolonged in preeclamptic women with a ratio below the fourth quartile ($p < 0.001$).

Conclusions: The automated measurement of the sFlt1/PIGF ratio is able to discriminate between different types of pregnancy-related hypertensive disorders. The measurement of the ratio is able to provide a short-term prediction of pregnancy duration and outcome. Thus, the ratio gives additional valuable information on the severity of the disease and can therefore be used to adapt clinical management.

PO-Geb 01.56

Influence of progressive muscle relaxation training on anxiety and depression levels during pregnancy and puerperium

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Objective: Relaxation training is an integral part of psychosomatic prenatal classes. The aim of this study was to determine whether progressive muscle relaxation training affects anxiety and depression levels during pregnancy and puerperium. Another aspect was to assess the satisfaction of the participants regarding the PMR-courses. **Materials and methods:** A total of 100 women attended this study. The control group, consisting of 50 women, received only general prenatal care. The other 50 women of the intervention group took part in a progressive muscle relaxation training for 5 weeks including one guided group session each week and the instruction to practice at home regularly.

In both groups Anxiety (STAI) and depression (BDI) were measured three times: before and after 5 weeks of intervention and during puerperium. The level of satisfaction regarding the subjective effectivity was assessed at the end of the intervention period. There were no significant differences between the intervention and control groups regarding the age, parity, gravidity and frequency of complications at the beginning of the study.

Results: During the study progress a successive decrease of the State-Anxiety could be observed in the total number of participants

($p = 0.004$). This trend could also be shown in the two separate groups. Because of the higher level of State-Anxiety scores in the control group (mean 40.88; SD 11.76) compared to the intervention group (mean 37.54; SD 7.36), a significant change could only be exhibited in the control group ($p = 0.004$). No significant differences could be shown in the PMR-group ($p = 0.279$), probably because of the lower mean levels of State-Anxiety at the beginning of the study. A decrease of the Trait-Anxiety levels of the total of the participants could also be observed ($p < 0.05$ and $p < 0.01$). A significant reduction of the Trait-Anxiety during pregnancy and in the puerperium could be shown for both groups. There were no significant differences between control group and PMR-group. A reduction of depression levels could be detected at all three points of investigation in the total number of participants ($p < 0.01$). This significant effect could only be shown in the PMR-group ($p < 0.05$) if groups were looked at separately. After the weeks of PMR training the satisfaction and subjective learning effect of the PMR-group participants was assessed. 86.4% of the women stated an obvious improvement of their relaxation abilities. 97.7% of the PMR-group would attend another course during a following pregnancy as far as there would be one offered. All participants declared that they would recommend PMR to other pregnant women.

Conclusions: An additional offer of PMR-courses to the general prenatal care leads to an improvement of subjective relaxation abilities during pregnancy and gains a high acceptance within the participants. PMR leads to a reduction of depression scores during pregnancy. No significant effect on State and Trait-Anxiety could be shown in this study, maybe because of the small number of participants.

PO-Geb 01.57

Acute abdomen in pregnancy caused by torsion of an appendix epiploica

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Objective: To increase the awareness of rare causes of lower abdominal pain in pregnancy

Materials and methods: A 30 year old G3 P0 presented at 24 + 2 weeks of gestation with right lower quadrant pain since the previous evening. The ultrasound scan showed a normal singleton pregnancy with a normal amount of amniotic fluid. Cervical length was 34 mm. No contractions were visualized on the CTG. Laboratory results did not show elevated inflammatory markers. Localized right lower quadrant pain with marked guarding led to the decision of undertaking a laparotomy. A perioperative bolus tocolysis was given. Following a pararectal incision, a necrotic appendix epiploica was found at the location of maximal pain. No ascites, no intraabdominal pus and no localized inflammatory reaction could be found. The adipose tissue including its peritoneal basis and the completely unremarkable appendix were removed. Bolus tocolysis was stopped 24 h after the operation.

Results: Histological examination revealed old necrosis of adipose tissue with localized fresh haemorrhages suggesting repeated torsion of an appendix epiploica. Postoperative treatment included a course of iv Cefuroxim. The further recovery was uneventful.

Conclusions: Differential diagnoses of acute right lower quadrant pain in pregnancy should include less common causes such as torsion of an appendix epiploica.

PO-Geb 01.58**Micro-RNA expression after LIF stimulation of trophoblastic cells**

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Objective: Micro-RNAs are recently detected key regulators of the immune system and of carcinogenic processes, but their function in pregnancy is poorly investigated yet. Leukemia Inhibitory Factor (LIF), is a cytokine which plays a crucial role in human reproduction and which triggers trophoblast invasion via Signal Transducer and Activator of Transcription 3 (STAT3). Therefore, we aimed to determinate LIF-regulated micro-RNAs in a choriocarcinoma cell line model to their potential involvement in control of invasion.

Materials and methods: JEG-3 choriocarcinoma cells were stimulated with LIF for 1 to 24 h, and total mRNA was isolated. Phosphorylation of signal transducers ERK1/2 (thr 702 and tyr 704) and STAT3 (ser 727 and tyr 705) was assessed by gel electrophoresis and Western blotting. STAT3 gene expression was analyzed as control of induction by RT-PCR. Expression of five different micro-RNAs, which are either known to be expressed in placental tissue or involved in tumor invasion, was quantified at six time points by qRT-PCR.

Results: ERK1/2 and STAT3 were phosphorylated from 10 to 30 min after LIF stimulation. Three micro-RNA, miR-9, miR-141 and let-7g, were time-dependently down-regulated by LIF with a peak after 4 h of treatment, which correlates with an increase of STAT3 expression. **Conclusions:** Although LIF is an inducer of invasion in trophoblastic cells, it downregulates expression of three invasion-related micro-RNAs in JEG-3 cells. These results suggest a regulatory role of micro-RNAs in behavior of trophoblast cells and their malignant derivatives.

PO-Geb 01.59**Case report: rectal cancer developing during pregnancy**

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Colorectal carcinoma presenting during pregnancy is uncommon [1]. We present a 27 year old woman who was admitted to hospital because of lower abdominal pain in the 27th week of gestation. The ultrasonic examination revealed a retrocervical tumor, suspected to be a myoma with central necrosis. Because of increasing and unbearable pain as the only symptom of an otherwise unremarkable clinical picture, a caesarean section of a healthy child was accomplished in the 30th week. Intraoperatively, a tumour of 9 cm diameter was seen in the rectovaginal septum. Fearing major bleeding, and under the misleading assumption of a myoma no further exploration was done. After 4 weeks of continuing pain a re-laparotomy was performed. The frozen section revealed a highly malignant epithelial tumour probably originating from the paramesonephric duct, germ cell or anal tissue. It was decided to do an en bloc resection of the uterus, posterior wall of the vagina, rectum and the adjacent part of the sigma. A temporary artificial anus was placed. Histology and further staging revealed a HPV associated tumour of the anus pT4 pN0 (0/17), M0, R1, G3(L0,V0). Following surgery, radio-chemotherapy was completed. One year after the first diagnosis a reanastomosis of the intestines was done. In the process no residue of tumour in the anal's blunt was

found. With this case history we want to draw the attention to poorly symptomatic malignancies of the pelvic and genital region which may arise during pregnancy. Their signs and symptoms may be mistaken, and thus responsible for the late diagnosis. Although malignancies are generally rare during pregnancy, any atypical sign and/or symptom must be examined thoroughly.

PO-Geb 01.60**Ultrasound-guided laser coagulation of the umbilical cord in acardiac twins**

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We present two cases of successful treatment of twin reversed arterial perfusion (TRAP) sequence by ultrasound-guided laser coagulation of the acardiac twins' umbilical vessels. At 21st and 18th gestational weeks, respectively, ultrasound-guided laser coagulation of the intraabdominal part of the acardiacs' umbilical vessels was performed (Neodym YAG laser, 60 Watt). Blood flow was successfully stopped and both pregnancies carried on uneventfully. In order to prevent the pump-twin from congestive heart failure, different surgical methods such as fetoscopic laser or bipolar forceps coagulation of the acardiac's umbilical cord have been applied. Ultrasound-guided laser vaporisation of intraabdominal umbilical vessels is a simple and minimal-invasive procedure to cease perfusion of the acardiac twin and may replace the more invasive fetoscopic approaches in selected cases.

PO-Geb 01.61**Blood group immunization: rhesus incompatibility versus Kell incompatibility. Differences in the course of fetal disease**

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Objective: The Kell-antibody induced fetal anemia represents an exception beneath the fetal blood group immunizations. The Kell-antibody blocks early erythropoetic cells and thus leads to a hypoproductive anemia. We want to demonstrate the differences in the course of disease between Kell incompatibility and Rhesus incompatibility.

Materials and methods: Since 2006 we treated 23 pregnancies with blood group immunization induced fetal anemia in our department; 16 of these pregnancies with Rhesus incompatibility and 7 with Kell incompatibility. 117 intrauterine transfusions were performed.

Results: We found considerable differences in the number of necessary transfusions per pregnancy, the lowest hemoglobin level, the time between transfusions and the gestational age of the first transfusion between Rhesus incompatibility and Kell incompatibility. The differences could not shown to be statistically significant because of the relatively small number of patients.

Conclusions: We are able to demonstrate with our cohort of patients that the Kell incompatibility is due to its pathogenesis more aggressive than the Rhesus incompatibility. Therefore patients with Kell incompatibility need closer follow up than other patients with blood group immunization in pregnancy.

PO-Geb 01.62**Large ovarian mucinous cystadenoma during pregnancy. A case report**

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Objective: There are few data available on managing adnexal masses in pregnant patients. Most of these are benign tumors such as mature cystic teratomas and cystadenomas. Rates of malignancy range from 3.6 to 6.8 percent of persistent masses.

Materials and methods: A 22-year-old woman, gravida I, para 0, presented with a huge, asymptomatic left adnexal tumor, incidentally diagnosed at the gestational age of 31 + 2 weeks. Abdominal ultrasound showed a multilocular cystic left adnexal tumor with thin septations measuring 142 mm × 86 mm × 134 mm. Fetal development was appropriate for gestational age. CA 125 was elevated up to 102.9 IU/ml. Close clinical and sonographic monitoring was conducted initially. Because of rapid enlargement and increasingly massive upper abdominal pain a longitudinal laparotomy with cesarean section and left ovariectomy with removing of the cystic mass was performed in the 33 + 5 week of pregnancy. Histologically, a 2000 g multilocular mucinous cystadenoma measuring 250 mm × 200 mm × 600 mm was identified. The premature infant had to be treated for RDS postnatal with complete reconvalescence after 12 days.

Conclusions: Conservative treatment of adnexal masses during pregnancy requires close monitoring of the patients to prevent maternal and fetal complications. The rapid enlargement of the ovarian mass during pregnancy might indicate a steroid hormone-responsiveness of the tumor.

PO-Geb 01.63**Diagnostic tools to evaluate suspected placenta percreta**

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Objective: According to the literature abnormal placentation such as placenta accreta, increta or percreta occurs in 1:7000 deliveries, whereas placenta percreta makes up 5–7% of these cases of abnormally deep placental invasion. This high risk condition for mother and fetus requires an early and correct diagnosis and planning of delivery.

Materials and methods: In a retrospective study we searched 10102 deliveries between 1/2006 and 4/2010 in one perinatal centre. 10 cases of placenta percreta were identified. We retrospectively investigated the diagnostic tools that had been applied. It was correlated with the clinical history and the therapeutic approach.

Results: 8/10 women had MRI whereas the depth of infiltration was correctly measured in 6/8 cases. Cystoscopy was performed in 5 cases. An infiltration of the bladder wall occurred in two patients. Ultrasound could not reliably rule out bladder invasion. All but one patients had previous caesarean sections, 4 had curettages. The incidence of placenta praevia totalis was 6/10. Hysterectomy was performed in 4/10 cases. The presence of risk factors such as history of caesarean sections, curettages and placenta praevia—especially when combined—should rise awareness for abnormally deep placentation. If placenta percreta is suspected by ultrasound, MRI and—in doubtful cases—cystoscopy should be performed. Leaving the placenta in situ in cases of suspected or confirmed bladder infiltration appears to be beneficial.

PO-Geb 01.64**Molecular blood genotyping in rare rhesus blood group variants: a case report of a rhesus positive baby in two rhesus negative parents**

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Objective: This case report shows the necessity of molecular blood group genotyping in a newborn that was apparently Rh pos. in two Rh negative parents.

Materials and methods: Parents presented with paternal Rh– (Ccddee) and maternal Rh– (ccdde) and no Rh Prophylaxis was performed primarily. Surprisingly blood group determination was inconclusive in repeated gel and titration assessments and concluded a baby probably rhesus positive. Molecular BG genotyping (PCR-SSP) then revealed a rhesus partial D (Dv) variant CcDvee, K–. Then father was tested again and revealed A (+) CcDvee, Type VII, which proved paternal transmission of blood group variant.

Conclusions: In this case only genetic BG typing revealed a partial RhD variant which enables the counseling for blood transfusion as donor or receptor in the individuals and counseling for future pregnancies, namely Rh prophylaxis.

PO-Geb 01.65**The endoglycosidase heparanase is not differently expressed in term placentas of women with gestational diabetes or uncomplicated pregnancies**

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Objective: The endoglycosidase heparanase (HPSE) is believed to play a crucial role not only in the development of metastasis but also in the pathogenesis of other processes, such as nephropathy and diabetes-associated diseases. However, its role in pregnancy-associated complications is not well understood.

Materials and methods: A power analysis to calculate the number of patients needed was conducted. Placental tissue was obtained directly after delivery. We then examined the expression of HPSE in term placentas of 30 consecutive patients with gestational or pre-existing diabetes and 30 healthy controls by means of RT-PCR in relation to house-keeping enzymes. Protein expression was analysed by means of immunohistochemistry, using a monoclonal antibody against HPSE. Statistical analyses were performed with Prism 4.0 for Windows (GraphPad Software, 2003, San Diego, Ca, USA). For continuous data the Mann-Whitney-Test was assigned. The results were considered statistically significant when the two-sided analysis yielded a p value < 0.05.

Results: The patients were comparable with respect to age, parity and gestational week. We were unable to show significant differences of the expression of placental HPSE—both on RNA and protein levels—between the two groups ($p > 0.05$).

Conclusions: Placental heparanase does not seem to contribute to pathological processes at term in women with gestational or pre-existing diabetes.

PO-Geb 01.66**The clinical significance of base excess (BE_B) and BE_{Ecf}** *Volker Michael Roemer¹,¹Institut für feto-maternale Medizin, Detmold, Germany

Objective: BE_B ($ctH_{B,act}^+$ (mmol/l)) is important since it might reflect lactate acidosis due to hypoxia; In vivo ctH_B^+ is dependent from pCO_2 . Independence is achieved when using the extended extracellular fluid (Ecf) reducing cHb to 1/3 (foetus: about 1/4). Correction of ctH^+ to normally low fetal oxygen saturation by reoxygenation rises ctH_B^+ leading to four variables: $ctH_{B,act}^+$, $ctH_{Ecf,act}^+$ (called Standard BE), $ctH_{B,ox}^+$, and $ctH_{Ecf,ox}^+$. Which variable is most appropriate for perinatal acid-base studies?

Materials and methods: The APGAR- and the WAS-score were used measuring neonatal vigour and FHR characteristics of 475 foetuses delivered vaginally. FHR was evaluated by computation of the WAS-Index referring to: $(FHF*w1) * (OZF*w2) * (OZA*w3)^{-1}$. The three weighting functions w1–w3 were determined using optimizing software. WAS-score denotes the mean of the last 30 WAS-indices.

Results: In vivo $ctH_{B,act}^+$ is closely correlated with pCO_2 : $r = -0.288$, $P < 10^{-4}$; $ctH_{Ecf,act}^+$ becomes independent from pCO_2 : $r = -0.0068$, $P = 0.881$. The two blood gases pCO_2 and pO_2 are inversely correlated ($P \ll 10^{-4}$). The 1-Min. APGAR is best correlated with pH,UA ($r = 0.4078$, $P < 10^{-4}$, Spearman's Rho = 0.307). Correction of ctH^+ to $sO_2(\%)$ yields: $ctH_{B,ox}^+$, $ctH_{B,act}^+$, $ctH_{Ecf,ox}^+$, $ctH_{Ecf,act}^+$: Rho = 0.259, 0.239, 0.184 and 0.176, respectively, P all $< 10^{-4}$. The same pattern holds true for the 5-Min. APGAR. The WAS-score is best correlated with pH,UA: $r = 0.656$, $P \ll 10^{-4}$. The metabolic variables: $ctH_{B,ox}^+$, $ctH_{B,act}^+$, $ctH_{Ecf,ox}^+$, and $ctH_{Ecf,act}^+$ give: $r = -0.587$, -0.565 , -0.461 and -0.448 , respectively, (P all $< 10^{-4}$).

Conclusions: Actual pH always offers the closest correlation with essential parameters. The clinical advantages of $ctH_{B,act}^+$ and $ctH_{Ecf,act}^+$ are not evident; $ctH_{Ecf,ox}^+$ should be used with correction to actual oxygen desaturation i.e. after 100% reoxygenation of haemoglobin.

PO-Geb 01.67**Perinatal parameters which may predict preterm delivery at the boarder of viability in a decade***Isabelle Antwerpen¹, Tina Ernst¹, Anke Reitter¹, Rolf Schlößer², Frank Louwen¹¹J. W. Goethe-University, Department of Obstetrics and Prenatal Medicine, Frankfurt, Germany, ²J. W. Goethe-University, Department of Neonatology, Frankfurt, Germany

Objective: To provide the latest descriptive data about infant survival and morbidity after extremely preterm birth in infants with gestational age (GA) of <25 weeks in relationship to parameters which may predict preterm delivery. As well as to advance prenatal and perinatal care and to update clinical guidelines.

Materials and methods: Center-based retrospective study of mothers and their extremely preterm infants with a GA of <25 weeks to compare survival rates due to infectious disease, birth weight and multiples in the unit of obstetrics at the Johann Wolfgang Goethe-University Frankfurt/Main, during 2000–2009.

Results: 80 mothers were identified. Out of all mothers 15 had experienced once, 7 twice and 4 three or more times a previous miscarriage, a previous stillbirth or neonatal death. The current pregnancy was the result of artificial reproduction in 8 of the women. Parameters of an infectious disease were demonstrated: 24 mothers had increased C-reactive protein (CRP), 46 mothers had increased leukocytes and 25 mothers had elevated temperature. The relation of several parameters to the birth weight and to the antenatal treatment of corticosteroids was shown. 94 infants with a GA $<25 + 0/7$ were identified. Out of these infants 43 were stillborn or died in the

delivery room and 51 were admitted to the ICU. The neonatal morbidity and mortality is demonstrated including mechanical ventilation, retinopathy of prematurity (ROP), periventricular hemorrhage, periventricular leukomalacia.

Conclusions: The survival rate increased in addition to the GA and a lower risk of infant death was associated with perinatal treatment such as antenatal corticosteroids which both stands in accordance with previous studies. Furthermore the present study could show the relation to maternal disease, birth weight and multiples. Because of the low number of cases multicenter studies are recommended to evaluate further relevance of risk factors.

PO-Geb 01.68**Accuracy of intrapartum detection of Group B streptococcus with a new rapid PCR assay in a maternity ward***Martin Müller¹, Ariane Henle¹, Susanne Rohner¹, Andre Kind¹, Sara Christine Droz², Daniel Surbek¹¹Bern University Hospital, Department of Obstetrics and Gynecology, Bern, Switzerland, ²Bern University Hospital, Clinic of Infectiology, Bern, Switzerland

Objective: Early onset neonatal sepsis due to Group B streptococci (GBS) is responsible for severe morbidity and mortality of newborns. The optimal strategy consists of intrapartum antibiotic prophylaxis given to patients who are tested positive for GBS in the antenatal culture-based screening and a risk based approach for cases of unknown GBS status. Recently a new rapid real-time polymerase chain reaction (PCR) assay for intrapartum detection of GBS become available. Herein we test the accuracy and acceptability of the PCR based test in the daily routine of the labour ward.

Materials and methods: A prospective study was conducted. All pregnant women in the maternity ward from 25 weeks' gestation on giving birth with a risk of premature birth, or with a planned cesarean section were included. Patients under 25 weeks were excluded. Selective GBS culture (gold standard) and a molecular GBS test (Xpert GBS) were performed routinely on specimen.

Results: We prospectively enrolled 124 pregnant women from April 2009 to April 2010 in our hospital. As compared to the selective culture, the molecular GBS test had a sensitivity of 96% and a specificity of 95%. The positive predictive value of 83% and negative predictive value of 99% were registered. Most of the errors in the molecular GBS group were based on ineffective management in the labour ward.

Conclusions: The PCR based molecular GBS test is an accurate tool to identify intrapartum GBS vaginal colonization. The use in a daily routine of a maternity ward is possible but there is a learning curve how to analyse the specimen, and therefore professional training is necessary in order to minimize the human source of errors.

PO-Geb 01.69**Severe ovarian hyperstimulation syndrome (OHSS) in a spontaneous pregnancy: diagnose of fetal triploidy. A rare disease***Christina Bassler¹, Ismini Staboulidou¹, Lars Makowski¹, Peter Hillemanns¹, Constantin von Kaisenberg¹, Cordula Schippert¹¹Medical School of Hannover, Department of Obstetrics and Gynecology, Hannover, Germany

Objective: The incidence of severe OHSS ranges from 5.2 up to 30% when controlled ovarian hyperstimulation is used, however, in spontaneous pregnancy, OHSS is an extremely rare event.

Materials and methods: We report a case of a woman in the 11th week of gestation, presenting a severe OHSS with abdominal pain, ascites, pleural effusion and severe hyperemesis gravidarum after spontaneous pregnancy. A triploidy of fetus was diagnosed. OHSS declined after legal induced abortion.

Results: The patient, a gravida 2 para 1, was admitted in the 11th week of gestation. A transvaginal ultrasound showed a living fetus with a biparietal diameter of 13.4 mm and a crown-rump-length of 43.0 mm with a large nuchal oedema (3.13 mm). The ovaries were enlarged to 15 cm in diameter with multiple cysts on both sides. Ascites was present. The free β -HCG value was 1932 U/l (36.0905 Mom), serum-HCG was elevated up to 584689 U/l, PAPP A was 2.237 U/l (1.1354 Mom). A chromosomal abnormality was suspected and chorionic villous sampling subsequently performed. The cytogenetics of long-term chromosome chorionic villous culture showed a complete triploidy (69, XXX). A legal abortion was induced and performed. Material was sent to the pathologist, who described no signs of a choriocarcinoma. Triploidy was confirmed. The patient was discharged 2 days after the abortion with only mild complaints of abdominal pain and hyperemesis. Serum-HCG declined to 52770 U/l and was controlled within the next 14 weeks until it reached to a negative value.

Conclusions: To conclude, this case highlights two aspects of this rare disease: first, one must be aware of the occurrence of OHSS in spontaneous pregnancy, especially if additional pathologies such as triploidy are present and second, β -HCG do not decrease immediately after pregnancy, but may persist during weeks after abortion.

PO-Geb 01.70

Management of fetal urethral valve with reflux, dilated urether, urinoma of left kidney and uremic ascites

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Objective: Dilatation of kidneys is often seen in fetuses. Normally there is no specific therapy necessary, pregnancy is prolonged until due date if amniotic fluid index and renal function are normal. We present a case of fetal hydronephrosis based on urethral valve presenting in 29th week of pregnancy with urinoma of the left kidney and uremic ascites.

Materials and methods: First visit was in 20th week with mild dilated bladder and mild hydronephrosis of both kidneys. No additional markers for chromosomal abnormalities were found. Reevaluation took place in 28th week showing the same and a slightly dilated right urether. In 29th week the patient was sent by gynecologist due to ascites. Ultrasound examination showed a severe urinoma of left kidney and a non-dilated bladder, pelvis of the right kidney and both urethers and ascites. Pregnancy was prolonged, lung ripening was induced. Ascites was resorbed in the following week, reflux into the left kidney and a hypertrophic bladder were detected. In 33rd week the fetus showed severe dilatation of the right pelvis of the kidney and a dilated right urether. Delivery was performed by c-section.

Results: Post partum the urinoma was drained and the hypertrophic bladder was drained by suprapubic catheter. Severe reflux from the bladder especially to the left pelvis of the kidney was found. There were no hints for any complications due to the uremic ascites in pregnancy. The baby was discharged after 6 weeks with suprapubic catheter, ureteroscopic operation of the valve and reimplantation of urethers if necessary is planned with the age of 3 month after functional testing of both kidneys.

PO-Geb 01.71

Fetal kidney insufficiency with an-/oligohydramnion after ACE-inhibitor/sartane treatment during pregnancy: a case report

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Objective: We present cases of two patients with adverse effects of the contraindicated ACE-inhibitors treatment during pregnancy. In one case the patient continued the treatment because of unrecognized pregnancy, in the other the ACE-inhibitor treatment was continued despite of known pregnancy.

Materials and methods: Patients were a 27- and a 36-year old I-gravida/0-para with arterial hypertension, insulin dependent diabetes mellitus, diabetic nephropathy and diabetic retinopathy. During both pregnancies, in the 2nd trimester (23rd and 26th week of gestation) an an-/oligohydramnion was diagnosed by ultrasound.

Results: Both neonates had reduced kidney function at delivery and were treated in the department of paediatric nephrology. In both cases the kidney function improved after several months.

Conclusions: In the second half of pregnancy ACE-inhibitor treatment may cause a decreased circulation of the placenta with consecutive fetal hypotonia, oligohydramnion and anuria of the newborn with the need for dialysis. By a reduced tonus of the kidney-vessels a hypoxia dysgenesis of the kidney tubuli occur which cause a decreased fetal urine production. Beyond the 16th week of gestation the fetal urine production is the main part of the amniotic fluid, therefore the oligohydramnion is a consequence of anuria. Occasional a hypoplasia of the cranial bones is described, probably also explained by the reduced perfusion. A deterioration of the kidney function of older children, after intrauterine exposition to ACE-inhibitors in the 3rd trimester and only temporary anuric kidney failure, is described. It is necessary that patients with contraindicated medication during pregnancy have safe contraception and these patients are to be informed about the risks of treatment. The adverse effect of the ACE-inhibitor treatment needs to be considered as a differential diagnosis of reduced amniotic fluid diagnosed by ultrasound.

PO-Geb 01.72

Prophylactic cerclage: influence of the timing on prolongation of pregnancy

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Objective: Prophylactic cerclage is a widely used procedure to decrease the risk of prematurity. The optimal timing of this operation is still under discussion.

Materials and methods: By means of a retrospective study, all cerclages performed in the Dr. Horst Schmidt Kliniken 2008–2009 were analyzed for the duration of pregnancy, fetal morbidity and mortality and maternal outcome.

Results: In 39 women a cerclage was performed, 13 of which had an additional suture of the os externum in terms of a total occlusion of the cervix. The operations were performed between 12 and 26 weeks of gestation. One patient was lost for follow up. Two pregnancies ended as late miscarriages, one of them caused by a parvovirus B19-induced extreme fetal anemia. The remaining 37 pregnancies continued beyond 30 weeks of gestation with no major inflammation-

related perinatal complications. 26 pregnancies persisted for more than 37 weeks. Plotting the operation date (gestational week) against the duration of pregnancy—expressed in percentile prolongation—yielded a hyperbolic-shaped curve with a sharp decline when the cerclage was performed after 22 weeks.

Conclusions: Patients at risk for cervical incompetence resulting in prematurity have an enhanced benefit when the cerclage is performed early i.e. before 22 weeks of gestation.

PO-Geb 01.73

Challenging the MALDI-ToF-MS serum profiling analysis to distinguish women with preeclampsia from matching controls in a multicenter study using a clinical approach

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Objective: We recently demonstrated that serum analysis using affinity based MALDI-ToF-MS is capable to distinguish between patients with early-onset preeclampsia (PE) and matched controls (CN). The method is in detailed description by Pecks et al. 2010. We now aimed to evaluate the potential diagnostic value of this method in a multicenter setting.

Materials and methods: A total of 127 Serum samples of pre-eclamptic ($n = 60$) and healthy pregnant women ($n = 67$) were collected in 4 perinatal care centers. Serum analysis was performed as described previously using MALDI-ToF-MS. Statistical analysis was performed with the ClinProTools (Bruker Daltonik) software package.

Results: Our previous results could be confirmed by repeated measuring of the identical samples. Established rules however displayed restricted applicability to center 2, 3 and 4 since predefined cut off values failed at differing peak intensities. Standardizing intensities center-wise by grouping peak intensities of PEs and CNs provided applicability over all centers apart from center 4 where no CNs were available. Therefore those samples were excluded from further calculation. Aiming to improve accuracy on the m/z values, internal calibration based on calculated masses from single and double charged transthyretin ($[m + H]^+ : 13,761 \text{ Da}$; $[m + H]^{2+} : 6,881 \text{ Da}$) was introduced. Newly added samples with larger biological variability amended the pre-established analysis and sample classification reached a sensitivity of 87.8% and a specificity of 73.1%. Note that separate calculations for early-onset PEs only revealed a sensitivity of 90.6% and specificity of 87.2% which are quite comparable to the previously published data.

Conclusions: Our results imply that MALDI-ToF-MS serum-profiling together with center-wise standardization offers a robust method to classify PE from CN over several centers. Furthermore the used peak ratios might hold potential information about subclasses of PE. This is subject of current investigations.

PO-Geb 01.74

Prevalence of IgM antibodies to Cytomegalovirus, Toxoplasmosis, Rubella, Chlamydia, Parvovirus and Herpes Simplex virus infection in women with bad obstetrics history

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Objective: Maternal infection plays a critical role in pregnancy wastage and their occurrence in women with bad obstetrics history. To find out the prevalence of IgM antibodies to Cytomegalovirus, Toxoplasmosis, Rubella, Chlamydia, Parvovirus and Herpes Simplex virus infection in women with bad obstetrics history. Setting: A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos. This is a cross sectional study.

Materials and methods: Between June, 2000 and December, 2009, blood samples were obtained from 200 pregnant women with bad obstetrics history and 200 pregnant women without bad obstetrics history. Samples were centrifuged, separated and stored at -20°C until assay was carried out for IgM seropositivity using ELISA kits. **Results:** 162 (81%) were positive for CMV, Rubella, Toxoplasmosis, Chlamydia, Parvovirus and Herpes Simplex virus alone or in combination. The highest percentage of the antibodies to CMV, Rubella, Toxoplasmosis, Chlamydia, Parvovirus and Herpes Simplex virus was in cases of abortion.

Conclusions: Our study shows a strong association of these pathogens with bad obstetrics history. Therefore screening and early diagnosis of these agents in patients can help in proper management of these cases.

PO-Geb 01.75

Post term in out-of-hospital birth: a problem?

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Objective: Midwifery associations are about to identify the primary outcomes for mother and child in Germany with a home birth or birth centre setting. The study question here was: What are the outcomes when mothers giving birth post-term have their babies at home or in a birth centre?

Materials and methods: We used routine data collected by QUAG for a retrospective cohort study with an analysis based on the place where birth started (transfers during and after birth included). The out-of-hospital-births were documented by midwives all over Germany between 2000–2004 (about 80% of all out-of-hospital births and 1.5% of all births in Germany). The study population included 42,154 women starting birth at home or in a birth centre. We compared women at term (control group, $n = 39,830$; Ipara $n = 14,031$, >Ipara $n = 25,799$) versus women post term (study group, $n = 1,092$; Ipara $n = 458$, >Ipara $n = 634$). Odds ratio and 95% confidence intervals were calculated.

Results: The rate of meconium-stained amniotic fluid was higher in the study groups (for Ipara: OR 2.0, 95% CI = 1.5–2.8) as asphyxia was slightly higher (for Ipara: OR 2.4, 95% CI = 1.2–4.7). Caesarean section and transfer were twice as high in the study group, for Ipara and >Ipara. Prolonged labour was significantly higher in the study groups during the first stage of labour (for Ipara: OR 2.7, 95% CI = 2.2–3.3) but not in the second stage. Both maternal and infant outcomes show differences but no dramatic changes compared to term birth. The rise in transmission to hospital and surgical birth can be seen as an example for good cooperation between midwives and hospitals.

Conclusions: Midwives in the out-of-hospital-birth-setting in Germany are skilled to care for women, who go over their due date.

PO-Geb 01.76

The use of cervical ripening catheter as mechanical device for labour induction in case of previous caesarean section. First experiences in the University Hospital of Leipzig

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Objective: The increasing frequency of caesarean section leads to a growing number of uterine scars in the following pregnancy. As one consequence risks of labour induction are very obviously then. Due to higher risk of uterine rupture in these cases the use of prostaglandins is restricted and more dangerous. Alternatively mechanical methods of labour induction like the double balloon catheter/ foley catheter for cervical ripening are demanded.

Materials and methods: In an observational study we examined the security, practicability and economic aspects of application of this mechanical device for labour induction. We report all cases since introduction of the method in daily work in February 2010 in our department.

Results: We show descriptively duration to delivery, success rate of vaginal delivery, complications, patient's acceptance and costs of the method. First experiences showed a simple and cost effective use especially in risk patients. The double balloon catheter is accepted by patients and medical staff. In most cases amniotomy and oxytocin application is necessary for vaginal delivery.

Conclusions: The development of the double balloon catheter/foley catheter for cervical ripening (COOK medical®) offers a new careful method of labour induction. It widens the repertoire of labour induction when patients are at risk for uterine rupture or refuse other methods. The security and efficiency of cervical ripening catheter should be examined in randomized, controlled studies.

Gynecology

PO-Gyn 01.01

Large endometriosis tumour in the rectus abdominis muscle causing pain 13 years after a caesarean section

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Objective: Endometriosis, mostly located within the pelvis is prevalent in 5–10% of all women; however the time from the first

symptoms to diagnosis usually is 3–11 years. Endometriosis of the rectus abdominis muscle is very rare, and difficult to diagnose. It is often caused by grafting endometrial cells to the muscle during a laparotomy, mostly a caesarean section. Rectus abdominis endometriosis can cause severe pain.

Materials and methods: We report the case of a 7 cm-endometrioma located in the rectus abdominis muscle causing severe pain 13 years after caesarean section and discuss causes, diagnostic and treatment approaches.

Results: A 43-year-old woman presented with strong periodic abdominal pain (9/10 on visual analog pain scale (VAPS)), increasingly limiting her mobility since 8 month. Due to an intra-uterine device, the patient did not menstruate and not link the episodes of pain to her menstrual cycle. Anamnestic dysmenorrhoe (3/10 on VAPS) since her menarche waned with oral contraceptives and rose again after the cesarean section 13 years ago. A coloscopy and a computertomographie of the abdomen did not identify the cause of pain. Ultrasound did show a multinodal tumour (70 × 40 × 50 mm) in the abdominal muscle and fascia and endometriosis of the bladder. A wide resection of the tumour, including surrounding muscle fibres and fascia was performed entering via the caesarean section scar. Besides one spot of endometriosis on the bladder no intraabdominal endometriosis was found, substantiating the suspicion of the long dating back caesarean section as cause. The histological examination of the specimen revealed ectopic endometrial tissue.

Conclusions: Endometriosis of the abdominal wall can cause symptoms even more than a decade after the causing operation. Although it is very rare the clinician has to keep it in mind for the differential diagnosis of abdominal pain.

PO-Gyn 01.02

Endometriosis of perirectal lymph nodes in deep infiltrating endometriosis of the rectosigmoid colon: a new therapeutical consequence to be considered?

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Objective: Repeated finding of typical endometrial and tuber glands and stroma in the cortex of an perirectal lymph node and accompanying lymphatic vessel in a case of a rectosigmoid endometriosis in a 29 year old patient with deep infiltration endometriosis of the rectosigmoid colon.

Materials and methods: Retrospective case-report and review of the literature.

Results: Confirmation of endometriotic lesion in pericolic lymph nodes and lymphatic vessel in a patient being diagnosed with endometriosis in the rectosigmoid with a lesion size of 2.5 cm in diameter and a lesion thickness of 1.5 cm.

Conclusions: We can confirm the repeated findings of endometriotic lesions in local perirectal lymph nodes and especially accompanying lymphatic vessel, which could be a sign of at least regional or maybe even systemic spread. Likewise unclear as the question of origination is the clinical importance in means of surgical (e.g. standard sentinel LN?) and/ or other therapeutical consequences such as adjuvant hormonal therapies and potential patient benefit in terms of a lower recurrence rate or at least a longer interval of being pain free to legitimate such new procedures. Therefore a prospective study would be reasonable to evaluate possible benefits.

PO-Gyn 01.03

Analysis of differential gene expression in normal and peritoneal tissue of endometriosis patients

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Objective: Endometriosis is one of the most common gynecological diseases. Although it has been the subject of numerous scientific investigations, its pathogenesis is as yet unexplained. Irrespective of models for the pathogenesis of endometriosis (metaplastic or transplantation theory) invasiveness, cell differentiation, and cell survival should have an essential role in the disease. To gain further insight into the transcriptional changes that take place before and after the development of endometriosis, we carried out microarray analysis of normal peritoneum from healthy donors and endometriosis patients as well as peritoneal endometriotic lesions.

Materials and methods: The present study investigated transcriptional differences between normal human peritoneum ($n = 14$), corresponding peritoneal tissue from endometriosis patients ($n = 11$) and pelvic endometriotic lesions ($n = 21$) by microarray hybridization, real-time polymerase chain reaction (PCR) and immunohistochemistry.

Results: Cluster analysis of microarray data revealed two large transcriptionally related groups of genes. The first cluster contained genes overexpressed in endometriotic lesions and included glandular markers as CDH1 and members of the claudin gene family which are typically expressed in endometrium tissue. Both human peritoneum from patients without endometriosis as well as phenotypic normal peritoneal tissue from endometriosis patients displayed strongly reduced levels of those genes indicating the absence of endometrium cells. In contrast the second cluster encompasses genes showing elevated expression in peritoneum from patients without endometriosis but reduced levels in phenotypic normal peritoneal tissue from endometriosis patients as well as in endometriotic lesions.

Conclusions: Microarray profiling reveals differences between normal peritoneal tissues from healthy donors and endometriosis patients which may a role in the establishment of this disease.

PO-Gyn 01.04

Frequency of ureterolysis in a selected group of patients of a certified center for endometriosis

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This study concerns the frequency of urinary tract involvement in women with endometriosis. The assessed variables of ureterolysis include frequency, symptoms, asymmetry, correlation to stage, associated clinical and surgical problems. Further it was examined whether consequences for surgical-gynecological training could be drawn from these data. In the DEZB, 1032 patients with endometriosis and adenomyosis were operated laparoscopically from 2006 to 2008. The data from 189 patients who underwent either laparoscopic or open ureterolysis were analyzed retrospectively. The diagnostic procedures included: analysis of patient histories, bimanual recto-vaginal examination, trans-vaginal ultrasound and kidney sonogram and, in severe cases of endometriosis, an additional pelvic MRI. To rule out urinary blockage a double-sided kidney sonogram followed the second day after the operation. In 18.3% of the laparoscopies a ureterolysis was completed and in 5.3% an extrinsic ureter endometriosis was proven. The exhibited urinary symptoms, e.g., polyuria or dysuria, did not

correlate clearly with the existence of ureter involvement. Ureterolysis was performed bilaterally in 47% of the cases, in 34% on the left side and 19% on the right side. The frequency of ureterolysis was relatively high (40%) in endometriosis rASRM IV°. Before surgery, six patients showed urinary blockage and postoperative three patients. Preoperative estimates of ureter involvement are difficult but should be considered when urinary symptoms occur. Urogenital endometriosis, especially when it involves the ureter, requires a surgeon well-versed in the technology of ureterolysis. Whether a German-trained specialist can accomplish this must be clarified—also for legal reasons—in surveys.

PO-Gyn 01.05

High-resolution ultrasound imaging for the noninvasive in vivo analysis of endometriotic lesion and cyst formation in small animal models

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Objective: Endometriosis is a highly prevalent gynecological disease severely affecting the patient's quality of life. To analyze the mechanisms involved in the disease and to identify new molecular targets for the development of effective therapies, small animal models are an important approach. Herein, we report for the first time the use of high-resolution ultrasound imaging for the in vivo analysis of intraperitoneal endometriotic lesions in mice.

Materials and methods: Intraperitoneal endometriotic lesions ($n = 32$) were surgically induced in 8 C57BL/6 mice by transplanting 4 uterine tissue samples into each animal. The volume of developing lesions, their stroma and cysts were analyzed by means of a 40 MHz ultrasound probe (Vevo770, Visualsonics) directly after transplantation as well as at days 7, 14, 21 and 28. At the end of the experiments, the animals were laparotomized for volume measurement of endometriotic lesions by means of a caliper and histology.

Results: The noninvasive ultrasound technology allows for the repetitive and quantitative analysis of endometriotic lesion growth (d0: $0.90 \pm 0.04 \text{ mm}^3$; d28: $2.04 \pm 0.34 \text{ mm}^3$; $p < 0.05$), and adhesion formation with a low intra- and interobserver variability ($r^2 = 0.977$ and $r^2 = 0.970$). Moreover, it enables to easily differentiate between endometrial cysts and stroma. Accordingly, volume measurements of both endometrial cysts and stroma indicate that the initial establishment of endometriotic lesions is associated with enhanced cellular proliferation, followed by a phase of increased secretory activity of endometrial glands. Results of the ultrasound analysis correlate well with measurements of lesion volumes by caliper and histology ($r^2 = 0.874$ and $r^2 = 0.939$).

Conclusions: High-resolution ultrasound imaging represents an important tool for future preclinical small animal studies, which focus on the pathophysiology of endometriosis and the development of new treatment strategies.

PO-Gyn 01.06

Patients with endometriosis in gynecological rehabilitation

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Objective: Endometriosis as a chronic and recurring disease has adverse influences on the physical, mental and social functioning. The

present paper describes the initial status quo of patients at admission to inpatient rehabilitation and outcome parameters 2.5 years after discharge. The specific feature of the rehabilitation programme is an integrated education module especially developed for endometriosis. **Materials and methods:** Between 2003 and 2005 all patients with endometriosis were asked to take part in the study until attaining the number of 300 cases. They filled out questionnaires at admission and 2.5 years after discharge. The questionnaires included amongst others items concerning the severity of disease, quality of life (SF12) and the evaluation of single therapeutic modules.

Results: The response rate on admission was very good (86%, $n = 258$). The average age of the patients was 37.4 years. 73.2% of the patients were employed. The average time of incapacity for work was 9.8 weeks within the last 12 month. More than 50% of the patients were rated stage III and IV on endometriosis. In comparison with patients suffering from breast cancer or cardiac insufficiency patients with endometriosis rated their physical as well as their mental quality of life considerably worse. 127 patients took part at the follow-up survey (=49%). Above all their ratings on coping and pain showed substantial improvements. Within the education modules those units dealing with information and physical exercise were rated as having been especially helpful. The SF12 showed significant improvements of 4.0 points on the mental scale and 2.17 on the physical scale.

Conclusions: In-patient rehabilitation does reach a sample of highly stressed women who represent a difficult to treat group in inpatient and outpatient care. Rehabilitation can achieve sustainably positive effects, which are worth to be evaluated further in detail.

PO-Gyn 01.07

Acute bleeding by deep infiltrating endometriosis in a second trimester pregnancy: a case report and review of literature

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A 34 year old 2G/IP with a gestational age of 26 weeks was admitted at the labor board with acute abdominal pain. The gynecological examination showed signs of an acute abdomen with a very painful palpation. Ultrasound examination showed free fluid within the abdomen. The pregnancy showed no signs of growth retardation with a normal CTG. The pain was analgetic resistant and infection parameters were slightly elevated. The Laparotomy reviewed a normal appendix and 500 ml of blood within the abdominal cavity. The bleeding was due to papillary and nodular structures of unknown dignity on the peritoneal surface of the uterus and especially close to the recto-vaginal space. Pathological analysis showed a deep infiltrating endometriosis. Bleeding could be stopped by using an argon beamer for the distinct uterine surface bleedings and by application of a fleece, covered with human fibrinogen and human thrombin (TachoSil®), for a diffuse bleeding close to the recto-vaginal space. After eleven days the patient could be discharged in a good condition and pregnancy could be further prolonged. A review of literature, concerning these rare but relevant cases, will be given.

PO-Gyn 01.08

Menorrhagia and dysmenorrhea related to adenomyosis with or without uterine leiomyomata: long-term symptom control, frequency of re-interventions and quality-of-life after uterine artery embolisation

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Objective: The purpose of this retrospective study was to evaluate the long-term clinical outcome of women undergoing uterine artery embolization (UAE) for adenomyosis with or without uterine fibroids. **Materials and methods:** Forty pre-menopausal women aged 39–56 years (Median: 46.5 years) with menorrhagia and/or dysmenorrhea and magnetic resonance (MR) imaging findings consistent with adenomyosis of the uterus underwent UAE as an alternative to hysterectomy. Clinical symptoms were assessed at baseline on a yes/no basis and at follow-up by a questionnaire using the categories: resolved, markedly improved, improved, unchanged, worsened, markedly worsened. The Uterine Fibroid Symptom and Quality of Life (UFS-QoL) Questionnaire was used to assess residual symptom severity and health related quality-of-life (HRQOL). All treatments after UAE were recorded. Clinical failure was defined as no improvement or 2nd invasive therapy to control symptoms after UAE. Results were stratified based on the extent of adenomyosis at baseline MR imaging. Kaplan Meier analysis was performed to determine freedom from clinical failure. Associated log rank was used to test differences among groups.

Results: Patients were followed for a median of 40.5 months (range: 5–102 months). UAE lead to clinical improvement in 29/40 (73%) of patients. 11 patients had a clinical failure. 10 Patients underwent a 2nd intervention (hysterectomy, $n = 9$, repetitive D&C, $n = 1$). Based on MR imaging three different groups could be identified: pure adenomyosis ($n = 13$), adenomyosis with leiomyoma predominance ($n = 10$), or adenomyosis predominance ($n = 17$). Within the group of patients with leiomyoma predominance none had a clinical failure. This difference was significant ($p = 0.028$) compared to patients with adenomyosis predominance and almost reached significance in comparison to the group with pure adenomyosis ($p = 0.079$). After UAE residual symptom severity was highest and HRQOL lowest for women with pure adenomyosis.

Conclusions: UAE is clinical effective at long-term in the majority of patients with adenomyosis. Symptomatic control and improvement in quality-of-life was highest in patients with adenomyosis but predominant uterine leiomyomata. Clinical failure and hysterectomy occurs more often in patients with predominant adenomyosis.

PO-Gyn 01.09

Safety aspects of dienogest in endometriosis: pooled data from a clinical development program

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Objective: A clinical study program including dose-ranging, placebo-controlled, active comparator-controlled, and long-term studies has characterized dienogest 2 mg daily as an effective therapy for endometriosis, with efficacy significantly superior to placebo and equivalent to leuprolide acetate (LA). Individual studies reported a favourable safety profile for dienogest. Pooled analyses from the study program allow further characterization of the safety features of dienogest.

Materials and methods: In four key studies, 332 women with endometriosis were treated with dienogest 2 mg once-daily for periods of 12–65 weeks and included in pooled analyses. Safety assessments included adverse events, laboratory tests, vital signs, body weight, physical examination, and menstrual bleeding pattern.

Results: Adverse events associated with dienogest were mostly mild or moderate in intensity and related to low withdrawal rates. The most commonly reported adverse-drug reactions (ADRs) were headache (9.0%), acne (5.1%), and nausea (4.2%). Incidences of hypoestrogenic ADRs were less common with dienogest than LA. Laboratory parameters—including lipid and hormone variables—and vital signs remained generally stable during dienogest treatment. Change in body weight was not different from placebo (mean \pm SD 12-week change: 0.3 ± 1.3 kg and 0.4 ± 1.4 kg, respectively). The number (mean \pm SD) of bleeding/spotting days during 90-day WHO reference period 1 in dienogest-treated women (25.1 ± 16.9) was similar to placebo (22.4 ± 9.6); however, the bleeding pattern was more variable with dienogest. A progressive reduction in bleeding intensity over time was observed during 90-day WHO reference periods 2–4.

Conclusions: Pooled analyses from the study program confirm the favourable safety profile of dienogest in the treatment of endometriosis.

PO-Gyn 01.10

Expression of glucose transporter 1 (GLUT-1) in human endometrial tissue, peritoneal endometriotic lesions and deep infiltrating endometriosis

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Objective: Recent studies implicate that estrogen and progesterone play an role in the regulation of glucose metabolism by affecting the facilitative glucose transporter (GLUT) in endometrial tissue. There is some evidence that defective glucose metabolism leads to infertility due to changes in late secretory endometrium and decidualization. Like in malignancies, GLUT-1 seems to be one of the major factors in hypoxia, which might play an essential functional role in endometriosis. There are only few data concerning GLUT-1 expression in eutopic and ectopic endometrium of women with endometriosis.

Materials and methods: Using immunohistochemistry (EnVision FLEX-Kit (Darko Germany)), GLUT-1 expression was examined in endometrium, in peritoneal and in deep infiltrating endometriosis (DIE). Tissues were collected from 30 women with DIE who underwent rectum resection combined with hysteroscopy and curettage. A modified Remmele-Stegener-IHC-Score (0–3) was used for data analysis. Statistical analysis Mann–Whitney-Test was performed.

Results: In eutopic endometrium GLUT-1 expression was positive in epithelium cells as well as in stroma cells. In ectopic lesions mainly epithelium cells were positive. No expression was detectable in eutopic endometrium of the proliferative phase. GLUT-1 expression was strong in the late secretory phase ($p < 0.001$) in eutopic endometrium and in epithelium cells of DIE ($p < 0.01$).

Conclusions: We support the hypothesis that GLUT-1 is important for a sufficient glucose metabolism in eutopic endometrium. GLUT-1 is known to be a part of the hypoxia induced survival pathway. Our data suggests that there is a difference in the metabolism of stroma and epithelia cells in ectopic endometrial tissue due to hypoxia. Higher levels of steroid hormones receptors known to be common in patients with endometriosis. The cycle-dependent up-regulation of GLUT-1 in late the secretory phase is an indication for an endocrine modulation. This supports the idea that hormonal imbalance leads to endometrial dysfunction due to an altered glucose metabolism.

PO-Gyn 01.11

Cordycepin, a mRNA polyadenylation inhibitor, suppresses proliferation, activates apoptosis, and abrogates expression of the vascular endothelial growth factor (VEGF) in epithelial endometriotic cells in vitro

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Objective: Endometriosis is a benign but chronic disease and is often associated with pelvic pain and infertility in affected females. Endometriotic cells show increased proliferation, resistance to apoptosis, and epithelial endometriotic cells have an increased level of VEGF, an important factor in angiogenesis. We investigate the effects of Cordycepin on proliferation and survival and on the expression of VEGF in epithelial endometriotic cells. Cordycepin (3'-deoxyadenosine) is found in the parasitic fungus *Cordyceps militaris* and has biological activity including anticancer activity. Cordycepin is an inhibitor of poly(A) polymerase (PAP) and inhibits mRNA polyadenylation, leading to shortening of the poly(A)-tail of newly synthesized mRNAs, to de-stabilization of these mRNAs, and to disruption of proteins synthesis.

Materials and methods: Immortalized 11z cell cultures were treated with various concentrations of Cordycepin. The effects on proliferation (MTT-assay); expression of p21, cyclins, and VEGF (immunoblotting); apoptosis activation (immunoblotting), and VEGF secretion (ELISA) were determined.

Results: Cordycepin treatment inhibited the proliferation of 11z epithelial endometriotic cells, accompanied by upregulation of the cell cycle inhibitor p21 and downregulation of the cell cycle promoter cyclin D1. Cordycepin inhibited the phosphorylation of the p38 MAP kinase, leading to downregulation of this cytoprotective signaling pathway and thus contributing to inhibition of proliferation and survival. Cordycepin downregulated VEGF expression and reduced the amount of VEGF secreted into the culture medium. Cordycepin activated caspase-dependent, intrinsic apoptosis, as documented by the proteolytic cleavage of caspase-9, caspase-3, and the PARP-1 precursors into their fragments.

Conclusions: Cordycepin inhibits proliferation, VEGF production and secretion, and survival of epithelial endometriotic cells and therefore negatively affects three processes crucial to endometriosis. The PAP-inhibitor Cordycepin may therefore be a potential candidate to encounter endometriosis, perhaps presenting a possible alternative to currently available medical treatments against endometriosis.

PO-Gyn 01.12

Size and spatial orientation of peritoneally fixed uterine tissue samples crucially determine growth and cyst formation of surgically induced endometriotic lesions in mice

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Objective: Endometriosis is a frequent gynecological disease, which affects ~10–15% of all women of reproductive age. In many rodent studies, intraperitoneal endometriotic lesions are surgically induced by syngeneic or autologous transplantation of uterine tissue samples, which are sutured to the abdominal wall. Herein, we report the differences of endometriotic lesion growth in dependency of the surgical induction of the lesions in mice.

Materials and methods: Intraperitoneal endometriotic lesions were surgically induced in 22 C57BL/6 mice by transplanting uterine tissue samples into each animal. By means of noninvasive high-resolution ultrasound imaging over a time period of 4 weeks, we analyzed the growth and cyst formation of the lesions in dependency of the mode of transplantation (syngeneic vs. autologous), the type of tissue, which was fixed adjacent to the peritoneum (endometrium vs. perimetrium), and the size of transplanted uterine tissue samples (2 mm vs. 3 mm).

Results: Developing endometriotic lesions exhibited an increased growth rate (d28: $342.4 \pm 62.0\%$) with many proliferating cell nuclear antigen (PCNA)-positive cells in the endometrial glands and stroma, when the perimetrium with the underlying myometrium was sutured to the peritoneum, in comparison to controls (d28: $133.5 \pm 31.8\%$). In the group of 3 mm uterine tissue grafts lesion growth was decreased (d28: $183.1 \pm 44.4\%$), when compared to 2 mm samples (d28: $294.2 \pm 32.5\%$). However, the larger grafts developed significantly more cysts throughout the observation period than the smaller ones. Interestingly, there was no difference between syngeneic and autologous endometriotic lesions.

Conclusions: Taken together, our findings contribute to increase the standardization and reliability of future studies, performed in the frequently used mouse model of surgically induced intraperitoneal endometriosis.

PO-Gyn 01.13

TVT results in women with stress urinary incontinence and intrinsic sphincter deficiency: pelvic floor ultrasound evaluation

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Objective: The aim of the study was to evaluate the influence of urethral mobility, tape positioning, and profilometry on outcome after TVT placement in women with stress urinary incontinence (SUI) and intrinsic sphincter deficiency (ISD).

Materials and methods: In 43 women with maximal urethral closure pressure (MUCP) = < 20 cm H₂O TVT was performed with the incision starting at 1/3 of the ultrasonographically measured urethral length (1/3-rule, standard technique at our departments). In 2 patients, due to very little urethral mobility, the operation was done according to the 1/2 formula (as for TVT-O placement in our departments). Pelvic floor ultrasound was performed under standardized conditions using a 5–9 MHz vaginal probe. The parameters measured included urethral length, linear urethral dorsocaudal movement (LUDM), longitudinal urethral tape localization (LUTL), and distance between hypochoic urethra and tape (DHUT). After 6 months the patients were divided into 2 groups: cured versus not cured.

Results: 37/43 (86%) and 2/2 (100%) of patients were cured after 6 months. Our results suggest that urethral mobility and tape position affected cure results, while urethra pressure profilometry did not (MUCP between 5 and 20 cm H₂O). In women with good urethral mobility, especially hypermobility, suboptimal tape positioning (slightly increased DHUT and/or distance from center of urethral length (DCU)) may still lead to continence. Tapes not positioned

optimally in women with low urethral mobility usually do not restore continence.

Conclusions: Our results suggest that urethral mobility and tape position are the most important factors affecting outcome of TVT placement for SUI in women with ISD.

PO-Gyn 01.14

Impact of birth on levator morphology with 3D ultrasound early postpartum: a prospective observational study

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Objective: Pregnancy and delivery play a major role in the development of urogynecological problems. Using 3D perineal ultrasound we evaluated the morphology and integrity of the levator ani muscle (LAM) soon after vaginal delivery and cesarean section.

Materials and methods: Patients delivered at our department between January-June 2009 were included in this prospective observational study. 3D perineal ultrasound was performed between 48–72 h postpartum. Axial plane at level of minimal hiatal dimension was utilized to determine antero-posterior (hAP), latero-lateral (hLL) diameter, area (hA), circumference (hC) of levator hiatus and LAM thickness. LAM avulsion was defined as a defect present in at least 3 consecutive tomographic slices above plane of minimal hiatal dimension.

Results: During study period 200 women after vaginal delivery (group A) and after cesarean section (group B) were enrolled. Group A included 111 (55.5%) patients (99 spontaneous deliveries, 11 vacuum, 1 forceps) and group B included 89 (44.5%) patients (67 elective, 22 secondary cesarean sections). No difference concerning age, BMI, parital status was found. All biometrical indices of levator hiatus were higher after vaginal delivery ($p < 0.001$) but not LAM thickness (Table 1). Presence of LAM defects was significantly higher in group A than in group B, with OR = 7.13 (IC95%:3–16.8) (Table 2). In group A, 42 (37%) levator defects were found: 36 (36.3%) after spontaneous and 6 (50%) after operative deliveries. In group B, 6 (6.7%) levator defects were found: 2 (2.9%) after primary (2 pluri-parae), 4 (18%) after secondary sections (4 nulliparae).

Conclusions: Our findings suggest that, in comparison to cesarean section, vaginal delivery modifies and damages LAM. The risk of levator trauma after vaginal delivery is more than 7 times higher than after cesarean section. Our data also show, that secondary cesarean section has no complete preventive effect on LAM trauma.

Table 1. Biometrical indices of Levator ani (A: vaginal delivery, B: cesarean section)

	A (111)	B (89)	p value
hAP (cm)	6.0	4.9	<0.001
hLL (cm)	4.1	3.6	<0.001
hA (cm)	14.68	10.64	<0.001
hC (cm)	15.98	13.55	<0.001
Levator thickness R (cm)	0.7	0.67	0.117
Levator thickness L (cm)	0.69	0.65	0.222

Table 2. Levator ani defects (A: vaginal delivery, B: cesarean section)

	A (111)	B (89)	<i>p</i> value
LAM defect	42 (37%)	6 (6.7%)	<0.001
LAM defect monolateral	28/42 (66.6%)	4/6 (66.6%)	
LAM defect bilateral	14/42 (33.4%)	2/6 (33.4%)	
no LAM defect	69/111 (63%)	83/89 (93.3%)	

PO-Gyn 01.15**Nerve-preserving sacropexy: anatomical study and surgical approach**

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Objective: After sacrocolpopexy, de novo bowel, urinary and sexual dysfunctions are described. These dysfunctions could be caused by injury of the autonomous nerves of the presacral space. The aim of our study is to describe the course of the autonomous nerves of the presacral space and to find the best nerve preserving approach for sacropexy.

Materials and methods: The autonomous nerves of the presacral space are dissected on six specially preserved female cadavers. Our analysis of the autonomic innervation focused on the following parameters: the exposition of the superior hypogastric plexus with the right and left hypogastric nerves; the dissection of the right sympathetic trunk, paying particular attention to the sacral splanchnic nerves; and the exposition of the ventral rami of the sacral spinal nerves S1–S4 with identification of the origin of the pelvic splanchnic nerves.

Results: The superior hypogastric plexus is located in front of the abdominal aorta and its bifurcation and deviates to the left of the midsagittal plane. At the level of the promontory, or just below, the superior hypogastric plexus branches into two hypogastric nerves that run in front of the sacrum. In the presacral space the parasympathetic pelvic splanchnic nerves from the ventral rami of the sacral spinal nerves (S2–S3) join the hypogastric nerves, forming the inferior hypogastric plexus on both sides. From the inferior hypogastric plexus, nerve fibres spread out bilaterally to the pelvic organs. In 2 of 6 cadavers sacral splanchnic nerves could be identified leading from the sacral sympathetic ganglion S1 of the sympathetic trunk to the inferior hypogastric plexus. The anterior longitudinal ligament above the promontory is a safe area for sacropexy. Thus awareness of the autonomous nerves in the presacral space may significantly improve functional outcomes of sacrocolpopexy.

PO-Gyn 01.16**Uterine artery embolization as a treatment option for symptomatic adenomyosis**

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Objective: Adenomyosis is a common disease in 5–70% in surgical series and affects premenopausal women. Adenomyosis is the

presence of heterotopic endometrial glands and stroma in the myometrium with adjacent myometrial hyperplasia. Epithelial and stromal elements are situated at least 2.5 mm below the endometrial-myometrial junction. Adenomyosis appears in two forms: diffuse (adenomyosis) or focal (adenomyoma) and coexisting myomas are common. This study was performed to evaluate the MR imaging appearance and clinical response of patients undergoing uterine artery embolization for the treatment of adenomyosis.

Materials and methods: A retrospective analysis of 15 premenopausal women with adenomyosis, who underwent uterine artery embolization was performed. The diagnosis of adenomyosis was based on established MR imaging criteria. Follow-up MR imaging was performed and at the same time clinical response was assessed at 1, 3, 6, 12 months after embolization.

Results: The presenting symptoms of the study participants aged 37–55 (mean: 46.3 years) were: hemorrhage, anemia pain, dysmenorrhea, dyspareunia, bulk symptoms, uteral sensitivity combination. Of the 15 patients, 3 had coexistence of adenomyosis and myomatosis, 5 diffuse adenomyosis, 2 focal adenomyosis, 5 diffuse and focal adenomyosis. Bilateral uterine artery embolization was successfully performed in all patients. We observed elimination of clinical symptoms and restoration of normal menstruation after 3 months: in 14/15 women (93%) In the remaining case we noticed 45 days after embolization a parturition of necrosed part of focal adenomyosis. This woman underwent in surgical excision of necrosed parts under reservation of the uterus.

Conclusions: Uterine artery embolization is a promising nonsurgical alternative for women with adenomyosis.

PO-Gyn 01.17**Conception rate and safety during pregnancy and vaginal delivery after laparoscopic myomectomy**

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Objective: Laparoscopic myomectomy (LM) has become the surgical treatment of choice in patients, presenting with infertility related to a uterine fibroid. Patients treated with LM might have an augmented risk of uterine ruptures in subsequent pregnancies. We evaluated the type and prevalence of LM-related complications in subsequent pregnancies.

Materials and methods: 65 infertile patients with the finding of an uterine myoma, referred to our institution from January 2001 to December 2006, underwent LM. Information and results from 59 patients were obtained with an average follow-up of 40.1 months.

Results: Conception rate after LM was 78% in a total of 81 pregnancies in 46 patients. We observed an abortion rate of 9.9% with 5 early abortions and 2 late abortions. One ectopic pregnancy was reported. Preterm delivery occurred in 5 cases. From a total of 73 deliveries, 13 patients opted for a primary cesarean section (CS) (17.8%). Vaginal delivery was successful completed in 50 (83.3%) of the remaining 60 patients. In the remaining 10 patients a secondary CS was necessary due to uterine rupture (4 cases), non reassuring fetal state during labor⁴ and failure to progress in labor (2).

Conclusions: In case of infertility related to a uterine fibroid, LM resulted in a high success rate. Still, we observed a significant increased risk for uterine rupture during labor (5.5%). Detailed risk-benefit information should be given when treating patients with LM for uterine fibroids.

PO-Gyn 01.18**Comparison of sonographic and magnetic resonance imaging (MRI) in patients with uterine artery embolization (UAE) for uterine fibroids***Matthias Schulze¹, Kathrin Schindler², Ralf Robel¹¹HELIOS Klinikum Borna, Gynecology, Borna, Germany, ²HELIOS Klinikum Borna, Radiology, Borna, Germany

Objective: Uterine artery embolization (UAE) was established in 1995 as a safe, effective, nonsurgical alternative for symptomatic fibroids. Ultrasound (US) and MRI are important tools in the selection of patients. It is the aim of our examination to differentiate the advantages of both methods for the diagnosis and prognosis of success of UAE.

Materials and methods: In an 1 year period (2009) 47 women with symptomatic uterine fibroids were treated with UAE at a standard protocol. US examination including power Doppler vascular visualisation was the key method to decide if the patient was applicable for UAE. At the day of admission MRI was performed for comparison of number, size and localisation of fibroids and for documentation of pelvic vascularisation. US and MRI examination were repeated after three to four month at a follow up examination. The number, structure, and size of the myomas were examined and compared to the symptoms of the patients (bleeding, pain, pelvic discomfort).

Results: The average age of patients was 46 years and 2.2 fibroids were detectable before treatment. In MRT especially small myomas <1 cm could be seen and the grade of vascularisation could be established with both methods, but the advantage of MRI was the visualisation of pelvic vessels. At the follow up examination US revealed a reduction of uterine size of 22% and size of fibroids of 40%. MRI presented equal results but shows some liquid fibroid necrosis. We could show a reduction of bleeding disorder by 86%, of pelvic pain by 60% and of pressure complaints by 75%. In the 3 failures especially persistent perfusion was remarkable.

Conclusions: US including power Doppler are the key examinations for application of UAE in symptomatic fibroids. MRI is important for the visualisation of pelvic vessels but not necessary for follow up.

PO-Gyn 01.19**Morphological changes of the Fallopian tubes in a relation to uterine myome (fibroid)***Gregory Brodsky¹, Leila Adamian¹, Nikolai Kondrikov²¹Scientific Center for Obstetrics, Gynaecology and Perinatology, Gynaecologic Surgery, Moscow, Russia, ²Scientific Center for Obstetrics, Gynaecology and Perinatology, Pathology, Moscow, Russia

Objective: Our objective was to investigate the effect of uterine myoma (fibroid) on the morphological structure of the uterine tube.

Materials and methods: A retrospective, comparative study has been carried out on 100 uterine tubes of 50 women at reproductive age, with using histological, immunohistochemical and morphometrical methods. The data were obtained on peculiarities of the structure of different part, thickness of the layers, changes of the arterial and venous blood vessels supply, nervous tissues and microarchitecture of the uterine tube wall in various phases of menstrual cycle in uterus myoma group. The data was compared with histological and morphometrical data from 60 cases from control group without genital tract pathology. The data was analysed statistically.

Results: In the preliminary analysis of the 50 cases (100 Fallopian tubes) with uterine myoma, we found morphological abnormalities Fallopian tubes, which were classified, as mild, moderate and severe. We found evidence of severe morphological abnormalities in 50

Fallopian tubes (50%). In 48 Fallopian tubes (48%) we observed moderate abnormalities, and in 2 Fallopian tubes (2%)—mild grade of abnormalities.

Conclusions: We conclude, that evidence based changes in morphological structures of the uterine tube in uterus myoma group could play a significant role as a morphological substrate for clinical data associated with significantly lower outcome of assisted reproductive technology. Our findings have implication on the use of diagnostic and therapeutic strategies in women with uterus myoma who seek fertility assessment and treatment.

PO-Gyn 01.20**Long-term results of UAE for symptomatic leiomyomata***Thomas Kröncke¹, Elke Zimmermann¹, Christian Scheurig¹, Matthias David²¹Charité – Universitätsmedizin Berlin, Radiologie, Berlin, Berlin,²Charité – Universitätsmedizin Berlin, Gynäkologie und Geburtshilfe, Berlin, Berlin

Objective: To evaluate long-term outcomes of UAE with trisacryl gelatin microspheres (TGMS) in women with symptomatic leiomyomata.

Materials and methods: In a prospective single-centre study 57 women with symptomatic leiomyomata underwent UAE using TGMS. Changes in fibroid-related symptoms and patient satisfaction as well as long-term re-intervention rates were assessed. Magnetic resonance (MR) imaging was used to determine imaging outcome with respect to changes in uterine and dominant leiomyomata volume.

Results: Baseline and clinical follow-up data was available in 57 patients after a median of 42 months. MR imaging follow-up was completed by 44 patients at a median of 15.5 months after UAE. After UAE, persistent improvement of menstrual disorders such as hypermenorrhagia, menorrhagia and dysmenorrhagia was reported by 92, 85 and 95% of women, respectively. Sustained improvement of bulk-related and other less common symptoms was reported in the majority of women. Seven/50 (14%) patients underwent additional treatment. Patient satisfaction was high (92%, $n = 46$). 47/50 (94%) women would recommend the procedure to others.

Conclusions: UAE using TGMS in women with symptomatic uterine leiomyomata can achieve long-term freedom from menstrual and bulk-related symptoms. The rate of therapeutic failure at 3.5 years is acceptable while patient satisfaction and recommendation of this minimal-invasive procedure are high.

PO-Gyn 01.21**Surgery of recurrence after stress urinary incontinence operations***Kurt Lobodasch¹,¹DRK-Krankenhaus, Frauenklinik, Chemnitz, Germany

Objective: The standard therapy of stress urinary incontinence is the placement of suburethral urinary slings. The objective cure rates are 90% after 11 years. In general hospitals the cure rates are about 80%. The kind of treatment in recurrent cases is analysed by the use of an online database with 3354 patients.

Materials and methods: 402 patients with recurrent surgery are evaluated. That means 11.9% of all patient with urinary incontinence need a second treatment. The database was evaluated and a meta-analysis of literature was performed.

Results: 254 Patients had a bulking procedure. That are 63.1%. 81 = 20.1% of the patients undergo a second tape procedure.

45 patients are operated with a Burch procedure. In 94.4% was the second treatment of recurrence a surgical procedure. Only 5.5% of the patients had a follow up with pelvic floor exercises or duloxetine.

Conclusions: The main treatment of recurrent urinary incontinence is a bulking procedure. The following are second tape, Burch operation and non surgical treatment. If diagnosis and first operation are correct in cases of recurrent incontinence an other surgical treatment should be considered. If the operation was faulty the same procedure can be correctly performed. In each case of recurrence a very careful examination and analysis is necessary.

PO-Gyn 01.22

Results of a urogynaecologic survey regarding modifications and differential therapy of pelvic organ prolapse repair by vaginal sacrospinous ligament fixation (Amreich-Richter)

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Objective: Repair of vaginal fault prolapse by sacrospinous ligament fixation (AR) was described by Amreich and Richter. The operation has low perioperative morbidity and a recurrence rate of 5–15% with high patient satisfaction, good anatomical results and quality of life. A lot of modifications are known regarding the sutures, needles and instruments used, blunt or sharp preparation, kind of perforation of the ligament and the stitching of the vagina. But every modification and its combination can change the outcome of the procedure. In the light of pelvic repair with meshes and sacrocolpopexy the actual significance of AR in clinical practice in Germany is not known.

Materials and methods: We did an urogynaecologic survey and asked all members of the AGUB addressing the favoured operative technique and differential therapy. A questionnaire was sent to all members of the AGUB ($n = 1116$). The results were statistically analyzed.

Results: 212 members replied. Each member performed 157 ± 129 corrections of pelvic organ prolapses (118 ± 106 vaginally, 22 ± 19 abdominally, 22 ± 29 laparoscopically, 24 ± 47 combined). Regarding AR 98 perform a unilateral and 24 a bilateral fixation. 15 use fast, 58 late resorbable and/ or 43 non resorbable sutures. 45 stitch transepithelial and 67 transepithelial for vaginal fixation. 46 knot with and 66 without intervening bridge. Most of the members prefer AR in the setting of women 70 years or older.

Conclusions: AR is still broadly used. In comparison to pelvic repair with meshes and abdominal or laparoscopic sacrocolpopexy most surgeons use it preferably in older patients.

PO-Gyn 01.23

Bilateral transcervical sacrospinous hysteropexy: a mesh-implant-free technique in the uterus preserving pelvic organ prolapse surgery

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Objective: Uterine prolapse is a common problem in women that negatively affects one's quality of life. Uterine preservation is becoming more important in pelvic organ prolapse. Recent literature describes vaginal, open abdominal and laparoscopic approaches. Most of these procedures use mesh-implantations. The well-supported

unilateral vaginal sacrospinous hysteropexies without mesh had a recurrence rate of nearly 20%. We assessed the bilateral transcervical sacrospinous hysteropexy and present 1 year follow up data.

Materials and methods: 52 pre- and postmenopausal women (range 35–72, median 55.6) were operated between 2007 and 2009. All women presented with uterine descent stage 2–4 according to the classification of the International Continence Society. The sacrospinous hysteropexy was performed bilaterally. A midline incision in the anterior and posterior wall was extended to the cervical part. After dissection of the sacrospinous ligament two Prolene 2/0 sutures were implanted with a Stitch-instrument (I-Stich, AMI, Germany) in the ligament both side. One suture was placed through the posterior left and right side of the cervix. One suture left and right passed the cervix to the anterior side. The hanging knot stabilizes the uterus in level 1 (de Lancey). In 40 women we combined the hysteropexy with anterior and posterior colpoperaphy and 12 patients received additionally a paravaginal repair.

Results: The mean operating time was 58 min. No intra- or postoperative complications occurred. After 12 month a subjective success rate was 96%, nobody had recurrent prolapse. One patient had pelvic pain for 6 month, 3 women developed a Cystocele and also 3 women a denovo stress urinary incontinence.

Conclusions: The bilateral transcervical sacrospinous hysteropexies is safe method and a good alternative technique compared to the laparoscopic or abdominal approach. The uterus is stabilized in the apical compartment without using mesh implantation. Further randomized trial are needed to confirm the data.

PO-Gyn 01.24

Intravenous leiomyomatosis: a case report

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Objective: Intravenous leiomyomatosis (IVL) is a rare benign disease characterized by nodular masses of histologically benign looking smooth muscle cells growing within the uterine or extrauterine venous system. IVL imitates a malignant neoplasm concerning the pattern of growth and extension. Unusual growth patterns and recurrent forms may be seen as shown in this case report.

Materials and methods: We report the case of a 42-year-old woman who was referred to our hospital for a big abdominopelvic tumor. Last history revealed abdominal pain and dyspnoea. An excretory urogram showed an urinary stasis on the right side. A magnetic resonance imaging of the pelvis demonstrated the presence of a tumor of the uterus with bladder impression, measuring 12 cm. Physical examination revealed a mobile uterus with a non-fixed tender mass in the pelvis, transvaginal ultrasound the presence of a myomatous uterus. Cystography was negative despite the impression of the bladder. Laboratory findings were normal. In an explorative laparotomy the abdominal tumor was resected and a total hysterectomy without adnexectomy was performed. Histological examination indicated intravenous leiomyomatosis of the uterus. The patient was followed up in our hospital every four months. Three years later the woman presented with a new tumorous mass at the right ovary. Gynaecological ultrasound was suspicious for sactosalpinx. Diagnostic laparoscopy was first performed followed by laparotomy. On surgical exploration an intraligamentary myoma was found on the right pelvic side and successfully resected. Histological examination confirmed the intraoperative diagnosis of an intraligamentary leiomyoma.

Conclusions: IVL is an uncommon neoplasm of the uterus that usually follows a benign course. Nevertheless, metastatic potential seems to play a role in intravenous leiomyomatosis and its recurrence.

PO-Gyn 01.25**Angiogenesis and lymphangiogenesis in ectopic human endometrial lesions in mouse models of endometriosis**

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Objective: Endometriosis, characterized by the presence of ectopic endometrium outside the uterine cavity mainly causing dysmenorrhoea, abdominal pain and subfertility, affects 10–20% of women of reproductive phase. Current therapeutical treatment, however, is still insufficient since it is associated with high recurrence rate and unwanted side effects. To develop novel therapeutical approaches, the cell biological mechanisms underlying this disease have to be evaluated. We here focussed on angiogenesis in endometriotic lesions as well as on lymphangiogenesis, the role of which in the pathogenesis of endometriosis is still not understood, in two different immunodeficient mouse strains after transplantation in different ectopic locations.

Materials and methods: Human premenopausal endometrium was implanted subcutaneously (s.c.) as well as intraperitoneally (i.p.) into immunodeficient nude mice and Rag1^{-/-} mice and cultured for up to 12 weeks. While nude mice lack functional T-lymphocytes, Rag1^{-/-} mice in addition lack functional B-lymphocytes. After 4, 8 and 12 weeks, blood vessel endothelia were evaluated by immunohistochemical staining with anti-CD31, mature pericytes stabilizing the vessels with anti-alpha smooth muscle actin (α -SMA), and lymphatic vessels with anti-LYVE-1.

Results: Implanted ectopic lesions showed a well preserved morphology up to 12 weeks of culturing independent of mouse strain used or localization (s.c. or i.p.). Blood and lymphatic vessels grown into the ectopic lesions were observed after subcutaneous as well as intraperitoneal transplantation. Amount of blood and lymphatic vessels as well as depth of invasion into the human tissue increased with time of culturing. In parallel, all specimens investigated showed blood vessels stabilized by pericytes. Microvessel density of stabilized blood vessel as well as ingrown lymph vessels revealed to be slightly enhanced in intraperitoneal compared to subcutaneously implanted lesions.

Conclusions: Human endometrial tissue is well preserved after subcutaneous as well as intraperitoneal transplantation in both immunodeficient mouse strains and is invaded by lymphatic as well as by blood vessels which in part are stabilized by pericytes.

Oncology**PO-Onko 01.01****Prognostic impact of metric tumour size in pT2 breast cancer**

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Objective: pT2 tumors comprise a wide size scale, ranging from >2 cm to \leq 5 cm. pT stadium is an important prognostic factor, thus

it was aimed to evaluate, if metric tumor size within one T-stage shows different prognosis.

Materials and methods: Early breast cancer patients (pts.) diagnosed between 1998 and 2008 and treated in HSK Wiesbaden.

Results: After a median follow-up of 48 months, 1011 pts were identified and classified in three groups: A) 2.1–3.0 cm (714 (70.6%) pts.), B) 3.1–4.0 cm (222 (22.0%) pts.) and C) 4.1–5.0 cm (75 (7.4%) pts.). Median age was 60, 57 and 54 years ($p = 0.04$) in groups A, B and C and axillary lymphnode involvement (pN+) was apparent in 37.7%, 50.0% and 49.3% ($p < 0.05$), respectively. Radiotherapy was conducted in 72.8% in group A, compared to 81.5% in group B and 88.0% in Group C ($p = 0.03$), chemotherapy in 57.6%, 69.8% and 69.3% ($p = 0.03$). In multivariate analysis, including classic prognostic factors (ER/PR, Her2neu, Grade, N-status), group C was associated with a significant elevated risk for recurrence HR: 2.61; (95% KI: 1.59–4.28) in comparison to group A. 5 year recurrence free survival was significantly different: A 85%, B 80% and C 65%; $p = 0.004$.

Conclusions: Pts. with pT2 breast cancer do not exhibit a homogenous prognosis and tumor size stratification into three groups could provide further information for the risk of recurrence.

PO-Onko 01.02**Bone density in postmenopausal women with non metastatic breast cancer before starting aromatase inhibitor therapy: comparison of QUS, DEXA and QCT**

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Objective: Aromatase inhibitor induced bone loss (AIBL) can have a great impact on women's health. Women at high risk for potential fractures should be detected and receive preventive measures along with AI therapy. We therefore investigated three different methods for measuring bone density: QUS, DEXA and QCT.

Materials and methods: $N = 60$ patients received QUS, DEXA and QCT. The T values were measured and osteopenia ($T -1.0$ to -2.4) and osteoporosis ($T \leq 2.5$) were diagnosed according to WHO criteria. The T values of all three methods were compared to each other with DEXA as the reference method.

Results: QUS measured a normal bone density in 56/69% of cases compared to DEXA of hip/spine, osteopenia in 53/59% and osteoporosis in 75/29%. QUS measured a normal bone density in 71/88% of cases compared to QCT of hip/spine, osteopenia in 70%/27% and osteoporosis in 67/19%. QCT measured a normal bone density in 62% (hip) and 27% (spine) of cases compared to DEXA, osteopenia in 57/19% and osteoporosis in 100 and 86% respectively.

Conclusions: Assuming DEXA as the reference measuring method QUS could detect normal bone density, osteopenia and osteoporosis acceptably depending on site of measurement. QCT has a high false positive rate compared to DEXA due to lacking own reference values of QCT. WHO criteria for DEXA cannot be applied to QCT one by one. QUS can help detect women with normal bone density. DEXA still cannot be replaced for diagnosis of therapeutically relevant bone density loss.

PO-Onko 01.03

Implementation of various biomarkers and gene/tests for breast cancer in the current AGO guideline 2010 and comparison of their costs and reimbursement

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Objective: Breast cancer is not a homogeneous entity. Several subgroups show different responds regarding standard therapies. Biomarkers and gene expression/tests can be used to individualize the outcome of adjuvant therapies as “personalized medicine” regarding prognosis, prediction or side effects. In the following a variety of these tests for primary breast cancer is analyzed according to the latest breast cancer guideline regarding implementation and costs vs. reimbursement.

Materials and methods: Identification of various biomarkers and gene/tests according to a selective Medline search and analysis of current breast cancer guideline 2010 version 10.1.0 of AGO Breast Commission for their implementation. Analysis of their costs versus revenues according to DRG Report Browser V2008/2010HA by InEK as well as potential additional payments (NUBs, Neue Untersuchungs- und Behandlungsmethoden; ZE, Zusatzentgelte) for 2010.

Results: The following biomarkers or gene/tests were identified and analyzed: 1. Estrogen and progesterone receptor, 2. Her2 receptor, 3. KI67 antigene, 4. uPA + PAI-1 proteases, 5. CYP2D6 (Tamoxifen metabolism), Oncotype DX, 7. MammaPrint, 8. Rotterdam 76-gene signature, 9. DPD test (5-FU toxicity) and 10. Topoisomerase II α (anthracycline sensitivity test). No. 1–7 + 10 are listed in the AGO guidelines breast cancer (80%), no. 8 + 9 not. The costs of the tests vary from approx. 25–2.600 € and are only for no. 1 + 2 implemented as standard of care in the DRG calculation (20%). No. 3–10 are neither pictured in DRGs nor reimbursed as NUB or ZE (80%).

Conclusions: Most biomarkers and gene/tests are listed in the AGO guidelines 2010. Due to limited use and timely delayed calculation the costs of the majority are not included in DRGs 2010. At present time most tests can only be offered in cost-covering clinical trials or as out-of-pocket payment by patients or have to be subsidized by hospitals from their own budget during implementation phase.

PO-Onko 01.04

ER and PR expression profile of circulating tumor cells (CTC) in metastatic breast cancer patients in comparison to the primary tumor

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Objective: Several studies have indicated that the expression of predictive markers including ER and PR can change during course of

disease. Therefore, reassessment of the predictive markers at the time of disease progression might help to optimize treatment decisions. Metastatic tissue may be difficult to obtain for repeated analysis. In this context, characterization of CTC could be of relevance. Therefore, the purpose of the present study was: (1) to reevaluate the ER/PR expression by CTC and (2) to compare the hormone receptor status expression profile of CTC with the primary tumor.

Materials and methods: We evaluated 193 blood samples from metastatic breast cancer patients at the time of first diagnosis of metastatic disease or disease progression. All samples underwent immunomagnetic enrichment using the AdnaTest BreastCancerSelect followed by RNA-isolation and subsequent gene expression analysis by reverse-transcription and Multiplex-PCR in separated tumor cells using the AdnaTest BreastCancerDetect. CTC were analyzed for the three breast cancer associated markers: GA733-2, Muc-1, Her-2 and actin as an internal PCR-control. Expression of the ER and PR receptor was assessed in an additional RT-PCR. The analysis of PCR products was performed by capillary-electrophoresis on the Agilent-Bioanalyzer-2100.

Results: The overall detection rate for CTC was 45% (87/193 patients) with the expression rates of 71% for EpCAM (62/87), 73% for MUC1 (64/87), 48% for HER2 (42/87), 19% for ER (17/87) and 10% for PR (9/87), respectively. Comparisons with the primary tumor were only performed in CTC + patients ($n = 87$). In 48/62 (77%) patients with ER-positive tumors, CTC were ER-negative and 46/53 (87%) patients with PR-positive tumors did not express PR on CTC. Primary tumors and CTC displayed a concordant ER and PR status in only 41% ($p = 0.260$) and 45% ($p = 0.274$) of cases, respectively.

Conclusions: Most of the CTC were ER/PR-negative despite the presence of an ER/PR-positive primary tumor. The predictive value of hormone receptor status expression profile of CTC for palliative endocrine therapy has to be prospectively evaluated.

PO-Onko 01.05

Clinical data and outcome in stage IV breast cancer at first diagnosis

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Objective: A subgroup of breast cancer consists of cases with detectable metastasis at first diagnosis. In an average sample this subgroup occurs in less than 10%. Are there special epidemiologic features and how is the prognosis?

Materials and methods: In this retrospective study we concentrated on the cases treated between 1968 and 2006. 191 cases could be included. The data were analyzed by SAS programme procedures as proc freq, proc univariate and proc lifetest (actuarial). Endpoint was Dec 31, 2009.

Results: Clinical data: The median age was 59.1 years. 73% patients had postmenopausal status. The clinical tumor size categories showed a shift to the larger tumor diameters. cT1 occurred in only 10% whereas cT3 and cT4 amount together to 58%. An unsuspected axillary status cN0 was palpated in only 27%. The tumor specimens were positive for ER in 69% and PR in 36%. Bone metastases were diagnosed in 65%.

Course: 184 of 191 women died within the observation period with a median/mean survival time of only 1.5/2.2 years. 7 patients were alive at endpoint. The cases with cT1 or cT2 had a significant better survival function than the patients with larger tumors. The same was valid for ER+ vs. ER- cases. By dividing the study period in 3 intervals of about 12 years the cases in the last period treated had the better outcome. However their tumors were smaller.

Conclusions: Analogue to the situation with distant recurrence there does not seem to be a chance of cure in the considered situation. Unfortunately we could not test the recently published result that operation of the primary in these cases yields a significant better

outcome. Our cases without resection had a much larger tumor burden than the cases with removable tumors.

PO-Onko 01.06

Circulating tumor cells (CTC) in peripheral blood of breast cancer patients before and after adjuvant chemotherapy predict increased risk for relapse: the German SUCCESS-Trial

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Objective: The prognostic significance of CTCs in MBC has been demonstrated. We evaluated whether the presence of CTC before and after adjuvant chemotherapy increases the risk of subsequent relapse and death.

Materials and methods: We analyzed 23 ml of blood from 1489 N+ and high risk N– breast cancer pts before and after adjuvant taxane based chemotherapy. CTC were assessed with the CellSearchSystem (Veridex, USA). After immunomagnetic enrichment with an anti-EpCam-antibody, cells were labelled with anti-Ck8/18/19 and anti-CD45 antibodies. Pts were followed for a median of 32 months.

Results: In 9.4% of pts ($n = 140$) >1CTC was detected before the start of treatment (median 1, range 1–827), while 8.7% ($n = 129$) presented with >1CTC (median 1, range 1–124) after chemotherapy. Pts with CTC before treatment had more lymphnodes involved ($p < 0.01$), but no correlation to tumor size, grading and HR-Status could be found. 85 recurrences occurred and 33 pts died of their disease. The presence of >1CTC before treatment was a prognostic factor with respect to poor DFS ($p < 0.0001$) and OAS ($p = 0.023$), whereas the persistence of >1CTC after chemotherapy only predicted reduced DFS ($p = 0.054$; $p = 0.154$ for OAS). A significantly better DFS and OAS was detected between the groups with persistently negative CTC status compared to those with persistently positive CTC status ($p = 0.0031$ and $p = 0.0187$). >5CTC were a significant indicator of poor prognosis for DFS and OAS at all time points. In multivariate analysis, >1CTC before treatment was an independent predictor for OAS, >1CTC after treatment for DFS, while tumor size, lymph node involvement, grading and HR-status were relevant for both time points.

Conclusions: We demonstrated the prognostic relevance of CTC in blood of early breast cancer pts before and after chemotherapy. Therefore, CTC detection could serve as clinically useful prognostic marker and treatment monitoring tool.

PO-Onko 01.07

Obesity and disease free survival in patients with nodal positive breast cancer: the ADEBAR trial

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Objective: The prevalence of obesity increases throughout all evolved civilizations. On the other hand several epidemiological studies have shown not only an increase in breast cancer among obese women but also an adverse impact of obesity on survival of breast cancer patients. This analysis focuses on the impact of obesity on patients (pts) treated within the ADEBAR study protocol.

Materials and methods: The ADEBAR Trial compared 4 cycles of EC followed by 4 cycles of Doc vs. 8 cycles of FEC (120) in pts with primary breast cancer (≥ 4 LN). 1500 pts have been accrued from sep/01 through may/05. For this analysis data of 1361 pts has been analyzed about the impact of obesity on disease free survival. Therefore pts have been grouped to either “underweight” (BMI < 18.5 kg/m²), “normal weight” (BMI 18.5–25 kg/m²), “overweight” (25 kg/m² $<$ BMI $<$ 30 kg/m²) or “obese” (BMI $>$ 30).

Results: 13 pts (1.0%) were “underweight”, 557 pts (40.9%) were normal weight, 491 pts (36.1%) were overweight, 300pts (22.0%) were obese at the time of study enrollment. After a follow up period of 60 months 87.5% of the underweight group, 70.4% of the normal weight group, 70.7% of the overweight group and 58.6% of the obese group were alive with no signs of recurrent disease. This difference was significant (Chi-square = 9.355; $p < 0.0249$).

Conclusions: This analysis strongly implicates an impact of obesity on disease free survival in patients with early stage node positive breast cancer in the prospectively randomized ADEBAR multicenter trial. It is therefore in line with earlier findings in epidemiological research and raises the question whether a weight reduction might be an additional approach on breast cancer therapy.

PO-Onko 01.08

Peptidomimetic GnRH antagonist AEZS 115 inhibits the growth of triple negative breast cancers in vitro by induction of apoptosis and inhibits phosphorylation of AKT

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Objective: AEZS-115 (Aeterna-Zentaris GmbH, Frankfurt/Main) is an orally active peptidomimetic antagonist of GnRH. In various tumors an autocrine growth promoting loop has been described for GnRH. Our study evaluates the anti-tumor activity and mechanisms of action of AEZS 115 in models of triple negative breast cancers (TNBC).

Materials and methods: Human TNBC cell lines MDA-MB 468, HCC 1806, HCC 1937 were analyzed for GnRH receptor expression. These cell lines were incubated with AEZS-115, peptidic GnRH-antagonist Cetorelix and GnRH-agonist Triptorelin at 1, 10 and 100 μ m and the number of viable cells was determined. Cleavage of caspase 3 and PARP as well as inhibition of AKT and ERK1/2 was determined by Western blot analysis.

Results: MDA MB 468, HCC 1806 and HCC 1937 cells expressed GnRH receptors as demonstrated by immunocytochemistry and western-blot analysis. GnRH-antagonist AEZS-115 dose dependently inhibited growth of all three cell lines, while Triptorelin and peptidic Cetorelix showed marginal growth inhibition. At 10 μ m AEZS-115 inhibited cell growth by 40–60%. At 100 μ m growth inhibition was 60–80%. These results obtained by crystal violet staining were confirmed by additional luminometric evaluation of the ATP content. AEZS 115 at 100 μ m induced cleavage of caspase 3 and PARP in all cell lines indicative of apoptosis. AEZS 115 and Cetorelix at 100 μ m

inhibited phosphorylation of AKT, but not of ERK 1/2 as determined by Western blotting.

Conclusions: GnRH antagonist AEZS-115 showed substantial anti-tumor activity in TNBC cell lines by induction of apoptosis, while GnRH-agonist Triptorelin and peptidic antagonist Cetrorelix showed minor growth inhibition. This finding could be explained by atypical GnRH-receptors on tumor tissue to which the different GnRH-antagonists might bind with different affinity. Both GnRH antagonists inhibited the phosphorylation of AKT, which may be one, but not the only mechanism of action of GnRH antagonists.

PO-Onko 01.09

Simultaneous study of Gemcitabine–Docetaxel combination adjuvant treatment, as well as biological targeted treatment: the SUCCESS B-Trial

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Objective: Taxane based chemotherapy, like the PACS 01 regimen (3× FEC followed by 3× Docetaxel 100) has been established as standard treatment option for early breast cancer. The combination of gemcitabine and taxanes might develop synergistic efficacy, whereas toxicity profiles of the two substances combine favorably. The prognostic relevance of isolated tumor cells in bone marrow has recently been proven (Braun et al.; Janni et al.) and early data indicates a prognostic relevance of circulating tumor cells in peripheral blood (Cristofanilli et al.; Rack et al.; ASCO 2008).

Materials and methods: The SUCCESS B Trial is an open-label, multicenter randomized controlled, Phase III study for early, HER2/neu-positive breast cancer patients. The study will compare the disease free survival after randomisation in patients treated with 3 cycles of Epirubicin-Fluorouracil-Cyclophosphamide-chemotherapy (FEC) 500/100/500, followed by 3 cycles of Docetaxel (D) 100 q3w versus 3 cycles FEC 500/100/500, followed by 3 cycles of Docetaxel 75 (D) q3w and Gemcitabine (G) 1000 d1,8 q3w, in both arms followed by anti-HER2 treatment. All women will be required to have HER2/neu-positive disease and histopathological proof of axillary lymph node metastases (pN1-3) or high risk node negative disease, defined as: pT2 or histopathological grade 3, or age <35 or negative hormone receptor. Evidence of distant disease is an exclusion criterium. After R0 resection of the primary tumor, patients will be randomized to one of the treatment arms. Furthermore, a translational research program will focus on the role of CTCs as valuable marker of treatment failure and early disease progression. At three predefined time points peripheral blood will be drawn.

Results: A total number of 799 patients is planned to be recruited, start was in June 2008. Results of the toxicity analysis and the translational research program will be available at the end of

treatment (~June 2011). First conclusions about the effects on the disease-free-survival are expected 2 years after the end of chemotherapy.

PO-Onko 01.10

Evaluation of breast reconstructions after breast ablation at the Breast Cancer Center Regensburg

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Objective: At the Breast Cancer Center Regensburg about 80% of breast cancer patients are treated with breast-preserving surgery and 20% receive breast ablation. Primary and secondary breast reconstructions are suitable methods to preserve or regain quality of life for those patients. For this study data from 2007 to 2009 about breast reconstructive surgery procedures either with implants or flaps were evaluated concerning number, complications and patient satisfaction. **Materials and methods:** Patients experienced pre-surgery a detailed consultation procedure for a joint decision-making process. Patient satisfaction was evaluated post-surgery. As breast reconstructive methods implants, LDF (latissimus dorsi flap) and DIEP flaps (deep inferior epigastric perforator) were exerted and complications intra- and post-surgery were assessed.

Results: From 2007 to 2009, 120 patients underwent primary or secondary breast reconstruction after breast ablation. The distribution of methods was almost equal between the groups. The distribution of primary (pri.) or secondary (sec.) breast reconstruction considering the method was 77% pri. vs. 23% sec. for implants, 34% pri. vs. 66% sec. for LDF and 47% pri. vs. 53% sec. for DIEP-flap. The rate of complications over all was < 4%. Patient satisfaction was high for all groups.

Conclusions: Primary and secondary breast reconstructions after breast ablation is safe and patients satisfaction is high.

PO-Onko 01.11

HistoCore®: a new single-use core cut breast biopsy system

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Objective: Examination of the diagnostic accuracy with a new single-use breast biopsy system (HistoCore®) in daily clinical routine.

Materials and methods: Between 12/2009 until 1/2010 we performed in the context of the mammography screening (assessment) at 25 patients with a lesion BI-RADS® 5 a sonographical guided core cut biopsy with the new HistoCore® system. The age of the patients was 51–67 years (median: 59 years), the tumor size 12–31 mm (median: 17 mm). At least 4 samples/specimen could be extracted of every lesion. The HistoCore® system (Caliber: 12–20G, length of the needle: 10–24 cm, length of the notch: 18 resp. 25 mm) characterize the

following innovations: complete handle with one hand, alternatively full resp. halfautomatic biopsy, minimizing of the haematoma by a shortened needle peak and in the first time the additional possibility of the locking and resetting of the coaxial needle.

Results: In 24 of the 25 lesions (accordant 96%) the malignancy was confirmed, at 1 lesion (accordant 4%) there was the histological result B3 and the histology of the following operation was benign, a papilloma.

Conclusions: The new single-use breast biopsy system (HistoCore®) is a technical innovative, perfected and applicable diagnostic method especially with the possibility of the locking and resetting of the coaxial needle under aseptic conditions, because a sterilisation is not necessary (one-time disposable product). Under these considerations as well as the analysis of the costs/reimbursement this product is a real competition to the established high speed core cut breast biopsy systems.

PO-Onko 01.12

Facial paralysis by contralateral metastasis in parotid gland in advanced breast cancer: case report

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Objective: Breast cancer is the most common malignancy of women and nearly responsible for 27% of all female malignant diseases in general. Despite improved screening methods at time of diagnosis 6 to 10% of women have a primary metastatic breast cancer. The way of metastasis of breast cancer may be hematogenous and lymphatic. The most common ways include regional metastasis, axillary lymph nodes and distant metastasis in lung, liver or bone. Metastasis of breast carcinoma in the parotid gland are very rare. So far in literature only few cases have been reported.

Materials and methods: Described in this case report is a 74-year-old woman with an invasive lobular carcinoma of the left breast, which represents 3 years after initial diagnosis a nodular change in the cicatrice of the mastectomy. The patient also had a contralateral peripheral facial paralysis, caused by a distant metastasis in the right parotid gland.

Conclusions: Patients with breast cancer and a new onset swelling of the parotid gland, or an acute peripheral facial paralysis may have a differential diagnosis of metastasis of breast cancer. If there is a histologically classified adenocarcinoma of the parotid gland it should be thought of a potential metastasis of breast cancer. If necessary a breast diagnosis should be encouraged to search for primary malignancy. In this situation, according to the personal disease progress, a palliative surgical repair is performed, followed by irradiation to achieve local control.

PO-Onko 01.13

Importance of the matrix metalloprotease 1G/2G promoter polymorphism for breast cancer incidence

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Objective: As the major proteases that degrade the extracellular matrix metalloproteases play an important role in tumor invasion. Overexpression of certain MMPs, such as MMP-1, in breast cancer is often associated with an unfavorable prognosis. The promoter region of the MMP-1 gene contains a 1G/2G polymorphism. In the 2G genotype, an additional guanine is inserted at position –1607 leading

to an extra binding site for Ets transcription factors. Some Ets proteins, such as Ets1, are proto-oncoproteins and are involved in the regulation of cellular invasion. We analyzed whether the incidence of breast cancer is linked to the MMP-1 1G/2G polymorphism.

Materials and methods: We genotyped 105 breast cancer patients and 135 age-matched women with no diagnosed breast cancer. Genotyping was done by combining PCR-based amplification with restriction enzyme analysis.

Results: Our analysis revealed that women carrying a MMP1 1G/1G genotype have a 2.2-higher chance to develop breast cancer. No correlation could be observed between clinical-pathological factors and the MMP1-1G/2G-Polymorphism.

Conclusions: The result that the 1G allele is correlated with a higher breast cancer incidence was unexpected because an additional Ets binding site is created by the 2G allele, but not by the 1G allele. It is possible that the MMP1 1G/2G promoter region is also been used by other transcription activators or repressors that contribute to MMP1 gene expression.

PO-Onko 01.14

Translational research program of the PlanB clinical trial: comparison of anthracycline-free adjuvant chemotherapy (4× TC) and standard chemotherapy (4× EC–4× Doc) among patients with HER2 negative breast cancer

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Objective: Therapeutic decision regarding adjuvant chemotherapy based solely on conventional prognostic and predictive factors is suboptimal potentially causing significant over- or under treatment. The 21-gene-signature (recurrence score, RS) is an important prognostic and predictive factor among patients with hormone receptor positive (HR +) breast cancer. There is yet no prospective comparison of centralized pathology, proliferation markers (i.e. KI-67) and modern biomarkers (i.e. uPA/PAI-1) with the RS. Furthermore, the predictive value of the RS regarding modern taxane-containing chemotherapy in prospective clinical trials remains to be demonstrated.

Materials and methods: The goal of the PlanB clinical trial is to randomize 2,448 patients with HER2–breast cancer and either N+ status or N– status in combination with high risk parameters (pT > 2 cm, grade 2–3, age <35 years, increased uPA and/or PAI-1, HR-) to receive either 4× E90/C600–> 4× Docetaxel100 q3w or 6× T75C600 q3w. Patients with 0–3 positive lymph nodes and low RS (<11, conservatively) should receive endocrine therapy only. Pathologic criteria, grading, KI-67, HR, HER2 and 2T Score (Topo-IIa/TIMP-1) (all centralized) and uPA-PAI-1 (decentralized) will be measured.

Results: Between 3/2009 and 3/2010 1,089 patients have been registered. RS results are available for 662 of 678 yet tested patients. Results are shown in table 1. Tissue blocks are currently undergoing centralized pathological evaluation. Interim data for correlation of centralized pathology (HR, proliferation) and RS will be presented. **Conclusions:** The PlanB trial will for the first time allow for a prospective comparison of centralized pathology and invasion markers with a modern multigene signature as part of a randomized multicenter clinical trial.

Table 1

RS:	<11/12–25/>25
pN0:	15%/62%/23%
pN1(1–3):	20%/63%/17%
pN > 2(4 +):	20%/56%/24%
All:	17%/62%/21%

PO-Onko 01.15 Sentinel lymph node detection with intraoperative 3D freehand SPECT in breast cancer patients

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Objective: This study proves the feasibility of using innovative freehand SPECT (fhSPECT, CSS300 SurgicEye GmbH) for axillary lymphatic mapping in breast cancer patients and defines the border conditions for large scale comparison studies.

Materials and methods: To date, 14 patients undergoing sentinel lymph node (SLN) biopsy were recruited and scanned intraoperatively using fhSPECT before excision of SLNs. The localization of SLNs with fhSPECT was compared to the position of SLNs detected using gamma probe and blue dye.

Results: Preoperatively, 22 primary and 4 secondary SLNs were mapped with conventional scintigraphy. In the pre-excision scan (performed in 13 of 14 patients) fhSPECT managed to map all but 2 SLNs in the identical position as compared to node location at planar scintigrams (23/25). Gamma probe failed to detect any SLN in 2 patients and mapped in total 17 of 26 nodes. 18 SLNs were resected and confirmed to be radioactive. FhSPECT detected 8 remaining lymph nodes in 8 patients after removal of the SLN. In 3 cases additionally detected nodes were resected and confirmed to be radioactive, while in 5 cases no additional lymph nodes were removed as radioactive uptake was low. Pre-excision fhSPECT acquisitions took approx. 3.3 min (SD, 1.3 min) while post-excision scans took 3.2 min (SD, 1.0 min). The surgical procedure was extended by 12 min (6 min before incision and 6 min after excision of SLNs).

Conclusions: Preliminary experience indicates that intraoperative imaging with fhSPECT for lymphatic mapping in breast cancer patients is feasible. Alteration of the surgical workflow can be considered minimal given potential clinical advantages like intraoperative 3D realtime imaging, documentation of complete resection and minimized invasivity. Due to the promising results fhSPECT will be further evaluated in ongoing studies. This research was partly funded by the DFG's SFB-824 and SurgicEye GmbH.

PO-Onko 01.16 Microarray analysis of differentially expressed genes in luminal B subtype of breast cancers reveals NHERF1 as a new marker of endocrine resistance

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Objective: Gene expression profiling has recently been used to identify a group of high proliferating estrogen receptor positive breast cancers (the luminal B subtype), which are associated with a prognosis that is even worse than that of high proliferating estrogen receptor negative tumors. The analysis of those tumors might provide valuable information about breast cancer biology and could be helpful for adjuvant or neoadjuvant treatment decisions.

Materials and methods: To gain insight into genes which play a role in estrogen receptor signalling we analyzed microarray data from breast cancer specimens. Genes were identified showing strong expression in high proliferating ER-positive tumors but no expression in either Ki67–/ER+ or Ki67+/ER– samples. Among these genes the Na⁺/H⁺ exchanger regulatory factor NHERF1 was found. We assessed the clinical relevance using a total of 2469 breast cancers.

Results: Our analysis indicates that enhanced NHERF1 expression is associated with metastatic progression and poor prognosis of breast cancer patients. We found no correlation between NHERF1 and the nodal status as well as age, but positive correlations for tumor size ($P < 0.001$), grade ($P < 0.001$) and erbb2 ($P = 0.033$). Weak NHERF1 expression correlated with longer disease free survival (DFS) in grade 1 and 2 tumors, but not in grade 3 breast cancers. Since NHERF1 expression is strongly linked to the presence of ER, the predictive value for endocrine treatment was analyzed. For samples with weak or none NHERF1 expression a treatment benefit was observed ($P = 0.007$). While untreated patients display a 10 yr DFS rate of $67.2 \pm 3.8\%$, endocrine treatment resulted in $80.1 \pm 4.0\%$. In contrast no differences in disease free survival were found for corresponding NHERF1 expressing breast cancers.

Conclusions: Our data indicate that expression of NHERF1 defines a state of differentiation, where breast cancer cells are refractory to endocrine treatment.

PO-Onko 01.17 Primary metastatic neuroendocrine breast cancer: an extraordinary case report

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Objective: Neuroendocrine tumors of the breast are rare malignancy in general, their prevalence is about 0.1% of all breast cancer and less than 1% of all neuroendocrine tumors. They arise most commonly in the bronchopulmonary system and gastrointestinal tract. We present a case of bilateral breast cancer with two different histological types which already showed pulmonary metastases likely of the neuroendocrine cancer and discuss the clinical management.

Materials and methods: A 65 year-old woman presented with an ulcerated right breast mass with pain and enlarged breast.

Mammography revealed also a malignancy in the left breast. A bilateral biopsy was performed and a neuroendocrine carcinoma was diagnosed on the left side, and an invasive ductal carcinoma in the right breast. She received a bilateral mastectomy with axillary lymph-node dissection by tumor size of 9 cm each side. In the CT-scan were detected multiple pulmonary metastases which could be verified in an octreotide scan (PET-scan) most likely for neuroendocrine metastases. **Results:** A bilateral breast cancer (left bifocal, solid, neuroendocrine carcinoma, and right bifocal, solid invasive ductal carcinoma) with predominantly neuroendocrine lung metastases has been diagnosed. Because of the two cancer types we started a therapy with somatostatin-analogs (lanreotid) which has been claimed as a useful therapy for metastatic neuroendocrine tumors and a standard palliative chemotherapy (taxan with bevacizumab) for metastatic breast cancer. After 3 cycles a restaging has to be performed and further management as 90 Yttrium-Dotatoc (somatostatin analogue) has to be discussed.

Conclusions: The neuroendocrine carcinoma of the breast is very rare. There is no standard treatment protocol and a large variety of chemotherapy protocols have been employed in treating this disease. Systematic therapy principles are based on poor data base and are extrapolated from studies of non breast neuroendocrine carcinomas.

PO-Onko 01.18

Metronomic low dose cyclophosphamide therapy in metastatic breast cancer: immunomodulation of regulatory and tumor-specific T cells in respect to overall survival

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Objective: Tumor-specific memory T cells (TCs) are detectable in a majority of primary breast cancer patients while in metastatic disease anti-tumor immune responses are inhibited by CD4+CD25+Foxp3+regulatory TCs (Treg) which might, therefore, lead to tumor progression. Recently, however, metronomic low dose chemotherapy with cyclophosphamide has been shown to reduce Tregs in rodent models. In this study, we investigated the effect of metronomic low dose cyclophosphamide on the clinical benefit in metastatic breast cancer patients and monitored individual modulations of anti-tumoral immune responses.

Materials and methods: We included a total of 12 patients with progressive, metastatic breast cancer. 50 mg of cyclophosphamide p.o. was administered daily for three months. Flow cytometry was used for quantification of T cell populations and proliferation rates. Tumor-specific memory TCs were assessed in IFN- γ EliSpot assays. Disease progression was monitored by CT/MRT of the lesions and/or—if significantly elevated—by tumor markers CEA/CA 15-3.

Results: Circulating Tregs were significantly reduced by 50% within the first 14 days of therapy. In the further observational period, however, Treg numbers recovered completely. Nevertheless, we detected a significant increase in tumor-specific memory TCs, which were maintained at high levels throughout the entire study. We observed disease stabilization (SD) in almost 60% of the patients after 3 months of treatment. In patients with SD a significant increase in tumor-reactive TCs was found as compared to pretreatment levels. In a follow-up analysis, we observed a significant correlation between the overall survival of patients and the frequencies of tumor-reactive TCs after cyclophosphamide treatment.

Conclusions: In metastatic breast cancer, metronomic low dose therapy with cyclophosphamide leads to transient reduction of regulatory TCs and stable induction of tumor-specific TCs. In this context, we could show a strong correlation of tumor-specific TCs with overall prognosis of the individual patient.

PO-Onko 01.19

Applying guidelines of adaptive management for the evaluation of data quality in cohort studies and registers

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Objective: High data quality of cohort- and register studies is indispensable for striking results. Therefore Nonnemacher et al. (2007) developed an ethodological framework to assess and increase data quality for both study types. The aim of this study was to apply the developed guidelines for a retrospective cohort study of breast cancer patients. Data sources steamed from two different cohorts (1996–97, 2003–04), which were resumed in one database named Breast Cancer Query Database (BCQDB). Data quality of BCQDB was assessed.

Materials and methods: The database BCQDB included cohort 1996–97 ($n = 389$) primary breast cancer patients with 1,389 variables and cohort 2003–04 ($n = 488$) with 150 variables. After synchronization of codings, data fusion and merging processes in the BCQDB the source data verification (SDV) was performed. Data quality indicators (DQI) for the levels of plausibility, organization and correctness were defined. Quotes were defined by the number of checked items/cases (denominator) and the number of deviant items/cases (enumerator) for each DQI. Proposed threshold values of Nonnemacher et al. (2007) served as a criterion to detected low data quality on DQIs and triggered SDV. Original data sources of periods and BCQDB data were compared by distributions and individual values to detect data failures and to improve data quality in the BCQDB. A data quality score before and after SDV was calculated. **Results:** Eleven of 24 possible DQIs were calculated. Applying the guidelines of adaptive management for the evaluation of data quality improved the BCQDB quality substantially.

Conclusions: The guidelines for assessing the data quality of cohort and register studies are capable of an objective framework to assess and increase data quality. The framework is flexible in terms of the study type and enables clinicians to ensure high data quality. High data quality is fundamental for striking results in clinical research.

PO-Onko 01.20

Evaluation of an automated breast ultrasound system—SomoVTM—in comparison to the hand-held ultrasonography and to mammography in 2252 cases

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Objective: Findings of hand-held ultrasonography (HHUS) are difficult to reproduce with relatively low sensitivity and specificity. Within this study the performance of an automated breast ultrasound

system (SomoVTM) will be analysed in comparison to HHUS and mammography.

Materials and methods: 1126 patients were included in this monocentric, explorative, prospective cohort study. All received a HHUS with a 13.5 MHz transducer and a mammography. In addition we performed a SomoVTM exam of both breasts that altogether 2252 cases were included. All exams were analyzed, blinded to the patients' history, clinical examination and to the result of the HHUS/mammography. All detected lesions were classified according to the BI-RADS assessment. Results of the SomoVTM were compared to HHUS and mammography. Sensitivity and specificity were calculated. To give an estimation of the agreement of the three different methods the kappa coefficient and the p-value of the McNemar Test were determined.

Results: The data showed for the comparison between SomoVTM and HHUS as well as for SomoVTM and mammography a high specificity (in average 0.94) and a medium sensitivity (in average 0.58). The Kappa coefficient indicated a moderate agreement for both settings (0.4), while the McNemar-test revealed no significant tendency that one of the methods tends to show opposite results to the other two. **Conclusions:** The automated breast ultrasound system (SomoVTM) can be considered as a promising new method. The level of specificity shows that a negative result can be considered with a high likelihood to be true, while positive results need further evaluation with other diagnostic methods. Therefore the system could be used as a screening tool.

PO-Onko 01.21

Gene expression signatures induced by stromal factors are a predictor of survival in breast cancer

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Objective: Recent findings present the tumor microenvironment as an innovative therapeutic target in cancer therapy. Fibroblasts have been identified to play an important role in breast cancer progression. Our aim was to analyze the effect of normal mammary fibroblasts on gene expression in human breast epithelial cells and its correlation to clinical data.

Materials and methods: Nonmalignant HMT3522 S1 human breast epithelial cells were cultured in 3D-collagen-gels as mono- or coculture with normal human mammary fibroblasts. Gene expression profiles of S1-cells from 3D-culture were analyzed using the Affymetrix HG-U133 Plus 2.0 GeneChip. Signal values were calculated by means of RMA using R Bioconductor 2.4, then log₂ transformed. Transcripts with a log ratio $\geq \pm 1.5$ were defined as differentially expressed. Using published microarray profiles of 295 human breast tumors with associated clinical data hierarchical cluster and Kaplan Meier analysis were performed to stratify the patients according to the generated gene expression profiles.

Results: S1-cells in coculture differentiated into polarized acinus like structures and underwent growth arrest after 10 day of culture, whereas S1-cells in monoculture showed unorganized and progressive growth. 99 transcripts were upregulated in S1-cells from co- compared to monoculture. Functions of these genes mainly relate to extracellular matrix constitution and differentiation. 36 transcripts were upregulated in S1-cells from monoculture,

predominantly involved in cell cycle regulation. Hierarchical cluster analysis stratified the patients into poor and good prognosis groups. Kaplan Meier analysis showed that 21 selected genes were highly informative in identifying patients with poor or good outcome ($p < 0.01$).

Conclusions: Gene expression changes in human breast epithelial cells induced by normal mammary fibroblasts provide gene expression profiles that clearly stratify patients into prognostic groups. Our 3D-culture-model proves to be a valuable in vitro model for research and emphasizes the relevance of the tumor microenvironment as target for breast cancer therapy.

PO-Onko 01.22

Impact of BRCA1 on expression of microtubulus-associated proteins in-vitro and in-situ

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Objective: BRCA associated breast cancer show a typical undifferentiated basal-like phenotype. Recent evidence shows, that BRCA1 is required for terminal differentiation of mammary epithelial cells. One of the hallmarks of terminal differentiation is regulation of microtubule nucleation at centrosomal and non-centrosomal sites which requires coordinated expression of microtubule associated proteins like the hyaluronan receptor RHAMM and its major kinase aurora-kinase A (AURKA).

Materials and methods: We investigated expression of AURKA and its kinase substrate pT703-RHAMM in BRCA1 mutated, sporadic undifferentiated breast cancers and normal breast tissue of reduction mammoplasties. Sections were scored by blinded investigators using the Remmele score.

Results: Breast cancer but also mammary epithelial cells showed a cytoplasmic staining pattern for AURKA whereas pT703RHAMM immunoreactivity was restricted to the nuclear envelope of distinct cells and the mitotic spindle of cells in pro- and metaphase chromosomes.

PO-Onko 01.23

Selective escape of breast cancer stem cells immunoselected with Trastuzumab and natural killer cells

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Although trastuzumab (Herceptin) has substantially improved the overall survival of patients with mammary carcinomas, even initially well-responding tumors often become resistant. Considering that clinical efficacy of trastuzumab correlates with the infiltration of natural killer (NK) cells into the tumor site, we established a cell-culture-system to select for ovarian cancer and mammary carcinoma cells that survive a challenge by trastuzumab and NK cells. Under these conditions, NK cells can eliminate tumor cells either via antibody-dependent-cell-mediated-cytotoxicity (ADCC) or by direct recognition of tumor-associated ligands for NKG2D or DNAM-1. The most striking phenotypic alteration observed in immunoselected

ovarian cancer cells was a down-regulation of HER2 expression, leading to an ADCC-resistant phenotype. All breast cancer cells tested (MCF7, SK-BR-3, MDA-MB231, BT474), however, failed to develop resistance in vitro. Instead, treatment with trastuzumab and polyclonal NK-cells resulted in the preferential survival of individual sphere-forming cells that displayed a CD44^{high}CD24^{low} “cancer-stem-cell-like” phenotype (CSC) and expressed significantly less HER2 compared with non-stem cells. Moreover, the molecular determinants for the direct recognition of transformed cells, most notably the NKG2D ligands MICA, MICB, ULBP1-4 and the DNAM-1 ligands CD112 and CD155, were virtually absent from CSC. When immunoselected breast cancer cells were then re-expanded, they mostly lost the observed phenotype and regenerated a tumor cell culture that displayed initial HER2 surface expression and ADCC susceptibility, but was enriched in CD44^{high}CD24^{low} CSC. This translated into increased clonogenicity in vitro and tumorigenicity in vivo. We provide evidence that recruitment of NK-cells and induction of ADCC by trastuzumab may spare the actual tumor-initiating-cells, which could explain clinical relapse. Moreover, our observation that “relapsed” in vitro cultures show identical HER2 surface expression and susceptibility toward ADCC suggests that administration of trastuzumab beyond relapse might be considered, especially when combined with proteasome inhibition which increases the expression of NKG2D ligands.

PO-Onko 01.24

The prognostic impact of SATB1-expression in breast cancer is correlated with estrogen receptor status

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Objective: Several recent reports have linked the expression of SATB1, a genome organizer recruiting chromatin remodeling/modifying enzymes and transcription factors, to the potential for metastasis of breast cancer cells and therefore its negative prognosis on survival. Still uncertain remains the relation of estrogen receptor (ER) status of the cancer cells to the prognostic value of the higher expression of the SATB1 in primary breast cancer cells.

Materials and methods: A database of 3030 Affymetrix microarrays and clinical characteristics from primary breast cancer patients was established. Log-transformed values were median centered over arrays and gene normalization was done separately in each dataset. To allow comparison of SATB1 expression between different datasets we used a quartile split of each dataset. Chi-square test was used to test for associations between SATB1 expression of tumors and categorical parameters. Kaplan–Meier curves were constructed and the log-rank test used to determine the univariate significance of the variables.

Results: Univariate analysis revealed no significant difference of SATB1 expression according to lymph node status, patho–histological grading, PgR-status and erbB2-status. However, a strong correlation was found for patients’ age ($p < 0.006$), tumor size and ($p < 0.02$) and Ki67 expression ($p < 0.0001$) among ER-positive samples. The survival analysis of our cohort revealed that while there was no significant difference among ER-negative cancers there was instead a benefit for high SATB1 expression among ER-positive tumors.

Conclusions: The prognostic impact of SATB1 expression is mainly confined to ER-positive breast cancers, suggesting that SATB1 is an estrogen dependent marker when analyzing gene expression data.

PO-Onko 01.25

Reversion of the malignant phenotype in breast cancer by stromal factors

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Objective: The tumor microenvironment plays a major role in tumor control and progression. Manipulation of the tumormicroenvironment can induce the reversion of the malignant tumor cell phenotype. Thus little is known about the underlying mechanisms. The aim of this study was to elucidate the reversion process and to identify the molecular signature of revertable and non-revertable tumors.

Materials and methods: Primary breast cancer cells (PBC) were isolated from fresh surgical specimen from 13 patients with primary invasive breast cancer and cultured in 3D collagen gels as either mono- or coculture with normal human mammary fibroblasts (HMF). After 10 days of culture collagen gels were fixed and cell growth and morphology was evaluated by immunofluorescence. Gene expression profiles of 5 revertable and 5 non-revertable tumors were analyzed using the Affy-metrix HG-U133 Plus 2.0 GeneChip. qRT-PCR was performed to validate the array results.

Results: In 5 out of 13 cultures PBCs in HMF-cocultures differentiated into polarized acinus like structures, whereas PBCs in 3D monocultures showed unorganized and progressive growth. Reversion was characterized by the expression of golgi apparatus at the apical cell pole or by basally localized β 1- and 4-intergrin, indicating the formation of a basalmembran surrounding the acinus. Gene expression analysis revealed 42 upregulated transcripts in the revertable tumors, mainly related to cell adhesion, signal transduction and transcription. 49 transcripts with known functions in e.g. mRNA splicing and cellular transport were downregulated. qRT-PCR analysis of 7 genes validated the array results.

Conclusions: Our results prove that normal fibroblast can induce reversion of the malignant phenotype of PBCs in co-culture. This significant role of fibroblasts in controlling cancer progression reveals them as a viable target for new breast cancer therapies.

PO-Onko 01.26

Knockdown of icb-1 gene affects both lactoferrin and E-cadherin expression and the differentiating effect of all-trans retinoic acid and vitamin D3 on MCF-7 breast cancer cells

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Icb-1(C1orf38) is a human gene initially described by our group to be upregulated during in vitro differentiation processes of cancer cells. To

further approach the function of *icb-1* in differentiation of breast and endometrial cancer cells, we now examined the effects of an *icb-1* gene knockdown on expression of differentiation markers E-cadherin and lactoferrin and on the differentiating effect of all-trans retinoic acid (ATRA) and vitamin D3. MCF-7 breast cancer and HEC1B endometrial cancer cells were stably transfected with an *icb-1* shRNA plasmid followed by G418 selection. Knockdown of *icb-1* gene was confirmed by real time RT-PCR. Expression of differentiation markers also was analyzed by qPCR. Knockdown of *icb-1* inhibited upregulation of E-cadherin triggered by ATRA treatment both in MCF-7 and in HEC-1B cells. Upregulation of E-cadherin induced by vitamin D3 or insulin/IGF1 was also blocked in MCF-7 (*icb-1* knockdown) cells. Furthermore, knockdown of *icb-1* gene inhibited upregulation of lactoferrin gene in MCF-7 cells treated with ATRA, vitamin D3 or insulin/IGF1. Our data support our hypothesis that *icb-1* is involved in differentiation processes of breast and endometrial cancer cells. *Icb-1* is suggested to be a mediator of differentiation signals to breast cancer cells triggered by ATRA, vitamin D3 and insulin/IGF1.

PO-Onko 01.27

Evaluation of microRNA expression profiles of formalin-fixed paraffin-embedded breast cancer specimens to predict locoregional recurrence after mastectomy

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Objective: To date the risk assessment for locoregional recurrence after mastectomy is still based on conventional measures of tumor size and nodal status. To tailor the indication for Postmastectomy Radiotherapy (PMRT), prognostic markers that correlate with relapse of locoregional breast cancer have to be defined. MicroRNAs (miRNA) are 20-25nt non-coding RNAs that have been extensively implicated in several human cancer, including breast cancer due to modulation of post-transcriptional gene expression.

Materials and methods: MiRNA was extracted (Qiagen) from formalin-fixed and paraffin-embedded archived breast cancer tissue for ten cases with recurrence and ten cases without recurrence (matched pairs regarding age, histology, hormonal receptor status). Global miRNA expression profile was performed on all samples using TaqMan microarrays (Applied Biosystems) containing 752 human miRNAs (representing 85% of human miRNAs in the miRBase 15.0 database).

Results: Unsupervised hierarchical clustering of the two case groups based on miRNA expression profiles detected eight miRNAs that were differentially expressed (p-value < 0,1), including miR-34c (underexpressed) and miR-450b (overexpressed). MiR-34c had previously been shown to be a critical regulator of targets involved in cell cycle control, apoptosis and DNA repair.

Conclusions: Our findings are under way to identify cases with high risk of recurrence to administer individualized therapy. To confirm the pattern of differential expression shown by microarray analysis, quantitative RT-PCR of this eight selected miRNAs has to be performed on further matched pair cases (a total of 68 cases). These results will be presented at the DGGG conference.

PO-Onko 01.28

Mifepristone (RU-486) modulates Wnt-1 signalling in MCF-7 breast cancer cells and induces apoptosis

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Objective: Breast cancer is the most common cancer in women and the Wnt signaling pathway is activated in 50% of the cases. Wnt-1, in particular, is known to regulate the progression of cancer as it promotes cell proliferation and prolongs cell survival. In this study, we investigated the effects of mifepristone (RU-486) on the expression of the proto-oncogene Wnt-1 and its effects on proliferation and apoptosis of breast cancer cells.

Materials and methods: MCF-7 and MDA-MB-231 cells were treated with RU-486 (1 µM) for 72 h. Proliferation was determined using the CellTiter-Blue assay (Promega) and apoptosis using the Cell Death Detection ELISAPLUS (Roche). To inhibit caspase activity, cells were pre-treated for 45 min with a specific inhibitor of caspase 1/3 or caspase 7 (25 µM, Calbiochem). Gene and protein expression of Wnt-1 was assessed by real-time PCR, Western blot analysis, and immunofluorescence.

Results: Analysis of the hormone receptor status showed the presence of estrogen-receptor- α and progesterone-receptor (PR) in MCF-7 cells but not in MDA-MB-231 cells. In line with this observation, RU-486 significantly inhibited Wnt-1 expression only in MCF-7 cells by 98% but not in PR-negative MDA-MB-231 cells. Western Blot analysis and immunofluorescence images confirmed the gene expression data. Treatment of MCF-7 cells with RU-486 diminished cell proliferation by 33% and concomitantly induced apoptosis almost 3-fold. This effect was partially blocked by the pre-treatment with the caspase 1/3 but not with the caspase 7 inhibitor.

Conclusions: RU-486 profoundly inhibits the expression of the proto-oncogene Wnt-1 in MCF-7 cells and induces apoptosis. This effect may at least partially be mediated by caspase 1, as MCF-7 cells lack caspase 3. Thus, our data show that RU-486 exerts apoptosis-inducing effects on PR-positive MCF-7 cells. Further experiments are needed to clarify the anti-tumor effects of RU-486 in breast cancer cells.

PO-Onko 01.29

Distribution of G-protein-coupled estrogen receptor GPR30 in primary breast cancer and its prognostic significance

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Objective: GPR30 is a member of the superfamily of G-protein-coupled receptor and mediates the rapid “non-classic” estrogen action. This study was undertaken to evaluate the expression of GPR30 in breast cancer tissue and to evaluate its correlation with classic prognostic factors and clinical outcome.

Materials and methods: GPR30 protein expression was quantified by immunohistochemical analysis in 321 primary breast cancer patients.

The immunostaining pattern of GPR30 was correlated to various clinicopathological variables and patient outcome including relapse-free survival (RFS) and 5-year overall survival (OS). The association of all tested factors with the risk of recurrence under anti-hormonal therapy was studied by logistic regression analysis, and survival by Cox uni- and multivariate regression method.

Results: GPR30 expression was detected in 56.1% of the breast cancer specimens investigated and positively correlated to overexpression of HER2 ($P = 0.008$) and development of metastasis ($P = 0.047$). In a trend analysis, a correlation of GPR30 expression with shorter RFS was observed (HR = 3.97; 95% CI, 1.319–5.709; $P = 0.011$). Survival analysis also showed that GPR30 was negatively correlated to RFS, but not to OS. In a subset of patients treated with tamoxifen, as opposed to aromatase inhibitors, GPR30 positivity was associated with a significantly decreased RFS (HR = 2.666; 95% CI, 1.335–5.324; $P = 0.005$). Moreover, this association remained significant in multivariate analysis.

Conclusions: This is the first study showing that the expression of the new estrogen receptor GPR30 in breast cancer cells independently predicts a short RFS in patients treated with tamoxifen. GPR30 expression correlates significantly to HER2 overexpression. These data are consistent with our recent results obtained in vitro.

PO-Onko 01.30

Is the expression of Rad51 an independent prognostic marker of recurrence free survival breast cancer patients?

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Objective: High-level expression of Rad51, a key factor in homologous recombination, has been observed in a variety of human malignancies. This study was aimed to evaluate Rad51 expression to serve as prognostic marker for the disease free survival in invasive breast cancer.

Materials and methods: A total of 143 invasive breast cancer tumours which had been diagnosed between 1992 and 1998 were analysed immunohistochemically. The expression of rad 51 and Ki67 was determined, the conventional parameters were re-evaluated. The median age of the patients was 63 years (range 32–91 years). The median follow up was 62 month (range 4–120 month). 41% of the patients suffered a distant metastasis, 28% a local recurrence.

Results: Patients whose tumours displayed high-level Rad51 expression showed a significantly shorter median recurrence free survival ($p = 0.033$, log-rank test) as well as a distant free survival ($p = 0.024$, log-rank test). Similarly Ki-67 appeared as an independent prognostic parameter related to recurrence free survival and overall survival ($p = 0.0001$, log rank test). T status, N status, M status, clinical stage and histological tumour grade were significant prognostic markers in univariate Cox survival analysis as well.

Conclusions: Our results suggest that Rad51 expression provides additional prognostic information for surgically treated breast cancer patients. We hypothesise that the decreased survival of breast cancer patients with high-level expression of Rad51 is related to an enhanced propensity of tumour cells for survival, antiapoptosis and chemo-/radioresistance.

PO-Onko 01.31

Modulation of CXCL9 release by prostaglandin e₂ and cyclooxygenase inhibitors in human breast cancer

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Objective: In murine breast cancer models the IFN- γ inducible chemokine CXCL9 impairs tumor growth and metastasis formation through recruitment of natural killer (NK) cells and activated T-lymphocytes. In human breast cancer we and others have shown that CXCL9 mRNA expression correlates with response to different chemotherapeutic regimens and tumor infiltrating lymphocytes, indicating that enhancing intratumoral CXCL9 could be a feasible therapeutic way to improve tumor suppressive immune infiltration. However, little is known about the regulation of CXCL9 in human breast cancer. Since overexpression of cyclooxygenases (COX) has been shown to correlate with impaired NK cell infiltration, this system is a conceivable candidate for modulating intratumoral CXCL9 concentration.

Materials and methods: CXCL9 was localized in human breast cancer samples by immunohistochemistry. For regulation studies, MCF-7 and MDA-MB 231 breast cancer cells were stimulated with IFN- γ with or without prostaglandin E₂ (PGE₂) or COX inhibitors (indomethacin, aspirin, celecoxib). CXCL9 release was measured by ELISA. Expression of CXCL9 and cyclooxygenases in 60 breast cancer samples was determined by ELISA and western blot, respectively.

Results: Within the tumor microenvironment, the cancer cells are the major source of CXCL9, thus making them the appropriate cell type to study CXCL9 regulation. PGE₂ significantly reduces IFN- γ mediated CXCL9 release from MCF-7 and MDA-MB 231 cells, and inhibition of endogenous cyclooxygenases by indomethacin or aspirin correspondingly augments this secretion. However, the COX-2 specific antagonist celecoxib has PGE₂-agonistic effects and impairs CXCL9 release, probably via COX independent mechanisms.

Conclusions: Suppressing endogenous PGE₂ by cyclooxygenase inhibition increases CXCL9 release from breast cancer cells and is therefore a pharmacologic candidate to enhance intratumoral immune infiltration. However, due to COX independent mechanisms the choice of the appropriate COX inhibitor seems to be crucial. The predictive value of CXCL9 as a novel biomarker and its correlation with COX overexpression in human breast cancer is discussed.

PO-Onko 01.32

Automated breast ultrasound in breast diagnostics: first experience of an unicentral pilot study

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Objective: Ultrasound is a routine tool in breast diagnostics, but is not yet part of screening programmes. An automated breast ultrasound system is a standardized, reproducible and investigator-independent method that could be used for ultrasound screening. The aim of our analysis was to compare clinical findings collected by analysis of an automated breast ultrasound system with findings detected by conventional methods (handheld breast ultrasound and mammography).

Materials and methods: Prospective analysis of an unselected group of patients from 9/2009 to 2/2010 at the University Hospital Homburg/Saar, Department of Gynaecology. All Patients received a conventional breast ultrasound and mammography. Additionally all patients were examined by an automated breast ultrasound system (Somo-Vu). Classification of these findings were made according to BIRADS criteria and afterwards compared to the findings collected by conventional methods (handheld breast ultrasound and mammography).

Results: A total of $n = 110$ patients received an automated ultrasound breast scan plus a handheld breast ultrasound and mammography. Findings (BIRADS I-V) in conventional investigation methods could be reproduced by automated breast scan in 82% of all cases. A discrepancy of BIRADS-classification could be shown in 33% of the investigations. Additional findings could be detected by automated breast scan in 18 patients (16.3%).

Conclusions: Findings of conventional breast ultrasound and mammography can be detected by automated ultrasound breast scan. Automated ultrasound systems can complete but cannot replace conventional methods. Further investigations about value and significance of automated ultrasound breast scans have to follow.

PO-Onko 01.33

Evaluation of two different vacuum-assisted breast biopsy systems: Ethicon Mammotome ST 11G/8G- versus ATEC Suros-system 12G/9G

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Objective: Two stereotactically guided vacuum-assisted breast biopsy systems were compared measuring time-effectiveness and quality of harvested material.

Materials and methods: 146 patients with suspicious microcalcifications on mammography were included in the study. Biopsies were carried out with either the Mammotome[®] Breast Biopsy System from Ethicon Endo-Surgery (11/8G) or the Suros Surgical's ATEC[®] Sapphire-system (12/9G). Lesions with a diameter smaller than 15 mm on mammography were biopsied with 11G ($n = 37$)/12G ($n = 38$) devices whereas lesions larger than 15 mm were targeted with 8G ($n = 34$)/9G ($n = 37$). Time-effectiveness was evaluated. Histological quality was judged by a pathologist in a blinded fashion according to a specimen grading classification.

Results: Median overall-time for the Ethicon-system was 879 s (11G) and 934 s (8G), for the Suros-system 671 s (12G) and 673 s (9G). The Suros-system displays a significantly shorter overall-time for small and large biopsy devices (U -test, $p < 0.001$). Time-savings were 268 s for 12G- and 245 s 9G-Suros-system. Comparing the histologic quality the Ethicon-system shows significantly higher values for the large and the small system (Chi-square test, $p < 0.001$).

Conclusions: Both biopsy systems meet all requirements for daily practice. The Suros-system was significantly faster, the Ethicon system provided a significantly better histological quality.

PO-Onko 01.34

Expression of Mucin-1, Galectin-1 and Galectin-3 in human myometrium, leiomyoma and leiomyosarcoma

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Objective: Leiomyomas of the uterus are the main reason for hysterectomies. The potential mechanism of malignant transformation from leiomyomas to leiomyosarcomas is still debated. The aim of this study was the evaluation of Mucin-1 (VU-4-H5), Galectin-1 and Galectin-3 in human myometrium and leiomyomas and its comparison to leiomyosarcomas in order to elucidate a potential pathway for malignant transformation of leiomyomas.

Materials and methods: Tissues from human myometrium, leiomyomas and leiomyosarcomas were obtained from 160 patients. 44 women received a laparoscopic myomectomy, 35 women received surgical intervention because of leiomyosarcomas. Samples from myomas, myometrium and leiomyosarcoma were analyzed regarding expression of MUC-1, Gal-1 and Gal-3 by immunohistochemical staining of paraffin-embedded material. Analysis was by the Kruskal-Wallis-test and Mann-Whitney test.

Results: We found a significant up-regulated expression of MUC1 (VU4-H5) in leiomyomas ($p = 0.007$) and leiomyosarcomas ($p = 0.039$) as compared to myometrium. In contrast there were no significant differences in expression of Gal-3 in tissues from myometrium, myomas and leiomyosarcomas. Concerning Gal-1 expression, differences were not significant comparing myometrium and leiomyosarcomas ($p = 0.277$). Only myomas had elevated levels of Gal-1 compared to myometrium ($p = 0.007$) and leiomyosarcoma ($p < 0.0001$).

Conclusions: MUC1 and Gal-1 might be useful in the future to evaluate the potential of leiomyomas to transform into leiomyosarcomas and, therefore, help in risk adapted consultation and adjusted treatment. Inhibition of MUC1 and Gal-1 might be an encouraging target in therapeutic developments.

PO-Onko 01.35

Overexpression of HLA-G in tumor-associated macrophages in ovarian cancer: implications for tumor immune escape

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Objective: HLA-G is a non-classical HLA class I molecule, reported in extravillous cytotrophoblasts. HLA-G is also found in tumour

specimens from ovarian cancer or in malignant ascites and is known to inhibit NK cell function. In ovarian cancer, immune tolerance inversely correlates with prognosis. Accordingly, the objective of the current study was to analyze the expression and induction of HLA-G as well as its role in tumour immune escape in ovarian cancer.

Materials and methods: Membranous HLA-G was evaluated by flow cytometry, immunohistochemistry and double immunofluorescent staining. mRNA expression levels of HLA-G were measured by real time PCR. Soluble HLA-G and IL-6 in malignant and benign effusions were determined by ELISA. NK cell function was measured by a luciferase-based cytotoxicity assay. Macrophages used in cytotoxicity assays were stimulated by IL-6 and membranous HLA-G was blocked by specific antibodies.

Results: Flow cytometric analysis of ovarian cancer cells and immunohistochemistry of tumour sections showed only minimal expression of HLA-G in malignant cells. Immunohistochemical and double immunofluorescence staining revealed that HLA-G is mostly expressed in tumour-associated macrophages (TAM, CD68+ cells). Macrophages stimulated with malignant ascites show higher HLA-G mRNA levels. Soluble HLA-G and IL-6 were increased in ascites of ovarian cancer patients compared to benign effusions as demonstrated by ELISA. IL-6 increased membranous HLA-G expression in macrophages. Cytotoxicity studies showed that IL-6 treated macrophages inhibit tumour cell lysis by NK cells, which could be reversed by HLA-G-specific antibodies.

Conclusions: Our observations demonstrate that HLA-G is not a marker of malignant cells but expressed in tumour-associated macrophages. IL-6 may contribute to elevated HLA-G expression in macrophages. Macrophage-bound HLA-G inhibits NK cell function. Thus, expression of HLA-G may be a new immunosuppressive effector mechanism of tumour-associated macrophages.

PO-Onko 01.36

Massive ascites associated with borderline ovarian tumor

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We present the case of a 45-year-old female with a body weight of 210 kg who was referred to our institution because of a suspected ovarian mass, progressive abdominal distension and massive ascites. CA125 was elevated at 967 kU/L. Preoperatively the patient was treated symptomatically with repeated paracentesis over 16 days draining 32 L of serous, exudative fluid with Psammom bodies but no malignant cells. An explorative laparotomy was performed with hysterectomy, bilateral salpingoophorectomy, omentectomy, appendectomy and peritoneal biopsies. Intraoperatively additional 24 L of ascites were drained. Histology revealed adenofibroma of both ovaries with transition to borderline ovarian tumors (BOT). Implants of the omentum were confirmed to be non-invasive by reference pathology. Postoperatively the clinical course was unremarkable with a significant CA125 decrease, no more relevant ascites and a post-operative body weight of 146 kg. Based on the clinical and pathological findings this patient suffered from a Pseudo-Meigs' syndrome presenting with a FIGO stage IIIb BOT and non-invasive implants associated with the largest amount of ascites ever reported for BOT.

PO-Onko 01.37

Schloffer tumor of the abdominal wall in a patient with carcinoma of the uterus

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Objective: The so-called Schloffer tumor is a very rare inflammatory pseudotumor of the abdominal wall, which normally occurs many years after abdominal surgery or trauma.

Materials and methods: We report the case of a 70-year-old woman, who was referred to our hospital with histologically proven endometrial cancer. Almost 30 years ago the patient has had a unilateral oophorectomy by laparotomy. On CT-scan a bone-like structure was described as an additional finding. During abdominal hysterectomy a rigidification of the abdominal wall was found and a bone-like tumor removed from the abdominal wall. In the following x-ray of the tumor, typical trabecular structures of bone were described. Also histological preparation revealed a bone-like tissue and was described as a Schloffer tumor. TNM-staging of the adenocarcinoma of the uterus was pT4 Nx Mx pR0. An interdisciplinary expert panel recommended percutaneous irradiation with single-time after loading and no systemic therapy. On follow-up visits no recurrence of the carcinoma or the Schloffer tumor were found so far.

Conclusions: The findings indicate that in rare cases of previously performed abdominal surgery formation of bone-like tissue, the so-called Schloffer tumor, can be found. Thus surgeons should be aware of this rare tissue formation within the abdominal wall.

PO-Onko 01.38

Frequency of elderly patients among women with acute gynecological complaints

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Objective: To investigate the frequency of elderly patients (>65 years) among women with acute gynecological complaints and to identify leading symptoms and diagnoses.

Materials and methods: Retrospective analysis of all women with acute gynecological complaints that required medical diagnosis and treatment by a gynecologist at the emergency room of a university hospital during a one-year-period. Known outpatients or former in-patients with medical problems during chemotherapy or after operative therapy were excluded in order to select patients with spontaneous and not therapy-induced symptoms. Frequency of patients above 65 years of age was calculated. Symptoms were documented following patients' history. Diagnoses were attributed to each patient after all diagnostic procedures and after the discretion of the attending gynecologist.

Results: Altogether 3134 women sought for help because of acute gynecological complaints. In 66 cases patients were older than 65 years resulting in a frequency of 2.1%. Leading symptoms were lower abdominal pain (30%), and vulvar or vaginal lesions (25%), and vaginal bleeding (20%). Leading diagnoses were genital prolapse, urinary tract infections, vulvar or vaginal lesions, non-gynecological diagnoses, and uterine bleeding with about 10%, respectively.

Conclusions: In women seeking for medical help at the emergency room of a university hospital, the frequency of patients above

65 years is only about 2%. This is much lower than the frequency of elderly patients at the department of surgery or general medicine. The underlying causes differ from those in younger women.

PO-Onko 01.39

Long term survival in a young patient with metastatic adenocarcinoma of the cervix and successful pregnancy after oncologic therapy: a case report and eight year follow up

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Objective: We report about the long term survival of a 37 year old patient with metastatic cervical cancer firstly diagnosed in 2002 and her clinical outcome until now.

Materials and methods: Her medical history reports a conisation of the cervix in 1998 with diagnosis of adenocarcinoma in situ and questionable microinvasion. No further therapy was performed because of the patient age. After multiple thrombotic events (both lungs, vena poplitea on the right side, both venae subclaviae) at the beginning of 2002 a paraneoplastic cause was presumed and further investigations with PET-CT and laparoscopy revealed lymph node metastasis of an adenocarcinoma. Laparotomy with complete pelvic lymphadenectomy on the right side, paraaortic lymph node dissection until the left kidney vein was performed with diagnosis of lymph node metastasis of an adenocarcinoma of the cervix, G2-G3. Consecutive combined radio-chemotherapy with 5 cycles Cisplatin 40 mg/m² BSA and daily radiation (1.5 Gy in five fractions per week) was performed. First successful pregnancy after the beginning of the down regulation with GnRh- analog (Nafarelin) in course of the ICSI protocol occurred in 6/2009. Prior performed PET-CT revealed no metastasis. The healthy child was delivered via c-section without difficulty in 2/2010.

Conclusions: In 1998 the patient was probably under treated with the conisation alone considering the diagnosis of an adenocarcinoma in situ with questionable microinvasion. With this histology we have to consider a progression rate of up to 70%. The relative 5 year, respectively 10 year survival rates for all stages are 64.5% versus 59.0%. Considering a relative 5 year survival rate of 12–35% in patients with metastatic cervical cancer our patient has a long term survival.

PO-Onko 01.40

Pleomorphic adenoma of the breast initially misdiagnosed as metaplastic carcinoma in preoperative stereotactic biopsy: a case report and review of the literature

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Objective: Pleomorphic adenoma (PA) is a benign mixed tumor found commonly in the salivary glands but rarely in the breast. Histopathology is characterized by a mixture of epithelial and myoepithelial cells and can display areas of chondroid or myxoid differentiation. The differential diagnoses include fibroadenoma, phyllodes tumor and metaplastic carcinoma. Metaplastic carcinoma is the most important

differential diagnoses, as surgical overtreatment, i.e. mastectomy may be the result. We describe one of the first cases of PA initially misdiagnosed as metaplastic carcinoma in a preoperative stereotactic biopsy.

Materials and methods: A 58-year-old Caucasian woman was referred to us with external performed stereotactic biopsy and the diagnosis of a metaplastic carcinoma (osteoid-chondroid type). Mammographic features showed a well-circumscribed lobulated tumor with pleomorphic microcalcifications. The patient underwent a wide excision and sentinel lymph node biopsy. The excision was complete. Further treatment was not recommended. A 1 year follow-up period was uneventful.

Results: The wide excision contained a 1.3 cm well-circumscribed bright mass with a fibrous pseudo-capsule. The neoplasm had a biphasic morphology consisting of trabecular and glandular structures with epithelial cells surrounded by myoepithelial cells. The mesenchymal differentiated areas showed chondroid and small areas of osseous metaplasia. Myoepithelial cells showed reactivity for CK5/6, 34BE12, S100, GFAP, actin and CD10. CK7 stained strongly positive in the luminal epithelial cell layers.

Conclusions: Because of the extreme rarity and confusing imaging findings suggestive of carcinoma a correct preoperative diagnosis might be difficult. 30–50% of cases reported were initially misdiagnosed as carcinoma. Pathologists and clinicians should be aware of this extremely rare tumor to avoid unnecessary aggressive surgical treatment. The complete excision is the therapeutic treatment of choice. A follow-up period of 5 years with yearly examinations should be recommended.

PO-Onko 01.41

Case report: endometriosis in a 79-year-old woman

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Objective: We present the case of a 79-year-old woman who had surgery at our institution for a 9.3 × 7 cm cystic mass behind the rectum.

Materials and methods: Case report.

Results: The patient had a laparotomy with hysterectomy and adnectomy as well as the excision of the large mass behind the rectum. The surgery was conducted without complications. Histologically, the cystic mass revealed an endometriosis cyst.

Conclusions: Retro-rectal tumors may be of diverse origin. Endometriosis is an unusual diagnosis in postmenopausal patients, however, the differential diagnosis should be remembered on unexplained tumors.

PO-Onko 01.42

The use of emergency contraception in Thrace in teenagers

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Objective: The aim of the present study is to explore postcoital contraceptive behavior of women belonging to two different religious

populations in Thrace in order to determine the effectiveness of the method.

Materials and methods: A retrospective study involving 65 teenagers, was conducted between January 2006 and December 2009 in our family planning centre. The age of the patients ranged between 13 and 18 years. The study included representatives from two female subgroups: 45 Christian Orthodox (group A), 20 Muslims living in Thrace (group B). Participants from each group were asked to answer a detailed questionnaire extensively, concerning sexual activity and contraceptive practices. The hormonal emergency contraception treatment initiated within 72 h with a progestin-only pill (levonorgestrel 1.5 mg) one pill.

Results: Information regarding the outcome of emergency contraception treatment was available in 97% of the cases in Group A, and in 86% of the cases in Group B. About 44.8% of cases came to our centre within the first 8 h after unprotected intercourse. Only 30% in group A and 9% in Group B have previously asked for postcoital contraception. Approximately 72% of the women reported unprotected intercourse during that time because they had problems with condom use. Breakage of condom was the most common reason for requesting (95%) a doctor's advice. There were no serious side effects. Nausea and vomiting (11.66%) were the most prevalent ones and 79% of the users menstruated at the expected time, whilst menses were delayed in 8.5% of the cases. Only one pregnancy occurred with perfect use in 1 women.

Conclusions: Teenagers, who have experienced failure of their contraceptive method or used no contraceptive at all, must be use correctly the postcoital contraception.

PO-Onko 01.43

Case report: treatment of recurrent squamous cell carcinoma of the vulva with angiosarcomatoid components with Caelyx and Bevacizumab

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Objective: Squamous cell carcinoma of the vulva with angiosarcomatoid components are rare malignant tumors of the female genital tract.

Materials and methods: A 64-years-old woman who initially presented a squamous cell carcinoma of the vulva (FIGO II, pT2, pN2, G2, R0) underwent a radical vulvectomy with bilateral inguinal-femoral lymphadenectomy followed by adjuvant chemo-radiation in December 2007. Nine months later she presented a lesion in the left inguinal region. Histopathology showed a recurrence of vulvar cancer. We did a radical excision of the lesion and reconstruction with a myocutaneous flap. Five weeks later two small tumours appeared in the scar of myocutaneous flap. The histopathology showed a squamous cell carcinoma with angiosarcomatoid components, a review of the primary tumour-tissue also presented angiosarcomatoid aspects. Because of sudden recurrence of a now high malignant (G3-4) tumour entity we decided a systemic therapy with Caelyx (pegylated liposomal Doxorubicin, 20 mg/m²) and Bevacizumab (10 mg/m²) repeated every 2 weeks.

Results: After 10 cycles of systemic chemo- and antibody therapy clinical examination showed a partial of one and a complete response of the other lesion in the left inguinal region. Residua were local excised and the histological examination underlined the CR/PR. After systemic treatment and final operation we can report an 11-months recurrence-free follow up.

Conclusions: This case shows the successful treatment of recurrence of high-malignant vulvar cancer with angiosarcomatoid components with Caelyx and Bevacizumab.

PO-Onko 01.44

Iatrogenic breast carcinoma after 20 years from radiotherapy for Hodgkin lymphoma

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Objective: Iatrogenic second neoplasms are a common late complication of radiotherapy, and breast cancer is a typical long-term sequela after mantle radiation for Hodgkin's lymphoma.

Materials and methods: A 50-years-old woman applied our Senology Outpatients Facility after radiological detection of a 2 cm-wide mass with suspicious calcifications in the upper outer quadrant of her left breast. The breast histological examination after mastectomy revealed an indifferntiated breast carcinoma with areas of condrosarcomatous differentiation, probably due to breast irradiation for Hodgkin lymphoma at the age of 30.

Conclusions: The relative risk to develop breast cancer after irradiation for Hodgkin lymphoma inversely correlates with the age at diagnosis and results to have a pick of incidence at 15–30 years after last irradiation. Therefore, we suggest the importance of a long-term surveillance in order to early detect breast neoplasms secondary to previous breast irradiation.

PO-Onko 01.45

Transvaginal sonographic prognostic value to detect endometrial pathology in postmenopausal asymptomatic women without hormone replacement therapy

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Objective: Endometrial cancer is the fourth most frequent malignancy in most of the developed countries. The aim of this study was to evaluate retrospectively the usefulness of transvaginal sonography for the detection of endometrial disease in postmenopausal women without symptoms.

Materials and methods: This study involved 850 postmenopausal women aged 51–64 (mean 57.5) who were examined at the Department of Obstetric-Gynecology of Democritus University. None of them were on hormone replacement therapy and all had amenorrhea of more than 2 years. The ultrasound evaluation of the uterus was both in the transverse and longitudinal axis. If there was fluid in the endometrial cavity the thickness was calculated by adding the two layers. Endometrial thickness was considered to be normal if it was less than 5 mm. When the endometrial thickness was more than 5 mm, we performed a diagnostic curettage in combination with hysteroscopy.

Results: Transvaginal sonography was performed in 850 women and well tolerated of all women. An endometrium of <5 mm and non-measurable (701 women) was not investigated further. The 701 cases

of this group were re-assessed 1 year later. In the rest of 149 postmenopausal women with suspicious endometrium, 115 cases had an endometrium 5–7 mm and 34 cases >7 mm. Every woman underwent diagnostic curettage under hysteroscopic control. The histological results were as follows: 21 endometrial polyps, 3 cervical polyp with extension in the cavity, 110 endometrial atrophys, 13 atrophic endometritis, 1 simple hyperplasia, 1 hyperplasia with atypia (0.8%). **Conclusions:** The transvaginal sonography is an efficient and acceptable, noninvasive method for early detection of endometrial pathology in uterine cavity in postmenopausal asymptomatic women.

PO-Onko 01.46

Cutaneous postradiation angiosarcoma of the breast after breast conserving treatment for breast cancer: a clinicopathologic case report

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Objective: Breast angiosarcoma may occur de novo, or as a complication of radiation therapy for mammary carcinoma. Radiation-induced angiosarcoma of the breast is being reported with increasing frequency as a result of the increased use of radiation therapy in conjunction with breast conservation surgery

Materials and methods: A case of coetaneous angiosarcoma of the breast that arose in irradiated skin tissue in a 71 year-old woman who had previously undergone treatment for breast carcinoma is reported. Initial diagnosis was reported as bilateral breast cancer (9 year ago) and the patient underwent breast conserving operation (BCO) and radiation of the breasts. Clinical examination shows multifocal blue areas (2–3 cm) in left breast. The diagnosis of angiosarcoma was made by skin biopsy performed by the patient's gynaecologist on routine follow-up examination. Ultrasound- and mammography examination shows regularly breast parenchyma. The patient was treated with mastectomy. **Conclusions:** With the increasing use of breast conservation therapy for breast cancer, reports of postradiation angiosarcoma have increased. Angiosarcomas may present with bruise-like skin discoloration, which may delay the diagnosis. Multifocal blue areas may be suspect for angiosarcoma. Imaging findings are nonspecific. For the histological diagnosis of angiosarcoma a skin biopsy should be performed. Surgical resection with mastectomy is the usual treatment for postradiation angiosarcoma.

PO-Onko 01.47

The decision to perform a sentinel lymph node biopsy is a prognostic factor

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Objective: The sentinel lymph node biopsy (SNB) is an established procedure in breast cancer to evaluate the nodal status. In the follow up of patients who underwent an SNB, in a retrospective study, the low rate of recrudescence attract attention. The aim of this research was to check whether this is accompanied with a feasible biology of the breast cancer.

Materials and methods: To check the result of the SNB at the University of Heidelberg of the Department of Gynecology and Obstetrics the procedures from the years 2003 to 2006 were retrospectively analyzed. 485 patients have been analyzed to correlate the technique, the staging, the biology and the progress of the cancer.

Results: In a follow up time of 14 to 65 months and a median of 34.6 months a very low rate of relapse was found. Besides 4 events of intra mammary recrudescence, 5 peripheral metastases (1%) were documented. Analysing the biology of the tumors, there was a significant higher rate of estrogen- and progesterone positive cancers than in the normal distribution. In contrast, there was a significant rare frequency of positive HER2neu oncogene amplification found. Only a few cancers with a high proliferation index were documented as well. **Conclusions:** By deciding to perform an SNB, a selection is made which is apparently associated with a high chance of histological free sentinel lymph nodes and as we can show here also an advantageous biology of the cancer and therefore a more favorable prognosis. This explains the low rate of metastases in our patient population.

PO-Onko 01.48

Concept of study: vinorelbine and tyverb in advanced 1–2 L ErbB2+ metastatic breast cancer

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Objective: Primary endpoint: Assessment of progression-free survival (PFS) in women with ErbB2-overexpressing metastatic breast cancer, treated with either a combination of lapatinib and vinorelbine or lapatinib and capecitabine. Secondary endpoints: Overall response rate, complete and partial response, overall survival, duration and time of response, clinical benefit rate, quantitative and qualitative toxicities and description of the pharmacokinetic of vinorelbine alone or in combination with lapatinib.

Materials and methods: VITAL is a randomized, parallel-arm, open-label, multi-centre, phase II study and evaluates the efficacy and safety of lapatinib combined with vinorelbine or capecitabine in women with ErbB2-overexpressive metastatic breast cancer, who received previously only one chemotherapeutic regime. About 105 patients will be included and randomized 2:1:

- Arm A: Lapatinib orally + vinorelbine intravenously
- Arm B: Lapatinib orally + capecitabine orally

In cases of disease progression there is the possibility to cross-over the treatment schedule.

Main inclusion-criteria:

- histologically-confirmed invasive breast cancer (WHO IV)
- metastases located visceral, in soft tissue or bone-only
- documented overexpression on ErbB2 (immunohistochemistry, FISH, CISH)
- progressive disease or relapse following prior anticancer therapy (anthracyclines, taxane), patients who have not received prior treatment for metastatic breast cancer should have either relapsed following trastuzumab in the adjuvant setting or have either a

contraindication to receive trastuzumab or unsuitability of taxane-based chemotherapy

- no prior therapy with lapatinib, vinorelbine or capecitabine
- Women ≥ 18 years, any menopausal status, ECOG 0 to 1, adequate organ and marrow function

Results: Until April 2010, 11 patients were randomized, 14 patients screened, there was 1 screening failure and 4 patients in pre-screening. 29 out of 45 centres are open/active and ready to recruit patients.

Conclusions: To administer a combined therapy with vinorelbine and lapatinib offers the possibility of further treatment options for ErbB2 + metastatic breast cancer. Two potent agents with non-overlapping signature toxicities are combined and pharmacokinetic interactions can be evaluated. Research Funding Source: Pharmaceutical/Biotech Company, GlaxoSmithKline.

PO-Onko 01.49

Additive effects of a GPR30 agonist and trastuzumab on proliferation of breast cancer cells *in vitro*

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G-protein coupled receptor GPR30 is proposed to act as a membrane-bound estrogen receptor. In contrast to ER α , activation of GPR30 is able to exert growth-inhibitory effects on tumor cells under certain conditions. In this study we examined, to what extent GPR30 activation would be able to modulate the antitumoral effect of HER2-targeting antibody trastuzumab. For this purpose, we studied the effect of GPR30 agonist G1 alone and in combination with trastuzumab on proliferation and gene expression of breast cancer cell lines SKBR-3, BT-474 (both HER2-overexpressors) and MDA-MB-231 cells as negative control. All cell lines employed were GPR30-positive. Proliferation was examined by means of the resazurin-based Cell Titer Blue assay, gene expression was analyzed by means of real time RT-PCR. Treatment with G1 alone inhibited cell growth of all cell lines tested in a dose-dependent manner, and growth inhibition positively correlated with GPR30 expression level. Addition of G1 significantly increased the antiproliferative effect of trastuzumab on BT-474 and SKBR3 cells. On the molecular level, this additive effect of G1 and trastuzumab was accompanied by downregulation of c-fos and cyclin A2 expression. In conclusion, we demonstrated that GPR30 agonist G1 is able to increase the antiproliferative effect of trastuzumab *in vitro*. The relevance of these data in the clinical setting has to be examined in further studies.

PO-Onko 01.50

Patient-perceived aesthetic and functional outcomes after breast conserving surgery as correlates of quality of life: validation of the German version of the Breast Cancer Treatment Outcome Scale (BCTOS)

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Objective: The Breast Cancer Treatment Outcome Scale (BCTOS) is a questionnaire designed to assess aesthetic and functional outcome

after breast conserving therapy. The purpose of this prospective cohort study was to validate the German version of the BCTOS and to examine its relations with quality of life (QoL).

Materials and methods: The study included 189 patients with one-sided, primary breast cancer, treated conservatively. All patients completed a newly developed German version of the BCTOS. QoL was measured by the EORTC Quality of Life Questionnaire C30 BR23 (EORTC). In order to define different relevant scales of the German BCTOS, a factor analysis on all constituting items was performed. Subsequently, the relations between outcomes of these BCTOS scales and specific EORTC scales were evaluated by performing a correlation and a multiple regression analysis. In addition, we assessed the impact of patient-, tumor- and therapy-related covariates on the outcome of the BCTOS scales.

Results: The factor structure indicated three internally consistent scales of the German BCTOS: Aesthetic Status, Functional Status and Breast Sensitivity Status. All BCTOS scales were correlated with scales of the EORTC. Correlation magnitudes ranged from 0.24 to 0.67 ($p < 0.001$). The multiple regression analyses confirmed these results. The analysis of relevant covariates demonstrated that younger patients revealed poorer status on all BCTOS scales than older patients.

Conclusions: Aesthetic and functional outcome seems to be closely related to quality of life. The German BCTOS demonstrated to be a useful instrument to measure aesthetic and functional outcome after breast conserving surgery.

PO-Onko 01.51

Low back pain (LBP) in the late pregnancy: a case report of lumbar bone metastases from a breast carcinoma

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Objective: LBP or discomfort is common during pregnancy. Because the pain should be expected to some degree by most women, especially in the late period of pregnancy, referral to a health care specialist is often delayed. We report of a young woman who developed LBP during her third pregnancy. Unfortunately, final diagnosis of lumbar metastases of a breast cancer (BC) was delayed. Algorithm of diagnosis and oncological management of the problem are presented in this report.

Materials and methods: Patient (25y, P3, G4, 33 + 1 week of gestation) with a family history of BC suffered from LBP, which was associated with third trimester pregnancy and lead to partial immobilization and hospitalization. Moderate LBP as well as lumb in the breast were existing since breast feeding period of her last pregnancy as reported by the patient.

Results: Pregnancy was without complication but right breast showed a lumb, that was self-detected by the patient. An inflammatory, multicentric carcinoma of the right upper quadrant and biopsy specimen was found (TNM: T4b, cN1, cM1, G2, Rx, Her2/neu 2+, genetic testing was denied by the patient). Irritation of S1 and neurological deficiency was seen. Pregnancy was ended in 36th week and diagnostic steps were completed (CT, MRI, serum markers). Metastases in spine, lung, liver were found. Patient received radiation of breast and spine lesions and chemotherapy was administered (Taxol/Avastin/Bisphosphonates). Follow up of palliative situation lasted 24 months.

Conclusions: LBP or discomfort is common during pregnancy and mostly interpreted as pregnancy associated symptoms. We present a

severe case of systemic metastases of a newly diagnosed inflammatory breast cancer in a very young pregnant patient. The presented case should teach to be aware of these exceptional findings and differential diagnosis, especially in case of a family history for breast cancer and breast lumb.

PO-Onko 01.52

Lobaplatin as single agent and in combination with TRAIL inhibits the growth of triple negative p53 negative breast cancers also by induction of necroptosis

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Objective: We investigated anti-tumor activity of 3rd generation compound Lobaplatin (Aeterna/Zentaris GmbH, Frankfurt/Main) as single agent, in combination with TRAIL and mechanisms of induction of programmed cell death (PCD) in in vitro models of triple negative breast cancers (TNBC).

Materials and methods: TNBC cell lines HCC1937 and HCC1806 were evaluated for p53 status by a luciferase-assay and treated with Lobaplatin alone and in combination with TRAIL. Cytotoxic effects were evaluated by crystal-violet assay. Induction of apoptosis was tested by cleavage of PARP and Caspase3. Subsequently cells were cocubated with Lobaplatin and multi-caspase-inhibitor ZVAD-fmk and inhibitor of necroptosis necrostatin, in order to check if cell death induced by Lobaplatin can be abrogated by inhibition of classical apoptosis or necroptosis, a recently discovered alternative way of PCD. To investigate in which phase of the cell cycle cytotoxicity is most pronounced, cell cycle FACS analysis was performed.

Results: In HCC1937 and HCC 1806 cells luciferase activity was decreased as compared to positive controls indicative of mutated p53. Lobaplatin demonstrated cytotoxic effects comparable to Cisplatin in HCC 1806 and HCC 1937 cells. Adding TRAIL to lobaplatin induced an increase of cytotoxicity by 30–50%. Western blot analysis revealed cleavage of PARP and caspase 3 after treatment. Cotreatment with ZVAD-fmk or necrostatin could weaken, but not abolish the cytotoxic effect of lobaplatin and cisplatin, indicative of apoptosis and necroptosis. FACS analyses are suggestive for induction of PCD at the G1/S as well as G2/M checkpoint.

Conclusions: Platinum derivative lobaplatin has good anti-tumor activity in models of TNBC. Co-treatment with TRAIL increases the cytotoxic effect of lobaplatin, suggesting a rationale for clinical studies. Additionally, we could show for the first time that platinum derivative cisplatin and lobaplatin induce necroptosis, which explains that PCD could only be partly inhibited by caspase inhibition.

PO-Onko 01.53

The development and determinants of Internet use for health information among breast cancer patients

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Objective: The number of people with access to the Internet and who actually use it to obtain health information is continuously on the rise. Gynecologists must, therefore, adapt their practice to these changing

circumstances. In Germany, however, there is still virtually no data available on patient Internet use. This study aims to determine the percentage of breast cancer patients using the Internet for health information. The study also seeks to ascertain whether this use is dependent on age and social status.

Materials and methods: The study population consisted of female patients with primary breast cancer who had undergone surgery in one of the breast centers in the German state of North Rhine-Westphalia between February and July of the years 2007 to 2009. Patients were surveyed postoperatively by mail using the Cologne Patient Questionnaire for Breast Cancer (KPF-BK). Of the patients who consented to participating in the survey (consent rate: 90%), an average of 88% responded to the questionnaire. The total sample size for the study in 2007 to 2009 was $N = 11.197$. Frequency and logistic regression analyses were used for statistical analysis.

Results: Over the 3 years of the study, there was an increase in the percentage of breast cancer patients using the Internet to obtain information on their condition (2007: 30.9%; 2008: 32.7%; 2009: 34.3%). Significant differences were found in the correlations between the different age and social status groups and Internet use. Older patients, patients with lower levels of formal education and patients without private medical insurance are significantly less likely to search for health information online.

Conclusions: One-third of breast cancer patients in the breast centers of North-Rhine Westphalia use the Internet to obtain information on their condition, and this number is rising. Determinants of patient Internet use are social status and age.

PO-Onko 01.54

Benign breast disease: diagnostic and therapeutic management in women younger than 40

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Objective: Considering the high prevalence of benign breast disease (BBD) in the fertile age, our study aims to analyse the accuracy of different diagnostic methods for BBD in women younger than 40.

Materials and methods: We collected data about all women younger than 40 with a diagnose of BBD who applied the Senology Outpatients during 2008, focusing on the diagnostic approach and the eventual surgical intervention. Data was analysed by R(version 2.8.0), considering significant $p < 0.05$. Also multivariate analysis was performed.

Results: Among 342 women with BBD, 92 were younger than 40. Definitive diagnose was 45.65% histological, 8.7% cytological, 20.65% clinical, 25% imaging. Ultrasonography and mammography prevalence is, respectively, 77.17 and 22.83%, this last directly correlated with age ($p < 0.05$). Magnetic resonance execution was very rare. Considering as pathology any objectivable breast lesion, objective examination, ultrasonography and mammography result to have a sensibility of respectively 85, 91 and 95%, and a specificity of 75, 71 and 100%. Surgery was performed in 39.13% of cases, directly correlating with age >35 years and lesion size greater than 30 mm ($p < 0.05$).

Conclusions: Despite the good accuracy of ultrasonography in evaluating young breasts, mammography remains the more sensible and specific diagnostic method for breast masses, and clinic examination should not be underestimated as a good alternative by the follow-up.

PO-Onko 01.55**Aesthetics before and after breast conserving therapy: can an objective evaluation predict patients' perspectives?**

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Objective: The leading question of this prospective, exploratory cohort study is to evaluate if the BCCT.core (breast cancer conservative treatment.cosmetic results) software, a semi-automated objective symmetry evaluation tool, is able to predict patient's perspective on aesthetics before and after breast conserving therapy. As the BCCT.core software is only semi-automated, it is moreover necessary to assess the inter-rater reliability.

Materials and methods: 128 patients with one sided, primary breast cancer, treated conservatively were included. To evaluate the relationship between objective and subjective measurements of breast aesthetics we compared the BCCT.core software results with the scores of the Aesthetic Status of the BCTOS (Breast Cancer Treatment Outcome Scale) preoperatively, shortly and 1 year after surgery. The inter-rater reliability for the BCCT.core software was assessed by calculating agreement rates and multiple kappa (mk) coefficients for four different raters; the agreement between the BCCT.core software and the BCTOS by analysing agreement rates and weighted kappa (wk) coefficients.

Results: The inter-rater reliability for the semi-automated BCCT.core software was very good indicated by agreement rates up to 84% (mk = 0.80). The agreement rates of the BCCT.core software and the BCTOS Aesthetic Status ranged between 35% and 60% according to the different times of assessment (wk = 0.37 at best). The patients seem to judge their aesthetic outcome more positively than the BCCT.core software.

Conclusions: The inter-rater reliability of the BCCT.core software is very good, but it shows only fair agreement with patient's perspective on aesthetic outcome measured by the Aesthetic Status of the BCTOS. A prediction of patient's perspective by the software is hence not possible.

PO-Onko 01.57**Results of a three months strength training of breast cancer patients during chemo therapy on the symptom of fatigue**

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Objective: Fatigue describes a sensation of physical and mental exhaustion which is associated with tumor diseases. 96% of breast cancer patients declare to suffer of symptoms of fatigue during chemotherapy. These exhaustion symptoms are not correlated with physical activity and don't improve through physical rest. Previous attempts to therapy fatigue in clinical trials demonstrated positive effects of strength training on the symptoms of fatigue. Therefore the

influence of strength training on fatigue symptoms for breast cancer patients was evaluated.

Materials and methods: Prospective trial of 21 breast cancer patients participating in a 12 weeks strength training parallel to neoadjuvant or adjuvant chemotherapy. 18 patients (85.7%) trained continuously twice a week for 60 min, 7 exercises at different sport equipment, 8–12 follow ups, intensity of 75%. 3 patients (14.3%) quitted the training due to stronger side effects of medical therapy. Before and after exercises, muscle power was measured using ISOMED 2000. Before and after the intervention and 6 weeks after starting the training program, fatigue symptoms were evaluated with the MFI (Multidimensional Fatigue Inventory).

Results: The mean age of study participants was 52.6 ± 9.4 years. Strength training resulted in a significant reduction of fatigue symptoms during training: less general fatigue ($p = 0.042$), less reduced activity ($p = 0.015$) and less physical fatigue ($p = 0.022$). Also an increase of muscle power in the arm on the side next to the operation field was seen under current chemotherapy ($p = 0.001$).

Conclusions: This ongoing clinical study shows that strength training reduces fatigue symptoms and raises quality of life of tumor patients. Based on these positive results of strength training in breast cancer patients under chemotherapy, strength training can be integrated in a program of rehabilitation for breast cancer patients.

PO-Onko 01.58**Heterotopic pregnancy and voluntary interruption with mifepristone**

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Objective: Heterotopic pregnancy is a multiple pregnancy with one normal implantation in the uterus and one ectopic pregnancy. It has a prevalence of 0.08–1.9% and an incidence from 1:2,600 to 1:30,000 in normal conception. Sonographic identification is very specific, but has low sensitivity. Signs of normal pregnancy associated with abdominal pain and an adnexal mass are the most significant symptoms, final diagnosis has to be verified by laparoscopy.

Materials and methods: A 30 year-old GIV/PII attended the emergency department with acute abdominal pain and vaginal bleeding 2 weeks after voluntary interruption of a sonographically documented, intrauterine pregnancy in the 5th week of gestation elsewhere. It was a spontaneous conception. She underwent laparoscopic appendectomy two months ago, where also an infection with *Chlamydia trachomatis* was found, which has not been treated. Hb 12.9 g/dl, Beta-HCG 2152mIU/ml. Transvaginal sonography revealed an empty uterus and a regular right ovary. The 17 × 11 × 12 mm mass on the left ovary was suspected to be a corpus luteum cyst. IV Antibiotic treatment was started for the Chlamydia infection and the patient was hospitalised for surveillance. On the 3rd day the patient developed acute abdominal syndrome and instability of circulation. Emergency laparoscopy was carried out and a left ruptured tubal ectopic pregnancy and hemoperitoneum (2000 ml) were found. Histological examination verified the tubal pregnancy. The lady recovered well and was discharged on the 4th postoperative day after ferinject infusion.

Conclusions: Only very few heterotopic pregnancy cases have been reported in natural cycles like our patient had. Salpingitis primarily because of Chlamydia is the main cause of tubal pregnancy and seems to play a crucial role also in this case. After diagnosis of intrauterine pregnancy, adnexal sites should always be assessed carefully for heterotopic pregnancy in order to prevent secondary rupture and excessive intra abdominal bleeding.

PO-Onko 01.59**Extending platinum-free interval (PFI) in partially platinum-sensitive (PPS) patients (pts) with recurrent ovarian cancer (ROC) treated with trabectedin (Tr) plus pegylated liposomal doxorubicin (Tr + PLD) versus PLD alone: Results from a PPS cohort of a phase III study**

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Objective: OVA-301, a phase III study comparing Tr + PLD vs. PLD alone in 672 ROC pts progressing after (Monk, Ann Oncol 2008).

Materials and methods: PFI >6 month was found in 430 (64%) of 672 randomized pts, including 214 (32%) pts with PPS disease (PFI 6–12 month). Outcomes of this non-platinum combination on PFS, RR and OS (protocol-specified interim analysis, cutoff May 08) are shown for the PPS population. We evaluated time from randomization to subsequent platinum (SP) and survival time from SP.

Results: Baseline characteristics of pts with PPS were balanced and consistent with those of the overall study population. Median (med) no. cycles, 6 (Tr + PLD) vs. 5 (PLD); 40% vs. 24% pts received ≥ 7 cycles. RR and PFS by IR significantly favored Tr + PLD: 33% vs. 15% ($p = 0.0041$); med PFS 7.4 vs. 5.5 mo (HR 0.65; $p = 0.0152$), with consistently superior outcomes by both IO and IA. Med OS from randomization was in favor of Tr + PLD: 20.7 vs. 17.2 month (HR: 0.59; $p = 0.0090$). The proportion of pts receiving SP was comparable in both arms. A significant delay in the administration of SP with the combination (med 15.3 vs. 11.6 month; HR 0.60, $p = 0.0093$) was observed. Med survival time from start of SP until death or last contact was 11.0 vs. 9.2 month (HR 0.72, $p = 0.2480$). The Tr + PLD safety profile of PPS cohort agreed with that of the overall study population and was consistent with known toxicities of each agent. No new or unexpected toxicities were seen.

Conclusions: In the PPS cohort of OVA-301, Tr + PLD induced significantly superior RR, PFS and OS (3.5 month prolongation in med OS). Significant delay in time to SP and longer survival after SP therapy was seen after this non-platinum regimen. Safety was manageable rendering a highly favorable benefit/risk ratio in this population with high unmet need for new therapeutic options.

PO-Onko 01.60**Heterogeneous expression of serine protease inhibitor maspin in ovarian cancer**

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Objective: Despite improvements in treatment, ovarian cancer (OC) is still perceived as a disease of unfavorable prognosis. Established clinical prognostic markers are highly dependent on the variation of the biological behaviour of OC. There is still need for molecular markers who will be able to predict the course of the disease in

respect to optimize treatment individually. Maspin is a serine protease inhibitor and is heterogeneously expressed among different types of cancer. Only limited data concerning the expression of maspin in ovarian cancer are available. This study investigates the possible prognostic value of maspin expression in various ovarian cancer cell lines as well as in clinical tissue specimens.

Materials and methods: Paraffin embedded tissue of 87 ovarian cancer patients was analyzed. The nuclear and cytoplasmic expression was recorded by an immune reactive score (IRS). The IRS value was correlated with clinical-pathological factors like grading, stage, histopathological subtypes and overall survival. Maspin expression was evaluated in established ovarian cancer cell lines (HEY, SKOV3, OVCAR3/8) and Paclitaxel- and Docetaxel-resistant HEY cells by qRT-PCR.

Results: The analysis revealed a significant correlation between cytoplasmic maspin expression and overall survival ($p < 0.05$). OC patients with tumors expressing high levels of maspin have a median survival of 28 versus 57 month for patients with low maspin expression. Significant differential maspin expression can be detected between benign, borderline ovarian lesions and OC, as well as among different tumor grading. Normal ovarian epithelial cells express less maspin than ovarian cancer cells. Docetaxel and Paclitaxel resistant ovarian cell lines show an increased level of maspin expression suggesting the unfavorable role of maspin expression in ovarian cancer cell lines.

Conclusions: In OC the serine protease inhibitor maspin is expressed differentially and somewhat paradoxical in comparison to other tumor entities. Low expression levels of maspin are significantly correlated with a longer survival.

PO-Onko 01.61**Working and educational conditions of gynecological trainees in North Rhine-Westphalia, Germany**

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Objective: In 2002 the gynecological society of North Rhine-Westphalia asked the gynecological trainees about their contentment concerning working and educational conditions. In the meantime new working archetypes have been introduced to meet the current working time act while the specializations in our profession have increased as well. Due to these circumstances the working conditions of junior residents in OBGYN have changed tremendously. A current extended survey among the trainees has been performed to figure out if the amendment to the training act in 2005 has influenced the quality of training and working contentment and how these conditions can be improved.

Materials and methods: 1200 questionnaires with 52 questions about labour contracts, training, working conditions, contentment, private life und health have been sent to the trainees of 150 departments of gynecology in North Rhine-Westphalia after being introduced by telephone. The answers to be given were dichotomic, multi-level or quantitative. Differences regarding age, sex, family status and type of clinic were supposed to be detected by creating subgroups. Re-evaluated questions were tested for differences compared to the 2002 survey.

Results: By evaluating the questionnaires conclusions concerning working and educational conditions with impacts on private life and individual career management are expected. These issues are important regarding many vacant positions of employment.

Conclusions: Both the training and the general working contentment have to be improved to preserve the attractiveness of our field for young academics and to avoid the emigration of prospective OBGYN

into non-medical fields and to keep them from going abroad. This survey is expected to help identifying the main factors which are responsible for (dis)contentment.

PO-Onko 01.62

A case of missed abortion with an incidental finding of a borderline tumour in a 30-year-old woman

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We describe a case of a 30-year-old woman, who was referred to our gynecological outpatient clinic for suspected missed miscarriage at gestational age of 10 weeks. This was the second pregnancy after the first has been ended in a first trimester miscarriage five months before. A transvaginal scan performed by an expert revealed an intrauterine pregnancy with a gestational sac of a mean diameter of 23 mm with an embryo of 6 mm length and negative cardiac activity. As the patient had a scan report of this pregnancy performed 3 weeks before, the diagnosis of a missed miscarriage could be confirmed. A corpus luteum cyst was seen in the left ovary. The right ovary was enlarged with a unilocular cyst of 59 mm in largest diameter. The cyst was of hypochoic content and showed echogenic papillary projections around the inner wall, which were moderate vascularised with colour Doppler. The scan report summarized a missed miscarriage and a right ovarian cyst, which was highly suspicious of a borderline tumour. All tumour markers showed normal levels, except of a slightly increased CA 125 of 49.9 kU/l (0–35). The patient was informed about all findings and recommended to have a right ovariectomy, which she agreed to. A laparoscopic ovariectomy and curettage was performed and a frozen section revealed a serous papillary borderline tumour, which was confirmed on final histology. Follow up management was planned for half year control visits for the next 3 years, followed by yearly control visits for a period of 2 years.

PO-Onko 01.63

Importance of the 4G/5G PAI-1 promoter polymorphisms for ovarian cancer incidence

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Objective: PAI-1 (plasminogen activator inhibitor-1) is an important protein in tumor progression and is a prognostic and predictive marker in breast cancer. Its clinical relevance in ovarian cancer is less well studied. PAI-1 gene expression is regulated by several growth factors and cytokines. In addition, a 4G/5G polymorphism in the promoter region of this gene has been shown to influence PAI-1 gene activity. In contrast to the 4G genotype, the 5G genotype contains an additional guanine in the PAI-1 promoter at position -675. It has been assumed that this additional guanine allows a transcriptional repressor to bind to this site and downregulate PAI-1 expression. We studied the importance of this promoter region for the incidence of ovarian cancer.

Materials and methods: We genotyped 105 patients suffering from ovarian, tube and peritoneal carcinoma and 157 age-matched women with no diagnosed gynecological cancer. Genomic DNA was isolated from blood and the promoter region containing the 4G/5G-polymorphism site amplified by PCR. Genotyping was done by restriction site analysis.

Results: There was no difference in the distribution of the genotypes in patient and control group. However, we found that patients carrying the 5G/5G genotype tend to be less likely to develop ascites and tend to show lower FIGO stage. In addition, there was a tendency that the 4G allele was overrepresented in patients with serous ovarian cancer.

Conclusions: Alterations in PAI-1 expression by the 4G/5G promoter polymorphism does not seem to have any importance for the chance to develop ovarian cancer. However, patients who have developed an ovarian cancer may sooner progress when they carry the 4G PAI-1 allele.

PO-Onko 01.64

A tension-free mesh used for the treatment of apical and anterior vaginal prolapses in continent and incontinent women

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To assess the safety, efficacy and functional results of Nazca TC, a tension-free mesh used for the treatment of apical and anterior vaginal prolapses in continent and incontinent women. The rational of this procedure is to create new sufficient barrier mechanism to repair anterior vaginal hernias and support the urinary bladder including the vaginal apex and the bladder neck using one mesh. Surgical technique: A median incision is carried out in the anterior vaginal wall starting 21/2 cm from the external urethral meatus to the uterine cervix or to the apex of the vagina in post hysterectomy patients. The urinary bladder is dissected all the way to the sciatic spine. Two small skin-incisions are made on each side of the Alba line 1 cm cranially and 1 cm laterally from the upper edge of the pubic bone. Additional two small skin-incisions are made in the posterior area of the obturator foramen. A proper needle is introduced laterally to the urethra and guided pre pubically between the insertion of the ischio-cavernosus muscle and the pubic bone along the major labia to the previously made supra pubic incisions. The armpit of the mesh is connected to the tip of the needle and brought to the supra pubic region. The mesh remains tension free in the sub med-urethral segment. The posterior arm tip of the mesh are brought around the arcus tendineus of the levator ani muscles closed to the ischiadic spine and connected to the trans obturator inserted helix tip. The helix is carefully pulled out. The posterior segment of the mesh is fixed to the cervix or to the sacro-uterine ligaments with non resorbable stitches. The vaginal wound is closed in the usual manner in overlapping-technique till the perineal body that was corrected when necessary.

PO-Onko 01.65

Regulation of the retinoid-X-receptor α and the leptin receptor pathway in choriocarcinoma cells in vitro

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Objective: Enhanced retinoid-X-receptor α (RXR α) expression is found in miscarried placentas and decreased expression in hydatidiform mole. Additionally, leptin receptor (Ob-R) expression is upregulated in both pregnancy disorders. The aim of the study was to investigate the impact of the retinoids 9-cis-(9-cisRA), all-trans-

retinoic acid (ATRA) and the PPAR γ agonist 15-Deoxy- Δ 12,14-prostaglandin J2 (15d-J2) on the expression of RXR α and Ob-R in choriocarcinoma cells in vitro.

Materials and methods: The choriocarcinoma cells BeWo and JEG-3 were stimulated with 10 nmol/ml 9-cisRA, ATRA and 15d-J2 for 24 h, respectively 48 h. Anti-RXR α or anti-Ob-R served as primary antibodies. The intensity of the stained cells was determined by a semiquantitative score. In real-time TaqMan PCR (RT-PCR) Ob-R and RXR α were analyzed after cell stimulation with 9-cisRA and 15d-J2 for 1, 2, 3, 4 and 8 h. Placental tissue from spontaneous miscarriages was incubated with M30 CytoDEATH antibody (M30) as well as RXR α or Ob-R and stained using a double-immunofluorescence method.

Results: 9-cisRA, ATRA and 15d-J2 downregulated RXR α expression in BeWo and JEG-3. Immunocytochemistry could be verified on mRNA level with RT-PCR. Retinoids enhanced Ob-R expression in JEG-3 which could be demonstrated via dotblot and RT-PCR. 15d-J2 had no effect on Ob-R expression. Double-immunofluorescent staining showed a simultaneous expression of M30 and RXR/Ob-R in extravillous trophoblasts (EVT).

Conclusions: The impact of the retinoids on Ob-R expression underlines the interaction of RXR α with the Ob-R pathway and highlights their cross talk in the signal transduction cascade. Downregulation of RXR α expression in stimulated choriocarcinoma cells might serve as a protection against apoptosis as miscarriage is associated with apoptosis of EVT. Upregulation of Ob-R might be understood as a response to low leptin levels found in miscarriage.

PO-Onko 01.66

Laparoscopic supracervical hysterectomy: what happens with the stump?

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Objective: Supracervical hysterectomy is discussed to be a good alternative to complete hysterectomy. Semm advised to excise the cervical channel vaginally to reduce the risk of cervical stump carcinoma and spotting. We here report our stump infection and spotting rate after usual LASH and LASH with additional laparoscopic excision of the cervical channel (eLASH).

Materials and methods: 260 premenopausal patients underwent LASH at our institution between January 2006 and June 2009. Until July 2007 we detached the cervix rather straight and coagulated the remaining cervical channel (LASH). Since July 2007 we excised the cervical channel laparoscopically (Ultracision) and coagulated the remaining very small cervical channel (eLash). All patients were asked to fill in a self administered questionnaire concerning the spotting rate, postoperative infections and smoking attitudes.

Results: We had a response rate of 70% ($n = 183$). 88 patient of the LASH group and 85 patients of the eLASH group completed the questionnaire. Questionnaire was incompletely filled in by nine patients. We had a postoperative stump infection rate of 6.8% (6/88) in the Lash group and 5.9% (5/85) in the eLASH group. No statistic significant differences between smokers and non-smokers were found. 21.6% (19/88) of the LASH group and 5.9% (5/85) of the eLASH group reported on spotting continuing more than 1 year after operation.

Conclusions: The laparoscopic excision of the cervical channel reduces the spotting rate. Stump infection rate is moderate and comparable to LASH. There seems to be no negative influence concerning smoking and infection rate.

PO-Onko 01.67

Transvaginal sonography as a prognostic value to detect endometrial pathology in postmenopausal symptomatic women without hormone replacement therapy

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Objective: Postmenopausal bleeding occurs in 80–95% of patients with endometrial cancer. The differential diagnosis includes a broad range of conditions, but the vast majority of postmenopausal women who present with irregular or excessive vaginal bleeding have benign disease. The aim of this study was to evaluate retrospectively the value of transvaginal sonography for the detection of endometrial disease in postmenopausal women with bleeding.

Materials and methods: The women were examined in the Department of Gynaecology of the General Hospital in Didimoticho during the time period from January 1998 to December 2008. None of them were on hormone replacement therapy and all had amenorrhea for more than 2 years.

Results: This study involved 60 postmenopausal women aged 47–66 years (Median 56.5). Transvaginal sonography was performed in 60 women. About 97.5% of the malignant diseases were discovered in study-women, whose endometrial thickness was above 4 mm, but we found endometrial cancer in 2.5% of the cases, in women, whose endometrial thickness was below 4 mm. A satisfactory visualization of the endometrium has been obtained in all 60 examined cases. The thinnest endometrium was 0 mm while the thickest one was 10 mm. Of the 60 study-patients, four had endometrial cancer, three had atypical hyperplasia, eight had complex hyperplasia, ten had simple hyperplasia, twenty-two had an atrophic endometrium and twelve had polyps. Endometritis was found in one case of the study population. Histology was available in all cases.

Conclusions: Concerning the age in the study patients, we confirm that endometrial cancer occurs at any age, but more commonly in ages above 58 years. In postmenopausal symptomatic women premalignancy or malignancy causes of bleeding can not be excluded with just transvaginal ultrasound and a fractional curettage is necessary.

PO-Onko 01.68

The first description of docetaxel-induced recall inflammatory skin reaction after previous drug extravasation

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We present for the first time a case of severe recall soft tissue injury after docetaxel extravasation in a patient with metastatic breast cancer. In general, extravasation of docetaxel causes mild local skin reactions without further necessity of intervention. For known anthracyclines and paclitaxel, inflammatory recall phenomena at sites of previous drug extravasation are rare and often occur following administration of the same cytotoxic drug. A 65-year-old female with 1997 first diagnosed pT1c pN1biii cM0, Her2 negative, hormone receptor positive, invasive ductal carcinoma of the right breast was treated at our institution with docetaxel (Taxotere[®]). After breast-conserving surgery and axillary dissection with

10 of 26 tumor afflicted lymph nodes followed by irradiation, our patient received multiple chemotherapeutic regimes and antiestrogenic therapies between 1997 and 2008. In the course, she developed lung, osseous and liver metastases, whereas re-induction with taxane-containing chemotherapy always led to tumor remission with less side effects and good general state of health. Drug extravasation of docetaxel in the antecubital fossa occurred and was treated with hyaluronidase s.c. and application of cold packs. A few days after the following chemotherapy cycle, she developed a severe erythema with edema, hotness on touch, and pain in the area of previous extravasation necessitating treatment with local steroids, analgetics and antibiotics. The recall dermatitis continued to exacerbate after each course of systemic docetaxel chemotherapy, and finally led to termination of this therapy. In conclusion, recall soft tissue injury after the use of docetaxel in a site of previous extravasation is a new type of skin toxic effect of this chemotherapeutic drug. When skin damage seems to have been fully resolved, caution is needed after an episode of drug extravasation. Even after a therapy interruption of several weeks, resumption of chemotherapy with docetaxel might lead to recrudescence of the inflammatory skin reaction.

PO-Onko 01.69

A case of primary pulmonary choriocarcinoma

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Objective: Primary pulmonary choriocarcinoma is a rare disease with only 25 reported cases in literature so far. In this report we present the case of a 31-year-old female with primary pulmonary choriocarcinoma initially noticed because of a positive urine pregnancy test.

Materials and methods: A 31-year-old woman presented to our outpatient department of gynaecology. A urine pregnancy test performed by the patient because of a delayed period had shown a positive result although her husband is sterilized and the patient was under oral contraceptives because of skin problems. A gynaecologic ultrasound showed normal anatomy and no signs of pregnancy. Quantitative β -HCG serum levels were 516 U/l. A laparoscopy failed to reveal an ectopic pregnancy. Biopsies of both ovaries showed no signs of malignancy or scarring which would have been consistent with old trophoblastic disease or ovarian choriocarcinoma. A D&C obtained no trophoblastic tissue and the endometrium was described as being in the secretory phase. Over several weeks, β -HCG-levels raised up 812 U/l. In order to rule out a mediastinal extragonadal germ cell tumor a CT-scan of the thorax was performed, revealing a peripheral nodule of 1.6 cm \times 1.7 cm in the right upper lobe of the lung. A diagnostic operative excision of the tumor was performed, revealing a choriocarcinoma. At 3 weeks postsurgery β -HCG dropped to less than 5 U/l. Further staging of the patient using PET-CT showed no hypermetabolic lesions, making a metastatic disease highly unlikely. The patient is at well being and refused adjuvant chemotherapy.

Conclusions: Besides the common differential diagnosis of elevated β -HCG levels one should also consider extragonadal choriocarcinomas. The diagnosis is of great importance for the patient, because notably primary pulmonary choriocarcinomas are mostly unresponsive to surgical and chemotherapeutic treatment. In addition they are associated with a poor prognosis.

PO-Onko 01.70

Identification of a novel type II Plk1 inhibitor and validation in gynecological cancer cells

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Objective: Human polo-like kinase 1 (Plk1) is a key component of mitotic progression. It is over-expressed in all today analyzed human cancer types. It is a negative prognostic factor for cancer patients and a measure for the aggressiveness of a tumor. Thus, Plk1 represents a promising target to develop new selective and specific therapeutic strategies. Kinase inhibitors are divided in type I inhibitors, targeting the highly conserved active conformation, and the more selective type II inhibitors, targeting the inactive conformation of kinases. These type II inhibitors occupy a hydrophobic pocket with less conserved surrounding amino acids [1].

Materials and methods: We did virtual screening using a homology-based structural model of human Plk1 to identify inhibitors against the inactive conformation of Plk1. Potential Plk1 inhibitors were analyzed using proliferation studies and kinase assays.

Results: We identified one potent inhibitor (SBE13) which leads to inhibition of Plk1 activity (200 pM), decreased cell proliferation, induces apoptosis and abnormal mitotic figures in cancer cells [2, 3]. Notably, SBE13 did not influence activity of other kinases (Plk2, Plk3, Aurora A).

Conclusions: This study suggests that kinase inhibitors targeting the inactive conformation of Plk1 may be considered for the development of highly selective and specific cancer therapeutics.

PO-Onko 01.71

The oncological emergency case: breast cancer patient with paraneoplastic hypoglycemia

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Objective: Hypoglycemia in the context of a paraneoplastic secretion of insulin-like peptide (IGF-II) is rarely described in Oncology. It can lead to severe adverse effects up to hypoglycemic coma (de Groot et al., 2007).

Materials and methods: A 60 year old patient with metastatic breast cancer was admitted to our hospital in pre-comatose state. The laboratory data revealed glucose of 9 mg/dl, other blood parameters were normal. Under treatment with constant infusions of glucose (100 ml/h, 20%) patient's state normalised rapidly. Eight years ago a primary breast carcinoma with bone metastases was diagnosed (stage: ypT3/ypN2/cM1/G2/hormone receptors positive/Her2-neu negative). Over the years the patient developed metastases in liver and lung. Recently she obtained her 5th-line chemotherapy containing Caelyx, Faslodex and bisphosphonates. Due to significantly decreased levels of IGF1-, Insulin- and C-Peptid and a normal IGF-II, the suspicion of a paraneoplastic hypoglycemia was raised, which was substantiated by a progress in imaging and serology (CA 15-3 > 3000kU/l). Under glucose infusions, glucocorticoides (Dexamethason 4 mg/day) and

somatostatines (Octreoid 100 µg/d) the patient was free of symptoms.

Conclusions: Paraneoplastic hypoglycemia is a rare emergency case in oncology. It can contribute to either primary diagnosis or awareness of progression of cancer. The rapid diagnosis and immediate treatment in terms of a specific tumor-therapy is of central interest. In the palliative situation the symptomatic treatment has priority (de Groot et al., 2007).

PO-Onko 01.72

Single pulmonary lesion detected by pet scan indicates choriocarcinoma

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Objective: GTD forms a heterogeneous group of abnormal trophoblastic tissues. Choriocarcinoma (CC) is a malignant form of GTD. CC is much more likely than other types of GTD to grow quickly and spread to organs away from the uterus. We present a rare case of exclusive lung manifestation of CC, initially treated as ectopic pregnancy (EP). State of the art algorithms of diagnostic and therapeutic regimen as well as current classifications are given.

Materials and methods: Patient (30 year, G2,P2) presented 12 months after term spontaneous delivery with metrorrhagia. Subsequent hCGs-levels persisted high. Ultrasound, hysteroscopy and laparoscopy were performed, revealing neither intra- nor EP. Curettage were performed but histology showed not trophoblast tissue. Methotrexate (MTX) was given but hCGs-levels persisted indicated MTX-resistant trophoblastic disease. A PET scan was performed showing a singular apical lesion of the right lung which corresponded with a subpleural nodule in CT-scan. Resection (VATS) was performed and histologic examination revealed CC.

Results: The Lesion was classified GTD Stage II/III high risk (WHO Index score >7) and resection was followed by EMA-CO. The lesion was cleared after this regimen and hCGs decreased.

Conclusions: High risk GTD spread to genital structures or lungs and without treatment prognosis is generally poor. In this presented case 12 months after delivery a high risk CC occurred. Patient had no evidence of GTD in genitourinary organs, but a single lesion of CC in the lung as found in a PET scan. Standard treatment is usually an intensive combination chemotherapy regimen such as EMA-CO in combination with surgical removal if possible. Blood hCGs levels serve as tumour markers indicating response or resistance to chemotherapy. All different staging systems (FIGO, WHO scoring system and the currently adopted TNM-system) are able to define high risk patients as prerequisite for state of the art therapy.

PO-Onko 01.73

YT521 isoform 1 and 2 exert the same impact on CD44 alternative splicing *in vivo*

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Objective: YT521 acts as a splicing factor in alternative splicing mechanism. The existence of two isoforms was confirmed due to

exon 6 inclusion (isoform 1) and exon 6 exclusion (isoform 2). Recently, isoform 1 was identified as a prognostic factor for endometrial cancer, while isoform 2 was rarely detected in this tumour type. However, exon 6 is not located in YT521 functional domain YTH and its skipping will not give rise to downstream nucleotide frameshift. Here we explored whether isoform 2 is as functional as isoform 1.

Materials and methods: Increasing amounts of expression plasmids of YT521 isoform 1 and isoform 2 were co-transfected in cancer cell lines with constant amounts of a minigene containing CD44 v4/v5 (ESTGLv2), respectively. The influence of both YT521 isoforms on alternative splicing profiles of ESTGLv2 was examined by RT-PCR with primers specific for the ESTGLv2 minigene.

Results: In a concentration-dependent manner, both YT521 protein isoforms cause a similar increase of CD44 v4 inclusion in minigene ESTGLv2 ($p < 0.01$). Thus, the protein YT521 isoforms 1 and 2, originating from inclusion or exclusion of YT521 exon 6, respectively, display no difference in affecting alternative splicing pattern of CD44.

Conclusions: YT521 isoform 2 displays a similar function in alternative splicing like isoform 1 in *in vivo* assay. Thus, the different expression levels of these two isoforms in endometrial cancer might be caused by their tissue-specific distribution.

PO-Onko 01.74

Exenteration in the treatment of advanced or recurrent vulvar and vaginal cancer

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Objective: Vulvar and vaginal cancer are the rarest of all genital carcinomas. While in advanced primary cancer pelvic exenteration (PE) can be an alternative to chemoradiation, PE is often the only therapy available in cases of recurrence.

Materials and methods: In a retrospective study we analyzed patients having undergone exenteration for vulvar or vaginal cancer in our department within the last 10 years.

Results: We identified 28 patients, 22 of them suffering from vulvar cancer, the other 6 from vaginal cancer. 8 of the vulvar malignancies were primary, 14 a recurrence, in vaginal cancer it were 5 and one, respectively. 18 patients presented with a stage FIGO III, in 9 patients the disease had advanced to stage IV. In 11 patients the disease had spread to the inguinal lymph nodes, in 3 patients also to pelvic nodes. At the end of surgery, all patients were macroscopically free of tumor, which was confirmed microscopically in 21 patients (75%, R0), the other 7 patients (25%, R1) having microscopic tumor remnants ($n = 2$, 7%) or lymphangiosis found in the surgical margins ($n = 5$, 18%). Over all patients, mean time of survival was 68 months, 5 year survival rate (5 YSR) 42%. For patients with primary disease mean survival was 74 months and 5 YSR 47%, for the others 47 months and 29%, respectively. Spread of disease to lymphatic nodes showed a decrease in survival: Patients with free lymph nodes lived a mean of 89 months and had a 5 YSR of 85% vs. 32 months and 36%, respectively, for patients with tumorous spread to the nodes ($p = 0.05$)

Conclusions: PE is a therapeutic option in advanced primary or relapsed vulvar or vaginal carcinoma, offering median- to long-term survival for a considerable part of patients. Carcinomatous spread to regional lymph nodes is the most important prognostic factor.

PO-Onko 01.75**27 Year old patient with residual uterine tumor of a choriocarcinoma after chemotherapy. A case report***Nikolaus de Gregorio¹, Rolf Kreienberg¹, Georg Sauer¹¹Universitätsfrauenklinik, Ulm, Germany

Objective: Malignant gestational trophoblastic neoplasia (GTN) is a rare gynecologic entity. Although there is a risk of metastatic disease, most women with GTN can be successfully managed with preservation of their normal reproductive function.

Materials and methods: We report the case of a 27 year old nulliparous, who was transferred to our hospital with elevated β -HCG levels after two curettages following an incomplete abortion. After 13 cycles of methotrexate, β -HCG Level reached the detection limit, however transvaginal sonography showed a highly vascularised uterine tumor. Operative hysteroscopy was performed; because of the high risk of hemorrhage, complete resection was not achieved. Pathological findings showed amorphi-necrotic tissue without viable cells. After a 3 year follow up, no relapse has occurred and a recovery of menstruation taken place.

Conclusions: A “watch and wait” strategy with regular ultrasound scans and close meshed β -HCG level control can be an option in treating patients with residual disease after GTN.

PO-Onko 01.76**The small vulvar cancer of the anterior fourchette: a specific tumor entity?***Monika Hampl¹, Dimitri Panyatopoulos¹, Judith Roos², Hans Ulrich Petry on behalf of the Study Group Colposcopy³, Matthias Dürst⁴, Magnus von Knebel Döberitz⁵, Miriam Reuschenbach⁵¹University of Düsseldorf, Obstetrics and Gynecology, Düsseldorf, Germany,²Lukaskrankenhaus, Frauenklinik, Neuss, Germany,³Klinikum Wolfsburg, Frauenklinik, Wolfsburg, Germany,⁴University of Jena, Gynecologic Molecular Biology, Jena, Germany,⁵University of Heidelberg, Applied Tumor Biology, Institute of Pathology, Heidelberg, Germany

Objective: The incidence of vulvar cancer in young women has increased in Germany during the last decade. The mean age has dropped significantly (by about 8 years) and we observed an increase of small tumors located between clitoris and urethra. We initiated a multicenter study in Germany asking members of the Study Group for Colposcopy and gynecological centers specialized in the treatment of vulvar cancer to provide tumor samples from patients with invasive tumors (max. T2) strongly located between clitoris and urethra.

Materials and methods: We received 129 tumor samples from vulvar cancer of the anterior fourchette including clinical/histological data and treatment characteristics of all patients reported in a standard questionnaire. We are right now analyzing these tumor samples and more than 60 control samples (vulvar cancer from other localizations) for the presence of HPV DNA and if positive HPV-type, presence of Herpes simplex DNA, p53/p16ink4a/Ki 67 expression and presence of immune-infiltrating cells by IHC.

Results: Preliminary results of 13 tumors show that two third of the tumors are p16 negative with a strong or moderate expression of p53. Of the p16 positive samples ($n = 5$), only two are p53 negative. HPV DNA and Herpes simplex DNA results as well as the IHC studies are still pending.

Conclusions: Our preliminary results suggest that this specific entity of vulvar cancer is HPV induced in about 30% of the cases whereas in the majority of the tumors p53 as a key tumor suppressor gene seems to play a role in tumorigenesis besides factors we are still working on.

PO-Onko 01.77**Amplification of epithelial growth factor receptor (EGFR) plays a role in the progression of high-grade vulvar intraepithelial neoplasia (VIN) to vulvar squamous cell cancer (VSCC), whereas HER-2 amplification is not detectable***Eleftherios Samartzis¹, Nicolas Samartzis¹, Patrick Imesch¹, Konstantin Dedes¹, André Fedier¹, Daniel Fink¹, Rosmarie Caduff², Mathias Fehr³¹UniversitätsSpital Zürich, Klinik für Gynäkologie, Zürich, Switzerland, ²UniversitätsSpital Zürich, Institut für Pathologie, Zürich, Switzerland, ³Kantonsspital Frauenfeld, Frauenklinik, Frauenfeld, Switzerland

Objective: Epidermal growth factor receptor (EGFR, HER-1) and HER-2 are transmembrane receptors that possess tyrosine kinase activity, playing essential roles in cancerous and physiological conditions. They are, together with HER-3 and HER-4, part of the ErbB family. EGFR-signalling suppresses apoptosis and induces proliferation, invasion, and the formation of metastases in cancer cells. Our objective was to compare the expression of EGFR and HER-2 in a series of VIN and VSCC tissues.

Materials and methods: We performed a tissue micro array (TMA) with specimen from 107 patients with high-grade VIN and 70 patients with vulvar cancer (p16-negative and p16-positive as surrogate marker for HPV-infection). EGFR- and HER-2-expression has been analyzed using immunohistochemistry (IHC). We applied a semi-quantitative scoring system from 0 to 3+. For the statistical evaluation EGFR scores were dichotomized by combining negative (0), weak (1+) and moderate positive (2+) versus strong positive (3+) results, which according to other authors is correlating with the amplification of EGFR with a sensitivity of 100% and a specificity of 79%.

Results: We found a significantly ($p = 0.007$) increased EGFR-Expression in vulvar squamous cell cancer ($n = 14/59$, 23.7%) compared to high-grade VIN ($n = 8/106$, 7.5%). The staining for HER-2 was negative for all tissue samples, whereas positive controls were positive. Similar results were found for the group of p16-positive tissues only.

Conclusions: Our results suggest that the amplification of EGFR plays a considerable role in the progression of high-grade VIN to VSCC. EGFR-amplification observed in 24% of patients with vulvar cancers may be exploited for targeted treatments. In addition, we demonstrate in one of the largest series analyzed so far that HER-2 amplification is not detectable in both VIN and VSCC.

PO-Onko 01.78**Elevated infect parameters after laparoscopic sacropexy: infection or posttraumatic reaction?***Carolin Banerjee¹, Heiko Leufgen¹, Martin Hellmich², Wolfgang Hatzmann³, Karl-Guenter Noe¹¹KKH Dormagen, Gynecology, Dormagen, Germany, ²University Köln, Institut Medical Statistics and Epidemiology, Köln, Germany, ³University Witten, Gynecology, Witten, Germany

Objective: Leucocytes and C- reactive protein (CRP) levels are often used to detect infections. Dependent on the degree of tissue trauma, elevated levels are also found after open surgery. The aim of this study was to evaluate the diagnostic validity of leucocytes and CRP levels after laparoscopic sacropexy for a better differentiation between infection and tissue response.

Materials and methods: 287 patients suffering from genital prolapse higher than I and laparoscopic sacropexy were included. LASH was

performed in case of pre-existing uterus ($n = 171$). Leucocytes and CRP levels were analysed pre-operatively and four days after operation. Additionally early (day 1–5) and late onset (>1 day after demission, at least day 7) infection rate was analysed. The discriminatory capacity of leucocytes and CRP levels were evaluated by receiver operating characteristic (ROC) analysis.

Results: Early infections (wound infections) were found in $8/287 = 2.8\%$. Late onset infections were found in $3/287 = 1.0\%$ (0.66% stump-infection after LASH, 0.33% unknown origin). Areas under ROC curves were low for both leucocytes (0.52, 95% confidence interval 0.37–0.66) and CRP levels (0.60, 95% CI 0.44–0.77), where a value of 1 (or 0) means perfect discrimination and 0.5 corresponds to tossing a coin. Thus thresholds yielding acceptable sensitivity and specificity could not be defined.

Conclusions: We found little evidence to support the diagnostic validity of leucocytes or CRP levels to differentiate infection and traumatic reaction four days after laparoscopic sacropexy. Our findings query the benefit of a routinely determination of leucocytes and CRP levels at that time. However, significance of our findings is limited by the low frequency of infections in the study sample. Sensitivity and specificity of leucocytes and CRP levels maybe better after normalisation of the initial tissue response (day 8–10).

PO-Onko 01.79

Fertility sparing surgery of borderline ovarian tumors: laparoscopy vs. laparotomy

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Objective: (1) To evaluate the role of minimal invasive surgery of borderline ovarian tumors (BOT) with regard to recurrence rate compared with radical surgical management and (2) to investigate the reproductive outcomes following fertility preservation.

Materials and methods: Medical reports of all 69 patients with BOT who underwent surgery between 1996 and 2009 at our institution were reviewed. Outcomes from patients who underwent fertility sparing surgery (FSS) were compared with outcomes from patients with radical surgery defined as hysterectomy, bilateral salpingo-oophorectomy and infracolic omentectomy.

Results: Forty-four patients with BOT were treated laparoscopically and 25 patients underwent laparotomy. One recurrence occurred in a woman treated with radical surgery (1/45) while 5 cases of recurrence were diagnosed in the fertility-sparing group (5/24; premenopausal $n = 2$, postmenopausal $n = 3$). The recurrence risk in the fertility sparing group was significantly higher than in radical surgery group ($p = 0.021$ Fisher Test). No difference regarding recurrence was observed between laparoscopy and laparotomy. No major intra- and postoperative complications occurred when patients were treated laparoscopically. Altogether, 24 patients underwent FSS (laparoscopically 16, laparotomically 8). In both groups, radical surgery and fertility-sparing surgery, 100% survival rate has been assessed. In the FSS group, out of 16 women in child bearing age, 3 had full-term deliveries, one is currently pregnant, 4 are considering to have a child, 4 don't wish to have children, 2 had a secondary radical surgery due to recurrence and 2 were lost to follow-up.

Conclusions: Laparoscopic radical surgery of BOT was feasible and safe. FSS of women in reproductive age carries an increased risk of recurrence. Women beyond child bearing age or who have completed family planning, should be informed about the option of secondary radical surgery.

PO-Onko 01.80

Surgical treatment of patients with breast cancer at the Cancer Center Regensburg 1998–2007

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Objective: Breast cancer is the most frequent malignancy in women. All modern prospective randomized clinical trials comparing mastectomy and breast conserving therapy have shown an equivalent survival. Today surgery of breast cancer allows a breast conserving rate of over 70%. New methods like sentinel lymph node biopsy and primary and secondary breast reconstruction were established.

Materials and methods: The Cancer Center Regensburg is an institution of 50 hospitals of Oberpfalz, the University Hospital of Regensburg and 1100 physicians. The region Oberpfalz consists of 1.1 million of inhabitants. Until now over 100,000 follow ups of tumor patients are reported in the register of the Cancer Center Regensburg. This study is a retrospective analysis of patients with diagnosed primary breast cancer between 1998 and 2005. The dates of 6773 patients undergo analysis concerning the surgical treatment of primary breast cancer.

Results: From 1998 to 2007 we observed an increase of breast conserving therapy from 42.4 to 65.4%. Patients with pT1-tumors were treated with breast conserving surgery in 76.3% in 2003 and 83.7% in 2007. SLN biopsy was performed in 8.7% of the cases in 2003 and 59.8% in 2007. The rate of axillary lymph node dissection decreased from 91.3% in 1998 to 40.2% in 2007. Breast reconstructive surgery was mostly performed in patients aged between 40 and 60 years. An increasing rate of autolog technics was performed, in 1998 10.2%, in 2007 28.1%. The rate of complications over all was $<4\%$.

Conclusions: The surgical treatment of the patients with primary breast cancer at the Cancer Center Regensburg showed increased rates of breast conserving surgery and SLN biopsy from 1998 to 2007. Reconstructive surgery after mastectomy can be performed with low rate of complications.

PO-Onko 01.81

Fast-track hysterectomy: a pilot study

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Objective: Fast-track concepts have been applied in many perioperative settings. Short length-of-stay with vaginal hysterectomy has been shown to be feasible and safe. We developed an interdisciplinary fast-track vaginal hysterectomy protocol for selected patients.

Materials and methods: Inclusion criteria were planned simple vaginal hysterectomy without concomitant procedures, ASA status 1–2, patient desire, and patient support at home. Patients were operated on early on the day of admission with regional or general anesthesia. Intraoperative points included preemptive analgesia, antibiotic pro-

phylaxis, bipolar vessel sealing, and nonuse of drains and catheters. Postoperative points included pain management with PO medications, mobilization on the afternoon of surgery and early eating. Complications and readmissions were recorded. Patients were contacted with a questionnaire at 8 weeks.

Results: 12 patients were enrolled into the protocol in the pilot phase. Seven patients went home on the first, three on the second and two on the third postoperative day. Reasons for extended stays were postoperative nausea and vomiting (PONV) and organizational problems at home. There were no readmissions for complications. Nine women were satisfied with the duration of the stay, three considered it too short.

Conclusions: Fast-track hysterectomy is feasible after accurate patient selection. The main barriers to discharge on day 1 were PONV and organizational problems at home.

PO-Onko 01.82

One step nucleic acid amplification (OSNA) as an intra-operative diagnostic tool for the assessment of the sentinel lymph node status in breast cancer patients

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Objective: The detection of sentinel lymph node (SLN) metastases in breast cancer patients is conventionally determined by intra-operative histopathological examination of frozen sections or touch imprints. Due to a poor sensitivity of these techniques, postoperative identification of metastases on paraffin embedded sections can lead to second surgery axillary lymph node dissection. A new molecular assay called One Step Nucleic Acid Amplification (OSNA) for intra-operative identification of metastatic disease in SLN has been evaluated in several clinical studies. We present here the results from the intra-operative use of OSNA.

Materials and methods: OSNA includes a sample preparation step followed by automated measurement of cytokeratin 19 mRNA copy number directly from the homogenate and can be carried out by a technician.

Before homogenisation of the whole node a 1 mm middle slice was reserved for histology. 257 SLN from 110 breast cancer patients were investigated. If OSNA was negative then Haematoxylin & Eosin (H&E) staining was performed every 200 µm; in case OSNA was positive, only one H&E section was made.

Results: Fourteen patients were positive and 81 were negative with both methods. In 4 patients OSNA indicated the presence of a macrometastasis and in 9 patients a micrometastasis whereas histology was negative. The positivity rate obtained by OSNA was 24.5%. In one patient a micrometastasis was found in the 1 mm middle slice and OSNA was negative. One SLN was histology +/OSNA-, indicating CK19 low expression on a protein and RNA level.

Conclusions: OSNA is a standardised procedure for intra-operative detection of SLN metastases in breast cancer patients and prevents patients from a diagnostic delay or second surgery. Since most or all of the tissue can be analysed by OSNA, the chance of a sampling bias due to uninvestigated material is very low.

PO-Onko 01.83

Vaginal assisted laparoscopic sigmoidectomy with hysterectomy and bilateral salpingoovarectomy in diverticulitis. A case report

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Objective: Case report of a vaginal assisted laparoscopic hysterectomy and bso in diverticulitis.

Materials and methods: We report about a 65 year old woman with recurrent diverticulitis. After vaginal perforation of an abscess, caused by the diverticulitis a diagnostic laparoscopy was performed to prove the diagnosis. It showed an inflamed sigma with peridiverticulitis and involvement of uterus, pelvic wall and left ovary. After conservative therapy with antibiotics definitive surgical treatment was planned. The surgical approach was laparoscopic assisted through the vagina. Sigma, uterus and bilateral ovaries were removed with no need for laparotomy or anus praeter. Colorectal anastomosis was done by EEA.

Results: Laparoscopy was performed without complications, retrieval of the tissue implemented through the vagina. Operation time was 147 min, blood loss 50 ml. Postoperative no complications occurred, the patient left hospital after 7 days.

Conclusions: The laparoscopic approach assisted through the vagina is suitable & feasible to remove the sigma, when simultaneous hysterectomy is performed.

PO-Onko 01.84

Hysterectomy rates for benign indications in Austria

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Objective: Hysterectomy is the most common gynecologic operation following cesarean section and the large majority of hysterectomies is performed for benign indications [1, 2]. Several surveys in Europe and the USA have shown stable or decreasing hysterectomy rates since the 1980s [1, 3–6]. We ascertained annual hysterectomy rates in Austria from 1997 to 2008.

Materials and methods: Analysis of number of inpatient stays in Austrian public hospitals with the intervention “HYSTERECTOMY”. Data were derived from the Austrian DRG system (leistungsorientierte Krankenanstaltenfinanzierung, LKF; Österreichisches Bundesinstitut für Gesundheitswesen, ÖBIG).

Results: The number of hysterectomies performed for benign indications decreased from 12,283 in 1997 to 8,470 in 2008. This amounts to a decrease of 31%. 92% of all hysterectomies were for benign indications in 1997, compared with 89% in 2008. The age-adjusted overall hysterectomy rate decreased from 308/100,000 women in 1997 to 191/100,000 women in 2008. Between 1993 and 1997 the hysterectomy rate was relatively stable, at about 300 hysterectomies/100,000 women. But data prior to 1997 have to be interpreted with caution because the Austrian DRG/LKF system was implemented in 1997.

Conclusions: The hysterectomy rate for benign indications in Austria declined markedly (by 31%) between 1997 and 2008.

PO-Onko 01.85**Therapeutic impact of MRI in the work-up of indeterminate adnexal masses at ultrasound**

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Objective: To evaluate the therapeutic impact of MRI including diffusion weighted imaging (DWI) for the work-up of indeterminate adnexal masses at ultrasound.

Materials and methods: 39 patients with indeterminate ovarian lesions scheduled for surgery were included in this prospective clinical study. MRI of the abdomen and pelvis including DWI was performed on a 1.5 T Siemens scanner. The gynecologist performing the ultrasound characterized the lesions based on the Kawai score and determined the surgical procedure. He reevaluated his assessment in knowledge of the MR findings. The signal of solid and cystic parts of the tumors was evaluated on T2w and b = 800 DWI, and ADC values were obtained. Where available, results were correlated to histopathology. Sensitivity and specificity of MRI were determined and the number of surgical procedures altered due to MRI were assessed.

Results: MRI resulted in a change of therapy in 54% of cases (21/39): in 13% (5/39) follow-up instead of surgery was performed, in 41% (16/39) MRI influenced the surgical procedure. Final diagnosis was a malignant lesion in 4 and a benign entity in 35 patients. Diagnostic accuracy of MRI was 97%; sensitivity 97% and specificity 100%. ADC values of benign teratomas ($n = 4$) were significantly lower than those of malignant lesions (78 ± 16 vs. $111 \pm 21 \times 10^{-5} \text{ mm}^2/\text{s}$; $p = 0.04$).

Conclusions: MRI is a helpful tool in the preoperative evaluation of sonographic indeterminate adnexal masses. It reduces the number of unnecessary surgical interventions in case of benign lesions and is helpful for surgical planning. DWI might allow better characterisation of ovarian lesions in selected cases.

PO-Onko 01.86**Self assessment of Swiss gynaecologists regarding clinical care for sexual dysfunctions**

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Objective: Female sexual dysfunctions, e.g. sexual desire disorder or arousal disorder, have a high prevalence. Nevertheless previous studies show that many physicians hesitate to address sexual issues (Platano et al. 2008). The aim of the study is to evaluate the approach of gynaecologists towards patients with sexual problems.

Materials and methods: In this pilot study at the Department of Gynaecology, University Hospital of Basel, gynaecologists were asked about their current care for patients with sexual issues and their attitude towards this topic by a self administered questionnaire (28 items). Statistic analysis was performed with SPSS 12.0.

Results: 35 of 58 questionnaires were returned. 46% of the gynaecologists quoted to ask less than 15% of their patients actively about sexual problems. 69% of the respondents estimated that 10–15% of their patients have a sexual problem and that less than 15% of the patients actively address this kind of problems. Only 6% of the gynaecologists stated to be uncomfortable to talk about sexual

problems. Dyspareunia was quoted as the most or second most prevalent diagnosis of female sexual dysfunction in 71% of the questionnaires. Overall the issue of sexual medicine was estimated to be important or very important by over 50% of the respondents.

Conclusions: A high percentage of cases with a subjective suspicion for a sexual problem are not further evaluated though only very few gynaecologists reported to be uncomfortable to address sexual problems. Another interesting finding is the high subjective prevalence of dyspareunia compared to sexual desire disorders or arousal disorders, which is not consistent with results of epidemiologic studies (Lindau et al. 2007). This pilot study demonstrates that gynaecologists consider the issue of sexual medicine to be important. In April 2010 an extension of the study is planned to include gynaecologists in private practices.

PO-Onko 01.87**Are there genetic causes for Mayer–Rokitansky–Kuester–Hauser syndrome? First results showing differentially expressed genes in the field of hormone and growth factor receptors**

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Objective: Vaginal and uterus aplasia in patients with Mayer–Rokitansky–Kuester–Hauser syndrome (MRKHS) are found in 1 out of 4000 female live births. Until now there was no molecular genetical cause identified, in spite of familial clustering. Animal models indicate the importance of hormones, especially estrogens, in the development of the female genital tract.

Materials and methods: From April 2007 until now there were 80 myometrial biopsies taken from uterine rudiments during laparoscopically assisted creations of a neovagina in MRKH patients and compared to age matched controls. Using microarray analyses we detected differentially expressed genes as well as differences in methylation (8 patients versus 8 controls).

Results: The first analysed probes show differentially expressed genes in the field of hormone and growth factor receptors which could be partially validated by RT-PCR. Differential methylation could be seen in genes which are known to play a role in embryological development. There were no copy number variations found in monozygotic twins in which only one suffered from MRKHS.

Conclusions: Gene expression analyses indicate that hormonal feedback systems may play a role in the proper development of the human female genital tract. Nevertheless data from monozygotic twins as well as methylation assays point to epigenetic causes for uterine and vaginal aplasia. In order to get significant and reproducible results the number of experiments has to be increased.

PO-Onko 01.88**Laparoscopic phenotypes in Mayer–Rokitansky–Kuester–Hauser syndrome and the histological structure of uterine rudiments—what about endometrium in uterine buds?**

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Objective: There are no numbers found in the literature concerning the percentage of the different laparoscopic phenotypes. No data was

found describing the histological structure of uterine rudiments in MRKH patients. The existence of functional endometrium in those rudiments is seen controversially.

Materials and methods: From 2000 until March 2010, 192 MRKH patients underwent laparoscopically assisted creation of a neovagina. Of those 47 complained about cyclic lower abdominal pain. As a first step during surgical treatment the exact phenotype was described. If laparoscopic signs of a hematometra were apparent, recently those uterine horns were excised completely in symptomatic patients. In other cases wedge shaped biopsies were taken from one of the uterine rudiments ($n = 10$).

Results: The majority of patients showed uterine rudiments on both pelvic walls connected by a more or less prominent uterine strip. Using ultrasound in none of all 192 patients, using MRI only in 5 out of 31 patients endometrium could be clearly differentiated. In a very small number of patients unilateral hematometra was clinically suspected. In 5 of the excised tissue samples proliferating endometrium could be histologically identified. Three of the tissue samples contained structures resembling müllerian ducts.

Conclusions: Within uterine rudiments of MRKH patients proliferating endometrium and structures of müllerian ducts can be found. The existence of functional endometrium cannot be clinically predicted and therefore the excision of uterine rudiments should, in our opinion, so far only be performed in symptomatic patients.

PO-Onko 01.89

A delicate balance between growth and senescence in the development of uterine leiomyomas

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Objective: Uterine leiomyomas (UL) result from the monoclonal proliferation of myometrial cells. Despite their high prevalence surprisingly little is known about their pathogenesis. Oncogene-induced senescence (OIS) is a frequent phenomenon in premalignant lesions that leads to a growth arrest mainly by the activation of two potent growth-inhibitory pathways as represented by p16Ink4a and p19Arf. The relevance of OIS for the development of UL has not been addressed, but HMGA2, encoded by a major target gene of recurrent chromosomal abnormalities in UL, has been implicated in the repression of the Ink4a/Arf (CDKN2A) locus. This prompted us to examine if HMGA2 contributes to the growth of leiomyomas by repressing this locus.

Materials and methods: Cytogenetic subgroups of uterine leiomyomas were determined by conventional cytogenetics. Gene expression patterns within a possible OIS-network have been studied by quantitative RT-PCR.

Results: Contrary to the expectations, we were able to show that generally UL express significantly higher levels of p19Arf mRNA than myometrium and that UL with 12q14_15 rearrangements showed higher expression levels than UL with other cytogenetic aberrations. Furthermore, the finding of a significant correlation between the expressions of p19Arf and CDKN1A shows that p19Arf triggers senescence rather than apoptosis in UL. Furthermore, the expression levels of HMGA2, p19Arf, and CDKN1A were found to be correlated

with the size of the tumors, indicating that an enhanced growth potential is counterbalanced by the p19Arf pathway. Mechanistically, the UL may thus execute a program already present in their cell of origin, where it can be activated to protect the genome, for example, in the case of enhanced proliferation. This also explains the low frequency of malignant transformation towards leiomyosarcomas.

Conclusions: In summary, the results identify the p19Arf-TP53-CDKN1A pathway as a major player in the growth control and genomic stability of uterine fibroids.

PO-Onko 01.90

Fatal course of a necrotizing fasciitis during adjuvant chemotherapy in a patient with early-stage breast cancer

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Objective: Necrotizing fasciitis is a rare, but rapidly progressive, life-threatening bacterial infection of the soft tissue. Immunocompromised patients, e.g. due to chemotherapy, are more susceptible to develop this disease.

Materials and methods: We report a case of a 42-year-old woman with early-stage breast cancer who presented a fulminant course of necrotizing fasciitis during a chemotherapy nadir.

Results: The patient was admitted to our hospital with elevated body temperature, nausea and pain in the left gluteal region, presenting as a small perianal erythema. She had received her last cycle of chemotherapy following the regimen of FEC/DOC nine days before. Blood examination data indicated extreme leukopenia (white blood cell count 300/μL) and an elevated CRP level of 4.36 mg/dL. Following the diagnosis of cellulitis of unknown origin after exclusion of an acute abscess, she received antibiotic therapy and G-CSF injection. Within a few hours her pain worsened, and erythema continued to spread over the left gluteal region and vulva, showing hemorrhagic bullae. Because of this rapid deterioration the patient was transferred to the emergency department of the neighboring university hospital. The CT scan showed an extended phlegmonous inflammation with soft tissue gas from the left upper leg to the gluteus muscle, vulva, perineum and ventral abdominal wall, indicating necrotizing fasciitis. The patient was taken to the operating room immediately and aggressive surgical debridement of the infected tissue was done. Despite all intensive care measures taken, she died from septic and hemorrhagic shock with multi-organ failure about 18 h after first consulting our clinic.

Conclusions: Immunosuppression due to chemotherapy predisposes patients to potentially life-threatening bacterial infections. Because necrotizing fasciitis is rare and early aggressive treatment is most important for the outcome of these patients, we want to raise the awareness of this disease.

PO-Onko 01.91

Case report: endometrial stromal sarcoma

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Objective: We present the case of a patient with a uterus with fast-growing fibroids.

Materials and methods: Case report.

Results: Upon D&C, no sign of malignancy was found. The patient had a laparotomy with partial morcellation of the large uterus. Histologically, a low-malignant endometrial stromal sarcoma (ESS) was found. Two months later, we performed a staging laparoscopy with bilateral salpingoovarectomy. In the area where the ligamenta rotunda were cut during hysterectomy, a suspicious lesion could be shown on both sides. These lesions were completely removed. Histologically, cells of the ESS were found. Laparoscopically, no other lesions could be detected.

Conclusions: After morcellation of a low-malignant ESS during hysterectomy, we detected a spread of the ESS per continuitatem to the ligamenta rotunda, but not to the rest of the abdomen.

PO-Onko 01.92

Evaluation of RAD001 (everolimus) in the setting of resistance to letrozole or anastrozole in postmenopausal ER-positive breast cancer patients: BOLERO-2 trial

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Background:

- Studies detected the mTOR-inhibitor RAD001 as promising drug. The serin/threonine kinase mTOR is a key factor in the intracellular signaling network. It takes part in the regulation of proliferation, angiogenesis and cell metabolism. Defect regulation of mTOR is found in numerous tumours and leads to an increase of cell proliferation and angiogenesis.
- In case of resistance to endocrine therapies the mTOR signaling pathway is up-regulated due to crosstalks between signaling pathways.
- RAD001 is thought to increase the efficacy of endocrine therapies by inhibiting the mTOR signaling pathway.

Materials and methods: BOLERO-2 (Breast cancer trials of Oral Everolimus) is a randomised, double-blind, placebo-controlled study that evaluates the efficacy of RAD001 (everolimus) in combination with exemestane in postmenopausal women with ER-positive breast cancer who have local progress or distant metastases and who are resistant to letrozole or anastrozole. The patients receive either exemestane plus RAD001 or exemestane plus placebo. Therapy is continued until progression.

Objective: The primary objective is to show the advantage of exemestane plus RAD001 over exemestane alone in regard to the progression free survival. Secondary objectives are the evaluation of overall survival, response rates, time and duration of response, ECOG performance status, safety and side effects, quality of life as well as pharmacokinetics and serum estradiol levels. Furthermore, the effect of RAD001 on bone marrow and on markers of angiogenesis and apoptosis is investigated.

Results: Recruitment was initiated in autumn 2009. Worldwide, 705 patients are planned to be enrolled until the end of 2010. First results are expected in 2012. First toxicity analyses will be presented at the meeting.

PO-Onko 01.93

Evaluation of health care needs of women with disabilities at a specialty gynaecologic outpatient service

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Objective: about 445.000 disabled women live in Bavaria, who face a lot of unique challenges in accessing medical care. They report an insensitivity to their specific health care needs. More than healthy individuals disabled women have a wide array of health-related issues, including multiple concurrent co-morbidities, psychosocial issues, an socioeconomic concerns. Overall, they experience a fragmented health care delivery-system that often is inadequate in important areas such as reproductive health, post-reproductive health and sexuality. In order to address these issues, the Klinikum Dachau institutionalized an outpatient service for disabled women in the rooms of the hospital. The mission of this clinic is to develop a model of comprehensive women-centered care with special focus to their disabilities.

Materials and methods: From November 2007 to January 2010 we performed 263 examinations of disabled women, the majority of them had neurologic disorders such as cerebral palsy, multiple sclerosis, and paraplegia after injuries of the spine. We evaluated the reasons for their presentation and the special needs of gynaecologic care.

Results: Approximately 80% of the women with a median age of 39 years were severely disabled. They needed special assistance and a lifter for climbing the gynaecologic chair. Over 32% of the women presented uterine fibroids, endometriosis or ovarian cysts, irregular menstrual periods and reported deterioration of their neurologic conditions (esp. epilepsy) during menstruation. Together with the growing experience of the gynaecologists questions concerning sexuality and sexual help became more often. The ability to identify and survey a representative sample of disabled women and to develop a database linking demographic, physical disability, economic, and health care access information is a key step in implementing a cross-functional approach towards improving the level and scope of health-care for disabled women.

PO-Onko 01.94

Fertility preservation: patients characteristics, spectrum, efficacy and risks of applied preservation techniques in >1000 patients of the network

FertiPROTEKT

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Objective: Fertility preservation in young female patients before chemo- and radiotherapy has become a clinical and scientific topic of increasing interest. However, data concerning the characteristics of

patients that need to be counselled, the efficacy and risk of the applied procedures are still poor. We therefore analysed the registry of the network FertiPROTEKT (www.fertiprotekt.eu) which includes 69 infertility and oncology centers in Germany, Switzerland and Austria. **Materials and methods:** 1280 patients (age 15–40) were counselled regarding fertility preservation before cytotoxic therapies in 2007–2009. Depending on tumour characteristics, oncologic therapeutic regime and time till start of the chemotherapy, patients were treated by ovarian stimulation and cryopreservation of unfertilized and fertilized oocytes, cryopreservation of ovarian tissue, GnRH analogues and/or by transposition of the ovaries. We analysed the characteristics of the patients, spectrum of chosen techniques, number of aspirated and cryopreserved oocytes and complication rates.

Results: Among 1280 counselled patients, main diagnosis were breast cancer (34.8%) and hodgkins lymphoma (30.5%). 51.2% of the counselled and 49.4% of treated patients were between 26 and 35 years old and 86.1% of the counselled and 87.4% of the treated patients had no children. In 1168 patients 1568 fertility-preserving methods were undertaken: ovarian stimulation (14.1%), removal and cryopreservation of ovarian tissue (31.9%), GnRH analogues (52.5%) and/or transposition of the ovaries (1.5%). We further focused on the acute complication rates of these techniques. This was 2.9% in patients with ovarian stimulation and 0.4% in patients undergoing removal of ovarian tissue.

Conclusions: Fertility preservation programmes mainly involve women without children diagnosed breast cancer or hodgkins lymphoma. As the efficacy of the methods still is restricted, patients need careful counselling. Combination of the techniques should be considered to increase success rate, especially as the fertility preservation techniques can be applied with low risk.

PO-Onko 01.95

Retroperitoneal dissection of the ureter-uterinecrossing during TLH

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Objective: Total laparoscopic hysterectomies have the highest complication rate of all hysterectomies. Iatrogenic ureteral injuries during total laparoscopic hysterectomies are well-known complications and an important cause of morbidity. In attempting to prevent these injuries we do laparoscopic ureterolysis and dissection in every total laparoscopic hysterectomy.

Materials and methods: We performed about 100 laparoscopic hysterectomies since October 2009. After dissection of the round ligament, we open the retroperitoneum and identify the ureter and the uteri artery. Under Vision the uterine artery is ligated.

Conclusions: The procedure is feasible and we noticed a learning curve for the procedure. We expect a reduction of ureter injuries and diffuse bleedings. Furthermore the gynecologist is trained for the dissection of the retroperitoneum.

PO-Onko 01.96

Robotic instruments: feasibility of a new precision-drive articulating instruments for laparoscopy

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Objective: Endoscopic surgery compromises triangulation of the instruments. This drawback has recently been overcome with active

robots for endoscopic surgery. Nevertheless these robotic surgery devices are extremely expensive and need a large room and team training. The costs for maintenance and disposable parts are excessively high. We aimed at evaluating the feasibility of a new hand-held robotic endoscopic instrument for advanced laparoscopy.

Materials and methods: The Precision-Drive Articulating Instruments is a motor driven instrument which instrument tip can be rotated and triangulated with controls connected to the handle. The instruments are available as Monopolar Scissors, Needle Driver, L-hook cautery, Maryland Grasper and Bipolar Forceps. The instruments can be re-sterilized approximately ten times. The new device was used for 30 min on a pelvic trainer followed by 3 cadaver trials. We performed and videotaped TLH, pelvic and paraaortic lymphadenectomy to evaluate the feasibility and possible benefits.

Results: In three cadaver trials the procedures were accomplished. Total operating time took 20 h and the time decreased with experience. After the first 2 h the surgeons felt familiar with the controls and simultaneously used two Precision-Drive Articulating Instruments in each hands. Instrument movement and tissue handling was more precise compared to regular laparoscopy. Especially in advanced procedures, two articulating instruments helped to ease up the surgical performance. No instrument related complications were noted.

Conclusions: The help of robotic articulating instruments might enhance advanced laparoscopic surgical procedures. This new reusable Precision-Drive Articulating Instrument proved to be feasible and helped performing advanced laparoscopic procedures as TLH, pelvic and paraaortic lymphadenectomy.

PO-Onko 01.97

Minimal modifications of LSH technique significantly reduce postoperative spotting

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Objective: The objective of this study was to evaluate the excision of the endocervix during laparoscopic supracervical hysterectomy (LSH) with regard to postoperative cyclical bleeding.

Materials and methods: We evaluated 300 patients who underwent LSH for benign bleeding disorders. In 150 patients the uterus was transected from the cervix using a monopolar loop. In a second series of 150 patients a unipolar needle electrode was used for the uterine amputation and the excision of cervical canal.

Results: The mean duration of the transection was 65 s (lap-loop) versus 168 s (needle). There were no differences between both groups regarding mean age, body mass index and uterine weight. The excision of the endocervix was performed without any complications in 148 procedures. Histologic examination of the removed tissue revealed endocervical tissue in 83.3% ($n = 125$), endometrium in 9.4% ($n = 14$), cervico-isthmic mucosa in 3.3% ($n = 5$) and myometrium only in 4% ($n = 4$). All 300 patients were contacted 12-month postoperatively to inquire about bleeding status and 282 (94%) responded. In patients who underwent excision of the endocervix postoperative cyclical bleeding was significantly reduced compared to the control group (1.4% versus 10.7%).

Conclusions: The results of this study indicate that the routine excision of the endocervix is a quick safe procedure which allows a significant reduction of postoperative cyclical bleeding in patients who undergo LSH.v.

PO-Onko 01.98**First experiences with Umbilical Single Entry Laparoscopy (U-SEL) in adnexal surgery**

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Objective: Laparoscopic surgery was one of the important developments of the last 3 centuries in medicine. Now further progress to scarless surgery was introduced by attempts of performing surgical interventions in the abdomen cavity only through natural body orifices (NOTES). Preexisting embryonic scar of umbilicus is another option. The problem so far was handling of laparoscope and instruments through one single aperture. New technical developments try to overcome this restrictions and to enable surgery with invisible scars. **Materials and methods:** We performed 13 Umbilical Single Entry Laparoscopies (U-SEL). Procedure: pneumoperitoneum with Veress-needle, three tiny circular incisions at the inner border of the umbilicus, 3 small-headed single-use trocars, a 5 mm-60°-laparoscope, additional to conventional instruments used distally bendable instruments, for tissue extraction Tyco EndoCatch.

Results: Patients aged from 28 to 57. Number of different surgery indications were: sterilisation 5, sterility 2, polycystic ovaries 1, serous cystadenoma 1, dermoid cysts 3. Type of interventions: 3 unilateral adnexectomies, 1 cyst resection, 5 bilateral tubal coagulations, 1 ovarian drilling, 2 adhaesiolysis, 2 chromopertubations, 4 EndoCatch tissue removals. Additionally in 5 cases we used Valchev uterine manipulator. In one case secondary trocar incision in lower abdomen was necessary. 4 patients had additional interventions. Average surgical times were 20% longer. There were no intra- or postoperative complications, except one prolonged wound healing. Degree of patients satisfaction 4–6 weeks after surgery was high.

Conclusions: Adnexal surgery with method described is effective and safe and can be done with low complication rate. Use of special introductory devices and open umbilical incision is not necessary, same goes for traumatic removal of tissue through the vagina. Patients satisfaction with surgery results was high, particularly in case of absent visible scars. Further experiences must show if this method can also be used for interventions on the uterus.

PO-Onko 01.99**Non-pegylated liposomal doxorubicin as second-line therapy for patients with platinum-refractory recurrent ovarian cancer: preliminary data of a multicenter phase II trial**

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Objective: The prognosis of patients with platinum-refractory recurrent ovarian cancer is poor. There is a need for salvage therapies with anti-tumor activity and acceptable toxicity for maintaining quality of life. Non-pegylated liposomal doxorubicin (Myocet®) is a promising drug fulfilling these demands. We present preliminary data of a multicenter phase II trial to study tolerability of non-pegylated liposomal doxorubicin in second-line setting.

Materials and methods: Patients with platinum-refractory recurrent ovarian cancer received non-pegylated liposomal doxorubicin 75 mg/m² d1q22 and 60 mg/m² d1q22 after study dose modification, respectively. Toxicity was evaluated according to CTC-NCI criteria. Quality of life was assessed using the QoL-30-questionnaire. Response was evaluated every three therapy cycles by CT/MRI imaging and course of Ca 125.

Results: 29 patients have been enrolled in the trial so far. 153 cycles of non-pegylated liposomal doxorubicin have been administered altogether. 29 patients were evaluable for toxicity. ORR was 22 %, further activity data will be presented. Main non-hematologic toxicity was nausea and vomiting (16 patients grade I/II), whereas no PPE was observed. A grade III hematologic toxicity occurred in two patients. As a consequence, treatment schedule was modified to 60 mg/m² d1q22. After dose reduction no grade III/IV hematologic toxicity was noted. There were three patients with grade III allergic reactions on infusion that could uncomplicatedly be managed. Quality of life could be maintained during treatment according to the QoL-30-questionnaire analysis.

Conclusions: Non-pegylated liposomal doxorubicin administered in a treatment schedule with 60 mg/m² d1q22 seems to be well manageable without relevant hematotoxicity and with tolerable non-hematologic toxicity (mainly nausea). Further observations are needed to confirm these preliminary experiences on a larger number of patients.

PO-Onko 01.100**Role of secondary cytoreductive surgery in the 1st relapse of epithelial ovarian cancer: who will benefit?****An analysis of 240 consecutive patients**

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Objective: In contrast to primary ovarian-cancer (OC), the value of surgery in relapsed OC (ROC) remains unclear. Primary objective of the present study was to evaluate clinical predictors of operability and the impact of tumor-debulking surgery on overall-survival (OS) in patients with the first relapse of OC.

Materials and methods: All consecutive patients who underwent secondary tumor-debulking surgery due to the first OC-relapse were prospectively analyzed as based on a validated intraoperative documentation-tool. Logistic-regression-analysis was performed to identify independent predictors of mortality. Kaplan–Meier curves were calculated for OS.

Results: Between 9/2000 and 10/2008, 240 operations were evaluated; 184 patients (81.1%) were platinum-sensitive and 43 (20%) platinum-resistant. 47.5% of the patients had ascites, while 85.8% presented a multifocal tumor dissemination-pattern. In 53.8% a complete tumor resection was achieved; in another 24.2%, postoperative tumor-residuals were <1 cm. In multivariate analysis, no tumor resection (OR: 7.6; 95% CI: 2.9–19.9), ascites >500 ml (OR: 6.76; 95% CI: 3.77–12.1), platinum-resistance (OR: 3.1; 95% CI: 1.26–7.7) and initial FIGO-stage-IV (OR: 2.86; 95% CI: 1.16–7) were the most significant risk factors for mortality. Median OS was 42.3 months (95% CI: 24.37–60.2); 17.7 months (95% CI: 12.27–23.13) and 7.7 months (95% CI: 3.1–12.3) for patients with complete tumor-resection, tumor-residuals ≤1 cm and >1 cm, respectively (trend *p* value < 0.001).

Conclusions: Absence of ascites, platinum-sensitivity, initial FIGO-stage <IV and complete tumor-resection correlate with a significantly better long-term prognosis after ROC-surgery. However, a significant trend of continuously improving survival associated with increasing tumor reduction rates could be identified even in patients where a complete tumor resection is not achievable. Extrapelvic tumor-involvement, interval to primary diagnosis and age do not seem to have any independent impact on survival.

PO-Onko 01.101

The reverse transcriptase inhibitor Truvada induces cell cycle arrest in ovarian cancer cells

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Objective: The first HIV drug AZT (azidothymidine) was originally developed as a nucleotide antagonist for cancer treatment purposes, though AZT is currently being replaced for both HIV and cancer treatment by more effective, more specific, and more tolerable drugs. We re-evaluated current HIV nucleotide antagonists on their potential usefulness as anti-cancer drugs.

Materials and methods: Several currently applied HIV NRTIs were tested for their effect on ovarian cancer cells in cell culture by means of cell survival analysis (MTT assay) and cell cycle distribution analysis (FACScan).

Results: Truvada, a combination drug of emtricitabine (a cytidine analogue) and tenofovir (an adenine analogue), significantly induced cell cycle arrest in ovarian cancer cells. Inhibition of cell proliferation was associated with marked changes in the cell cycle distribution and cyclin expression. The Truvada constituents induced BRCA1 activation, suggesting DNA damage-induced by misincorporation of these nucleotide analogues into the DNA. Although the DNA damage and cell cycle arrest did not result in apoptosis, as confirmed by FACS analysis, pre-incubation of ovarian cancer cells with Truvada markedly enhanced the sensitivity of ovarian cancer cells to doxorubicin-mediated apoptosis.

Conclusions: The nucleotide reverse transcriptase inhibitor Truvada can induce cell cycle arrest in ovarian cancer cells that could be used to sensitize ovarian cancer cells to doxorubicin-mediated apoptosis.

PO-Onko 01.102

Evaluation of aberrant promoter methylation as prognostic marker for ovarian cancer

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Objective: Most cases of ovarian cancer (OvCa) are detected at a late stage thus exhibiting a poor prognosis. The outcome is related to the residual tumour mass and the chemotherapeutic response. To date, no reliable prognostic markers are available for OvCa. Therefore the aim of this pilot study is to evaluate the possible use of epigenetic aberrations as prognostic markers.

Materials and methods: Using methylation-specific PCR we retrospectively analyzed tumour samples for the promoter status of genes known to be methylated in OvCa. These genes are involved in proliferation, apoptosis or drug metabolism. Samples with complete clinical data ($n = 25$) were classified according to the progression free period (>18 months $n = 16$; <18 months $n = 9$). The groups were compared for clinical parameters and methylation frequencies.

Results: Both prognostic groups comprised pT3 tumours (mainly pT3c serous adenocarcinomas) and exhibited the same frequency of lymph node metastasis (67% vs. 69%) and an equal median age (59 and 59.5 years). As expected we detected a higher proportion of incomplete resected tumours within the poor prognosis group (67% vs. 38%) thus confirming the prognostic value of free resection margins. Three genes showed different hypermethylation frequencies in both groups: DAPK 33% vs. 68%; HIC1 56% vs. 38% and OPCML 22% vs. 56% in the poor vs. good prognosis group respectively. Although noticeable these differences do not reach statistical significance (Chi-square test) but should be explored further using larger patient cohorts.

Conclusion: The differential outcome-related promoter methylation of some genes points to the possible use of epigenetic aberrations as prognostic markers. At present we are using array-based genome-wide methylation analyses to identify genes differently methylated in patient groups exhibiting identical clinical characteristics beside the occurrence of relapse (median time to progression 841 days vs. median recurrence free time 1270 days).

PO-Onko 01.103

Ovar 2.9: A Phase III Study compare PLD-Doxorubicine-Carboplatin (CD) with Carboplatin-Paclitaxel (CP) in recurrent platin-sensible ovarian cancer. A GCIG study

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Objective: In this multicentric phase III study the combination of PEG-Doxorubicine (30 mg/m²) in combination with carboplatin AUC 5 d1 q 21d, compare with carboplatin and paclitaxel (175 mg/m²) d1 q 21d in the treatment of platin-sensible (>6 month after platin-taxan first-line therapy) ovarian cancer. 976 pts after 1st- or 2nd-line platinum-based therapy who had been pretreated with a taxane were randomized to either C-D. The primary endpoint was PFS. Randomization was stratified according to therapy-free interval of (1) 6–12 months (2) > 12 months. The patients characters were not different between the both arms. From 4/05 to 09/07, 976 pts were enrolled, 467 to C-D arm and 509 to C-P arm. Pt parameters were well balanced. 85% of C-D and 78% of C-P pts received ≥ 6 cycles. Median follow-up is 21mo. Overall survival is still too early to be reported ($n = 308$ deaths). This is the final analysis for PFS and toxicity.

Results: For the trial are below. In 35% of the cases was the time to progression 6 to 12 months. The adverse reaction rate in this group did not differ from the total population.

Conclusions: This trial, the largest in relapsed ovarian cancer, showed significant superiority of PLD-carboplatin combination in terms of PFS. In addition, compared to paclitaxel-carboplatin, PLD-carboplatin was well tolerated with lower rates of severe and long-lasting (neuropathy) toxicities.

Table 1. Results Ovar 2.9

	CD	CP
PFS in months 824 events $p = 0.005$	11.3 month	9.4 month
Neutropenia G3 or 4	35%	46%
Thrombocytopenia G3 or 4	16%	6%
Non-haematol. toxicity G3 or 4	28%	37%
Alopecia >G1	7%	84%
Hypersensitivity G > 2	5%	18%
Neuropathy G > 2	4%	27%
Skin G > 2	13%	2%
Mucositis G > 2	14%	7%
Stop of treatm. by toxicity reasons	7%	15%

PO-Onko 01.104

A new encouraging attempt for conservative treatment of lymphfistulas after lymphadenectomy during Staging laparotomy due to ovarian cancer with Somatostatin

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Objective: One severe complication of lymphadenectomy in ovarian cancer patients is postsurgical lymphfistulas causing chyloric ascites. Treatment of this complication ends often in surgical closure of the fistula. Here we report a new conservative treatment of such patients with Somatostatin. This hormone is produced naturally in the pancreas, in particular cells of the gastrointestinal and in the hypothalamus. A synthetic Somatostatin is Octreotid which inhibits the production of pancreas enzymes to treat severe bleedings of the gastrointestinal and postoperative fistulas of the pancreas and upper gastrointestinal.

Materials and methods: From January 2007 until April 2010 five patients with massive chylous ascites due to extended lymphadenectomy during Staging laparotomy because of ovarian cancer were treated with the peptide hormone Somatostatin at the department of Gynecology University Hospital Ulm, Germany. All patients had a higher stage of disease. They all had positive lymph nodes and underwent typical radical surgery including pelvic and paraaortal lymphadenectomy. Due to high loss of chylous ascites (average amount of 1000 ml per day) after surgery the patients received a treatment with either Bendatreotid 100 µg 3 × a day or Sandostatin 100 µg twice a day accompanied by parenteral nutrition due to fasting.

Results: At the end of the Somatostatin treatment average loss of fluid was 200 ml to a trace. Nutrition carence and parenteral nutrition was followed by a diet with fatfree, followed by fatpoor alimentation.

Conclusions: Patients who suffer from massive postoperative chylous ascites after lymphadenectomy often underwent another surgery to

treat the fistulas. Rational of the somatostatin treatment was to reduce lymphatic transport by reduction of fatty acid absorbtion in the small intestine to obtain natural closure of the fistula. In our case this treatment worked in all cancer patients so that an attempt with somatostatin should be made in patients suffering from fistulas after lymphadenectomy.

PO-Onko 01.105

Long time results of 178 women with Borderline ovarian cancer: results of the multicenter tumour register of the tumour centre of Berlin

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Borderline tumors of the ovary are rare and differ considerably from ovarian cancer in means of tumor biology and disease progression. However, the data base on this very rare entity and its clinical behaviour is weak. To improve this situation clinical data of the Tumour Center Berlin, a joined venture of eight cancer centers in Berlin have been analysed from 2005 to 2008 in regard to epidemiological data and outcome. The median age of patients with borderline tumor of the ovary was 50 years (range 12–90 years) and therefore significantly lower than ovarian cancer patients (range, p etc). The median follow-up period was 21 month (range 0–54). During the analysed period 6 patients died. The 3-year survival rate was 98% and therefore significantly higher than in patients with ovarian cancer. On the basis of these data a prospective data register has been established, which takes special concern in operative aspects and ways of fertility preservation.

PO-Onko 01.106

Malignant ovarian teratoma (neurogenous cell carcinoma) arising from mature dermoid cyst: a case report

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Objective: Teratomas are germ cell tumors which in gynaecology mostly occur to be benign (i.e., dermoid cyst). Malignant transformation in females is a rare event (<3%), while male teratomas commonly have malignant entity. The median age of patients with teratomas is during the reproductive years. Female patients who

undergo malignant transformation of a formerly benign dermoid cyst are often elderly women. Malignant teratomas have a very poor prognosis. We report about the rare situation of a severe malignant ovarian teratoma in a young female patient.

Results: This 37-year-old patient underwent a laparoscopic excision of a cyst of the left ovary in 04/09. Histology showed a mature teratoma. In June 2009, she recognized loss of life-efficiency and painless proceeding growth of abdominal girth. We performed explorative laparotomy with instantaneous section. Histopathologic results showed a big (dm 16 cm) premature malignant teratoma with hepatic and peritoneal metastases. Final result of tumor notation: pT3c, pN0 (0/37), pM1 (OTH), FIGO IV. For further therapy, the patient was treated with 4 chemotherapy series of Bleomycin, Etoposid und Cisplatin, which led to stable disease till 1/10. Despite that, in 2/10 a routine restaging showed new suspicious liver formations. We performed re-laparotomy for exploration and resection of these areas. Unfortunately, operation had to be abandoned due to inoperability. Further palliative chemotherapy in combination with autologous stem cell support is intended.

Conclusions: Due to the rare event of malignant transformation of teratomas, no standard guidelines exist for sufficient diagnosis and therapy. R0 surgery should be achieved, but often fails because of late and unspecific clinical symptoms. Regimes with Cisplatin, Vincristin, Mitomycin-C, Bleomycin have been tested, but overall and disease-free-survival dates were very poor. Due to the rarity of the disease, further investigations on this subject will be needed.

PO-Onko 01.107

Feasibility of bevacizumab and metronomic chemotherapy in heavily pre-treated patients with ovarian cancer (OC)

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Objective: Treatment of recurrent ovarian cancer is still challenging, since standard chemotherapy fails to demonstrate long term disease control in most cases. On the other hand preliminary data indicate, that bevacizumab is active and well tolerated in patients with heavily pre-treated ovarian cancer. Moreover there is some evidence that a so called metronomic (i.e. low dose continuous) application of orally available cytotoxics may increase their antiangiogenic properties.

Materials and methods: The aim of this retrospective analysis is to evaluate the feasibility and efficacy of bevacizumab given every 3 weeks (15 mg/kg), combined with orally administered cyclophosphamide (C) and methotrexate (M) according to a metronomic scheduling.

Results: To date a cohort of 17 patients is assessable for safety as a primary endpoint. All of them received prior chemotherapy with a median number of 3 regimens. Key toxicity included fatigue and gastrointestinal disorders such as nausea and vomiting. But no G3/4 side effects except neutropenia were observed. Efficacy analysis is pending.

Conclusions: Our data support that bevacizumab plus metronomic cyclophosphamide and methotrexate is a salvage therapy with a favourable toxicity profile even in heavily pre-treated patients with

ovarian cancer. An updated safety and efficacy analysis will be presented at the meeting.

PO-Onko 01.108

The effect of age at the time of diagnosis on stage and overall survival in patients with ovarian carcinoma: data of the Cancer Center Regensburg

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Objective: With an incidence of 9660 cases per year ovarian carcinoma represents the fifth most common malignancy in women in Germany. Many approaches in surgical technics and medication e.g. chemotherapy increased over all survival rates. In this study we evaluated the data of the Tumorzentrum Regensburg concerning age at the time of diagnosis as a prognostic factor for over all survival in patients with ovarian carcinoma.

Materials and methods: The Cancer Center Regensburg consists of a recording network including the University of Regensburg, 50 hospitals and 1100 medical practices in the region of Oberpfalz and Niederbayern. A retrospective analysis of the data from 1998–2005 with 581 patients was performed. Compared to the expected incidence in this region, this maps 75.9% of cases.

Results: The mean age at the time of diagnosis was 62.5 years for patients registered at the Cancer Center Regensburg compared to 68 years statewide (Germany). 50.4% of the patients were diagnosed at an age younger than 65. 132 patients were diagnosed with early stage disease FIGO I. 62.1% of these patients with favorable prognosis were diagnosed at an age younger than 65. After the median follow up period of 120 months more than 80% of these patients were alive. For patients older than 65 the median overall survival was 99.2 months. 41.3% of patients were diagnosed with stage FIGO III disease. The median overall survival for the cohort of patients older than 65 was 27.8 months, for patients between 50 and 65 51.5 months and for patients younger than 50 105 months.

Conclusions: Patients younger than 65 were more often diagnosed with early stage disease. Patients younger than 65 have a better outcome concerning median overall survival. In this study we could show that age is an important prognostic factor for overall survival in patients with ovarian carcinoma.

PO-Onko 01.109

Gene-therapy for pretreated chemo-resistant ovarian-cancer with a modified MDR1-driven oncolytic Adeno-Virus

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Objective: Ovarian cancer (OC) is the fourth most common cause of death in gynecologic malignancies. Ovarian cancer cells rapidly become chemo-resistant by multi drug resistance gene (MDR) 1 expression. Therefore conditionally replicating adenoviruses (CRAds) are a promising therapeutical approach. We designed a genetically

modified mdr-1 specific CRAd. Objective is the specific induction of oncolysis in chemo-resistant ovarian cancer cells.

Materials and methods: MDR1 expression in chemotherapy naïve and pretreated OC cell lines and primary patient cells was determined by RT-PCR. We designed Ad5/3MDR1, a fiber modified mdr1 targeted vector. Replication of and oncolysis by Ad5/3MDR1 was measured in naïve and chemotherapy pretreated OC cell lines and primary patient tumor cells. Specificity of the vector was confirmed in co-cultures of pretreated ovarian cancer cells with human fibroblasts. The in vivo efficiency of a combined chemo and gene-therapy administration was studied in an ovarian cancer xenograft mouse model.

Results: We could determine significant ($p < 0.05$) increased expression levels of MDR1 in pretreated ovarian cancer cell lines and primary patient tumors by RT-PCR. MDR1 promoter activity was significantly increased in chemo resistant ovarian cancer cell lines (7.3–11.5%) and primary patient tumor cells (8.8%–12.4%) compared to the ubiquitous expressed CMV control promoter. Normal human fibroblasts did not show any significant MDR1 promoter activity (<1%). Ad5/3MDR1 activity/replication was specific to chemo pretreated ovarian cancer cells in co-culture experiments with normal human fibroblasts. Ad5/3MDR1 treatment in an orthotopic peritoneal ovarian cancer mouse model showed a distinct survival benefit in compare to the control treatment group in vivo. Moreover by simultaneous administration of chemo and gene-therapy a synergistic treatment effect could be clearly shown

Conclusions: Ad5/3MDR1 is a promising candidate for gene-therapy of chemo resistant, metastatic ovarian cancer with huge impact for future clinical trials.

PO-Onko 01.110

Interval debulking surgery after induction chemotherapy for patients with advanced epithelial ovarian cancer: a retrospective analysis

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Objective: Primary complete debulking surgery is not always possible in the management of advanced stage epithelial ovarian cancer (EOC) due to anatomic, intraoperative or disease-related limitations. Induction chemotherapy is still under debate to play a role if surgery results in suboptimal debulking. To evaluate efficacy and complications of interval debulking surgery in patients with advanced ovarian cancer.

Materials and methods: All patients who underwent interval debulking surgery for advanced EOC between 2004 and 2009 at the Department of Gynecology and Obstetrics at Heidelberg University were included in this study. All data were obtained retrospectively by chart review. A descriptive statistical analysis was performed using SPSS 17.0 software.

Results: 26 patients were included in this study after primary surgery for EOC with suboptimal debulking. All patients were treated with 2–4 cycles of a platinum/taxane-based chemotherapy before secondary interval debulking surgery was performed. The toxicity of the chemotherapy was commonly moderate, only two patients developed grade III side effects, grade IV side effects did not appear. After induction chemotherapy all patients showed response to the treatment in terms of decreasing Ca 125 levels, furthermore, 12 patients showed response according to MRI or CT imaging. In 23/26 patients optimal

debulking (residual tumour masses < 1 cm) was possible after induction chemotherapy.

Conclusions: Interval debulking surgery after induction chemotherapy can be an option in the treatment of well selected patients with advanced EOC. In this retrospective study 23 of 26 patients reached a stage of resectability (<1 cm residual tumour masses) after 2–4 cycles of platinum/taxane-based chemotherapy. Future directions should focus on the definition of prognostic parameters to characterize suitable patients for this treatment concept.

Reproductive medicine

PO-Repro 01.01

Effect of host ovariectomy on the follicular developmental potential, morphological integrity and follow-up of xenografted adult ovarian tissue

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Objective: Ovarian cryopreservation allows for fertility preservation in cancer survivors. The developmental potential of ovarian tissue fragments may vary individually and depends on various factors. Here we used the common marmoset monkey as a non-human primate model to study the effects of host treatment and graft duration on the number and morphological integrity of unadvanced follicles in xenografted adult ovarian tissue.

Materials and methods: Ovarian tissues were collected from healthy adult marmosets. Tissue fragments were cryopreserved, stored for at least 4 weeks and thawed prior to grafting to ovariectomized and intact nude mice. Grafts were retrieved after 2, 4 and 8 weeks. Following exgrafting, the tissue was routinely processed and evaluated for number and morphological appearance of follicles.

Results: Following xenografting of cryopreserved ovarian tissue fragments, the mean number of primordial follicles decreases dramatically 2 weeks post grafting (39.1 ± 4.7 vs 6.9 ± 0.7 , $p < 0.05$), and then remains unchanged after 4 weeks (6.9 ± 2.2) and 8 weeks (4.8 ± 0.5), respectively. This effect, however, is limited to the subclass of primordial follicles; the population of primary follicles remains stable after grafting when compared to tissues prior to grafting. No significant difference is shown between fresh and cryopreserved tissues regarding the relative number of primordial follicles; however, the proportion of morphologically normal unadvanced follicles is significantly lower in cryopreserved tissues post grafting. Host ovariectomy does not change the ratio between primordial and primary follicles, but allows for a higher mean unadvanced follicle number in grafted fresh tissues ($24.8 \pm 3.2\%$ vs $12.5 \pm 3.6\%$, $p < 0.05$). More advanced follicular stages up to antral follicles were documented.

Conclusions: Initial follicular loss following xenografting is consolidated over an extended grafting period, and graft sustainment is positively influenced by host ovariectomy. (Funded by the German Cancer Aid)

PO-Repro 01.02**Ovarian tissue cryopreservation and oocyte in vitro maturation: effect on the meiotic competence of the murine oocyte**

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Objective: Ovarian tissue cryobanking is a new and promising technique to preserve women's fertility compromised by gonadotoxic therapies. Autologous grafting of frozen ovarian tissue exposes patients to the potential risk of reseeded vital tumor cells. In contrast, the combination of cryopreservation followed by tissue and oocyte in vitro maturation (IVM) might be a safer and therefore preferable alternative for oncologic patients. The aim of this study was to investigate the effect of ovarian tissue cryopreservation on the oocyte's meiotic competence in a mouse model.

Materials and methods: Ovaries were collected from 7- to 17-week-old female C57BL/6 mice ($n = 9$) and cryopreserved following a slow freezing protocol using DMSO, ethylene glycol and sucrose as cryoprotectants. After thawing, oocytes were mechanically isolated with 27G needles and in vitro maturation (IVM) of oocytes was performed for 16–20 h under administration of 1.5 mIU/ml LH and 1.5 mIU/ml FSH. Subsequently, oocytes were classified using an inverted microscope according to their meiotic stage as germinal vesicle (GV), germinal vesicle break down (GVBD) and metaphase II (MII). Oocytes isolated from non-cryopreserved ovaries from comparable mice served as controls.

Results: The number of GV oocytes resuming meiotic development was similar between the two groups. After cryopreservation, 79 out of 90 oocytes (88%) resumed meiosis (GVBD and MII), compared to 114 out of 124 (92%) oocytes, which matured after isolation from fresh tissue, without previous stimulation- or superovulation-treatment of the animals.

Conclusions: Isolation and IVM of murine oocytes derived from cryopreserved ovarian tissue was successfully performed and showed no major difference in meiotic resumption compared to controls. Further investigations evaluating fertilization rates of these in vitro matured oocytes need to be performed.

PO-Repro 01.03**Analysis of PKA-dependent signal transduction in human granulosa cells after substitution of LH with a TaqMan[®] real time Mikro-Array**

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Objective: Gonadotropins are responsible for cyclic transformations in the ovary. Follicle stimulating hormone and luteinizing hormone (FSH and LH) bind to G-protein-coupled receptors and the activation of adenylatecyclase leads to an increase of intracellular cyclic AMP (cAMP). cAMP controls and induces the cAMP-dependent protein-kinase A (PKA) which is important for the regulation of the cell cycle. To gain further information about the signal transduction in human granulosa cells (GCs) after the LH-Peak we performed a PKA-specific Mikro-Array. Analysis were made on mRNA-level.

Materials and methods: GCs were collected from seven patients undergoing in-vitro-fertilization at the I. Department of Obstetrics and Gynaecology, Innenstadt, Maistrasse, Ludwig-Maximilians-University. After seven days of cultivation, 100 mIU/ml r-LH or

plain culture-medium was substituted. Isolation of mRNA was performed after 2 h and mRNA-concentrations were measured photometrically. 300 ng of each culture were pooled and put into a Real-Time (TaqMan[®] Mikro-Array analysing 92 PKA-dependent genes.

Results: Out of a number of 92 simultaneously investigated G-protein-receptor related genes, substitution of 100 mIU/ml r-LH lead to an inhibition of mRNA under 0.6 fold expression compared to the unstimulated control in eight genes. Six genes were upregulated at least 2 fold compared to unstimulated controls. Inhibition of the mRNA for G-protein-coupled receptors corticoreleasing hormone receptor (CRFR) and glucagonreceptor (GCG) could be detected.

Conclusions: LH and FSH bind to G-protein-coupled receptors on their target cells. The results of our study show that high doses of LH inhibit G-protein-coupled receptors in human GCs. Interestingly; CRFR which is involved in stress actions is inhibited. Furthermore, GCGR which is essential for the blood sugar concentration is less expressed after stimulation with LH.

PO-Repro 01.04**Mannose-binding lectin 2 (MBL2) gene polymorphisms and their impact on pregnancy outcome**

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Objective: Genetically determined deficiency of plasma mannose-binding lectin 2 has been shown to predispose to infectious and inflammatory diseases. Low MBL levels have been reported to have negative impact on pregnancy outcome in women with recurrent miscarriages (RM). We investigated the association of MBL2 genotypes and pregnancy outcome in RM-patients.

Materials and methods: 126 women (>2 idiopathic miscarriages) were analyzed for genetic polymorphisms in the MBL2 gene, which largely determine serum MBL levels. 57 patients suffered from early RM (ERM) <14th week of gestation and 69 from late RM (LRM) > 14th week of gestation. LRM were further subdivided into those with clinical signs of infection ($n = 23$) and idiopathic ($n = 46$). 124 healthy women with >2 uncomplicated deliveries served as controls. Genotypes were determined by DNA sequence analysis and categorized into high- (HYA/HYA, LYA/HYA, LYA/LYA, HYA/LXA, LYA/LXA), intermediate- (HYA/0, LYA/0, LXA/LXA), and low-producing genotypes (0/0, 0/LXA).

Results: Our results show no significant difference in frequency of high-, intermediate-, and low-producing MBL2 genotypes between RM-patients and controls. High genotypes were found in 46.8% RM-patients, 43.8% ERM, 49.3% LRM, and 45.9% controls (n.s). Intermediate genotypes were present in 34.9% RM, 38.6% ERM, 31.9% LRM, and 35.5% controls (n.s). Low genotypes were detected in 18.3% RM, 17.5% ERM, 18.8% LRM, and 18.5% controls (n.s). We also did not detect any differences in the frequency of the various MBL2 genotypes in the two subgroups of LRM patients. Compared with the literature, our analyses demonstrated a higher prevalence of the low genotypes in controls (18.5%) than previously reported for European females (6–12%).

Conclusions: We failed to confirm the reported increased prevalence of low-producing MBL2 genotypes in idiopathic LRM as well as in LRM with signs of infection. This might be explained by the high frequency of the low genotypes in our controls.

PO-Repro 01.05

In vitro maturation: 5-year experience in Heidelberg

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Objective: Although several patients may benefit from reduced FSH application, in vitro maturation (IVM) belongs to the rare treatment options in assisted reproduction. We summarize our 5-year IVM experience at the University of Heidelberg.

Materials and methods: Women with polycystic ovary syndrome (PCOS) as well as patients after ovarian hyperstimulation syndrome (OHSS) were offered IVM. Stimulation started between day 3–10 of the menstrual cycle and FSH dosage was 125 IU/day over 3 days. Ovulation was induced on the third day of FSH injection or one day after and oocyte retrieval was performed 33–38 h later. Oocytes were cultivated for 24 h in IVM medium. Fertilisation took place one day after oocyte retrieval and embryo transfer two days afterwards.

Results: From February 2005 to December 2009, 115 patients were included and 215 oocyte retrievals (ICSI ($n = 125$, 59%), IVF ($n = 73$, 34.4%)) with 177 embryo transfers performed. Main reasons for IVM were: PCOS (64.6%) and OHSS (15.0%). Mean number of oocytes was 8.9/oocyte retrieval with 5.9 (64%) becoming matured, 2.8 (45.1%) getting fertilized and 2.1 being transferred. Pregnancy rate per transfer was 15.3% ($n = 27$), with $n = 12$ live births (6.8%), $n = 2$ ongoing pregnancies (1.1%), $n = 4$ abortions (2.3%) and $n = 9$ biochemical pregnancies (5.1%). In 61 cases, fertilized oocytes were frozen and 32 cryotransfers were performed resulting in 3 pregnancies (1 biochemical, 1 live birth, 1 ongoing pregnancy).

Conclusions: Within the last 5 years, 115 patients with PCOS or OHSS underwent IVM at our department. Although pregnancy rate was low, IVM is very convenient for patients due to low FSH dosages and rare appointments implicating low cost rates.

PO-Repro 01.06

Postpubertal mumps orchitis: a case report

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Objective: The overall reproductive ability of men and women is decreasing with age, leading to an increasing need for reproductive procedures (e.g. IVF, ICSI, IUI). Therefore age-related degenerative changes of the reproductive system should be an important aspect of anti-aging research. Reasons why a couple may not have children are manifold and even unexpected some times, as our case report shows.

Materials and methods: At first the cause of infertility in a married couple (male 57 years, female 37 years) was not obvious, since there were only normal findings for the female and the male partner had already two adult children out of his first marriage. However, sperm analysis showed a complete azoospermia. The reason was not as expected, an age related azoospermia, but an epidemic parotitis (mumps), which the male received at the age of 32, years after his two children were born. Mumps is known to cause sterility in men; a postpubertal mumps orchitis is associated in 20–40% of the males with azoospermia. In such cases regular infertility treatment is not successful. However, testicular sperm extraction (TESE) could provide some mobile sperms, enabling Intracytoplasmic sperm injection

(ICSI). The case observed, emphasizes two aspects: Firstly, complex reproductive medicine is a powerful tool to overcome severe infertility problems, and secondly, simple, but careful anamnesis of the individual case is important, to exclude misinterpretations.

PO-Repro 01.07

Molecular effects of heparins on the human endometrium are not directly related to the coagulation system

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Objective: We have demonstrated that heparins modulate the decidualization of human endometrial stromal cells (ESCs) and the action of the inflammatory cytokines IFN (interferon)- γ and TNF (tumor necrosis factor)- α . The molecular mechanisms of these heparin effects are still unknown and it remains open, whether they are associated with classical anticoagulation or not. In the present study we therefore further specified this non-coagulatory mode of action of unfractionated heparin and the clinically well established LMWHs (low molecular weight heparins) in human ESCs in vitro.

Materials and methods: Human ESCs derived from hysterectomy specimens were decidualized in vitro using 17 β -estradiol and progesterone. The cells were incubated with IFN- γ , TNF- α , heparin, dalteparin, enoxaparin, certoparin, dextran sulfate or fondaparinux. The secretion of IGF (insulin-like growth factor)-I was measured by ELISA. IL (interleukin)-6 mRNA expression was determined using real-time RT-PCR. The activation (phosphorylation) of STAT (signal transducer and activator of transcription)-1 was detected by in-cell western assay.

Results: During early decidualization of ESCs heparin enhanced the up-regulation of IGF-I secretion. This dose dependent effect showed a characteristic bell-shaped curve. Similar effects were mimicked by dextran sulfate but not by fondaparinux. The LMWHs certoparin, dalteparin and enoxaparin also showed an augmentation of the IGF-I secretion. Comparable effects of the mentioned agents were seen on TNF- α induced IL-6 as well as IFN- γ mediated activation of STAT-1.

Conclusions: Heparin and LMWHs have an influence on the cell biology of the human endometrium. These heparin effects seem to be independent of their classical anticoagulatory function but one could presume a dependency on the electric charge of the molecules. Therefore heparin and LMWHs seem to be an interesting pharmacological approach for the therapy of endometrial pathologies. Especially the effects independent of anticoagulation should be further taken into account.

PO-Repro 01.08

Antigen-presenting cells in pregnant and non pregnant human myometrium

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Objective: Inflammatory cells and mediators play a crucial role in human parturition. Different populations of leukocytes invade cervix, placenta and fetal membranes as well as the myometrium. Numerous studies have described the decidual immune cell population in preg-

nant and non-pregnant endometrium. However, little is known about the presence of immune cells in human myometrium which is in direct contact to the endometrium.

Materials and methods: We herein analyzed a broad spectrum of immune cells in human myometrium comparing tissue samples from non-pregnant ($n = 8$) and pregnant ($n = 10$) uteri. Applying immunohistochemistry and a panel of antibodies which are specific for T-cells, monocytes, NK-cells, B-cells and antigen presenting cells (CD4, CD8, CD14, CD15, CD16, CD19, CD56, CD68, CD83, HLA-DR, DC-Sign, mastcelltryptase), we characterized the immune cell population of human myometrium.

Results: A significantly higher number of CD14, CD15, CD16, DC-SIGN as well as CD4 positive cells was found in myometrium of pregnant compared to non-pregnant uteri, while mast cells were significantly reduced in pregnant myometrium.

Conclusions: All markers found increased in pregnant myometrium indicate monocyte/macrophage lineage cells and thus suggest a possible involvement of these cells in healthy pregnancy maintenance. Monocytes/Macrophages might produce a microenvironment that permits a controlled invasion of trophoblast cells into the myometrium while preventing a rejection of the semiallogenic conceptus and providing an important barrier against invading pathogens.

PO-Repro 01.09

Cryopreservation of oocytes before chemotherapy in a patient with breast cancer and intrauterine pregnancy

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Objective: Increasing survival rates of cancer patients and progress in reproductive medicine have resulted in the development of different options of fertility preservation: ovarian stimulation and freezing of fertilized and unfertilized oocytes, ovarian tissue banking, in vitro maturation and medicinal methods like GnRH-agonists during chemotherapy. Short protocol with GnRH-antagonists is usually used for stimulation. If the tumor is oestrogen-dependent, stimulation may be combined with 5 mg letrozol daily applied simultaneously with the gonadotropin.

Materials and methods: A 38-year old gravida 2 para 0 with newly diagnosed breast cancer pT2, pN2 (6/12), G2, L1, M0, ER 10/12, PR 10/12, Her2neu 1+ wished to cryopreserve her unfertilized oocytes before chemotherapy (3× FEC, 3× Paclitaxel). A breast ablation had already been performed. We immediately started stimulation in midluteal phase on cycle day 26 with 300 IE HMG, GnRH-antagonists and letrozol 2× 250 mg daily during the first five days of stimulation. Ovulation was induced on day 11 (10,000 IE HCG, 0.2 mg Triptorelin). 17 oocytes had been aspirated and cryopreserved with slow freezing. During stimulation luteolysis did surprisingly not occur, so a pregnancy test was performed on day 11 (HCG 3,493 mIU/ml). Sonography showed an intrauterine pregnancy (5+0 SSW). The aspirated follicles showed a normal morphology (metaphase II) despite high progesterone levels during stimulation. The patient decided to interrupt her pregnancy before she started chemotherapy.

Conclusions: This case shows a successful stimulation with cryopreservation of oocytes during pregnancy which had been conceived in the same cycle before stimulation was started in midluteal phase. Stimulation was performed in the shortest possible time maintaining lowest possible levels of estradiol. The quality of oocytes had not been influenced negatively by high progesterone levels in pregnancy.

PO-Repro 01.10

The moral status of the embryo: in the light of David Hume's moral sentimentalism

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The current study applies the ethics of moral sentimentalism, based on the reflections of David Hume (1711–1767), a Scottish philosopher of the age of enlightenment on the moral status of the embryo. The fact that in Germany abortion is common and socially accepted, while at the same time preimplantation diagnostics (PID) is forbidden, represents a paradox, which we try to explain resorting to the ethical concept of moral sentimentalism. David Hume observed that moral reflections and decisions in humans are rather driven by the passions than by reason. This speculative concept is supported by recently published neuroimaging studies. Scientific innovations are often seen with distrust, due to modern myths, such as Mary Shelley's Frankenstein or Aldous Huxley's "Brave New World". Secondly, our Christian background causes a special sensitivity towards science concerning the beginnings of life. Last but not least, in Germany due to our particular history, genetic testing has a negative connotation. Thus, a scientific innovation, such as PID, frequently induces a vague feeling of anxiety in the spectator. Accordingly, such new methods are at first morally rejected by the majority. However, by sheer force of habit these innovations are frequently meet with indifference and finally morally approved in the course of time. This development could be observed in different areas of medicine, such as heart transplant and in vitro fertilization. According to David Hume's ethical concept the different moral value of the embryo in the uterus and in the petri dish are based on different stages of moral adaption. Thus, moral sentimentalism cannot establish the moral status of the embryo as a fixed constant. By clarifying, that our moral judgement does not base exclusively on reason and rationality, it can however raise the ongoing debate paradoxically to a more rational level.

PO-Repro 01.11

Heparin has anti-inflammatory effects on the human endometrium by interacting with TNF- α - and IFN- γ -signaling

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Objective: The pro-inflammatory cytokines tumor necrosis factor (TNF)- α and interferon (IFN)- γ are secreted by immune cells and have an influence on the implantation of the embryo in the endometrium. Both mediators seem to play an essential role in the pathophysiology of repeated implantation failure and habitual miscarriages. The use of heparins might be beneficial in the prophylaxis and treatment of these implantation disorders. We therefore investigated whether heparin has a regulatory effect on TNF- α - and IFN- γ -signaling in human endometrial stromal cells (ESCs) in vitro.

Materials and methods: Human ESCs were isolated from hysterectomy specimens and decidualized by the use of 17 β -estradiol and progesterone. After incubating the cells with TNF- α or IFN- γ with/without heparin the activation of the connected signaling pathways was analysed by flow cytometry (I (inhibitor of) κ -B α , IFN- γ R (receptor)), transcription-factor-assays and confocal microscopy (NF (nuclear factor)- κ B), In-Cell-Western-assays (STAT (signal transducer and activator of transcription)-1-phosphorylation) as well as real-time RT-PCR (IRF (IFN-response-factor)-1 and Nmi (N-myc-interactor)).

Results: In human ESCs heparin had no influence on the TNF- α -mediated degradation of cytoplasmatic I κ B α , but inhibited the transcriptional activity of NF- κ B in the nucleus. However, the nuclear translocation of activated NF- κ B was not disturbed by heparin. Heparin dose-dependently inhibited the IFN- γ -induced phosphorylation of STAT-1 and the consecutive induction of the IRF-1 gene. Thereby heparin interfered with the binding of IFN- γ to the cell surface of ESCs. The expression of the IFN- γ R was not regulated by heparin.

Conclusions: Heparin inhibits signaling pathways of inflammatory cytokines (TNF- α and IFN- γ) in human ESCs via different mechanisms. These molecular observations further underline the role of heparin beyond its classical anti-coagulatory effects. In daily practice heparin and its derivatives might be interesting anti-inflammatory agents for the improvement of implantation rates in reproductive medicine as well as for the prophylaxis of habitual miscarriages.

PO-Repro 01.12

Outcome of frozen-thawed embryo transfer: artificial versus spontaneous cycle

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Objective: To evaluate the outcome of frozen-thawed Embryo transfer (FET) a retrospective analysis was performed comparing the pregnancy rates of patients undergoing FET either in a spontaneous or an artificial cycle.

Materials and methods: Data of 203 patients undergoing FET at the Department of Endocrinology and Reproduction in Ulm between 2000 and 2008 were included, retrospectively. 148 women received FET with spontaneous cycle (group A) and 55 women with an artificial cycle (group B). Subgroup analysis was performed in the cohort receiving two embryos in total; $n = 93$ spontaneous cycle (group A1), $n = 36$ artificial cycle (group B1). Pregnancy rates, endometrial thickness, Estrogen (E2)-, Progesteron (P)- and Luteal Hormone (LH) Levels were measured.

Results: In the total cohort, pregnancy rate was 34.5% and 21.8% in the group A and B, respectively without statistical significance; $p = 0.084$. There was no difference in endometrial thickness or P-Level, but as well LH-level as E2-level were significantly higher in group B than in group A ($p < 0.0001$). In the subgroup analysis, pregnancy rate was 37.6% and 27.78% in group A1 and B1, respectively; $p = 0.2921$. Again there was no difference in endometrial thickness or P-level. LH-level and E2-level were significantly higher in group B1 than in group A1; $p = 0.0068$ and < 0.0001 respectively.

Conclusions: Our retrospective study shows a trend towards higher pregnancy rates in spontaneous FET compared to artificial FET despite lower estradiol levels and lower endometrial thickness. Large randomized controlled trials are needed to confirm this trend.

PO-Repro 01.13

Cumulus cell glycodelin relates to oocyte maturation

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Objective: The protein Glycodelin (Gd) shows inhibitory or enhancing effects on the fertilization process depending on its glycosylation pattern. Only the mature oocyte has the best chance to become

fertilized, and the surrounding cumulus oophorus cells must create an optimal microenvironment for the passage of the spermatozoa. Therefore the aim of this study was to evaluate the relationship of egg maturity and the amount of Gd in cumulus cells.

Materials and methods: Cumulus cell samples derived from 75 individually denuded cumulus oophorus complexes (COCs) of 14 patients attending our clinic for ICSI treatment were stained for Gd. A Gd-staining index (Gd-SI) per oocyte for at least 100 cumulus cells was calculated. The maturity characteristics of the COC and the morphology of the corresponding oocyte after hyaluronidase treatment were evaluated, and at least the calculation of the mean Gd-SIs for the premature, mature and post-mature stages followed.

Results: The Gd-SIs are related to egg maturity, since Gd-SIs were the lowest in cumulus cells from premature stages, and during oocyte maturation the Gd-SIs increased ($P < 0.05$).

Conclusions: The difference in Gd-SIs of oocytes with morphological features of prematurity, maturity and postmaturity indicates that there is a relationship between oocyte maturity and the amount of Gd in the corresponding COC.

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Endocrinology

PO-Endo 02.01

The “special” situation of genetic testing and prenatal diagnosis in Germany: remarks on the influence of history

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The situation in Germany is quite different to that in Europe and the USA. The legal regulation on prenatal diagnosis and genetic testing are ‘special’. In law and in fact this is determined by the act on abortion (§§ 218, 1976, then 1995), on protection of embryos (Embryonenschutzgesetz, 1990, then 2001) and on genetic testing (Gendiagnostikgesetz, 2009). Those regulations are stricter than in other countries. I.e. preimplantation diagnosis (PID) is forbidden.

Objective: What are the reasons for those strict legal regulations?

Results: Since 1945 we have in Germany a lively debate on questions of genetic testing and prenatal diagnosis. This is dominated on the one side by the organisation of disabled persons (Aktion Mensch) and on the other hand by persons claiming their right of self-determination and also freedom of research. Till today this discussion is going on and the arguments of both sides are reflected in a heterogeneous legislation. Some of the reasons are

- The reference to the Third Reich till today works as discussion stopper
- Personal continuities in science and politics
- Consequences of KZ medical experimentation in the 1940s
- Necessity to break with Third Reich
- Increasing Focus on ethical implications of diagnosis and therapy

Conclusions: The situation in Germany is mainly determined by historical experiences and reasons. But there is decreasing knowledge about the situation in the Third Reich, i.e. of the politics of eugenics and euthanasia. So it is hardly possible to discuss without any reservations about genetic testing and prenatal diagnosis in Germany: The influence of history is dominating the discussion about genetic testing and prenatal diagnosis direct or indirect.

PO-Endo 02.02**Selective venous catheterization led to the diagnosis of an ovarian hilus cell tumor**

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Objective: We present a case of a 74 year old patient with increased sexual desire who had elevated serum testosterone levels without further symptoms of hyperandrogenism.

Materials and methods: For diagnosis, ultrasound and CT-examinations, laboratory analyses, selective venous catheterization and, after surgical removal of the ovaries, histopathological evaluations have been carried out.

Results: While pelvic ultrasonography and CT were not successful, a selective venous catheterization led to the diagnosis of an occult tumor of the right ovary. Laparoscopic bilateral salpingoophorectomy was performed, and histopathological examination revealed a hilus cell tumor of 7 mm in diameter. After removal of the ovaries, the serum levels of testosterone returned rapidly to the normal range.

Conclusions: Although rare, in postmenopausal women with high testosterone serum levels, a hilus cell tumor should be taken into consideration as differential diagnosis. The performance of selective catheterization is a valid approach to identify the origin of elevated androgen production.

PO-Endo 02.03**Inhibin A, Inhibin B and Activin A in patients with oral contraceptives: are these markers of residual ovarian function?**

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Objective: To assess whether the secretion of Inhibin A, Inhibin B and Activin A changes during the therapy with hormonal contraceptives and to evaluate if these changes have a clinical relevance for therapy.

Materials and methods: 18 healthy females aged 21 to 25 with normal body weight, regular menstrual periods and an uneventful gynaecologic history were divided into two groups. Group 1 (9 patients) was given no medication (control group). Group 2 (9 patients) was given a monophasic combined oral contraceptive (OC). We obtained whole blood samples on cycle day 1, 4, 8, 12, 16, 24 and 28 of menstrual period from each patient and measured hFSH, hLH, progesterone, estradiol, testosterone and prolactin by Beckmann Access Immunoassay and Inhibin A, Inhibin B and Activin A by ELISA Oxford Bioinnovation. Statistical analysis was performed with SPSS and Wilcoxon Test, Friedman Test, Spearman correlation and Bonferroni adjustment.

Results: Group 2 showed a breakup of cyclic secretion of Inhibin A, Inhibin B and Inhibin Pro- α -C. Inhibin A and Inhibin Pro- α -C were suppressed by OC. In group 2, Inhibin B showed an increase by day 4 (higher than control group) and a decrease by day 7. No difference between the two groups could be detected for Activin.

Conclusions: There is a significant effect of OC on ovarian proteo-hormones: suppression of Inhibin A, Inhibin B and Inhibin Pro- α -C as well as a change in secretion pattern. As we showed a suppression of Inhibin A, B and also Inhibin Pro- α -C, there must be not only a suppression of hormonal release, but also of hormonal synthesis, caused by missing follicular development. Not all follicular endocrine activity is suppressed: We detected an increase of Inhibin B by day 4. This effect could be used to determine an individual minimal hormonal level for a safe contraconceptive action of OCs.

PO-Endo 02.04**The predictive value of antiTPO-antibodies for Hashimoto's thyroiditis and its relevance in gynecology**

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Objective: Hashimoto's thyroiditis (HT) is the most prevalent cause of subclinical or overt hypothyroidism and is known to affect female health issues such as fertility, pregnancy outcome and others negatively. It is mostly defined by elevated levels of auto-antibodies against thyroid peroxidase (antiTPO); based on these, patients are treated. The aim of the study was to evaluate the predictive value of antiTPO for the presence of HT as confirmed by histologic examinations in women undergoing thyroidectomy.

Materials and methods: In a preliminary analysis of a prospective study 320 women undergoing thyroidectomy were included. Preoperative antiTPO-levels (normal range: 0-63 IU/mL) were compared to histological results including thyroiditis grading. In addition, all patients answered a questionnaire about general symptoms and female health.

Results: A total of 55 patients (17.2%) revealed elevated preoperative antiTPO-levels. Histological signs of thyroiditis were found in 130 patients (40.6%). Elevated antiTPO-levels were significantly associated with histological result of thyroiditis ($p < 0.01$) with positive and negative predictive values, sensitivity and specificity of 90.9, 69.8, 38.5 and 97.4%, respectively. Thyroiditis grading was positively associated with antiTPO-levels ($p < 0.01$; $r = 0.579$). All patients showed euthyroid preoperative TSH-, fT3- and fT4-levels. Several health issues were significantly associated with increased antiTPO-levels such as early miscarriage, chronic irritability and history of breast cancer ($p < 0.01$).

Conclusions: Normal antiTPO levels do not rule out lymphocytic thyroid inflammation. HT is diagnosed serologically in only about 40%. AntiTPO-positive patients form a group at risk for several female health issues, who need extensive gynecological and thyreological care.

PO-Endo 02.05**Effects of estrogenic compounds, SERMs and SPRMs on gene-expression biomarkers in human endometrial Ishikawa cells**

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Objective: Human endometrial function is controlled by 17 β -estradiol and progesterone as well as many local mediators. Its functions can be also altered by desired effects (e.g. contraceptives) or undesirable side-effects of drugs (e.g. tamoxifen) and environmental chemicals (e.g. pesticides). Besides pure receptor agonists and antagonists selective estrogen receptor modulators (SERMs) and selective progesterone receptor modulators (SPRMs) are in the focus of current research. Many endometrium-specific effects can only insufficiently be assessed in animals due to species differences. Here we describe a cell culture model to assess functional effects of exogenous compounds on human endometrium *in vitro*.

Materials and methods: The human endometrial Ishikawa cell line was applied to study effects of compounds interacting with estrogen and progesterone receptors in a tissue-specific model. Test compounds were applied for 24–48 h. Reverse transcription quantitative real-time PCR (RT-qPCR) with assays from the Universal Probe Library (UPL; Roche) was used as highly sensitive and flexible method to detect chemical effects on the expression pre-selected molecular biomarkers (e.g. progesterone receptor mRNA).

Results: In Ishikawa cells sigmoidal dose-response curves and EC₅₀ values were established for up-regulation of PR mRNA by 17 β -estradiol, diethylstilbestrol and the xenoestrogens bisphenol A and nonylphenol. 17 β -estradiol and DES acted as strong and bisphenol A and nonylphenol as weak estrogens, respectively (EC₅₀ approx. 10⁻¹¹ M vs. 10⁻⁷ M). Endometrial effects of SERMs (4-hydroxytamoxifen, raloxifene) and SPRMs (RU 486) were investigated in the presence of the respective agonists. The PR-down-regulating effects of progesterone were antagonized by RU 486 in a dose-dependent manner. Results were confirmed on the protein level by Western Blotting.

Conclusions: Our findings demonstrate that the Ishikawa cell line is a suitable model to predict tissue-specific endometrial effects of drugs and chemicals by a highly flexible molecular approach.

PO-Endo 02.06**Treating menopausal symptoms with a complex homeopathic remedy: a prospective randomized double blind clinical trial**

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Objective: To evaluate the efficacy and safety of a complex homeopathic remedy for the treatment of menopausal symptoms compared with placebo.

Materials and methods: 102 peri- and postmenopausal women requiring treatment for menopausal symptoms received treatment for 36 weeks. They were randomized in 3 groups to take as well the homeopathic remedy (2 \times 12 weeks) as placebo (12 weeks) with different order of remedy (M) and placebo (P) in a cross-over design (1: M/M/P, 2: P/M/M, 3: M/P/M). Efficacy was measured with Menopause rating scale II (MRS II).

Results: Reduction of symptoms after 12 weeks of treatment did not differ between remedy and placebo (−1.4 vs. −2.3 of total score MRS II, $p = 0,441$) and did not reach clinical significance (−3.5). Treatment with remedy for 24 weeks resulted in a total reduction of menopausal symptoms of −1.7 or −2.0. However reduction of symptoms after 36 weeks in group 1 (M/M/P) and 2 (P/M/M) reached clinical significance (−4.2 and −4.6) including a substantial contribution of placebo (−2.5 vs. −2.6). In contrary reduction of symptoms in group 3 (M/P/M) after 36 weeks (−0.3) did not reach clinical significance. No difference between verum and placebo was found regarding safety.

Conclusions: Treatment with the complex homeopathic remedy for 12 or 24 weeks proved to be safe but did not result in clinical significant improvements of menopausal symptoms. However treatment phases of at least 24 successional weeks should be recommended for further evaluation of efficacy.

PO-Endo 02.07**The degree of cycle irregularity correlates with the grade of endocrine and metabolic disorders in PCOS patients**

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Objective: PCOS (polycystic ovarian syndrome) is a clinically heterogeneous, endocrine disorder, which affects up to 4–10% of women in their reproductive age. A standardized definition is still difficult because of a huge variety of different phenotypes. The aim of this study was to evaluate possible correlations between the degree of cycle irregularity and the grade of endocrine and metabolic abnormalities.

Materials and methods: a cross-sectional study was carried out. Hyperandrogenic and/or hirsute women with regular menstrual cycles and polycystic ovaries in ultrasound (PCOS eumenorr, $n = 45$), PCOS patients with oligomenorrhea (PCOS oligo, $n = 42$) and PCOS patients with amenorrhea (PCOS amenorr, $n = 31$) were recruited from the Department of Gynecological Endocrinology and Reproductive Medicine Heidelberg.

Results: Normocyclic patients demonstrated metabolic parameters (BMI, Fasting Insulin, HOMA-IR) significantly better than patients with oligo/amenorrhea. Hormonal parameters (LH, FSH, FAI and testosterone) were significantly different between patients with different menstrual patterns and patient with regular cycles.

Conclusions: determining the degree of cycle irregularity as a simple clinical parameter might be a valuable instrument to estimate the degree of metabolic and endocrine disorders. Emphasis should be given to those parameters as a first step to characterize PCOS patients with a risk of endocrine and metabolic disorders leading to consequent detailed examination.

PO-Endo 02.08**The bisphosphonate compliance protocol: a study to determine influence factors and impact of non-compliance and non-adherence with bisphosphonate therapy**

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Objective: Antiresorptive therapy (ART) with bisphosphonates (BP) is effective in reducing the risk of fractures by maintaining bone mineral density (BMD), however discontinuation and non-adherence are common in patients treated with ART. Reasons for this are discussed controversially, and little is known about the impact of noncompliance on therapy outcome.

Materials and methods: In this prospective, observational study, women with an indication for BP therapy (group I) were questioned every six months about compliance/adherence, side effects, and quality of life. The patients are subdivided into two subgroups according to their underlying disease: 25 women with breast-cancer induced bone disease (BCIBD) are compared with 16 women with postmenopausal osteoporosis in whom ART was also indicated ($n = 16$). Bone density was measured at the beginning of the study and after 24 months using DXA scans and compared with a control group (II).

Results: 103 patients were recruited. Mean baseline-age of patients in treatment was 63 years, compared to 60 years in the control group. 84 (81.6%) women had a history of BC. Patients in group I had significant lower BMD at baseline compared to group II. In group I, 12 patients had been treated with tamoxifen prior to baseline (29.3%), in group II this proportion was 22 (35.5%). 14 (34.1%) women had AI therapy in group I, and 33 (53.7%) in group II. 15 women took oral BP, 13 women were on i.v. BP in group I. So far, 3 patients stopped BP therapy, while another 3 patients discontinued BP-therapy for >6 month between the visits due to potential/ expected side effects (i.e. tooth extraction).

Conclusions: Careful consideration of patients' medical history and priorities when choosing a bisphosphonate and attention to side effects plus appropriate co-medication can help to meet therapeutic goals towards preventing osteoporotic fractures.

PO-Endo 02.09**Ovulation and loss of bone density during the perimenopausal transition: the PEKNO study**

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Objective: The PeKnO-Study is a prospective observational study on the influence of perimenopausal luteal phase hormones and ovulation patterns on bone mineral density (BMD) changes over 2 years.

Computer-based cycle monitoring, pre-menstrual serum hormones, and BMD measurements by QCT are used to answer the question: Is there a correlation between decreasing rates of ovulation during the menopausal transition and increased perimenopausal bone loss?

Materials and methods: Cycle-length and ovulation were monitored by participants using a commercially available cycle-monitor. Serum hormones and bone-markers were drawn during the luteal phase of every 6th cycle. At baseline and after 2 years, trabecular bone density was determined by QCT in lumbar vertebrae 1–3.

Results: 68 women aged 45–53 years have been recruited so far, 50 participants completed the 24 month study. A total of >1200 cycles was evaluated, including 270 cycles with serum parameters. The rate of ovulatory cycles decreased from 67 to 47% during 2 years. The decreasing rate of ovulation correlated significantly with an increased loss of bone density ($r = 0.68$; $p < 0.001$). 13% of the women (95% CI: 5–27%) left the normal range of bone density and were osteogenic after 2 years. After 2 years a total of 29% participating women had osteopenia. The profile analysis will be presented.

Conclusions: The decreasing number of ovulations in the aging ovary seems to influence the bone density of perimenopausal women. This ongoing study will further investigate the connection between anovulatory cycles in pre- and perimenopausal women and the later development of osteoporosis.

PO-Endo 02.10**Smoking and AMH levels in normal fertile women**

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Objective: To investigate the effect of age and smoking on the AMH levels in healthy, normally cycling, fertile women.

Materials and methods: In 152 healthy, normally cycling, fertile women (aged 20–50 yr), with BMI ranged from 17.7 to 29.4 kg/m², blood samples were taken on day 3 of a spontaneous cycle. Serum FSH, LH, E2, progesterone and AMH were measured in all blood samples. Eighty five of the women (56%) were smokers. For the statistical analysis of the data, t test, Pearson's correlation and linear regression analysis were performed.

Results: Age was positively correlated to serum FSH and LH levels ($r = 0.613$, $p < 0.001$ and $r = 0.321$, $p < 0.001$ respectively) and negatively correlated to serum AMH levels ($r = -0.894$, $p < 0.001$). There were no significant differences in FSH, LH, E2, progesterone and AMH levels between smokers and non-smokers. Multiple step-wise linear regression analysis showed that in both smokers and non-smokers, the age was the most significant determinant of AMH levels ($r = -0.887$, $p < 0.001$ and $r = -0.942$, $p < 0.001$, respectively).

Conclusions: Aging significantly decreases AMH levels in normally cycling, fertile women, while smoking does not seem to have significant effects on AMH levels

PO-Endo 02.11**C60 fullerenes may be used in very low doses for applications in human ovaries**

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Objective: Lately, various nanomaterials have raised interest in numerous potential biomedical applications. C60 fullerenes which consist of 60 carbon atoms in the shape of a football are considered for imaging probes, antioxidants, or drug carriers. However, since they are insoluble in aqueous media it is difficult to study their activities in biological systems. Therefore, organic solvents are used for solubilization of fullerenes in water. The aim was to determine if fullerenes may also be used in ovarian applications by examining the interleukin 6 (IL-6) and 1beta (IL-1beta) production in cultured granulosa cells.

Materials and methods: Granulosa cells obtained during in vitro fertilisation treatment were cultured in microplates either with 0.025, 0.1, or 0.4 mg/ml C60 fullerenes, respectively, which were prepared by two methods: a) Wells were coated with a fullerene-methanol-suspension following solvent evaporation and cell seeding. b) Fullerenes dissolved in toluene were transferred into water by sonication and added to the cells. After four days IL-6 and IL-1beta were quantified in the culture supernatant by enzyme-linked immunosorbent assay (ELISA) and compared between fullerene-treated and untreated cells.

Results: As shown by ELISA granulosa cells secreted much more IL-6 than IL-1beta. Cells cultured with 0.025 and 0.1 mg/ml C60 fullerenes prepared by the methanol method produced the same amounts of IL-6 and IL-1beta like the controls. Merely cell treatment with 0.4 mg/ml fullerenes resulted in significant 5-fold and 4-fold increases in the IL-6 and IL-1beta concentrations. However, granulosa cells incubated with fullerenes prepared by the toluene method already showed with 0.1 mg/ml significant IL-6 and IL-1beta increases of 39% and 88% in comparison to untreated cells.

Conclusions: Our results show that C60 fullerenes do not influence the IL-6 and IL-1beta production of granulosa cells at the very low dose of 0.025 mg/ml and may be used for diverse ovarian applications.

PO-Endo 02.12

The expression of the vascular-endothelial-growth-factor-receptor Neuropilin-1 reveals a complex angiogenic network at the Human Fetal-Maternal Interface

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Objective: Angiogenesis is required for a successful implantation of the invading blastocyst. The vascular endothelial growth factor (VEGF) is known as an important key player of angiogenesis during the implantation process. Neuropilin-1 (NRP-1) was shown to play a role in angiogenesis in human endometrium during the menstrual cycle. These findings showed that besides VEGF receptor 2 (VEGFR2) NRP-1 might additionally play a role in the vascular remodelling process during embryo implantation and establishment of a pregnancy. **Materials and methods:** NRP-1 protein expression was investigated in human trophoblast cell lines (JEG-3, Jar and BeWo) aiming to evaluate the expression of NRP-1 in vitro—as well as in human decidua of all three trimesters of pregnancy by western blot analysis. The localization of NRP-1 in human decidua of all three trimesters of pregnancy was further investigated by immunohistochemistry.

Results: NRP-1 protein was expressed in all cell lines examined. Corresponding to the analysis of human tissue by western blot, NRP-1 protein was higher expressed in the early pregnancy in comparison to the end of pregnancy. NRP-1 was expressed in the decidua and villi of all samples investigated. Regarding the localization, the strongest expression of NRP-1 was shown in the vessels, stroma and glands of decidua as well as in the invading cytotrophoblast of first trimester samples, followed by a decline in expression towards the third trimester samples with only a moderate to low staining in the decidual compartment of NRP-1, and no to low staining in the corresponding cytotrophoblast.

Conclusions: This is the first study clearly showing the expression of NRP-1 in human decidua and trophoblast suggesting an important role for the VEGF co-receptor NRP-1 besides the established receptor VEGFR2 at the fetal-maternal interface during the process of embryonic implantation and placentation.

PO-Endo 02.13

Signalling cascades mediating decidual chemokine ligand 1 (CXCL1) expression

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Objective: The early fetal-maternal dialogue is a necessary prerequisite to establish a successful pregnancy. Chemokines like the chemokine ligand 1 (CXCL1) are known to be a key player in the process of decidualization and implantation. Therefore, the aim of this study was to identify the signalling cascades involved in the expression of CXCL1 induced by embryonically derived IL-1β in human decidua in vitro.

Materials and methods: Culture and decidualization (induced by progesterone and cyclo-AMP incubation for 72 h) of immortalized human endometrial stroma cells (dES) (cell line St-T1) was followed by a pre-incubation with MAPKinase, STAT3- and JNK-inhibitor for 2 h and a subsequent treatment with 0.1 ng/ml recombinant human IL-1β for 48 h. Cell culture supernatants were collected and frozen, RNA and protein isolated after the modified single-step method. Subsequent 2 μg RNA each were reverse transcribed and PCR performed for β-actin and prolactin mRNA. Supernatant of β-actin and prolactin positive samples were then measured for CXCL1 secretion via ELISA.

Results: Incubation with 25 μM of MAPKinase inhibitor lead to a statistically significant decrease of about 60% of the CXCL1 secretion in dES cell culture supernatants compared to only IL-1β treated controls. 250 μM of STAT3 and 100 μM of JNK inhibitor reduced the CXCL1 secretion in dES cell culture supernatant of about 35 and 30%, respectively.

Conclusions: The early fetal-maternal dialogue between embryonically derived IL-1β and decidual CXCL1 is primarily mediated via MAPK-signalling in vitro. Chemokines are key players in this early dialogue influencing implantation, angiogenesis and mediating maternal acceptance of the semi-allograft. Further knowledge about these early interactions might increase pregnancy rates after IVF-treatment and reduce implantation-related pathologies, for example pre-eclampsia.

Perinatal medicine

PO-Geb 02.01

Direct costs of delivery: is there a difference between spontaneously conceived twins and twins after ART?

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Objective: Healthcare expenditures are rising steadily. There are no data about delivering costs of gemini pregnancies. This study should provide data about the financial situation of delivery costs of Gemini deliveries after spontaneous conception and assisted reproduction in Northern Germany.

Materials and methods: Retrospective cohort-analysis about obstetrical data of gemini deliveries between January 2000 and December 2008 in the department of obstetrics and gynecology of the university hospital Schleswig-Holstein, Campus Lübeck.

Results: Patients delivering gemini after assisted reproduction are staying 1.1 days longer at the hospital, are average 2.5 years older and gravidity and parity is lower compared with women after spontaneous conception of gemini. Fetal outcome (weeks of gestation, birthweight, APGAR, umbilical arterial pH, intensive care unit etc.) and other maternal data (maternal height, maternal weight, length of operation etc.) were not significant different. The 1.1 day longer hospital stay lead to about 250 Euro more costs per patient.

Conclusions: Additional costs in gemini deliveries after assisted reproduction are due to longer stay at the hospital. This additional stay of average 1.1 day was not obvious for medical reasons. Main delivery costs for the substantial outcome-parameters are therefore not significant different in both groups.

PO-Geb 02.02

Placenta praevia marginalis increta—hysterectomy—the only operative option?

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Objective: Placenta increta is an uncommon and potentially life-threatening diagnosis. In case of a placenta increta all or part of placenta is adherent to the uterine wall, caused by extensive villous invasion into the myometrium. Usually abnorm placenta localisation is caused either by primary deficiency or secondary damage to the decidua basalis, most commonly considered in patients with a history of uterine surgery and advanced maternal age. Hysterectomy is a common therapeutic intervention, but the results involve the loss of the uterus and the ability to conceive. This raises the question if we can take responsibility of a hysterectomy sparing operative intervention after suitable preparation.

Materials and methods: A placenta increta appears in 15% of all cases. In a period from 5/2008 to 4/2010 we noted a number of 13 cases suffering from placenta praevia, 3 of them with the additional diagnosis of placenta increta. 2 of those patients underwent hysterectomy as the only option to control severe and life-threatening hemorrhage. The following case report of a concerned patient shows a successful hysterectomy sparing operative intervention in face of the pre-known risks.

Results: A hysterectomy sparing operative intervention in face of the pre-known risks might be practicable in specific cases and credible preliminary.

Conclusions: Incomplete separation of the placenta after delivery is a high risk of postpartum hemorrhage and undergoing hysterectomy. Reconstruction might be a further operative option to avoid hysterectomy. Cesarean-section should be done by an experienced surgeon and in a facility of available resuscitation and intensive care.

PO-Geb 02.03

Comparison of effectiveness and safety of dinoprostone and misoprostol for labour induction at term

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Objective: The aim of this study was to compare the effectiveness and safety oral misoprostol with intravaginal dinoprostone applications for assisted labor induction each other and to control group of spontaneous singleton deliveries. The influence of maternal properties on the duration of induction was investigated.

Materials and methods: The Jena perinatal database of 5 years (2003–2007) was analysed, where 644 women initially receiving 50 µg misoprostol and 99 women receiving 1 mg dinoprostone for labor induction. In the misoprostol group, a repeated dose of 100 µg was applied every 4 h until beginning regular contractions. A repeated dose of 1–2 mg was applied every 6 h in the dinoprostone group. Control group data was surveyed from 699 records fulfilling the inclusion criteria.

Results: Maternal age and body weight, gravidity and parity have independently significant effects on duration of labor induction. The mean interval from starting misoprostol to delivery was 18, 3 ± 12, 9 h compared to 25, 5 ± 48, 3 h in the dinoprostone group. Within 24 h after the first medical application 81% of the misoprostol vs. 68% of the dinoprostone group could deliver ($p < 0.05$). After misoprostol more women could deliver spontaneously and the number of caesarian section was less (22% vs. 33%; $p < 0.05$). A potential or occurring uterus ruptures were noticed in one and two cases after receiving dinoprostone and misoprostol, respectively. A duration of first and second stage of labor < 8 h was significantly more to record after misoprostol priming compared to the controls ($p < 0.01$), whereas the risks of perineal injuries and anaemia were decreased ($p < 0.01$).

Conclusions: Due to essential advantages with regards to effectiveness and safety, a labor induction with misoprostol is strongly suggested following an appropriate assessment of potential contraindications.

PO-Geb 02.04

Hellp-syndrome as early complication in molar pregnancy

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Objective: Preeclampsia and HELLP-syndrome are serious complications of pregnancy. Development of preeclampsia prior to 24 weeks' gestation seems to be associated with hydatidiform mole, a gestational disorder with a very low incidence rate in all pregnancies. The fetal outcome usually is poor and continuation of pregnancy in such cases bears severe maternal risks such as preeclampsia and persistent trophoblastic disease.

Materials and methods: We report a case of a 30-year-old woman with partial molar pregnancy in one placenta of dichorionic diamniotic twins. She presented with hyperemesis, severe hyperthyroidism at 12 + 1 weeks' gestation and markedly elevated beta-hCG levels. On ultrasound examination hydatiform mole was suspected. Despite growth retardation of both fetus and the risk of severe maternal complications the patient decided to continue pregnancy. Karyotypization analyses revealed a diploid fetus and no placental triploidy. Finally termination of pregnancy was performed at 19 + 6 weeks' gestation due to development of HELLP-syndrome.

Conclusions: Partial molar pregnancy with living fetus of a diploid karyotype poses a challenge for clinical management. Based on currently available information termination of pregnancy seems not to be indicated in such cases if close check-up during and after pregnancy is performed. This case demonstrates the dilemma of clinical management as well as the importance of close check-up even during early pregnancy to prevent life-threatening maternal conditions if the affected pregnancy is continued.

PO-Geb 02.05

Choice of collection system does not influence the quality of umbilical cord blood units

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Objective: Umbilical cord blood is used as hematopoietic stem cell source for transplantation. The success is highly correlated with the number of total nucleated cells (TNC), CD34+ cells, and colony forming units (CFU). We compared two collection systems regarding their efficacy for stem cell harvesting.

Materials and methods: Prospective study between 8/09 and 2/10 including consecutive vaginal deliveries with cord blood donations using either Fenval[®] or MacoPharma[®] collection bags randomly. In comparison to the Fenval[®] bag, the MacoPharma[®] bag is sterile for use during cesarean sections, has a thicker needle (12 g vs. 16 g) and a satellite bag containing additional anticoagulant solution to rinse the tubing and to achieve better cell recovery. TNC, CD34+ cells, and CFU were determined as described previously.

Results: During 6 months, 140 cord blood donations were registered. After exclusion of 26 donations due to low volumes (n.s.), 114 samples were available for analysis, 57 in each group. Maternal age, gestational age, parity, rate of spontaneous deliveries, umbilical cord blood pH, birth weight and sex did not differ between groups. Comparison of banking rate (52.6% vs. 71.9%), clotting rate (7.0% vs. 10.5%), contamination rate (6.7% vs. 2.4%), TNC (115.7 ± 47.7 vs. $134 \pm 59.7 \times 10^7$), CD34+ cells (3.7 ± 2.2 vs. $3.3 \pm 2.1 \times 10^6$), and CFU (227.1 ± 117.0 vs. $191.7 \pm 104.4 \times 10^4$) showed no statistically significant differences.

Conclusions: Choice of collection system does not increase the yield of hematopoietic stem cells in umbilical cord blood donations. In our study, we could not prove an advantage of the refined collection system using a thicker needle and a satellite bag for rinsing. Since most public cord blood banks struggle for funding and most deliveries are vaginal deliveries, the use of a cheaper bag does not compromise stem cell yield.

PO-Geb 02.06

Late onset malaria in non-endemic region during pregnancy can mimic a HELLP-syndrome

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Objective: Gestational malaria infection and HELLP syndrome show a big overlap in clinical and laboratory findings. Malaria not only increases maternal morbidity and mortality but also contributes to significant perinatal morbidity and mortality. Incubation time between mosquito bite and clinical symptoms may in rare cases exceed two months complicating early diagnosis. This is of specific interest in non-endemic regions like Western-Europe with little expert knowledge and experience of malaria disease and its treatment.

Materials and methods: A 34 year-old Primigravida at the beginning of the 36th gestational week presented with fever chills, headache and general malaise which quickly resolved with supportive treatment. CTG-controls showed a slightly increased fetal heart rate with a baseline of 160 bpm. Within two days the laboratory controls revealed aggravating thrombocytopenia, signs of hemolysis and an increase in transaminases to the 1.5–2 fold upper normal limits. At the fourth day after onset of symptoms the patient had a new fever chill. The decision to perform a cesarean section was made because of a pathologic CTG and under the impression of the beginning of a HELLP syndrome. The use of a rapid diagnostic test (Binax now[®]) after postoperative ongoing recurrent fever chills in a regular quartan pattern together with a history of travels to Cameroon 2 years before and China 3 months ago finally led to the diagnosis of Malaria quartana after two negative thick peripheral blood smears. After treatment with chloroquin as recommended by the German guidelines the patient quickly recovered and was discharged at well being.

Conclusions: Malaria in pregnant women can mimic the constellation of a HELLP-Syndrome. A thorough case and travel history together with the newer rapid diagnostic test can help not to miss this curiosity with devastating consequences.

Keywords: Pregnancy, Malaria, HELLP-syndrome.

PO-Geb 02.07

Postpartal sexual disorders. Results from the FRAMES (Franconian Maternal Health Evaluation Studies)

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Objective: Postpartal sexual disorders is not a negligible matter, since chronicifications may not only impair the quality of the partnership. Both somatic and psychosocial factors contribute to the development of these disorders. Aim of this study was to identify pre-, peri-, and postnatal factors of postpartal sexual discomfort.

Materials and methods: Within a prospective study (FRAMES) 1100 women were interviewed by standardized questionnaire concerning their physical, mental and sexual conditions in the pre- and postpartal period.

Results: 85.5% of the women stated that they had sexual relations in the first 6 months after birth. The mean duration before beginning of sexual activity was 9.6 weeks. The mean coital frequency was 4/month. The desire for the sexual intercourse was raised by the women in 4.7%, by the man in 8.0% and by both partners in 87.3%. Noteworthy significant facts: women, who had born a child before, scored their sexuality better; high school degree leads to an later sexual relation and less coital frequency pp; the better the anaesthesia during delivery, the better the impact on postpartal sexuality; helpless during delivery, had less sexual relations and evaluated the sexual feeling more negative; breast feeding had an negative impact on postpartal intimacy; the partner's encouragement was associated with the earlier begin of sexual activity and higher coital frequencies.

Conclusions: A lot of factors influence postpartal sexuality. While personal constitution of the mother cannot be modulated, there are still changeable factors. Therefore sufficient anaesthesia and good supervision of the women during birth should take place to minimize the psychic trauma. To prevent misconceptions, adequate education of the couple should take place in an early stage and the partners support should be highlighted. However, this study could not show significant associations between the form of delivery and the woman's sexual activity pp.

PO-Geb 02.08

Maternal and fetal mortality and morbidity in 10 hospitals in Kano and Kaduna State, Nigeria: reduction of MMR by Quality Assurance in Obstetrics

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Achieving the Millennium Development Goals 4 and 5 has continued to be a challenge in Nigeria, with a maternal mortality ratio (MMR) being one of the highest in the world.

Objective: The activities are aimed towards establishing an Institute of Quality Assurance in Obstetrics to improve the chances of survival for mothers and their children.

Materials and methods: The project commenced in January 2008 with 10 hospitals from Kano State and Kaduna State of Nigeria. With an audit the structure of the hospitals were investigated: equipment status and hygienic conditions were established using a "hospital score". The hospitals participated in a continuous monthly collection of data pertaining to maternal and child mortality and morbidity. In half yearly quality circles, staff from the participating hospitals discuss under supervision the unrecognizable results of each hospital.

Results: The structure and hygienic status of the hospitals exhibited deficits in many areas. There was a close relationship between the "hospital score" and maternal mortality. Following the continuously collection of data and discussion of the results, average MMR decreased from 1790/100,000 in first half year 2008 to 0.94/100,000 in second half year 2009. The average FMR remained roughly unchanged during the time of observation: 84.9/1000 in 2008 and 83.5/1000 in 2009. The MMR was related to the total number of deliveries in a hospital, increasing in hospitals with lower delivery rates. A similar relationship was found for FMR. There was no correlation with the CS-rate, which fell from 6.6% in 2008 to 5.3% in 2009.

Conclusions: Quality assurance in obstetrics is a continuous process of analysing, discussing and reducing the MMR and FMR with the guidance of an Institute of Quality Assurance. This might be a model

for Nigeria and other countries to reduce the unacceptable high MMR and FMR.

PO-Geb 02.09

Morbidity and mortality of obstetric patients admitted to the ICU of a tertiary hospital

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Objective: Due to extremely low rates of maternal mortality in the modern medical setting, new indicators for the monitoring of maternal health like need for transfer to an intensive care unit (ICU) have to be identified. This study aims to assess the causes of obstetric admissions to ICUs at the General Hospital of Vienna, Austria, and to evaluate the predictive ability of the APACHE II Scoring System in obstetric patients. Furthermore the most seriously affected patients and the factors most likely associated with severe morbidity are identified.

Materials and methods: A retrospective chart review of obstetric patients who were admitted between the second trimester of pregnancy and 6 weeks post partum to an ICU of the General Hospital of Vienna, a tertiary care university hospital, between 1996 and 2009 was carried out.

Results: 252 patients were included which makes this data pool one of the largest ones of its kind. The observed mortality rate amounts to 2.8% while the mean one calculated by the APACHE II Scoring system is 13.3%. A majority of patients (77.6%) was admitted for complications associated with pregnancy, the most common indications being (pre-)eclampsia and HELLP (31.6%) and major hemorrhage (32.8%). **Conclusions:** The APACHE II Scoring system overestimates mortality in obstetric patients. Women suffering from puerperal sepsis had the poorest outcome. Complications associated with preeclampsia and postpartum hemorrhage account for the largest number of ICU-admissions.

PO-Geb 02.10

Pregnancy management in a women with systemic mastocytosis

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Objective: Systemic mastocytosis, a rare disorder of mast cell proliferation in connective tissues, may lead to mast cell degranulation due to lots of different stimuli and (medical) drugs. Especially in pregnancy this might lead to life-threatening situations for the mother but also for the unborn.

Materials and methods: A 30-year-old german women presented with systemic mastocytosis in her first pregnancy in 20th gestational week for planning her further pregnancy and the mode of delivery. Whole pregnancy the patient had mainly gastro-intestinal symptoms like diarrhoea and enterospasms. She received Prednisolon 10–30 mg in 27th gestational week and improved.

Results: We could give birth to a healthy boy by elective Cesarean section with a special pharmaceutical management for the mother. Furthermore, we tried to avoid any stress by providing for a family room and also offered the patient child care whenever needed. A year

after her delivery she was diagnosed a steroid-induced Addison's disease. To date she is in 34th gestational week in her second pregnancy. **Conclusions:** Women with systemic mastocytosis, although rare, need close control and follow-up during pregnancy and confinement. Otherwise a mast cell degranulation may lead to life threatening situations for the mother and her baby. Interdisciplinary counselling is crucial.

PO-Geb 02.11

Management of placenta percreta: delayed planned hysterectomy after arterial embolization

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Objective: Major obstetric hemorrhage is the leading cause of maternal morbidity and mortality. Abnormal placentation occurs in approximately 1:2500 pregnancies, including about 5% placenta percreta. It occurs when the villi penetrate the full thickness of the myometrium and may invade neighbouring organs. Approximately 75% of placenta percreta cases are associated with placenta previa.

Materials and methods: A 32-year-old woman, gravida 4, para 2 (vaginal delivery, cesarean section), who had been diagnosed with a placenta previa, was referred at 24 weeks of gestation. The findings of our ultrasound examination with color Doppler and MRI were consistent with a diagnosis of placenta previa percreta. The cystoscopy showed no mucosal invasion. An elective cesarean with vertical fundal incision was performed at 33 weeks of gestation. A healthy, 2015-g female was delivered. Hysterectomy was postponed to avoid major bleeding as bladder was closely adhered to uterine wall and massive varicose veins were present. The placenta was not removed. A bilateral transarterial embolization of the uterine arteries was performed by radiologists on the 10th postoperative day. A total hysterectomy was planned. On the day of hysterectomy, endovascular catheters for balloon occlusion were placed within the internal iliac arteries. They were deflated after closure of the vaginal cuff with hemostasis. The estimated blood loss was about 4000 mL. The postoperative recovery was uneventful and the patient was discharged on the 14th postoperative day without any complications. The histopathology of the uterus confirmed a placenta previa percreta.

Conclusions: Placenta percreta is a life-threatening condition. The increased frequency of cesarean delivery over the past years has resulted in a greater incidence of abnormal placentation. Every attempt should be made to achieve the diagnosis antenatally, to minimize maternal morbidity. A multidisciplinary approach, the use of new interventions techniques and alternate surgical approaches are the key to successful management.

PO-Geb 02.12

Combination of prostaglandins and mechanical dilatation of the cervix helps to improve induction of labour

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Objective: Prostaglandins, and especially the synthetic prostaglandin E1 analogue misoprostol, are successfully used for induction of labour in cases with unfavourable cervix. However, prolonged induction-delivery intervals and failure in therapy still occur.

The aim of this study was to evaluate a combined treatment of prostaglandins and mechanical dilatation of the cervix, an also established method of cervical ripening, in order to reduce the induction-delivery interval.

Materials and methods: In this randomized trial over 100 term pregnancies with indications for induction of labour were included. In both groups, women received a standard therapy with misoprostol. Additionally in the study group, a COOK[®] balloon was inserted in the cervix for a maximum of 24 h. The study was approved by the ethics committee, and informed consent by the patients was obtained. Main outcome parameters were duration of induction of labour, rate of failure in therapy, and rate of adverse events.

Results: Compared to the control group, the induction-delivery interval was significantly shorter and failure rate was lower when using the combination of prostaglandins and mechanical dilatation. There was no difference in the incidence of necessary cesarean section and surgical vaginal delivery between both groups.

Conclusions: The combination of misoprostol and COOK[®] balloon is very beneficial for induction of labour in cases with unfavourable cervix.

PO-Geb 02.13

Influence of the centralisation of perinatal medicine on perinatal outcome in a maternity clinic with more than 1000 deliveries

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Objective: The initiation of perinatal centres with different characteristics should contribute to a reduction of risks in obstetrics.

In this analysis we wanted to explore the effect these measurements have on the clinical outcome in a maternity clinic with more than 1000 deliveries under the same head physician.

Materials and methods: We selected 3 years with a similar number of deliveries, first 1995 to account for the time factor, second 2005 before initiation of perinatal centres according to the GSG and third 2007 after the effective initiation.

We evaluated the data from the perinatal statistic of Baden-Württemberg and compared our own data with the data from other maternity clinics with a similar number of deliveries and with all deliveries of Baden-Württemberg.

Results: In the period 1995 to 2005 first of all the general risk factors changed, as increasing age, obesity, diabetes, other illnesses and state after caesarean section, but not so much the clinical outcome of the newborn. In the aftermath we recognised as intended from GSG a shift to mature babies with a corresponding higher birth weight and a decreasing number of deliveries with risk factors. Accordingly the outcome of the newborn is better which shows the pH at birth and the APGAR score. The difference between the years is not very grave as our clinic has always found itself on a good level of outcome compared to the other maternity clinics of Baden-Württemberg.

Conclusions: GSG has lead to the intended changes in clientele in the maternity clinics. Predictable emergencies in peripheral clinics are getting less and thus the clinical outcome better. But the overall perinatal outcome for Baden-Württemberg shows no improvement in spite of the better structure and supply of the perinatal centres.

PO-Geb 02.14**Correlation between cardiac radial ventricular velocity in growth-restricted fetuses and normal controls by Tissue Doppler Imaging (TDI) echocardiography***Ralf Schmitz¹, Jörg Heinig², Ludwig Kiesel¹, Johannes Steinhard¹¹University of Münster, Obstetrics and Gynecology, Münster, Germany, ²Obstetrics and Gynecology, Hamm, Germany

Objective: Tissue Doppler Imaging (TDI) echocardiography is a recent imaging tool that allows direct evaluation of myocardial velocities. Cardiac function is often impaired in fetuses with intra-uterine growth restriction (IUGR). The aim of this study was to compare radial mechanical velocities measured by Tissue Doppler Imaging (TDI) in pregnancies complicated by IUGR with normal controls.

Materials and methods: A prospective study was performed on fetuses with IUGR ($n = 37$, group 1) and normal fetuses ($n = 60$, group 2) between the 20th and 40th week of gestation by TDI transversal four chamber view raw data. Ventricular peak velocities of the left (LV) and the right ventricle (RV) were analysed offline with TDIQ-Software (Toshiba Medical Systems).

Results: Radial mechanical ventricular velocities are feasible in all scans. The frame rate was $141 \pm 24/s$ and the mean week of gestation was the $27th \pm 5$. The velocities of group 1 differ not significantly from group 2 (LV: group 1 14.5 ± 6.7 cm/s; group 2 14.9 ± 8.1 cm/s, $p = 0.75$ /RV: group 1 13.5 ± 5.7 cm/s; group 2 12.6 ± 4.7 cm/s, $p = 0.181$).

Conclusions: Evaluation of radial ventricular velocity by novel TDI technique is feasible. In our data myocardial velocities of IUGR fetuses are similar compared to normal controls. Limitations of our study are low number of cases and inclusion of IUGR cases with unsuspected Doppler indices. The clinical role of radial mechanical ventricular velocities in IUGR fetuses needs to be defined in larger studies including cases with defined Doppler alterations.

PO-Geb 02.15**Metabolic differences in neonates born by caesarean section compared to those by vaginal delivery***Hénar Ortega-Senovilla¹, Katrin Meitzner², Emilio Herrera¹, Matthias Schmitter³, Kristof Graf⁴, Klaus Vetter⁵, Michael Abou-Dakn², Ute Schäfer-Graf²¹Universidad San Pablo-CEU, Department of Biology, Madrid, Spain,²St. Joseph Hospital, Obstetrics and Gynecology, Berlin, Germany,³University of Münster, Obstetrics and Gynecology, Münster,Germany, ⁴German Heart Institut, Cardiology, Berlin, Germany,⁵Vivantes Klinikum Neukölln, Obstetrics, Berlin, Germany

Objective: The number of babies born by elective caesarean section (CS) has increased dramatically in the last years. Although it is known that CS results in significant changes of the hormonal milieu, there are very few studies related to its metabolic consequences. Present work was therefore addressed to compare the metabolic profile of cord blood serum in newborns born by CS with those born by vaginal delivery (VD).

Materials and methods: Cord blood was obtained after 83 deliveries by CS and 98 deliveries by VD from healthy women with normal OGTT at 26–27 weeks of gestation, accurate gestational age, singleton pregnancy and absence of congenital anomalies. Neonatal fat mass was derived from measurement of skinfolds within 72 h postnatal.

Results: Maternal age was slightly higher, pre-pregnancy BMI was similar while gestational age at delivery, birth weight and fat mass were lower in CS vs. VD. Cord blood serum glucose, triglycerides,

glycerol, and nonesterified fatty acids, as well as total-saturated, monounsaturated and polyunsaturated fatty acid concentrations were lower but insulin and insulin/glucose ratio were higher in CS than in VD. These differences maintained after adjustment for maternal pre-pregnancy BMI gestational age at delivery, birth weight and fat mass of neonates.

Conclusions: Lower circulating glucose and lipid levels in newborns born by CS could be related to the known delay in their post-partum surges in catabolic hormones, like catecholamines and cortisol which is further enhanced by hyperinsulinemia. These metabolic changes resulting in lower available circulating substances might contribute to problems in perinatal adaptation observed in newborns born by CS without experience of labor.

PO-Geb 02.16**Biobanking and networking: take a chance***Harald Zeisler¹, Lorenz Küssel¹¹Medical University Vienna, Department Obstetrics and Gynecology, Wien, Austria

Biobanks are a collection of biological material (blood, DNA, tissue, biopsy specimens, etc.) and the associated data and information stored in an organised system, for a population or a large subset of a population. By combining and comparing biological tissue samples with patient information, researchers will be able to investigate the fundamental mechanisms of diseases. So Biobanking offers new abilities for translating new biomedical knowledge into new clinical practices, diagnostic techniques and preventative treatments. “Networker” is a colloquial expression for people who actively build up and enlarge a network. Networking is a “marketing” method by which research opportunities are created through networks of like-minded researchers. Due to specific research fields it is often necessary that Networking is conducted on a larger scale via the Internet in order to connect people from all over the world. In addition, being part of this network on specific platforms it is easier to find suitable sponsors. Networks now make globalization accessible also for small and medium sized companies. Biobanks form the base for networks in which enterprises and researchers cooperate. Networks have internationally established themselves as one of the most important instruments of the economic policy turned over.

PO-Geb 02.17**A case of facial nerve paralysis as a rare neurological complication of HELLP syndrome***Michael Wilhelm¹, Karl Ulrich Petry¹¹Clinical Centre, Department of Gynecology and Obstetrics, Wolfsburg, Germany

Objective: To report on a case of facial nerve paralysis as a rare neurological complication of HELLP syndrome.

Materials and methods: A 32 year old primigravida was referred to our obstetrical department at 33 weeks of gestation with left-sided facial paralysis and ptosis. Laboratory findings included a thrombocyte count of 69/nl, GOT at 219 IU/l, and GPT at 183 IU/l. Besides the neurological manifestation the patient showed no other clinical signs of HELLP syndrome.

Results: Caesarean section was immediately performed. A healthy boy of 1860 g was delivered and transferred to the neonatal intensive care unit. The patient herself clinically and chemically recovered with intravenous corticoid application, and was released from care on the 8th day after delivery. Neurological and otolaryngological examinations, as well as MRI of the neurocranium, showed no other pathologies.

Conclusions: Facial nerve paralysis is a rare complication of HELLP syndrome, and can lead to full recovery when treated accordingly.

PO-Geb 02.18

Prenatal diagnosis of neural tube defect a review of 1,000 cases

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Objective: Neural Tube Defects is among the most common major congenital malformation World Wide. Prenatal Detection is possible in about 95% of the cases through amniotic fluid Alfa-Feto Protein (AFP), with levels from the open lesion. To assess the ability to detect neural tube defect by assaying amniotic fluid Alpha Feto-Protein levels. **Setting:** A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos. **Study and Design:** A prospective study **Materials and methods:** Amniotic fluid samples were collected from patients at risk of having offspring with Neural Tube Defects or from those undergoing prenatal diagnosis for biochemist or cytogenetic studies between 1994 and 2009. AFP was assayed using Elisa kits method. **Results:** Out of a total amniotic fluid assayed for AFP only 1.1% (110) showed elevated values. 56% (16) had open Neural Tube Defects, 21.2% (23) had other fetal defects or conditions. In about 0.01% (1) there were no reasons for the elevation. **Conclusions:** Patients at risk for delivery results with Neural Tube Defects should be counseled and offer prenatal diagnosis.

PO-Geb 02.19

Fetal Magnetocardiographie (fMCG): a non-invasive method to detect the development of fetal cardiac time intervals (fCTI) and to monitor pregnancies at risk of congenital AV-block

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Objective: fMCG is a non-invasive method to detect magnetic fields generated by electric cardiac currents. Morphology and duration of fetal cardiac time intervals (fCTI) can be analyzed from 20 weeks onwards. With increasing signal quality during gestation. Pregnancies with maternal autoimmune diseases and presence of SSA-/SSB-antibodies are at risk of irreversible fetal AV-node damage through the diaplacental transferred autoantibodies particularly between 18–24th week of gestation. Markers for AV-node affection are missing and a total AV-block only can be diagnosed by ultrasound after manifestation. Early investigation of the cardiac conduction system is necessary for fetal monitoring. A new 156 channel-fMEG device dedicated for obstetrical measurements was used. Our aim was to evaluate fCTI detection starting before 20 weeks to investigate physiological changes of fCTI during gestation and to compare fCTI's between healthy fetuses with fetuses exposed to maternal SSA-/SSB-antibodies. **Materials and methods:** 95 fMCGs were recorded in healthy fetuses (controls) and 23 in fetuses exposed to SSA-/SSB antibodies (study group) between 15 and 41 weeks of gestational age. After bandpass filtering (1–100 Hz) and signal subtraction of the maternal heart

signal, automatic and manual signal detection was used to obtain an averaged fMCG-graph to measure fCTI according to recommended MCG standards.

Results: fCTI's could be analysed from 17 weeks onwards. Both groups showed increasing P wave- and QRS-duration with GA. Other CTI's increased only in the control group during gestation. PQ interval was longer in the study group (50.8 ms vs. 60.2 ms; $p \leq 0.001$). **Conclusions:** CTI's of atrial and ventricular depolarization increased with GA in both groups and reflect the growing cardiac muscle. PQ interval was longer in the risk group. This indicates a prolonged transmission at the AV node. PQ-interval could be a possible marker for AV-node affection.

PO-Geb 02.20

Long-term amnioinfusion through a subcutaneously implanted amniotic fluid replacement port system for treatment of PPRM in humans

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Objective: Preterm premature rupture of the membranes (PPROM) is a serious condition and one of the most important causes of perinatal morbidity and mortality. Nowadays the possibilities for the treatment of PPRM are still limited.

Materials and methods: We here report the case of a 39 years old 5th-gravida with PPRM in 18 weeks of gestation in which we implanted an Amniotic Fluid Replacement Port System (AFR-Port) for long-term saline infusion (100 ml/h) into the amniotic cavity. **Results:** The gestation was terminated by caesarean section at 29th week of gestation due to umbilical cord prolapse. The newborn boy did not have any signs of lung hypoplasia and was successfully extubated one day after delivery. Six months after the delivery the child did not have any deviation from the normal development. **Conclusions:** This is the first report of successful use of a subcutaneously implanted AFR port system in humans for long-term amnioinfusion as a treatment of PPRM for prolongation of pregnancy and avoidance of lung hypoplasia.

PO-Geb 02.21

Arterial stiffness of young women with previous gestational diabetes

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Objective: Gestational diabetes (GDM) is a cardiovascular risk factor later in life. Our aim was to investigate the relationship between carbohydrate intolerance, obesity and arterial stiffness in women with previous GDM (pGDM).

Materials and methods: Follow up examination was made in 66 women with pGDM and 27 after normal pregnancy at $38,2 \pm 5,4$ weeks after delivery. A 75 g 3-hOGTT was performed. Parameters of arterial stiffness (carotid femoral and carotid radial pulse wave velocity (c-fPWV, c-rPWV); carotid augmentation index (c Aix)) was assessed by using PulsePen device. Investigating them is useful, noninvasive method to assess the atherosclerosis and cardiovascular risk.

Table 1 (PO-Geb 02.21). Clinical and analytical characteristics at follow-up for women with previous gestational diabetes and controls

	Control, NGT	pGDM, NGT	pGDM, AGT	Significance 1 vs. 2 group	1 vs. 3 group	2 vs. 3 group
N	26	44	22			
Age (years)	32.8 ± 3.1	34.9 ± 3.7	34.6 ± 5.5	NS	NS	NS
BMI (kg/m ²)	24.5 ± 4	24.8 ± 4	28.2 ± 7.9	NS	<0.05	<0.05
Waist hip ratio	0.8 ± 0.06	0.8 ± 0.07	0.8 ± 0.08	NS	NS	NS
Parity	2.3 ± 1.2	2.5 ± 1.4	2.7 ± 1.3	NS	NS	NS
OGTT AUC glucose (mmol/l)	958 ± 159	1159 ± 178	1600 ± 362	<0.01	<0.001	<0.001
OGTT AUC insulin (uU/ml)	6479 ± 3294	10842 ± 7675	11736 ± 6932	<0.05	<0.05	NS
HOMA-IR	2.2 ± 1.2	2.6 ± 1.6	4.7 ± 6.7	NS	<0.05	NS
HOMA-B	115.1 ± 66.8	124.8 ± 69.8	109.3 ± 78.5	NS	NS	NS
HbA1C	5.3 ± 0.3	5.5 ± 0.3	5.7 ± 0.4	NS	<0.001	<0.05
Mean c Aix	-2.3 ± 11.7	1.5 ± 12.7	-1.2 ± 14.1	NS	NS	NS
Mean c-f PWV	6 ± 0.9	6.3 ± 0.8	6.5 ± 1.1	NS	NS	NS
Mean c-r PWV	6.4 ± 1.1	6.4 ± 1.2	6.7 ± 0.9	NS	NS	NS

Results: Abnormal glucose tolerance (AGT) was diagnosed in 23 women (IFG:5, IGT:11, IFG + IGT:2, DM:5). We divided the women into 3 groups: 1: without pGDM, normal glucose tolerance (NGT) at the follow up; 2: pGDM but NGT; 3: pGDM and AGT. There was no age difference between the groups (34.2 ± 4.1), but BMI was elevated in those with AGT, same was seen for blood pressure. The values of the area under the curve (AUC) of insulin levels at the OGTT was only lower in the control group. There was no difference among arterial stiffness parameters in the 3 groups. However we found linear association among c-fPWV and BMI and waist hip ratio (WHR) using univariate linear regression analysis ($P < 0.001$, $R^2 = 0.19$, $R^2 = 0.28$). In the AGT group were the correlations even stronger ($P < 0.001$, $R^2 = 0.44$, $R^2 = 0.65$), in the two NGT group weaker (pGDM: $P = 0.01$, $R^2 = 0.13$, $R^2 = 0.14$; control: $P = 0.03$, $R^2 = 0.18$). There was no correlation between c-fPWV and BMI in the control group.

Conclusions: Our findings could not confirm any difference in arterial stiffness parameters among young women with normal or abnormal carbohydrate tolerance after pGDM or without it. However there is a linear association of c-fPWV, representing the arterial stiffness, and BMI and waist hip ratio.

PO-Geb 02.22

Analysis of amniotic fluid and maternal plasma concentrations of glucose, insulin, adiponectin and leptin at the 16th gestational week in women who will develop gestational diabetes mellitus: a case-control study

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Objective: To determine the differences in glucose homeostasis at the 16th gestational week in women who will develop gestational diabetes mellitus (GDM) compared to controls.

Materials and methods: Between 2006 and 2007, samples of foetal amniotic fluid and maternal plasma were prospectively collected at

the time of amniocentesis by routine prenatal screening, after obtaining women informed consent and the institutional reviewer board ethical approbation. 8 patients who completed the follow up, were found affected by GDM, and were compared with 10 control patients with a normal pregnancy course.

Results: Mean maternal age was 38.22 years (±2.82), and all considered women delivered at term, with no significant difference in the Apgar scores between cases and controls. Mean foetal weight at birth was 3512 g (±651.84) in women with GDM and 3148 g (±537.92) in controls, but the difference was not statistically significant. The adiponectin concentration was higher at the 16th gestational week in women who would develop GDM than in controls. The leptine and insulin concentrations in the amniotic fluid were higher in controls, and the plasmatic glucose concentration was higher in GDM, but only the insulin concentrations achieved the statistical significance ($p < 0.05$).

Conclusions: Our data suggests that in pregnancies which will be complicated by GDM, amniotic fluid adiponectin is higher and insulin level is lower in the early foetal period, while no statistically differences among plasma concentrations were found. This let us suppose that an earlier alteration in the foetal glucose metabolism would probably influence the later maternal glucose dysmetabolism, and the consequent development of maternal GDM.

PO-Geb 02.23

Placental transport of the amino acid taurine is not altered in preeclampsia

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Amino acids are important nutrients for fetal growth and development. Placental amino acid transport is decreased in pregnancies with growth-restricted infants (IUGR) and results in decreased fetal amino acid concentrations. Taurine is an essential amino acid during fetal life, and placental taurine transport and fetal taurine plasma concentrations are decreased in IUGR.

Objective: Since IUGR and preeclampsia share a similar spiral artery pathology that decreases perfusion but manifest different placental

pathology; we investigated whether placental taurine transport was reduced in pregnancies complicated by preeclampsia.

Materials and methods: The uptake of 3H-aurine over time (10, 20, 40, 60 and 120 min) was investigated using primary villous fragments isolated from placentas of primiparous women with preeclampsia ($n = 5$) compared to AGA controls ($n = 7$).

Results: Placental taurine uptake increased linearly over time in villous fragments from both preeclamptic and control subjects ($p < 0.0001$). However, there was no difference in taurine uptake between preeclamptic (2.85 ± 1.06 pmol/min/mg) and control villous fragments (2.81 ± 0.51 pmol/min/mg, $p = 0.94$). This included one placenta from a small for gestation age infant (>5th centile) from a preeclamptic pregnancy.

Conclusions: In contrast to IUGR, placental uptake of the amino acid taurine is not decreased in preeclampsia compared to controls. This is consistent with greater villous surface area previously reported in placentas from preeclamptic pregnancies as compared to IUGR pregnancies. These data suggest that placental amino acid transport may not limit placental/fetal nutrient availability in preeclampsia. However, more data is required, especially from preeclamptic pregnancies with growth-restricted infants.

PO-Geb 02.24

Planned caesarean delivery does not protect breech babies from intrapartum injury

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Objective: Planned caesarean section is better than planned vaginal birth for the term fetus in the breech presentation. This was the interpretation given by the term breech trial, a randomised multicentre study. A follow up trial with analysis of outcome after 2 years has not shown any differences between vaginal and abdominal deliveries of breech babies. By reason of study design and methods most cases of neonatal death and morbidity in the term breech trial cannot be attributed to the mode of delivery.

Materials and methods: Both of our cases deal with women with breech presentation at term. (1) Case: The patient was I gravida/0 para and had a planned caesarean section. A fetal femur fracture occurred during birth. (2) Case: The patient was II gravida/I para and had a vaginal delivery. A fetal humerus fracture occurred during birth. Casually incised wound of the newborn in addition to maternal injury can occur during a caesarean section. Particularly caesarean section assumed to be safer for breech babies.

Conclusions: In comparison of the two cases it has shown that a caesarean delivery is not always safer than vaginal delivery for breech babies. Different studies have shown that there have been no differences in the outcome of the breech babies concerning the mode of delivery. For this reason the pregnant with breech presentation should be informed about both modes of delivery. At the same time we have to point out the equality of both modes of delivery and that the caesarean section is not less of risk for newborns.

PO-Geb 02.25

External cephalic version: a safe and successful procedure to reduce caesarean section rate

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Objective: The purpose of this study was to evaluate the rate of caesarean delivery after successful external cephalic version.

Materials and methods: Between 01.01.2005 and 12.31.2009 we performed 239 external cephalic versions (ECV). 144 fetuses have successfully been turned into a cephalic presentation (60%). In 108 cases of successful ECV we collected or received data according to the delivery. ECV was performed in singleton fetuses in breech position most times beyond 36 + 0 weeks. After information, exclusion of contraindications and consent we performed ECV at the labour ward after half an hour of cardiotocography (CTG), using intravenous Tocolysis with Fenoterol aided by ultrasound and CTG and caesarean stand-by. After the procedure all fetuses were monitored continuously for half an hour or longer by means of CTG, and again the following day. In one case we performed an emergency caesarean section (CS) because of persisting fetal bradycardia.

Results: From 144 Fetuses after successfully ECV only one Fetus turned back immediately after version but remains in cephalic position after a second attempt one week later. We had 2 cases of elective CS, one because of HELLP-syndrome and one because of IUGR. Emergency CS took place in 12 cases. Indications: 4 times pathological CTG changes, 6 times protracted labour during active-phase first-stage labour, and one time second-stage. One time Chorioamnionitis, two times malpresentation of the fetal head. Operative vaginal delivery was performed in 16 cases. Indications: pathological CTG changes 6 times, protracted second-stage 10 times (combined with malpresentation in 5 times). 78 women delivered spontaneously. The rate of vaginal birth after successful ECV was 87%.

Conclusions: ECV remains a safe procedure and should be offered in cases of breech presentation beyond 37 weeks. Successful ECV significantly decreases the caesarean section rate, the higher costs connected with CS and the risks related to breech delivery.

PO-Geb 02.26

The elective caesarean section and its impact on the newborn

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There is ongoing debate, whether elective C-section affects health conditions of the newborns. We investigated the outcome of the newborns within the first 24 h after birth, with particular focus on differences between C-section without labor and vaginal delivery. We retrospectively investigated a cohort of all children born in a secondary-care-hospital (Tulln/Lower Austria) between January/2007 and December/2008 after the 37th week of gestation, comparing elective caesarean delivery, emergency caesarean delivery and vaginal delivery, in order to show the differences of the rates of admission to a Neonatal-Intensive-Care-Unit (NICU) in the first 24 h after birth, the APGAR-Score and the umbilical cord pH, between these groups. We included 1064 children in this study. Our results show significant differences in the rates of admission to a NICU. After vaginal delivery only 18 of 678 (2.7%) children, after caesarean section (labored) 19 of 198 (9.6%) and after caesarean section (unlabored) 44 of 188 (23.4%) children required admission to a NICU ($p < 0.001$). After adjustment for gestational age and birth weight by means of multiple regression, caesarean delivery still remained an independent risk factor for the newborns' admission to a NICU (OR 6,084; 95% CI 3,438–10,766). Also for the APGAR-Score and the umbilical cord pH we identified significant differences between our study groups. The results of this study clearly show considerable disadvantages of elective C-section for the child regarding the rate of admission to a NICU

within the first 24 h after birth as well as an impairment in the ability of the newborn to adapt to the world outside the uterus. These results are in line with the present literature. We conclude from this study that C-section increases the risk of admission to a NICU and the risk of a worse outcome in the newborn within the first 24 h after birth.

PO-Geb 02.27

Sudden infant death syndrome in Berlin, Germany, from 2001–2008

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Different factors that increase the mortality due to sudden infant death syndrome (SIDS) have been statistically proven by several studies. The most important risk factors are sleeping in prone and side position, smoking during pregnancy and in the environment of the child, the so-called “co-sleeping”, as well as sleeping under too soft and thick coverage and on soft mattresses. The use of a dummy, co-rooming without co-sleeping and breastfeeding the child are protective factors by different mechanisms, which are not yet completely understood. The aim of the study was to determine to which extend the different risk and protective factors play a role in cases of SIDS in Berlin, Germany. Therefore, the autopsy files of the institutes for forensic medicine in Berlin from the years 2001–2008 and the files of the prosecution were analysed as to the known risk and protective factors. 63% of the children were male, 37% female. The highest death rate was between the 2nd and 4th month of life. 40% of the children were found dead in prone position, 30% in spine and 2.5% in side position. 90% slept with a blanket and 9% had a cushion in the bed. 26% died in their one bed, 14% in the parental bed, the rest elsewhere. 18% had a room of their own, 23% slept in the parental sleeping room. Of those 70% slept in the parental bed. 31.5% were exposed to cigarette smoke before and after birth. Only 8% were breast fed until death. Most of the results of other studies could be confirmed for the cases of SIDS in Berlin.

PO-Geb 02.28

Induction of labour with Cytotec (Misoprostol) or Dinoprost (Prostin) in postterm nulliparas

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Objective: The object of this study was to investigate the efficacy of vaginal administration of Misoprostol versus Dinoprost as a useful alternative method to predict successful labour in nulliparas 1 week postterm.

Materials and methods: The first group A included of 100 pregnant women, who requested pregnancy termination 1 week after labour term and received vaginal misoprostol 50 µg (1/4 Cytotec 200 µg). The second group B included of other 100 pregnant, who vaginal administrated 3 mg (1 dinoprost). In all examined women the Bishop Score was ≤ 7 and the CTG-controls had no pathology were divided in two groups regarding their gestation age. According our protocol this procedure was repeated after 6 h until maximal two times. If the Bishop score was >8 , oxytocin was administrated. The aim of this study was to evaluate retrospectively the usefulness of misoprostol to cervical priming, the duration for delivery and the fetal perinatal outcome for statistical analysis, categoric variables were compared with SPSS 11.5 for Windows, Kolmogorov-Smirnov Mann Whitney and Pearson Chi Square

Results: In both groups were the participant age and the pregnancy week were similar. $p = 0.907$. The Labour duration was longer in the Group B ($p = 0.000$), while the APGAR score was better in Group A ($p = 0.015$). In the Group A was the labour modus as following: 86.9% normal vaginal labour, 3.8% Vacuum extraction, 9.3% caesarean Section. The labour modus in the Group B was 82.83% normal vaginal labour, 3.07% Vacuum extraction, 14.1% caesarean Section. The mean induction—labour n interval was 4.5—1.2 h in group A, while 6.5—1.5 h in group B. There was no serious side effects.

Conclusions: Misoprostol is an effective agent for postterm pregnancy medical termination.

PO-Geb 02.29

Blood transfusion policy in obstetrics at the University Hospital Zurich over 10 years

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Objective: In Switzerland no recent study has been published in regards to the administration of blood products in obstetrics, therefore the goal of our retrospective study is to calculate the trend and evaluate the practice of transfusion medicine at the University Hospital of Zurich in the department of Obstetrics.

Materials and methods: Women who gave birth and received at least one red blood cell, platelet or fresh frozen plasma (FFP) transfusion where selected from the department’s database. Complete information was found for 241 cases from January 1996 to February 2007. Information was collected from the department’s computer programs and completed and compared with archive data. Data was collected in regards to: demographics, type of delivery, blood loss, number and type of transfusions received, hematological lab values, patient complications, complications during and after labor, and type of anemia treatment.

Results: Although we expected to see a decreasing trend in red blood cell transfusions, our results show an increasing percentage of patients receiving blood transfusions after the year 2004. Furthermore our data shows a number of FFP, platelet and red blood cell (RBC) transfusions being administered inappropriately with discrepancies in data administration.

Conclusions: Educational outreach and quality assurance checks are options, which could help improve the acknowledgment, understanding and administration of the practice of blood product transfusion at the University of Zurich Hospital.

PO-Geb 02.30**Surveillance of a fetus with FIUV****(fetal intra-abdominal umbilical vein) varix**

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Objective: We present the rare case of a patient with a fetal intra-abdominal umbilical vein varix and a possible explanation for the development of the varix.

Materials and methods: The patient, a 41 year-old IVg/Ip was diagnosed at 32 weeks of gestation with an intraabdominal varix of the umbilical vein as a sign of a presumptive stenosis of the umbilical part of the vein. Further ultrasonic evaluation showed no other irregularities. Amniocentesis had been performed in the first trimester because of a history of trisomy 13 with normal results. In color Doppler ultrasound there was normal blood flow in both the middle cerebral and the umbilical artery. Blood flow was normal in the periumbilical portion of the umbilical vein and in the ductus venosus. The intra-abdominal part of the umbilical vein showed varicose dilation up to 12 mm over a distance of 22 mm. Blood flow velocity in this part of the vein was elevated to 85 cm/s. Due to the risk of intrauterine fetal death primary cesarean section was performed at 36 weeks of pregnancy.

Results: The neonate was a healthy female, weight 2640 g, APGAR score 9/10/10. There were no further malformations.

Conclusions: A fetal intra-abdominal umbilical vein varix is a rare condition in pregnancy. A possible explanation for the dilation of the poststenotic vessel is the high velocity of blood flow in the low pressure area, caused by a jet phenomenon. The degree of poststenotic widening of the vein may be due to the decrease of pressure from the jet. Conducting a survey of literature the risks for the fetuses are found to vary strongly. When a FIUV varix is diagnosed in pregnancy, frequent controls of the baby's well-being are essential in order to prevent intrauterine fetal death. The varix can be detected on routine sonography.

PO-Geb 02.31**Intrauterine midgut volvulus without malrotation: a case report**

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Objective: Midgut volvulus is a condition in which the small bowel or proximal colon twist around the superior mesenteric artery. This condition most commonly presents during the first year of life and is associated with a high rate of morbidity and mortality. Midgut volvulus without malrotation is an extremely rare surgical condition which may also occur during intrauterine life. Most cases of volvulus are associated with intestinal malrotation or other congenital anomalies. Dilated bowel loops on prenatal ultrasound may be an indicator of this anomaly. In these cases close monitoring of the fetal condition is mandatory to tailor the appropriate treatment.

Materials and methods: A 25 year-old pregnant woman was referred to our hospital at 33 weeks of gestation with reduced fetal movements and onset of preterm labour. Ultrasound examination revealed a dilated intestine but no other fetal abnormalities. Intrauterine volvulus was suspected. Fetal biometry and Doppler measurements were appropriate for gestational age. Within two days of admission,

however, fetal Doppler indices and gross fetal movements deteriorated, cardiocography became abnormal and fetal ascites developed. A 1940-g male was delivered by Cesarean section. Neonatal examination showed a tense, distended abdomen. Laparotomy was performed at 6 h of age, during which the suspected volvulus was confirmed. A de-torsion and segmental bowel resection were performed.

Conclusions: Prenatal diagnosis of a volvulus requires close monitoring in a prenatal care center and immediate post partum intervention to ensure optimal

PO-Geb 02.32**Obesity decreases the chance to deliver spontaneously**

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Objective: To evaluate the impact of maternal obesity on labour, intrapartum assessment, delivery and fetal outcome.

Materials and methods: Retrospective cohort analysis of $n = 11.681$ deliveries supervised between 1.01.2000 and 31.12.2009. Results were analyzed dividing the patients in 2 main groups according their BMI: group 1, control: BMI 18–24.9 and group 2 BMI, test >25 . Subgroups were built: (0) BMI 25–29.9, (I) BMI 30–34.9, (II) BMI 35–39.9, (III) BMI >40 . Exclusion criteria were defined: delivery $<37 + 0$ weeks p.m., multiple pregnancy, comorbidity other than GDM, abnormal presentation, BMI <18.5 , incomplete data. Main outcome parameter was defined: mode of delivery, maternal injury and fetal outcome (arterial cord ph, APGAR score, birth weight). **Results:** $n = 8.379$ patients met the inclusion criteria and were divided in two groups: (1) $N = 4.464$ patients and (2) $n = 3.915$. Basic maternal characteristics including fetal vital parameters were equal in all groups. GDM occurred more frequently in obese patients ($P < 0.001$). Concerning the main outcome parameters a significant decrease in the rate of spontaneous delivery between control (71.97–65.95%, <0.001) and test groups (71.97% vs. 50.27%, <0.001) could be observed. The rate of secondary c-section increased significantly according to higher BMI (>40 : OR 2.5, 95% CI 1.841–3.611, $\times 2 P < 0.001$). The groups showed no difference in the rate of injuries during delivery though fetal birth weight increased significantly with higher BMI (3412–3681 g, $P < 0.001$).

Conclusions: Obesity decreases the chance to deliver spontaneously. Moreover, the obese patient suffers from a significant longer trial of labour (7.89 vs 9.52 h) and elevated risk of surgical delivery.

PO-Geb 02.33**Does gender of the supportive companion during labor influence delivery outcome: a retrospective cohort study**

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Objective: Previous retrospective and prospective controlled studies demonstrated positive effects of a continuous presence of a supportive companion with respect to length of labor, type of delivery, and need of epidural analgesia. Whether or not the gender of the supportive companion influences delivery outcome is unknown.

Materials and methods: We conducted a retrospective cohort study to compare delivery outcome, ie spontaneous delivery versus vaginal-operative delivery or cesarean delivery, in patients with a singleton pregnancy between 38/0 and 41/6 weeks, who planned a vaginal delivery at the Department of Obstetrics, University of Vienna,

between 1/2007 and 12/2009, with respect to the gender of the supportive companion. Univariate and multivariate logistic regression was used to assess the influence with respect to the gender of the supportive companion, patient's age, parity (nulliparity vs multiparity), body mass index, induction of labor, fetal birth weight, regional anesthesia, and education of the patient (>10 vs. <10 years of school education).

Results: A total of 1707 women were enrolled in this study. Of those, 1493 women (87%) were accompanied by a male supportive companion and 214 women (13%) were accompanied by a female supportive companion. 1399 women (82%) had a vaginal delivery, whereas 308 (18%) had a vaginal operative delivery or caesarean section. In a univariate analysis, delivery outcome was significantly associated with age ($p < 0.0001$), parity ($p < 0.0001$), and fetal weight ($p = 0.004$), but not with gender of the supportive companion ($p = 0.8$), body mass index ($p = 0.1$), induction of labor ($p = 0.3$), regional anesthesia ($p = 0.09$), and education ($p = 0.8$). In a multivariate analysis, age ($p < 0.0001$), parity ($p < 0.0001$), and fetal weight ($p = 0.001$) were all independent predictors of delivery outcome.

Conclusions: Age, parity, and fetal weight, but not gender of the supportive companion during labor and delivery influences the rate of vaginal-operative deliveries and cesarean deliveries in singleton term pregnancies.

PO-Geb 02.34

The partograph in daily practice: it's quality that matters. A follow-up after 12 years

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Objective: Worldwide an estimate of 585,000 women per year die due to factors directly related to pregnancy and childbirth. Substandard care factors and avoidable mistakes at health facilities are the major causes. The partograph has shown to be an important tool to monitor labour. The partograph increases the quality of all observations on the fetus and the mother in labour, is effective in preventing prolonged labour, reduces operative intervention, and improves neonatal outcomes. However, after partograph implementation and training there is only little supervision and assessment of daily practise. This study measures the performance quality of partograph use in three regional hospitals in southern Tanzania. Aim is to compare assessment data of 1996 and 2009 and identify the influence of performance quality on neonatal outcome.

Materials and methods: In the present study, an indicator-based quality assessment tool was used developed by German and Tanzanian health care experts. Within the maternity departments, independent observers quantitatively assessed the quality of daily partograph use on an itemized scale from 0 (0%) to 2 (100%). Neonatal outcome was assessed using the 1 min APGAR score. An APGAR < 7 was classified as unsatisfactory.

Results: Poor partograph-based monitoring was related to unsatisfactory neonatal outcome, with an odds ratio of 2.94 (95% CI = 1.32–6.58; $P < 0.005$). A non-significant increase in the performance quality of monitoring normal delivery and a decrease in monitoring complicated delivery was measured.

Conclusions: Evidently the partograph improves the outcome for mother and baby, this study finds that poor performance quality of monitoring labour by partograph appears as a risk factor for

unsatisfactory neonatal outcome. At the same time, those women with complicated deliveries seem to receive the monitoring with the least quality. Generally, the use of partograph needs continuous reinforcement and quality assurance to successfully reduce morbidity and mortality for mother and baby.

PO-Geb 02.35

Perinatal management and surgical repair of a severe congenital diaphragmatic hernia in an extremely preterm infant

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The overall survival rate in isolated congenital diaphragmatic hernia (CDH) is about 60%. The prognosis is determined by the grade of lung hypoplasia and impaired lung development. Transient fetoscopic tracheal occlusion may improve lung growth and thereby outcome. We report a case of an extremely preterm infant, born at 27 weeks gestational age (GA) with diagnosis of isolated left sided CDH, liver herniation and expected lung hypoplasia (Lung to head ratio 0.8). A 31 year old patient was referred at 21 weeks GA for prenatal diagnostics at our centre. US confirmed the diagnosis of left sided CDH (Lung to head ratio 0.8 (LHR)) with liver herniation. Multi-disciplinary counselling considered a prospective management including fetal surgery with tracheal balloon occlusion. At 23 weeks GA the patient developed prolaps of the amnion bag. Lung maturation was induced with betamethason. At 27 3/7 weeks GA rupture of membranes occurred and amnion infection syndrome was suspected. A female infant, birth weight 1060 g (54th percentile) was vaginally delivered (Apgar score: 4/7/8; cord-blood pH 7.4). Postnatal treatment followed a protocol including, prophylactic surfactant and inhaled nitric oxide application, high frequency ventilation and inotropic support. Pulmonary circulation was stabilized and surgical closure of the CDH on NICU was performed at day 6 postnatal age. The patient was extubated on day 14 postnatal age. She developed grade II° intraventricular hemorrhage and was discharged at term equivalent age. Follow up at 3 month corrected age shows a normal somatic and neurological development. This is a rare report of a surviving extremely preterm infant with CDH and a LHR <1. One may speculate whether the infant did benefit from preterm delivery before fixation of pulmonary hypertonus occurred. It should be systematically evaluated in CDH with very poor prognosis, whether this may be an alternative procedure.

PO-Geb 02.36

Long-term developmental outcome of preterms after tocolysis with NO donors or betamimetics: an 8 years follow up of the Thuringia Tocolysis Trial

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Objective: While tocolysis were used to treat preterm labor for decades only very limited knowledge exist about neurodevelopmental

long-term effects of the used medication. Whereas there is increasing suspicion for beta mimetic long-term effects (Witter et al. 2009) no studies exist about effects of NO donors. To explore the impact of tocolytic therapy with fenoterol (Partusisten®) or nitroglycerid patches (Nitroderm TTS®) on neuropsychological development in children aged 7–9 years. Their mothers participated the prospective randomized multicenter Thuringia Tocolysis Trial 1999–2002 (Schleussner et al. 2003).

Materials and methods: 19 children intrauterine affected with fenoterol and 21 children after NO tocolysis between the 27th and 34th weeks gestation underwent neuropsychological assessment. All subjects were appropriate for gestational age (delivered after 34 + 0 weeks gestation), without intensive care requirements, invasive procedures, or malformations. The test battery consists of testing cognitive performance (IQ-CPM) and movement performance (Movement ABC-2), attention test (CPT), parents questionnaires for ADHD symptoms (DISYPS/ADHS), socioeconomic status and child development, general psychiatric problems (CBPL), behavioural problems (SDQ) and children questionnaires for emotional irritability (PFK) and live events (ZLEL).

Results: All children developed within the normal ranges of all performed tests. Significant differences were observed in the parents questionnaire CBPL ($p < 0.05$), but also within the normal range of the scale. No significant differences were to detect in all other tests.

Conclusions: Antenatal tocolytic therapy with the NO donor nitroglycerid seems to be without long-term effects on neuropsychological development.

PO-Geb 02.37

Chorioamnionitis, an absolute contraindication for delayed interval delivery? A case report

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Objective: Implementation of assisted reproduction has increased the incidence of multiple gestations. 1–2% of all twin pregnancies are complicated by premature contractions with following premature rupture of membranes before 26 weeks of pregnancy. Prolongation of pregnancy after the delivery of the first twin can improve the outcome of the remaining twin. This is a case report of fortunate delayed delivery even though chorioamnionitis occurred after very early PROM of the first amniotic sac.

Materials and methods: A 33 year old nulliparous woman was admitted to the hospital at 18 + 4 week of gestation of a dichorionic, diamniotic twin pregnancy achieved by assisted reproduction, because of cervical incompetence without premature uterine contraction. The patient was treated with bed rest and antibiotic. Two days later PROM of the first amniotic sac occurred. The mother developed chorioamnionitis and at 21 + 3 week premature labour and stillbirth of the first (male) twin took place. Nevertheless with new antibiotic uterine contractions ceased, CRP declined, a cervical cerclage was placed and the second twin was left in utero. RDS prevention had been carried out at 24 + 0 and 24 + 1 week of gestation. Caesarean section was performed at 24 + 3 weeks and a female infant of 610 g was born successfully.

Conclusions: Each of these pregnancies is a unique medical situation. Therapy is a complex of tocolysis, cervical cerclage, bed rest, antibiotics and RDS prevention with antenatal corticosteroids. In literature we find a mean prolongation interval of 16 (1–96) days. Benefits are reduced neonatal mortality and morbidity. Serious maternal risks of delayed delivery are severe chorioamnionitis and sepsis.

PO-Geb 02.38

Fetal right heart defects: antenatal management and outcome in 120 cases

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Objective: We sought to determine the characteristics of antenatally diagnosed right heart anomalies over a 15 years period in a tertiary referral centre.

Materials and methods: In this retrospective analysis the medical records and pediatric charts of 120 fetuses with prenatally confirmed right heart anomalies were reviewed. According to the origin and localization of the morphologically and functionally altered cardiac structures we searched our data base for cases affected by tricuspid dysplasia, tricuspid atresia, Ebstein's anomaly, tetralogy of Fallot (ToF), double outlet right ventricle, pulmonary stenosis/atresia ± VSD. The course of affected fetuses throughout advancing pregnancy and their postnatal outcome with respect to the necessity of surgical interventions were analysed. Follow up ranged from 0.1 to 14.9 years.

Results: Targeted ultrasound confirmed diagnosis before 24 gestational weeks in 58% and 42% were detected beyond 24 weeks. Karyotype examination (94/120) revealed fetal aneuploidies in 31%. 35 pregnancies were terminated on parental request, 12 pregnancies resulted in intrauterine demise or spontaneous abortion. From the remainder of 72 live born infants 5 died perinatally, 4 after 3 months and 6 within 1 year of life. ToF accounted for the majority of right heart anomalies (35%), followed by tricuspid disorders (32.5%). 62 fetuses had additional cardiac abnormalities, predominantly occurring when the tricuspid valve was affected (50%). 15 women refused autopsy after TOP or IUFD/postpartal death, in all other cases prenatal diagnosis had been confirmed or further specified. 73.6% of the newborns underwent 1 or more corrective surgical interventions (average 2) resulting in satisfying cardiac function of the survivors. **Conclusions:** Prenatal diagnosis of anomalies of the right heart enables their correct classification, assessment of severity of the obstructive lesions (including flow via foramen ovale and ductus arteriosus) as well as proper delivery scheduling and adequate perinatal management.

PO-Geb 02.39

Fetomaternal transfusion syndrome: a case report of life-threatening perinatal complication

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Objective: We present the case of a serious fetomaternal transfusion syndrome which may develop in the last three months of pregnancy. Fetomaternal transfusion syndrome is defined as the transfer of fetal erythrocytes to the maternal circulation and presents as a rare but potentially life-threatening complication for the fetus/newborn. About 0.1 to 0.2 ml of fetal blood are transfused under physiological conditions, larger volumes can be transferred under pathological

conditions like a caesarian section or placental abnormalities. We present the case of a patient whose child developed a life-threatening complication due to fetomaternal transfusion.

Results: We report the case of a 37 year old woman (GI/P0) who was admitted to the hospital with premature rupture of membranes in the 37th week of pregnancy with previously uncomplicated course of pregnancy. During the initial phase of labor CTG abnormalities developed which mandated an urgent secondary cesarean section. A vital child, appropriate for gestational age, was delivered and—after showing signs of serious anemia—immediately transferred to the neonatal intensive care unit. Haemoglobin concentration was 5 g/dl and the child was transfused with consecutive improvement of the child's cardio-circulatory status. Since no obvious reason for the newborn's anemia could be identified (e.g. no Rhesus/ AB0 incompatibility, no parvovirus B19 infection, no signs of bleeding or premature abruption of the placenta) maternal blood was tested for fetal Hb (HbF) to evaluate for fetomaternal transfusion syndrome. Fetal Hb was significantly elevated in maternal blood (+900%, maternal HbF 5%) proving the child's anemia to be due to fetal-maternal transfusion.

Conclusions: This case report of a serious fetomaternal transfusion syndrome emphasizes the necessity of keeping this differential diagnosis in mind when CTG abnormalities develop and an anemic child is subsequently delivered.

PO-Geb 02.40

Fetal micro-/retrognathia: an ominous sonographic finding? Retrospective analysis of 56 prenatal cases

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Objective: We sought to determine the characteristics and prognostic value of antenatally diagnosed fetal micro-/retrognathia in a mixed referral population.

Materials and methods: In this retrospective analysis the medical records and pediatric charts of all pregnancies with the suspicion of fetal micro-/retrognathia were reviewed. During the study period from January 1993 and December 2009 a total of 28.935 pregnancies were screened by ultrasound. A total of 56 eligible cases have been identified. The initial diagnosis was established between 11 + 5 and 35 + 1 gestational weeks. The affected fetuses were classified according to the previously described criteria of micro-/retrognathia. Once the diagnosis has been made a detailed analysis for additional structural defects and/or chromosomal anomalies was carried out.

Results: In 33/56 cases (59%) the parents opted for termination of the pregnancy. Four fetuses died immediately after birth, in 5 cases a stillbirth occurred. Karyotype examination was prompted in 43/56 cases (77%). In 38% an abnormal karyotype was found (mainly

fetuses with trisomy 18 and triploidy). Additional structural abnormalities mainly affected the musculoskeletal system (44%). 18% of the cases had non-skeletal anomalies (multicystic kidney disease, congenital heart disease and other syndromal disorders). Fourteen fetuses were live-born (25%), of which two infants were healthy and the prenatal diagnosis could not be confirmed. Of the remainder 4/12 fetuses had minor structural abnormalities and showed a favourable postnatal outcome.

Conclusions: The diagnosis of fetal micro-/retrognathia poses a considerable impact on both the antenatal and postnatal outcome of the affected individuals due to its potential association with minor and major structural abnormalities. Thus, detailed sonographic anatomical survey is mandatory. In certain cases adjunctive use of fetal MRI may be reasonable. Once the diagnosis has been confirmed, a comprehensive parental counseling together with pediatricians, oral surgeons and geneticists is needed.

PO-Geb 02.41

Life threatening complication in the postnatal period of a patient with myasthenia gravis

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Objective: We present a case with a complication from maternal myasthenia gravis and raise awareness for optimization of perinatal management.

Materials and methods: The heterogeneous group of congenital and acquired myasthenia syndromes is clinically characterized by an insufficient neuromuscular transmission leading to progressive paresis. In the case of maternal myasthenia gravis both the mother and the child may develop myasthenia symptoms with varying degrees of weakness and progressive fatigability of the skeletal muscles. We present the case of a patient with a life threatening complication due to myasthenia gravis shortly after an elective cesarean section. We emphasize the necessity of interdisciplinary diagnostic and therapeutic strategies during the perinatal period.

Results: We report the case of a 38 year old patient with immune-mediated myasthenia gravis, who underwent a secondary cesarean section with spinal anesthesia at 35 + 3 weeks of pregnancy, after a premature rupture of membranes. The newborn was transferred to the pediatric hospital for surveillance and did not show any signs of muscular weakness throughout the first week of life. The mother developed a myasthenic crisis characterized by progressive dyspnoea leading to a respiratory insufficiency during the second postpartum day. A generalized seizure with cardiac-circulatory arrest followed. After successful cardiopulmonary resuscitation the patient was transferred to the intensive care unit. The interdisciplinary therapeutic approach included ventilatory assistance via endotracheal intubation, parenteral pyridostigmine, azathioprine and steroids. A stable state was regained, so that after five days of intensive care treatment the patient was transferred to normal ward and in the course of time could be dismissed.

Conclusions: Myasthenia gravis can lead to a life threatening situation in the postnatal period. Literature review reveals that a high per-

centage of myasthenia gravis patients develop postnatal myasthenic crisis. To avoid further complications interdisciplinary perinatal management is mandatory.

PO-Geb 02.42

Seroprevalence of HTLV infection in a prepregnancy class group in Lagos

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Objective: Human T-Cell lymphotropic viruses are Human RNA retroviruses not related genetically to HIV but have similar routes of transmission as HIV. HTLV causes T-Cell leukemia and T-Cell lymphoma in adults and may also be involved in certain de-myelination diseases. HTLV is transmitted transplacentally, parenterally, by sexual contacts and by infected blood. The infection in women occurs primarily during their reproductive years; hence pregnancy provides a unique opportunity for implementing prevention strategies against the infection. To study seroprevalence of HTLV infection during pre-pregnancy period. If we estimate the seroprevalence in pre-pregnancy patients, the effective and timely intervention will reduce transmission of infection to their new born. **Setting:** A Prenatal Diagnosis & Therapy Centre of a Tertiary Hospital in Lagos. **Design:** A cross-sectional study.

Materials and methods: Blood samples of males and females referred to the pre-pregnancy class between 2003 and 2009 with written consent were collected and tested for HTLV antibodies. Sera from 252 patients were tested for HTLV I&II antibodies by ELISA technique (DIA-PRO Diagnostic Bioprobes Srl, Milano/Italy).

Results: Out of a total of $n = 252$ patients screened, 2 (0.79%) were found to be seropositive.

Conclusions: In the present study, seroprevalence of HTLV infections was found to be 0.79% among patients attending the pre-pregnancy class in Lagos. There is need to prevent this prevalence from increasing by targeting an intervention program towards high risk and vulnerable groups in the society.

PO-Geb 02.43

Rupture on the posterior side of an unscarred uterus on onset of labour at 41 + 4 weeks of gestations

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Objective: The rupture of an unscarred uterus is a very rare and one of the most dangerous complications in obstetrics, associated with a high risk for maternal and fetal mortality.

Materials and methods: A 33-year-old gravida 4, para 2 with 2 prior vaginal deliveries without any complications received 25 µg misoprostol to induce labour at 41 + 4 weeks of gestation. In patient history there was an abortion and the patient underwent curettage. 5 hours 30 min after application of misoprostol the patient presented a sudden pain and a minimal vaginal bleeding while she had mild

contractions. Simultaneously a fetal bradycardia was registered. An emergency Caesarean section was performed. A rupture of the uterus on the left posterior side from uterine fundus to the internal cervix was seen. The cervix itself was unaffected and 2 cm open. The child was lying in the abdominal cavity. After cutting the umbilical cord the baby was given to the attendant paediatrics (NpH 6.82, APGAR 1/5/7). The time from diagnosis to delivery of the baby was 8 min. A partial placental abruption on the anterior side of the uterus could be demonstrated. The patient underwent a total hysterectomy with a totally blood loss of 1500 ml. Packed red blood cells were substituted. The postoperative inhabitation was without any complications.

Conclusions: The symptoms of a rupture of the uterus have to be recognised as fast as possible to induce immediate emergency interventions. Every induction of labour has a higher risk of an uterus rupture even by an unscarred uterus.

PO-Geb 02.44

Early gestational diabetes mellitus (GDM) screening based on risk factors

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Objective: Women with early diagnosis of GDM represent a high-risk population with an increased incidence of severe obstetric complications. Early GDM testing in women with high diabetes risk is recommended by the HAPO consensus without definition of risk factors. ADA, WHO and DGGG early screening recommendation had been incoherent regarding definition of risk factors (Table 1). Our aim was to investigate the predictive value of single risk factors by itself and in combination for early-onset GDM using patient data obtained from a population-based universal screening study with oGTT at 10–18th and 26–28th week of gestation (case-control study)

Materials and methods: 3607 pregnant women were screened according to WHO GDM criteria. In a database of all GDM women ($n = 155$ early onset, $n = 123$ late onset) and a control group ($n = 319$), we compared the predictive value of ADA, WHO and DGGG risk factors

Results: All investigated risk factors (except for previous macrosomia) identified women with risk for early onset GDM. Previous GDM (pGDM), age and obesity discriminates best between women with early and the late onset GDM. Combinations of risk factors according to ADA, to WHO and to DGGG could identify 47, 54, 53.2% of the early onset GDM patients with a specificity of 85, 70 and 74.9% respectively. Stepwise logistic regression analysis revealed pGDM (OR: 7.8; $P < 0.0001$), BMI ≥ 30 kg/m² (OR: 3.4; $P < 0.01$), strong family history of diabetes (OR: 2.4; $P < 0.01$) and age ≥ 35 years (OR: 1.9; $P < 0.05$) as independent risk factors. Including maternal age ≥ 35 years in ADA and DGGG risk factor definition elevates sensitivity to 59.7 and 64.3% with a specificity of 71.8% and 63.3% respectively.

Conclusions: More than half of all GDM women were diagnosed by early screening. Including an age limit of >35 years, early screening based on the risk factors of DGGG (BMI ≥ 27 kg/m², pGDM, family history, previous macrosomia, habitual abortion) or ADA (BMI ≥ 30 kg/m², pGDM, family history) could identify almost two thirds of these patients

Table 1. (PO-Geb 02.44). WHO, ADA and DGGG guidelines: indication for early oGTT during pregnancy

	Age	Weight	Previous history of glucose intolerance	Family history of diabetes	Previous macrosomia	Other
WHO 1999	Older women	–	Previous history of glucose intolerance	–	History of LGA babies	Elevated fasting/random blood glucose Ethnicity
ADA 2010	–	Marked obesity	Previous GDM	Strong family history of diabetes	–	Personal history of glucosuria PCOS
DGGG 2001	–	Overweight BMI ≥ 27 kg/m ²	Previous GDM	Strong family history of diabetes	Previous macrosomia (≥ 4500 g)	Habitual abortion Previous congenital malformations and intrauterine death

Table 2. (PO-Geb 02.44). Patients characteristics

	Early onset GDM	Late onset GDM	Control	<i>P</i> early vs. late onset GDM	<i>P</i> early onset GDM vs. control	<i>P</i> late onset GDM vs. control
<i>N</i>	155	123	319			
Age (years)	31.8 \pm 4.3	30.3 \pm 3.9	30.2 \pm 4.3	<0.05	<0.05	NS
BMI (kg/m ²)	24.9 \pm 5.4	24.1 \pm 4.1	23 \pm 4.1	NS	<0.0001	<0.05
Strong family history of diabetes (%)	24.7	29.8	7.9	NS	<0.0001	<0.05
Previous GDM (%)	20.8	11.3	2.2	<0.05	<0.0001	<0.05
Age ≥ 35 year (%)	25.3	11.3	15	<0.05	<0.05	NS
BMI ≥ 27 kg/m ² (%)	27.3	20.3	16.3	NS	<0.01	NS
BMI ≥ 30 kg/m ² (%)	19.5	9.8	5.8	<0.05	<0.0001	NS
Habitual abortion (%)	2.6	0.8	0.3	NS	<0.05	NS
Previous macrosomia (≥ 4000 g)	4.6	5.8	5.5	NS	NS	NS
Previous macrosomia (≥ 4500 g)	0	0	0.6	NS	NS	NS

PO-Geb 02.45

Fetal megacystis: an interdisciplinary challenge

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Objective: Fetal megacystis is an infrequent disorder with varying prognosis depending on the amount of amniotic fluid, the appearance of the kidneys and a variety of other associated abnormalities.

Materials and methods: We present the case of a Gravida I Para 0 with a fetal megacystis diagnosed at the time of first trimester and report the postpartum follow up until 2 years of age.

Results: The megacystitis was diagnosed at 14 + 3 weeks of gestation. An interdisciplinary consultation was organized. At 17 + 4 weeks of gestation the bladder displayed a maximum diameter of 7 mm and a function of the bladder was performed. As a prognostic parameter the fetal urine showed no pathologies. Further sonographic controls revealed a mild dilated bladder with prominent bladder wall. At all times of examination the amniotic fluid index impressed normal as well as no hyperechogenicity of the kidneys could be detected. After a spontaneous delivery at 38 + 0 weeks of gestation the child was taken care of by the neonatal department. The boy showed signs of a prune-belly like symptom complex with cryptorchism and flappy

abdominal wall. For urination catheterisation was necessary and the renal function was unrestricted at all times.

Conclusions: In case of fetal megacystis a precise prenatal sonographic examination and diagnosis allow for individualized treatment and prognosis of these patients. Interdisciplinary logistics and expertise are necessary to handle those complex cases under optimal conditions.

PO-Geb 02.46

Adenosine receptor A2A and A2B activation reduces trophoblast migration

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It is hypothesized that the pathophysiology of preeclampsia begins with shallow trophoblast invasion leading to placental hypoxia. Hypoxia is a potent stimulus for the release of adenosine. Women with preeclampsia show increased circulating concentrations of adenosine and placental expression of adenosine receptors is increased in preeclampsia.

Objective: We are working on the hypotheses that adenosine is involved in placental development and tested the hypotheses that the adenosine receptor subtypes A2A and A2B are involved in trophoblast migration. **Materials and methods:** Human HTR-8/SVneo trophoblast cells were grown to confluence in RPMI 1640 medium supplemented with 5% fetal bovine serum and 100 IU/ml penicillin–streptomycin. Monolayers were scratched with a sterile pipette tip. The ability of the cells to migrate into the “wound” in the presence or absence of adenosine receptor A2A or A2B agonist, antagonist or a combination of both in growth media was observed under hypoxic (2% O₂) or standard tissue culture conditions (21% O₂) over a 22 h time period and analyzed using Image J software. Data are presented as medians and standard errors of remaining wound area. Statistical analyses were performed with Kruskal–Wallis and Wilcoxon-rank sum test. Probability values were considered significant at $p < 0.05$.

Results: The ability of trophoblast cells to migrate was reduced and the remaining wound area was increased after adenosine receptor A2A and A2B stimulation compared to control at hypoxic (A2A: 46.7 ± 2.1 vs. 40.95 ± 3.0 ; A2B: 41.37 ± 4.7 vs. 24.8 ± 4.8 ; $p < 0.05$, $N = 7$) and normoxic (A2A: 48.8 ± 2.2 vs. 43.0 ± 2.2 ; A2B: 37.2 ± 7.7 vs. 23.3 ± 4.0 ; $p < 0.05$, $N = 7$) conditions.

Conclusions: Our results suggest a role for adenosine receptors A2A and A2B in placental development and possibly in the pathophysiology of preeclampsia.

PO-Geb 02.47

Management of an IUGR with an intraabdominally anastomosis of the umbilical artery and vein

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We describe a case of malformation of the umbilical vessels resulting in an IUGR. We explain diagnostic and clinical management. First visit of the 32-year-old first Gravida was in 27 + 5 week showing a dysproportional IUGR, especially of the fetal abdomen. Sonomorphology of the organs was normal, TORCH and amniotic fluid index as well. Doppler of the maternal system showed normal uterine perfusion. Umbilical Doppler was normal but Doppler of Arteria cerebri media (ACM, PI 0.94, RI 0.59) and ductus venosus (DV, PI 1.02) showed pathological results. The fetus did not show any abdominal growing over the next 3 weeks, while the BIP and the femur were growing normally. Doppler did not deteriorate any further but remained as described above. Repeated sonographical screening for fetal malformation resulted in the diagnosis of an anastomosis between the umbilical artery and the umbilical vein in the abdominal wall and a crossing of both umbilical vein in the same location. Pathophysiological patterns focussed on normal Doppler of the umbilical artery while ACM and DV are pathological are discussed as well as management of surveillance and timing of delivery. The baby was delivered by caesarean in 30 + 5 weeks with a weight of 980 g.

PO-Geb 02.48

Influences in neurodevelopment of children at school age receiving antenatal glucocorticoid treatment

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Objective: Antenatal glucocorticoid (GC) therapy is used to treat women at risk of preterm delivery to enhance fetal lung maturation. There is increasing suspicion that this therapy programs mental and cardiovascular disturbances in later life. To explore the impact of antenatal GC therapy on neuropsychological development in children aged 7–9 years.

Materials and methods: 39 children (21 females) treated with 2×8 mg betametasone (GC) 24 h apart (and repeatedly if necessary) between the 25th and 34th weeks gestation and 39 controls underwent neuropsychological assessment. Controls were pair-matched for gestational age at delivery, gender, and current age. All subjects were appropriate for gestational age (delivered after 34 + 0 weeks gestation), without intensive care requirements, invasive procedures, or malformations. The test battery consists of testing cognitive performance (IQ–CPM) and movement performance (Movement ABC-2), attention test (CPT), parents questionnaires for ADHD symptoms (DISYPS/ADHS), socioeconomic status and child development, general psychiatric problems (CBPL), behavioural problems (SDQ) and children questionnaires for emotional irritability (PFK) and live events(ZLEL). A matched pairs analysis by mixed linear models were fitted to examine the impact of antenatal GC exposure.

Results: Significant differences were observed in cognitive performance (IQ) ($p = 0.001$), movement performance ($p = 0.04$), ADHD symptoms ($p = 0.01$) and behavioral problems ($p = 0.004$), but all within the normal range of the scales. The results have to be thoroughly explored for residual confounding which could not be eliminated by matching.

Conclusions: Antenatal GC-treatment or GC-treatment related factors may cause a long-term influences on neuropsychological development, yet performances in normal range.

PO-Geb 02.49

Changed HPA axis and autonomic stress reactivity of children at school age as long-term effect of antenatal glucocorticoid treatment

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Objective: To explore the impact of antenatal Glucocorticoid (GC) therapy on stress reactivity mediated by the autonomic nervous system (ANS) in children aged 7–9 years.

Materials and methods: 39 children (21 females) treated with at least 2×8 mg betametasone (GC) 24 h apart between the 25th and 34th weeks gestation and 39 controls underwent the Trier Social Stress Test adapted for Children (TSST-C). Controls were pair-matched for gestational age at delivery, gender, and current age. All subjects were appropriate for gestational age (delivered after 34 + 0 weeks), without intensive care requirements, invasive procedures, or malformations. Before, during and after TSST-C salivary cortisol levels were measured. Standard indices of heart rate variability (HRV) were derived from the electrocardiogram as outcome measures: mHR (mean heart rate), SDNN (overall variability), RMSSD, HF (both related to vagal activity), LF (related to vagal and sympathetic activity), LF/HF (sympatho-vagal balance), AIF (autonomic information flow, reflects complex short term ANS mediated communication). A matched pairs analysis by mixed linear models were fitted to examine the impact of antenatal GC exposure on ANS stress response.

Results: Whereas no differences in basal cortisol levels the cortisol stress response was blunted in the GC group ($p = 0.015$). Significant differences were observed stress test induced for SDNN ($p = 0.035$), RMSSD ($p = 0.030$), mHR ($p = 0.011$), HF ($p = 0.001$), LF/HF ($p < 0.001$) and AIF ($p = 0.021$). Adjusted for baseline activity TSST-C induced a attenuated increase in mean HR, LF/HF and AIF and a attenuated decrease in SDNN, RMSSR and HF in the GC group compared to controls. This suggests a blunted stress response of all parts of ANS in GC group. The results have to be thoroughly explored for residual confounding which could not be eliminated by matching.

Conclusions: The reduced stress response of the humoral and autonomic nervous system in children may have been programmed by antenatal GC administration.

PO-Geb 02.50

Abruption of placenta praevia: a case report

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Objective: Vaginal bleeding during the second half of pregnancy is always a threat to mother and fetus. The most important differential diagnoses are placenta praevia and abruption of placenta. Diagnosing placenta praevia does not rule out abruption of placenta, however. This case report demonstrates that placenta praevia is rather a risk factor for abruption of placenta.

Materials and methods: A 28 year old woman with a singleton gestation at 26 weeks presented with vaginal bleeding and known placenta praevia. At admission the lively fetus with an estimated weight of 1000 g appeared to be in breech presentation. The ultrasonic scan showed a placenta praevia totalis and normal cervical length. Tocolysis, induction of fetal lung maturity and an antibiotic therapy were conducted. The following day bleeding ceased. In the course of the hospital stay contractions and slight bleeding emerged, but could be controlled. Another ultrasonic scan revealed a hematoma in the region of the cervical os. At gestational age of 28 weeks bleeding restarted, this time accompanied by a diffuse slight abdominal pain. After consultation of our neonatologists the decision was made to carry out caesarean section during which a partial abruption of the placenta was confirmed. The newborn weighed 1400 g and received APGAR-scores of 1/4/9. The following days he remained stable and could be transferred to the hospital of the family's hometown.

Conclusions: This case report illustrates that vaginal bleeding of women with placenta praevia should carefully be questioned concerning abruption of placenta.

PO-Geb 02.51

Breastfeeding rates in Freiburg/Germany

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Objective: Purpose of this study was to assess the motivation, behaviour and duration of breastfeeding of women delivering in 2 "babyfriendly Hospitals" in Freiburg/Germany.

Materials and methods: The prospective observational study included 443 births between august and December 2008. We performed a standardized interview the day after delivery in the maternity ward.

Thirty-four women decided for primary weaning. Breastfeeding women were followed up by telephone interview 3, 6 and 12 month after delivery. Statistical analysis was performed with univariate and multivariate regression analysis.

Results: 92% started breastfeeding and 61% were still breastfeeding at 6 month. Women still breastfeeding 6 month post partum are significant older, have higher education, had not delivered by elective caesarean section, decided to breastfeed already in pregnancy, were not in doubt about the amount of milk, did not use a pacifier, did not deliver in the university hospital and felt supported by their partners. In a multivariate analysis the independent variable was higher education.

Conclusions: Breastfeeding promotion should be implemented in school education and pregnancy counselling. Multidisciplinary breastfeeding support could help to sustain breastfeeding continuation as recommended by WHO/UNICEF.

PO-Geb 02.52

Preeclampsia: first nationwide and representative study in Germany of prevalence, risk groups, and possible prevention mechanisms based on the data of the German Perinatal Quality Register 2006

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Objective: Preeclampsia (PE) is one of the most serious pregnancy complications. It is among the leading causes of maternal and fetal morbidity and mortality. This study evaluated risk groups and prognostic factors as well as the consequences of PE on neonatal outcome based on the German Perinatal Quality Registry 2006.

Materials and methods: The German Perinatal Quality Registry is a complete collection of pre- and perinatal data of all German hospital deliveries in 2006. The evaluated cohort exists of 658,145 newborns of 647,385 women. Data evaluation was approved by the University of Heidelberg's Ethics Committee and the "Gemeinsamer Bundesausschuss für Qualitätssicherung" (BQS). For statistical analysis chi-squared testing was used to determinate the relationship between categorical variables of interest. Afterwards, multivariate logistic regression models were used to estimate odds ratios (OR) and the 95% confidence intervals of risk factors. Statistical significance was assessed at $p \leq 0.05$.

Results: In Germany 2–3% of all pregnancies develop PE. High risk groups are pregnant women at higher age (>35 years), low socio-economic status, preexisting obesity, and gestational diabetes. Moreover, nulliparity and multiple pregnancy are associated with an increased risk for PE. Adverse neonatal outcome parameters include: microsomia (OR growth <10 percentile: boys 2.12 (1.98–2.26), girls 1.86 (1.76–1.97)), hypoglycemia, preterm delivery, emergency cesarean section and decreased vital parameters (5-min APGAR <7). **Conclusions:** Based on analysis of the full set of German hospital deliveries, PE imposes enormous health risks not only for neonates, but also demonstrates problematic accumulation of risk factors among specific groups of pregnant women. For initiation of target-group aimed interventions, knowledge of demographic factors as well as psychosocial structures of high risk groups is the key: thus older, obese pregnant women with low social status and gestational diabetes

form an important target-group for diagnostic and therapeutical measures.

PO-Geb 02.53

Prevalence and outcome of gestational diabetes in Turkmenistan

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Objective: Very few data are available about the health care system in Turkmenistan a central Asian country with rapidly increasing wealth and rates of obesity. As for other central Asian countries the prevalence of gestational diabetes (GDM) is unknown. The aim of this investigation was to prospectively determine the prevalence of GDM in Turkmenistan and the frequency of complications in newborns from GDM mothers.

Materials and methods: From March 2008 until September 2009 all pregnant women presenting to the perinatal center at the Ene Maehri Merkezi Hospital (University of Ashgabat) obtained a glucose screening (after 26 weeks of pregnancy; 50 g glucose orally). If the 60 min glucose concentration was ≥ 7.8 mmol/l an oral glucose tolerance test (75 g) was performed. GDM was diagnosed if one or more glucose values were abnormal (≥ 5.0 , ≥ 10.0 , ≥ 8.0 mmol/l at 0-, 60-, 120-min, respectively). Birth weight, APGAR and 30 min glucose concentration were determined in all newborns.

Results: 25.4% of 1271 screened patients had a pathological screening test. Of those, 28.5% had GDM (overall prevalence 7.3%). Screening glucose (60 min) correlated with age ($r = 0.13$; $p > 0.001$), BMI ($r = 0.12$, $p < 0.001$), gravidity ($r = 0.12$, $p < 0.001$) and blood pressure ($r = 0.06$, $p = 0.03$). GDM patients were older (30.2 ± 5.3 years vs. 27.1 ± 4.9 years; $p < 0.001$) and more obese (BMI 27.7 ± 4.9 vs. 26.5 ± 4.5 kg/m²; $p = 0.03$) than controls. GDM patients delivered more frequently by scheduled caesarean sections (12.0% vs. 8.9%, ns) and less frequently by emergency caesarean sections (8.8% vs. 13.3%, ns). In newborns delivered after ≥ 37 weeks gestational age (controls vs. GDM) birth weight (3500 ± 462 vs. 3605 ± 409 g, $p = 0.06$) and APGAR (8.4 ± 1.5 vs. 8.3 ± 1.3 , ns) did not differ between both groups. However, hypoglycemia (blood glucose < 2.5 mmol/l) occurred twice as often in GDM children compared to controls (13.9 vs. 27.3%, $p < 0.05$).

Conclusions: In Turkmenistan GDM is characterized by the same risk factors as in European countries. Because of the rapidly increasing wealth and increasing prevalence of obesity the prevalence of GDM will probably further increase. Newborns from GDM patients tended to be heavier and had high rates of hypoglycemia. This study shows that medical prevention programs can also be successfully implemented in Turkmenistan.

PO-Geb 02.54

Fetal megacystis with oligo-anhydramnion in 21st week of gestation

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Objective: First presentation of a 23 years old primigravida in 20 + 3 weeks of gestation for malformation ultrasound scan: normal fetal weight, anhydramnion, bilateral hydronephrosis and megacystis with hypertrophic bladder wall. Last normal amount of amniotic fluid was anamnestic in 14th gestational week. So the strong suspicion of a lower urinary tract obstruction (LUTO) existed. The objective of this case report was to determine whether vesico-amniotic shunting could prolong pregnancy and improve fetal outcome.

Materials and methods: The puncture of the fetal urine bladder for kidney function diagnostic ($\beta 2$ -microglobulin, cystatin C, Na⁺, K⁺, Cl⁻) showed a still acceptable kidney function. Amniocentesis revealed a normal male karyotype. To prevent lung hypoplasia a vesico-amniotic shunt was implanted. The following ultrasound examinations showed a regular amount of amniotic fluid and an orthotopic shunt. Furthermore a fetal hydronephrosis on the left side persisted. In week 26 the shunt was dislocated, ascites and fetal hydronephrosis on the left side with normal AFI (amniotic fluid index) was observed. Infant respiratory distress syndrome (IRDS) prophylaxis and re-shunting was conducted. The following examinations demonstrated normal AFI with appropriate fetal development, still hydronephrosis on the left side, no more ascites, shunt in situ. From 35th week amniotic fluid decreased (AFI 7-8), hydronephrosis progressed and a megacystis developed again. Caesarean section was performed in 36 + 5 weeks of gestation.

Results: Fetal outcome: 3380 g, Apgar 8/8/9, arterial-pH: 7.29, good cardiopulmonary adaption. Sonographically infravesical obstruction with bladder hypertrophy and bilateral dilated ureters was seen. By micturating cystourethrogram a LUTO was confirmed. Additionally a dysplastic right kidney was suspected. 6-month-follow-up: Left kidney with normal function and dysplastic right kidney in state after urethral stricture and pyelocutaneostomy. The child showed a normal development.

Conclusions: Vesico-amniotic shunting in sonographically suspicion of a LUTO prolongs pregnancy and improves fetal outcome.

PO-Geb 02.55

Case report: diagnosis of familial Beckwith–Wiedemann syndrome by a small exomphalos at 12 weeks of gestation

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The 33 year old I-Gravida was referred for a nuchal scan. Her previous medical history was uneventful. However, she reported on a small exomphalos at birth. The ultrasound examination showed a small exomphalos containing bowel only. The crown rump length was

67.5 mm, fetal NT 2.9 mm and free β -hCG and PAPP-A were 11.5 MoM and 1.9 MoM, respectively, resulting in an increased risk of trisomy 21 of 1:20 and a risk of trisomy 18/13 of 1:8400. However, the most likely diagnosis was Beckwith–Wiedemann syndrome based on the maternal history, the small exomphalos and the largely increased free β -hCG level. Invasive diagnosis was declined. Initiated by the ultrasound findings, molecular genetic analysis revealed, that the patient herself was affected (mutation in gene CDKN1C). Meanwhile her sister, a 35 year old II-Gravida I-Para with one healthy child came for a nuchal scan. She also reported on a small exomphalos at birth, otherwise her medical history was uneventful. Her nuchal scan showed a crown-rump length of 68.1 mm, a fetal NT of 2.0 mm and free β -hCG and PAPP-A levels of 1.0 and 0.4 MoM. Although the risk profile was not indicative for Beckwith–Wiedemann syndrome, the fetus had a similar small exomphalos. Both cases of Beckwith–Wiedemann syndrome were confirmed after birth. Further genetic analysis of the remaining family members showed that the two sisters and one brother were affected by Beckwith–Wiedemann syndrome.

PO-Geb 02.56

Prenatally diagnosed partial monosomy 21: ultrasound findings, karyotyping results and fetal outcome

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Objective: We describe a prenatally diagnosed case of monosomy 21 which is a very rare finding resulting in live births with severe mental retardation. Ultrasound findings, karyotyping and postnatal findings are described.

Materials and methods: A 36 year old 4 gravida 2 para was sent to our tertiary clinic for perinatal medicine for reasons of moderate retardation at 24 weeks of gestation. She reported a normal first trimester screening including normal biochemistry performed by her doctor. At 20 weeks of gestation a mild fetal growth retardation was diagnosed. Ultrasound findings at 24 weeks presented a mild ventriculomegaly with suspected partial agenesis of the corpus callosum, hyperechogenic bowel, abnormal profile and a dilated colon. Maternal and fetal Doppler sonography was normal. Under suspicion of a chromosomal or genetic abnormality we performed an amniocentesis. The karyotype was described as: 47,XX,del(21)(q22), +mar[15]. Karyotypes of both parents were normal. Pregnancy was monitored regularly by ultrasound. Fetal growth restriction was obvious onward. By the end of pregnancy the patient revealed clinical signs of pre-eclampsia so that the pregnancy was terminated at 41 + 3 weeks of gestation by spontaneous delivery. Birth weight was 2240 g, Apgar 1/8/9. Postnatally a high nasal root, down-slanting palpebral fissures, retrogenia, posterior rotated, slightly deep-set ears, a long philtrum, and a thin upper lip red were noticed. To confirm the prenatal findings and further characterise the chromosomal changes DNA was extracted from cord-blood taken at birth and subjected to karyotyping. Karyotype was described as: mos47,XX,del(21)(q22), +mar[22]/46,XX,del(21)(q22)[7]/46,XX,-21, +mar[5]/45,XX,-21[4]. Results were confirmed by molecular karyotyping using array CGH and SNP arrays.

Conclusions: Deletion of part of long arm in Chromosome 21 is a very rare finding normally coherent with growth retardation and mental retardation. Exact prenatal diagnosis of the karyotype can be difficult if mosaicism occurs. Thus prenatal genetic counselling can be difficult.

PO-Geb 02.57

Case report: two moles with living healthy fetuses

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Objective: Partial moles arise from the trophoblastic epithelium of the placenta. The availability of ultrasonography has led to early diagnosis.

Materials and methods: We present two cases with a partial mole and different pregnancy outcome.

Results: In both cases an abnormal placental structure was diagnosed at second trimester ultrasound examination. The first patient presented with transient vaginal bleeding. The fetus had normal anatomy and size for gestational age. An echogenic placenta was located on the right and a normal placenta on the left uterus wall. Amniocentesis revealed a normal karyotype. hCG was 449503 mIU/ml. After pregnancy with decrease of the mole part of the placenta, a healthy child was spontaneously born at 40 weeks of gestation. The histologic examination showed a regressive hydatidiform mole combined with a placental retardation in dichorionic twin pregnancy. Invasive growth did not appear. The second patient had an echogenic placenta with cystic structures and a normal fetus. At 27 + 0 the fetus showed a significant growth retardation and massive increase of the cystic part of the placenta. With normal uterine and umbilical doppler parameters. V_{max} in the middle cerebral artery was elevated. A distinct anemia with hemoglobin 4.7 g/dl, thrombopenia and signs of consumptive coagulopathy was found. Fetal blood transfusions were performed twice. A maximum of hemoglobin 6.8 g/dl was achieved. The preterm delivery through cesarean section was performed because of persistent anaemia and thrombopenia. Blood transfusion after birth was necessary. The histologic examination showed a partial mole with a hypertrophic placenta with no signs of invasive growth. **Conclusions:** Our examples show that in case of moles with vital fetuses a close follow-up of the fetal and placental development should be done by ultrasound. Patients have to be counseled about severe complications. In case of growth restriction or anemia a pre-term delivery might save the child.

PO-Geb 02.58

Status post sectioned and induction of labor with oral misoprostol: a prospective observational study

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Objective: Aim of the study is to show the safety and effectiveness of a dosage ascending regime of oral misoprostol for induction of labor after a prior uterine scar (97.5%C-section).

Materials and methods: 440 women in total had one prior uterine scar. In the first group (76 Patients) misoprostol was applied to induce labor with an ascending doses (day 1: 25–50–50 μ g, day 2: 50–100–100 μ g, following days 100–100–100 μ g). The second group includes 364 women (spontaneous labor, oxytocine, amniotomy, Dinoprostone gel 0.5 mg, primary caesarean).

Results: In the first group 53/76 women achieved vaginal delivery (success rate 69.73%), compared with 159/231 of those who tried to achieve vaginal delivery in the second group (success rate 68.83%). In the first group 31/53 (58.49%) gave birth within the first 24 h, needing ≤ 125 μ g misoprostol in total. Only one rupture in the first group was noted 1/76 (1.31%), compared with 6/364 (1.64%) or 5/231 (2.16%) in the second group. Labor has been completed with

vacuum extractor or forceps in 14/53 (26.41%) in the first group, compared with 34/159 (21.38%) in the second group.

Conclusions: There were no significant differences in the rate of uterine ruptures or the emergency C-sections between the misoprostol and the other methods for induction of labor in women with a single prior uterine scar. Misoprostol has significant rate of success in these cases. Our data do not prove, that a single uterine scar is a contra-indication for oral misoprostol.

PO-Geb 02.59

Ferritin in maternal and cord blood at delivery in Nigerian women

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Objective: One of the most prevalent disorders of man is the dietary deficiency of iron and the resulting anaemia. Measurement of ferritin is useful in determining changes in body iron store, early detection of iron deficiency anaemia, and for monitoring the iron status of pregnant women. High serum ferritin may indicate Iron overload without apparent liver damage and other clinical conditions like inflammation and malignancy. To evaluate the ferritin level in maternal and cord blood at delivery. **Setting:** A Prenatal Diagnosis & Therapy Centre of a Tertiary Hospital in Lagos. **Design:** A cross-sectional study.

Materials and methods: Blood samples were taken with written consent from 90 healthy women and from the umbilical cord of their babies at delivery for serum ferritin estimation using ELISA method (Diagnostic Automation Inc., USA).

Results: The mean ferritin level in maternal blood at delivery was 103.9 ng/ml with a range of (13–516 ng/ml) and 174.6 ng/ml (14–573 ng/ml) in the cord blood.

Conclusions: In the present study, the ferritin level in cord blood is significantly higher than in the maternal blood at delivery.

PO-Geb 02.60

Heterogeneity within the different vaginal *Lactobacillus* species isolated from pregnant women

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Objective: Lactobacilli form a critically important component of the vaginal ecosystem and are the predominant vaginal microorganisms in healthy premenopausal women. Especially during pregnancy they are protective against infection and preterm birth. However, only about 5 of >40 different *Lactobacillus* species isolated from human stool samples or added to food colonize the human vagina. Up to now there exist no data on the heterogeneity as well as the different functions within the *Lactobacillus* species isolated from the human vagina of pregnant women. Our aim was to analyze the heterogeneity of *Lactobacillus* spp., their functional role and the interaction with other inhabitants of the vaginal microflora.

Materials and methods: We analyzed vaginal swabs from a total of 120 healthy pregnant women at week 35–41 for the presence of

lactobacilli. Colonies with a phenotype indicating *Lactobacillus* species were isolated and identified by species-specific PCR, by 16SrRNA sequencing. Typing was performed by rep-PCR and terminal-restriction-fragment polymorphism (T-RFLP).

Results: Among the 120 patients around 30% harboured more than one *Lactobacillus* species. We mainly isolated *L. acidophilus*, *L. crispatus*, *L. gasseri*. Further analysis of the respective *Lactobacillus* species by rep-PCR and T-RFLP indicated a wide heterogeneity. In this regard, the 26 *L. gasseri* strains belonged to 3 different clusters each subdivided into 2–4 subclusters. Similar results were obtained for the additional *Lactobacillus* species.

Conclusions: Knowledge about the heterogeneity within the *Lactobacillus* species in correlation to the additional microorganisms isolated from the respective vaginal swabs is a prerequisite for the study of the respective functionality.

PO-Geb 02.61

Magnetographic actocardiogram-recordings to detect fetal behavioral states and heart rate variability changes during gestation

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Objective: Fetal heart rate variability (fHRV) is a marker for fetal well being and neurovegetative development. Nijhuis classified fetal behavior (quiet/active, asleep/awake) after 32 weeks of gestational age based on fHRV and movement by CTG and ultrasound. Starting at 23 weeks rest and activity states can be distinguished. However CTG has limited temporal accuracy for fHRV analysis. Fetal magnetocardiography (fMCG) detects fHRV with high temporal resolution and fetal movement. Both can be plotted as actocardiogram. fMCG allows fHRV analysis with statistical measures indicating the neurovegetative influence. Actocardiogram inspection was used to define fetal behavior states added by statistical fHRV parameters to assess neurovegetative development. An automatic state detection algorithm was introduced and compared to the visual analysis.

Materials and methods: 55 fMCGs were collected in healthy fetuses between 24 to 41 weeks (recordings up to 45 min). Actocardiograms were plotted and visual analysed according to Nijhuis. Automatic classification algorithm was based on fHRV-criterias of heart rate, oscillation and acceleration. Standard deviation of the beat-to-beat intervals (SDNN), root mean square of successive differences (RMSSD) and mean permutation entropy (PE_mean) were calculated. **Results:** Visual and automatic state detection classified similarly (quiet sleep: 26% vs. 32%, active sleep: 54% vs. 59%, active awake 4: 10% vs. 10%) with no difference between the two schemes. SDNN increased ($p < 0.01$) and PE_mean decreased ($p < 0.05$) with increasing GA. RMSSD increased in late gestation ($p < 0.05$).

Conclusions: fMCG allows automatic state classification and differentiation of active and quiet cycles in early gestation (<32 weeks). SDNN reflects increasing overall HRV, RMSSD indicates pronounced vagal influence during gestation. Decreasing PE_mean suggests higher heart rate complexity with increasing GA. This confirms earlier reports of fetal states development. Detection of fetal state and neurovegetative maturation could be valuable for fetal monitoring.

PO-Geb 02.64**T1 meconium colonography in fetal MR imaging: volumetric measurement of the meconium at different gestational ages depending on abdominal anomalies**

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Objective: The fetal MRI is an increasingly used method to detect fetal anomalies. The aim of the study was the volumetric measurement of the meconium at different gestational ages and the evaluation depending on abdominal anomalies.

Materials and methods: This retrospective study consists of a review of 83 fetal MRI examinations. 58 examinations were performed with a 1.5-T system, 18 examinations were performed with a 3-T system. TRUFI, HASTE and T1f2D sequences were acquired. The region of interest was determined by outlining the areas of hyperintense signal of meconium slice by slice manually. A three-dimensional model of the meconium with an automatically calculation of the intestinal volume was reconstructed. Patients without abdominal anomalies (group A) were compared to patients with abdominal anomalies (group B).

Results: Seven of the 83 examinations (8%) were excluded because of movement artifacts and incomplete visualization. The meconium volumetry demonstrates in both groups an exponential correlation to gestational age. The range of meconium volumes at 20–38 weeks' gestational age was 0.4–43 ml. No meconium could be detected in 2 fetuses before 20 weeks' gestational age and in 2 fetuses with abdominal abnormalities. A missing hyperintense meconium signal in rectum could be observed in three fetuses with gastrointestinal anomalies.

Conclusions: This study shows an exponential correlation between gestational age and meconium volume. Deviations of this exponential trend could sign abdominal anomalies. A missing signal in rectum was only observed in fetuses with gastrointestinal abnormalities.

Perinatal medicine and Reproductive medicine**PO-Geb/Repro 02.01****Acute aortic dissection in pregnant women with Marfan syndrome: case report and review of the literature**

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Objective: The Marfan syndrome (MFS) is one of the most common inherited disorders of connective tissue with an incidence of approximately 1:5000 individuals. Aortic root disease, leading to aneurysmal dilatation, aortic regurgitation and dissection, is the main cause of morbidity and mortality in the MFS. Pregnancy is a high-risk period for aortic dissection and rupture in women with MFS.

Materials and methods: We report a case of a 26 year old woman with known MFS in a singleton pregnancy at 32 weeks of gestation with acute severe upper back pain. A MRI of the abdomen and backbone suggested a type A aortic dissection prolonging to the common iliac arteries. After extensive counseling and because of the life threatening character of this finding we performed a CT with contrast agent of the thoracic aorta what verified a type B aortic dissection. After fetal lung maturing induction a caesarean section was performed. Child and mother did very well after delivery. The vascular surgeons recommended a yearly diagnostic follow up and a strict antihypertensive therapy with betablockers.

Results: The risk of dissection has been estimated to be approximately 1 percent per year in women with an aortic root diameter ≤ 40 mm and 10 percent per year in women with an aortic root diameter > 40 mm. Serial clinical assessment should therefore include echocardiographic monitoring. Additionally beta blockers should be given to all MFS patients in an attempt to minimize aortic dilatation and risk of aortic dissection during pregnancy. Moreover preconceptual counseling is important to explain the risks during pregnancy, the restricted lifespan and the possibility of inheritance of MFS.

Conclusions: We recommend a multidisciplinary approach to prenatal care in pregnant women with MFS, preferably at a center with experience in the management of patients with MFS.

PO-Geb/Repro 02.02**Increased concentration of tubular parameters in the amniotic fluid of male fetuses in the 2nd trimester of pregnancy**

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Objective: The male gender demonstrates a higher prevalence of renal dysplasia associated with increased tubular loss. The aim of the study was to compare the concentration of sodium, chloride, potassium, calcium, phosphate, magnesium and alpha1-microglobulin in the amniotic fluid of male and female fetuses to search for gender-related differences in renal function at the beginning of the 2nd trimester of intrauterine life.

Materials and methods: During routine diagnostic amniocentesis amniotic fluid was taken from 92 male (age of gestation 101–128 days, on average 112.8 days) and 111 female fetuses (age of gestation 101–123 days, on average 111.8 days). Concentration of sodium, chloride, potassium, calcium, phosphate, magnesium and alpha1-microglobulin was determined in these samples. Exclusion criteria were a known prenatal renal disease or other major structural anomaly.

Results: We found no gender difference in the amniotic concentration of sodium, chloride, calcium or magnesium. However, the concentration of potassium (4.57 ± 0.18 vs. 4.05 ± 0.12 mmol/l, $p = 0.01$), phosphate (1.19 ± 0.05 vs. 1.03 ± 0.03 mmol/l, $p = 0.05$) and alpha1-microglobulin (52.58 ± 2.50 vs. 46.25 ± 1.87 mg/l, $p = 0.04$) showed significantly raised levels in male fetuses.

Conclusions: Increased concentration of potassium, phosphate and alpha1-microglobulin in the amniotic fluid of male fetuses indicates a higher urinary excretion of these substances. We speculate that sex-specific differences of tubular function are already apparent at the beginning of the 2nd trimester.

PO-Geb/Repro 02.03**Cervical hydatidiform mole pregnancy after missed abortion presenting with severe vaginal bleeding: case report**

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We report on a 28 year old women presenting with a complete hydatidiform mole localized to the cervix. Two months after curettage of missed abortion she presented with severe vaginal bleeding. Clinical examination revealed a lesion of the epithelial outside surface of the cervix. Due to the bleeding immediate surgical intervention was necessary. Histological examination revealed a complete hydatidiform mole. Currently, only three cases of this exceedingly rare diagnosis have been published. Two cases are reporting on a partial hydatidiform mole and only one case on a complete hydatidiform mole. All cases presented with vaginal bleeding and needed surgical intervention, although in one case initially methotrexate was applied. In this case, we hypothesize that the pathogenesis took place in two steps. Initially, during fertilization, a hydatidiform molar pregnancy developed. Normally this abnormal trophoblast tissue would adhere to the endometrium, but in this case we assume that the endometrial lining was damaged and intrauterine implantation was not possible because of the prior curettage. This circumstance provided the possibility for the abnormal trophoblast tissue to pass the endocervix and to emerge into vaginal vault. Presumably, during the curettage an epithelial defect was set on the outside surface of the cervix. This defect was set by clamping the cervix while dilatation. We speculate that this weak spot of the epithelial surface was responsible for the adherence to the cervix and subsequent bleeding was caused by injury of maternal blood vessels. We present a case with cervical hydatidiform mole as a rare differential diagnosis in vaginal bleeding after dilatation and curettage. We speculate that the defect set by dilatation of the cervix has provided the possibility for the adherence of the abnormal trophoblast tissue and therefore propose that careful holding of the cervix with atraumatic clamps while curettage is important to avoid subsequent complications.

PO-Geb/Repro 02.04**Obesity and pregnancy: maternal BMI over 15 years**

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Objective: This retrospective cohort study aims to illustrate the continuous change of maternal BMI categories 1994–2008. One focus of our attention was the influence of maternal age and parity. Furthermore we wanted to demonstrate the portion of normal weighty women over 15 years. Which portion do extreme weights have? The obesity frequency was computed with underweight, regular weight and overweight.

Materials and methods: We analysed the perinatal statistics of Mecklenburgia—Pommern, German federal state, from 1994 up to 2008. We identified a total of 138 232 singleton pregnancies. Computation of the BMI only for the mothers, whose weight was admitted before 17 gestational weeks.

Results: Especially in the maternal age groups 13–20 years and 21–29 years was registered a rise of the maternal BMI—values on the average. The frequency of obesity (BMI >30) amounted to 8.75% 1994 vs. 12.34% in the year 2008; morbid obesity (BMI >40) 0.61 vs. 1.43%; overweight (BMI >25) 19.66 vs. 21.29%. The proportions of

women having the first child were regarding to BMI >30 5.91% vs. 9.84; BMI >40 0.49% vs. 1.02; BMI >25 16.79 vs. 19.61%. Likewise smaller rates were found in the BMI category 18.50–24.99 in the process of the years.

Conclusions: BMI >40 means that complications such as pre-eclampsia, gestational diabetes, threatened fetal hypoxia, fetal macrosomia, neonatal infections and hyperbilirubinaemia are significantly more common in the process of the years 1994–2008.

PO-Geb/Repro 02.05**Placental thickness and gestational age**

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Objective: A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos.

Materials and methods: A total of 420 normal pregnant women of all gestational ages participated in the study conducted using Kretz Technik Combison 350S and Aloka Machine with a 3.75 MHz sector probe.

Results: Our result shows that placental thickness gradually increases from 14.5 mm at 11 gestational weeks to 37.7 mm at 39 weeks of gestation. As from the 21st to the 35th week of gestation, the placental thickness corresponded exactly with calculated gestational age in weeks.

Conclusions: Our study confirms that placental thickness could be used for the calculation of gestational age in weeks apart from other common parameters between 21 and 35 weeks, i.e. second and third trimester.

PO-Geb/Repro 02.06**MIC-1: a novel modulator of dendritic cells in early pregnancy**

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Objective: Macrophage inhibitory cytokine-1 (MIC-1), a novel member of the transforming growth factor-beta (TGF- β) superfamily has recently been described to be produced in high levels by placental tissue. Detected in decreasing levels in sera of women who subsequently miscarried, it is even speculated to play an important role in the establishment and maintenance of pregnancy. So far, little is known about the modulatory effects of MIC-1 on immune cells found in elevated numbers in decidual tissue during pregnancy. We therefore characterized the impact of this factor on dendritic cells (DC), which are thought to play a distinct role in the establishment of peripheral tolerance in pregnancy.

Materials and methods and results: To detect the decidual cells expressing MIC-1, immunohistochemical staining, PCR experiments and Western blot analysis were performed. Thereby, we ascertained that it is mainly expressed by trophoblast cells and stromal cells. Analysing the MIC-1 secretion of decidual cells by ELISA, trophoblast cells and stromal cells again could be characterized as main producers. We then investigated the effects of MIC-1 on immune cells in decidual tissue. Therefore, immature DC were generated from blood-derived monocytes and differentiated in the presence of MIC-1. MIC-1 was able to modulate the phenotype of DCs by decreasing the expression of CD25, CD40 and CD83 during cytokine-induced DC maturation similar to Dexamethasone (Dex), which was used as a

control. Furthermore, T-cell stimulatory capacity of DCs was significantly reduced after MIC-1 exposure

Conclusions: Thus, we have identified a novel factor that could promote the generation of a tolerogenic micromilieu at the feto-maternal interface.

PO-Geb/Repro 02.07

Is there a risk for pre-eclampsia in pregnancies after ovum donation?

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Objective: Pregnancy risks after ovum donation (OD) to patients with ovarian failure or idiopathic low ovarian response are still under debate. As OD is prohibited in Germany couples refer themselves to IVF centres abroad sometimes without adequate information. We present two pregnancies with very early fetal retardation and severe pre-eclampsia resulting in pregnancy terminations for maternal health problems.

Materials and methods: In patient 1, 37 year, after unsuccessful ICSI treatments (low ovarian response, andrological subfertility) a singleton pregnancy was achieved after OD. Due to treatment resistant hypertension decompensated mitral regurgitation developed with pulmonary hypertension. Pregnancy was medically terminated in the 20th week. The patient recovered from her nephrological and pulmonary conditions. A low grade compensated mitral incompetence remained. The dead female fetus weighed 120 g. Placenta measured 55 cm² and weighed 54 g. Patient 2, 47 year, healthy, primary sterility. Embryo-transfer from OD resulted in a singleton pregnancy. She was referred to our clinic for decompensated hypertension, pulmonary oedema and HELLP-syndrome. Pregnancy was terminated in the 23rd week by Cesarean section. 14 months later she is still treated for hypertension. The dead female fetus weighed 260 g. Placenta measured 100 cm² and weighed 201 g. We observed 8 pregnancies during the past 4 years after OD in healthy patients with primary sterility. All pregnancies were complicated by pre-eclamptic symptoms.

Conclusions: Based on literature and the presented data risk of pre-eclampsia after OD seems to be at least 2–3 times higher than in spontaneous pregnancies (3.4). Lasting conditions may arise in formerly healthy patients.

PO-Geb/Repro 02.08

Stimulation of syncytium formation in vitro in human trophoblast cells by galectin-1

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Objective: Galectin-1 (gal-1) recognizes appropriate glycotopes on the syncytiotrophoblast and extravillous layer from second trimester human placenta and choriocarcinoma cells BeWo. The aim of this study was to investigate the effect of gal-1 on syncytium formation in BeWo and human villous trophoblasts (HVT) cells.

Materials and methods: The effect of gal-1 on syncytium formation was investigated with immunocytochemical and double immunoflu-

orescence stainings, cell-labeling and Real-time RT-PCR. BeWo and HVT cells were incubated with 60 µg/ml gal-1 for 48 h (BeWo) or 96 h (HVT) and cell fusion was detected by fluorescent cell-labelling solution. Finally, BeWo cells were incubated for 1 h in the absence and presence of 60 µg/ml gal-1 and Real-time RT-PCR was performed.

Results: We showed downregulation of the β -catenin and E-cadherin expression in the 48 h BeWo cell culture. The inhibition of E-cadherin was demonstrated on mRNA level too. Increased cell fusion was also showed with DiO and DiI fluorescent cell-labelling. In addition, we demonstrated the downregulation of Ki67 protein expression. Similar results were obtained with the HVT cells.

Conclusions: Our data suggest that gal-1 stimulates the syncytium formation in choriocarcinoma cells BeWo and HVT cells in vitro and inhibits the expression of β -catenin, E-cadherin and in addition Ki67 in BeWo cells. Therefore gal-1 may be a major trigger for the exceptional process of trophoblast cell fusion.

PO-Geb/Repro 02.09

Follicular fluid proteomic profiling analysis of patients with the 5,10-methylenetetrahydrofolate reductase 677C>T mutation by using SELDI-TOF-MS technology

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Objective: 5,10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme of the folate metabolism. Patients homozygous for the 677C>T mutation in the MTHFR gene develop moderate hyperhomocysteinemia under conditions of impaired folate status. We have reported that this mutation affects ovarian responsiveness to FSH and estradiol synthesis. To assess if patients with the MTHFR 677C>T mutation have different protein profiles in follicular fluid compared to controls, we used Surface Enhanced Laser Desorption and Ionization-Time Of Flight (SELDI-TOF) mass spectrometry.

Materials and methods: Follicular fluids from 677TT homozygous individuals- ($n = 16$) and 677CC wildtype ($n = 16$) patients, undergoing controlled ovarian hyperstimulation (COH) for IVF/ICSI, were collected and analyzed by SELDI-TOF mass spectrometry in order to detect differences in the amount of proteins between 2 and 200 kDa molecular weight. All controls (677CC) were matched with 677TT subjects regarding age, BMI and number of retrieved follicles after COH. For biostatistical analyses, the implemented software was used.

Results: One protein of 3967 Da was significantly reduced in patients carrying the MTHFR 677C>T mutation. In addition, three proteins were diminished in the follicular fluids of women who became pregnant during the index IVF/ICSI cycle, compared to those who did not, but this did not correlate with the MTHFR 677C>T genotype.

Conclusions: A correlate of the MTHFR 677C>T mutation is detectable in follicular fluid in form of a downregulated, not yet identified protein. However, its reduced concentration does not influence the success of assisted reproduction treatment.

*Authors contributed equally

PO-Geb/Repro 02.10**Fas-stimulated secretion of cytokines in human endometrial stromal cells is mediated by caspases***Henriette Wenig¹, Herbert Fluhr¹, Marek Zygmunt¹¹University of Greifswald, Department of OB/GYN, Greifswald, Germany

Objective: The Fas/Fas-ligand system belongs to a pathway typically inducing apoptosis. It is expressed at the feto-maternal interface and has been assumed to play an important role at the process of implantation. Previously we could show, that human endometrial stromal cells (ESCs) express Fas, but are primarily resistant to Fas-mediated apoptosis. Under emerging evidence of Fas playing a role in non-apoptotic signaling, we investigated possible Fas-mediated effects on cytokines/chemokines in ESCs in vitro.

Materials and methods: Human ESCs derived from hysterectomy specimens were isolated and decidualized in vitro, using 17 β -estradiol and progesterone. After treatment with an activating anti-Fas monoclonal antibody and a caspase-inhibitor the respective amounts of LIF (leukaemia inhibitory factor), IL (interleukin)-11, -6, -8, MCP (monocyte chemoattractant protein)-1 and RANTES (regulated and activated normal T-cell expressed and secreted) were determined by ELISA and real-time RT-PCR. Activation of NF- κ B was analyzed by in-cell western assay and nuclear transcription factor assays. The enzymatic activity of caspases was measured using luminescent assays.

Results: Fas-stimulation increased the secretion and expression of LIF and IL-11 in undifferentiated ESCs, whereas IL-8 was upregulated in decidualized cells. Fas-treatment had no impact on the secretion of IL-6, MCP and RANTES. In undifferentiated ESCs there was no activation of NF- κ B upon Fas-stimulation. However, the Fas-mediated effects on LIF, IL-11 and -8 were dependent on the activation of caspases.

Conclusions: The Fas/FasL-system selectively modulates cytokines in human ESCs, using distinct signaling pathways and underlining its non-apoptotic function. As the subtle balance between apoptotic and non-apoptotic effects might be essential for the success of early implantation, a better physiological understanding of these processes could reveal new therapeutic targets for woman suffering from repeated implantation failure.

PO-Geb/Repro 02.11**Illegal termination of pregnancy: vitamin-K-antagonist?**Dita Cupisti¹, Tamme W. Goecke¹, Bernd Schwarze², Jürgen Ringwald³, Michael Schroth⁴, Matthias W. Beckmann¹, *Susanne Cupisti¹,¹Universitätsfrauenklinik, Universität, Erlangen, Germany,²Rechtsmedizin, Universität, Erlangen, Germany,³Transfusionsmedizin, Universität, Erlangen, Germany,⁴Kinder- und Jugendklinik, Universität, Erlangen, Germany

Objective: In Germany there is a number of about 110,000 pregnancies per year terminated. A number of further 90,000 pregnancies are estimated to be terminated without report. There are different options for legal termination of pregnancy by medikaments and surgical procedure. It is supposed that these options are used for illegal termination of pregnancy as well. There are no current reports about other medikaments with different purpose used illegally for termination of pregnancy. Antikoagulation with vitamin-K-antagonists in pregnancy is usually not allowed. However there can be occasions of maternal health problems where vitamin-K-antagonists are needed. In these rare cases the application has to be monitored carefully because of severe site effects for the mother and the baby.

Materials and methods: We report two cases of intoxication with vitamin-K-antagonists in pregnancy where we suppose a self-intoxication of the mother with the intention to get rid of the pregnancy.

Results: The current legal and historical options for termination of pregnancy are shown.

Conclusions: Self-intoxication with vitamin-K-antagonists seem to be a new current option for illegal termination of pregnancy, gynaecologists should be aware of.

PO-Geb/Repro 02.12**Hormone production and follicular development after in vitro culture of fresh and frozen murine ovarian tissue in a new dynamic culture system***Mahmoud Salama¹, Katharina Winkler¹, Karl-Friedrich Murach¹, Susanne Hofer¹, Ludwig Wildt¹, Stephanie C. Friess¹¹Medical University of Innsbruck, Department of Gynecological Endocrinology and Reproductive Medicine, Innsbruck, Austria

Objective: Ovarian tissue autotransplantation in cancer patients seeking fertility preservation may reintroduce malignant cells. Therefore, ovarian tissue cryopreservation followed by oocyte in vitro maturation and fertilization could be a safer option. As a first step to this end, the objective of this study was to establish a new dynamic culture system for fresh and frozen murine ovarian tissue.

Materials and methods: 72 ovaries were obtained from 36 female C57BL/6 mice 7–14 weeks old. 18 ovaries were frozen/thawed via slow freezing/rapid thawing protocol. 27 dynamic culture chambers (DCCs) were compared to 21 static culture chambers (SCCs), serving as controls. Each chamber contained 3 ovarian halves cultured in 2 ml blank G-MOPSTM medium (Vitrolife, Sweden) for 6 days (1 estrus cycle) in a 38°C water bath. Estradiol (E2) and Progesterone (P) were measured daily in all effluents to assess folliculogenesis. After 6 days of culture, tissues were examined histologically for viability and follicular development.

Results: DCCs with fresh tissue ($n = 21$) showed combined E2 and P peaks in 81% of chambers. Viability was 100% in 52.2% of chambers; Corpora Lutea (CL) were seen in all chambers producing E2. DCCs with frozen/thawed tissue ($n = 6$) showed combined E2 and P peaks in 50% of chambers. Viability was >60% in 50% of chambers; CL were seen in all chambers producing E2. SCCs with fresh tissue ($n = 15$) showed combined E2 and P peaks in 80% of chambers. Viability was 100% in 26.6% of chambers; CL were seen in all chambers producing E2. SCCs with frozen/thawed tissue ($n = 6$) showed no E2 peaks. Viability was >60% in 50% of chambers; CL were not seen.

Conclusions: We preliminarily established a new dynamic culture system for fresh and frozen ovarian tissue in mice with superior results to the conventional static culture regarding tissue viability and hormone production.

PO-Geb/Repro 02.13**Effect of sperm count and morphology on results of intrauterine insemination***Godwin Ajayi¹, Oluseyi Ogunsola¹, Adeola Alamu¹¹College of Medicine, University of Lagos, Prenatal Diagnosis and Therapy Centre and Department of Obstetrics and Gynaecology, Lagos, Nigeria

Objective: To assess the effects of the count of mobile sperms inseminated and percentage of morphologically normal sperms on the

results of IUI. *Setting:* A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos. *Study and design:* A prospective study *Materials and methods:* The study is made up of 201 couples who underwent 614 IUI cycles. Intervention: All IUI cycles were preceded by ovarian superovulations with clomiphene citrate 50 mg tablets orally twice daily for 5 days, starting on the second day of the cycle and one HMG ampule 75 IUIM daily for 5 days start by day 5 of the cycle. Cycles were monitored with Basal Temperature Charts and transvaginal follicleometry. The IUI was performed with a catheter 36 + 4 h after HCG Injection. Main outcome measures clinical pregnancy.

Results: 44 clinical pregnancies were obtained, for a pregnancy rate per cycle of 10.4%. The pregnancy rate percentage was 6.1% when the number of mobile sperm was $<5 \times 10(6)$ and 19.8% with normal mobile sperm $>5 \times 10(6)$. When the normal sperm morphology was $>30\%$ and number of mobile spermatozoa inseminated $>5 \times 10(6)$, the pregnancy rate was 21.3%.

Conclusions: Intrauterine insemination is less successful when the number of mobile sperm inseminated is $<5 \times 10(6)$, or normal sperm morphology is $<30\%$.

Keywords: IUI, Sperm Morphology, Count, Success.

PO-Geb/Repro 02.14

German infertile couples' attitudes towards their cryopreserved pronuclear stages and potential embryos

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Objective: Two new treatments for couples experiencing infertility, cryopreservation of pronuclear stages which is a routine practice in Germany, and cryopreservation of embryos, which is mostly done in foreign countries, gives these couples a chance to make additional attempts at pregnancy. Nonetheless, there is wide-spread debate about the moral and legal status of the early stages of life. This German survey of 700 infertile patients analyzes the attitudes and decisions of patients about potential cryopreserved embryos and their cryopreserved pronucleus stages.

Materials and methods: 223 German infertile patients with cryopreserved pronuclear stages in storage for 1–5 years returned completed standardized questionnaire. Several multivariate regression models were performed in order to assess influencing factors that contributed to the infertile couples' decision and attitudes (e.g. socio-demographical factors and individual parameters).

Results: The vast majority of German infertile couples (92%) are in favor of an overall legalization of embryonic cryopreservation. Couples are also in favor of donating surplus frozen embryos (69%). The multiple regression analysis showed that there is a high correlation between the extent to which couples were aware of possible risks associated with the freezing, the stage of treatment, the age and religious beliefs of the couples with the couples' opinions about legalization ($p < 0.05$). The majority of respondents considered the pronuclear stage as well as the embryo as deserving dignified treatment (40%).

Conclusions: In contrast to the German Embryo Protection Law, infertile German couples are in favor of legalizing the cryopreservation of surplus embryos created as part of a fertility treatment. Infertile German couples are in favor of using supernumerary frozen pronucleus life stages and embryos in a meaningful manner instead of discarding. In general, the findings of the study could help redefine

the public debate on the legalization process for embryos and the moral and legal status of embryos in Germany.

PO-Geb/Repro 02.15

Differential gene expression profiles in cells of the corona radiata and outer cumulus oophorus in relation to oocyte competence

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Objective: Identification of oocytes with superior developmental capacity remains a challenge in assisted reproduction. Cumulus cells are mediators of oocyte maturation which are in turn regulated by oocyte-secreted factors. Cells of the corona radiata are immediately apposed to the zona pellucida and connected with the oocyte via transzonal projections. Outer cumulus cells show a lower level of intercellular adhesion and molecular exchange. Differences in gene expression patterns in those cell subpopulations might be relevant for evaluation of oocyte quality. We compared expression levels of three candidate genes in corona radiata and cumulus cells of the same oocyte and correlated results with nuclear maturity, zona birefringence and ART success.

Materials and methods: Cumulus cells were collected from 48 oocytes of 14 ART patients. Nuclear maturity and zona birefringence intensity were determined in every oocyte. Cumulus and corona cells were removed separately during oocyte preparation for ICSI. Real time PCR analysis was done on the Light Cycler system. Expression of candidate genes was compared between cumulus and corona cells and correlated with oocyte quality. Candidate genes were chosen based on their central role in oocyte metabolism (BMP15) or steroidogenic activity (STAR) and maintenance of gap junctions between oocyte and corona cells (CX43).

Results: Significant ($p < 0.001$) differences in mRNA-expression between corona radiata and outer cumulus cells were identified for all candidate genes. Expression of STAR and CX43 in corona cells showed a better correlation with oocyte competence than in cumulus cells. No correlation of expression any of the candidate genes with zona birefringence intensity could be established.

Conclusions: Subpopulations of the cumulus-oophorus complex exhibit different expression profiles for certain candidate genes, thus the choice of appropriate candidate genes and the relevant cell cohort is essential. Expression analysis of the corona radiata might be more useful for oocyte selection for ART.

PO-Geb/Repro 02.16

Maternal serum ADAM12 and total β -HCG in early pregnancy after assisted reproduction

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Objective: ADAM12, a pregnancy associated multi-domain metalloprotease with additional cell adhesion activities, has proteolytic activities directed against insulin-like growth factor binding proteins indicating a regulatory function on the bioavailability of insulin-like growth factors in early pregnancy and placentation. The aim of this study was to examine the course of ADAM12 and human chorionic

gonadotropin (total β -hCG) in early pregnancy after assisted reproduction.

Materials and methods: ADAM12 was determined retrospectively from frozen serum samples obtained between day 14 and day 35 after ovulation/ovum pickup from 192 early pregnant women after assisted reproduction (45 after low-dose gonadotropin stimulation with ovulation induction, 22 after in vitro fertilization, 76 after intracytoplasmic sperm injection, 49 after transfer of cryopreserved pronucleus cells). In all samples previously routine measurement of total β -hCG had been done. For sensitive measurement of ADAM12 the new DELFIA-ADAM12 assay was slightly modified to lower the detection limit to 0.4 ng/mL. Multiples of the median (MoM) were calculated from ADAM12 results.

Results: In 77% of samples obtained up to day 23 after ovulation/ovum pickup the ADAM12 levels were below the detection limit. For those samples with elevated ADAM12 levels there was no correlation with gestational age. After day 23 an exponential rise of ADAM12 was observed with increasing gestational age. There was a linear correlation of ADAM12 with total β -HCG. The ADAM12-MoMs were inversely correlated with the mothers weight ($p = 0.016$). In pregnancies ending in spontaneous abortions ADAM12-MoMs (median of MoM = 0.4) were significantly lower compared with ongoing pregnancies (median of MoM = 1.31; $p < 0.001$).

Conclusions: With the modified assay version ADAM12 can reliably be measured already 23 days after ovulation in pregnant women. The ADAM12 levels show an exponential increase strongly correlated with gestational age in intact pregnancies, whereas they were significantly reduced in spontaneous abortions

PO-Geb/Repro 02.17

Case report: continuation of pregnancy after severe head trauma in early pregnancy

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We present a case of a 31 year-old patient with severe craniocerebral trauma after motor vehicle accident in her 8th week of pregnancy. During the course of intensive care, the case was complicated by recurrent infections and fever, treated with a wide spectrum of antibiotics. The patient was admitted to our emergency room unconscious with severe head trauma after an automobile accident. Multiple skull fractures were accompanied by multiple brain hematomas and cerebral edema. After acknowledgment of the patient's state of pregnancy, radiological diagnostics were limited to head and upper spine. The patient was eventually transferred to intensive care unit ventilated and under analog sedation. In order to maintain an adequate brain perfusion, therapy with catecholamine and noradrenalin was started. In the following months the patient had to undergo intermittent antibiotic therapy with ceftriaxon, imipenem, vancomycin, tazobactam and amphotericin B. Due to repetitive seizures the patient received treatment with carbamazepin. The fetal prognosis under the severe condition and the aggressive therapy of the patient was discussed with family members and the continuation of the pregnancy as well as maximal therapy for the unborn child was decided on. During the following months fetal development was without pathological findings both in ultrasound and fetal heart tracking. In her 15th week of pregnancy, after seven weeks of intensive care treatment, the patient was transferred to a rehabilitation clinic. At this point the patient was capable of breathing spontaneously with stable vital parameters and started to react to her surroundings. Despite fecal incontinence and therefore limited hygienic circumstances, ascending infection did not occur. The patient is now in her 30th week of

pregnancy with normal fetal biometry, normal fetoplacental and uteroplacental perfusion, all fetal organs seem to be developed as expected by ultrasound diagnostics. Delivery of the baby is planned at 37 weeks of pregnancy by cesarean section.

PO-Geb/Repro 02.18

Prenatal predictive ultrasound findings for gastroschisis

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Objective: Identification of predictive prenatal ultrasound findings during pregnancy complicated with fetal gastroschisis.

Materials and methods: Retrospective observational study from 3/1997 to 12/2009 including 78 pregnancies complicated by fetal gastroschisis. After the diagnosis of gastroschisis follow up were performed continually with special attention to the diameter of the fetal colon, amount of amniotic fluid and fetal Doppler parameters.

Results: Prenatally 6, 84 and 10% of the bowel malformations were found in the first, second and third trimester respectively. There were three stillbirths and three neonatal deaths. In four cases the pregnancy was terminated, mainly because of complex structural abnormalities. We found that the dilated bowel in the third trimester accurately predicted postnatal complications and correlated with the development of a severe intrauterine growth restriction (<3th percentile).

Conclusions: The majority (91%) of fetuses with antenatally diagnosed gastroschisis survived to delivery. Dilatation of the fetal bowel seems to be the most important predictive factor in terms of survival.

PO-Geb/Repro 02.19

High prevalence of vitamin D deficiency in winter periods

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Objective: Vitamin D is a prohormone that plays an important role in various physiological processes, e.g. calcium metabolism, cellular growth and differentiation, immunity and cardiovascular regulation, and also for maintaining oral health through effects on bone and mineral metabolism and immunomodulatory action by interference with proinflammatory cytokines. The vit D receptor has dual functions as an endocrine receptor and metabolic sensor. The activity of vit D3 in preventing rickets and osteoporosis is well known, but the extent of inadequate supply in Germany is uncertain.

Materials and methods: Screening was prospectively performed in the winter period (end of October-April) and included a total of 206 consecutive women, who attended the outpatient endocrine clinic for menopausal complaints or disorders of the menstrual cycle, and who were not on vit D3 substitution. The median age was 54 (range 14–86) years. 25-hydroxy(OH)D3 (25-hydroxycholecalciferol) as the major form of vit D in the circulation was determined by means of a standard serum assay. Vit D deficiency was defined as concentration <20 ng/ml, severe deficiency as serum levels <10 ng/ml.

Results: Serum levels of vit D ranged from <4.0 ng/ml to 42.8 ng/ml. Vit D deficiency was detected in 71.4% (147/206) of women; and this

screening identified a high proportion of individuals (28.6%) (59/206) with a severe vit D deficiency. Low levels of vit D were found in 76.9% of patients >50 years of age compared to 74.6% of younger women (<50 years), and a severe vit D deficiency was detected in 25.9% of patients >50 years compared to 35.6% in younger individuals.

Conclusions: Inadequate vitamin D3 supply is a very common finding in pre- and postmenopausal women, and severe deficiency of vitamin D in the winter period was unexpectedly high.

PO-Geb/Repro 02.20

Factors influencing the duration of second-trimester termination of pregnancies with prostaglandin derivatives

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Objective: To examine the time interval between first induction and fetal expulsion in fetal defect related termination of pregnancy and to determine the relevant factors that influence this time interval.

Materials and methods: Retrospective study involving singleton pregnancies that were terminated due to fetal abnormalities between 2005 and 2009. Induction was done by either 200 µg misoprostol, 1 mg gemeprost or in case of a previous caesarean section by 0.5 mg dinoprostone gel or 1 mg gemeprost. The length of the induction interval between first induction and fetal expulsion was examined according to different maternal and fetal characteristics. Univariate and multivariate logistic regression analysis was used to determine the significant contributors for a delivery within 24 h.

Results: 184 singleton pregnancies fulfilled the inclusion criteria. The median gestational age at first induction was 19.2 weeks of gestation. The median time interval between first induction and expulsion was 18 h (25–75th centile 11–30 h) and in 59 (32.1%) cases, the induction interval was longer than 24 h. Multivariate logistic regression analysis in the prediction of fetal expulsion within 24 h after first induction indicated significant contribution from gestational age and history of spontaneous delivery without previous caesarean section.

Conclusions: The only relevant contributors for the time interval were gestational age and previous history of spontaneous delivery. By combining this information it was possible to correctly anticipate fetal expulsion within 24 h after first induction in 90% of the cases.

PO-Geb/Repro 02.21

Recent changes of indications and recipients of stem cell transplantations from umbilical cord blood of private cord blood banks worldwide

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Objective: Experimental cord blood transplantation (CBT) was initially described in 1972 but became clinically relevant after CBT in 1988 in Fanconi anemia was first published. Soon afterwards private banks were established to store umbilical cord blood and stem cells individually. To better understand adult stem cell application and underlying trends, an analysis for indication and transplant recipient was performed.

Materials and methods: From the database of published CBTs worldwide from private storage between 12/1993 and 11/2009 a

comprehensive analysis was performed for two time periods: 12/1993–12/2004 vs. 1–11/2009. Indications and transplant recipients of cord blood transplantations were identified and analyzed. A comparison of CBTs with NETCORD's database from 3/2010 was performed to estimate the ratio of applications between public and private CB banks.

Results: Until 11/2009 $n = 400$ CB transplantations from private cord blood banks including clinical trials are confirmed worldwide. From 12/1993–2004 $n = 52$ CBTs are documented vs. $n = 69$ from 1–11/2009, an increase of $\Delta n = 4.7/\text{year}$ to $n = 75.3/\text{year}$ (+1.492%). In the first time period $n = 6/52$ (11.5%) CBTs were autologue, in the second $n = 59/69$, (85.5%). Main indications were in the first period 1. ALL $n = 20/52$ (38.5%), 2. + 3. AML and Sickle cell anemia $n = 6/52$ each (11.5%) vs. 1. Cerebral palsy $n = 43/59$ (72.9%), 2. other Brain damage $n = 9/59$ (15.3%), 3. Diabetes mellitus type I $n = 4/59$ (6.8%) in the second. Ratio of public vs. private CBTs is 9.305:400 = ~23:1.

Conclusions: Umbilical CBTs from private storage have seen a remarkable increase recently. The recipient in 2009 was in 85.5% the donor (=autologue transplantation), supporting the intended purpose. Primary CBT indication has changed from oncological to regenerative. This analysis shows CB from private blood banks serves as additional source of adult stem cells for a variety of regenerative indications for the donor him/herself.

PO-Geb/Repro 02.22

Predictive factors for breech presentation: our experience in 14,433 singleton pregnancies and a literature review

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Objective: Breech presentation represents in the developed Countries a typical indication for a primary caesarean section in women presenting for parturition. The aim of this population-based retrospective cohort study is to investigate the incidence and predictive factors of breech presentation.

Materials and methods: We collected data about the 14,433 singleton deliveries happened in the University Clinic of Gynaecology and Obstetrics in Udine between 2001 and 2009, considering the risk factors and trends in breech presentation prevalence. We analysed data using R (version 2.9.2), considering significant $p < 0.05$. Also a multivariate logistic regression analysis was performed

Results: Mean maternal age is 31.78 years (± 5.17) and mean gestational age at delivery 38.67 weeks (± 2.54). Prevalence of breech presentation is significantly different ($p < 0.05$) among nulliparous women (5.36%, 415/7743) and multiparous ones (3.53%, 236/6689), and significantly lower ($p < 0.05$) among African women (2.62%, 14/535) compared to the whole population (4.59%, 636/13852). In the subgroup of breech presentation, maternal age, gestational age at delivery and neonatal weight are significantly different than in the whole population. By multivariate logistic regression, maternal age results a risk factor for breech presentation, while African ethnicity, multiparity and advanced gestational age seem to be protective factors.

Conclusions: Primiparity, young maternal age, ethnicity other than African, early gestational age and low neonatal weight at delivery result to be predictive for foetal breech presentation at delivery.

Gynecology

PO-Gyn 02.01

First experiences in robotic-assisted laparoscopy with prosurgics freehand camera-holding system

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Objective: Prospective analysis of 16 patients undergoing gynaecological laparoscopy using freehand robotic camera-holding device. This study evaluates its introduction into clinical praxis.

Materials and methods: A total of 16 patients underwent robotic-assisted laparoscopic surgery such as hysterectomy, adnexectomy and cystectomy at the same institution, during the same period and with the same surgeon. Perioperative data (operation time, blood loss, time for assembly, comfort for the surgeon, roboter-handling, obstructions for the surgeon or the assistance caused by roboter) was collected prospectively. Demographic data, pre-existing diseases, previous abdominal or pelvic operations, postoperative development and length of stay were retrieved from patient's records. We used the freehand camera-holder, attached to the surgical table, controlled via surgeon's head movements by a head-mounted optical emitter. Movements are detected by a sensor mounted atop laparoscopic video monitor. The sensor indicates intended direction of motion through displaying a LED arrow. Surgeon initiates and terminates movements with a foot pedal.

Results: Mean time from suture to docking the robotic-arm was 5.13 min ($\sigma = 2.6$ min). 10 procedures were successfully completed without any intra-operative complication. No conversions to laparotomy were necessary. No major intra- or post-operative complications occurred. In only one case post-operative minor complication was detected (suspected urinome). In all cases camera-positioning was steady with barely no inadvertent movements. In 56% human assistance could be saved.

Conclusions: Robotic devices permit tremor-free imaging and can eliminate need for assistance. Moreover they offer greater vision control to the surgeon and allow complete autonomy over the laparoscopic surgical view. Further studies comparing roboter-assisted laparoscopy to conventional laparoscopy are needed to prove its superiority in clinical routine.

PO-Gyn 02.02

Secondary cervical stump resection after laparoscopic supracervical hysterectomy

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Objective: Cohort retrospective analysis to evaluate complication rates and postoperative problems resulting in secondary cervical stump resection in women with laparoscopic supracervical hysterectomy (LASH).

Materials and methods: 300 women underwent LASH between January 2002 and December 2009 at Department of Obstetrics and Gynecology, Erlangen University Hospital, Erlangen. Retrospective

analyze of LASH procedures and follow-up including secondary cervical stump resections.

Results: The intraoperative complication rate was low with 1% at all. No conversion to abdominal hysterectomy was necessary. In the postoperative phase the complication rate was also low with 0.66%. Six patients were identified who had a secondary cervical stump resection (2% of all cases). In three patients cervical stump resection was performed because of atypical endometrial hyperplasia found in the histological examinations of the uterus. Two women had a coincident neoplasm. Another woman developed pain in the cervical stump and had still menstruation bleeding.

Conclusions: LASH is a safe and feasible procedure in women undergoing hysterectomy. However some postoperative problems may occur resulting in secondary cervical stump resection. Those should be taken into account when hysterectomy procedures were discussed with women.

PO-Gyn 02.03

Discriminant function analysis as decision making system for patients considered for pelvic exenteration: decision making before exenteration

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Objective: Pelvic exenteration (PE) is a potentially life saving procedure. Because of the heterogeneity of patients who might profit from a major surgical procedure an assortment of those patients who underwent PE is difficult. Therefore the influence of risk factors on survival is analysed and a decision making model based on the model of discriminant function analysis (DFA) is created.

Materials and methods: In a retrospective study medical findings of a heterogeneous group of patients who underwent PE were analysed. The operations had been performed exclusively by two surgeons, both experienced in multivisceral surgery of the small pelvis. For collecting and categorizing data we used the following tests: SF 12 questionnaire, Statistic Program SPSS®, Mann–Whitney Test and Fischer–Yates Exact Test. For calculating the DFA patients were grouped according to the outcome measure of death or survival from January 1999 to December 2005.

Results: 63 patients with different anamnestic requirements underwent exenterative surgery. The probability that the DFA sorted the patients correctly to survival or death was 88.9%. The function found by plotting the predictive values against the probability of survival had a high discriminatory power predicting the patients' outcome with high accuracy. Additional by plotting diagnostic sensitivity against specificity we got the ROC being 0.5 in our study, allowing cut-off point and diagnostic reliability to be calculated. The resulting score with a sensitivity and positive predictive value for survival of 95 and 93% leads to allocate those patients correctly to the major surgical procedure.

Conclusions: Even if a randomized evidence level I based study is unfeasible yet, DFA helps to objectify the assessment of prognosis and leads to decide upon major surgical procedure. A decision making model based on DFA allows the prediction of survival by clinical findings with high accuracy, even if results based on retrospective examinations.

PO-Gyn 02.04**Three-year follow up comparing NovaSure with ThermaChoice and endometrial loop resection**

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Objective: In this study we compared different techniques of endometrial ablation. Therefore we compared the bipolar impedance-controlled endometrial ablation (NovaSure) with balloon ablation (ThermaChoice) and endometrial loop resection at 3 years after administration.

Materials and methods: A total of 91 women suffering from menorrhagia underwent endometrial ablation in our hospital from January 2007 till March 2010. All patients underwent a diagnostic hysteroscopy and fractional abrasio before endometrial ablation in the same setting. We evaluate the average age, duration of the operation, duration of hospitalisation and intraoperative or postoperative complications retrospectively.

Results: At 3 years of follow up we include $N = 34$ patients in the NovaSure group with an average age of 42.59 years, $N = 30$ patients in the ThermaChoice group with an average age of 47.39 years and $N = 27$ patients in the group of endometrial loop resection with an average age of 47.44 years. In the NovaSure group the operation took on average 18.62 min, the average duration of hospitalisation was 1.97 days. In the ThermaChoice group the operation took on average 33.20 min, the average duration of hospitalisation was 1.80 days. In the group of endometrial loop resection the operation took on average 36.67 min, the average duration of hospitalisation was 1.18 days. We found no patient with intra- or postoperative complications.

Conclusions: At 3 years follow up, bipolar thermal ablation shows the shortest duration of operation but the longest duration of hospitalisation. The endometrial loop resection was associated with the shortest duration of hospitalisation but the longest duration of operation. Our clinical experience shows a superiority of bipolar impedance-controlled endometrial ablation technique over balloon ablation and endometrial loop resection in the treatment of menorrhagia. We are currently investigating amenorrhoea rates, hysterectomy rate and quality of life associated with the different techniques of endometrial ablation in our hospital; the results are still outstanding and will be published soon.

PO-Gyn 02.05**Prognostic factors for the success of thermal balloon endometrial ablation**

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Objective: To identify prognostic factors for successful treatment of menorrhagia using THERMACHOICE—a hot fluid balloon ablation device.

Materials and methods: Retrospective clinical study on 115 patients who have undergone THERMACHOICE at St. Hedwig's Hospital between 2002 and 2008. About 2 years after THERMACHOICE these women were asked by a questionnaire about satisfaction, earlier therapies, menstrual symptoms, postoperative discomfort.

Additionally patients were offered a gynecological examination including vaginal sonography and laboratory analysis of FSH and estradiol.

Results: From 115 patients 70 returned the questionnaire and 50 underwent examination. The mean age was 45.27 years. The average time between the intervention and the survey were 739 days. 88.6% of the women were satisfied. 31.7% of the women reported amenorrhea, 38.1% hypomenorrhea and 27.0% eumenorrhea. Menorrhagia persisted in only two patients. Women with postoperative amenorrhea were older ($p = 0.001$) and had statistically significant higher FSH- ($p = 0.0$) and lower estradiol-levels ($p = 0.019$) than women who still reported uterine bleeding. ROC analysis found that a FSH-level of 39.65 IU/l implicates a chance of 50% to reach postoperative amenorrhea. Preoperative dysmenorrhea and premenstrual symptoms were associated with a lower postoperative rate of amenorrhea. Postoperative dysmenorrhea and use of non steroidal analgetics seem to influence patients' satisfaction negatively. No difference in postoperative bleeding patterns could be found between satisfied and not satisfied women.

Conclusions: The THERMACHOICE intrauterine balloon system is an effective procedure in women suffering from menorrhagia. Significant prognostic factors for a favourable outcome are increased age and high FSH. Further prospective studies are needed to prove whether the cut off of 39.65 for FSH could be used to select patients with a probably positive result. Uterine position, length and depth and endometrial thickness did not influence any result.

PO-Gyn 02.06**Intraabdominal adhesions: what is our patients' awareness?**

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Objective: To analyse and to compare how female patients are generally informed about adhesions (patient's awareness) and their related problems by surgeons pre-operatively.

Materials and methods: Multi-centre study including data from a German women's university hospital, a teaching hospital and a general district hospital in the UK, as well as an online survey. Patients and interventions: Over eight weeks $n = 105$ patients (Germany) and $n = 82$ (UK) patients admitted for laparoscopic or open abdominopelvic surgery were interviewed pre-operatively. $N = 212$ responses to an online survey were also analysed.

Results: Less than 50% of patients are made aware of adhesions. Even less patients were told about complications caused by adhesions (<70% of patients who were told about adhesions). Lack of knowledge is cited by 46% of patients as a reason for health professionals not informing them about adhesions. 41% answered that adhesions are considered as not sufficiently important. Patients who had previously heard of adhesions were most commonly informed by physicians.

Conclusions: There is lack of information among patients and physicians about adhesions and their complications of which surgeons do not appear to inform their patients regularly. Written information prior to surgery and computer-based applications would possibly help to raise patient's awareness.

PO-Gyn 02.07**Expression of CD68, COX-2 and IL-6 in a rat model of postoperative peritoneal adhesions**

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Objective: Acute and chronic inflammatory processes are supposed to be of relevance in adhesiogenesis. This study was designed to investigate the expression pattern of important inflammatory mediators in peritoneal adhesions.

Materials and methods: In 60 male Sprague-Dawley rats a standardized peritoneal defect was performed. On 3rd, 5th, 14th, 30th, 60th and 90th postoperative day 10 animals were sacrificed respectively. The formed adhesions were analyzed using immunohistochemical stains for macrophages/monocytes (CD 68), cyclooxygenase-2 (COX-2) and interleukin-6 (IL-6).

Results: During the whole observation period none of the animals died, or showed signs of infections or complications. At each time point formation of peritoneal adhesions was observed in all animals respectively. A notable expression of CD68 was observed in all animals with a peak on day 3. Although the number of CD68 positive cells decreased over time, CD68 positive stained cells could still be observed even on postoperative day 90. Analysis of COX-2 protein expression levels showed a highly positive staining up to the 90th postoperative day. IL-6 was detected in between the adhesion tissue up to 2 weeks postoperatively, with the highest levels 3 days postoperatively and a continuous decrease until the 14th postoperative day.

Conclusions: The detection of macrophages/monocytes and COX-2 indicate a chronic inflammatory process within peritoneal adhesions. The initially high number of macrophages/monocytes leads to the conclusion that this cell population may be essential in adhesiogenesis. Influencing IL-6 or the IL-6 pathway may serve as a novel target to minimize the formation of postoperative peritoneal adhesion.

PO-Gyn 02.08**Nerve-sparing Vaginal Assisted Laparoscopic Radical Hysterectomy (VALRH): evaluation of type C1 radicality for low and high-risk early cervical cancer**

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Objective: (1) To evaluate the morbidity and oncologic outcome of our modification of LRH using the classification of radical hysterectomy by Querleu and Morrow 2008 and (2) to compare nerve sparing VALRH with common LRH.

Materials and methods: Retroperitoneal staging was performed on patients with early or locally advanced cervical cancer starting with removal of sentinel nodes. Systematic paracervical, paravesical, external and internal iliac, common iliac, and risk-adapted presacral, aortic infra-mesenteric and aortic infrarenal lymph node dissection was performed laparoscopically. Radical hysterectomy was performed dissecting uterosacral ligament close to the rectum and vesicouterine ligament close to the bladder. Ureter was mobilized according to type C. Autonomic nerves were lateralized in VALRH and the vaginal resection line was prepared under direct vision. Vaginal cuff was closed with a running suture.

Results: From 2005 until 2008, 64 patients with pT1B1-pT3A were treated by LRH, 53 of which received VALRH. No conversion to

laparotomy was necessary. Parametrial width was median 32 mm, resected lymph nodes were 39 (14–118). Hb dropped median by 1.27 mmol/l. Spontaneous bladder voiding was median on d 3 postop versus d 5 median without nerve preparation ($p = 0.02$). High risk patients who did not receive postoperative radiation therapy had an unfavourable prognosis with early relapse. None of the 17 low risk patients (tumor <2 cm, N0) relapsed so far.

Conclusions: Nerve-sparing VALRH was feasible and safe, allowing closure of the vaginal cuff to avoid tumor cell contamination and judgement of the vaginal length as well as early bladder control.

PO-Gyn 02.09**Laparoscopic Subtotal Hysterectomy (LASH) or Laparoscopic Total Hysterectomy (TLH): the critical question in non-oncologic patients**

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Objective: Minimal invasive surgery in benign indications for hysterectomy requires the least radical organ preserving intervention to solve the patient's problem.

Materials and methods: TLH is only indicated if the uterine cervix has a problem or when the fibroids are too big. If LASH solves the patient's problem no TLH and more radical surgery is necessary. LASH is unique partial organ preserving surgery, easily done by laparoscopy with less side-effects than TLH. Laparoscopic Subtotal Hysterectomy = LSH is done in 4 steps: Step 1 Dissection of adnexa from uterus or pelvic side wall, Step 2 Dissection, presentation and coagulation of ascending branches of uterine vessels, Step 3 Delimitation of uterine cervix from corpus uterine, Step 4 Morcellation of uterus. Whether to cover the cervical stamp with peritoneum or not is up to the surgeon's decision. A collective of 416 laparoscopic hysterectomies is analysed.

Results: In 60% hysterectomies were performed as LASH in the two analysed centres: Dept. Obst. Gyne. at Universitätsklinikum Schleswig-Holstein/Kiel and Dubai Health Care City(DHCC)/ U.A.E.

Conclusions: The choice of the type of hysterectomy, be it per laparotomy or laparoscopy, in benign indications is clearly for subtotal hysterectomy, in our case for Laparoscopic Subtotal Hysterectomy (LASH)

PO-Gyn 02.10**Endoscopically assisted construction of a neovagina by a variation of the Vecchietti method in patient with Mayer-Rokitanski-Küster-Hauser syndrome**

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Objective: The most common cause of an aplastic vagina is Mayer-Rokitanski-Küster-Hauser syndrome with an incidence of 1:4000–5000. This congenital abnormality of the female genital tract is based on agenesis of the Müllerian duct. In patients with MRKH you find a short or aplastic vagina and a rudimentary or absent uterus. Usually they have functioning ovaries, so the secondary sexual characteristics are normal. The predominant symptom is primary amenorrhoea and the patients are unable to practice sexual intercourse.

Materials and methods: Woman aged 22 with MRKH. Uterus and vagina are aplastic, there is only a short vaginal stump (0.5 cm). Secondary sexual characteristics and sex steroid levels are normal.

Surgical procedure: A few weeks prior to the surgical procedure the patient was asked to dilate the vaginal stump with a vaginal dilator. Thereby the length of the vaginal pit was about 3 cm. The patient was operated under general anaesthesia. For the endoscopic approach three additional suprapubic incisions are needed. The pouch of Douglas is opened up and a tunnel is prepared between the bladder and rectum. For a better orientation we place a thick Hegar's dilator into the vaginal stump during this preparation. The tension thread is then passed with a straight needle from the vaginal stump through the prepared tunnel into abdominal cavity and connected to a vaginal dilator. Cystoscopy and laparoscopy confirm absence of injury of the bladder or rectum. Now the threads in the abdominal cave are retrieved and withdrawn by a laparoscopic grasper after creation of an extra-peritoneal tunnel through to the abdominal wall and fixed at a tension apparatus. Preoperative the patient got an epidural catheter for analgesia during the tension period.

Results: Tension was increased day by day. After 10 days the neovagina had a length of 10–12 cm. The tension threads and tension apparatus were removed under general anaesthesia. The patient was informed to use a vaginal dilator after instillation of oestrogenic cream 1 h twice a day for at least 6 months until onset of regular sexual intercourse.

Conclusions: The endoscopically assisted method for construction of a neovagina gives very good results in cases where there is a vaginal stump. It avoids the stress of a laparotomy, the rate of complication is low, the risk of injury of the bladder can be minimized by doing a cystoscopy during the surgical procedure. However, the most important thing for a satisfying long-term result of this procedure is the regular postoperative dilatation.

PO-Gyn 02.11

Gene expression profiles: a new approach towards the diagnosis of interstitial cystitis/painful bladder syndrome?

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Objective: Interstitial cystitis (IC) or painful bladder syndrome (PBS) is a chronic bladder disease with increasing incidence. Today, its diagnosis relies on symptoms evaluation (urgency, frequency, pain) in combination with cystoscopic and histological evidence. A molecular marker for an objective diagnosis is highly desired. Towards this goal, comparative gene expression profiles of bladder biopsies from patients with ulcerative IC/PBS and control patients have been performed.

Materials and methods: Cold-cup biopsies from bladder tissue were collected from five ulcerative IC/PBS patients and from six healthy controls. After total-RNA extraction, gene expression profiles have been generated using Affymetrix Human Genome U133 Plus 2.0 expression arrays. HE staining of paraffin sections has been performed. Selected gene expressions were quantified by real-time polymerase chain reaction (TaqMan Assays, Applied Biosystems).

Results: GeneChip expression arrays cover all known human mRNAs. More than 31,000 of over 54,000 tested probe sets were present (detection p value <0.05). The difference between the disease and the control group was significant for over 3,500 signals (t test p value <0.01), and approximately 1,000 genes showed a disease-to-healthy expression ratio greater than two. The found gene expressions show similarities to patterns from immune system, lymphatic, and

autoimmune diseases. The dominant biological processes were the immune and inflammatory reactions. Many of the up-regulated genes were expressed in leukocytes, suggesting leukocyte invasion into the bladder wall. Histopathological data support these findings. Selected gene expressions were tested in bladder biopsies of patients with non-ulcerative IC/PBS.

Conclusions: Gene expression profiles with total-RNA isolated from bladder biopsies suggest a strong inflammatory infiltration in ulcerative IC/PBS. A current field of research deals with the question whether this is also true for non-ulcerative or early stages of IC/PBS.

PO-Gyn 02.12

Experience with vaginal mini-sling ophira: first interim analysis

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Objective: The placement of Mini Slings is a new type of incontinence treatment developed in the past decade. This study was performed to evaluate success and patient satisfaction of the Ophira Mini Sling System.

Materials and methods: A prospective open-label multicenter study of treatment of female stress urinary incontinence with Mini Sling Ophira was started in July 2009 and is ongoing. By April 2010 thirty-nine patients were treated in DRK Krankenhaus Chemnitz Rabenstein. This System has a polypropylene monofilament mesh for the sub urethral area and two self-fixating arms with multiple fixating points in fishbone design. The tapes are placed mid-urethral low tension anchored to the obturator internus muscle. Pre-operative assessment consisted of a careful history, ICIQ- SF questionnaire, clinical exam, ultrasonic and urodynamics. The patients were re-evaluated 3 months and 6 months after the operation.

Results: 39 patients mean age 56 years (range 37–78) underwent Mini sling Ophira placement. 36 patients had a primary Stress urinary incontinence and 3 a recurrent incontinence. The procedure was combined with prolaps-surgery or laparoscopic procedures in six patients. The mean operating time was 10 min (range 7–15 min) in patients with Mini Sling placement alone. We had no significant intraoperative and early postoperative complications such as bladder perforation, urethral injury or bleeding. Postoperative pain was very mild (average 1–2/10). One patient with persistent pain was re-operated with complete removing of the tape. Success rate after 3 month was 92% ($n = 36$). Two Patients with recurrent or persistent stress urinary incontinence underwent a bulking therapy after 4 month. 6-months follow-up data will be available in October 2010 and will be presented.

Conclusions: According to the interim analysis of our first 39 patients, the placement of Mini Sling Ophira is a safe and efficient method for the treatment of female stress urinary incontinence.

PO-Gyn 02.13

The fat component of the urogenital diaphragm is an important determinant of the success of a conventional anterior wall repair

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Objective: The prolapse of the anterior compartment represents the most frequent reason for surgical intervention. Because of failure

rates of conventional surgery up to 60% of the cases, it is challenging to relate the histological structure of the supporting layer created by the intervention to the clinical outcome.

Materials and methods: In eleven patients undergoing a conventional anterior wall repair by reconstruction of the urogenital diaphragm, punch biopsies were taken from the rebuilt diaphragm layer. The relative composition of connective tissue, fat cell, and muscle areas was determined with the Leica Qwin morphometry system (Leica, Cambridge, UK).

Results: The spreading of tissue fractions resulted in $24 \pm 10\%$ collagen, $24 \pm 16\%$ muscle and $13 \pm 15\%$ fat. The percentage of collagen decreased with increasing age ($n = 11$, $r = 0.68$, $p < 0.05$). Four of the eleven patients presented with a relapse of cystocele. All recurrent descents were at or beyond the hymenal ring (Ba 0 to +5 cm). Age, BMI and parity did not differ between patients with and without relapse, respectively. The relative contribution of the individual tissue components to the composition of the diaphragm revealed no difference between the groups for collagen. The fraction of fat tissue was significantly increased in the group of successful surgery compared to the relapse group ($p < 0.05$) whereas the mean fraction of muscle tissue was decreased, though not significantly. In the total group minor values of Ba shift (i.e. actual re-displacement) were correlated to low fractions of muscle tissue ($n = 11$, $r = 0.61$, $p < 0.05$). No relation was found between BMI and percentage of fat tissue.

Conclusions: The rigidity of the urogenital diaphragm and the success of surgical repair is a function of fat tissue rather than connective or muscular tissue.

PO-Gyn 02.14

Paraurethral injection Bulkamid® for the treatment of female urinary incontinence

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Objective: Bulkamid® is made from a homogeneous polyacrylamide hydrogel for paraurethral injection. This gel contains 2.5% cross-linked polyacrylamide and 97.5% aqua and has been used in Germany since 2005. At the Brandenburg continence center, this method has been introduced in March 2009. Here we evaluate effectivity and complications in all treated patients, and investigate the success rates in those patients with mixed urinary incontinence, hypotonic and hypomobile urethra, for whom the insertion of a tension-free vaginal tape was indicate in question.

Materials and methods: Data were analyzed retrospectively from 42 patients of the Brandenburg Continence Center. Preoperatively, all patients received a complete examination with urodynamic tests including UDP, flow-EMG and introital sonography. All women included in this study were injected with 2 ml paraurethral Bulkamid® in three equal-size bulks at 2, 6 and 10 o'clock positions under urethroscopic view. Preoperatively and six weeks after surgery the patients completed the King's health questionnaire, and a detailed history of voiding was obtained.

Results: Of 42 treated patients, more than 85% reported a reduction in pad use by more than a half. 6 patients (38%) were completely continent at post-treatment examination. The lower the degree of initial stress incontinence, the higher was the effectiveness of treatment: 100% of the patients with initial stress incontinence grade I achieved at least a reduction of pads use by half, and nearly 60% of these patients became completely continent. In the subgroup with mixed urinary incontinence, the same success rates were observed, and even the presence of hypotensive or hypomobile urethra had no influence on this outcome. No complications were observed.

Conclusions: The paraurethral injection of Bulkamid is a safe and largely complication-free method for the treatment of stress incontinence, regardless of the presence of additional symptoms of urge, a hypotensive or hypo-mobile urethra. The effectiveness of this method depends inversely on the degree of incontinence.

PO-Gyn 02.15

Is there a chance to cure patients with total urinary incontinence?

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Objective: In previous studies we observed that the elevation of the perineal body with a mesh fixed between the levator ani muscles and the os sacrum (VARESA I) could substantially improve urge incontinence. We therefore assumed that the combination of VARESA I and a TOT could be helpful in those patients who were totally incontinent (always wet).

Materials and methods: Between 2007 and 2009, 28 patients with a total urinary incontinence were operated in our institution.

Results: Immediately after surgery 12 patients (43%) were cured, 9 patients (32%) could hold the urine but for some minutes (improved) and 7 patients remained incontinent. Multivariate analysis could not delineate those patients who could not be cured. Between 12 and 36 months after surgery only one patient recurred. She had a rupture of the mesh fixation. After surgical repair she was continent again.

Conclusions: Totally wet patients suffer extremely by their disorder. After our treatment (VARESA I and TOT) 75% of the patients felt absolutely happy and reported about a second life. We therefore believe that absolute urinary incontinence can be cured by surgery. This approach definitively needs further evaluation.

PO-Gyn 02.16

TVT sling incision: indications, outcome and recurrent incontinence

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Objective: This study retrospectively investigated suburethral tape incision and indications for this procedure, outcome in terms of cure of tape-related symptoms and frequency of recurrent stress urinary incontinence.

Materials and methods: Between 2003 and 2009, 174 women underwent surgical cutting of a suburethral tape. In 85 of them, the initial sling procedure was performed at our hospital, corresponding to a 7% revision rate.

Results: In 107 patients the TVT was severed because of disturbed bladder voiding, among them 70 women with recurrent urinary tract infection. A significant proportion of these women had a sonographic tape distance from the urethra of ≤ 3 mm ($p = 0.008$). Urge incontinence was reported by 112 women, frequently associated with a tape position too close to the urethra or bladder neck. Thirty patients reported dyspareunia; 24 showed tape erosion; 30 reported constant pain. Bladder voiding was improved after repeat surgery in 97%. The cure rates for urge and dyspareunia were 65 and 93%. Chronic pain persisted in 19%. Recurrent stress urinary incontinence occurred in 63 patients (52%) who were continent before TVT severing.

Conclusions: Indications for sling incision are disturbed bladder voiding, recurrent urinary tract infection, irritable bladder, pain, and

dyspareunia. Sling incision often normalizes bladder voiding but is less successful in improving irritable bladder, pain, or dyspareunia. The recurrent stress urinary incontinence rate is 52%. Dystopic tape positions account for most cases of tape cutting. Therefore optimal TVT positioning is important. Surgeons should assess their performance by preoperative and postoperative ultrasound.

PO-Gyn 02.17

Vaginal estrogens do not improve mesh extrusion rates in vaginal mesh surgery

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Objective: Mesh extrusion is a common complication in surgery for pelvic organ prolapse (POP). It is hypothesized that local estrogens reduce this complication. We analyzed the association between vaginal estrogen application and mesh extrusion rates in a prospective multicenter study.

Materials and methods: 199 women with cystoceles had anterior mesh implantation in 6 German hospitals. The application of local estrogens was recommended pre- and postoperatively. Nevertheless, estrogens were often not used for different reasons. A clinical examination, vaginal fluid pH-value determination and a history were performed preoperatively, 3 and 12 months postoperatively. A vaginal tissue specimen was taken during surgery.

Results: There was no association between menopause status or patients age and extrusion rate. Equally there was no effect between preoperative vaginal estrogen application and extrusion rate ($p = 0.8$). But extrusion rate was significant higher in patients using estrogen 3 months postoperatively ($p = 0.032$) (12 (9%) using estrogen; 0 using no estrogen). Comparing extrusion rates 3 or 12 months postoperatively with the preoperative vaginal fluid pH-value there was no significant association. But 3 months postoperatively vaginal fluid pH-value was higher in the extrusion group (5.2 vs. 5.8; $p = 0.009$), this may be a side effect by the vaginal lesion.

Conclusions: In our study, there was no effect between vaginal estrogen application preoperatively and extrusion rate in vaginal mesh surgery, the extrusion rate was even higher using estrogen 3 months postoperatively.

PO-Gyn 02.18

Perigee mesh for treatment of descensus genitalis anterior: efficiency and postoperative outcome

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Objective: While a pulsion cystocele as a midline defect of the fascia pubocervicalis can be operated by an anterior vaginal kolporrhaphia with good results, this operative treatment is not appropriate for a defect of the anterior vaginal wall caused by a defect of the lateral attachment of the vagina. A mesh system like the Perigee mesh offers a vaginal operative procedure for lateral defects.

Materials and methods: 26 of 52 patients, who were treated in our hospital with a Perigee mesh between 2/06 and 11/08 were seen for follow-up. We checked the efficiency of the operation method and the subjective satisfaction rate by use of a questionnaire and a gynecological examination.

Results: In the follow up examination of 26 patients we found 5 relapses type cystocele II° with insufficient apical fixation. Subjectively 23 patients constituted their condition as better or healed, 3 as unchanged and only one as worse than before the surgery. Micturition was better in 15 patients, worse in only one. Preoperatively 12 patients suffered from stress incontinence, of which 10 stated their condition to be better postoperatively. In one patient the stress incontinence was worse, one patient reported a de novo stress incontinence. No patient had pathological residual urine. One patient reported dyspareunia. Only 15 patients still applied vaginal estrogen as it was recommended.

Conclusions: The subjective satisfaction rate was better than the objective results. It seemed to us that the recurrent prolapses were caused by insufficient apical support by the operation. In case of cystoceles with insufficient apical fixation of the vagina the Perigee-mesh procedure should be combined with an apical fixation of the vagina, i.e. sacrospinal fixation.

PO-Gyn 02.19

Vaginal sacrocolporectopexy-a safe and cost effective approach for sub-/total uterine and vaginal vault prolapse surgery-description of the method and perioperative results

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Objective: As alternative to sacrospinous fixation, laparoscopic/open vaginosacropepy, use of meshes; vaginal sacrocolporectopexy is described as alternative in patients with prolapse. We present this “minimal invasive” mesh free vaginal technique and perioperative results.

Materials and methods: (1) Incision of the posterior vaginal wall, opening Douglas pouch, ±vaginal hysterectomy, (2) Blocking rectum left, small intestinal convolute upwards, (3) Incision of the praesacral peritoneum (level S2), (4) Dissection of anterior longitudinal ligament, (5) Fixing non-absorbable monofile suture (No. 0) to posterior wall of vaginal cuff, moving to the peritoneum on the right lateral margin of the rectum to os sacrum, (6) Suture placed two times through longitudinal ligament, (7) Advancing suture in the opposite direction, taking the posterior vaginal wall, (8) Anterior and/or posterior vaginal wall repair if necessary, (9) Closure of vagina and fixing the suture with elevation of vagina in a naturally axis.

Results: 83 patients with sub-/total uterine ($n = 50$, grade 2–3) and vaginal vault ($n = 33$, grade 2–3) prolapse were treated with sacrocolporectopexy. Cystocele (grade 2–3) was found in 76 and rectocele (grade 2–3) in 38 patients. In 8 patients masked stress incontinence was identified. Mean age of patients was 65 (39–88) years; mean duration of sacrocolporectopexy was 81 min. (35–165) without, and 80 min. (45–100) with hysterectomy. Anterior and/or posterior repair were performed in 79 (95%) patients. Three bladder lesions occurred and corrected without squeals (two in patients with history of hysterectomy). Haemoglobin decreased pre-/postoperative a mean of 1.8 mg/dl (range 0.3–3.3). Four patients has been revised (1 hematoma, 3 for suture removing in history of sciatica). Five of eight patients with masked incontinence were continent after surgery. In two patients TVT-O was performed.

Conclusions: Vaginal sacrocolporectopexy represents a safe, easy to perform, cost effective method for treatment of sub-/total uterine/vaginal vault prolapse.

PO-Gyn 02.20

Laparoscopic sacropexy for grade III–IV uterovaginal prolapse: short term results

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Objective: Evaluation of short term results of laparoscopic sacral colpo-, cervico- and hysteropexy performed between June 2009 and April 2010 at the Department of Gynaecology and Obstetrics, Jena University Hospital.

Materials and methods: 19 Patients with predominant apical prolapse stage III–IV underwent laparoscopic sacral colpo- (n11), cervico- (n7) or hysteropexy (n1). Suspension as performed by tension free application of Prolene mesh (Gynaemesh PS) using monofilament nonabsorbable sutures at the pelvic as well as at the presacral site. No staplers or bone screws were applied. For valid evaluation P-QOL/D questionnaire was used.

Results: Nine patients presented with recurrences secondary to prolaps surgery. In 2 patients alloplastic materials had been applied to the perineum in prior procedures. Median age was 68 years (range 42–81) and median BMI 27 (range 21–39). At presentation patients complained of vaginal discomfort (n19), urgency (n9), voiding difficulties (n12), stress urinary incontinence (n6) and ulcerations of vaginal skin (n7). Operating time ranged 151–305 min (median 223). In all patients postoperative recovery had been without complications. In 17 patients the anatomic results were satisfying with no recurrent apical prolapse so far. All of them described their subjective situation as fully cured. In 2 cases recurrent prolapse occurred after 1 and 8 months. One of them with massive uterovaginal prolapse underwent consecutive abdominal repair. The other patient who primarily underwent LASH and sacral cervicopexy is now scheduled for anterolateral fasciocervicopexy (Waaldijk).

Conclusions: Abdominal sacropexy is considered to be a gold standard in prolapse surgery. Combined with the advantages of minimal invasive surgery these short term results appeared as effective and safe. Using suture techniques at the presacral site we found no complications such as vertebral osteomyelitis or mesh expulsion as previously described by others.

Oncology

PO-Onko 02.01

Cold shock domain family member YB-1 expression in endometrium and endometriosis

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Objective: The Y-box binding protein YB-1 is involved in a variety of biological functions such as DNA transcription and repair and translational control of protein synthesis. The protein is highly expressed in a number of malignant diseases and is described as an oncogen regarding ovarian cancer in particular. The benign, chronic inflammatory disease endometriosis shares many characteristics with malignant diseases, like strong dissemination and invasion in affected

tissues, increased angiogenesis and high numbers of recurrence. The objective of our study was to examine the expression of YB-1 in human endometrium and endometriosis.

Materials and methods: Endometrium, endometriotic tissues and peritoneal fluid were obtained from patients undergoing laparoscopy at the Department of Obstetrics and Gynecology of the University of Lübeck. Immunohistochemistry and immunocytochemistry were performed in tissues and primary cultures of epithelial and stromal cells respectively. Cell cultures were prepared from endometriotic tissues and control endometrium and peritoneal macrophages were isolated from peritoneal fluid of patients with endometriosis as well as from healthy controls. YB-1 gene and protein expression were analyzed by quantitative real time PCR and Western Blot.

Results: YB-1 was statistically significant and more strongly expressed in endometrium, endometriotic lesions and peritoneal macrophages of patients with endometriosis in comparison to controls. Strongest YB-1 expression was observed in the epithelial compartment of endometriotic lesions.

Conclusions: Stronger YB-1 expression in endometriosis could have an impact on the development and/or progression of the inflammatory disease.

PO-Onko 02.02

Cluster analysis of endometriosis patients in an outpatient education programme

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Objective: The complexity of endometriosis and its diverse physical, emotional and social medical impacts pose major problems not only for the patient but also for the physician. Women with endometriosis differ greatly in terms of coping-strategies. The present study aimed to identify different patient groups to improve care.

Materials and methods: The population of a study on the development and implementation of an outpatient education programme for women with endometriosis served as the basis of the analysis. Two-step cluster analysis was performed to identify three clusters based on the variables “age”, “disease duration”, and “delayed diagnosis”. A unifactorial variance analysis variance (ANOVA) was used for comparison of mean values.

Results: In total, 115 cases were included in the three clusters. The first cluster was a group of 44 women characterized by the highest mean age (44 years) and the longest duration of disease (13 years). Deep exhaustion was the most important symptom in this group. The second cluster consisted of a subgroup with a mean age of 36 years and a disease duration of 3.4 years. These patients had the highest pain scores and the worse quality of life scores. The most striking feature in this group was the extremely long delay in diagnosis, amounting to 16 years on average. The third cluster consisted of young women (31 years) with a short duration of disease (3.4 years) and a short delay in diagnosis (2.1 years) who had a problem-oriented approach to dealing with the disease.

Conclusions: We expect that the analysis of psychological comorbidities at the 12-months-follow-up will show starting points to produce strategies for more selective treatment of endometriosis. In particular, it is crucial to identify “difficult” patients in Cluster 2 early and to ensure that they receive specific services.

PO-Onko 02.03**Inpatient costs for women with deep infiltrating endometriosis: a comparison of data from the years 2006 and 2007 of the Deutsche Endometriosezentrum Berlin (DEZB) Stufe III**

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Objective: In 2006 and 2007 respectively 13 women underwent surgical interventions because of deep infiltrating endometriosis (DIE) in the Deutsche Endometriosezentrum Berlin (DEZB). In these special cases the preoperative diagnosis is clearly more extensive. The costs of inpatient treatment of women with DIE increase in all clinical areas. Until now the payment occurs with the German DRG-System. The aim of this study is to show that the G-DRG-System do not lead to an adequate cost recovery for these patients. Therefore it is important to measure the correct costs. We want to put up a basis for discussion with the healthcare system to create an adequate cost recovery.

Materials and methods: We re-evaluated 26 cases of women with DIE in 2006 and 2007 with rASRM score I–IV°. Until now we examined the general duration of stay in days (day) and the costs for MRI and laboratory in Euro (€).

Results: The general duration of stay in 2006 were 13 days and in 2007 14 days. In 2006 five patients and in 2007 twelve patients achieved a MRI. The costs for the MRI had the amount of 2826€ in 2006 and of 5496€ in 2007 for all patients. The laboratory costs had the amount of 204€ in 2006 and 195€ in 2007.

Conclusions: Complex DIE-cases need special diagnostic and treatment. That leads to an increased demand of the costs due to special diagnostic, therapy and a prolonged duration of stay. We fear that the G-DRG-System is not able to cope the real costs of DIE, which could lead to a reduced quality of treatment of patients with endometriosis.

PO-Onko 02.04**Endometriosis between AFS and ENZIAN: a critical assessment of classification systems for endometriosis staging in an own patient group**

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Objective: Several classification systems are currently in place to classify the disease severity of endometriosis, many of which provide a very detailed description of some aspects of endometriosis. So far there is not one single classification system which would allow to depict the disease in all its facets such as the desire to have children, pain and extent. The AFS classification system is currently the most widely used system of classification, but it does not take deep infiltrating endometriosis into account. This is why, complementary to AFS classification, the ENZIAN score was developed as a staging system which also includes deep infiltrating endometriosis. The aim of the following study is to demonstrate that the ENZIAN score is a proper tool for classifying deep infiltrating endometriosis when combined with the AFS classification system. However, it can be

shown that certain localisations of endometriosis may be classified in both systems.

Materials and methods: Between 1st January 2009 and 31st January 2010, a total of 219 female patients underwent surgical treatment of endometriosis at Linz General Hospital and were post-operatively classified using the rAFS and ENZIAN scores. Retrospective study. **Results:** Classification of endometriosis using AFS and ENZIAN scores to assess disease severity and distribution pattern of deep infiltrating endometriosis.

Conclusions: The AFS classification system has proven a valuable tool in classifying endometriosis at international level. The ENZIAN score is a useful complementary tool to depict deep infiltrating endometriosis, yet needs to be adapted accordingly to avoid double classification in both systems. Both classification systems are to be regarded as morphologically descriptive, the inclusion of pain and the desire to have children as leading symptoms is urgently needed.

PO-Onko 02.05**Endometriosis in Pfannenstiel scar: a case report**

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Objective: To raise the awareness of scar endometriosis. Pathogenesis as well as different approaches to diagnosis, treatment and prevention based on current literature are discussed.

Materials and methods: In the present case report a 38 year old G2 P2 presented with premenstrual pain and bloody discharge from her caesarean scar. On ultrasound examination a 13 × 13 × 16 mm nodule was found at the level of the scar tissue. As scar endometriosis was suspected, the nodule was removed under general anesthesia.

Results: Histological findings were compatible with scar endometriosis. The postoperative recovery was uneventful.

Conclusions: Differential diagnosis of scar tissue pain in women following gynaecological or obstetric surgery should include scar endometriosis. Endometriosis is functional endometrial tissue outside the uterine cavity. Abdominal surgery involving the uterine cavity can lead to a spread of endometrial tissue in the abdominal cavity and may also involve the Pfannenstiel scar. Caesarean sections as one of the most frequently performed obstetric operations play a significant role in the development of scar endometriosis with an incidence of up to 1.7%. However, the pathogenesis of scar endometriosis remains unclear and gives rise to many theories. Important methods of preoperative diagnosis are ultrasonography including Doppler, computer tomography and magnet resonance imaging. Surgical removal is the treatment of choice. Histological examination confirms diagnosis. Preventive measures include thorough cleaning of the wound. In case of recurrent lesions malignancy has to be excluded.

PO-Onko 02.06**Peritoneal fluid level of TNF α , IL-1B, IL-6, IL-8, IL-12 and IL-13 in Nigerian women with endometriosis**

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Objective: The objective of this study is to look at the peritoneal fluid levels of six cytokine (TNF α , IL-1B, IL-6, IL-8, IL-12 and IL-13) in patients with endometriosis. Setting: A Prenatal Diagnosis and

Therapy Centre and Dept. of Obstetrics and Gynaecology of a Tertiary Hospital in Lagos. Study and Design: A cross sectional study. *Materials and methods:* Serum and peritoneal fluids samples were obtained from a total of $n = 57$ women, while undergoing laparotomy for infertility surgery (tubal repair, myomectomy and hysterectomy). Concentration of TNF alpha, IL-1B, IL-6, IL-8, IL-12 and IL-13 were measured in serum and peritoneal fluid. 17 were diagnosed with endometriosis externa, 6 adenomyosis uteri, 16 uterine leiomyoma and 18 normal results.

Results: Peritoneal fluid levels of TNF alpha, IL-6, IL-8, were significantly higher in the endometriosis and adenomyosis group ($p < 0.01$) respectively. There were no significant differences in the peritoneal fluid levels of IL-1, IL-12 and IL-13 in the entire group.

Conclusions: The elevated levels of TNF alpha, IL-6 and IL-8 in peritoneal fluid but not serum may show the importance of local cytokine profile in serum and peritoneal fluid from infertile women with and without endometriosis.

PO-Onko 02.07

Establishment of endometriosis centers of excellence: facts, problems and fiction

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Forced since 2005 by Stiftung Endometriose-Forschung e.V., Endometriose-Vereinigung Germany e.V., the European Endometriosis Liga, and the German Society of Gynecologic Endoscopy (AGE), the establishment of Endometriosis Centers in Germany did significantly improve the development of quality strategies in more than 25 Centers founded so far. From 2006–2009, our own experiences based on the diagnostic and treatment of more than 1500 patients (Table 1).

Out-patient (year)	2006	2007	2008	2009
Summary (N)	354	523	502	493
Pain (N)	343	515	479	413
Infertility (i)	23	86	81	111
Surgery (year)	2006	2007	2008	2009
Summary (N)	192	324	343	439
Pain (N)	114	230	245	400
Infertility (N)	40	71	98	109

Facts, Problems, and Fictions:

1. The establishment of a Center will lead to a increase of patients
2. The whole team should be able to handle the dramatic increase of complex and very complex cases
3. The Center structure should provide sufficient opportunities for qualification (doctors, nurses and patients)
4. Advanced Endometriosis is a surgical challenge—you will experience the urgent need in surgical training and cooperation.
5. In the out-patients setting, deficiencies in financial resources can lead to restrictions

6. The payment for Endometriosis procedures (diagnostic and treatment) which is based on the G-DRG-System should be optimized in the next future.
7. The growing number of patients will offer the opportunity for basic and clinical research.
8. In Europe, the german model of Centers of Excellence is unique and might influence the future of research and treatment.

PO-Onko 02.08

Expression levels of hnRNP G and hTra2β1 have opposite effects in endometrial cancer biology β

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Objective: Endometrial cancer (EC) is the most common gynecological malignancy in developed countries. The underlying molecular pathogenesis of EC, however, is poorly understood. Two well characterised alternative splicing factors hnRNP G and hTra2β1 were found exert antagonistic effects on alternative splicing in vitro and in vivo. In this study we explored the impact of these two factors in tumor biology of endometrial cancer (EC).

Materials and methods: EC tissues ($n = 139$) were tested for hnRNP G and hTra2β1 expression on mRNA level by real-time PCR and on protein level by immunohistochemistry.

Results: hTra2β1 mRNA level was found being induced in advanced FIGO stages ($p = 0.044$). HnRNP G protein nuclear expression was found more prominent in patients without distant organ metastasis ($p = 0.033$), and in FIGO stages I/II group ($p < 0.001$). hTra2β1 protein nuclear levels were elevated in poorly differentiated ($p = 0.007$) and lymph node metastases ($p = 0.003$) cancers. Kaplan–Meier survival curves revealed that elevated hnRNP G mRNA ($p = 0.029$) and protein ($p = 0.027$) levels were associated with a favourable patient outcome. Elevated hTra2β1 nuclear protein level was correlated with worse overall survival. Multivariate Cox-regression analyses identified nuclear hnRNP G level (hazards ratio 0.468, $p = 0.026$) as well as hTra2β1 level (hazards ratio 5.760, $p = 0.004$) as independent prognostic factors for EC progression-free survival.

Conclusions: Our results indicate that the antagonistic functional effects of hnRNP G and hTra2β1 on alternative splicing correlate directly to their opposite clinical effects on EC patient outcome.

PO-Onko 02.09

The sentinel concept for lymph node staging in endometrial cancer: is it possible?

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Objective: The sentinel concept is on the step into surgical routine in gynecologic malignancies. In endometrial cancer there are some difficulties in labeling of the sentinel nodes (SLN). Transfundal or hysteroscopic injections are described for application. The aim of this

study was to show the practicability of the sentinel concept using an trans-cervical application of the marker preoperative. We record the number of SLN found in lymphoscintigraphy, single photon emission computed tomography combined with computed tomography (SPECT/CT) and intra-operative.

Materials and methods: Between August 2008 and March 2010 21 patients underwent SLN labeling for staging of endometrial cancer. We applying 10 MBq Technetium-99 m-nanocolloid (2×5 MBq; 0.5 ml volume each) trans-cervical into the fundal myometrium. 45 min p.i. planar lymphoscintigraphy was performed followed by SPECT/CT and surgical therapy. We registered the number and location of SLNs in lymphoscintigraphy as well as in SPECT/CT. Additional the number of SLN found intraoperative, lymph nodes found within the obligatory performed conventional lymph node dissection and positive SLN were registered.

Results: Lymphoscintigraphy could be detecting SLNs in 15 of 21 patients, SPECT/CT detecting SLNs in 19 of 21 patients (90.5%). One of the two patients with non-marked SLN had an distinctive lymph node metastasis in 24 of 50 lymph nodes. One labeled SLN in SPECT/CT (5.3%) could not be found as SLN intraoperative using the gamma probe. Three patients had SLN metastasis as well as further lymph node metastasis. One patient (5.5%) had lymph node metastasis with an unaffected SLN. In average 3 SLN and 34 non-SLN were removed.

Conclusions: In endometrial cancer the sentinel concept is possible to perform using a trans-cervical labeling procedure. The SPECT/CT improved the pre- and intraoperative detection of SLNs. It's increased the number of sentinel lymph nodes found during surgery. But, currently a complete lymph node dissection must be carried out obligatory.

PO-Onko 02.10

Cyr61 (CCN1) protein expression as a predictive marker in endometrial cancer

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Objective: Cysteine rich 61 (Cyr61/CCN1) is involved in a multitude of physiologic and pathologic processes such as cell adhesion, migration, angiogenesis and apoptosis. It is an important player in tumorigenesis due to its pro-angiogenic activities. Cyr61 undergoes alternative splicing resulting in two different mRNA variants. Hypoxia triggers the predominant expression of only one mRNA variant that is solely capable to code for biologically active protein. Cyr61 expression studies in endometrial cancers found both, a downregulation as well as an overexpression of the protein. We studied the expression of Cyr61 and its splicing isoforms in endometrial cancer.

Materials and methods: Cyr61 protein expression in 138 tissue samples originating from endometrial cancer patients was evaluated by immunohistochemistry (IHC) and correlated to clinicopathologic factors separating histological types I and II. Survival of tumor patients was calculated by using Kaplan–Meier curves and Log-rank-test. In addition, expression of both Cyr61 mRNA variants was investigated in these samples by real-time PCR. Immunohistochemical results were correlated to expression levels of Cyr61 mRNA isoforms.
Results: Cyr61 overexpression was detected in 15% of endometrial cancer samples. Multivariant-analyses confirmed correlation of high protein expression levels (IHC) with lymph node metastasis, lymph-angioinvasion and tumor-grading. Patients with an overexpression of Cyr61 had a lower overall-survival and a shorter receive-free-survival compared to patients exhibiting low or moderate expression of Cyr61.

We could not find any significant correlation between immunohistochemistry and expression of the protein-generating mRNA transcript.
Conclusions: Overexpression of Cyr61 in endometrial cancer correlates well with poor survival, lymph node metastasis, lymph-angioinvasion and tumor-grading. Therefore, it could represent a new molecular marker in predicting survival of patients with estrogen-dependent endometrial cancer. Posttranslational modifications may account for the discrepancy of Cyr61 protein expression examined by IHC and no significant correlation with expression levels of the protein-generating Cyr61 mRNA variant obtained by realtime PCR.

PO-Onko 02.11

Paraneoplastic peripheral neuropathy in a premenopausal patient with endometrial carcinoma

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Objective: A paraneoplastic syndrome refers to a group of symptoms which are not directly caused by the primary or metastatic tumor. Paraneoplastic polyneuropathies are most frequently associated with lung cancer and in a gynecological setting with breast cancer. A manifestation in the course of a neoplasm of the female genital organs is an uncommon finding and has only been reported in a few cases.

Materials and methods: We report about a 48 year old nullipara who presented with subacute symmetric weakness of the limbs and paresthesia. Nerve conduction studies were consistent with sensorimotor neuropathy, biopsy revealed an axonal degeneration. Within 4 months, she turned from a regularly healthy woman into a disabled and wheel-chair depending patient. A suspicious uterine sonogram was found while accomplishing the oncological screening. Curettage was performed, which proved the presence of endometrial adenocarcinoma. Corticosteroid therapy and radical hysterectomy with bilateral adnexectomy was conducted. Secondly a radical lymphonodectomy was performed rendering the final tumor stage: pT1b, pN1 (4/25), G2, R0. Postoperatively the neurological symptoms improved. The patient is now scheduled for a adjuvant radiotherapy.

Conclusions: Neurological symptoms such as neuropathy, paresthesia and weakness, which occur in otherwise healthy women with no medical history, are always suspicious. The phenomenon of a paraneoplastic syndrome can point to an underlying malignancy and can be used as marker of progression or regression of the tumor. Usually paraneoplastic symptoms occur before the tumor is diagnosed. Due to the rarity of PNP, there is no standard treatment, but surgical and/or chemotherapeutical oncological treatment is recommended.

PO-Onko 02.12

Impact of CAIX and TIMP-1 serum levels at the diagnosis of metastatic breast cancer

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Objective: The tissue inhibitor of metalloproteinase (TIMP-1) plays a role in angiogenesis and invasion of cancer cells. CAIX (Carbonic anhydrase IX) forms part of the family of zinc metalloproteinase, which is involved in regulation of cell growth. Limited data has shown an association between an elevation of both factors and worse

prognosis in breast cancer patients. Therefore, we investigated the prognostic impact of CAIX and TIMP-1 serum levels in a cohort of metastatic breast cancer patients.

Materials and methods: Blood samples were taken at first diagnosis of metastatic disease before initiation of therapy in 90 breast cancer patients who were treated at the University Medical Center Hamburg-Eppendorf between 1994 and 2006. CAIX and TIMP-1 were measured by commercially available ELISAs (Oncogene Science, Siemens Healthcare Diagnostics). CAIX levels above the published cut-off of 506 ng/ml and TIMP levels above the cut-off of 454 ng/ml were regarded as elevated.

Results: 21% of the patients ($n = 18$) had elevated CAIX levels and only 19% of the patients ($n = 14$) had elevated TIMP-1 levels at the onset of metastatic disease. Increased TIMP-1 levels correlated with HER2/neu negativity ($p = 0.017$) but no other correlation could be observed between CAIX and/or TIMP-1 and traditional clinicopathological parameters. A shorter overall survival could be seen in the group of patients with increased CAIX levels (17 vs. 32 months; $p = 0.029$). We were not able to demonstrate a difference with regard to progression-free survival for patients with elevated CAIX serum levels. Elevated TIMP-1 serum levels were not associated with shorter progression-free or overall survival. However, in the subgroup of patients with estrogen receptor negative primary tumors elevated TIMP-1 levels correlated with shorter overall survival (5 vs. 18 months; $p = 0.003$).

Conclusions: In our group of patients with metastatic breast cancer, we were able to demonstrate a prognostic impact of CAIX and TIMP-1 serum levels.

PO-Onko 02.13

Multiple tubular adenomas of the breast: a case report and review of the literature

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Objective: Tubular adenomas of the breast are rare benign lesions mainly diagnosed in women younger than 35 years. In 1982 the classification of adenomas of the breast firstly included tubular adenomas distinguished from fibroadenomas by the predominance of epithelium and relative lack of stroma. These tumors with a reported incidence of about 4% of all benign breast lesions and about 11% of breast adenomas could be misdiagnosed as breast cancer.

Materials and methods: We here present a case of bilateral tubular adenomas in a 21 year old Chinese woman. She presented with a palpable tumor mass of the left breast measuring up to 11 cm. She reported a continuous tumor progression within the past 6 years. On physical examination the tumor affected the entire left breast, while lymph nodes were inconspicuous. Breast ultrasound showed a 110 mm solid hypochoic lesion of the left breast with partially irregular edges and inhomogeneous echo structure. The patient underwent a core biopsy. The histologic examination showed a tubular adenoma without any special histologic features. Therefore a mammography was not performed. Personal pathologic anamnesis revealed a malignant tumor of the parotid gland at the age of 11 years treated with radiation. The patient presented good general health. She underwent a total resection of the tumor in the left breast.

Conclusions: Tubular adenomas are rare lesions of the breast and often difficult to differentiate from breast cancer by clinical examination. Surgical examination is the treatment of choice and allows the correct histopathologic diagnosis. Core biopsy should be performed before surgery to avoid unnecessary misdiagnosis.

PO-Onko 02.14

Simultaneous study of docetaxel based anthracycline free adjuvant treatment evaluation, as well as life style Intervention strategies: concept of the SUCCESS C trial

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Objective: Taxane based chemotherapy, like the PACS-01-regimen (3× FEC followed by 3× Docetaxel 100) has been established as standard treatment option for early breast cancer. Anthracycline-based regimens don't seem to be superior in HER2-negative patients (Gennari et al., Slamon et al.). Dietary intervention seems to improve outcome in patients with early breast cancer (WINS, Chlebowski et al.). The prognostic relevance of isolated tumor cells in bone marrow has recently been proven (Braun et al., Janni et al.) and early data indicate a prognostic relevance of circulating tumor cells in peripheral blood (Rack et al., ASCO 2008, Rack et al., ASCO 2009).

Materials and methods: The Success C Trial is an open label, multicenter, 2 × 2 factorial design, randomized controlled, phase-III study for early, HER2/neu-negative breast cancer patients. The first randomization of the study will compare the disease free survival in patients treated with 3 cycles of Epirubicin–Fluorouracil–Cyclophosphamide (FEC)-chemotherapy, followed by 3 cycles of Docetaxel (D)-chemotherapy versus 6 cycles of Docetaxel–Cyclophosphamide (DC)-chemotherapy. The second randomization will compare disease free survival in patients with BMI of 24–40 kg/m² getting an individual lifestyle intervention versus not getting this lifestyle intervention. Women assigned to the weight reduction arm will receive an intervention program that consists of weight loss, diet and physical activity goals in the framework of a 2-year standardized and structured telephone and mail-based intervention. Furthermore, a translational research program will focus on the role of CTCs as valuable marker of treatment failure and early disease progression. At four predefined timepoints peripheral blood will be drawn.

Results: Results of the toxicity analysis and the translational research program will be available by the end of treatment (~ June 2012). First conclusions about effects on disease-free-survival are expected 2 years after the end of chemotherapy or lifestyle intervention respectively.

PO-Onko 02.15

Development of breast-dimensions to use in 3D-mamma-scanners in plastic breast surgery

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Objective: Aim of this study is the identification of relevant breast-dimensions and their conversion into technical parameters of a

computer animated breast modell, to predict the outcome of operations in plastic breast surgery.

Materials and methods: The 3D-breastmodell is supposed to be used previously to a plastic surgery procedure of the female breast. The system aims to provide the patient with a visualization of the outcome of the planned operation. The dimensions of 100 probands were determined, medically interpreted and evaluated. In order to provide the 3-D computer program with a basis of standard values, the results were supplied to the program.

Results: Until now the different breast distances and details of 33 probands were measured and standard values (age, weight, height) determined. Average values and standard deviations were calculated. First Analysis shows following results of standard values: age 36.21 years, height 166.45 cm, weight 69.49 Kg.

Breast details (cm)	
Breast breadth circular	97.89
Breast breadth right	27.68
Breast breadth axilar	54.44
Breast breadth left	27.62
Under breast breadth circular	86.20
Under breast breadth axilar	45.74
Breast height left	18.26
Breast height right	18.47
Distances (cm)	
Breast base bottom to nipple right	8.85
Breast base bottom to nipple left	9.00
Breast base top to nipple right	14.62
Breast base top to nipple left	14.29
Nipple right—suprasternal notch	24.71
Nipple left—suprasternal notch	24.80
Nipple right—medioclavicular point	23.82
Nipple left—medioclavicular point	24.30

Conclusions: The aim was to develop out of the collective of probands, breast dimensions according to age, height, weight etc., which could be used in the 3D-computer program. These standard values should be compared to patient data previous to a planned operation.

PO-Onko 02.16 Correlation between tumor burden and detection of sentinel lymph nodes in early breast cancer

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Objective: Sentinel lymph node biopsy (SLNB) is a standard treatment in the operative care for early nodal negative breast cancer. In literature a success rate of 95% is reported for SNLB. Intraoperative there are remarkable differences in the presentation e.g. the amount of radioactivity, the accumulation of blue dye and the total number of removed sentinel lymph nodes. A correlation between detection of the SLN and the nodal status is assumed.

Materials and methods: We studied in retrospective all SLNBs performed at our clinic from 7/2005 to 12/2009 regarding the intraoperative presentation and the histological tumor burden of the SLN. 406 patients received a SLNB. 1147 SLNs were removed totally, thereof 243 were positive in histological analysis. The positive SLNs were classified in 40 immunohistochemically positive SLN, 60 micro- and 143 macrometastases. Staining with blue dye and the measured radioactivity (99 m Tc) as ex vivo count and as ratio to the background count were compared.

Results: Over all SLNs there was a significant difference between the nodal positive and the nodal negative SLNs, for blue dye $p = 0.008$ (Fisher's exact test), and for the cps ex vivo count $p < 0.001$ (Kruskal–Wallis). Within the group of nodal positive SLNs the ratio was significantly attributed to the tumor burden, $p < 0.003$ (Kruskal–Wallis). For the immunohistochemically positive SLNs a mean ratio of 93.6, for the micrometastases 69.7 and for the macrometastases 62.3 was found.

Conclusions: Based on the enrichment of radiocolloid the SLNs could be differentiated significantly according to their tumor burden. We will show additional parameters as the amount of radioactivity of the primary tumor, the size of the nodal metastases as well as perinodal tumor occurrence with respect to blue dye, radioactivity and the number of SLNs removed.

PO-Onko 02.17 Peritoneal metastases in breast cancer patients: differences in survival depending on histological subtype. A subgroup analysis from the BRENDA database project

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Objective: Distant spread from breast cancer is commonly found in bones, lungs, liver and central nervous system. Metastatic involvement of peritoneum and retroperitoneum is unusual and unexpected. The aim of the study was to perform a comprehensive analysis of breast cancer patients with peritoneal metastases and to compare survivals depending on biological subtypes.

Materials and methods: 44 breast cancer pts with peritoneal metastases were detected out of a collective of 2500 bc patients treated in one institution between 1995 and 2005. Clinical characteristics such as estrogen receptor and progesterone receptor as well as survivals were analyzed based on breast cancer subtypes.

Results: Mean patient age was 54 years, 25 patients (56%) had ductal invasive carcinoma while 19 (44%) were diagnosed lobular invasive carcinoma. 30 (68%) patients had endocrine responsive tumors. A Her 2 percentage is not provided due to the lack of data bevor the year 2000. Median survival calculated from peritoneal metastases in histologic subgroups was as follows: Median progression free survival was 36.5 months for ductal invasive carcinoma, and 23.5 months for lobular invasive breast cancer. Median overall survival was 46 (Std 38.5) months for ductal invasive breast cancer and 32 (Std 54.5) months for lobular invasive breast cancer.

Conclusions: Patients with peritoneal metastases are a heterogenous group with a different outcome. The histologic subtype seems to be an important predictive factor as lobular invasive breast cancer is associated with worsened progression free an overall survival rates.

PO-Onko 02.18**Alteration in proliferation, apoptosis and expression of receptor-tyrosine-kinases of breast cancer cell line CAMA1 after incubation with a Thomsen-Friedenreich-antibody (NM-TF1)**

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Objective: The Thomsen-Friedenreich (TF) antigen is an onco-fetal carbohydrate epitope, associated with diverse carcinomas. Former studies showed, that a majority of mamma carcinomas and their disseminated tumor cells in the bone marrow express TF. In this study we investigated the effect of a TF-antibody (NM-TF1) on proliferation and apoptosis of the breast cancer cell line CAMA1 and furthermore alterations in receptor tyrosine kinase-expression in vitro. **Materials and methods:** After immunocytochemical staining of CAMA1 cell slides with NM-TF1, confirming the positivity of CAMA1 for the TF-antigen, CAMA1 cells were each incubated 48 h with 60 µg/ml NM-TF1 for all following examinations. A Glycophorin antibody functioned as an isotype control applied in the same concentration as NM-TF1. Proliferation rates were measured by a BrdU cell proliferation ELISA, apoptosis rates were determined by nick translation, immunocytochemistry with a M30 Cytodeath antibody and a cell death detection ELISA. Receptor tyrosine kinase-expression was analyzed by a Phospho-RTK Array and evaluated with the “Quantikine” software.

Results: NM-TF1 treated CAMA1 cells showed a significant inhibition of proliferation compared to the control group. Further with regard to apoptosis we found significantly elevated rates confirmed by all three examination methods after incubation with NM-TF1. The analysis of the Phospho-RTK Arrays, showed a down regulation of the Erb B2-, Erb B4-, Eph A1- and Eph A4-receptor phosphorylation for NM-TF1 treated CAMA1 cells.

Conclusions: The TF1-antibody NM-TF1 facilitates an inhibition of proliferation and an elevation of apoptosis in breast cancer cell line CAMA1. Therefore this antibody could be a hopeful candidate for an antibody-based tumor therapy for TF-positive mamma carcinomas. The analysis of the Phospho-RTK-Array allows insights in RTK inhibition. The TF1-antibody affects cell signaling pathways especially of the Erb-family, which influence not only cell proliferation and apoptosis, but also protein synthesis, cell motility, invasion and metastasis.

PO-Onko 02.19**Defining clinical and tumor characteristics to predict non-sentinel lymph node status in breast cancer patients with sentinel node metastasis**

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Objective: The current practice is to perform a complete axillary lymph node dissection (ALND) in breast cancer patients with tumor-involved sentinel lymph nodes, although only some of them have non-sentinel metastasis. In the most cases the axillary staging by sentinel node biopsy is probably sufficient, first of all considering the high morbidity of ALND. We inquired, if there exist any clinical or tumor characteristics, which predict the probability of having non-sentinel involvement.

Materials and methods: We analysed 765 breast cancer patients, who were treated with a sentinel node biopsy in the years 1998 to 2008 in our hospital. If they had sentinel lymph node metastasis, they underwent ALND. We evaluated the following clinical and tumor characteristics as predictors for non-sentinel lymph node involvement: age of patient, menopausal status, localisation of the tumor, tumorsize, tumor histology, tumor grading, hormone receptor status, HER2-status, lymphangiosis carcinomatosa and multifocality of the tumor.

Results: 160 patients (21%) had sentinel lymph node metastasis. In 16 patients (10.0% of the 160 patients with sentinel node metastasis) we found a non-sentinel lymph node involvement. Big tumorsize, negative hormone receptor status, negative HER2-status, lymphangiosis carcinomatosa and multifocality were significantly associated with non-sentinel lymph node involvement. We could not find any correlation of non-sentinel metastasis considering patient's age, menopausal status, tumor localisation, tumor histology or tumor grading.

Conclusions: We could show that there exist tumor characteristics, which we correlated to low probability of non-sentinel involvement. In the case of low probability of non-sentinel tumor burden the ALND should be discussed. Changing the current management could be an advantage for many patients.

PO-Onko 02.20**Supplementary preoperative breast MRI compared to mammography and ultrasound alone in women with invasive lobular breast cancer**

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Objective: Breast MRI is superior in the staging of invasive lobular breast cancer (ILC) compared to ultrasound and mammography alone. Yet, evidence that the implementation of breast MRI leads to a benefit for the patient is relatively weak and it could also lead to an overestimation of the tumor and respectively to an overtreatment of the patient.

Materials and methods: At the Heidelberg Breast Unit we included 92 ILC patients in a retrospective but confirmatory analysis who received a preoperative breast MRI and subsequent surgical therapy. If breast MRI revealed additional suspicious lesions or increase in tumor size estimation these cases were presented to a fictitious interdisciplinary preoperative tumorboard. The recommendation of the fictitious tumorboard given without the knowledge of the breast MRI result was compared with the recommendation of the real tumorboard what integrated the results of the breast MRI. In the case of surgical change, we analyzed if this was adequate according to the postoperative pathology findings.

Results: New MRI findings resulted in a change of surgical therapy in 23 of all patients (25%). According to the postoperative pathology findings this change was appropriate in 20 of these patients (22%). Assuming a minimal acceptable benefit rate of 5% clinically relevant this change turned out to be significant on a confirmatory basis ($p < 0.0001$). Three patients (3%) who underwent mastectomy due to breast MRI, a breast conserving therapy would have been possible.

Conclusions: Patients usually benefit from a preoperative breast MRI in terms of appropriate change of surgical change due to breast MRI. The risk of overtreatment on the contrary is limited.

PO-Onko 02.21**Diagnostic accuracy of HER2 immunohistochemistry in breast core needle biopsies**

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Objective: Currently, core needle biopsies (CNBs) are widely used to determine HER2 status in breast cancer. Recent publications reported up to 20% false-positive results on CNBs if immunohistochemistry (IHC) is compared to fluorescence-in-situ-hybridization (FISH). To clarify, if confirmation of IHC positivity by FISH is generally required, we analyzed the reliability of IHC positivity on CNBs versus surgical specimens in a multi-institutional study.

Materials and methods: Five pathological laboratories contributed to this study by performing IHC on 500 CNBs and the corresponding surgical specimens overall. If IHC revealed score 2+ or 3+, HER2 status was confirmed by FISH in a central laboratory. We compared evaluation according to FDA-approved scoring criteria and recently published ASCO-CAP guidelines.

Results: CNBs scored 3+ revealed 5 false-positive results if scoring followed the FDA criteria (5/40 = 12.5%) and 2 false-positives in terms of the ASCO-CAP criteria (2/33 = 6.1%). IHC was false-negative in one CNB only. By contrast, IHC on surgical specimens revealed 5 false-negative results, but only one false-positive result (1/35 = 2.9%) if scored following FDA-approved criteria. With the aid of the ASCO-CAP criteria, false-positive IHC results were obtained in only one of the five participating institutions.

Conclusions: IHC 3+ scores on CNBs proved to be reliable in 4 of the 5 participating institutions if scoring followed the ASCO-CAP criteria. Therefore, accurate determination of HER2 status in breast cancer is possible on CNB using the common strategy to screen all cases by IHC and re-test only 2+ scores by FISH. Prerequisites are quality assurance and the application of the new ASCO-CAP criteria. (J Clin Oncol. 2010, in press)

PO-Onko 02.22**MSCs recruitment by breast cancer cells and the effect of breast cancer on MSCs**

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Objective: Drug or suicide gene delivery to breast cancer by mesenchymal stem cells (MSCs) has been reported to be a treatment option due to migratory properties of stem cells. In contrast, stem cells have also been shown to enhance tumor growth, metastasis and invasiveness. However, little is known about cytokines involved in the recruitment of MSCs by breast cancer. Here we investigate the interaction between breast cancer cells and MSCs.

Materials and methods: Breast cancer was generated in Balb/C mice ($n = 5$) by injecting 4T1 cells into the mammary fat pad. Seven days after injection of tumor cells, mice received an i.p. injection of GFP-Luc-labeled human MSCs, which were tracked by bioluminescence. In vitro migration assay were performed to assess migration of MSCs towards conditioned medium of 2 breast cancer cell lines (4T1, MDA-MB231). PDGF-BB protein was used in ascending concentration to investigate its migratory properties on MSCs. MSCs were incubated with tumor conditioned medium (4T1, MDA-MB231) and stem cell lysates were harvested after 48 h. Afterwards, reverse phase protein array (RPPA) was used to investigate quantitative measurement of protein expression and activation by 139 distinct antibodies.

Results: MSCs migrate in a xenograft breast cancer model towards breast cancer. We could show in vitro that the migration of MSCs towards breast cancer cells (4T1, MDA 231) is PDGF-BB dependent. In addition, MSCs treated with conditioned medium of breast cancer revealed a significant change in the expression of proteins involved in regulation of cell cycle and cell growth (e.g. c-Myc, Cyclin E1, EGFR, STAT3).

Conclusions: Proteins involved in regulation of cell cycle and cell growth are upregulated in MSCs after interaction with breast cancer cells. Thus, drug or gene delivery approaches using MSCs as carrier is a double-edged sword and requires more in depth investigation.

PO-Onko 02.23**Two years of mammography screening program in eastern Thuringia: effects on tumor stages and surgical options in two certified breast centers**

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Objective: Population-based digital mammography screening was implemented in East Thuringia in May 2007. We analysed differences in tumour stages and operative therapy comparing patients from the Mammography Screening Program (MSP) and patients with breast cancer diagnosed otherwise. Furthermore, we analyzed how the MSP influences the total number of breast cancer patients with a special view to tumor stage and type of operation performed.

Materials and methods: Data from the breast cancer patients of the two quality controlled, DKG-certified Breast centres in Jena and Gera (East Thuringia) were analysed for the following periods: from May 2006 until April 2007 (407 patients), from May 2007 until April 2008 (588 patients) and from May 2008 until April 2009 (623 patients). Breast cancer was diagnosed in a total of 344 patients from May 2007 until April 2009 by the MSP. Patient groups were compared regarding tumour stage, nodal status and breast conserving surgery (BCS).

Results: In the MSP-diagnosed patients we found not only a higher number of DCIS (15.3 vs. 7.6%), but also an increased number of carcinoma smaller than 2.0 cm (65.6 vs. 50.4%). Accordingly, Breast cancers larger than 2.0 cm were less frequent in the MSP-group (15.6 vs. 31.9%). In the MSP-group, 67.7% were node negative vs. 62.6% from the era before MSP. BCS was performed in 90.7% of the MSP-patients but only in 71.2% of other patients. In the period from May 2008 until April 2009, the percentage of patients presenting with carcinoma of less than 2.0 cm went up by 8% in comparison to the period from May 2006 until April 2007, $p = 0.007$. The quota of BCS could be increased by 4% in all patients.

Conclusions: MSP participation led to a significantly increased detection of smaller, node negative breast carcinomas and an increase of the rates for BCS.

PO-Onko 02.24**Sequential treatment with epirubicin/cyclophosphamide, followed by docetaxel is equieffective, but less toxic than FEC120 in the adjuvant treatment of breast cancer patients: the German ADEBAR phase III study— subgroup analyses**

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Objective: Based on evidence from single trials as well as meta-analysis, taxane containing adjuvant chemotherapy has been established as standard treatment in node-positive breast cancer. However, in the MA-21 study, AC-P was significantly inferior to FEC120. We prospectively compared a sequential epirubicin-docetaxel chemotherapy regimen to FEC120.

Materials and methods: The ADEBAR study was a multicenter phase III trial ($n = 1502$) to evaluate whether breast cancer (BC) pts with ≥ 4 axillary lymph node metastases benefit from a sequential anthracycline-docetaxel regimen (E90C–D: 4 cycles epirubicin [E] 90 mg/m² plus cyclophosphamide [C] 600 mg/m² q21 days followed by 4 cycles docetaxel [D] 100 mg/m² q21 days) compared to dose-intensive anthracycline-containing chemotherapy (FE120C: 6 cycles E 60 mg/m² day 1 + 8, 5-FU 500 mg/m² day 1 + 8 and C 75 mg/m² day 1–14, q4 weeks).

Results: Treatment was stopped prematurely in 3.7% of the pts in the E90C–D arm and in 8.0% in the FE120C arm due to toxicity ($p = 0.0009$). Antibiotic treatment was given in 10.4% (E90C–D) vs. 19.7% (FE120C), G-CSF support in 39.2% vs 61.4% and erythropoietin stimulation in 8.7% vs. 20.0%, respectively ($p < 0.0001$). Haematological toxicity was significantly higher in the FE120C-arm. 128 events of recurrence were observed in the FE120C group and 153 in the E90C–D group. Overall survival in the two groups was not significantly different: HR 0.99, 0.73–1.35, $p = 0.99$. Subgroup analyses, stratifying for tumor size, lymph node involvement, hormone receptor and HER2-neu status showed no significant difference between the two treatment arms and will be presented in detail.

Conclusions: Different toxicity profiles given, hematological toxicity in the FE120C group was more severe than in the E90C–D. In contrast to AC-P in an earlier study, EC-Doc provides a feasible and effective alternative option to dose-intensified FEC with different safety profile in this high risk breast cancer cohort.

PO-Onko 02.25**Clinical risk factors for complications associated with ECG-guided portacath use in breast cancer patients**

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Objective: Totally implanted venous access systems (portacath) are increasingly used in cancer patients in order to make the application of

chemotherapy for patients more comfortable and safer. Nevertheless these portacaths are associated with short- and long-term complications. These vary between different types of malignancies. Complication rates in breast cancer patients have not yet been analyzed broadly.

Materials and methods: We performed a retrospective analysis at the university hospital Frankfurt, Germany. Records from 405 breast cancer patients who had received an ECG-guided portacath insertion from years 2003 to 2009 were reviewed to evaluate risk factors for port associated complications. Two different insertion techniques were used: surgical cut down to the cephalic vein or if not possible direct puncture of the subclavian vein. The device was placed on the fascia pectoralis. All patients were followed through December 2009 or until death, catheter failure, or catheter removal upon completion of chemotherapy. Beside clinical tumor parameters disease specific events have been evaluated.

Results: Of 405 breast cancer patients 9 were excluded because of incorrect portacath insertions. Among the remaining 396 patients the most frequent complication was thrombosis (9.8%). Surgical complications were infrequent with catheter leakage (0.8%) and pneumothorax (0.5%). We found no significant correlations between the rate of thrombosis and several different clinical variables (primary vs. metastatic disease, tumor size, lymph node status, and histological grading). Moreover no differences were found regarding to the two applied insertion techniques or the chest side in which the portacath was placed. Interestingly, the rates of thrombosis were lower in patients older than 50 years (7.1 vs 14.0%; $P = 0.037$).

Conclusions: The thrombotic complication rate in breast cancer patients is rare. We found younger age as the only patient related risk factor for the development of port-related thrombosis.

PO-Onko 02.26**High sensitive pool screening of point mutations in breast cancer using chemiluminescence detection**

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Objective: A nonisotopic pool-screening method of point mutations (e.g. SNP) and small insertions/deletions in genetic samples is presented. Based on a formerly described allele-specific pool-screening, the semi nested PCR is substituted by a one-step method in combination with solid-phase technique and chemiluminometric detection.

Materials and methods: The allele-specific PCR was designed to discriminate between T and G changing the amino acid 300 from Cysteine to Glycine in the breast cancer gene 1 (BRCA-1). The PCR products were coupled via their Biotin label to Streptavidin-coated microtiter plates. For chemiluminometric measurement an A(lcaline)-P(hosphatase)-labeled monoclonal anti-Digoxigenin-antibody was added. The antibody detects the PCR products resulting out of the amplification of the mutant allele. AMPPD with amplifier was used as the chemiluminescent substrate for AP.

Results: The method is able to detect one mutant allele in a total of 2048 alleles. Pool sizes from 32 up to 128 samples are practicable (=64 to 256 alleles). The signal-to-noise-ratio is better than 3:1 vs. cut-off for pools with 128 specimens.

Conclusions: The method is very useful in following applications: for population studies, especially for rare mutations, for determination of allele frequencies in a population or in modified manner: for screening, e.g. for HIV- or Hepatitis B exclusion in blood donors, for cancer therapy monitoring to evaluate the risk of a minimal residual disease, e.g. Philadelphia chromosome in chronic myeloid leukaemia. Furthermore the use of microtiter plates allows an automated execution of the post PCR steps i) PCR product extraction, and ii) detection & measurement of the mutant allele. The method is able to reduce the costs about 60 to 90% for PCR per sample (depending on pool size).

PO-Onko 02.27**Menopausal status in breast cancer patients with past chemotherapy determines long-term hypoactive sexual desire disorder**

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Objective: Chemotherapy and endocrine treatment in young breast cancer patients are frequently associated with abrupt menopause. Little is known about the long term prevalence of hypoactive sexual desire disorder (HSDD) in these patients. We want to examine the effects of adjuvant endocrine therapy on sexual desire in pre-menopausal patients with breast cancer and past chemotherapy.

Materials and methods: A controlled, cross-sectional study enrolled 47 women with breast cancer or benign breast disease at a tertiary-care center. A standardized questionnaire (SIDI-F) on HSDD was utilized. Serum concentrations for estradiol, testosterone and Anti-Müllerian hormone (AMH) were measured by specific assays. The SIDI-F interview was applied in 35 women with breast cancer (mean age: 42.3 years) with eventual adjuvant endocrine therapy, 2–8 years after chemotherapy, and 13 women with benign breast tumors (mean age: 39.8 years), 2–5 years after diagnosis.

Results: Mean SIDI-F scores were similar in the breast cancer group (32.9) and the benign breast disease group (34.0). Subgroup analysis revealed no statistical differences in the mean SIDI-F scores with respect to the actual endocrine therapy. However, in breast cancer patients with menopause induced by chemotherapy or gonadotropin-releasing hormone (GnRH) agonists, the SIDI-F scores were significantly lower (30.7) compared to breast cancer patients with menorrhagia (40.4). Mean estradiol and testosterone levels were not statistically different. Mean AMH levels were significantly lower in the breast cancer group (0.1 ng/ml) as compared to the benign breast disease group (0.7 ng/ml).

Conclusions: Adjuvant endocrine therapy with GnRH agonists in breast cancer patients with past chemotherapy has a negative impact on sexual desire. Patients with menopause induced by chemotherapy or GnRH agonists show significantly reduced sexual desire as compared to menstruating patients with past chemotherapy.

PO-Onko 02.28**Description and first results of BRENDA II project: is the preexistent fear of chemotherapy reason for violations of guidelines in breast cancer?**

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Objective: Therapy of breast cancer according to guidelines leads to a better recurrence free and overall survival of patients as it could be shown in BRENDA I project. But there are still only about 70% of patients getting a therapy according to guidelines. Brenda II should identify and characterize reasons of non-guideline-adherent therapy and develop strategies to improve the outcome of patients.

Materials and methods: Standardized and well implemented questionnaires (e.g. EORTCQLQ-C30, PHQ-D) are used at three points of therapy to figure out inter alia social and psychological status and medical history: Before surgery, after surgery and tumorboard and 6 month after finishing adjuvant treatment. At this point there are $n = 56$

patients who had passed all three, $n = 160$ who had passed two inquiries and $n = 228$ who had passed only one.

Results: Under therapy the fear of endocrine, operative and radiation therapy gets tendentially less, while fear of chemotherapy seems to stay equal or even to get more. All patients refusing chemotherapy had a higher score of fear in all items. Fear of loss of hair and fear of nausea was always pronounced the most.

Conclusions: There seems to be sort of psychological disposition remaining unchanged under therapy experiences and which complicates the guideline adherent therapy. It has to be discussed, if this could be point of intervention to improve outcome of patients.

PO-Onko 02.29**Parvovirus H-1 is cytotoxic for human breast cancer cells**

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Objective: Despite effective systemic therapies tumor of approximately 50% of all breast cancer patients will relapse. Therefore, new therapeutic approaches are needed. A promising new candidate is oncolytic virotherapy. Replication-competent oncolytic viruses like parvovirus H-1 (H-1PV) selectively kill cancer cells and have low toxicity in non neoplastic cells. H-1PV does not cause any known human disease and was shown to have oncosuppressive properties in a number of tumor entities. The aim of this study was to evaluate the cytotoxic effect of H-1PV in human breast cancer cells.

Materials and methods: Human breast carcinoma cell lines MCF-7 and MDA-MB-231 were infected with H-1PV at different multiplicities of infection (MOI). The cytopathic effect was evaluated on day three after infection by counting the number of surviving cells. Survival was calculated as the number of living infected cells divided by the number of living mock-treated control cells.

Results: Both cell lines were susceptible to H-1PV induced cell killing. This cytopathic effect was dose dependent. Whereas in MDA-MB-231 a MOI of 1 led to a survival rate of 0.69, this low MOI was unable to result in significant cell killing in MCF-7. At higher MOIs (MOI = 10 and 100, respectively) survival rates were 0.16 and 0.05 in MDA-MB-231 and 0.81 and 0.63 in MCF-7, respectively.

Conclusions: H-1PV leads to a dose dependent cell killing in human breast cancer cells. Wildtype H-1PV therefore seems to be a promising new candidate for the treatment of breast cancer. Furthermore, as transgene carrying vectors have been produced from H-1PV, the virus could be used for gene therapy of breast cancer.

PO-Onko 02.30**Detecting sentinel lymph node metastasis in breast cancer patients on a molecular level: a new multi-marker RT-PCR panel**

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Objective: To compare the diagnostic accuracy of mRNA marker panels as detected by RT-PCR to histological examination of SLN from breast cancer (BC) patients.

Materials and methods: 314 SLN from 150 patients were analysed histologically and with RT-PCR for various mRNA-markers. A marker panel consisting of CK19, MGB1, MGB2, EGP2 and NYBR1 was decided upon and a SLN defined as metastases-positive by PCR when at least 2 out of 4 markers were expressed. The panel was then validated in a second collective of 315 SLN from 235 patients. Analyses were performed on SLN level and on patient level, where a patient was correctly identified as node-positive when at least one of the histologically-positive SLNs was PCR-positive as well.

Results: In the first collective, 74/314 SLN were histologically metastases-positive. Individually analyzed the mRNA-markers attained the following sensitivities/specificities: CK19 94.6%/97.9%, MGB1 82.4%/91.7%, MGB2 82.4%/96.7%, CEA 71.6%/97.5%, EGP2 91.9%/97.1%, NYBR1 82.4%/93.8%. The RT-PCR panel consisting of at least 2 positive out of the 4 markers CK19, MGB1, EGP2 and NYBR1 led to 95.9% sensitivity, 95.0% specificity, 85.8% positive predictive value (PPV), 98.7% negative predictive value and 95.2% overall concordance with histology. On patient level, sensitivity was 97.1%, specificity 95.7%, PPV 87.2%, NPV 99.1% and overall concordance with histology 96.0%, respectively. In the validation collective, 84/315 SLN were histologically-positive and panel sensitivity was 88.1% with 95.2% specificity and 93.3% overall concordance on SLN level. On patient level, sensitivity in the validation collective was 90.3%, specificity 93.9%, PPV 86.7%, NPV 95.6% and overall concordance with histology 92.8%, respectively.

Conclusions: Molecular staging of SLN using real-time this RT-PCR multi-marker panel in BC patients could serve as a useful complement to standard diagnostics.

PO-Onko 02.31

WSG PLAN B trial: Evaluating of molecular based risk assessment according to Oncotype DX and uPA/PAI-1 in primary HER2 negative breast cancer: interim analysis

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Objective: Anthracycline- and taxane-based adjuvant chemotherapy (CHT) is standard of care in N+ breast cancer (BC) and shown to be the most effective regimen in N- BC, but overtreatment remains a major problem. Gene signatures identify patients at low risk of recurrence currently misclassified by conventional prognostic factors. Plan B incorporates the 21-Gene Recurrence Score (RS) as mandatory risk stratification in hormone-receptor (HR)+ patients with N(0–3)+. Recent data suggest that patients with low RS do not derive significant benefit from adjuvant CHT regardless of nodal status.

Materials and methods: Patients with high-risk primary BC are eligible. A total of 2448 patients are planned to be randomized to receive either 4× Epirubicin90/CPM600 q3w followed by 4× Docetaxel100 q3w or 6× Docetaxel75/CPM600 q3w. Importantly, patients with N(0–3)+ and RS <11 will be spared CHT but receive endocrine therapy alone. Pharmacogenomic e.g. will be performed prospectively. The primary study endpoint is event-free survival.

Results: Between 3/2009 and 4/2010, 1089 patients have been registered and 855 randomised. Baseline characteristics are comparably. RS results actually exist in 662 cases: 113 with RS <11, 412 with 12–25 and 137 > 25. 55 (49%) of the patients with low level RS don't get any CHT. The two regimes have been shown equal acceptance and analog toxic profile (169 SAE).

Conclusions: WSG PLAN B trial helps to identify the most effective regimen in HER2–BC. It's a prospective trial to evaluate RS. Registration constant in time and high acceptance of RS in clinical practice means that we have feasibility for genomic tests.

PO-Onko 02.32

Secondary plant derived substances, food ingredients in interaction with breast cancer cell lines

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Objective: Plants produce more than 100,000 different low-molecular-mass natural products, known as secondary metabolites. Numerous of them are non-steroidal phytoestrogens, classified to lignans, isoflavonoids and coumestans. Within 2 interdisciplinary research projects (Deutsche Krebsstiftung, BMBF) plant derived substances and food ingredients were proved systematically regarding their anti cancer effects under in vitro conditions by means of different breast cancer cell lines. Expected results have meaning for the nourishing medicine, the development of phytomedicine, e.g. development from screenings to the determination of estrogen receptor modulators, structural analysis and structure design.

Materials and methods: Project 1: At first, investigation of molecular and cell biological to prove mechanisms of established and potential phytoestrogens as a condition for the development of strategies in cancer prevention and therapy. Present conditions: extraction, substance analysis, testing of extracts and lignans in cell culture models. At present technologies are compiled to resuming cracking steps by excerpts of the flax root. Project 2: Innovative regional competence for the development of biofunctional food ingredients from lupinus seed.

Results: According to the method of Lyengi it was possible to enriched lignans. The analysis of secondary derived substances was carried out by Pyrolysis Field Ionization Mass Spectrometry: lignans, flavonoids, terpenes, sterols, peptides among others. At different concentrations it could be estimate antiproliferative effects of flax root extractions; control substances were estradiol and tamoxifen. The antiproliferative effects were present at ER positive and ER negative cell lines. Root extract from *L. usitatissimum* at concentrations of 0.01 µg/ml to 50 µg/ml didn't have significant cytotoxic effects to MCF7 and BT20 cells.

Conclusions: It was prepared a flax root extract from *Linum usitatissimum* with measurable lignan concentrations reducing cell growth of two breast cancer cell cultures in vitro.

PO-Onko 02.33**Cervical cancer screening by self-sampling for p16 with two different sampling systems**

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Human papillomavirus has been identified as the major causal agent of invasive cervical cancer. Primary screening by HPV testing has a high sensitivity, however its specificity remains limited. In contrast, p16INK4a is only expressed in the oncogenic process of cervical cancer. The majority of cervical cancer cases are still associated with absent or deficient screening because of inconvenience often associated with obtaining Pap smears. Patient-obtained vaginal sampling for analysis of HPV DNA has a sensitivity of detection of high-grade cervical lesions that is at least as equivalent compared to Pap smear. It remains unclear what sampling method is best for self sampling and what diagnostic assay provides high sensitivity and specificity. We compared efficiency and patient-handling of two self sampling devices such as vaginal brush and vaginal lavage sampling. Gynaecological examination including smears for Pap, Cervatec and HPV testing and colposcopic examination with biopsies was performed. All samples were examined by p16 ELISA. This pilot study included 152 patients recruited at our colpo clinic. 43% presented with atypical Pap smear, 46% were hr-HPV positive and 31 patients had CIN 2+. Handling of the self sampling devices was rated acceptable or good in 62% of the cases. But only in 2% of atypical pap smears the self sampled p16 ELISA turned out to be positive. Comparing vaginal sampling with vaginal lavage, we could not find any significant difference in respect to the detection rate for HPV and p16-expression. In conclusion, our results showed that self-sampling followed by p16 ELISA analysis is not suitable to detect CIN. Neither self-sampling with the vaginal brush nor with the vaginal lavage showed sufficient results. A subsequent main study in larger scale is planned whereby a self-sampling system for the screening of dysplastic lesion of the cervix only on the basis of HPV-analysis will be tested.

PO-Onko 02.34**Effects of sex hormones in oral contraceptives on the female sexual function score: a study in German female medical students**

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Objective: Female sexual dysfunction (FSD) is a very common disorder, with an estimated prevalence of having at least one sexual dysfunction of about 40%. To investigate the prevalence and types of FSD and the relationship between hormonal contraception (HC) and FSD in female German medical students. Female Sexual Function Index (FSFI) with additional questions on contraception, sexual activity, and other factors that may influence sexual function.

Materials and methods: An online questionnaire based on the FSFI was completed by students from six medical schools. Obtained data were screened for inconsistencies by programmed algorithms.

Results: A total of 1,219 completed questionnaires were received, and 1,086 were included in the analyses after screening. The mean total FSFI score was 28.6 ± 4.5 . 32.4% of women were at risk for FSD according to FSFI definitions. Based on domain scores, 8.7% for were at risk for FSD concerning orgasm, 5.8% for desire, 2.6% for

satisfaction, 1.2% for lubrication, 1.1% for pain and 1.0% for arousal. The method of contraception and smoking were factors with significant effect on the total FSFI score whereby hormonal contraception was associated with lower total FSFI scores and lower desire and arousal scores than no contraception and non-hormonal contraception only. Other variables such as stress, pregnancy, smoking, relationship and wish for children had an important impact on sexual function as expected according to earlier studies.

Conclusions: The prevalence of students at high risk for FSD was consistent with the literature although domain subscores differed from samples previously described. The contraception method has a significant effect on the sexual functioning score and women using contraception, especially hormonal contraception, had lower sexual functioning scores. Stress and relationship among other variables were found to be associated with sexual function and may thus provide insight into the etiology of sexual disorders.

PO-Onko 02.35**The benefit of clinical pharmacists' interventions in a gynecology department of a German university hospital: a pilot project from clinical and quality management perspective**

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Objective: Drug therapy management is increasingly complex from the physicians' point of view. According to international studies ward-based clinical pharmacists' interventions (PI) may improve cost-effectiveness as well as treatment outcomes. To assess PI benefits from clinical and quality management perspective a one-year pilot project was initiated.

Materials and methods: A clinical pharmacist as part-time staff was implemented on a once-weekly base in the ward round of three operative and/or oncological teams. The scope of duties was systematic chart and medication process analysis, patient-oriented drug information, Adverse-Events-management, optimization of drug substitutions according hospital formulary, avoidance of special medications' orders, improvement of drug storage and reimbursement. Consecutive PI were prospectively recorded and classified in the ADKADokuPIK[®] database from 10/08–7/09. PI's clinical relevance was categorized using the NCC MERP Index out of clinical pharmacist's perspective. Moreover monetary effects on drug costs or reimbursement were estimated and stratified according intervention category groups. Effects on process costs were not considered.

Results: Within this time frame 274 PI were documented, among them 60 medication errors: $n = 53$ NCC MERP categories A-C (no harm), $n = 5$ category D (no harm but monitoring required) and $n = 2$ categories E/F (temporary harm, intervention or hospitalization required). Higher severity grades were not recorded. The PI acceptance by physicians or nurses was 90.7%. With €23.603 quantifiable return on investment (ROI) the project-related staff costs were almost completely financed by reduced drug costs or increased reimbursement rates. Measures to optimize DRG-rates were particularly efficient.

Conclusions: The benefit of PI during gynecological ward rounds could be demonstrated out of clinic and quality management perspective. Due to the provided evidence for ROI the project was extended for another year. Further research should identify and quantify the value of improved patient outcomes.

PO-Onko 02.36**Observational data of 274 women treated with loop electrosurgical excision procedure (LEEP) for cervical intraepithelial neoplasia (CIN)**

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Objective: Conisation for suspected high grade CIN is often performed based solely on abnormal cervical cytology results. LEEP is a common surgical procedure in this context. This study was designed to analyze concordance rates of cytology, colposcopic examination including targeted cervical biopsy and postoperative histology as well as to assess the efficacy of LEEP.

Materials and methods: Two-hundred and seventy-four consecutive patients treated with LEEP for CIN at our center were analyzed. All patients underwent Pap-smear, HPV-DNA testing, colposcopy and, if indicated, targeted cervical biopsy/endocervical curettage before and 3–6 months after surgery.

Results: Median age of the patients was 34 years. Preoperative HPV testing was positive for high risk types in 77.9%. All patients underwent a LEEP without further ablative procedures. Complete excision of the lesion could be achieved in 84.3%; in 13.6% pathological findings were ambiguous and in 2.1% the lesion was clearly not excised entirely. Overall complication rate was 5.4% (mainly postoperative bleedings and pain). Of the patients with initial recurrent Pap III/IV or Pap IVa 74.1% had a CIN II/III lesion in postoperative histology. Adding colposcopy to preoperative assessment increased concordance with postoperative histology to 88.2%, with additional preoperative targeted biopsy the concordance rate was 95.0%. Median follow-up was 50 months; 9 patients (3.4%) had persistent disease and 4 (1.5%) developed disease recurrence and underwent re-conisation. HPV testing at 3–6 months after surgery was negative in 78.5%; 2 of the patients developing disease recurrence had a persistent HPV infection after LEEP.

Conclusions: Assessment of cervical lesions with colposcopy and targeted biopsy is a highly accurate method and can potentially help to avoid overtreatment. Surgical treatment of high grade CIN with LEEP is a safe procedure with low recurrence rates, resulting in a clearance of cervical HPV infection in the majority of cases.

PO-Onko 02.37**Detection of breast cancer cells in lymph node tissue by quantitative alu real-time PCR**

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Objective: To establish the detection of metastatic breast cancer cells in lymph nodes.

Materials and methods: MDA-MB-435 cells were injected into the second mammary fat pad of female nude mice. Genomic DNA was isolated from axillary lymph nodes and subjected to quantitative alu real-time PCR by using specific primers. 18S rRNA was used as an internal reference. PCRs were carried out using the ABI PRISM™

7700 Sequence Detector (Applied Biosystems). Serial dilution steps of genomic DNA obtained from human MDA-MB-435 cells in genomic DNA obtained from mouse lymph node tissue served to construct the calibration curves. The amount of the alu PCR signal was correlated to the amount of amplified genomic DNA, by using the internal control 18S rRNA against which the alu signal was normalized.

Results: Preliminary data show that the correlation coefficient for all measurements demonstrated an excellent relationship between the alu signal and the relative amount of human DNA with a detection limit of 0.001% human DNA in murine DNA. Preliminary results of alu PCR indicated the presence of human DNA in lymph node tissue of tumor bearing mice.

Conclusions: Quantitative real-time alu PCR may allow the detection of metastatic cancer cells in lymph node tissue on a single cell level.

PO-Onko 02.38**Adoption of a critical incidence reporting system (CIRS) in routine outpatient care of patients receiving chemotherapy**

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Objective: In the day case chemotherapy an efficient and transparent documentation of chemotherapy-associated events is very important to ensure an optimal risk management and secure treatment.

Materials and methods: We reviewed all adverse events (hospitalisation, dose reduction, interruption or preterm finish of chemotherapy cycles and blood transfusions) in 2008 and 2009. Potential impact on management of cancer patients was analyzed.

Results: A total of approximately 9000 chemotherapy application were recorded in 2008/09. 471 adverse events were documented (201 interruptions of therapy, 131 hospitalisations, 77 preterm finishes, 13 dose-reductions and 49 blood transfusions). The most frequent causes were leucopenia, infections, anaemia and impairment of general state of health without specific diagnosis. Analyses of adverse events had serious impact on routine management of cancer patients and content of pre-treatment counselling including the following examples. (1) After occurrence of multiple pulmonary embolisms of patients with ovarian cancer (6 patients in 2 years) the threshold for prophylactic heparinization was subsequently lowered. (2) Due to insufficient sun protection, exanthema was observed in a high fraction of patients receiving anti-EGFR directed therapies and led to modifications of pre-treatment counselling.

Conclusions: The CIR-system implements a feed back loop which allows identifying and responding to unknown, neglected and underreported events caused by modern oncologic therapies.

PO-Onko 02.39**Caesarean section and simultaneous total mesometrial resection (TMMR) in pregnancy related cervical cancer**

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Objective: Pregnancy-related cervical cancer is a rare event and has an incidence of 1:1000–1:2000 (CIN3/CIS 1:750) pregnancies. The average maternal age is rising steadily since the last 3 decades and along with that, malignancies during pregnancy are more frequent.

The following case report describes the surgical treatment of a 29 year old pregnant woman diagnosed of a poor differentiated invasive cervical cancer by conization in the 27th week of gestational age. The surgical treatment was performed at the 31st week of gestation age after induction of fetal lung maturity.

Materials and methods: After consensus on the optimal time of delivery a caesarean section with simultaneous longitudinal laparotomy and a total mesometrial resection (TMMR) according to Höckel including pelvic lymphadenectomy and bilateral salpingectomy was performed. TMMR based on developmentally defined topographic anatomy with nerve-sparing contrary to the classical Wertheim-Meigs-surgery.

Results: The uterus showed no further manifestations of the cervical cancer, the parametria and pelvic lymph nodes and the pelvic wall biopsies being tumor-free. The surgery was very bloodless, the structures were defined clearly due to the bulked tissue. TNM: pT1b1, pN0 (0/51), L1, V0, G3, R0, M0. The preterm baby developed well and the mother had no postoperative complications. No adjuvant treatment is necessary.

Conclusions: There are no recognised guidelines for treatment of pregnancy-related cervical cancer. Thus it must be based on recommendations for non-pregnant women. The therapy has to be adjusted individually considering interest of the mother as well as the unborn. The therapy depends on the gestational age, stage of the cervical cancer, ethnic and individual wishes and psychological aspects. In general, the prognosis of cervical cancer is not worse for pregnant women compared with non pregnant women and the surgery is very bloodless.

PO-Onko 02.40

Differential diagnosis in symptomatic adnexal masses

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Objective: Symptomatic adnexal masses (SAMs) are among the most frequent causes for emergency consultation in gynecology. The underlying causes include a variety of pathologies such as benign cysts, extra-uterine gravity, infectious processes or malign tumors. The aim of our study was to identify the most common diagnosis related to SAM in different age groups and their associated clinical findings.

Materials and methods: We evaluated all patients, treated at our institution from 2004 to 2008 for SAM by laparoscopic exploration. 1302 women were included (870 pre-menopausal; 432 postmenopausal). For each case we compared the final histopathological diagnosis with the pre-operative work-up including patient's history and clinical examination upon presentation. The obtained results were compared with data from published collectives.

Results: 55% of all encountered SAM were found to be uncomplicated benign cysts. Endometriotic cysts (8.3%) and dermoid cysts (7.8%) were the following most common causes. 7.4% of all cases were related to internal genital infections, a value which was notably lower than data, published by other authors. In 3.2% of all cases, the laparoscopy revealed a malignant neoplasia, which was a surprisingly high value compared to data in previous studies. In postmenopausal patients we observed an increased frequency of malignant tumors and infectious pathologies.

Conclusions: In this large study collective we further evaluated the character and prevalence of underlying pathologies in SAMs. Compared to previous studies, considerable differences were found regarding the frequency of malignant tumors as well as internal genital infections.

PO-Onko 02.41

Thyroid receptor alpha 1 expression in normal controls, misoprostol treated and abortion placental tissue

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Objective: Thyroid function influences the outcome of human pregnancy as a sufficient availability of thyroid hormones is required for fetal development. Thyroid hormone receptors are expressed in placental tissue from early pregnancy. The aim of our study was to investigate the expression of TR α 1 in placentas of normal and miscarried pregnancies and in placentas treated with the progesterone receptor antagonist Misoprostol.

Materials and methods: Placental tissue was obtained from 45 patients ($n = 15$ miscarriage, $n = 15$ normal pregnancy without Misoprostol treatment, $n = 15$ normal pregnancy with Misoprostol: 200 mg oral 24 h before induced abortion). Paraffin sections of the placentas were stained with specific antibodies against TR α 1 followed by a semiquantitative evaluation and statistical analysis.

Results: TR α 1 is expressed in cytotrophoblast cells to a higher degree than in syncytiotrophoblast cells both in miscarried and in normal placentas beside of Misoprostol treatment ($p < 0.04$). In addition, TR α 1 is upregulated in miscarried placentas as compared to normal placentas ($p = 0.001$ in syncytiotrophoblast cells). With regard to Misoprostol application before curettage, a downregulation of TR α 1 in treated placentas as compared to untreated placentas was observed ($p = 0.007$ in cytotrophoblast cells).

Conclusions: Differences in the expression of TR α 1 were present in normal and disturbed pregnancies. The higher expression of TR α 1 in cytotrophoblasts might indicate the central role of thyroid hormones during proliferation. Upregulation of TR α 1 in miscarried placentas is accompanied with upregulation of RXR and PPAR γ/δ . This could possibly be linked to an insufficient supply of the placenta with ligands of this nuclear hormone receptor family. Downregulation of TR α 1 after Misoprostol treatment indicates an interaction between the progesterone receptor antagonist and the expression of thyroid hormone receptors. Further in vitro studies focusing on the possible crosstalk of these hormonal receptors are part of ongoing research.

PO-Onko 02.42

ACT-FASTER: an epidemiological prospective cohort study to describe treatment patterns of Fulvestrant and exemestane in postmenopausal patients with advanced HR+ breast cancer under real-life conditions in Germany

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Objective: Fulvestrant is an estrogen receptor antagonist with a distinct mode of action for the treatment of hormone receptor-positive (HR+) postmenopausal (PMP) women with advanced breast cancer (ABC) progressing or recurring on an antiestrogen. As a result of the CONFIRM study, fulvestrant was approved in Europe in the 500 mg dose (2 × 250 mg injections days 0, 14, 28, then monthly) in March 2010. CONFIRM included ABC patients on 1st to 2nd line treatment. Another trial, FIRST, explored fulvestrant 500 mg against anastrozole in patients newly diagnosed with ABC. Outcomes research to evaluate the performance of therapeutic interventions in daily practice is becoming increasingly important. ACT-FASTER aims to generate data on fulvestrant 500 mg and exemestane under real-life conditions with a focus on the use of fulvestrant in different treatment lines.

Materials and methods: ACT-FASTER is a prospective non-interventional cohort study sponsored by AstraZeneca that will collect clinical, epidemiological and pharmaco-economic data on PMP patients with HR + ABC on treatment with fulvestrant 500 mg or exemestane under real-life conditions in Germany. Enrolment starts in July 2010. It is planned to include 660 patients at approx. 40 specialised clinics and 100 office-based gynaecologists or oncologists. The study has two co-primary objectives: For patients receiving fulvestrant, to compare the effectiveness in terms of time to progression as a function of line of treatment (1st- vs. 2nd- vs. 3rd-line), and for all patients, to collect and explore real-life data on epidemiology and management of all patients treated with fulvestrant or exemestane, including tumour characteristics, data on co-morbidities and treatments received. Additional effectiveness data, pharmaco-economic data (resource use, etc) and information on health-related quality of life will also be explored for both fulvestrant and exemestane.

Conclusions: ACT-FASTER aims to collect real-life data on the endocrine treatment of PMP patients with HR + ABC with a focus on the effectiveness of the newly approved dose of fulvestrant 500 mg. Additionally, data on patient management, quality of life and pharmaco-economics will be generated. As such, ACT-FASTER constitutes an important project of outcomes research in this patient setting.

PO-Onko 02.43

Efficacy and safety of vaginal application of estriol (Gynoflor®) on atrophic vaginitis in postmenopausal breast cancer patients treated with aromatase inhibitors

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Objective: More than 50% of postmenopausal women suffer from vaginal dryness, atrophic vaginitis or urogenital disorders. The most common symptoms like burning, pruritus or dyspareunia are leading to a decreased quality of life. The median age of patients with breast cancer is 64 years. Most of them are postmenopausal. The majority of tumor cells express estrogen and progesterone receptors. The current treatment strategy in hormone receptor positive breast cancer is the use of an aromatase inhibitor (AI) which potentially induce or enhance the symptoms of an atrophic vaginitis. To reduce atrophic vaginitis intravaginal estradiol is a safe alternative to systemic estrogen therapy in a healthy population. However in postmenopausal patients with breast cancer on AI therapy a possible benefit of local

estriol therapy is poorly understood. We therefore evaluate the local and systemic effect of vaginal application of 0.03 mg estriol (Gynoflor®) on atrophic vaginitis and serum estrogen concentrations in postmenopausal breast cancer patients treated with an nonsteroidal AI.

Materials and methods: In this bicentric, blinded trial study serum of postmenopausal patients with estrogen receptor positive breast cancer on non steroidal AI therapy is analyzed concerning clinical symptoms of vaginal atrophy, vaginal dryness and dyspareunia. We analyze serum concentrations of estrogen, estrogen metabolites, FSH, LH, testosterone, androstendion, inhibin, SHBG, DHEAS at Day 0 and 28 (t = -0.5, 0.5, 1, 2, 4, 6, 8, 24 h). The initial therapy concludes the daily application of one Gynoflor® vaginal tablet (0.03 mg estriol) over a period of 28 days (n = 24). In the following eight weeks three tablets per week are given. Further blood samples are drawn at, week 8 and week 12.

Conclusions: The goal of this study is to analyse the potential systemic and local effect of local applied estriol (Gynoflor®) in breast cancer patients on AI treatment.

PO-Onko 02.44

Thyroid hormone receptor (TR)alpha- and (TR)beta-expression in breast cancer

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Objective: Until now the relationship between thyroid status and breast cancer is controversial. Hormone dependency of the mammary gland and the similarity of TR with ER and PR lead to remark of TR as marker in breast cancer patients.

Materials and methods: In this trial, 181 patients with anamnestic sporadic breast cancer were randomized after written form of consent. The expression of TRalpha1/2 and TRbeta1/2 was examined by immunohistochemical staining. Staining reaction was performed with the ABC method and staining intensities were analysed using the IRS-score.

Results: Both TRs were detected in the nuclei of the breast tumours. Expression of TRalpha1/2 was detected about 57% of these patients by median IRS score of 1. The TRbeta1/2 expression showed positive results in almost 60% of the breast cancer patients. Significant correlations of the expression of TRalpha or TRbeta and clinical parameters were found.

Conclusions: Our results reveal specific alterations of the expression of TRalpha and significant low values of TRbeta in this cohort of breast cancer patients. The expression of TR seems to be an important point in the pathophysiology of malignant breast tumours.

PO-Onko 02.45

Definition of resection margins in breast cancer by 2-D ultrasound

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Objective: The aim of the study was to improve the operation for breast cancer and to reduce the need for second operations because of

insufficient resection margins. Close resection margins in breast cancer operation is the most important risk factor for local recurrence. The prediction of resection margins is important in breast cancer operations. The results of pathological fresh frozen diagnostic for resection margins are not exact enough, and the results of the final histological diagnosis are too late. The study was done to analyse the efficiency of intraoperative ultrasound to define resection margins.

Materials and methods: 88 specimens of 81 patients with sonographically detectable tumors were examined with ultrasound before there being sent to the pathologic examination. 507 measurements had been done and correlated with the histological measurement of the resection margins. There was no selection based on the histological tumor type.

Results: In the evaluation of the correlation between the sonographical and histological measurement we could show, that a resection margin of 5 mm by ultrasound correlates to a histological margin of 1 mm in 95% of the cases. The intraoperative ultrasound seems to be a method that is able to give fast and reliable further information to the surgeon about resection margins. This information can help to decide about the necessity to remove additional margins.

PO-Onko 02.46

In vitro angiogenesis testing as a tool for treatment individualisation in patients with cervical cancer

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Objective: Angiogenesis is an important prerequisite of development and differentiation of organs and tissues, and it plays a key role in tumour growth and metastasis. Angiogenesis factor expression has been implied as a marker for tumour malignity, and it may help to identify patients with a benefit from emerging anti-angiogenetic treatment modalities. The present study examines the relationship between angiogenesis factor expression and clinical tumour criteria.

Materials and methods: 81 patients with cervical cancer who underwent follow-up examinations between October 2002 and June 2005 were enrolled, and serum samples were examined for VEGF, bFGF, endostatin and VEGF-R1 by means of an ELISA. Based on an endothelial-cell proliferation assay, an angiogenesis score was calculated.

Results: Higher endostatin and VEGF expressions indicated advanced disease, and VEGF allowed for a reliable distinction between patients with non-invasive and recurrent disease, respectively. There were no correlations between the angiogenesis score and clinical criteria or individual angiogenesis factors.

Conclusions: The utility of angiogenesis factor notwithstanding, the angiogenesis score assessment's value for the identification of patients who will benefit from anti-angiogenetic treatment is arguable. In contrast, VEGF plasma concentration may be a promising marker for cervical cancer.

PO-Onko 02.47

Visualization of cervical intraepithelial neoplasia (CIN) by optical coherence tomography (OCT)

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Objective: Optical coherence tomography (OCT) is an optical high-resolution imaging modality that permits characterization of micro-architectural features up to 2 mm in depth. The purpose of this study was to evaluate the accuracy and reproducibility of OCT in the characterization of cervical intraepithelial neoplasia (CIN).

Materials and methods: Colposcopy-guided OCT images were taken from unsuspected and suspicious areas in women with suspected CIN. Each woman then underwent directed biopsies. Based on a 6-grade classification (normal, inflammation, CIN1, CIN2, CIN3, squamous carcinoma) all OCT images were independently evaluated by two investigators blinded for the final histological diagnosis and later compared to the corresponding histology. Sensitivity and specificity of OCT in detecting CIN were determined. To assess the interobserver agreement, unweighted Cohen's kappa was calculated from the ratings of each investigator for each OCT image seen.

Results: A total of 189 OCT images were compared with their corresponding histology in 106 women undergoing colposcopy for suspected CIN. Sensitivity calculated for both investigators with the threshold at CIN1 was 98 and 95% respectively. The specificity was 39 and 41% respectively. Cohen's kappa calculated to 0.70 (0.95 CI: 0.55–0.85) showing substantial interobserver agreement.

Conclusions: OCT is a rapid, easy-to-use modality that provides microarchitectural information of the cervical epithelium. Further refinement of this technology will lead to OCT systems with higher resolution and improved image acquisition rates at or near video quality. Therefore, OCT has the potential to become a valuable investigative tool in the management of pre-invasive and invasive cancer of the cervix.

PO-Onko 02.48

Invasive cervical cancer during pregnancy: laparoscopic nodal evaluation and neoadjuvant chemotherapy with cisplatin before oncologic treatment delay

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Objective: Cervical cancer is the most frequently encountered malignancy during pregnancy. The decision for termination or delay of pregnancy is always a challenge. The presence of nodal metastasis is the most important negative predictive factor and its assessment represents a crucial parameter to decide if pregnancy can safely continue. Cisplatin is recommended to prevent cancer progression during waiting time for fetal maturity but knowledge about passage of platinum through placenta is very limited.

Materials and methods: 18 patients who underwent laparoscopic pelvic lymphadenectomy during pregnancy at Charité–University Berlin and Friedrich-Schiller-University Jena between 1999 and 2009 were analyzed retrospectively. Among these six consecutive patients with cervical cancer diagnosed in second trimester underwent neoadjuvant chemotherapy because of local residual tumor, high risk situation or advanced disease. After 3 cycles (one patient 2) of cisplatin chemotherapy caesarean section together with radical (1× simple) hysterectomy was performed not less than 32 week of gestation. At the time of delivery synchronous samples from maternal blood, umbilicalcord blood and amnion fluid were taken and analysed for cisplatin concentration.

Results: All of the laparoscopic procedures were successful completed; there was no mortality, morbidity, or conversion to laparotomy. Additionally, there was no complication for either mother or child related to the general anesthesia. The mean number of lymph nodes removed was 17 (6–46). Lymph nodes were positive in 16% of the cases (3/18) and these patients received immediate cancer treatment. Cisplatin concentration in the umbilical cord and amnion fluid was 31–60% and 13–43% of the maternal blood, respectively.

Conclusions: Laparoscopic pelvic lymphadenectomy during pregnancy is feasible and safe without complications neither to mothers nor to infants. The knowledge of relevant lower cisplatin concentrations in umbilical cord and amniotic fluid overcomes prejudices and concerns about neoadjuvant chemotherapy to delay second trimester pregnancy in patients with cervical cancer.

PO-Onko 02.49

Role of BNIP3 in tumor cell dissociation and peritumoral stromal remodelling in carcinomas of the uterine cervix

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Objective: Pattern of invasion (PI; representing different grades of tumor cell dissociation) and peritumoral stromal remodelling, characterised morphologically by different grades of desmoplastic stromal reaction (DSR), are involved in infiltrative tumor growth. Apoptotic pathways, including BNIP3 a proapoptotic member of the bcl-2 family plays important roles in tumor cell invasion.

Materials and methods: Fifty cases of squamous cell carcinoma of the uterine cervix (CX) were evaluated immunohistochemically for BNIP3. Staining for cancer cells was counted as percentage of positive cells and by performing an immunoreactive score (IRS = staining intensity (0–3) × calculated percentage of positive cells (1–4). Staining for peritumoral stromal cells was counted as positive or negative, regardless of staining intensity and percentage of positive stromal cells. Staining results of tumor and stromal cells were correlated to PI (finger-like and spray-like) and DSR (counted as none/weak and moderate/strong).

Results: CX with spray-like PI represented a higher percentage of positive stained tumor cells than those with finger-like PI (50.6 + 33.0% versus 36.3 + 27.2%; $p = 0.98$) and higher IRS. CX with strong and moderate DSR showed more BNIP3-positive tumor cells compared to cases with none and weak DSR (53.2 + 29.0% versus 36.2 + 28.6%; $p = 0.078$), a higher IRS was also observed. The most CX represented BNIP3-staining of the peritumoral stromal cells (76%), without any correlation to PI or DSR or staining pattern of cancer cells.

Conclusions: There might be a putative role of BNIP3 in tumor cell dissociation (i.e. pattern of invasion) and peritumoral stromal

remodelling in CX. Further studies are required to get an insight in the mechanisms behind these features.

PO-Onko 02.50

Photodynamic therapy of cervical intraepithelial neoplasia using hexylaminolevulinate and methylaminolevulinate

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Objective: Cancer of the human cervix is the second most common female cancer with about 500.000 cases per year and develops through precancerous lesions called cervical intraepithelial neoplasia (CIN). Established ablative treatment methods like conisation procedures may cause substantial complications in following pregnancies including premature delivery and the birth of low-weight babies. Photodynamic therapy (PDT) of CIN using modern esters of 5-aminolevulinic acid (5-ALA) like hexylaminolevulinate (HAL) or methylaminolevulinate (MAL) represents a promising alternative.

Materials and methods: Between 2006 and 2010, over 150 PDT cycles were carried out in our institution in patients with CIN 1–3 within clinical studies. After local application of a photosensitizing agent, dysplastic cells become susceptible for light of a defined wave length, which is delivered to the cervix using a PDT laser and a special cylindrical light catheter. This procedure is easily supported by the patients and can be performed on an outpatient basis. We report summarized outcome data from all present clinical studies.

Results: PDT for CIN 1–3 achieved response rates of about 70% six months after PDT using HAL or MAL as the photosensitizer. Furthermore, colposcopic, histological and immunohistological data show no suspicion of sustained damage to the cervical tissue like scarring or inflammation which could lead to cervical insufficiency.

Conclusions: PDT seems to be a non-invasive, repeatable procedure for CIN and cervical HPV infection with minimal side effects and preservation of cervical function which can be easily performed on outpatient basis.

PO-Onko 02.51

Evaluation of a new multiplex real-time PCR assay for the detection of high risk human papilloma viruses in a clinical routine setting: an interim report

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Objective: Assessing analytical and clinical performance of the new Abbott RealTime High Risk HPV test in a routine setting by comparison to digene hc2 (Qiagen).

Materials and methods: 311 routine cervical smears were collected in liquid based cytology medium (PreservCyt LBC) by two centres and tested for HR-HPV. The Abbott test detects 14 HR-HPV types and simultaneously identifies HPV16 and HPV18, while hc2 detects 13 HR-HPV types without further differentiation. Discordant specimens

were genotyped (Roche Linear Array; LA) and analytical performance was assessed based on HPV types targeted by both tests. Clinical performance was evaluated based on cytological (ThinPrep) and histological diagnosis, if available.

Results: The Abbott test identified HR-HPV in 126 cases, while 129 samples tested positive with hc2. Concordant results for 288 specimens and good overall agreement (92.6%; $k: 0.85$) were observed. Discordant specimens (24 of 25) were further examined by LA. HR-HPV overall-detection rate (Abbott: 99.21%; hc2: 93.65%) of both assays were comparable. Analytical specificity (Abbott: 99.46%; hc2: 92.93%) and accuracy (Abbott 99.04%; hc2: 92.93%) were significantly higher with the Abbott test. 14 cases with negative or low grade histology tested positive only with hc2 did not contain targeted HR-HPV types. Both assays demonstrated correlation of HR-HPV detection with high grade cytological (Pap IIIID+) and histological (CIN2+) categories. Mixed infections (7%) were mainly HPV16/Other HR. HPV16 was identified in 16% (mainly PapIIIID+) and HPV18 in 3.2% (PapIIIID+) of the population.

Conclusions: Preliminary study results demonstrate comparable analytical sensitivity of Abbott RealTime HR HPV and hc2, while analytical specificity and typing accuracy of the new assay are clearly superior. Identification the two HPV genotypes with the highest oncogenic potential in combination with the ability to detect infections of clinical relevance will enable the test to contribute to improving cervical cancer prevention.

PO-Onko 02.52

Pregnancy after laparoscopic lymphadenectomy and neoadjuvant chemotherapy followed by radical vaginal trachelectomy in bulky stage IB1 cervical cancer

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Objective: Radical vaginal trachelectomy (RVT) is an oncologically safe therapy option in patients with early stage cervical cancer and wish for pregnancy but it is limited to women with lesions measuring less than 2 cm. Neoadjuvant chemotherapy can be applied to down-stage the tumour so that patients can become eligible for RVT. We report a case of pregnancy after chemotherapy and RVT.

Materials and methods: A 27 year old G₀ patient was diagnosed with adenosquamous cervical cancer stage IB1 (4 cm in diameter) in December 2005 and persisted on fertility-sparing therapy. First, the laparoscopic pelvic and paraaortic lymphadenectomy was performed and showed no metastasis in the lymph nodes. The patient received chemotherapy with Paclitaxel 200 mg/m² and Cisplatin 100 mg/m². Goserelin was given for fertility protection. The cycle was repeated after 3 weeks with Cisplatin reduced to 50 mg/m² because of creatinine-increase. MRI followed showing tumour reduction to 8 mm. RVT was performed in April 2006

Results: Except for the creatinine-increase, the chemotherapy was well tolerated. After RVT, only focal carcinoma of 2 mm in diameter was found in the final specimen. The patient recovered and resumed a normal menstrual pattern 6 weeks after surgery. In December 2008 she conceived. She reported no problems during pregnancy except for gestational insulin-dependent diabetes. The cervix measured 25 mm during pregnancy. The patient gave birth to a boy in August 2009 by caesarean section after 38 + 0 gestational weeks. The newborn (weight 3500 g, length 52 cm, APGAR-scores 5/8/10, pH-value 7.28) was monitored on a neonatal ward for 24 h. The patient is followed up regularly and there is no evidence for recurrence.

Conclusions: Neoadjuvant chemotherapy followed by a fertility-sparing surgery may become a valuable option for women with bulky stage cervical cancer who wish to preserve their fertility potential.

PO-Onko 02.53

Chief medical clinic manager: an innovative job description for increase of quality of care and physicians' economic freedom of action

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Objective: Leadership structures in German hospitals are adjusting parallel to DRG-induced economic reorientation of the health care system. Due to limited resources physicians have to take increasing responsibility not only for the clinical core process of patient care but also for the integration of financial, administrative and organizational aspects.

Materials and methods: A Chief Medical Clinic Manager (CMCM) is a new job description and an innovative approach to combine medical competence and business economics embedded at the operational level of care. Ideal qualification is a medical specialist in the clinic's field with practical experience in patient care and leadership as well as in hospital economics and quality control. A CMCM is placed as staff position at a superior level in the clinic, with authorizing competence for the entire physician team and takes part in all daily physicians' meetings.

Results: Main tasks are cost transparency within the clinic, identification and elimination of illegitimate cost drivers, organizational development by structured processes especially focusing on quality of care and guideline-based treatment as well as financial and strategic controlling of all business aspects. A CMCM improves horizontal communication within the department and hospital, induces change management and financial adjustment of care to reimbursement without reducing standard of care. In cooperation with the director of the clinic, a CMCM develops a vision for clinic development, an investment strategy and a business plan. The success parameters are positive clinic's operative results, cost covering care, increased investment rate, employees' satisfaction and implementation of innovations in research and therapy.

Conclusions: A CMCM assures quality of care and increases financial and organizational freedom of action at clinic level in a non-profit public health care system. This concept has been developed over several years and has been proven to be financially successful. The financial return of investment for the clinic is 3–10-fold the income of a CMCM.

PO-Onko 02.54

Value of ultrasound in preoperative local staging in early breast cancer

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Objective: The purpose of this study was to determine the precision of breast ultrasound in the measurement of breast lesions compared to the histological measurement. A number of other dependent variables were also analysed.

Materials and methods: 460 patients with 445 malign lesions were examined using breast ultrasound and the lesions were measured and set in comparison to the histological measured size. The data was further analyzed according to histology, tumor stage, age, grading and therapy.

Results: Metrical comparison showed good correlation between sonography and the pathological measured size of breast lesions, especially in tumor stage T1 and T2 and within ductal invasive carcinomas. Higher tumor stages leads to imprecise measurements and the histological type of lobular invasive carcinoma also shows imprecise measurements. Age and grading do not influence precision of measurement.

Conclusions: Breast ultrasound allows precise measurement of breast lesions especially in lower tumor stages. The larger the tumor stage the more imprecise the measurement gets. Multivariate analysis shows no cross impact between tumor stage and histological type concerning quality of measurement.

PO-Onko 02.55

Peritoneal enterobiasis causing endometriosis like symptoms

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Objective: The Enterobiasis is the most common parasitic disease of the temperate zones and infects the human intestinal tract. In rare cases extraintestinal infections with *Enterobius vermicularis* may occur and can affect the female genital tract and the peritoneal cavity. In most cases the infection is asymptomatic, but there are also cases described in which the peritoneal Enterobiasis can cause abdominal pain.

Materials and methods: Case report and review of the pertinent literature.

Results: A 32 year old patient was admitted with cyclical lower abdominal pain. With suspected endometriosis a laparoscopy for diagnostic autofluorescence (DAFE) was performed. At surgery extensive peritoneal deposits were seen. Macroscopically these deposits were not typical for endometriosis. The histological examination showed granuloma caused by *Enterobius vermicularis* eggs. The patient was treated with mebendazole over two months. After completion of treatment the patient was asymptomatic. At the Second Look Laparoscopy no more peritoneal changes were detected.

Conclusions: *Enterobius vermicularis* may cause symptoms similar to endometriosis. In cases with reasonable suspicion it should therefore be considered in the differential diagnosis.

PO-Onko 02.56

Cost of inpatient treatment for endometriosis in Germany: an analysis based on the G-DRG-coding

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Objective: Endometriosis is a chronic disease with an enormous economic burden placed on the society. We tried to estimate the financial burden of the inpatient treatment.

Materials and methods: The design of the study is a descriptive analysis of data from national inpatient database taken from all hospital admissions in Germany. The design of the study is a retrospective one. We identified the number and type of hospital admission involving surgical interventions for endometriosis. We estimated the costs of these hospitalisations to payers in Germany using the DRG rates.

Results: There was a total number of 20,835 inpatient patients in 2006. The average cost per patient was estimated to be 3,056.21 Euro. The total inpatient cost in 2006 was estimated to be 40,708,716.26 Euro. The most frequent procedure in the treatment of an endometriosis was a hysterectomy. The estimated mean length of the stay is 4.96 days. Further on is the diagnosis of the endometriosis of the ovaries the most frequent one. The most expensive DRGs were N07Z (other interventions on uterus and adnexes).

Conclusions: We present a calculations of real costs based on official national databases, our results can be used as a proxy of costs for inpatient treatment of endometriosis. This may allow the responsible persons to improve the allocation of resources and to apply a more sustained management of expenses.

PO-Onko 02.57

Functional analysis of CRYAB, a putative tumor suppressor gene in ovarian cancer

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Objective: Improving the molecular understanding of ovarian cancer development and progression could contribute to novel strategies for the management of this malignancy. Loss of heterozygosity (LOH) is a hint for the inactivation of tumor suppressor genes (TSGs) located in deleted regions. In breast and ovarian cancer frequent LOH has been demonstrated at the chromosomal region 11q23-q25.

Materials and methods: Gene expression of candidate gene CRYAB was performed with cancer profiling arrays and RT-PCR. Mutation analysis was done by DHPLC. For functional characterization CRYAB was subcloned in a retroviral vector and transfected in ovarian carcinoma cell lines and correlation of CRYAB expression and chemoresistance was analysed

Results: CRYAB (alpha-Crystallin-B) was downregulated in 56% of ovarian carcinomas (OC), however, 19% of OC displayed more than 2-fold CRYAB overexpression compared to normal tissue. No inactivating mutations could be identified in the coding region. We could demonstrate 8-fold CRYAB overexpression in ADR-resistant compared to ADR sensitive SKOV-3 cells, however CRYAB expression was not induced by ADR or Cisplatin within 96 h. CRYAB expression in transfected SKOV-3 and HEY cells (SKOV-3-/HEY/CRYAB S11-IEG3) was increased 8-fold and over 10-fold, respectively, but no increase in resistance against ADR, Cisplatin, Etoposid could be observed in CRYAB transfected cells. CRYAB expression will be silenced in ADR resistant SKOV-3 by siRNA experiments to confirm that CRYAB overexpression is rather an effect than the cause of chemoresistance in this OC cells. Correlation of CRYAB expression and chemoresistance is further analysed by immunohistochemistry in tumor tissues of chemoresistant compared to chemosensitive ovarian carcinomas.

Conclusions: Frequent LOH on chromosome 11q23 and CRYAB downregulation in ovarian cancer identify CRYAB as a putative tumor suppressor gene in OC. Chemoresistance is correlated with but not caused by CRYAB overexpression.

PO-Onko 02.58**Intestinal malrotation in adults as rare differential diagnosis of chronic (lower) abdominal pain: a case report**

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Objective: Intestinal malrotation is a rare congenital disease. In most cases first symptoms present during childhood with acute or chronic, partial or total intestinal obstruction, complicated by volvulus or intestinal necrosis. The diagnosis of malrotation in adults is not often taken into consideration leading to a time lack to its recognition. We present a case where symptoms of malrotation were misdiagnosed as endometriosis.

Materials and methods: A 36 year old nulliparous woman came to our outpatient clinic suffering from chronic recurrent lower abdominal pain that was independent of menstrual cycle. She had a known endometriosis, so that external colleagues proposed hysterectomy. Until then she has had five laparoscopies, where signs of endometriosis and a mobile blind intestine have been described. In our institution clinical examination, blood count and Ca 12-5 as well as cystoscopy and colonoscopy were normal so that we proposed another laparoscopic examination to evaluate the extent of endometriosis. During this operation no signs of endometriosis could be verified but an abnormal position of the bowel was obvious. The whole small intestine appeared to lie in the right part of the abdomen, the blind intestine was dislocated upwards in the middle right part of the abdomen and the mesentery was dislocated to the right. A contrast enhanced MRI arranged after the operation confirmed suspicion of intestinal malrotation: the small intestine lying on the right side of the abdomen and the colon on the left side. Hysterectomy was not performed.

Conclusions: This case demonstrates that malrotation in adults is a rare but clinically relevant entity, which has to be kept in mind as differential diagnosis to avoid unnecessary examinations or operations.

PO-Onko 02.59**Müllerian cysts of the vagina in a 15 year old: a case report**

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Objective: Müllerian cysts are an ontogenetic disorder deriving from the Müllerian duct (paramesonephric duct), the embryologic structure-forming the uterus, the tubes and the upper part of the vagina. As Müllerian cysts are a rare diagnosis, we want to present a case report concerning a 15 year old female patient with a large tumor in the lower abdomen, sonographically detected during a routine gynecological examination.

Materials and methods: All findings of the patient were collected, like medical history, lab values, MR-images, operation reports and images. **Results:** The 15 year old girl was admitted to hospital after routine vaginal ultrasound had showed an about 9 cm large polycystic tumor in the pelvic area, suspiciously from an ovarian origin. But a neuronal origin could not be excluded. MR-imaging was done without any additional findings. The patient had no signs or symptoms, especially no abdominal or rectal pain and no bleeding abnormalities. Values for Estrogen and CA 125 were normal. Beside an oral hormonal contraceptive, she did not take any drugs. Laparoscopy was performed

and a large retroperitoneal tumor 9 cm in diameter was found. It was not only attached to parametrial tissue next to the vagina and the rectum but also to the muscles of the pelvic floor. For reaching the tumor, the ligamentum rotundum had to be mobilised. The polycystic tumor had a very thick capsule containing a yellowish sticky fluid. The tumor could be totally extirpated. Histopathologically, cysts of the vaginal wall deriving from the Müllerian duct with typical squamous epithelium but without malignancy were diagnosed. The patient recovered fast from surgery without any complications.

Conclusions: Müllerian cysts of the vagina are a rare disease which is not easy to diagnose. As literature supports, laparoscopy is the preferred management, especially in large cysts.

PO-Onko 02.60**Preliminary data on combined treatment with the recombinant N-terminal domain of thrombospondin-2 and radiotherapy on the growth of squamous cell carcinoma xenografts**

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Objective: To study the effect of combined radiation therapy and antiangiogenic treatment with the recombinant N-terminal domain of thrombospondin-2 (N-TSP2-Fc) in human squamous cell carcinoma (SCC) xenografts.

Materials and methods: Human A431 SCC cells were injected intradermally into both flanks of female nude mice. Tumors were irradiated at a dose rate of 1.87 Gy/min by using a RS 225 X-Ray Research System (Gulmay Medical Systems). Irradiation was initiated at day 8 after tumor cell injection. Radiotherapy was applied on 3 consecutive days in doses of 2 Gy. N-TSP2-Fc was administered by daily intraperitoneally injection. N-TSP2-Fc application was either initiated at day 5 and continued until day 10 after tumor cell injection or was given on 15 consecutive days after completion of radiotherapy. **Results:** Preliminary data show that treatment with exogenous N-TSP2-Fc before and during radiotherapy may enhance the antitumor effect of irradiation. The growth delay was longer for A431 SCC given N-TSP2-Fc treatment and irradiation than for tumors given radiotherapy alone. After irradiation, A431 tumors given N-TSP2-Fc treatment grew more slowly during the regrowth period than tumors given radiotherapy alone.

Conclusions: Our preliminary data suggest that antiangiogenic N-TSP2-Fc may enhance the antitumor activity of radiotherapy. Further investigations on possible radiosensitizing effects of N-TSP2-Fc are currently being performed.

PO-Onko 02.61**Hyperemesis gravidarum triggering exacerbation of a maternal diaphragmatic hernia: case report and review of the literature**

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We report on a 30 year old woman presenting with hyperemesis gravidarum and subsequent vomiting at the end of the first trimester. The patient initially presented with nausea and vomiting, without any

abdominal pain. Clinical symptoms increased and the patient complained suddenly severe dyspnoe and intractable cough. Therefore immediately a chest x-ray was performed showing a severe left sided diaphragmatic hiatus hernia with an intra-thoracal stomach, making immediate surgical intervention necessary. Diaphragmatic hernias complicating pregnancy are a rare event, they normally occur in later periods of pregnancy due to the rising intra-abdominal pressure caused by the enlargement of the uterus. Also maternal diaphragmatic hernias during pregnancy are usually associated with minor complaints. However, they can be life threatening, due to mediastinal shift and cardio-respiratory failure. The majority of maternal diaphragmatic hernias complicating pregnancies occur in antenatal period, most of them in the 3rd trimester. More than 90% of maternal diaphragmatic hernias complicating pregnancy are localized on the left side of the diaphragm. Usually maternal diaphragmatic hernias become clinically obvious in advanced stage of pregnancy, in contrast hyperemesis gravidarum is normally occurring in the first trimester and is usually self-limiting. Guiding symptoms for hyperemesis gravidarum are nausea and vomiting, but can also be unspecific symptoms of a maternal diaphragmatic hernia. Therefore especially mild variants of maternal diaphragmatic hernias in early pregnancy can be misdiagnosed as hyperemesis gravidarum. Nevertheless the rising intra-abdominal pain while vomiting obviously can trigger exacerbation of a pre-existing maternal diaphragmatic hernia. We therefore speculate that there is a direct link between hyperemesis gravidarum and the exacerbation of the pre-existing maternal diaphragmatic hernia. Hence a diaphragmatic hernia should always be excluded, if symptoms of hyperemesis are intractable, mediastinal shift with dyspnoe occurs, failure of conservative treatment especially after 20th week of gestation and in very late onset of assumed hyperemesis gravidarum.

PO-Onko 02.62

Prevalence of female sexual dysfunctions in the gynecological practice: preliminary results from the EROS-Gyne study

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Objective: Aim of the EROS-GYNE study (Epidemiology and recognition of female sexual dysfunction in the gynecologist's practice) was to investigate the prevalence rate of hypoactive sexual desire disorder (HSDD) in the German gynecologist's practice.

Materials and methods: The study was conducted in 22 gynecological practices in the South Baden and Rhine-Main region. It comprised a survey which collected data about sexual problems, somatic diseases and depressive symptoms. A subsample of women, who agreed a telephone interview, was interviewed subsequently. This clinically validated interview asked for partnership, sexual satisfaction and complaints. Additionally, we asked for mental disorders. At the end of the interview it was possible to diagnose a sexual disorder. 1644 women were invited by medical staff to fill in the survey prior to their gynecological examination. One question "Altogether, are you satisfied with your sex life?" approved to dichotomize in a high-risk group of dissatisfied women and a low-risk group of satisfied women.

The clinical interview was performed in 70 women out of the high-risk group and 71 women out of the low-risk group.

Results: 1558 women filled in the questionnaire. The clinical telephone interview was performed in 141 patients and yielded a prevalence of 17% for acquired HSDD. Women who fulfilled the criteria for HSDD who were likely to suffer from at least moderate depressivity were excluded from this prevalence estimation. Out of the 17% of women with acquired HSDD, almost all patients reported personal distress due to the sexual problem and three out of four patients reported interpersonal problems.

Conclusions: About every sixth patient in gynecological care suffers from acquired HSDD. The recognition and diagnosis of HSDD is necessary since gynecologists are most often the first professional contact person for women suffering from HSDD. This study was funded by an unrestricted grant of Boehringer Ingelheim Germany.

PO-Onko 02.63

Relevance of the number of metastatic lymph-nodes for disease recurrence in vulvar cancer

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Objective: Nodal involvement is the most important prognostic factor for recurrence and survival in vulvar cancer. Adjuvant radiotherapy is currently recommended for > 2 metastatic nodes by German guidelines. This standard is based on small and heterogeneous patient cohorts. We therefore reanalyzed the impact of the number of affected nodes for disease-recurrence in a large and homogenous cohort.

Materials and methods: 157 consecutive patients with primary squamous cell cancer of the vulva treated at our center were analyzed. All patients underwent primary surgery by triple incision resulting in complete tumor resection.

Results: Median age was 61 years; 44% had FIGO stage I, 20% stage II, 28% stage III, 8% stage IV disease. 49 patients (31%) had lymph-node metastasis; 21 patients had 1, 13 had 2 and 15 had >2 metastatic lymph-nodes. Median follow-up was 23 months; 22 patients (14%) developed disease-recurrence (77% vulva, 18% groins and 5% both). Patients without nodal involvement had a significantly longer disease-free survival than the other groups ($p < 0.001$). However, the number of metastatic lymph-nodes did not result in a significant difference in disease-free survival; even in patients with only 1 or 2 affected nodes disease-free survival rates were significantly lower compared to node-negative patients (88% of node-negative patients were disease-free after 2 years and 59, 69 and 27% of the patients with one, 2 and >2 affected nodes). 31% of the patients received adjuvant radiotherapy. There was no significant difference regarding the number of patients receiving adjuvant radiotherapy between the different nodal positive subgroups.

Conclusions: Lymph-node metastases remain the most important prognostic factor in patients with vulvar cancer. In our cohort, the effect of nodal involvement appeared to be independent from the number of metastatic nodes. Therefore, it might be justified to consider adjuvant radiotherapy to the groins even in patients with only one metastatic node.

PO-Onko 02.64**Overactive bladder: a challenge to gynaecologists***Annett Gauruder-Burmester¹,¹Interdisziplinäres Beckenbodenzentrum, Berlin, Germany

There are a very large number of undetected cases of incontinence patients whose incontinence reduces their quality of life although this could largely be prevented by a preterm intervention. The continence function is one of the first social as well as control functions which is gained within a child's development and is generally considered to be an indicator for other social as well as control functions. Until today different definitions have been used for a complex of symptoms which is called overactive bladder. There is a big prevalence for this complex of symptoms which will increase due to the age development and, therefore, is of great interest. The hyperactive bladder (overactive bladder, OAB) includes the storage symptoms pollakisuria, imperative urge to urinate and nycturia with or without incontinence but these symptoms are always in the absence of local, metabolic, neurological or endocrine pathology. As a consequence the diagnosis "OAB" can initially only be suspected in the presence of those symptoms. It will become definite, however, once the symptoms have been properly diagnosed. Today a physician who works at a practise or hospital does not have enough time to review the large number of therapeutic recommendations of different sources and to verify whether the propagated treatment options are scientifically proven. Every year approx. 2 million articles are published in over 10,000 scientific journals. Especially from this point of view the guidelines regarding diagnostics and therapy of the hyperactive bladder are an integral part of the clinical daily routine.

PO-Onko 02.65**Bulking agents as periurethral injection for the treatment of stress incontinence***Kurt Lobodasch¹,¹DRK Hospital, Gynecology, Chemnitz, Germany

Objective: The prevalence of urinary incontinence leads to social and societal challenges. The bulking therapy is a viable option for patients, with failed alternative operations, anesthetic risks, other contraindications or who reject major surgery.

Materials and methods: Meta-analysis of the clinical studies on bulking agent in terms of their valuation in the current guidelines of the German-speaking medical associations.

Results: The substances bovine-collagen (Contigen[®]), silicone (Macroplastique[®]), hyaluronic-acid[®] (Deflux/Zuidex[®]) and polyacrylamide (Bulkamid[®]) differ substantially in terms of their side effect profile and the re-injection rates. Granulomas, abscesses and calcification occurred in particular in hyaluronic-acid and collagen. Urethral erosions were observed during treatment with hyaluronic-acid and silicone. Collagen did show a high allergy potential. Migration, embolism and granuloma formation were a potential risk in the treatment with silicone. These complications were not described with Polyacrylamid. The re-injection rates also differed among the agents. The Re-injection rate in the first year after treatment was 43–60% for hyaluronic acid, 31–74% for collagen, 38–52.5% for silicon and 20–44% for the polyacryamid therapy.

Conclusions: In the periurethral injection therapy, the choice of the substance used is crucial both in terms of effectiveness and in terms of

safety. The analysis of available bulking agents demonstrated striking differences. General differentiation has to be made for bulking substances in which the gel acts as a carrier material and substances where the gel itself achieves the bulking. A generalized assessment of bulking therapy, as currently observed in the guidelines is therefore not appropriate. The comparison of the substances shows that the Bulking therapy with Bulkamid[®] has a unique benefit-risk profile among the available substances, presents itself as highly feasible, effective, sustainable and safe, and as an option for many patients for whom no (other) causal-oriented treatment option would be available.

PO-Onko 02.66**Vaginal mesh extrusion rates are only slightly influenced by vaginal bacterial colonisation***Lisa Lahnstein¹, Annerose Serr², A. Niesel³, C. Fuenfgeld⁴,A. Kraus⁵, F. Lenz⁶, H. J. Augenstein⁷, Susanne Markert¹,Juliane Farthmann¹, Dirk Watermann¹, Gerald Gitsch¹

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Objective: Implantation of transobturatoric meshes is frequently used in the surgical treatment of cystocele. Wound healing problems with mesh extrusions are frequently observed. We determined bacterial colonisation of the vagina and analyzed the relation to mesh extrusions. **Materials and methods:** In our prospective multicenter study 200 patients with Cystoceles underwent surgical transobturatoric mesh implantation. The microbiological colonisation and the pH-Value of the vaginal fluid was analyzed before surgery, after 3 months and after 12 months.

Results: 194 patients were evaluated either after three months and 186 after 1 year. The extrusion rate at 3 months was 7.2% (14/194) and 5.9% at 12 months. The preoperative pH-values were not statistically different in patients with or without extrusions at 3 or 12 months follow up examination (5.0/5.3 at 3 months resp. 5.0/5.4). A colonisation with physiologic vaginal bacteria was observed in 64% of patients preoperatively, in 68% at 3 months and in 60% at 12 months. Colonisation with physiologic bacteria was not correlated to extrusions at 3 months, but we observed a statistically significant correlation between preoperative physiologic colonisation and extrusion rates at 12 months. Patients without an extrusion had a physiological bacterial colonisation in 67.7% in contrast to 34.4% Patients with an extrusion ($p = 0.046$). A colonisation with pathogenic bacteria like streptococci, staphylococci or pseudomonas species was observed in 17% of patients preoperatively, in 19% at 3 months and in 19% at 12 months. Colonisation with pathogenic bacteria was not correlated to extrusion rates.

Conclusions: An unphysiologic bacterial colonisation of the vagina is frequently observed in patients with POP. A colonisation of the vagina with physiological bacteria may prevent mesh extrusions in patients with mesh augmented surgery for POP, but overall mesh extrusion rates were only slightly related to bacterial colonisation of the vagina.

PO-Onko 02.67**Novel pelvic floor training approach in stress urinary incontinence: one-on-one physical therapy in combination with Galileo vibration training. Results of two prospective comparative studies**

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Objective: To investigate whether and why the outcome of physical therapy in stress urinary incontinence can be improved by combining one-on-one physical therapy with muscle stimulation using the Galileo (side-alternating vibration platform).

Materials and methods: Sixty women were randomized to 3 groups each in 2 studies. Treatment consisted of combined physical therapy and vibration training (Ph + V) in group A, physical therapy alone (Ph) in group B, and vibration training (V) in group C. The 30 patients in the first study received one-on-one Ph + V; the 30 patients in the second study received 2 30 min sessions/week of group physical therapy and 2 individual 8 min sessions/week of vibration training.

Results: In the first study, the cure rate of stress urinary incontinence after 12 weeks of treatment was 40% for Ph + V, 56% for Ph, and 40% for V versus 80% for Ph + V after 24 weeks. The corresponding cure rates in the second study were 50% for Ph + V and 20% for either Ph or V alone versus 72% for Ph + V after 24 weeks. Contractility of the pelvic floor muscles (EMG) significantly improved in both Ph + V groups compared with the groups receiving either Ph or V alone (study 1: +6.8 μ V, $p = 0.0077$; study 2: +7.4 μ V, $p = 0.0109$). In both Ph + V groups, sustained effects were reflected in subjective improvement 3 months after the end of treatment (study 1: improvement in 90% of women; study 2: improvement in 100%).

Conclusions: The best results in terms of cure of stress urinary incontinence, increase in muscle contractility, and sustained effects of treatment were achieved by physical therapy combined with Galileo muscle training administered on a one-on-one basis. The additive effect of these two forms of physical treatment results from the improvement of voluntary motor performance combined with vibratory stimulation of reflective muscles via the monosynaptic stretching reflexes.

PO-Onko 02.68**Case report: suburethral angiofibroma**

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Objective: Angiofibromas are benign tumors, composed of variable amounts of vascular and smooth muscle elements.

Materials and methods: A 44 year old woman was referred to a tertiary urogynecology center with the diagnosis of a cystocele. Perineal ultrasound examination revealed a suburethral hypoechoic mass. Urethrocytoscopy excluded contact with urethral lumen and urinary bladder cavity. Additional MRI study indicated a benign lesion such as leiomyoma or fibroma. Complete excision was performed later. No peri- and postoperative complications occurred. Histological examination reported an angiofibroma measuring 3.5 \times 2.5 \times 2 cm.

Conclusions: Angiofibroma should be considered as a possible diagnosis of a suburethral mass. This case emphasizes the importance

of perineal ultrasound examination as an essential part of urogynecological workup.

PO-Onko 02.69**The influence of bladder volume in the assessment of pelvic organ prolapse**

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Objective: The assessment of the maximum extent of the pelvic organ prolapse (POP) is essential for planning surgical treatment. The effect of bladder fullness on the degree of prolapse has rarely been addressed. This study compares the degree of prolapse using the POP quantification (POPQ) system.

Materials and methods: 120 consecutive patients without any prolapse and patients with POP stage I or II according to the POPQ were included. All women were examined with full and empty bladder with maximal straining by a Valsalva effort.

Results: The mean maximal bladder filling was 344 \pm 96 mL and the mean residual volume after spontaneous micturition was 24 \pm 35 mL. After catheterization of those patients with more than 100 mL residual volume (6 cases) we were able to perform the examination with the mean of residual volume of 18 \pm 19 mL. With empty bladder 54% had the same stage, 41% had a one step higher stage and 5% had a two step higher stage of prolapse. There was an increase in the extent of prolapse in the empty bladder setting at all six site-specific points (Aa, Ba, C, D, Ap, Bp; $p < 0.001$) but not in the results of genital hiatus, perineal body and total vaginal length.

Conclusions: The bladder filling affected the anatomy of the vagina, especially of the anterior wall and the central compartment in patients with no or moderate prolapse. Therefore we suggest to perform the examination with full bladder to apply the stress test and with empty bladder to evaluate the stage of prolapse.

PO-Onko 02.70**Modified treatment of vaginal vault prolapse fixation with a titanium coated extralight mesh (TiLOOP–TiFour)**

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Objective: To assess the clinical efficacy of TiLOOP TiFour titanium coated extralight mesh in the treatment of vaginal vault prolapse in a modified treatment. A reusable suture device (RDS-Ney) allows the surgeon to position a supportive mesh to correct the bladder's herniation into the vaginal wall.

Materials and methods: The study group consisted of 48 women (mean age 82.8 years) who underwent vaginal cuff prolapse surgery with titanized extralight meshes between September 2009 and February 2010. The procedure has the advantage of fast and secure fixating the proximal arms of the mesh on the sacrospinous ligament. 37 patients had vaginal cuff prolapse POP-Q stage IV and 11 patients POP-Q stage III with a subjective feeling of prolapse. 29 patients were diagnosed with sui. Bladder emptying difficulties were present in 41 cases and chronic infection in 18 patients as well.

Results: The total mean operation time was 40 min (14–19). All patients were available for follow up visits after 3 months. 1 patient had recurrence

of cystocele but to a much lesser extent than POP-Q stage II. Most patients were completely satisfied with the surgical outcome. However, the following complications were encountered among our study group: 1× Retrobubic Hematoma, 4× Post operative stress incontinence or de-novo urge syndrome, 1× Severe pelvic pain causing difficulty with walking and moving, 1× Dyspareunia and 1× Vaginal Erosion of the material

Conclusions: We can conclude from this study that titanium coated extralight meshes offer better outcomes for reconstructive treatment of vaginal vault prolapse. The modified treatment of sacrospinous ligament fixation with the reusable suturing device (RSD-Ney) is an effective and safe procedure with a low recurrence and complication rate. The procedure has the advantage of fast and secure suturing the proximal arms of the meshes on the sacrospinous ligament. Secondly, at the follow up period, there are far less reports of complications such as erosions, dyspareunia and pelvic pain.

PO-Onko 02.71

Anterolateral fasciocervicopexy: new minimal invasive surgery of massive uterovaginal prolapse in multi-morbid patients

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Objective: We focus on the assessment of feasibility and results of an innovative, minimal traumatizing and short surgical procedure for the treatment of grade III/IV uterovaginal prolapse.

Materials and methods: 10 elderly patients aged over 70 years suffering massive uterine prolapse who underwent long term vaginal pessary treatment, eventually suffering from chronic pressure ulcerations of the atrophic vaginal skin and presenting with prolapse symptoms such as voiding difficulties, post-void residual volume or recurrent urinary tract infections are included.

Results: We describe the surgical technique and report first results of a pilot project performing the Anterolateral Fasciocervicopexy (Waaldijk) in a selected patient group at the Department of Gynaecology, University of Jena

Conclusions: Minimal invasive modifications of standard methods are often beneficial for selected patients even though the restoration of the anatomy has to be seen as a compromise. Abdominal, laparoscopic or vaginal standard operations for genital prolapse are time consuming invasive procedures, not always suitable for elderly, multi-morbid patients without additional risks for peri- and postoperative morbidity and mortality. This selected group of patients may benefit from the innovative, minimal traumatizing and short procedure of Anterolateral Fasciocervicopexy (Waaldijk) by the relief of their main complaints related to grade III/IV prolapse.

PO-Onko 02.72

Urethral ultrasound for optimized TVT positioning: the one-third rule

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Objective: TVT insertion does not consider individual urethral length. Depending on urethral length, the tape may not come to lie in the

optimal functional position. We investigated whether positioning of TVT can be optimized by preoperative ultrasound measurement of urethral length.

Materials and methods: Urethral length in 50 women with stress urinary incontinence was measured by preoperative introital ultrasound. The site of incision was marked using the following formula: 1/3 of the measured urethral length = distance of the distal end of the 1.5 cm suburethral incision from the external urethral orifice. Shape of tape, position, and distance from urethral lumen were evaluated by introital ultrasound 6 months postoperatively.

Results: After 6 months, 94% were continent, 6% were improved. In 86% tape position was between <70% and >50% of the urethral length; in these cases the likelihood of being cured was significantly higher ($p = 0.048$). A too distal position was associated with a 17 times greater risk of not being cured. Bladder voiding was disturbed on the first postoperative day in 14% because of TVT-urethra distance < 3 mm. Tape loosening led to cure in 6/7 patients, while one had persistent voiding dysfunction (unchanged distance <3 mm). Three developed de novo urge (2 with tape-urethra distance <3 mm).

Conclusions: Preoperative sonographic urethral length measurement ensures optimal TVT placement. The optimal site is calculated using the aforementioned formula. Nonoptimal TVT placement is associated with a higher recurrence rate but rarely causes complications. Complications typically occur when the tape is too close to the urethra.

PO-Onko 02.73

Vertebral osteomyelitis as complication of laparoscopic sacral colpopexy with titanium bone screws

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Objective: Case report of vertebral osteomyelitis—a rare, severe complication after laparoscopic sacral colpopexy using alloplastic mesh material and titanium bone screws.

Materials and methods: 68 year old patient referred as an emergency from a neighboring hospital presented with weakness, pain in both legs and progressive signs of septicemia. Thirty nine days prior to admission she had undergone laparoscopic sacral colpopexy for vaginal vault prolapse performed at the Gynaecological Unit of the same hospital. On MRI intraspinal empyema L3–L5, spondylodiscitis L3–S1 and multiple abscesses of the surrounding soft tissue were diagnosed. Group C Streptococcus was found on blood cultures.

Results: Intensive care for septicemia and operative decompression of the spinal canal was immediately performed by neurosurgeons. One day later, after further stabilization of the condition, the patient underwent laparotomy at Dept. of Gynaecology and Obstetrics, Jena University Hospital. Mesh and bone screws were removed. Within the same procedure further dissection and stabilization of the vertebra and the vertebral disc were performed by neurosurgeons. Intraoperative swabs showed E. coli, group C Streptococcus and Morganella morganii. I.v. antibiotics were given according to resistogramm.

Conclusions: Some rare cases of severe complications after the use of titanium bone anchors or screws have been reported so far. Application of nonabsorbable sutures to the presacral ligament instead of tacker or screws to the vertebral bones should be preferred.

PO-Onko 02.74**Evaluation of the tension-free vaginal tape (TVT) by introital ultrasound**

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Objective: Until now, no standardization for ultrasound assessment of the tension-free vaginal tape (TVT) has been established in clinical practice. The aim of this prospective, observational study was to evaluate the position of the tape by using ultrasound and compare this data with clinical postoperative results.

Materials and methods: 296 patients with stress urinary incontinence (SUI) were treated with TVT and followed-up in our department. Further 12 patients, who were initially treated in other hospitals, and who had postoperative problems, were included in this study. Dependent on the outcome after 3 months, the patients were divided in groups with and without specific disorders. TVT was evaluated by introital ultrasound. The position of the tape was established by its site, in relation to urethral length [%] and the distance to the hypo-echoic center of urethra (HCU) [mm].

Results: Suitable position of the tape was determined in patients without any postoperative disorders. The position of the tape at rest in relation to urethral length was in the mean 61%. The distance to the HCU was 4.6 ± 1.5 mm. In patients with persistent SUI the tape was more often located under the inner (3 vs. 0%) or outer quarter (29 vs. 13%, $p = 0.004$). In patients with residual volume the distance to the urethra was significantly lower (2.7 vs. 4.6, $p < 0.001$).

Conclusions: Tape position may be regularly investigated by ultrasound. In combination with the clinical outcome, it represents an important method and assists in the planning of a future therapeutic course of action in cases of postoperative disturbances.

PO-Onko 02.75**Mode of delivery after tension-free vaginal tape procedure: literature review and case report**

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Objective: The popularity of the TVT procedure for treating stress urinary incontinence has led to more women of childbearing age undergoing this surgery. Therefore the incidence of pregnancy after TVT procedure is likely to increase. On the other hand, there is no consensus among obstetricians and gynaecologists for obstetric management of women who have undergone TVT procedure.

Materials and methods: We present a review of the current literature and we report the case of a 26 year old woman previously treated with TVT-O.

Results: There exist only a few reports on pregnancy and delivery after midurethral sling procedures. In the literature there is no evidence that an elective caesarean section protects against stress urinary incontinence in cases of pregnancy after TVT procedure. In our case an elective caesarean section was performed at 39 weeks' gestation. Postnatal pelvic floor exercises successfully controlled the incontinence with a recurrence of the stress urinary incontinence 4 months after delivery because of terminating physiotherapy. The woman was re-examined at 17 months postnatal. At this time she was doing well and reported no incontinence symptoms and no symptoms of an overactive bladder. The stress test was negative. Introital ultrasound

showed the tape in the same position as before pregnancy and no residual volume.

Conclusions: After a review of the literature, the best mode of delivery after TVT procedure is still unclear. Therefore it is not recommended to suggest a prophylactic caesarean section routinely. At present the mode of delivery must be considered individually, taking the woman's priorities into account.

PO-Onko 02.76**Sexual function and quality of life of women with urogynecological dysfunction**

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Objective: The aim of this study was to compare sexual function and quality of life in women with and without urogynecological dysfunction (stress urinary incontinence, overactive bladder and prolaps genitalis).

Materials and methods: A total of 210 women (urogynecological disorders; $n = 151$ and without such problems; $n = 59$) from 29 to 89 years old were included. To obtain QoL (Quality of life) and sexual function assessments, the interviewer-administrated pelvic floor questionnaire was used. This validated questionnaire included aspects to bladder dysfunction, bowel dysfunction, pelvic organ Prolaps and sexual function. Women with and without therapy were included.

Results: Of the four domains in the pelvic floor questionnaire, all domains were significantly different between the two groups ($p = < 0.05$). When comparing the sexual life, 74 of the 151 women with urogynecological disorders were sexual active (49%), in comparison 64% of the control group. 24.5% had a regularly sex life. 24.5% of the sexual active women had experience dyspareunia and 18.6% a coital urinary incontinence, this is 32.5% among the women with stress urinary incontinence. Coital urinary incontinence is more frequently during intercourse in the urogynecological group than the control group.

Conclusions: SUI, OAB and Prolaps genitalis have a detrimental impact on QoL and sexual life. In addition, our findings suggest that women with SUI had more coital incontinence than those with OAB. The aim of further studies should be to find therapy options for specific therapy to improve the QoL and sex life for these patients.

PO-Onko 02.77**Identification of CAR 4/6 as a new splice variant of the coxsackie adenovirus receptor (CAR) differentially expressed in cervical cancer progression**

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Objective: The coxsackie adenovirus receptor (CAR) is a component of the tight junction (TJ) complex and involved in cell adhesion. Functional loss of CAR could enhance both invasion and metastatic spread. Inactivation of CAR may result from the interaction with its soluble isoforms. CAR expression was analyzed for splice variants with regard to tumor progression.

Materials and methods: After amplification, cloning and sequencing of all splice variants we established specific qRT-PCRs for

quantification of CAR mRNA in normal tissue and cervical cancer. By generating expression constructs for transfection, we analyzed cell proliferation, anchorage independent growth, migration and invasion. **Results:** We identified a new splice variant termed CAR4/6 which lacked exon 5. Localization of CAR4/6 in the cell membrane was confirmed by ectopic expression in cell lines. Expression analyses revealed that most normal tissues, including those of the female genital tract, express full length CAR (CAR6/7) but not CAR4/6. In a set of 30 invasive cervical carcinomas, significantly increased levels of both CAR4/6 and CAR6/7 were found in micro-dissected tumor areas compared to normal cervical epithelial tissue. An increase in the ratio between CAR4/6 and CAR6/7 was observed with tumor progression. Ectopic expression of both membrane bound isoforms of CAR in HT1080 cells enhanced the proliferative and invasive properties of these cells. Proliferation and invasion was strongest in cells transfected with CAR4/6.

Conclusions: We identified a new isoform of CAR possibly contributing to progression of cervical cancer by enhancing proliferation and invasion.

PO-Onko 02.78

An unusual emergency in gynecology: uterine bleeding caused by cancer in the stomach in an HCG positive woman

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Objective: The determination of the serum beta-human chorionic gonadotropin (HCG) in gynecology serves to verify a pregnancy. But HCG is also a nonspecific tumor marker of malignant tumors of the gastrointestinal tract and for trophoblastic diseases in association with a pregnancy.

Materials and methods: We report a case of a 46 year old woman with extreme anemia, hypermenorrhea and an IUD as well as a positive pregnancy test. The patient, however, did not have a gynecological disease, but instead primary metastatic cancer of the stomach with partial choriocarcinomatous differentiation.

Results: The patient was sent to our hospital because of extreme anemia (Hb 6.1 g/dL) and a weak general condition. A new IUD had been inserted four weeks before. Blood examination data indicated an abnormally high level of HCG (522798 IU/L, normal <5), the hemoglobin concentration was 5.5 g/dL. We performed an abrasion and a laparoscopy to exclude a disturbed intra-/extra-uterine pregnancy as well as a trophoblastic tumor. There was no pathology to be found in the pelvis except for a small eminence on the surface of the liver. Microscopically, the abrasive material contained a decidual component. To exclude a tumor of the gastrointestinal tract, we performed an abdominal sonography that showed multiple liver metastases. CT revealed multiple pulmonary metastases as well. The gastrointestinal endoscopy diagnosed a bleeding tumor (5 cm) in the stomach. The biopsy of this confirmed a high-grade tubular adenocarcinoma with partial choriocarcinoma differentiation. The elevated HCG level is caused by the extended metastases and, on the contrary, is responsible for the decidual stroma transformation without any evidence of a pregnancy in the uterus.

Conclusions: The symptoms anemia, hypermenorrhea and a positive HCG are often signs of a disturbed intra- or extrauterine pregnancy. The HCG, however, can also be a sign of a malignant tumor of the gastrointestinal tract.

PO-Onko 02.79

SPECT-CT improved the detection of inguinal sentinel lymph nodes in vulvar cancer

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Objective: Due to location vulvar cancer is predestinated for the sentinel concept. We analyzed if the use of the single photon emission computed tomography combined with computed tomography (SPECT/CT) in detection of inguinal sentinel lymph nodes is helpful compared to conventional planar lymphoscintigraphy and improved the intraoperative detection with the gamma probe.

Materials and methods: Between August 2008 and March 2010, 16 patients with invasive vulvar cancer received peritumoral intracutaneous injection of 10 MBq technetium-99 m-nanocolloid (4 × 2.5 MBq; 0.5 ml each) followed by planar lymphoscintigraphy 45 min p.i., SPECT/CT and surgery. From tumor stage T1b we performed a complete inguino-femoral lymph node dissection. We recorded the number and localization of sentinel lymph nodes in lymphoscintigraphy and SPECT/CT, non-sentinel lymph nodes and lymph node metastasis found intraoperative.

Results: 16 patients underwent sentinel concept for inguinofemoral lymph node staging. All patients had pre-operative sentinel identification using SPECT/CT and lymphoscintigraphy. The SPECT/CT showed sentinel lymph nodes in all 16 (100%), the lymphoscintigraphy in 15 of 16 (93.8%) patients. With SPECT/CT a non-inguinal sentinel (gluteal) lymph node could be identified in one patient. This sentinel would not be found with routine intraoperative examination using the gamma probe. With lymphoscintigraphy the mean number of detected sentinel lymph nodes was 2.1, with SPECT/CT 4.1 ($p < 0.05$). In average 5 sentinel lymph nodes were removed. In 8 patients (50%) a complete lymph node dissection was performed. Four of these patients have sentinel lymph node metastasis without metastasis in further lymph nodes. One patient had lymph node metastasis with an un-affected sentinel. No patient with tumor stage T1a had sentinel metastasis.

Conclusions: The sentinel concept in vulvar cancer becomes routine in the surgical treatment of vulvar cancer. The pre-operative SPECT/CT improved the detection of inguinal and non inguinal regional sentinel lymph nodes compared to conventional lymphoscintigraphy and made the intraoperative detection easier to perform.

PO-Onko 02.80

The influence of elder berries and blossom extracts on the cell lines MCF-7, BT-20 and fibroblasts

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Objective: We tested the effects of phytoestrogen extracts from the blossom and the berry of elder, *Sambucus nigra*. Examined the effect of the extract becomes on the cell proliferation, cell lethality as well as the metabolism activity at the cell line, MCF-7, BT-20 and at fibroblasts.

Materials and methods: Microwave extractions as well as the extractions after Luyengi, a raw extract was won out of the elder berry as well as the elder blossom. Out of the raw extract of the elder berry, which was won by the microwave extractions, 7 parliamentary groups were

generated through the HPLC. The raw extracts of the elder after the extractions of Luyengi were used in the concentrations 1000, 500, 250, 100, 50, 20, 10 µg/ml for the subsequent tests. In order to examine the cell lethality, the metabolism activity as well as the cell proliferation, became the LDH test, MTT test and the BrdU test carried out.

Results: The blossom of elder as well as berry extracts as well as the 7 parliamentary groups show in MCF-7 a significant cytotoxic effect of 30%, cell proliferation ca. 40% and the metabolism activity 120%. In contrast to that the extracts show after Luyengi in MCF-7 significant cell lethality of –20%, cell proliferation 20% and metabolism activity around 90–110%.

Conclusions: The elder extracts show antiproliferative and cytotoxic effects on MCF-7. The extraction methods differ in its cytotoxic effect on MCF-7. It is to be supposed been preserved that in the microwave extractions connections, which cytotoxic influence MCF-7. For going on statements, yet numerous tests must be carried out at MCF-7, BT-20 and fibroblasts.

PO-Onko 02.81

Case-report: 57 year old woman with Wolffian adenoma

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A 57 year old postmenopausal woman with an asymptomatic pelvic mass increasing in size on a 1 year follow-up. The pelvic transvaginal ultrasound demonstrated an inhomogenous, solid and highly vascularized tumor mass with an approximate size of 3.6 × 2.9 cm. The patient underwent a laparoscopic adnexectomy. CA-125 was within norm range. Histopathology of the tumor showed a female adnexal tumor of probable Wolffian origin (FATWO). In our patient's specimen signs of malignancy such as high mitotic rates, necrosis or angioinvasions were absent. Wolffian adenoma is a rare neoplasm arising from the remnants of the mesonephric duct. Until 2009 there were only 63 patients with FATWO described. The tumor is considered to be mostly benign but there are also few cases reported which have shown malignancy and even metastasis. Therefore patients with FATWO should receive careful follow-up for possible local recurrence and metastasis.

PO-Onko 02.82

Early detection of disseminated tumour cells (DTC) in a case of a rare, aggressive breast tumour (Merkel Cell Carcinoma)

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Objective: Merkel cell carcinoma (MCC) is a rare, aggressive, malignant neuroendocrine tumour with an increasing incidence and also a high metastasis- and mortality-rate (five-year-survival rate 30–74%). The tumour cells express, among others, the cytokeratins 8, 18, 19 and 20. The following case report describes an unusual presentation of a breast tumour of a 79 year old female patient with an infiltrating MCC of the right breast. To recognize an early spreading of the cancer and to adapt therapy, we tried to detect micrometastases in the bone marrow.

Materials and methods: The procedure was complete excision of the biopsy-proven, CK 20 + MCC and axillary sentinel lymph node biopsy

(SLNB). Additionally, we took bone marrow aspirations of both iliac crests. Searching for the cytoskeleton of epithelial cells, a pan-cytokeratin antibody (mAb A45-B/B3) was used to identify cytokeratin 8, 18 and 19 positive cells. After immunohistochemical colour reaction, the samples were analyzed by Ariol SL-50 System automatically.

Results: Although the sentinel lymph node was free of tumour cells, we found cytokeratin 8-, 18- and 19-positive epithelial cells within the bone marrow indicating micrometastases. So far spreading of the MCC tumour is routinely only analyzed by SLNB. The patient received radiotherapy of the breast and the axilla. Systemically we administer bisphosphonates for 3 years (Clodronat 1600 mg/die per os or Zoledronat 4 mg i.v. every 6 months), to eliminate the micrometastases as an analogy to encouraging results of treatment of breast cancer micrometastases.

Conclusions: Few cases of primary MCC of the breast have been reported in literature only and—to our knowledge—so far no detection of disseminated tumour cells (DTC) as an early sign of spreading of disease. The authors recommend consideration of bone marrow aspiration and identification of potential DTC also with rare tumours of the breast and thus to adapt therapy sufficiently.

PO-Onko 02.83

A tissue's PTEN and ER status modulates AKT activation and tissue-specific reactions upon tamoxifen treatment

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Objective: Tamoxifen (TAM) is an important selective estrogen receptor (ER) modulator for treatment of ER positive breast cancer. However, TAM is one risk factor for developing endometrial carcinoma (EnCa). This study's aim is to contribute towards our understanding of the molecular mechanisms of TAM's tissue-specific contrary mode of action between mammary and endometrial tissues. **Materials and methods:** To determine total and phosphorylated protein expression Immunoblotting was performed on endometrial tissues, and with TAM-treated EnCa and Mamma-Ca cell lines time kinetics were analyzed. Using molecular cloning and transfections, the PTEN status of RL95-2 EnCa cells was rescued.

Results: We observed deregulation of phosphorylation within the IGF-AKT axis in endometrial tissues from patients with TAM therapy. Protein deregulations occurred in benign pre-stages of EnCa and included increased total protein and phosphorylation levels of ER, AKT, PTEN and mTOR. Kinetic studies following TAM treatment of the PTEN mutated RL95-2 EnCa cell line demonstrated induction of pER α -S118 and pAKT-T308. These effects occurred within minutes, pointing towards an additional non-genomic TAM mode of action. TAM treatment of four EnCa and MaCa cell lines, differing in their ER and PTEN statuses, was performed to compare PI3 K-AKT-mTOR signaling with RL95-2 EnCa cells (ER+, PTEN–) showing highest levels of AKT activation following TAM treatment and the Mamma-Ca HTB-26 line (ER–, PTEN+) exhibiting lowest levels.

Conclusions: We propose that following TAM treatment, the ER and PTEN status of a tissue dictates the level of AKT activation. Ongoing studies to re-express PTEN in RL95-2 cells will provide evidence for the role of PTEN in regulating the response upon TAM. Loss of PTEN occurs in ~80% of EnCa and could result in direct and rapid AKT activation upon TAM. Hence, low-molecular weight inhibitors

blocking AKT activation could be an additional treatment benefit for patients under TAM therapy.

PO-Onko 02.84

Differences of first and second opinion on the histopathology of borderline ovarian tumors (BOT)

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Objective: The histopathological diagnosis of BOTs is based on the criteria of epithelial cellular proliferation without stromal invasion. However, despite an additional number of standardized criteria, there are considerable diagnostic problems when assessing these tumors. Since the long-term outcome of patients with BOTs is mainly histology-dependent, the prognosis may change with the second reading of the histopathological slides.

Materials and methods: Retrospectively we compared the first and second pathologist's diagnosis on all BOTs of our department between January 1998 and December 2008. Furthermore the results of this comparison were correlated to recurrence and survival rates.

Results: In the above mentioned period of time 26 patients (ROBOT-trial) underwent primary laparotomy, laparoscopic procedures or reassessment surgery for BOT diagnosis and/or tumorectomy. The histological diagnosis of 4 cases was altered by the second pathologist: 3 BOTs changed to benign findings (endometriosis, 2 times cystadenoma), 1 BOT was classified as malignant (Psammon-carcinoma). Considering the clinical management after this reclassification, 3 patients had overtreatment and 1 patient had been undertreated. However, until now all 26 patients show a disease-free survival.

Conclusions: The histopathological classification of borderline ovarian tumors is difficult and ambiguous. The clinical management of patients with these tumors can be optimized under study conditions with a second opinion on pathology.

PO-Onko 02.85

Human Tra2-beta1 and acidosis regulate Cyr61 alternative splicing

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Objective: Recently, we first described alternative splicing for the tumor-relevant pro-angiogenic Cyr61 gene. Two mRNA isoforms were identified, whereas the expression of only one isoform that was significantly upregulated by hypoxia contributes to the generation of biologically active Cyr61 protein and could be correlated to an aggressive phenotype in cancers. Our latest studies were subjected to investigate the molecular account of the reversible alterations in Cyr61 alternative splicing caused by hypoxia or its impacts.

Materials and methods: Gynaecological cancer cell lines were treated with 0.2% lactic acid at a pH of 6.2 for 24 h. RNA was isolated followed by RT-PCR. Immunocytochemistry was carried out with the avidin/biotin method. Transfections of Tra2-beta1-shRNA-Plasmids were performed in various cell lines.

Results: Analogous to hypoxia, acidosis lead to an increased expression of the protein-generating transcript. The shRNA-mediated elimination of splicing factor Tra2-beta1 initiated the same effect on Cyr61 alternative splicing pattern like hypoxia or acidosis.

Interestingly, on the protein level, we were able to show, that Tra2-beta1 protein localization is also influenced by acidosis. Under normal culture conditions cancer cells displayed a nuclear localization of Tra2-beta1 protein. Acidosis caused complete deficiency of nuclear Tra2-beta1 protein, in contrast to a markedly cytoplasmatic expression. The alteration in alternative splicing pattern caused by acidosis could be detected on mRNA and protein level. The Tra2-beta1-knock-down effect on Cyr61 alternative splicing was detectable on the mRNA level only.

Conclusions: According to our recent findings Cyr61 alternative splicing is influenced by acidosis, a concomitant phenomenon of proliferating, hypoxic cancer cells. We hypothesize that Cyr61 alternative splicing is controlled by the splicing factor Tra2-beta1. Proof is provided due to the facts that Tra2-beta1 protein localization is acidosis-dependent, and that elimination of the transcription factor Tra2-beta1 triggers the same effect on Cyr61 alternative splicing like acidosis or hypoxia, respectively.

PO-Onko 02.86

Postoperative pain after laparoscopic sacropexy

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Objective: Laparoscopic surgery is associated with a reduced morbidity. Compared to open access, postoperative pain is reduced. The aim of this study was to analyse the intensity and course of postoperative pain and the influence of co-factors (adipositas, duration of operation, drugs).

Materials and methods: 287 patients suffering from genital prolapse higher than I° and laparoscopic sacropexy were included. Patients were asked postoperatively to evaluate their pain using a four point verbal rating scale (VRS). Additionally medical records were analysed concerning drug application and co-factors.

Results: Patients could distinguish between abdominal pain and shoulder pain after laparoscopy. Shoulder pain was rarely influenced by drugs, but disappeared after two to three days. Abdominal pain showed a maximum at day one and a good response to non-steroidal antiphlogistics. Best results were found after Diclofenac (3 × 50 mg/day) and Ibuprofen (2–3 × 400–600 mg/day). The few cases treated with specific Cox-2 inhibitors (Etoricoxib) showed a tendency to very good results (application of only one tablet at all).

Conclusions: Laparoscopic sacropexy is associated with a moderate degree of postoperative pain. Non steroidal antiphlogistics are sufficient to treat postoperative abdominal pain during the first days after operation but have no influence on shoulder pain. Alternatively specific Cox-2 inhibitors should be taken into consideration.

PO-Onko 02.87

Robot-assisted surgery in gynecology: experiences and results after 2 years of implementation of the daVinci system

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Objective: The daVinci system offers several advantages for patient and surgeon (3D sight, extreme flexibility of instruments, magnification of sight). Most limitations of conventional laparoscopy are

eliminated; thus the system is an advancement in MIC technology. In gynecology there is a broad spectrum of possible interventions.

Materials and methods: So far 125 patients underwent a surgical procedure with the daVinci system. Recruitment occurred by the outpatient clinic. Selection criteria were complex gynecological pathologies (complex fibroids, cervical and endometrial cancer, etc.). Principal aim was to avoid laparotomy.

Results: In 62% total hysterectomy and in 9% subtotal hysterectomy in benign disease has been done, in 3% radical hysterectomy; myomectomy in 20%, 3% LND (pelvic and paraaortic), 2% sacrocolpopexy. Mean uterine weight was 263 g (35–1000), the console time 138 min, the docking time 33 min (skin to console). The mean hemoglobin deficit was -1.4 g/dl; in case of LND 25.2 lymph nodes has been removed. The length of stay was 6d, postoperative need of analgesia 3d. Following complications occurred: 2 conversions to laparotomy (1.6%), 3 bladder lesions (intraoperative repair), 1 re-laparoscopy due to pelvioperitonitis has been done. Up to now no vaginal cuff dehiscence was observed. The rate of abdominal hysterectomies for benign disease between 2007 and 2009 decreased to 25%.

Conclusions: Gynecologic surgery is the ideal field for robotic surgery. The implementation of the daVinci surgery is feasible. The main advantage of robot assistance is in complex changes (radical hysterectomy, multiple myomas, etc.). The observed complications are equivalent to conventional laparoscopy. The patient satisfaction is high. There are open questions concerning long-term financing of the robot system and the absence of reference in the DRG system. So far data from prospective RCT are missing, especially in oncologic long term follow up. A critical application of the system in the framework of an surgical master plan is recommended.

PO-Onko 02.88

Activity of bevacizumab (rhuMAB VEGF) in combination with metronomic cyclophosphamide in advanced refractory epithelial ovarian cancer

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Objective: During the last decade new therapeutic strategies for the treatment of ovarian cancer have been evaluated, based on the most advanced knowledge of its molecular biology. Drugs like bevacizumab, either alone or in combination with metronomic chemotherapy, are showing antiangiogenic antitumour activity in ovarian cancer as well in preclinical models as in clinical trials. We present the outcome of a patient's case with recurrent heavily pretreated ovarian cancer which is currently under ongoing therapy with bevacizumab and metronomic cyclophosphamide in combination for 22 months.

Materials and methods: A 53 year old woman with no relevant pre-existing medical co-morbidities underwent four surgical interventions because of advanced recurrent ovarian cancer, each followed by chemotherapy in the following order: carboplatin, liposomal doxorubicin, paclitaxel, topotecan. Finally, the tumor progressed again with massive ascites that had to be drained several times. As a savage option, an individual therapy concept including bevacizumab 10 mg/m² q2w and metronomic cyclophosphamide 50 mg orally per day was induced.

Results: The patient showed a rapid improvement of all tumor symptoms and soon did not need any ascites drainages any more. Treatment was tolerated without any significant toxicities and the patient returned to activity with good quality of life. Tumor marker levels normalized and imaging attested a partial remission. Currently,

the patient is under treatment for 22 months in fine conditions and ongoing remission.

Conclusions: Bevacizumab in combination with oral metronomic cyclophosphamide shows activity and is an option in the palliative therapy of heavily pretreated patients with recurrent ovarian cancer. Further investigations have to clarify if there are molecular predictors like e.g. antiangiogenesis gene polymorphisms for a successful therapy and if there are risk factors that predispose to the complication of e.g. gastrointestinal perforation. Also, the duration of therapy is unclear. Perhaps a maintenance therapy is reasonable.

PO-Onko 02.89

Tumorradiosensitivity testing (TRCA) in gynecological cancers

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Objective: Ovarian cancer is the most lethal of all gynecological malignancies, being responsible for about 50% of all deaths for female genital tract cancer. Although there have been significant advances in treatment, 40–85% of patients who have FIGO stage 3 to 4 disease will relaps after primary therapy. There is a need for developed and improve new modalities of individual therapyregimes. In order to determine the in vitro efficacy of cytostatic drugs in combination with radiotherapy (5–30 Gray), it is necessary to obtain tissue samples representative for the tumor. These samples allow prediction of the in vivo responses towards radiochemotherapy.

Materials and methods: 14 patients, affected by advanced metastatic ovarian carcinoma, were treated with primary surgery, typically including a total abdominal hysterectomy, bilateral salpingoophorectomy, omentectomy, and lymphadenectomy. From the resicated tumour-material we produced cell suspensions and than the cell culture plates were treated in vitro with different cytostatic drugs and drug combinations. After this all plates are treated with a one single dose radiotherapy (5–30 Gray). After 7 days the cell culture were evaluated with ATP-TCA. Theoretically the combination of chemo- and radiotherapy should achieve the best tumour growth inhibition rates, than each therapy separately, but in reality the results are very individually different.

Results: 6 of the 14 tumour tissue show a higher response rate and a better improvement regarding tumour growth inhibition rate with radiochemotherapy, 5 tissue samples have a constant effectiveness with single or combination therapy and 3 samples show a worsen response rate.

Conclusions: The results are individually different, each tumour tissue shows different reaction and its difficult to make a prediction. Nevertheless it's a ability to improve end develop the therapy regimes for patients who have exhaust primary therapy.

PO-Onko 02.90

Relevance of two-marker combinations for discrimination of benign and malignant ovarian diseases

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Objective: During the last years lethality and course of ovarian cancer have improved only slightly. This may be due to the fact that three

quarters of patients have an advanced or disseminated stage of disease by the time of diagnosis. Thus we tried to identify combinations of biomarkers that permit a reliable classification of benign and malignant ovarian diseases.

Materials and methods: We measured the concentrations of 11 biomarkers in the blood sera of 133 patients with pelvic masses by Sandwich ELISA systems. The histological analyses of the resectates revealed 47 malignant and 86 benign diseases. Due to the limited sample size we restricted statistical analyses to combinations of only two biomarkers leading to 55 combinations using complete cases. To quantify the predictive power of all combinations we used the AUCs of the biomarkers and the biomarker combinations and calculated 95% confidence intervals by using casewise resampling.

Results: The biomarkers that performed best in univariate analyses were CA 125 (AUC 0.944), which has already provided to be a useful marker for monitoring ovarian cancer in the clinical routine and the marker HE4 (AUC 0.897). Predictiveness of CA125 improved by combinations with HE4 (AUC 0.961) and CA 19–9 and slightly improved with mouse-galectin-1, PP1490 and CA 15–3.

Conclusions: The performance of CA125 can be improved when combined with HE4, CA 19–9, mouse-galectin-1, PP1490 and CA 15–3. Especially the combination of CA 125 with HE4 seems to be promising. These results show that additional studies with larger cohorts are necessary to validate the discriminatory power between benign and malignant masses of the pelvis when using biomarker and biomarker combinations. Moreover our results could contribute to the development of a screening test for detection ovarian cancer at a curative stage.

PO-Onko 02.91 RIG-I activation causes immunogenic tumor cell death in ovarian cancer

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Objective: Advanced epithelial ovarian cancer (EOC) relapses in the majority of cases due to the growth of residual microscopic tumors. Therefore, new therapeutic strategies to extend remission are required. Compelling evidence has underlined the importance of the immune system in controlling EOC. Based on the fact that the innate immune system is essential to the function of adaptive immunity and thus to the generation of effective immune responses we sought to enhance tumor immunogenicity by activating RIG-I, an intracellular innate immune sensor of viral infection.

Materials and methods: We established ascites-derived primary EOC cell cultures. EOC cells were stimulated with RIG-I ligands and effects were assessed (apoptosis, HLA antigens, cytokines and chemokines). Coculture of RIG-I-treated EOC cells with monocytes and monocyte-derived dendritic cells (MoDCs) as well as natural killer (NK) cells was performed and activation determined (phagocytosis, HLA and costimulatory molecules, cytokines and chemokines).

Results: The targeted delivery of RIG-I agonists induced primary EOC cells to upregulate HLA-class I, and to secrete pro-inflammatory CXCL10, CCL5, IL-6, TNF- α and IFN- β . Moreover, EOC cells stimulated via RIG-I became apoptotic, and were readily phagocytosed by monocytes and MoDCs, which in turn upregulated HLA-class I/II as well as costimulatory molecules, and released CXCL10 and IFN- α . This overwhelming pro-inflammatory milieu further augmented the cytolytic activity of NK cells.

Conclusions: We provide proof-of-principle that RIG-I ligands are promising candidates for cancer therapy by potentiating EOC cell apoptosis as well as antitumor immune responses and may lead to the development of an effective immunotherapy of EOC.

PO-Onko 02.92 Impact of disseminated tumor cells in bone marrow on clinical outcome in ovarian cancer patients

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Objective: Data concerning the impact of disseminated tumor cells (DTC) in ovarian cancer on outcome are still rare. In 109 primary epithelial ovarian cancer patients, we evaluated whether first-line therapy including radical tumor debulking and chemotherapy (carboplatinum/paclitaxel) can impact upon DTC in bone marrow (BM) and analyzed associations of DTC on outcome.

Materials and methods: DTC were analyzed in bilateral BM-aspirates (10 ml) using density-gradient-centrifugation and immunocytochemistry, applying the anti-CK-antibody A45-B/B3. Disease-free survival (DFS) was estimated using the Kaplan–Meier method and evaluated using a two-sided log-rank test. Associations with other clinical data were tested by the chi-squared-test according to Pearson. A significant increase of DTC was assessed if the difference was ≥ 2 CK+ cells.

Results: Before chemotherapy, we identified CK+ cells in 45% (49/109) BM-samples with a mean number of 1.9 cells/ 9×10^6 BM-cells (range 0–37). After chemotherapy ($n = 67$), we detected CK+ cells in 37% (25/67) with a mean number of 3.7 cells/ 9×10^6 BM-cells (range 0–100). A significant increase of DTC in BM was noted in 24%. In 31%, chemotherapy eliminated pre-existing CK+ cells. In FIGO III/IV-stages, the presence of >5 CK+ cells before chemotherapy was associated with less macroscopic complete resection rates in primary surgery ($p = 0.042$). No other significant associations with clinical data including platinum-sensitivity, grading, tumor stage or patients' age were observed. FIGO III/IV-patients showed a trend for a diminished DFS in case of a significant increase of DTC in BM (estimated means: 24.6 and 36.2 months, respectively; $p = 0.061$).

Conclusions: An increase of DTC during therapy might be a prognostic factor in ovarian cancer patients.

PO-Onko 02.93 Gene expression analysis of primary ovarian cancer and corresponding in vitro cultivated cell lines: underlining evidence for the well-known problem of translating from cell culture results into clinical practice

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Objective: Results of cell culture experiments in ovarian cancer (OC) are only partly and heterogeneously assignable to clinical questions. Gene expression profiling of tumor tissue and their corresponding in vitro cultivated cell lines should help to clarify this issue of translational research.

Materials and methods: Gene expression data of 23 primary OC and 41 corresponding cultivated cells and ascites cell cultures were analyzed using the Affymetrix-chip HGU133 + 2.0 array. The cell cultures were also analyzed considering proliferation, time of duplication, and defining an IC50 score for specific cytostatic drugs. In order to determine the genomic integrity of individual cells an Interphase-in-situ-hybridisation (I-FISH) set was developed.

Results: For 27 cell culture lines an IC50 score was generated. In contrast, no IC50 score was found for 14 cell culture lines. A distinct cluster was seen in primary tumor cells, fast proliferating cell lines and slow proliferating cell lines using the principle component analysis (PCA). These clusters were also seen in paired samples of primary cancer tissue and corresponding cell culture lines. Gene expression profiles of primary OC and cell culture lines did not only differ in proliferation associated genes but also in the expression of stromal, mesenchymal and epithelial markers as well as steroid-modifying enzymes and drug-resistance-genes. Interestingly, an up regulation of drug-resistance-genes was observed in fast proliferating cell culture lines in contrast to primary tumor tissue. I-FISH analysis indicated genomic instability in the fast proliferating cell culture lines.

Conclusions: Gene expression profiles and in particular I-FISH-analysis are useful methods for a more distinct characterization of cell cultures from OC. The observed genomic change in cell culture lines in contrast to corresponding primary cancer tissue underlines the well-known issue for translation of cell culture experiments into clinical practice.

PO-Onko 02.94

Macrophage migration inhibitory factor levels in serum of ovarian cancer patients correlate with prognostic parameters in ovarian cancer

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Objective: In ovarian cancer cells prognostic parameters like Her2new or estrogen receptor expression in breast cancer cells are missing, but clinical and pathological features like response to platinum-based chemotherapy, histological grading or FIGO stages display a certain correlation with prognosis in ovarian cancer. Recently it was shown, that especially in ovarian cancer host immunity versus tumor cells is of importance for the course of the disease. Tumor guided immune escape mechanisms have nicely been demonstrated. One of these mechanisms is the secretion of tumor derived Macrophage Migration Inhibitory Factor (MIF) in serum of ovarian cancer patients. MIF suppresses antitumoral responses of CD8+ T-lymphocytes and NK-cells however the clinical relevance of this mechanism still remains unclear.

Materials and methods: We evaluated, whether MIF-serum levels in ovarian cancer patients correlate with clinical and pathological predictors of poor prognosis. Points of interest were responsibility to platinum-based chemotherapy, histological grading, FIGO-stages at primary diagnosis and disease free and overall survival. In addition, immunohistochemistry for CD8+ T-cell and NK-cell infiltration in the tumor stroma in tissue samples from the examined patients was performed.

Results: In all examined groups high MIF levels in serum correlated with poor prognosis. Tumor stroma infiltration by antitumoral immunologic effector cells correlates with poor prognosis in ovarian cancer. It was evident, that patients with high MIF serum levels displayed significantly less numbers of tumor infiltrating effector cells.

Conclusions: We feel encouraged to postulate, that the secretion of MIF in serum of ovarian cancer patients is of clinical significance based on MIF interference with antitumoral immune responses. A correlation between tumor guided MIF secretion and poor prognosis in ovarian cancer should potentially be considered.

PO-Onko 02.95

The clinical impact of circulating proteasomes in patients with epithelial ovarian cancer

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Objective: The ubiquitin-proteasome system exerts regulatory functions on crucial cellular processes such as cell cycling, differentiation, proliferation, gene transcription, apoptosis and signal transduction. Circulating 20S-proteasomes (c-proteasomes) can be detected in human serum by using the enzyme-linked immunosorbent assays technique. Increased levels of c-proteasomes have been reported in various malignancies including ovarian cancer. We evaluated whether c-proteasomes impact upon the clinical course of ovarian cancer patients.

Materials and methods: Circulating 20S-proteasomes were assessed by ELISA in the sera of 120 patients presenting with the initial diagnosis of ovarian cancer. Concentrations were measured by ELISA in blood plasma of all patients before and after ($n = 68$) primary treatment and 55 healthy controls. The median follow up time was 19 months. Tumor specimens of patients were immunohistochemically stained for 20S-proteasomes to evaluate associations of histopathological PSM expression with c-proteasomes.

Results: The median c-proteasome concentration was higher in untreated ovarian cancer patients (457.5 ng/ml, Range: 200–12,540 ng/ml) than in healthy controls ($p < 0.0001$; 290 ng/ml, Range: 140–425 ng/ml). Following completion of primary treatment, the median c-proteasome concentration increased significantly relative to baseline ($p = 0.003$; 595 ng/ml, Range: 200–20,000 ng/ml). The posttherapeutic proteasome concentration positively correlated with residual disease in primary surgery ($p = 0.031$). Patients with c-proteasome concentrations exceeding the cohort's median post-treatment concentration showed a diminished overall survival ($p = 0.045$). We found no correlation between proteasome concentrations and strength of proteasomal staining in tumor specimens.

Conclusions: Circulating proteasome concentrations correlate with residual tumor mass and might be a prognostic variable in ovarian cancer.

PO-Onko 02.96

Tolerability of long-term use of trabectedin in combination with pegylated liposomal doxorubicin (PLD) in patients (pts) with relapsed ovarian cancer (ROC)

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Objective: OVA-301 was an open-label, multicenter, randomized Phase III study comparing Tr+ PLD to PLD alone in 672 pts with ROC. The combination significantly improved PFS and RR, with a trend toward longer OS and manageable noncumulative toxicity (Monk, Ann Oncol 2008, Abs. N°LBA4). Protracted tolerability of

trabectedin 1.1 mg/m² and PLD 30 mg/m², 3 h–q3 weeks vs. PLD 50 mg/m² q4 weeks in pts receiving over 6 cycles was analyzed.

Materials and methods: Safety evaluated in 320 (of 663 treated) pts receiving ≥6 cycles by adverse events (AEs), laboratory data and physical findings (NCI CTC Version 3.0).

Results: Balanced baseline characteristics: median age 56 years; ECOG 0: 68%; median platinum-free interval: 9.2 months; prior taxanes: 78%; papillary/serous histology: 72%. (See Table 1)

Conclusions: This novel non-platinum, non-taxane combination is an efficacious regimen in pts with ROC with reasonable long-term tolerability in pts that received ≥6 cycles. Hematological toxicity and transaminase elevations were more common in the combination arm, yet transient, and not cumulative; and less frequent than at <6 cycles. HFS, mucosal inflammation and stomatitis were more common with PLD. Discontinuation rates due to AEs were low. Updated data will be presented.

Pts with ≥6 cycles	Trabectedin + PLD (173 pts/1580 cycles)	PLD (147 pts/ 1224 cycles)
Median cycles (range)	8 (6–21)	7 (6–22)
G3-4 hematologic AEs (per cycle)		
Neutropenia (a)	40%	17%
Anemia	4%	1%
Thrombocytopenia	5%	1%
Febrile neutropenia	1%	<1%
Elevations (per cycle) (b) (c)		
AST	11%	–
ALT	2%	–
Any grade Aes (per cycle)		
Hand-foot syndrome (HFS)	7%	22%
Mucosal inflammation	3%	10%
Stomatitis	5%	11%
Hypersensitivity*	0.3%	0.4%
Supportive therapies (per cycle)		
G-CSF	26%	7%
Antianemics	14%	5%
Reason for discontinuation (per pts) (d)		
Drug-related AE (mainly neutropenia and hand-foot syndrome)	9%	6%
(a) Neutropenia more common at cycle <6 for both arms		
(b) No hepatic failures (c) In contrast to cycle <6: ALT, 95%; and AST, 92%		
(d) Disease Progression is most common reason for both arms One drug-related death with trabectedin + PLD: acute myeloid leukemia,		
*Only occurred in cycle 1–2		

PO-Onko 02.97

The Impact of structured quality management on surgical outcome in primary advanced ovarian cancer (AOC)

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Objective: Surgical outcome in AOC is the most important prognostic factor. We report our results before and after introduction of a quality management program (QM) in AOC in 2001. The QM included: OP by dedicated surgical teams only, routine interdisciplinary pre-OP consultation, 2nd opinion intra-OP before closure in all patients with any macroscopic residuals deemed inoperable, and annual quality conferences.

Materials and methods: Analysis of 396 patients with primary surgery for AOC FIGO IIB-IV in our institution (1997–2008).

Results: Between 1997–2000 19/51 patients (37%) had complete debulking. This rate increased to 51% in 2001–2003 ($n = 86$) and 64% in 2004–2008 ($n = 259$). The corresponding rates of debulking to ≤1 cm residual tumor were 72, 87, and 90%, respectively. The utilisation of extended surgical procedures increased over time, e.g. bowel resection (33–67%), splenectomy (4–18%), diaphragmatic stripping (2–44%), and paraaortic lymphadenectomy (29–81%). Patients with complete resection had 5-YSR of 57% (median OS = 68 months) compared to 15.7% (median OS = 30.7 months) in patients with residuals 1–10 mm, and 15.1% (median OS = 17 months) in patients with residuals >1 cm ($p < 0.001$). The median OS increased from 30.7 months 1997–2000 to 37.0 months 2001–2003 and 53.3 months in 2004–2008 ($p = 0.049$).

Conclusions: Optimizing surgical skills and introduction of QM improved surgical and overall outcome. However, centralization effects were observed in parallel indicating that cluster effects and volume-training aspects might have contributed to this evolution. Further analysis will focus on evolution of morbidity rates over time as well.

PO-Onko 02.98

Primary therapy of malignant ovarian tumours.

Experiences of a gynecologic oncology center

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Objective: Evaluation of our patient's (pts.) data, the influence of increasing specialization, including certification as gynaecologic oncologic centre.

Materials and methods: Description of the prospective collected pts. data, the treatment and the quality of treatment in different time periods between 1997 and 2009 of all pts. with first diagnosis of an ovarian malignancy.

Results: 882 pts. with an ovarian malignancy were diagnosed between 1997 and 2009. 168 pts. (20.1%) had a borderline tumor (LMP), 668 pts. (79.3%) an invasive-epithelial carcinoma and 46 pts. (0.6%) a non epithelial cancer. Primary cytoreductive surgery was conducted in 842 pts. (95.5%). During the analyzed period of time, the degree of surgical extension was one of the most distinctive features observed. Between 1997 and 2000 laminal deperitonealisation of the diaphragm was conducted in 1.7% and pelvic and paraaortic lymphadenectomy in 39% and 31%, in comparison to 43%, 60% and 65% in the period between 2007 and 2009. Complete resection was achieved in a raising frequency of pts., 33% in the years 1997 to 2000, and 47% and 61% in the years 2004–2006 and 2007–2009. Pts. with ovarian cancer treated at our gynaecologic oncologic centre showed a 5 year overall survival (5YOS) rate of 56% (95% CI: 52–60%) in comparison to the benchmark (EUROCORE 4) with 35.4%. After splitting the observation period, a significantly increased 5YOS was observed, from 26 months between 1997 and 2003 to 45 months between 2004 and 2009 ($p = 0.011$).

Conclusions: An increasing number of pts. with ovarian malignancies were treated in the HSK Wiesbaden in the last 13 years. Pts. with advanced ovarian cancer were treated more aggressively, resulting in higher frequencies of complete resection and a higher-than-average life expectancy, consecutively. All pts. with ovarian malignancies should be offered a treatment in an experienced gynaecologic oncologic centre.

PO-Onko 02.99

Has bowel resection with R0-resection in advanced ovarian cancer influence on prognosis?

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Objective: In advanced ovarian cancer best prognostic factor is optimal tumour debulking with adjuvant platinum-based chemotherapy. Aim of this study is to determine if extent of surgery with bowel resection has influence on prognosis.

Materials and methods: 191 patients with primary ovarian cancer in FIGO III/IV were evaluated. All patients operated between 1/2000 and 6/2007 at the university hospital of gynecology and obstetrics, Tübingen. All patients got adjuvant platinum-based chemotherapy. Follow-up was 53.5 months.

Results: 191 patients in FIGO III/IV were evaluated. 157 patients were classified to FIGO III and 34 to FIGO IV. In FIGO III and IV 55 patients got a R0 resection (28.8%); and 135 patients (71.2%) had suboptimal debulking. In FIGO III bowel resection was done in 59 patients (37.6%) and in FIGO IV in 20 patients (58.8%). Bowel resection showed independent to residual tumour mass no significant positive effect on prognosis in advanced FIGO stages ($p = 0.36$). In FIGO III/IV optimal debulking with bowel resection was done in 27.8% ($n = 22$). R0-resection alone showed significant positive prognostic effect on prognosis on OS and PFS in advanced FIGO stages ($p < 0.001$). R0-resection with bowel resection showed a significant positive prognostic effect on OS and PFS in FIGO III/IV ($p < 0.001$).

Conclusions: R0-resection is a significant prognostic factor for OS and PFS in advanced FIGO stages. Optimal tumour debulking with bowel resection showed a significant prognostic factor for OS and PFS.

PO-Onko 02.100

Nuclear receptor cofactor gene ERAP140 polymorphism rs1567 and breast cancer susceptibility

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Estrogen exposure is known to increase breast cancer risk and to promote breast cancer progression. Estrogen actions are mediated by estrogen receptors (ER) α and β , but also require ER-binding of specific coregulatory proteins. ERAP140, also known as NCOA7, is a nuclear receptor coactivator protein which is involved both in ER α and ER β signal transduction. Therefore, polymorphisms in ERAP140 gene might affect breast cancer susceptibility. In this genotype-phenotype association study we analyzed the single nucleotide polymorphism (SNP) rs1567 located in the coding region of ERAP140 gene, which results in an amino acid exchange. We compared its frequency in 352 breast cancer patients and 346 women without any malignancy by means of an allele-specific tetra-primer PCR. After tests for deviation from Hardy–Weinberg equilibrium using the Fisher's exact and the χ^2 test, allele frequency, allele positivity and genotype frequencies were determined. Odds Ratio (OR) was calculated using the more frequent homozygous genotypes as reference group. We could not observe any significant difference of allele or genotype frequencies between the cancer and the control group, nor between cancer subgroups. Our data clearly suggest that the ERAP140 SNP tested is not associated with breast cancer susceptibility.

PO-Onko 02.101

HER2-status of disseminated tumor cells in bone marrow of breast cancer patients at the time of diagnosis and in the disease-free survival time

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Objective: Persistence of disseminated tumor cells (DTC) in bone marrow (BM) of breast cancer patients at the time of diagnosis and in the disease-free survival time (DFS) is associated with poor prognosis. The aim of this study was to compare HER2-status of DTC with HER2-status of the corresponding primary tumor.

Materials and methods: 156 BM aspirates from breast cancer patients, in which cytokeratin-positive cells were identified after double staining procedure and incubation with the A45-B/B3-pan-cytokeratin-monoklonal-antibody, were included into the study. HER2-status was obtained using the chromogenic-*in situ*-hybridization (CISH). Out of 156 BM aspirates 89 were obtained at the point of diagnosis, 50 in DFS, 9 at the point of relapse and 8 from patient with distant metastases.

Results: In the patient-collective with DTC in BM at the point of diagnosis ($n = 89$) HER2-status correlated with HER2-status of the primary tumor ($p = 0.021$). No correlation could be observed between positive HER2-status and any of the established prognostic markers, tumor size ($p = 0.33$), tumor grading ($p = 0.82$), ER-status ($p = 0.24$), PR-status ($p = 0.9$), nodal status ($p = 0.94$). In DFS (BM-aspiration Ø27.6 after the primary BM-aspiration, $n = 50$) no correlation could be observed between positive HER2-status and any of the established prognostic markers, including HER2-status of the primary tumor ($p = 0.071$). DTC with HER2-positivity were found in 34.8% of the patients at the point of diagnosis, whereas in 44% of the patients in DFS. In 21 of 72 patients with HER2 negative tumors HER2 positive cells were detected.

Conclusions: In our study HER2-status correlated with HER2-status on the primary tumor at the point of diagnosis, but not in the DFS. HER2 positive DTC can be detected in patients with HER2 negative primary tumors. These patients might benefit from trastuzumab treatment. The antigenic profile of DTC may therefore be included in adjuvant therapy decisions and provides promising targeted treatment options.

PO-Onko 02.102

Association of GnRHR gene polymorphisms with the tumor grading of breast cancer patients

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The role of gonadotropin-releasing hormone (GnRH) as master regulator of female sexual steroid hormone synthesis arises the question if single nucleotide polymorphisms (SNPs) in its receptor (GnRHR) might influence breast cancer susceptibility. In this genotype-phenotype association study we examined three SNPs in the GnRHR gene and genotyped a total of 565 women, 254 women with breast cancer and 311 women without any malignancy by means of allele-specific tetra-primer-PCR. No significant differences were observed between breast cancer patients and healthy women concerning genotype, allele frequency or allele positivity. In contrast, we observed significant associations after sub-grouping the breast cancer cases according to tumor grading. The C allele as well as the CC genotype of SNP rs13138607 were less frequent in patients with poorly differentiated (G3) tumors than in G1 or G2 tumors or than in the control group (CC: OR: 0.49, $p = 0.0208$; OR: 0.68, $p = 0.0377$). Furthermore, women with G1 or G2 tumors more frequently carried the T-allele of SNP rs12644822 than women with G3 tumors (OR: 0.65, $p = 0.039$ bzw. OR: 0.49, $p = 0.013$), the same was true for the heterozygous genotype (OR: 0.45, $p = 0.019$). In conclusion, we observed a significant association of GnRHR SNPs with tumor grading of breast cancer patients, but not with breast cancer susceptibility. The relevance of these data has to be examined in further studies on a larger patient cohort.

PO-Onko 02.103

Zoledronic acid inhibits invasiveness and migration of tumor stem cells derived from the human breast cancer cell line MDA-MB 231

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Objective: Recent clinical studies revealed that adjuvant zoledronic acid (ZA) correlates with a favorable prognosis for the patients: Not only bone metastasis but also overall metastasis was found to be reduced significantly. A surprising observation that supports the hypothesis of early micrometastases in the bone marrow followed by distant metastasis as a further (and later) event. This second step might be inhibited by bisphosphonates. The topical hypothesis of cancer stem cells suggests that dormant tumor cells in the bone marrow consists, at least partly, of stem like cells. We, therefore, evaluated the influence of ZA on migration and invasiveness of an isolated fraction of MDA-231 cells with stem cell properties.

Materials and methods: The stem cell fraction was prepared via spheroids and verified by high expression of CD 44 and low/no CD 24, the generally accepted properties of breast cancer stem cells. Invasiveness was quantified in Boyden chambers, 8 µm filter inserts coated with matrigel. Migration was observed and documented by time-laps videography and quantified with ImageJ software.

Results: Incubation of the cells with ZA reduced the invasiveness in a dose dependent manner. Invading cells were reduced by 62% at 1 µM ZA and by 79% at 10 µM ZA respectively. Migration was reduced even more by 75% at 1 µM and by 88% at 10 µM ZA.

Conclusions: The incubation with ZA results in significantly reduced invasiveness (as shown before for other cellular models). The cellular migration is also reduced severely. The remaining movement made not any headway but was more a kind of trembling on the spot. It seems to be of particular interest that also tumor cells with stem cell properties are reduced in malignancy by zoledronic acid.

PO-Onko 02.104

Postmenopausal breast cancer: biochemical markers to predict bone disease in contrast to bone mineral density measurement

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Objective: It is very important to detect bone loss at an early stage in women with breast cancer during endocrine therapy. In the present study biochemical markers and osteodensity measurements were compared in view of their value to detect bone changes during endocrine therapy.

Materials and methods: Postmenopausal women with breast cancer were included in this study. Blood samples were taken before surgery and after one year of endocrine therapy. The serum was analysed for BAP, an enzyme involved in bone formation and for TRACP-5b (BT), an enzyme involved in bone resorption. Bone density was measured by ultrasonic method.

Results: So far 22 patients could be analysed. After 1 year, 14 patients (63%) had a lower T-Score as compared to the first measurement. The bone marker BT was significantly increased at the second measurement, whereas BAP did not differed significantly. The ratio BAP/BT was nearly 30% lower at the second measurement point. A significant negative correlation could be found between T-Score and BT-levels.

Conclusions: The present results indicate that biochemical markers of bone metabolism might be valuable as predictive parameters for bone changes during endocrine therapy. To verify these data further patients will be included in this study.

PO-Onko 02.105**Differently regulated proteins in tear fluid of breast cancer patients and age-matched controls**

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Objective: The early detection of breast cancer is a key factor for a successful treatment. Despite of an increased survival, many patients die from metastatic relapse. Many biomarkers for breast cancer have been investigated, but they still do not provide useful clinical specificity and sensitivity. In this study we used tear fluid from 54 patients with breast cancer and 54 healthy controls to examine the protein profiles in both groups.

Materials and methods: Protein profile patterns in tear fluid of breast cancer patients (CA) and healthy donors of the same age (CTRL) were investigated with Surface-Enhanced Laser Desorption-Ionisation Time-Of-Flight Mass Spectrometry (SELDI-TOF-MS) on the cationic exchanger (CM-10) and a reverse-phase surface (H50) protein chip surfaces. The identification of significant biomarkers was performed after enrichment of samples with Matrix Assisted Laser Desorption Ionisation (MALDI-TOF-TOF)-MS. The obtained data were analyzed by multivariate statistical techniques and artificial neuronal networks.

Results: A panel of 11 significant biomarkers has been detected in both groups with 5 elevated proteins in CA. The specificity of 80% and sensitivity of approximately 70% of the biomarkers for the discrimination between CA and CTRL were achieved with the AUC of 0.77. In preview studies, some decreased peaks in CA were identified as Prolin-rich protein 4 (PRP4).

Conclusions: We could show that SELDI-TOF-MS can serve as a potential screening method for detection of breast cancer. The use of tear fluid is a non-invasive and simple method to obtain stable protein profiles. The form of identified PRP4 has been associated with nasopharyngeal carcinoma (NCAPP4). Its role remains unclear but it could have a protective function in the eye such as modulation of the microflora. Further subsequent de novo screening of the discovered biomarkers can help to understand cancer emergence and development and can possibly facilitate the early diagnosis of breast cancer.

PO-Onko 02.106**MRI, mammography and ultrasound compared to histopathological findings in patients with newly diagnosed breast cancer**

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Objective: To evaluate (1) the relation between preoperative findings in mammography, MRI, ultrasound and histopathological results and (2) the influence of MRI findings on surgery.

Materials and methods: From 2004 to 2008, 218 patients underwent breast cancer surgery in our hospital after an MRI evaluation of both breasts. Three of these patients presented with bilateral breast cancer. In cases with more than one lesion in one breast the largest lesion was considered for evaluation. Patients undergoing primary systemic

therapy were not included. The study was conducted retrospectively from the database of our breast center.

Results: The median volume of the breast carcinoma was 2.92 cm³ according to the histology. In MRI, the median tumor volume was 3.60 and 1.53 cm³ in ultrasound. More than one lesion occurred histopathologically in 25.9%. In mammography, MRI and ultrasound multiple lesions occurred 7.3, 45.5 and 20.0% respectively. Lymph node involvement was found in 33.9%. 83.0% of the tumours were invasive ductal carcinoma, 11.5% invasive lobular carcinoma, 2.5% tubular carcinoma, 1.5% medullar and 1.5% other carcinoma. During a median follow up of 57.1 months, 16 patients presented progressive disease. The median progression free interval was 32.5 months, the median overall survival 55.2 months. The surgical treatment was influenced by MRI in 27% of all cases. In 5.4% a mastectomy was performed instead of breast conserving surgery due to MRI findings.

Conclusions: MRI and ultrasound are more sensitive than mammography in order to diagnose malignant breast lesions. On the other hand, mammography is in most cases the first procedure to detect a tumor. MRI tends to over-, ultrasound underestimates the size and number of the lesions. MRI results influence the surgical treatment in nearly a third of all cases.

PO-Onko 02.107**A single nucleotide polymorphism (SNP) in close vicinity to CCND1 as potential risk modifier in BRCA related breast cancer**

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Objective: Germline mutations in *BRCA1* and *BRCA2* confer high risk of breast and ovarian cancer. Increasing evidence suggests that disease penetrance is modified by other genetic factors. A recent genome-wide association study performed by the German Consortium of Hereditary Breast and Ovarian Cancer (GC-HBOC) has shown that the rare allele of *rs606555* is associated with an increased risk in *BRCA1/2* negative breast cancer cases (OR = 0.796, 95% CI 0.718–0.883, $p = 1.44 \times 10^{-5}$, $n = 3049$ cases/3813 controls). In this study we evaluated the minor allele of *rs606555* in *BRCA1/2* mutation carriers.

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Moreover, we analyzed the association of *rs606555* with the estrogen receptor (ER) status in *BRCA1/2* affected carriers.

Materials and methods: A total of 1586 samples (*BRCA1/2* positive, affected and non-affected) collected in 12 centres of the GC-HBOC was genotyped for *rs606555* by real time PCR. Statistical analysis was performed using Cox-Regression analysis. Association analysis of *rs606555* with ER status was performed by multivariate logistic regression analysis.

Results: In *BRCA2* associated breast cancer, we found the rare allele of *rs606555* significantly associated with an increased risk (HR 2.37, 95% CI 1.00–5.62, p value = 0.049). Additionally, the minor allele of *rs606555* was associated with an increased risk for ER negative tumors in *BRCA1/2* mutation carriers (OR for ER positivity per minor allele 0.56, 95% CI 0.39–0.79, p = 0.001).

Conclusions: We found a significantly increased risk for breast cancer in *BRCA2* mutation carriers for the rare allele of *rs606555* and an association with ER negative tumors in *BRCA1/2* mutation carriers. *Rs606555* is located on chromosome 11q13, 71022 bp upstream of the cell cycle progression protein gene *CCND1*. Its product, Cyclin D1, is frequently overexpressed in breast cancer. Further investigations will include protein expression experiments and functional analyses to understand the nature of *rs606555* and its modifier role in BRCA associated breast cancer.

PO-Onko 02.108

Prognostic significance of Immunoglobulin Kappa C in node-negative breast cancer is conserved across molecular subtypes

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Objective: Immunological defense mechanisms play an important prognostic role in breast cancer. We examined the prognostic impact of Immunoglobulin Kappa C (IGKC) in 766 node-negative breast cancer patients without adjuvant systemic therapy according to molecular subtypes.

Materials and methods: IGKC (probe set ID 211645_x_at) was analysed utilizing microarray based gene-expression data of three independent and previously published cohorts of node-negative breast cancer patients (Mainz, Rotterdam, TRANSBIG). Additionally, we investigated the prognostic significance of IGKC in luminal (ER+/HER2-), *erbB2*-like (HER2+), and basal-like (ER-/HER2-) molecular subtypes, respectively. Metastasis-free survival (MFS) was analyzed with univariate and multivariate Cox regression.

Results: Patients with higher expression of IGKC showed better MFS in the whole cohort of patients (HR 0.795, 95% CI 0.711–0.890, p < 0.001). Using multivariate Cox regression, IGKC retained its independent prognostic significance (HR 0.731, 95% CI 0.621–0.861, p < 0.001). 521 patients (68%) belonged to the luminal subtype, 106 (14%) were *erbB2*-like, and 139 (18%) basal-like, respectively. Prognostic impact of IGKC was conserved across luminal (HR 0.796, 95% CI 0.688–0.923, p = 0.002), *erbB2*-like (HR 0.542, 95% CI 0.387–0.757, p < 0.001), and basal-like (HR 0.760, 95% CI 0.600–0.963, p = 0.023) subtypes, respectively. In multivariate analysis IGKC had independent prognostic significance additionally to molecular subtypes (HR 0.746, 95% CI 0.664–0.837, p < 0.001).

Conclusions: IGKC has independent prognostic impact in breast cancer. Its prognostic significance is conserved across molecular

breast cancer subtypes. Incorporating IGKC should lead to a more appropriate assessment of outcome in node-negative breast cancer.

PO-Onko 02.109

A biochip for simultaneous gene expression and SNP analysis in breast cancer

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Objective: By now microarrays are designed for mutation or transcript analysis. This project focuses on the development of a biochip technology platform that can simultaneously detect SNPs and uncover variances in mRNA levels. Furthermore the technology is optimized to analyse also clinical samples in our case formalin-fixed and paraffin-embedded (FFPE) breast cancer tissues.

Materials and methods: Specific oligonucleotides were immobilized in a hydrogel mounted on a polymethylmetacrylat (PMMA) chip. In a temperature-controlled flow cell total RNA, was directly on-chip amplified utilizing a labelling multiplex nucleic acid sequence based amplification (NASBA) assay. When the reaction takes place the labelled NASBA products gradually hybridize to the immobilized probes and fluorescence data can be collected. Northern blot analysis confirmed specificity of the NASBA reaction.

Results: In a proof of principle set up we were able to simultaneously amplify and detect on-chip the five targets (RPS18 (ribosomal protein S18), ESR1 (estrogene receptor), ERBB2 (erythroblastic leukemia viral oncogene homolog 2), CASP8 D302H (caspase 8), SOD 2 V16A (manganese superoxide dismutase 2)). Furthermore allelic discrimination of the two SNPs was possible. In view of clinical applications, we showed that NASBA as an isothermal nucleic acid amplification assay can be applied to RNA extracted from FFPE breast cancer tissues.

Conclusions: Our study indicates that simultaneous detection of SNPs and measurement of mRNA levels is possible on a single biochip-platform. This test can be easily performed in a single step and also applied to RNA extracted from patient samples such as FFPE tissues making an application in clinical routine throughout imaginable.

PO-Onko 02.110

Predictive factors for non-sentinel axillary lymphnode metastasis by sentinel lymphnode biopsy

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Objective: Sentinel lymphnode biopsy (SLNB) is progressively replacing complete axillary lymphnode dissection (CALND) in

patients with negative sentinel node. Our study aims to determine the predictive factors for non-sentinel axillary metastasis, in order to review the current SLNB indications and limits.

Materials and methods: We collected data about every SLNB performed in our Department of Surgery between 2002 and 2009, focusing on patient's characteristics, tumor histological type, grading, hormonal receptor status and TNM classification. Data was analysed by R (version 2.10.1), considering significant $p < 0.05$. Also multivariate analysis was performed.

Results: Younger age, greater tumor size, higher grading and hormone-receptors negativity, are predictive for the axillary metastatic involvement, while multifocality does not result associated with worse axillary nodal status. By multivariate analysis, only younger age and greater tumor size are confirmed to be significant risk factors for axillary non-sentinel lymphnode metastatic involvement, and DCIS results to be protective factor.

Conclusions: Great tumor size and undifferentiation are strongly predictive for non-sentinel lymphnode metastasis, as also the younger age, so that in spite of their tumor size, advanced aged women have a greater prevalence of negative axillary findings. Anyway, in our opinion, also young women continue to deserve SLNB as primary axillary approach, in order to avoid CALND when possible.

PO-Onko 02.111

Digital galactoscopy of the 2nd generation

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Objective: The complementary breast diagnosis implies clinical examination, mammography, sonography and under special conditions the MRI. Is it possible to improve the diagnosis at pathological nipple discharge with the digital galactography of the 2nd generation?

Materials and methods: On the basis of own experiences (RöFo 2002; 174: 1015-1017) we realised galactoscopies in clinical routine. Between 6–9/2009 we examined in the context of the assessment at 10 patients with a galactoscopy of the 2nd generation (PolyDiagnost LaduSkop[®]): for the first time exists the possibility, after implantation of an obturator (380 µm), to place an endoscopical system, which reduces the decontamination problems and simultaneously histological proof of an intraductal lesion. There exist endoscopy/fiber optical systems with outer diameter of 0.45–1.3 mm and a resolution until 30,000 pixel.

Results: We examined 10 patients with a pathological (bloody) nipple discharge by cytology, sonography, galactography and the galactoscopy. After local anaesthesia we used the new galactoscopy system of the 2nd generation (PolyDiagnost LaduSkop[®]) (Obturator, Insertion (Solex[®]), Endoscope, (Zoom[®])-Ocular): Die galactographical/optical/histological diagnosis intraductal papilloma was confirmed in 8 cases—in 2 cases there was a carcinoma. The examinations were well accepted by the patients—pain was nearly eliminated.

Conclusions: With the new galactoscopy system of the 2nd generation the diagnosis of intraductal proliferations by using of an obturators (380 µm) could be improved by elimination of decontamination problems.

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Membrane-initiated effects of progestins on proliferation in breast cancer cells

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Objective: Progesterone receptor membrane component 1 (PGRMC1) is expressed in breast cancer and may be important in tumorigenesis and thus may increase breast cancer risk. The aim of this project was to investigate the influence of different progestins on MCF7 breast cancer cells overexpressing PGRMC1.

Materials and methods: MCF7 cells transfected with PGRMC1 wild-type or mutants were established and incubated in RPMI/charcoal treated FCS supplemented with progesterone (P4), medroxyprogesterone acetate (MPA) or norethisterone (NET) at concentrations from 1 nM to 10 µM and cell proliferation was measured after 4 days by MTT-assay. The same cell lines were also incubated with P4, MPA and NET at 1 µM for 6 days. The proliferation was measured daily. **Results:** NET increased proliferation of MCF7-PGRMC1 (WT) and MCF7-PGRMC1 (S56A/S180A) cells reaching its maximal effect of X fold proliferation compared to untreated control at a concentration of 0.1 µM. MPA increased proliferation of this cells at concentrations higher than 1 µM with a maximum at 10 µM. No effects were observed in MCF-7 cells within the investigated concentration ranges. P4 did not increase proliferation of any cell line tested within the investigated concentration ranges. Incubation of cells with MPA and NET at 1 µM for 6 days increased proliferation in all cell lines with a maximal effect in MCF7-PGRMC1(WT) cells: around 3.5 times on the 6th day compared to the untreated control. A minimal increase of proliferation was observed in MCF7 cells: around 1–1.5 times on the 6th day. Only P4 had no obvious effect on cell proliferation on any cell line. **Conclusions:** The effect of progestins on breast cancer tumorigenesis may depend on the specific progestin used for hormone therapy and the expression of PGRMC1. The data presented are very important in terms of the positive results of progestins and breast cancer risk in clinical studies so far.

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Perinatal medicine

PO-Geb 03.01

An often unrecognized and underestimated problem during the lactation period: thrush of the breast

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Materials and methods: It is estimated that about 18% of pain in the breast and/or the nipple within the lactation period is caused by an infection with *Candida albicans*. Unless women describe severe, unbearable pain during breastfeeding often lasting much longer than the sucking itself, they often do not receive adequate help. One of the reasons might be the frequent absence of apparent lesions on the breast or nipple. Generally there are only very discrete alterations like light rose coloration and swelling of the areola, dry and squamous

skin or light swelling of Montgomery glands. In addition, microbiological proof of *Candida* is extremely difficult because it requires special culture mediums to verify it and lysozymes in breast milk can destroy the fungus. A possible way of infection seems to be the transmission of *Candida* from the maternal vagina during child birth and is then transmitted while breast feeding back to the mother's breast. It is necessary to treat this infection consequently with an antifungal agent to relieve the pain. One might try to treat the breast and the baby at the same time with local application of miconazol. If there is no immediate effect, it is necessary to switch to a systemic treatment with 100–200 mg fluconazol for at least 10–14 days. It is not necessary to stop breastfeeding while treatment. We believe that many women will not discontinue breastfeeding prematurely if we offer immediate and sufficient help.

PO-Geb 03.02

Diagnosis and conservative management of placenta increta: a case report

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Objective: Abnormally invasive placentation, like placenta accreta, increta or percreta are a rare but important and challenging complication in obstetrics. Hysterectomy seems to be the appropriate therapy but in some patients it seems to be important to preserve fertility and therefore conservative management is preferable.

Materials and methods: A 28 year old IIG 0P presented herself at our hospital with premature rupture of membranes with a gestational age of 19 weeks. She had one curettage after miscarriage in her medical history. Intrauterine fetal death was diagnosed with 22 weeks of gestation and delivery was induced with misoprostol. After vaginal delivery a curettage was performed and ultrasound control afterwards revealed a partially hypervascularized placenta, that was deeply invading into the myometrium. A β -HCG-level of 41 184 IU/l and MRI confirmed the diagnosis of placenta increta. On demand of the patient to preserve fertility a conservative treatment with methotrexat was attempted. The patient received 6 cycles of intravenous body-weight adapted methotrexat. Ultrasound and MRI controls showed reduced hypervascularisation but still two large vessels at the site of invasion into the myometrium, β -HCG was decreased to 84 IU/l. A MRI guided embolisation of the remaining arterial vessels into the placental tissue was performed and the following curettage succeeded in complete extraction of the placental tissue.

Conclusions: Conservative management and preservation of fertility is an option in selected cases of abnormally invasive placentation. Methotrexat and arterial embolisation are two options of treatment, close monitoring of the patients is necessary—ultrasound, MRI and β -HCG-levels are possible diagnostics to monitor the progress of therapy.

PO-Geb 03.03

Case report: internal version and cervical spasm in the 28th gestational week

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Objective: A 28 year old secundipara was referred to our clinic with PPROM at 28th gestational week. 7 years ago she underwent cold

knife conization due to hSIL; GBS and *U. urealyticum* in cervical swab received antimicrobial therapy until negative results. Cervical incompetence was diagnosed at 23rd week (CL 25 mm, Y-shaped) and cerclage was performed and tocolysis administered. At admission: PPROM, cervix was shortened and dilated 1 cm, cervical suture in situ. Ultrasound revealed cephalic presentation, EFW 1000 g, and normal amniotic fluid collection, CTG without uterine activity. All lab parameters were within acceptable range, intravenous antibiotic prophylaxis, prophylactic tocolysis and corticosteroids were administered. Patient was monitored, and in next several hours decrease of amniotic fluid was observed, as well as changes of fetal lie; firstly transverse dorsosuperior and then dorsoinferior transverse lie. Patient recognized uterine contractions; suture was released. Despite maximal tocolytic therapy contractions became very strong and resulted in cervical dilatation of 8 cm. At that time fetus is in dorsoinferior transverse lie, head left; complicated by immediate prolapse of the leg and umbilical cord. CTG showed fetal bradycardia, immediate delivery was indicated. Patient was intubated to produce uterine relaxation, umbilical cord was pushed back and internal version was performed; followed by breech extraction: traction of the feet, thighs and body, freeing of the hands by Mueller's maneuver. Because of cervical spasm, fetal head could not be delivered and therefore Dührssen incision was performed and fetal head delivered by MLVS maneuver. Female premature baby was delivered, 1000/38, Apgar score 6/8. The placenta was adherent what resulted in manual removal.

Conclusions: Neonatal outcome was characterized by RDS, GBS perinatal infection (purulent meningitis), IVH III degree with complete regression month after discharge. Normal neurological status was observed six months after the delivery.

PO-Geb 03.04

Intrapartum uterine rupture during vacuum extraction

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Objective: Uterine rupture is rare (ca. 1/1500 births) but a severe complication during delivery. With rising incidence, uterine rupture is associated with significant fetal and maternal risks. The major causes of uterine rupture nowadays are previous operations of the uterus (caesarean section, myomectomy, etc.). However, clinical presentation may vary and does not have to be acute.

Materials and methods: A 35 year old woman was delivered by vacuum extraction. In her history, there were no uterine operations beside a conisation and curettage. Intrapartally, the patient reported pain in the right lower abdomen, but clinical examination and CTG were normal. After vacuum extraction, the patient was in good condition without symptoms. She was discharged at the fifth day post-partum with persisting moderate pain in the right groin. She was then again admitted at day 13 post-partum with reduced well-being and severe pain in the abdomen. Vaginal examination showed marked bleeding. Sonography and MRI revealed a large haematoma in the right parametrium as a result of a lateral uterine rupture. Laparotomy confirmed the uterine lesion and reconstructed the uterus after preparation and removal of the haematoma. Intraoperative findings showed a complete right longitudinal uterine rupture, ranging from the isthmus uteri to the fundus. After surgery, the patient developed fever and clinical signs of infection. Due to suspected septic uterus, the indication for the relaparotomy was made and the hysterectomy without adnexa was performed at the 20th day post-partum. After the operation, the patient recovered quickly. The histological examination validated the clinical diagnosis of a septic uterus. Her postoperative recovery was uneventful. She was discharged well on day 32 post-partum.

Conclusions: A traumatic uterine rupture sub partu can occur during first pregnancy/delivery and its symptoms may come late and unspecific. Abdominal pain postpartum requires careful clinical (and sonographic) examination.

PO-Geb 03.05

Differential expression of VE-cadherin and flk-1 in the syncytiotrophoblast of preeclamptic placentas compared to healthy controls

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Objective: VE-cadherin is promoting intercellular adhesion of endothelial cells thereby regulating endothelial integrity and permeability. Moreover, VE-cadherin is involved in the regulation of Flk-1 receptor activity and thus cell cycle regulation. Preeclampsia has been associated with impaired syncytial function and altered trophoblast turnover. Therefore we investigated whether altered VE-cadherin and Flk-1 expression might be associated with preeclampsia.

Materials and methods: Biopsies of placentas from 19 patients with late onset preeclampsia and 24 healthy term deliveries as well as 20 cases of early onset preeclampsia and 20 preterm controls were stained for VE-cadherin and Flk-1.

Results: All biopsies showed VE-cadherin and Flk-1 expression in placental vessels and in the syncytiotrophoblast. VE-cadherin expression in the syncytiotrophoblast was significantly higher in late onset preeclamptic cases and flk-1 expression was less pronounced compared to term controls. Whereas in early onset preeclampsia VE-cadherin was significantly less and flk-1 significantly more expressed compared to preterm controls.

Conclusions: Differential expression of VE-cadherin and Flk-1 might contribute to the etiopathologic events at the fetomaternal interface in preeclampsia. Since reduction of VE-cadherin and increase of flk-1 could lead to pronounced cell activation in the syncytiotrophoblast these changes than would enhance necrotic shedding instead of apoptotic shedding. The syncytial material released into the maternal system on necrotic shedding is believed to cause the maternal syndrome of preeclampsia. Thus overexpression of VE-cadherin and downregulation of flk-1 would represent a more stable situation in the syncytiotrophoblast and could possibly display a compensatory mechanism in the late onset cases.

PO-Geb 03.06

Pitfall in case of severe fetal anemia: low middle cerebral artery velocities

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Objective: Clinical standard management to detect severe fetal anemia is the non invasive monitoring of the peak systolic velocities of middle cerebral artery (pMCA). Doppler measurements of the pMCA are a valuable tool for estimating haemoglobin concentration in fetus. The correlation between haemoglobin and pMCA seems to be more accurate as the severity of anemia increases.

Materials and methods: We monitored a pregnant gravida 2 para 1 since first trimester screening with a risk of rhesus alloimmunisation (anti D antibody 1:16). Follow-up showed altered antibody titers up to 1:4096 and borderline pMCA always below 1.5 MoM (multiple of median).

Results: At 37th week of gestation a suspected cardiocotogram was recognized. The middle cerebral artery showed low resistance indices and low pMCA. The resistance indices of the umbilical artery were decreased and venous flow in the ductus venosus was pathological. An unscheduled caesarean section was performed and a girl with a severe anemia haemoglobin concentration below 5 g/dl was born.

Conclusions: In the literature the detection rate of severe fetal anemia by pMCA monitoring with a cut-off value of 1.5 MoM is up to 100%. In our experience during the last decade pMCA measurements are a very helpful tool in the management of fetuses with the red cell alloimmunisation. We demonstrate a pitfall in case of severe fetal anemia with low pMCA. Due to this case it is important to integrate all clinical parameters of the biophysical profile in last weeks of gestation.

PO-Geb 03.07

Placenta percreta: severe complication after previous caesarean sections. A case report

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Objective: The incidence of caesarean sections (CS) is rising continuously and so are severe complications like placenta percreta are common (incidence higher than 1:1000). The evaluation of placental by ultrasonography is one of the most important elements of prenatal care, especially after previous CS.

Materials and methods: A 39 year old G6 P4, pregnant with diamniotic, dichorionic twins, presented at 30 weeks gestation with abdominal pain localized at the old section scar. Her obstetrical history included three CSs and one forceps delivery. A placenta percreta combined with a covered uterus rupture was suspected by ultrasound.

Results: Increasing abdominal symptoms necessitated an unscheduled CS. Due to severe intraoperative atonal bleeding an emergency hysterectomy was made with the requirement of multiple blood transfusions.

Conclusions: This case report should demonstrate the relevance of modern diagnostic procedure without the requirement of high definition ultrasound equipment. In the daily routine the diagnosis of implantation disorders is considered to be standard consultant proficiency. Especially in the presence of known risk factors, abnormalities have to be excluded. Prior to CS, particularly in the case of elective CS, patients must be informed about the higher risks of implantation disorders and bleeding complications in consecutive pregnancies.

PO-Geb 03.08

Comparison of effectiveness and safety of dinoprostone and misoprostol for labour induction at term

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Objective: Study was to compare the effectiveness and safety of oral misoprostol and intravaginal dinoprostone applications for assisted labour induction between each other and to a control group of spontaneous singleton deliveries. The influence of maternal properties on the duration of induction was investigated.

Materials and methods: The Jena perinatal database of 5 years (2003–2007) was analysed, where 644 women initially receiving 50 µg misoprostol and 99 women receiving 1 mg dinoprostone for labour induction were recorded. In the misoprostol group, a repeated dose of 100 µg was applied every 4 h until beginning of regular contractions. A repeated dose of 1–2 mg was applied every 6 h in the dinoprostone group. Control group data was surveyed from 699 records fulfilling the inclusion criteria.

Results: Maternal age and body weight, gravidity and parity have independently significant effects on the duration of labour induction. The mean interval from starting misoprostol to delivery was 18.3 ± 12.9 h compared to 25.5 ± 18.3 h in the dinoprostone group. Within 24 h after the first medical application, 81% of the misoprostol vs. 68% of the dinoprostone group could deliver ($P < 0.05$). After misoprostol more women could deliver spontaneously and the number of caesarean sections was less (22 vs. 33%; $P < 0.05$). Potential or occurring uterus ruptures were noticed in one and two cases after receiving dinoprostone and misoprostol, respectively. A duration of first and second stage of labour < 8 h was recorded significantly more often after misoprostol priming compared to the controls ($P < 0.01$), whereas the risks of perineal injuries and anemia's were decreased ($P < 0.01$).

Conclusions: Due to essential advantages with regards to effectiveness and safety, a labor induction with misoprostol is strongly suggested following an appropriate assessment of potential contraindications.

PO-Geb 03.09

Antepartum second trimester bleeding and preterm labour

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Objective: Preterm delivery is one of the most frequent complications during pregnancy. Preterm birth is cause of perinatal mortality and morbidity, indeed 75% of perinatal mortality and morbidity, are due to preterm delivery. Transvaginal cervical evaluation is more accurate than digital examination of the cervix in the assessment of the risk for preterm delivery. Our purpose was to assess the correlation of second trimester bleeding in the prediction of preterm labour.

Materials and methods: In a retrospective study, between 1998 and 2008, 150 pregnant women with singleton pregnancies and recurrent vaginal bleeding underwent gynaecological and transvaginal sonographic examination to assess the cervical length and the presence of cervical funnelling. We excluded patients with missed miscarriages in the past, known stillbirths, preeclamptic women and pregnancies with known fetal congenital abnormalities. They reported no risk factors for preterm delivery. For statistical analysis, categoric variables were compared with chi-square test.

Results: The management of hemorrhage was in all cases conservative. We have no Blood transfusions administrated. Of 150 women with transvaginal sonographic cervical assessment, 33 (22%) women had abnormal cervical length and abnormal dilatation of the internal cervical os at the same time. In 90% of the subgroup participants with cervical pathology was a preterm labour (mean 34 week) noticed. The remaining cases 117 with vaginal bleedings und no cervical pathology had a term labour. Perinatal fetal outcome was in all cases satisfactory.

Conclusions: Our data confirm that sonographic assessment in the second trimester has more prognostic value than vaginal bleeding for predicting preterm labour.

PO-Geb 03.10

A milk test for determining completeness of the placenta

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Objective: Completeness of the placenta is checked immediately after expulsion to ensure that no fragments remain in the uterus. However, visual and ultrasonographic assessment may be difficult in some cases and the assessment of completeness is often determined by the obstetrician experience, rather than objective evaluation. Retained placenta fragments increase the risk of postpartal haemorrhage and infection. In uncertain cases often a curettage of the uterine cavity has to be performed.

Materials and methods: We conducted a prospective, randomized and blinded study to evaluate the effectiveness and positive as well as negative predictive value of the so-called "milk-test". After the injection of a certain amount of milk in the umbilical vein of the expelled placenta its completeness was assessed by a blinded person. After randomisation the placenta was damaged before in a definitely and established way or was remained untouched.

Results: The used milk test provided good positive and good negative predictive values. Exact results will be demonstrated at the DGGG meeting.

Conclusions: The milk test is a valuable, simply and quick aid to the obstetrician during the assessment of the completeness of the placenta postpartal.

PO-Geb 03.11

Treatment of heterotopic cervical and intrauterine pregnancy

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Objective: To describe a rare case of a heterotopic pregnancy with a gestational sac in the cervix and one in the uterine cavity, managed successfully with subsequent delivery of a healthy neonate.

Materials and methods: A 25-year-old IG/OP woman was diagnosed with a twin gestation 8 weeks following IVF treatment for primary infertility of 2 years' duration. Transvaginal ultrasound scan revealed two gestational sacs containing two viable fetuses: one sac inside the uterine cavity and the other sac in the uterine cervix. Interventions: Selective termination of the cervical pregnancy by curettage in combination with cervical cerclage. **Main outcome measures:** Intra- or postprocedural complications, pregnancy outcome and fertility preservation.

Results: The termination of the cervical pregnancy was successfully performed without intra- or postprocedural complications with preservation of the patient's fertility. The intrauterine pregnancy progressed uneventfully through 39 1/2 weeks with delivery of a healthy newborn.

Conclusions: Cervical pregnancy is usually considered a life-threatening event. Other factors such as concomitant intrauterine pregnancy and the patient's infertility history generally would be secondary concerns. In this case, we were able to selectively terminate the

cervical pregnancy, while preserving the intrauterine one, allowing this couple to have a healthy newborn. Further cases will be necessary to appropriately define risk rates for such an approach.

PO-Geb 03.12

Misoprostol for induction of labour: a safe alternative for twin pregnancies and premature births?

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Objective: Misoprostol (MP) is being used with increasing frequency to induce labour. The intention was to clarify whether the administration of MP in twin pregnancies and premature deliveries had a different effect on the course of labour and foetal outcome compared with the conventional use of prostaglandin and the normal population. **Materials and methods:** PGE2 vaginal tablets were replaced with MP in our department beginning in 2006. Thirty parameters concerning course of labour and foetal outcome were compared. In the control group the indication for induced labour was over term pregnancy or rupture of membranes >37 weeks' gestations. The study group comprised twin pregnancies >37 weeks' gestation and pre term pregnancies <37 weeks' gestation with PROM. Both compared to each other and with regard to the use of MP versus prostaglandin. **Results:** The goal of this study is to compare induction of labour by oral MP vs. vaginal PGE vs. iv oxytocin application in normal singleton term pregnancies (A) vs. twin gestations ≥37 weeks (B) vs. preterm pregnancies <37 weeks with PROM (C) with regard to vaginal delivery rate, duration of labour and fetal outcome. Results: A (n = 1551): induction by MP: 807, PGE: 614, Oxy: 130 B (n = 100): induction by MP: 53, PGE: 28, Oxy: 19 C (n = 193): induction by MP: 103, PGE: 56, Oxy: 340 Vaginal delivery rate: A: MP: 86.2%, PGE: 83.8%, Oxy: 14.1%; B: MP: 75%, PGE: 70.9%, Oxy: 92.1% C: MP: 79.8%, PGE: 74%, Oxy: 76.7% Mean duration of Labour: A: MP: 7.53 h, PGE: 8.52 h, Oxy: 7.79 h; B: MP: 8.02 h, PGE: 7.46 h, Oxy: 5.41 h, C: MP: 10.09 h, PGE: 10.47 h, Oxy: 9.5 Umbilical cord pH <7.2: A: MP: 21.8%, PGE: 23.9%, Oxy: 25%, B: MP: 8.7%, PGE: 16.4%, Oxy: 13.2%, C: MP: 20.2%, PGE: 10%, Oxy: 10% Apgar >8: A: MP: 89.8%, PGE: 86.5%, Oxy: 87.5%, B: MP: 74.7%, PGE: 70%, Oxy: 76.7%, C: MP: 76.9%, PGE: 70.9%, Oxy: 73.7%. **Conclusions:** Beside normal singleton pregnancies at term misoprostol application seems to be a safe and successful option to induce labor in high risk pregnancies like twin and preterm pregnancies.

PO-Geb 03.13

The development of the German legal maternity guideline and the antenatal health care record

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Objective: This work evaluated two major documents in German obstetric health legislation: the legal maternity guideline (*Mutterschafts-Richtlinie*) and the antenatal health care record (*Mutterpass*). Our aim was to develop a comprehensive picture of the historical formation of their current editions.

Materials and methods: We investigated 15 editions of the German legal maternity guidelines and its 22 amendments, as well as nine versions of the antenatal health care record and its predecessor, the "Sprechstundenblatt." We developed two parallel analysis instruments, one tailored to the antenatal record and a second to the legal maternity guideline. Their main categories comprise "development", "layout" and "content". The development of the German legal maternity guideline and the antenatal health care record has been analyzed according to four periods, each defined by significant events in the documents' evolution: 1965–1973, 1974–1986, 1987–2003, 2004–2010 (Table 1).

Results: On average, the legal maternity guideline was published increasingly infrequently from the first to the third period (2.7 years first period, 4 years second, 8 years third). In contrast, the mean time interval between revisions in the fourth period was 0.9 years. The number of separately published amendments to the guideline rose during the first three periods (respectively 1, 3, 18) and fell in the fourth (8). The fourth period compares to the first, in that amendments were closely followed by guideline publications. The antenatal health care records were revised every 4.5 years on average. During the third period, an insert was added instead of publishing a new edition. This resulted in only two published antenatal records within this 16-year period.

Conclusions: The development of the German legal maternity guideline and the antenatal health care record has occurred unsystematically. Addressing the historical evolution contributes to a better understanding of contemporary aspects of maternity care.

Table 1. (PO-Geb 03.13). Mean time intervals between publications within each period

	Legal maternity guidelines (mean of intervals between revisions) [year]	Amendments of legal maternity guidelines (mean of intervals between amendments) [year]	Antenatal health care records (mean of intervals between revisions) [year]
Period I 1965–1973	2.7	3.0	3.0
Period II 1974–1986	4.0	1.0	4.0
Period III 1987–2003	8.0	0.9	8.0
Period IV 2004–2010	0.9	0.8	3.0

PO-Geb 03.14**Cases of twin reversed arterial perfusion (TRAP) sequence**

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Objective: Acranius acardius is characterized by a normally developed fetus and an unformed twin with retrograde blood supply, lacking a heart pump. This severe complication of monochorionic twin pregnancies occurs less than in 1:35,000 births. The higher cardiac output of the healthy twin because of the supply of the acardius increases the risk of heart failure. We present 3 cases of monochorionic diamniotic twin gestations with twin reversed arterial perfusion (TRAP) -sequence with different outcomes.

Materials and methods: The first patient was a 35 years old gravida 3 para 2 woman with spontaneously conceived twin gestation with diagnosed TRAP-sequence after missed abortion of the one twin in the 7th week of gestation. Fetoscopic laser photocoagulation was performed in the 2nd trimester. The second patient was a 30 year old woman gravida 2 para 1 who did not fulfil the requirements for laser treatment. The third patient, a 39 years old woman with pronounced uterine leiomyomas, primigravida after intracytoplasmic sperm injection (ICSI) was not referred to a tertiary centre.

Results: First and second patient delivered healthy infants near the estimated date of delivery after close follow up of the pregnancies. By the third patient preterm labour led to caesarean section in the 25 + 0 week of gestation. The neonate died 48 h after delivery.

Conclusions: The survival of the cardiac decompensated twin is ensured only after elimination of the reversed arterial perfusion. The only therapeutic option is the interruption of the blood circulation in the umbilical cord of the acranus-acardius. The successful outcome of the first two patients underlines the importance of early diagnosis and reference of patients with TRAP-sequence to a centre with the possibility of adequate evaluation and treatment.

PO-Geb 03.15**Case presentation: the Goldenhar Syndrome**

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Objective: The Goldenhar Syndrome (GS), also known as Oculoauricular Dysplasia, was first described by Maurice Goldenhar in 1952. It is a congenital birth defect with an asymmetrical face due to different deformations as partially formed/absent ear and eye, dislocation of the chin and mouth. In addition the skeletal, cardiac, central nervous and renal systems can also be involved. The incidence range from 1:3000–5000. A developmental disorder of the 1st + 2nd branchial arch or a vascular disruption during morphogenesis is assumed.

Materials and methods: We present a 35-years old gravidaII, paraI, who was referred due to abnormal results in the first trimester screening for trisomie21 (1:138) at 14 + 2 weeks' gestational age. Her first child has been born without any abnormalities. At this stage of pregnancy we diagnosed a vitium cordis, which was later specified as a double-outlet right ventricle (DORV), multicystic renal dysplasia and retrognathia. A amniocentesis was performed which showed a normal karyotype (46XY). A syndromic disease was assumed. At all her visits, fetal + maternoplacental doppler ultrasound, the fetal's development and amniotic fluid was within normal ranges. On January the 14th, an intrauterine fetal death (IFT) was diagnosed, one day later with 35 + 5 weeks' gestational age she gave birth to a dead

fetus, weight 2500 g, length 45 cm, head circumference 33 cm with signs of maceration. A autopsy was performed. The most obvious findings were as following: asymmetrical face morphology with an inclined lid, hypoplasia of the mandibular, hypoplasia and dysplasia of the right ear and pre-periauricular attachments, oesophagus atresia, DORV, multicystic renal dysplasia and abnormal structure of the thoracic vertebra.

Conclusions: To set the diagnose of GS, all clinical patterns need to be taken into consideration, it is hardly done by prenatal ultrasound only. The reason for the IFT is unclear and the newborns malformations do not the answer this question alone.

PO-Geb 03.16**Seroprevalence of rubella virus infection in Lagos prepregnancy class population 1997 to 2009**

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Objective: There is a little information on the incidence and prevalence of Rubella Infection in Lagos/Nigeria. The risk of congenital Rubella in sero-positive pregnant women has been found to produce congenital abnormalities even in developed countries. The aim of the study is to determine the prevalence of rubella virus antibody in prepregnancy class population of men and women. Study and Design: This is a cross sectional study of men and women attending the prepregnancy class facilities in the centre. Setting: A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos

Materials and methods: Between June 1997 and December 2009, the seroprevalence of rubella virus was determined in the study of 2529 men and women. A total of $n = 1.251$ Rubella IgG sero-positive were screened for IgM seropositive using ELISA kits.

Results: A total of 100 (14.6%) males out of 584, 269 (14.9%) females out of 1,881 and 10 (29.4%) unknown sex out of 24, were found to be susceptible to Rubella Infection and the seropositivity rate related to prior infection were 85.45% (584) in males, 85.1% (1,542) in females and 70.6% (24) in the unknown sex. Out of 1,251 Rubella IgG positive men and women, 19.4% (68) out of 351 males, 19.97% (170) out of 851 females and 16.3% (8) out of 49 unknown sex were found to be Rubella IgM positive.

Conclusions: This prevalence of Rubella antibody in prepregnancy class population of men and women shows high susceptibility and reinfection or active infection rates leading to a high risk of transmission among couples.

PO-Geb 03.17**Preeclampsia is associated with elevated plasma ADMA levels and severely decreased placental activity of dimethylarginine dimethylaminohydrolase (DDAH)**

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Objective: Asymmetric dimethylarginine (ADMA) is a key regulator of nitric oxide (NO) production. Dysfunction of the endothelial NO

pathway plays an important role in the pathophysiology of preeclampsia, and elevated ADMA levels were found in women with preeclampsia as compared to healthy pregnancies. ADMA levels are regulated by the enzyme dimethylarginine dimethylaminohydrolase (DDAH). We set out to study whether differences in plasma ADMA levels are mere markers of preeclampsia, or reflect pathophysiological changes in preeclamptic versus normal placenta. Further, we studied the role of single nucleotide polymorphisms (SNPs) of the DDAH gene in this pathophysiology.

Materials and methods: We measured plasma levels of L-arginine and ADMA by a validated LC-MS/MS method in 18 pregnant women with preeclampsia and in 28 healthy pregnant women (controls). DDAH activity was determined by measuring the degradation of (2H6)-labeled ADMA in tissue homogenates from placental biopsies in 15 women with preeclampsia and 16 controls. Finally, we determined the influence of a known SNP in the DDAH2 promotor region (rs805305) for DDAH activity and ADMA levels.

Results: Plasma ADMA levels were significantly elevated in preeclampsia as compared to controls (0.51 ± 0.14 vs. 0.42 ± 0.07 $\mu\text{mol/l}$; $p = 0.005$). Placental DDAH activity was almost undetectable in preeclampsia (0.03 ± 0.10 nmol [2H6]-ADMA/g protein/min) and significantly lower than in controls (0.32 ± 0.42 ; $p = 0.02$). Furthermore, women who were homozygous for the -449G DDAH2 genotype had significantly lower placental DDAH activity ($p = 0.04$) and a trend towards higher plasma ADMA levels ($p = 0.12$).

Conclusions: In preeclampsia, elevated ADMA levels in blood reflect major pathophysiological changes in this pathway. Our data suggest that high ADMA levels are caused by decreased activity of its degrading enzyme, DDAH, secondary to polymorphisms in the DDAH2 gene. Determination of ADMA in blood may be a novel, pathophysiology-related biomarker for detection of women at risk of preeclampsia.

PO-Geb 03.18

Evaluation of βhCG and PAPP-A during first trimester screening as a possible marker for preeclampsia

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Objective: Preeclampsia is one of the most important disorders affecting 5% of all pregnancies. Until now it was not successful to establish a clinical useful screening test for the prediction of preeclampsia before the onset of clinical symptoms. The existing screening tests are based on the angiogenetic approach or focus on placental function testing. The aim of our study was to investigate a possible correlation between the expressions of the placenta secreted hormones βhCG and PAPP-A during first trimester screening and the development of preeclampsia later in pregnancy.

Materials and methods: One-Hundred-fifty-five patients with uncomplicated singleton pregnancies between 11 + 0 and 13 + 6 weeks of gestation were enrolled in this study. All patients joined our department for the first trimester screening test. None of the fetuses had a numeric chromosomal aberration. Serum samples were collected between 11 + 0 and 13 + 6 weeks of gestation with informed consent and the approval of the Research Ethics Committee, and the PAPP-A and βhCG levels were measured using the KRYPTOR[®] random-access immunoassay system (KRYPTOR; BRAHMS, Henningsdorf, Germany).

Results: The expression of βhCG was significantly higher in pregnancies which subsequently developed preeclampsia. The PAPP-A concentration was lower in pregnancies complicated by preeclampsia

than in uncomplicated pregnancies, but this failed to reach statistical significance.

Conclusions: The placental expression of βhCG is significantly higher in pregnancies which subsequently developed preeclampsia than in uncomplicated pregnancies. These findings might offer new possibilities in the prediction of preeclampsia.

PO-Geb 03.19

Coincidental cervical pregnancy with placenta previa partialis and percreta

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Objective: The purpose of the present case report is to review the current epidemiological situation of pathological placentation and discuss different treatment options.

Materials and methods: A 38 year old gravida 3 para 2 presented at 17 + 0 weeks of gestation with the clinical suspicion of premature rupture of membranes (PROM). Past medical history included a caesarean section 15 years ago and a spontaneous vaginal delivery 11 years ago.

Results: On speculum examination purulent discharge was found. Ultrasonography revealed a cervical pregnancy and a placenta previa partialis with placental invasion of the lower uterine segment. Fetometry was adequate for gestational age but no vital signs could be detected. Laboratory results showed significantly elevated inflammatory markers (C-reactive protein: 12.8 mg/dl and leucocytosis). The diagnosis of septic abortion in combination with a pathological placentation led to the decision of undertaking a caesarean hysterectomy. Intraoperatively the uterus could be separated from the urinary bladder. Postoperative treatment included a course of iv Clindamycin and Cefuroxim. The further recovery was uneventful.

Conclusions: Due to rising caesarean section rates, the incidence of placenta previa and percreta is on the rise. At present 1 in 2500 live births is affected. However, cervical involvement is rare occurring in less than 1% of the cases. Abnormal placentation is linked with a significantly increased peripartur morbidity and mortality due to severe haemorrhage, disseminated intravascular coagulation and infections. Treatment of choice is hysterectomy. Alternatively, the placenta can be left in situ. This conservative approach might be followed by a course of iv Methotrexate and/or embolisation of afferent vessels. To decrease the incidence of pathological placentation, the indication of every caesarean section should be considered carefully.

PO-Geb 03.20

Effect of steroids on angiogenic factors in pregnant women with HELLP syndrome

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Objective: HELLP syndrome is a serious complication of pregnancy. Lacking a causal treatment, expectant management with glucocorticoids has been used to prolong pregnancy. It is still unclear whether this treatment improves outcome. Since angiogenic factors like sFlt1 and PlGF are closely linked to the pathogenesis of HELLP syndrome, we wanted to investigate if the sFlt1-PlGF ratio is altered by glucocorticoids.

Materials and methods: We report two cases of early-onset HELLP syndrome before 34 weeks of gestation where we monitored platelets and sFlt1/PIGF ratio frequently from the point of admission. Both women received a daily dose of 32 mg methylprednisolone IV (patient A four courses prior to delivery, patient B three courses prior to delivery).

Results: In both cases, we observed an increase of the platelet count. In parallel, as a result of increasing maternal serum sFlt-1 concentrations and decreasing maternal serum PIGF concentration, the sFlt-1/PIGF ratio increased (patient B) or remained almost unaffected (patient A) under steroid therapy. As expected, the ratio declined after delivery.

Conclusions: The observed effect as the temporary increase of platelet count seems to be a peripheral steroid effect without direct action on the anti-angiogenic status and therefore the underlying pathogenesis of HELLP syndrome. Thus, the use of glucocorticoids should be critically reviewed and needs further investigation.

PO-Geb 03.21

Actim Partus Test[®] as therapeutic guide in patients with preterm contractions

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Objective: To determine symptomatic patients less than 35 weeks of gestation without risk for preterm delivery and therefore avoid over-therapy as hospitalisation, tocolytics or corticoids by using the Actim Partus Test[®].

Materials and methods: Our multicentred prospective randomized trial underwent its pilot phase and includes patients with preterm contractions between 24 + 0 to 33 + 6 weeks of gestation with cervical shortening between 15 and 25 mm but negative Actim Partus Test[®] (rapid bed side test which measures cervical phosphorylated insulin-like growth factor binding protein-1 concentration under 10 µg/ml). 200 symptomatic patients will be enrolled in the study-group and 100 in the control-group. After written consent the study-group does not receive tocolytics nor are corticoids given, only bedrest is recommended. This group is compared by the control-group which receives the standard treatment.

Results: Within the pilot phase 9 study-patients presented with preterm contractions, all of them reached 34 + 0 weeks of gestation. In the control-group 17 patients were enrolled so far. Here 2 gave birth before 34 + 0 weeks.

Conclusions: The test is rapid and easily applicable and highly anticipates preterm delivery before 35 weeks of gestation in patients at risk. The patients are benefitting from the absence of tocolytics and steroids and are comparing to the control-group not undergoing a higher risk for neonatal complications.

PO-Geb 03.22

Myomectomy of two large myoma in pregnancy: a case report

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Objective: Illustrating that dissection of large myoma during pregnancy can be a safe procedure.

Materials and methods: We present a case of a 31y I/O, who underwent myomectomy of two large myoma at 18 weeks of

gestation due to massive abdominal pain and severe displacement symptoms.

Results: In early pregnancy a uterus myomatosus had been diagnosed. Hospital admission was required at 16 + 3 weeks of gestation due to rapid growth of the myoma and increasing symptoms. Magnetic resonance imaging (MRI) revealed 7 myoma measuring up to 190 × 110 mm and detecting a thick myometrium underneath the myoma. The largest myoma were classified as subserous in no distance to the placenta. Due to the patient's condition with till growing myoma a myomectomy was performed at 17 + 5 weeks of gestation (weights: 1583 and 310 g respectively). Operation sites were closed in 3 layers leaving an adequate thick uterus wall. The intra- and postoperative course were without complications. The pregnancy was monitored with weekly ultrasound examinations and another MRI showing constant sizes of the remaining myoma and a stable wall of the uterus (1 cm thickness) without signs of imminent rupture. The pregnancy was prolonged to 35 + 4 weeks of gestation with no maternal symptoms. A cesarean section was performed and a 2490 g girl was delivered. The intraoperative findings revealed the already known remaining myoma and a sufficient myometrium thickness at the resection sites.

Conclusions: Although the majority of myoma are asymptomatic and do not require treatment during pregnancy, their presence may be associated with complications. The location, total number and the dimension of the myoma play an important role for the course of the pregnancy. Optimal treatment of leiomyoma occurring in pregnancy is still controversial. Individual decisions are required. In selected cases myomectomy during pregnancy can be a necessary and safe procedure.

PO-Geb 03.23

Serum-based diagnosis and mouse models for preeclampsia: presentation of a novel protein

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The overarching goal of this study is to use serum as a blueprint to establish in vivo and in vitro diagnostic and treatment models for pregnancy disorders such as preeclampsia and intrauterine growth restriction (IUGR). When combined, preeclampsia and IUGR complicate 10–15% of all pregnancies worldwide and are a major cause of maternal, fetal and neonatal mortality and morbidity. Despite intense investigation, these complications have remained enigmatic and the mechanisms that contribute to their emergence are largely unknown. We have recently initiated serum-based studies to establish in vitro and in vivo predictive and mechanistic assays for IUGR/preeclampsia. Our data strongly suggest that serum from preeclampsia/IUGR patients contains an “activity” that disrupts cross-talk between placental invading trophoblasts and endothelial cells as well as causes preeclampsia and IUGR like symptoms in pregnant mice. The latter phenotype is particularly apparent in interleukin-10 (IL-10) deficient mice. A major task has been to expand these studies using a larger sample of human samples to verify these novel preliminary results and to identify the dysregulated protein component(s) by state of the art proteomic techniques such as mass spectrometry based Surface Enhanced Laser Desorption and Ionization-Time of Flight (SELDI-TOF). Results will be described with a focus on identification and biochemical and physiological properties of a novel protein (US Patent Application #WIH2009–01) that is invariably deficient in preeclampsia serum. This novel protein is able to counteract the above-mentioned disruption of the interaction between trophoblast

and endothelial cells as well as preeclampsia and IUGR like symptoms in pregnant mice. Supported by the NIH-NCRR grant P20RR018728 and the Rhode Island Research Alliance Collaborative Research Award and STIFT (Foundation for Technology, Innovation and Research in Thuringia, Germany).

PO-Geb 03.24

Strong influence of maternal lipids on fetal growth limited to pregnancies with gestational diabetes?

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Objective: To evaluate the potential contribution of maternal glucose and lipids to fetal metabolic environment and growth in pregnancies with normal glucose tolerance in comparison with pregnancies with well controlled gestational diabetes (GDM) previously reported by us. **Materials and methods:** In 190 pregnancies with normal OGTT (controls), serum triacylglycerol (TAG), cholesterol, free fatty acids (FFA), glycerol, insulin and glucose were determined in maternal serum close to delivery and in cord blood. Birth weight, BMI and neonatal fat mass were obtained after delivery.

Results: Maternal serum glucose, TAG, FFA and cholesterol levels did not differ between controls and GDM, whereas insulin, insulin/glucose ratio, HOMA and glycerol values were lower in the former. However, in cord blood serum glucose, insulin, insulin/glucose, HOMA, TAG and FFA were lower in controls than in GDMs, with no differences in glycerol and cholesterol. Similar to our findings in GDM, in controls maternal serum glucose, FFA and glycerol correlated with those in cord blood. In contrast to GDM, maternal glucose but not TAG or FFA correlated with neonatal weight, BMI and fat mass. In GDM, FFA levels had been the strongest predictor for neonatal macrosomia. Cord blood glucose, FFA and TAG positively correlated with birth weight and fat mass whereas in GDM a negative correlation between cord blood TAG and neonatal weight or fat mass was previously found.

Conclusions: In normal pregnancies, in contrast to GDM, maternal lipids do not influence fetal growth. Despite similar levels of maternal lipids in GDMs and controls, fetal lipids are higher in GDMs, indicating their enhanced placental transport and/or a different responsiveness of the fetus due to fetal hyperinsulinism.

PO-Geb 03.25

Homocysteine, Vitamin B6, Vitamin B12 and Folic acid concentration in pre-eclamptic women

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Objective: To investigate the relationship between pre-eclampsia and maternal blood concentration of homocysteine, Vitamin B6, Vitamin B12 and Folic acid. **Setting:** A Prenatal Diagnosis and Therapy Centre

of a Tertiary Hospital in Lagos. **Study and Design:** This is a cross sectional study

Materials and methods: 50 normal pregnant women with pre eclampsia and 50 healthy pregnant women were included in the study. Plasma homocysteine, Vitamin B6, Vitamin B12 and folic acid were assayed in all the pregnant women during the third trimester of pregnancy.

Results: Homocysteine plasma level were significantly higher in the pre-eclampsia group than in the control (11.48 + 5.61 $\mu\text{mol/e}$, 7.19 + 2.38 $\mu\text{mol/e}$ in the control group $P < 0.001$). Vitamin B6 (pyridoxal-5-phosphate) plasma level in pre-eclampsia group were lower than control group (5.97 + 2.76 $\mu\text{g/e}$ in pre-eclampsia group and 12.85 + 5.29 $\mu\text{g/e}$ in the control group $P < 0.001$). Vitamin B12 serum levels in the pre-eclampsia and the control group showed no significant difference (108.35 + 36.81 pg/ml in pre-eclamptic group, 121 + 46.92 pg/ml in the control group $P > 0.05$). Folic acid serum levels in the pre-eclampsia group were significantly lower (5.68 + 2.96 ng/ml in the control and 9.7 + 4.8 ng/ml in the pre-eclamptic group $P < 0.001$).

Conclusions: In the pathogenesis of pre eclampsia, high homocysteine levels and low Folic acid and Vitamin B6 levels play a role. **Keywords:** Pre eclampsia, homocysteine, Vitamin B6, Vitamin B12, Folic acid

PO-Geb 03.26

Persistent hyperemesis gravidarum as a symptom of a primary hyperparathyroidism

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Objective: Primary hyperparathyroidism in pregnancy is rare. Only about 200 cases have been reported in the literature. The prevalence in pregnant patients is underestimated due to changes in the hormonal milieu. Slightly elevated PTH and calcium levels may remain unnoticed. Primary hyperparathyroidism during pregnancy causes risks for mother and fetus, a particularly increased risk for preeclampsia is described. We present a case where persistent hyperemesis led to the diagnosis.

Materials and methods: A 35 year old woman IIIIG/0P presented in the University Hospital in Kiel at 21 weeks pregnancy with several days history of excessive nausea and vomiting. Hyperemesis had been a problem throughout pregnancy. First-trimester screening presented normal results with regular biochemistry. Ultrasound examination of the fetus and doppler parameters were regular. Calcium levels were elevated to 3.85 mmol/l (2.0–2.6 mmol/l), serum PTH amounted to 3315.7 pg/mol (1 15–65 pg/mol). An ultrasound examination of the neck revealed two hypochoic lesions of the left posterior lobe of the thyroid gland (2.3 × 1.4 × 0.8 cm), and posterior to the right lobe of the thyroid gland (0.6 cm), thus confirming the diagnosis of primary hyperparathyroidism. The patient subsequently underwent a para-thyroidectomy resulting in normal Calcium levels (2 mmol/l.) postoperatively. The rest of pregnancy was normal with vaginal delivery of a healthy female baby (3355 g).

Conclusions: In the literature, a significantly increased risk for both mother and fetus in untreated primary hyperparathyroidism is described, at a low prevalence of 0.15% in the pregnancy. This seems to rise up to 1.4% if one includes asymptomatic or unrecognized cases. As presented in this case report, the symptom of hyperemesis gravidarum with its unclear etiology led to the diagnosis.

PO-Geb 03.27**Evaluation of cervix length as predictive factor for successful labor induction for vaginal delivery**

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Objective: A variety of conditions in pregnancy require active obstetric management to end pregnancy. If time is not crucial, inducing labor is a lesser invasive alternative to caesarean section. In this study the cervix length as potentially predictive factor was evaluated regarding success of inducing labor for vaginal delivery.

Materials and methods: A retrospective study was performed from 8/2008–9/2009 at a university OB/GYN department. Included were all pregnant patients with completed 34th–42nd gestational week in which pregnancy could not be prolonged for fetal or maternal reasons. Excluded were all patients with emergency or elective cesarean section. In all other cases ($n = 59$) a standardized ultrasound measurement of length of cervix was done. Labor was induced according to DGGG guidelines with prostaglandins. All data was taken from medical files and statistical analysis performed.

Results: Patient age was $\bar{O}30.9$ years (16–44), gravidity 2.0 (1–6) and para 0.6 (0–4). The group included 59 deliveries with 64 neonates. Indication for inducing labor was $n = 39$ (66.1%) fetal and $n = 20$ (33.9%) maternal reasons. The vaginal delivery rate after labor induction was $n = 33$ (55.9%), vaginal-operative $n = 5$ (8.5%) and cesarean section $n = 21$ (35.6%). The vaginal delivery ratio with up to 76.5% ($n = 13/17$) in the 41st gestational week was in all gestational weeks higher or even the cesarean section rate, which prevailed in the 42nd gestational week with 71.4% ($n = 5/7$). Cervix length in vaginal group was 25.0 mm (4–58 mm), vaginal-operative 21.4 mm vs. vaginal 25.5 mm, in cesarean section group 28.7 mm (12–44). The preliminary results were n.s.

Conclusions: Due to small numbers and study concept, cervix length could not be identified as predictive factor for a successful induction of labor. Individual patient factors as well as professional aspects determine the birth mode, especially the predominating trend for cesarean sections in the 42nd week.

PO-Geb 03.28**Forceps delivery: a practical training DVD**

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Forceps delivery in Germany has declined once more from 1.4% to 0.7% between 2001 and 2008. This development can be explained by the tendency towards caesarean sections and the increasing percentage of vacuum extractions, which has increased from 4.4% to 5.3%. The reason for the decreasing amount of forceps deliveries is probably the attributed elevated maternal morbidity of forceps delivery. However, this delivery technique is an essential of the obstetrical repertoire. Specific indications for forceps delivery still exist especially when vacuum extraction does not work properly or is contraindicated. Among those indications are failed trial of vacuum extraction, premature birth before 35 + 0/7 gestational weeks, extensive caput succedaneum and occiput posterior position. In order to manage forceps delivery professionally it is essential for the obstetrician to know exactly the normal mode of delivery, birth mechanisms in prolonged labour and the technique of forceps delivery itself. In this practical video guide several didactical techniques—e.g. footage from delivery ward, use of obstetric mannequins and computer graphics—are used to present dedicated trainees more than plain text as a motivation to commit to this classical obstetrical method.

PO-Geb 03.29**Ovarian hyperstimulation syndrome in aneuploid pregnancy**

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Objective: Ovarian hyperstimulation syndrome occurs frequently after hormonal stimulation with human chorionic gonadotropin (hCG). Thus it must be assumed that hCG is a key factor in the pathogenesis of ovarian hyperstimulation syndrome. An association of aneuploid pregnancy with alterations in maternal serum hCG concentration has been described in the literature.

Materials and methods: A 40 year old patient presented to our clinic with severe ovarian hyperstimulation syndrome at 17 weeks of gestation of a spontaneous singleton pregnancy. The pregnancy had to be terminated shortly thereafter due to a vitally critical maternal condition caused by a beginning amnion infection syndrome. Karyotype analysis of the abort material showed a trisomy 16. In the follow-ups at the referring gynaecologist, the sonomorphologic polycystic aspect of the ovaries subsided entirely while serum hCG levels and infection parameters returned to normal values.

Conclusions: In cases of ovarian hyperstimulation syndrome in pregnancy that cannot be traced back to preceding exogenous hormonal stimulation, aneuploidy should be considered as a differential diagnosis.

PO-Geb 03.30**Spontaneous, VE-assisted delivery of a healthy child by a paraplegic woman without epidural anesthesia**

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Objective: Pregnant women with paraplegia have repeatedly been shown to be at an increased risk for autonomous hyperreflexibility and hypertensive crisis during and after delivery. To prevent and counter this condition elective epidural anesthesia is recommended.

Results: We report the case of a spontaneous, VE-assisted delivery of a healthy child by a paraplegic woman without epidural anesthesia. Epidural anesthesia is currently recommended for the delivery of paraplegic women as autonomous hyperreflexia and hypertensive crisis may be a complication for delivery. A 28 year old paraplegic GII/PO with a history of spinomedullary trauma at Th10 presented at 38 weeks of her pregnancy for induction as scheduled according to the recommendations for women with paraplegia. The history of her current pregnancy showed no significant pathological conditions, the induction period progressed well and epidural anesthesia was planned. However, in less than 15 min the cervix had dilated from 4 to 10 cm, followed by a sudden decrease in fetal heart-rate to 50 bpm. Elective epidural anesthesia could not be administered anymore, the call was made to perform a vacuum extraction: in the course a healthy child (APGAR 7/8/9) was born with the mother in continuously stable cardio-circulatory and neuro-muscular status. More specifically, no signs of autonomous hyperreflexibility were observed during the time of delivery and during the first days. This case report shows that autonomous hyperreflexia is not always a complication for spontaneous delivery in paraplegic women.

Conclusions: We report the case of a spontaneous, VE-assisted delivery by a paraplegic woman without epidural anesthesia and without development of maternal autonomous hyperreflexibility. Further research is required to identify parameters that may help to predict hyperreflexibility in paraplegic patients in order to plan for elective epidural anesthesia at an early stage of delivery.

PO-Geb 03.31**Preterm delivery with abscessing placenta mycosis and retained IUD**

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Objective: We report the case of an acute abscessing chorioamnionitis and funisitis by invasive candida with consecutive preterm labour. Pregnancy occurred under retained IUD.

Materials and methods: Admission of a 37 year old, gravida 7, para 6 at 30 weeks and 4 days of gestation with preterm uterine contractions and known presence of an intrauterine device (IUD). Patients' medical history comprised a preterm delivery at 28 weeks of gestation. Begin with lung maturation (Betamethason) and i.v.-tocolysis with Fenoterol. Cervical smear with habitual flora/without pathologic growth. After 18 h under tocolysis, premature rupture of the membranes and following CRP-increase occurred. Therefore induction of labour with prostaglandins was commenced. Spontaneous labour of a girl (1540 g, APGAR 1/4/7, Na-pH 7.39) 31 h after rupture of membranes. After initial respiratory problems age-appropriate development. Based on the suspicion of amniotic infection syndrome, antibiotic therapy of the newborn despite negative infection parameters was started. The placenta histology showed an acute chorioamnionitis and funisitis by invasive candida with abscesses. Primary smear from the newborn revealed candida in the ear and stool, however never signs of invasive candidiasis, and always negative infection parameters. Maternal smears were all negative for mycosis. Due to the histologic result initiation of a systematic therapy with Fluconazol for the mother, with liposomal Amphotericin B intravenously as well as topically and orally administered therapy with Nystatin for the child.

Conclusions: Cases of invasive mycosis are very rare in obstetrics. Still according to literature, pregnancies with a retained IUD are a particular risk collective for invasive mycosis. This is why in case of certain risk constellations the possibility of mycosis should be taken into account.

PO-Geb 03.32**Pregnancy progress in case of metastatical rectum carcinoma under chemotherapy and Avastin doses in early pregnancy**

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Objective: The treatment of a patient with a metastatical colorectal carcinoma is mainly palliative. Owing to a combine chemotherapy with 5-FU, FS and Irinotecan, a significant extension of the total survival time and the progressive-free interval has been demonstrated, which can be improved with a supplementary dose of Avastin. There

is little knowledge about the effects on a pregnancy, the most common dose is used in the 2./3. trimenon.

Materials and methods: A 37-year old 4 gravida 3. para in the 34 + 5 week of gestation is referred to our obstetrical consultation hour. The patient suffers from a rectum carcinoma with hepatic and pulmonal metastasis after operative therapy and an adjuvant chemotherapy according to the FUFIRI-protocol and Avastin (5 + 2 week of gestation). The pregnancy was determined in the 22 + 5 week of gestation with a control computer tomography. After a premature amniorrhexis the decision for a secondary cesarian section was taken as a result of a pathological CTG in the 36 + 4 week of gestation.

Results: Birth of a hypotrophic male premature infant in a moderate diminished general condition of health: birth weight 1770 g, length 42 cm, head circumference 32.5 cm. Additionally to a primary drink laziness the following features occurred: VSD, ASD, pulmonal stenosis, poly- and syndactylia of both hands, both thumbs anomaly and both hips joint luxation.

Conclusions: It is important to give empathically a detailed information to a sexual mature women about contraception before a planned chemotherapy. The patient has to be informed about the unknown facts of a chemotherapy during a pregnancy with all possible consequences. It is also significant to recommend a sufficient contraception after a completed treatment. The compliance of the patient is an indispensable condition for succeeding. We recommend a β -HCG test before the beginning of a zytostatical therapy or a consultation with a gynecologist.

PO-Geb 03.33**Acute lower limb compartment syndrome after cesarean section: a case report and review of the literature**

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Objective: Acute postpartal compartment syndrome of the lower limb (ACS) is a rare yet severe pathology encountered in obstetric patients, which requires undelayed diagnosis and treatment. The aim of our study was to further identify common causes, associated pathologies, presenting symptoms and treatment options in obstetrics patients with an ACS.

Materials and methods: A case report of a patient with ACS treated in our department and a review of the literature concerning ACS in gynecologic and obstetrical care.

Results: Prolonged episodes of hypotension during cesarean section, which might occur during extensive blood loss with subsequent hemorrhagic shock were identified as main risk factors for the development of a postpartal ACS. In the setting of vaginal delivery placenta retention was commonly associated with the onset of a postpartal ACS. Further predisposing factors for a ACS following labor, identified in our analysis were fluid deficit, the use of vasoconstrictive drugs, lithotomy position, prolonged surgery time, compressive bandages and obesity.

Conclusions: As the quality of the functional result in the setting of ACS is directly related to the promptness of diagnosis and surgical intervention, the knowledge of potential risk factors may be a valuable tool to correctly diagnose a postpartal ACS.

PO-Geb 03.34**Case report: fetal renal agenesis with contralateral hypoplastic kidney, postpartum development of adequate lung volume and neonatal peritoneal dialysis**

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Objective: Impaired fetal lung development is highly associated with decreased AFI in the 2nd trimester. We present the case of prenatal diagnosed unilateral renal agenesis and contralateral hypodysplastic kidney.

Materials and methods: Critical clinical case report.

Results: A 32 year old woman presented in our clinic at 30 weeks of gestation with anhydramnio since 24 weeks of gestation, renal agenesis of the right side and contralateral hypoplastic kidney. We ruled out premature rupture of membranes and applied betamethason for lung-maturation-therapy. Examinations by fetal-MRI or genetic testing were rejected by the patient. Fetal echocardiogram was regular but fetal lung-volume appeared to be reduced thus lung-hypoplasia had to be hypothesized. Due to preterm labour the patient was hospitalised at 33 weeks of gestation to get a second turn of lung-maturation-therapy because of limited neonatal prognosis. Fetal growth restriction was diagnosed <3 percentile. At 34 + 5 gestational weeks due to persisting preterm labour and vaginal bleeding delivery by caesarean section was performed (newborn parameters: 1980 g, pH art. 7.25, BE 1.6). The neonate was immediately transferred to the pediatric intensive care unit, where it had to receive peritoneal dialysis via Tenckhoff-catheter for rising renal parameters (creatinine 5.51 g/ml). Lung hypoplasia was confirmed and the child was intubated for 7 days due to beginning cyanosis. No other symptoms in terms of a Potter-Syndrome were detected. After 9 weeks of intensive care the child was dismissed in a sufficient health status. Transplantation of a kidney is planned after weight gain up to 10 kg.

Conclusions: Despite the severe bilateral kidney anomalies with oligo-anhydramnio since 24 weeks of gestation and consecutive hypoplasia of the lung the newborn reached satisfying pulmonary function under intensive care management and could be dismissed shortly with spontaneous breathing and adequate health status under peritoneal dialysis to aim for later kidney transplantation.

PO-Geb 03.35**The impact of prepartum anxiety on the incidence of surgical interventions during labour**

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Objective: Pregnancy and childbirth mostly represent a meaningful event in a woman's life. Especially for women who are pregnant for the first time pregnancy is often related to considerable changes. Although according to DSM-IV prevalence rates of mental axis-I-disorders do not generally increase during pregnancy, there are studies that found high prevalence rates of anxiety disorders during the postpartum period. The present study examined the question whether anxieties women suffer from during pregnancy have an impact on the course of childbirth and on the risk of a secondary caesarean section. It is assumed that on a physiologic level, anxiety

can disturb the natural process of birth due to altered hormone levels. Moreover, anxious women might have problems to relax.

Materials and methods: A sample of $N = 248$ women was recruited at the University of Heidelberg Women's Hospital. Prepartum anxiety was measured by the Anxiety Screening Questionnaire (ASQ) (anxiety), the State-Trait-Anxiety-Inventory (STAI) (anxiety) and by the Pregnancy Related Anxiety Questionnaire-Revision (PRAQ-R). Dependent variables were duration of labour and incidence of labour inducing procedures.

Results: The data show that pregnancy related anxiety measured by the PRAQ represents an important predictor of duration of labour. General anxiety which was not specific for childbirth did not contribute to duration of labour. Parity, peridural anaesthesia, inducing labour and birth weight were added as control variables to the regression analysis. The incidence of surgical procedures could partly be explained by regression analysis of pregnancy specific anxieties. This effect disappeared when parity and peridural anaesthesia were taken into the regression model as predictors.

Conclusions: Anxieties during pregnancy due to the exceptional situation and to upcoming delivery play an important role for the course of childbirth. Prospective studies should examine models on the aetiology of these anxieties.

PO-Geb 03.36**Early onset preeclampsia in a twin pregnancy with hydatidiform mole and coexisting fetus**

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Objective: We present a case of early onset preeclampsia in a twin pregnancy with hydatidiform mole after missed abortion of geminus II and a patient with a complete mole and a suspected twin pregnancy with good outcome for mother and neonate.

Materials and methods: At 24 + 0 weeks of pregnancy the patient was admitted because of preeclampsia and vaginal bleeding. Clinical chemistry showed severe anemia, HCG of 389855 mIU/ml and a hyperthyroid situation. Geminus I was vital, geminus II had been transformed to a giant mole. In the further course the symptoms aggravated; thyreostatic therapy was started in order to prevent thyreotoxic crisis. The patient received blood transfusions and antihypertensive medication, and magnesium was started as prevention of eclamptic seizures. Two days later she became oliguric without adequate rise in red blood count despite blood transfusions and abdominal symptoms worsened. In order to prevent further risk primary cesarean section was performed.

Results: The neonate was female; weight 560 g, APGAR score 4/7/7, pH 7.32, BE -3.7. She died after 3 days due to grade IV intracerebral hemorrhage. The mother had an intraoperative blood loss of approx. 2500 ml, postoperatively she was admitted to ICU for acute respiratory distress, interstitial lung edema and thyreotoxic crisis. On day 6 she could be discharged with almost euthyreotic values. In chest X-ray there was no sign of metastatic disease. Histology showed a hydatidiform mole without invasive growth. In the second patient, pregnancy could be prolonged until 33 weeks, when a healthy neonate was delivered.

Conclusions: These cases show that obstetricians should be aware of the rare situation after missed abortion of one geminus that there can be a transformation to hydatidiform mole. There need to be very close check-ups in order to prevent risks for the second fetus and the mother.

PO-Geb 03.37**Management during pregnancy and successful long-term therapy with subcutaneous protein C concentrate of a low birthweight preterm infant with compound-heterozygous protein C deficiency**

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Objective: In neonates with protein C deficiency the homozygous form regularly manifests as severe ophthalmic and cerebral vein thrombosis with purpura fulminans occurring even intrauterinely during late pregnancy. While the incidence of heterozygous congenital protein C deficiency is one in 200–300 births, the homozygous state is extremely rare. In case of a heterozygous protein C deficient mother and father the child has a 25% risk of being compound heterozygous protein C deficient, which equals functional homozygosity. **Results:** During pregnancy the mother's only treatment option with an acceptable and well defined risk profile after the first trimester were oral anticoagulants. Indeed, coumarin treatment resulted in significant elevation of the fetal INR as confirmed after delivery and can be viewed as effective in therapeutically inhibiting fetal coagulation. Maternal coumarin treatment was effectively antagonized for early planned cesarean section without influencing the fetuses' anticoagulant therapy at any point. In neonatal severe protein C deficiency the treatment options include fresh frozen plasma and protein C concentrate in the acute phase. The preterm infant was substituted with protein C intravenously until 3 kg of weight and corrected age of 38 weeks of gestation. Then the route of administration was switched to subcutaneous infusion resulting in nearly 40% reduction of protein C concentrate compared to intravenous infusion.

Conclusions: Prenatal diagnosis of fetal compound heterozygous protein C deficiency can be safely managed by maternal treatment with coumarins. Early planned cesarean section before 32 weeks limits significant maternal side effects and avoids the increasing fetal risk to develop intrauterine thromboembolic complications. After delivery intravenously administered protein C during prematurity and switching to subcutaneous infusion at 3 kg body weight resulted in sufficient protein C levels and enabled the family at-home treatment now for 2.5 years with excellent quality of life.

PO-Geb 03.38**Termination of pregnancy in a rudimentary horn of a bicornuate uterus at 12 weeks of gestational age**

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Objective: We report the case of a termination of pregnancy in a rudimentary horn of a bicornuate uterus in order to avoid the risk of uterine rupture and maternal hemorrhage.

Materials and methods: A 34 year old IIIg/Ip was diagnosed with a single pregnancy in a rudimentary uterine horn by ultrasound. Regarding her past obstetrical history she had one early miscarriage and an intrauterine fetal demise most likely due to placental infarction of unknown origin at 40 weeks of gestational age. During the first trimester of the current pregnancy an ultrasound revealed a uterine wall thickness of maximum 2 mm in the rudimentary horn. At the

implantation site of the placenta almost no uterine wall was detected as a possible sign for an accrete placenta.

Results: The following options were repeatedly discussed with the patient: continuing the pregnancy with a significant risk of uterine rupture in the second or third trimester followed by severe hemorrhage containing a significant risk of maternal and fetal mortality. Alternatively, the patient was counselled to terminate the pregnancy in order to avoid the mentioned risks. Finally, the patient opted to terminate the pregnancy at 12 weeks of gestational age. Thus, a laparotomy was performed and the rudimentary horn of the bicornuate uterus containing the viable pregnancy was removed completely. The postoperative course was uneventful.

Conclusions: A pregnancy in a rudimentary horn of a bicornuate is a rare condition with a significant risk for rupture of the uterine wall. In the literature there are only a few reports published, with only one out of nine reporting upon a successful pregnancy outcome. Therefore, prolongation of the pregnancy can only be justified with informed consent of the mother after thorough discussion of the risks for herself and the newborn.

PO-Geb 03.39**Multifactorial analysis of affinity: mass spectrometry data from serum protein samples. A strategy to distinguish patients with preeclampsia from matching control individuals**

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Objective: Preeclampsia is a major cause of maternal and neonatal morbidity and mortality. Preeclampsia usually manifests after the 20th week of gestation and is unpredictable in onset and progression. Early identification of the risk of developing preeclampsia would provide means for a better surveillance, and thus improve maternal and fetal outcome. In order to develop a strategy for a molecular-based diagnostic assay, we applied a multifactorial differential analysis of serum proteins using mass spectrometry.

Materials and methods: Samples from pregnant women with early-onset preeclampsia ($n = 11$) and gestational age matched pregnant women with uneventful pregnancies ($n = 13$) were assayed. Serum proteins were fractionated by magnetic beads (Profiling Kit 100 MB-HIC8, Bruker Daltonik, Bremen) and fractionated precipitation. Spectra were recorded with a Reflex III MALDI ToF MS (Bruker Daltonik) in linear positive ion mode in the mass ranges from 4–25 kDa and 20–250 kDa. Spectra were reproducible and rich of signals with a good signal to noise ratio. Statistical analysis was performed with the ClinProTools (Bruker Daltonik) software package.

Results: The on average most abundant ion signals were observed at m/z 9.390, 9.103, and 8.886. The best differentiating ion signals between the two sample groups were found at m/z 13.715, 13.834, and 13.891. The underlying proteins of these three signals were identified as transthyretin along with its posttranslational modified variants. Nephelometric measurements supported the tendency of a lower transthyretin concentration in preeclampsia. Ratios of peak intensities of all six ion signals enabled us to create cut off values by which preeclampsia were successfully classified from controls with a sensitivity of 91% and a specificity of 92%.

Conclusions: Our findings support the hypothesis of preeclampsia being a heterogeneous disorder that might be classified by a defined proteome signature in maternal blood using multifactorial analysis of affinity-fractionated serum samples.

PO-Geb 03.40**Detection-rates and false-positive-rates in comparison of 36 weight estimation formulae in macrosomic fetuses**

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Objective: The aim of this retrospective study was to compare the accuracy of 36 commonly used weight estimation formulae in macrosomic fetuses.

Materials and methods: Fetal weight estimation was carried out within seven days up to delivery in 350 singleton fetuses with a birth weight of ≥ 4000 g. The accuracy of the different weight estimation formulae was compared by firstly, the mean percentage and absolute percentage error, secondly, by the frequency distribution of differences between estimated fetal weight and fetal birth weight, and thirdly by comparing detection and false positive rates in screening for fetuses with a birth weight of 4000, 4300 and 4500 or more.

Results: Mean PE ranged from -62.2 to 9.6% and was closest to 0 with the Hard formulae. With 12 of the 36 weight estimation formulae mean APE was 10% or less, smallest with the Hart formulae (3.9%). The mean detection rate among all formulae for fetuses with a BW ≥ 4000 g, ≥ 4300 g and ≥ 4500 g was 29, 24 and 22% for respective mean false positive rates of 12% (for ≥ 4300 g) and 7% (≥ 4500 g). A detection rate of 50% or more was achieved with five formulae.

Conclusions: Some formulae showed advantages as far as mean and absolute percentage errors were concerned. But none reached a detection rate and false positive rate for fetuses ≥ 4500 g that could lead to clinical recommendation.

PO-Geb 03.41**Prenatal diagnosis of spina bifida: sonographic “head signs” show an association to poor motor outcome**

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Objective: To analyze the spectrum of sonographic signs in fetuses with spina bifida and to determine their impact on functional outcome in infants with spina bifida.

Materials and methods: Prenatal ultrasound examinations of all fetuses with prenatally confirmed spinal dysraphism between 1993 and 2009 ($n = 109$) were reviewed for myelomeningocele, “lemon sign”, “banana sign”, ventriculomegaly, talipes and level of the spinal defect. These signs were correlated with the antenatal course and the postnatal outcome (e.g. psychometric development, bladder and intestinal function) of all live-born children.

Results: The spectrum of prenatal ultrasound signs comprised 41 cases with myelomeningocele (37.6%), 52 cases with “lemon sign” (47.7%), 55 cases with “banana sign” (50.4%). Forty-two fetuses had a ventriculomegaly (38.5%) and in 23 cases talipes (21.1%) were diagnosed. The level of spina bifida was mainly the lumbosacral region in 70% (76 cases) or the thoracal region in 23% (25 cases). 72 pregnancies (66%) were terminated on parental request, 33 individuals were born alive (30.3%). Postnatal follow-up revealed 6 children (26%) with an impaired mental development. 10 individuals were wheelchair-bound (43.5%). 73.9% of the affected individuals suffered

from an impairment of bladder function and 36% showed a disturbed bowel control. 5 children died (4.6%) within the first year of life. The occurrence of poor motor function was significantly higher when “banana sign” (OR 13.3, 95% CI 1.78–100.14, $p < 0.05$) or ventriculomegaly (OR 20.3, 95% CI 1.88–218.39, $p = < 0.05$) were present during prenatal ultrasound exam.

Conclusions: Ultrasonographic finding of specific head signs appears to be associated to poor motor function in children affected by spina bifida. Due to the relatively small sample size, further studies are needed to confirm these findings.

PO-Geb 03.42**Seroprevalence of Parvovirus B19 from Lagos prepregnancy class. A retrospective analysis**

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Objective: An acute PVB19-infection of the mother during pregnancy can give rise to a high morbidity and mortality rate for the fetus and possibly through cardiac mispersistence to a cardiovascular risk for the mother.

Materials and methods: Since there is little valid information on the rate of Parvovirus B19 infection in reproductive age in our environment, we therefore decide to study the seroprevalence of this virus in patients attending the prepregnancy class. Setting: A Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos. Blood samples were tested serologically by ELISA technique for Parvo virus 19-IgG and IgM. No PVB19-DNA test was done in Parvovirus IgG/IgM positive patients in this study.

Results: Between February 2004 and June 2009, a total of $n = 510$ Patients (106 males/ 401 females and 3 unknown sex) were screened for Parvo IgG serologically using ELISA technique (DIA. PRO Diagnostic Bioprobes Srl, Milano, Italy). Out of 106 males screened 83/106 (78.3%) were IgG positive and out of 401 females screened 304/401 (75.8%) were IgG positive and out of the 3 unknown sex, 2 were IgG positive. Out of 358 patients who were IgG positive, 42 (61.8%) males, 148 (53.8%) females and 3 (100%) of the unknown sex were IgM positive to Parvovirus B19.

Conclusions: Our study shows that there is a high carrier rate of PVB19 in the population and this could be contributory to the high fetal morbidity and mortality rate and all patients should be screened before pregnancy.

PO-Geb 03.43**Treatment of growth restricted human fetuses with amino acids and glucose supplementation through a chronic fetal intravascular perinatal port system**

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Objective: Intrauterine growth restriction (IUGR) carries an increased risk of mortality and morbidity. The accepted procedure to treat IUGR fetuses is the preliminary delivery which may increase neonatal mortality and morbidity and deteriorates neonatal brain development.

Materials and methods: We report here on intravascular supplementation with amino acids and glucose of IUGR human fetus at 33 weeks of gestation with oligohydramnios and placental insufficiency using the port system (Norfolk Medical, Illinois, USA). The catheter was implanted into the umbilical vein (UV) by cordocentesis, and was then connected to subcutaneously implanted port system. The treatment course included daily infusions of amino acid solution and 10% glucose into UV.

Results: Daily intravascular fetal nutrition significantly improved both fetal condition and fetal weight gain. No complications were seen. The patient was delivered by cesarean section in 38th week of gestation. The female newborn weighted 2130 g and was 47 cm high. Blood sampling from UV after delivery showed no deviations of amino acids in comparison to standardized curves. In 1 year follow-up the child's development and the weight gain, was like these of children without IUGR in the anamnesis.

Conclusions: This is the first report of successful use of subcutaneously implanted intravascular perinatal port system in IUGR human fetuses for long term administration of nutrients into UV of fetus for treatment of IUGR and prolongation of pregnancy.

PO-Geb 03.44

Changes of angiogenic factors in severe HELLP-syndrome after fetal termination

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Objective: Preeclampsia is defined by high blood pressure and proteinuria in pregnancy. As a severe subtype of preeclampsia, HELLP-syndrome exhibits abdominal pain and typical laboratory signs in platelet count, liver enzymes and haemolysis markers. Preeclampsia is accompanied by a rise of angiogenic factors like sFlt1, which is a soluble VEGF receptor fragment and a decline of PlGF (placental growth factor) both produced by the placenta. These factor concentrations are in balanced relation in normal pregnancy. There are numerous studies about dynamics of angiogenic factor in clinical course of severe preeclampsia. Furthermore, there are hints and observations that fetal loss or termination leads to improvement of maternal condition in the case of severe early-onset preeclampsia.

Materials and methods: We report a case of a 29 year old primigravida in the 22 + 1 week presenting with signs and symptoms of an early severe HELLP-syndrome. At admission she was complaining of upper abdominal pain. Severe hypertension required urapidil i.v. medication. In addition, we report elevated liver enzymes and proteinuria of 1.5 g/24 h. Sonography showed a highly echogenic and thickened placenta. Because of the immaturity of the fetus and the severity of the disease, termination of pregnancy with fetocid was indicated. The quotient of sFlt1/PlGF was followed up very closely. Together with platelets and liver enzyme level dynamics of the named parameters are given. After fetocid, the sFlt1/PlGF ratio fell off 41% and raised again later. After expulsion of the placenta, the ratio went down to 41.

Conclusions: Termination of pregnancy due to the maternal condition can be necessary in very dramatic and early-onset forms of hypertensive complication in pregnancy. Little is known about effects of fetal death on angiogenic factor concentration. Breakdown of the fetoplacental circulation leads to a partly and temporary decline of the angiogenic ratio. Removal of the placenta is needed to stop finally the production of the anti-angiogenic surge.

PO-Geb 03.45

Fetal renal insufficiency following valsartan and trastuzumab in pregnancy: three case reports with different intrauterine course and outcome

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Objective: Some drugs are known for their fetal nephrotoxicity and are therefore contraindicated during pregnancy. However for many innovative drugs only scant data exist on the effect on the fetus and on their use during pregnancy. We report on three cases of drug-induced renal insufficiency with different intrauterine course and outcome.

Materials and methods: Case 1: A pregnant woman suffering from breast cancer received a neoadjuvant trastuzumab (Herceptin[®]) therapy from 16 weeks onward. Fetal renal insufficiency with anhydramnios and missing visualisation of the fetal bladder developed at 21 weeks of gestation. After discontinuation of Trastuzumab and repeated weekly instillation of amniotic fluid, spontaneous resolution of fetal renal function was noted at 24 weeks. The further course of pregnancy was complicated by massive intrauterine growth restriction. After caesarean section at 32 weeks the postnatal development and the renal function were normal. Case 2 and 3 both received valsartan during pregnancy (case 2 Diovan[®], case 3 Cordinate[®]). In Case 2 fetal renal insufficiency with anhydramnios was observed at 21 weeks. After discontinuation of Valsartan spontaneous resolution of fetal renal function was noted and a healthy male neonate with normal renal function was born at term. In case 3 the Valsartan-therapy was unknown to the attending physicians. At 32 weeks of gestation she presented with anhydramnios and preterm labour. The kidneys were massively enlarged and a biochemical examination of fetal cord blood confirmed terminal renal insufficiency with elevated cystatin C and beta 2 microglobulin levels. Following preterm delivery the renal function remained insufficient and the infant now requires dialysis.

Conclusions: During pregnancy the application of Valsartan and Trastuzumab should be avoided if possible. In pregnancies exposed to Trastuzumab or Valsartan the treatment should be discontinued and the fetus should be closely monitored with particular attention to the amniotic fluid volume as this reflects the fetal renal function.

PO-Geb 03.46

Seroprevalence of cytomegalovirus in Lagos prepregnancy class population 1997 to 2009

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Objective: There is a little information on the incidence and prevalence of Cytomegalovirus (CMV) Infection in Lagos/Nigeria. The risk of congenital cytomegalovirus in sero-positive pregnant women has been found to produce congenital abnormalities even in developed countries. The aim of the study is to determine the seroprevalence of cytomegalovirus antibody in prepregnancy class population of men and women. Setting: A Prenatal Diagnosis and

Therapy Centre of a Tertiary Hospital in Lagos. Study and Design: This is a cross sectional study of men and women attending the prepregnancy class facilities in the centre.

Materials and methods: Between June 1997 and December 2009, the seroprevalence of Cytomegalovirus was determined in this study from 2,857 men and women. A total of 1,547 CMV IgG sero-positives, were screened for IgM seropositivity using ELISA kits.

Results: A total of 190 (22.1%) males out of 860, 388 (19.8%) females out of 964 and 7 (21.2%) unknown sex out of 33 were found to be susceptible to CMV infection. The infection seropositivity rate related to prior infection were 77.9% (670) in males, 80.1% (1,576) females and 78.8% (26) unknown sex. CMV IgM seropositivity was found in 23.8% (99) out of 416 males, 32% (353) out of 1,103 females and 21.4% (6) out of 28 unknown sexes.

Conclusions: This prevalence of CMV antibody in prepregnancy class population of men and women shows high susceptibility and reinfection or active infection rates, leading to a high risk of transmission among couples.

PO-Geb 03.47

Prenatal and postnatal findings in a case of non-mosaic trisomy 22

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Objective: Early intrauterine growth restriction (IUGR) combined with structural anomalies is a frequent sign of chromosomal abnormalities.

Materials and methods: A 43 year old woman who had one prior pregnancy loss and was mother of one healthy child, was referred because of IUGR at 25 weeks gestation. Nuchal translucency examination and fetal karyotyping had been declined. Prenatal ultrasound revealed a dolichocephalus, flat profile, hypertelorism, unilateral renal agenesis and suspected contralateral renal hypoplasia, hypospadias and a single umbilical artery. After detailed counselling the parents decided in favour of the pregnancy and against karyotyping. Weekly ultrasound and Doppler examinations showed inadequate fetal growth and increasing signs of placental insufficiency. At 35 + 5 weeks a male infant was delivered by primary cesarean section (birth weight 1630 g). The major additional postnatal findings were multiple craniofacial stigmata, mild aortic coarctation, anal atresia and scrotum bipartitum. Genetical testing of lymphocytes and fibroblasts showed an additional chromosome in all analysed metaphases which was identified as chromosome 22 by in situ hybridization: 47, XY, +mar.ish22q11 (D22S75 × 3). ish22qter (×3). Because of the poor prognosis therapeutic interventions were not intensified. At the age of four weeks the child died of renal insufficiency.

Conclusions: Non-mosaic trisomy 22 is a rare finding in IUGR combined with structural anomalies. Due to multiple malformations the rate of life births as well as the postnatal survival rate is low. In this case the condition could be observed throughout ten prenatal weeks and 4 weeks after birth.

PO-Geb 03.48

Case report: prenatal diagnosis of an intestinal volvulus

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Fetal intestinal volvulus is a rare entity, mainly caused by intestinal malrotation or meconium ileus. Meconium ileus in combination with volvulus shows a high perinatal mortality and morbidity. Therefore an early diagnosis is essential for optimal treatment in order to improve neonatal outcome. Volvulus presents with a variety of symptoms. A definitive diagnosis by prenatal ultrasound has been described only in a few cases. We report a case of mild fetal bowel dilatation at 30 weeks of gestation with development of extreme bowel dilatation and volvulus, presented by the 'whirl-sign', in combination with fetal ascites and polyhydramnios at 33 weeks of gestation. At this time cardiotocography and umbilical artery blood flow were normal. Due to the ultrasound findings, elective cesarean section was performed in spinal anesthesia. A male neonate was delivered weighing 2620 g, Apgar scores of 9 at 1 min and 5 min each. Urgent laparotomy verified the diagnosis of meconium ileus with intestinal volvulation, and intestinal perforation. Resection of a long segment of necrotic ileum and enterostomy were necessary. The genetic testing showed a homozygous mutation ΔF508 of the CTFR gene. This case shows the importance of careful examination of the fetal intestine by routine ultrasound, and if necessary the need for rapid decisions for elective delivery to optimize neonatal intensive care and to allow early surgical treatment.

PO-Geb 03.49

Successful pregnancy after myocardial infarction

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Objective: Pregnancies after myocardial infarction are rare. Main reasons in young women are adipositas, smoking, hypertension, diabetes and frequently disorders of fat metabolism. Due to improved survival after myocardial infarction these young patients will be seen in a pregnant condition. We report of a 27 year old 1. Gravida/Nullipara (163 cm/54 kg) and status post inferior myocardial infarction at the age of 23 with cardiovascular arrest, ventricular fibrillation and reanimation. Coronary angiography showed an occlusion of the right coronary artery, which was re-canalized by stent in the same intervention. No history of smoking or thrombotic events in her own or family history was stated. After exclusion of thrombophilic risk factors a hyperlipoproteinaemia was discovered. Among therapy with statins and Omega-3-Acidethylester

normal blood fat results were achieved. Secondary prevention for coronary artery disease takes with acetylsalicylic acid (ASS) 100 mg/day and metoprolol 47.5 mg/day. After diagnosis of pregnancy medical care in our high risk pregnancy outpatient clinic took place every 4 weeks. The cardiologist performed cardiac control. Left ventricular ejection fraction was normal. Statins were dropped, Omega-3-Acidethylester, ASS 50 mg and metoprolol were continued. Cesarean in intubation narcosis was planned for 38 weeks of gestation (WOG) and anti thrombotic therapy after cesarean medication was changed to ASS 100 mg/day and low fragmented heparin after pre-deliver interdisciplinary counseling. But emergency cesarean was performed under ASS 50 mg/day at 34 weeks of gestation due to a vaginal bleeding (healthy newborn). Post caesarean course was normal, no clinical complains, ECG-variations or troponin T increase were observed. Statin treatment was discontinued due to post partum increased maternal blood fat results, heparin discontinued.

Conclusions: Pregnancy after myocardial infarction represents a risk factor. An early interdisciplinary surveillance is mandatory during the whole pregnancy. The best way of delivery is cesarean about the 38th WOG.

PO-Geb 03.50

Diagnosis and management of an unilateral giant fibroadenoma of the breast in pregnancy

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Objective: Fibroadenomas represent the vast majority of breast pathologies in young women. 2–4% of the fibroadenomas exceeds 5 cm in size or 500 g in weight and are called giant fibroadenomas. Due to their excessive growth they are usually enucleated to clarify a malignant origin and to prevent persisting deformities of the breast. The benign giant fibroadenoma has to be differentiated from phylloides tumors which hold a malignant potential.

Materials and methods: We present a 17 year old female who was pregnant in the 24th week and suffered from a giant fibroadenoma in the right breast. Besides massive and painful swelling of the breast since 8 weeks no other abnormalities were found. On clinical examination we found a mobile tumor of more than 10 cm in size with dilated veins and an erythema on the skin surface. A prior performed biopsy and ultrasound could not definitely differentiate the mass from a phylloides tumor. Because of the rapid growth and progressive deformation of the breast an enucleation was performed without complications under perioperative control of the fetal well-being by CTG and ultrasound. After pathologic examination the tumor- size was determined 13 × 12.5 × 4.5 cm with a final weight of 456 g. Histologically a fibroadenoma with signs of chronic inflammation was confirmed. The patient did well in the long- term follow up with an adequate cosmetic result. A reconstruction because of the pronounced ptosis was delayed until the end of puerperal. No affection of the newborn was noticed after delivery.

Conclusions: We present a rare case of a giant fibroadenoma in a pregnant young woman. Because of the progressive structural damage of the breast immediate surgical enucleation was indicated. Safety of the fetus was provided by perioperative monitoring. Besides the preoperative differentiation from phylloides tumor is still challenging.

PO-Geb 03.51

Diagnosing vaginal microflora disbalance in pregnant women using culture- and PCR-based T-RFLP analysis

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Objective: Bacterial vaginosis (BV) is a prevalent infection in women of reproductive age associated with numerous sequelae, including preterm delivery, amniotic fluid infection and an increase in risk of acquiring sexually transmitted disease. Diagnosis of BV is based on the presence of clinical signs as well as microbiological findings. Among the many laboratory methods used for the diagnosis of BV the Gram-stain criteria as defined by Nugent et al. are currently regarded as the standard procedure. Although this method has been repeatedly refined, morphological assessment alone may not reflect the microbiologic variations among BV individuals and should be extended by molecular methods. Quite recently we have shown that the PCR-based terminal-restriction-fragment-analysis (T-RFLP) provides a reliable technique to allow differentiation of the fluid of BV and healthy women. However, for prevention early detection of clinically relevant disturbance of the vaginal flora is necessary.

Materials and methods: Vaginal swabs from 163 pregnant women were analyzed by Nugent score, conventional culture and identification and T-RFLP as described previously by Thies et al.

Results: According to Nugent score 18 patients had BV which was verified by T-RFLP pattern. Among the remaining 146 specimen in 22 samples only lactobacilli were found. In addition to lactobacilli *Enterococcus faecalis*/koagulase-negative staphylococci (KNS)/E. faecalis + KNS/E. faecalis + *Escherichia coli* were detected in 14/36/27/27 specimen. However, culture results could not reflect the degree of vaginal flora disturbance. In contrast, using T-RFLP analysis covering aerobic and anaerobic microorganisms we could detect distinct pattern of phylotypes representing different degrees of microbiota disturbance. **Conclusions:** We have established a T-RFLP profiling as a molecular tool to consider the microbial community as a whole and to characterize subgroups of women who are prone to develop BV.

PO-Geb 03.52

Comparison of fetal MR imaging and US for diagnosis of fetal anomalies except of cerebral anomalies

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Objective: Ultrasound as the primary screening modality is used to detect fetal anomalies. The fetal MRI is further an increasingly used method to detect fetal anomalies. Because of the excellent soft tissue contrast and the large field of view sonographic gastrointestinal findings could be completed or further anomalies could be discovered. The aim of the study was to prove the additional value of fetal magnetic resonance imaging (MRI) for the diagnosis especially of fetal anomalies except of extracerebral anomalies.

Materials and methods: In 44 pregnant women with fetal anomalies diagnosed at US were evaluated. The gestational ages of the fetuses

ranged from 18–38 weeks. In these fetuses, prenatal MR imaging was performed within 14 days of US. 39 examinations were performed with a 1.5-T system, 5 examinations were performed with a 3-T system. TRUFI, HASTE and T1f2D sequences were acquired. Prenatal US and MR imaging findings were compared with postnatal diagnosis.

Results: Fetal anomalies involved the cardiopulmonary system, the musculoskeletal system, the genitourinary system and the gastrointestinal system. In 19 diagnostic cases, US and MR imaging findings were in complete agreement with postnatal diagnoses. MR imaging correctly provided additional information to the US determined diagnosis in another 6 cases and correctly changed the US diagnosis in 4 cases. MR imaging provided more information than did US in 7 cases. In 2 cases, the diagnoses at both US and MR imaging were incorrect when correlated with the postnatal outcome. The US yields a sensitivity of 67% and a specificity of 90%, the fetal MRI yields a sensitivity of 82% and specificity of 95%.

Conclusions: Our results showed that fetal MRI has a high impact as an addition to ultrasound in evaluating of fetal anomalies.

Gynecology

PO-Gyn 03.01

Treatment of endometriosis with GnRH-analogues: how do patients and their gynecologists comply with recommendations of a certificated level III center for endometriosis?

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Objective: Nearly 10% of sexually mature women suffer from endometriosis. Depending on stage and symptom severity a postoperative treatment with GnRH-analogues, oral contraceptives, Mirena-IUD or, in case of desired pregnancy, assisted reproductive technologies is advantageous.

Materials and methods: In 2007 and 2008, 692 endometriosis patients were operated in the DEZB and 437 (63%) of them received a recommendation for postoperative treatment. A standardized survey was conducted to determine whether or not patients followed the provided advice and if symptoms lessened. Basic facts such as age, preoperative complaints, primary or secondary infertility, BMI, social status or inability to work were considered.

Results: In total, data from 360 women (82%) was collected of which 263 women (73%) followed the postoperative medical advice and 214 of them (81%) felt symptom improvement. In 46 cases (17%) the symptoms did not change and three women (1%) felt worse. On the other hand, 97 patients (27%) did not comply. Of those, 51 (52%) felt better without postoperative treatment, 43 (44%) felt no change and in three cases (3%) symptoms worsened. The primary reason for treatment rejection was the wish for alternative treatment choices (31 cases/32%), such as homeopathy or TCM. Sixteen women (16%) criticized that cost of hormonal therapy and in 14 cases (14%) the gynecologist opted for a different treatment choice. Other reasons included the fear of side effects of hormonal treatment or the rejection of infertility treatment.

Conclusions: For optimal patient care it is important to know if women comply with our recommendations and if endometriosis symptoms are reduced thereby. We are dependent on patients' and treating gynecologists' compliance which are essential in the evaluation of our quality of treatment.

PO-Gyn 03.02

Ajust™ fully adjustable single incision sling for the treatment of stress urinary incontinence: 1 year follow-up on a new minimal-invasive treatment for female SUI

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Objective: Suburethral slings achieve excellent success with high continence rates in stress urinary incontinence. Conventional retro-pubic or transobturator tapes actually are preferred by most surgeons, but shows side effects and complications because of the blind passage of the tape. The sling Ajust™ has eliminated the need for blind trocar passing, utilizing a single vaginal incision and a push-in technique and allows a post-insertion bi-directional adjustability (loosen and tighten) after strong anchoring in obturator membrane. This study evaluates the efficacy and safety of this new procedure with 1 year clinical outcome.

Materials and methods: In our prospective, single-arm, observational study 52 patients with a mean age of 62.8 years (range 39–88 years.) were treated from November 2008 to March 2009 with Ajust™ in 4 centres. Each patient had a fully urogynecological assessment. Quality of Life was to be assessed using Kings Health Questionnaire, Patient Perception of Intensity of Urgency Scale, Visual Analog Score for pain and global satisfaction and short form of UDI 6 and IIQ7.

Results: These are first results after 1 year of 52 patients. All but 1 (98.1%, 51/52) of the Ajust Sling placement procedures was initially successful, changing in 1 case intraoperatively to TOT system. No complication of bleeding >200 ml, bladder lesions, erosions, perforations, hematomas or bladder outlet obstructions occurred during the period covered by this analysis. Overall, out of the 50 subjects who successfully received the Ajust Sling, 48 subjects demonstrated total restoration (86.5%) of their continence, 1 subject demonstrated improvement (2.0%).

Conclusions: First results showed a high efficacy with excellent continence rates because of the strong anchoring in the obturator membrane and no severe side effects in fact of using a small mini-sling and possibility of bi-directional adjustability after insertion. Further prospective studies with a longer follow-up have to prove the high efficacy.

PO-Gyn 03.03

Reoperation for pelvic organ prolapse within 10 years of primary surgery for prolapse

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Objective: The lifetime risk of undergoing at least one operation for pelvic organ prolapse (POP) or urinary incontinence is reported to be 11%. However, there are few data on the reoperation rate after primary surgery for POP. A recent American study found a 10-year-

reoperation rate of 17%. In recent years, new surgical concepts and procedures for treatment of POP have been developed and brought to market. A justification for the new techniques is the assumption of poor long-term results with the established operations. Long-term outcomes are essential to evaluate both established and new surgical procedures. The aim of the present study was to determine the reoperation rate within 10 years after primary surgery for POP.

Materials and methods: In a retrospective study we reviewed all patients who underwent primary surgery for POP at 4 large regional centers in 1997 and 1998. Hospital databases were searched to determine whether the patients had been reoperated through 2008. Reoperations for incontinence were not counted.

Results: A total of 456 patients underwent a primary operation for POP in 1997 and 1998. The most common primary operation was vaginal hysterectomy with colporrhaphy (89% of primary procedures). We identified 13 reoperations for prolapse, for a reoperation rate of (at least) 2.9%. The median interval between the operation and reoperation was 5.5 (1.5–10) years. The sacrospinous ligament fixation (Amreich-Richter) was the most common reoperation method (46%, $n = 6$) used. The mean age at the time of primary operation was 62 (31–93) years.

Conclusions: The reoperation rate for prolapse after primary vaginal hysterectomy and colporrhaphy for prolapse in this series appears to be modest. Surgery for pelvic floor disorders is common but it remains difficult to determine the long-term efficacy of these procedures and even to define success.

PO-Gyn 03.04

Pelvic floor ultrasound evaluation of TVT-O: do we place the tape where it is supposed to be?

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Objective: Significant differences exist in urethral length and mobility in incontinent women. Therefore, individual and exact placement of any anti-incontinence tape is assumed to be crucial for success. The aim of this study was to explore the differences between planned and achieved position of TVT-O.

Materials and methods: TVT-O surgery was performed in 63 incontinent women. The first 29 operations were performed according to the 1/3 rule—incision starting at 1/3 of the ultrasonographically measured urethral length (standard technique for TVT placement at our department). Due to unsatisfying results, we then switched to start the incision at 1/2 of the urethral length. Ultrasonographically assessed TVT-O biomechanics showed reduced mobility of the TVT-O compared with the TVT. We changed our approach assuming that results can be improved by TVT-O placement closer to the high pressure zone. Success was assessed 6 months after surgery, calculating the difference between planned and achieved TVT-O position according to the formula: planned LUTL (longitudinal urethral tape localization) minus achieved LUTL. + means a deviation toward the bladder base, – to the external urethral orifice.

Results: Deviations in the group operated according to the 1/2 and 1/3 rule were between + and –3 mm in 76% of women and between + and –3.5 mm in 84%. The greatest deviation was –8 mm in one case; all other deviations ranged between –6.8 mm and +4.3 mm.

Conclusions: In most cases, deviations did not exceed ± 3.5 mm, suggesting that the technique is precise and that the tape stayed where it was planned and placed and did not move after insertion at the 6-month follow-up.

PO-Gyn 03.05

Interdisciplinary treatment of genital descensus and coloproctical diseases: functional results after surgery

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Objective: Patients with genital prolapse often suffer from coloproctological diseases like the rectum prolapse with symptoms of obstipation and/or fecal incontinence. The purpose of the investigation was to determine the functional aspects of the anatomical defects by reconstruction of the anatomy. For example the symptom of fecal incontinence was examined before and after combined interdisciplinary prolapse-surgery.

Materials and methods: In the years 2004–2008, 313 patients with genital prolapse were treated in the Saint Josefs-Hospital in Wiesbaden. 38 of these women (average age 61.3 years) had a complete genital prolapse with rectum prolapse III°. The patients were seen by a gynecologic pelvic surgeon and a coloproctologist for initial diagnostic workup. The diagnostic workup of symptoms included the standard gynaecological speculum examination, bimanual examination, proctoscopy and colonoscopy. The patient was seen and examined 6 months post-operatively, after the specific surgical procedure was performed as determined by the interdisciplinary team. The examination results were evaluated to compare the pre- and post-operative findings.

Results: None of the 38 women had a recurrence of genital—or rectal prolapse. None reported genital discomfort. 4 patients with urinary incontinence were improved or cured subjectively. 6 women reported worsening of urinary incontinence symptoms and 6 reported incontinence who had no prior symptoms. Half of the patients with fecal incontinence were cured or were improved.

Conclusions: While surgical repair of pelvic prolapse is not a specific treatment for incontinence, in its preference it is a obligatory prerequisite for effective surgical treatment for urinary and fecal incontinence. Before the treatment of a combined urogynecological or coloproctological suffering the patient must be cleared up about the fact that an intervention like reconstruction of the anatomy is not synonymous with the immediate regaining of the organ function, and that for this if necessary another intervention or therapy could be necessary.

PO-Gyn 03.06

Assessment of quality of life in urogynaecological patients: the use of validated questionnaires

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Objective: The aim of this study was to review current literature on German pelvic floor questionnaires and to design and validate a pelvic floor questionnaire with an additional post-treatment module including improvement and satisfaction scales.

Materials and methods: Comprehensive pubmed literature search. Face and convergent validity and reliability testing was performed in a new German pelvic floor questionnaire on 80 patients before and after conservative or operative treatment for pelvic floor disorders.

Results: Literature search revealed that there was no German questionnaire that assesses all pelvic floor symptoms including bladder, bowel and sexual function and prolapse symptoms, symptom severity, impact on quality of life and bothersomeness in women with pelvic floor dysfunction. The new German pelvic floor questionnaire performed well. Missing data did not exceed 4%. Improvement and

satisfaction scales correlated significantly with bladder and bowel domain scores. Test-retest reliability showed moderate to good agreement. The questionnaire was sensitive to change with a large effect size. Results of an interviewer-administered version of the questionnaire were similar to the self-administered questionnaire.

Conclusions: The validated German Pelvic floor Questionnaire including a post-treatment module assesses symptoms, improvement and satisfaction in a reliable and reproducible fashion. There are no comparable instruments available in German. The German Pelvic Floor Questionnaire can be integrated in a routine urogynaecological clinic employing an interviewer- or self-administered version. To conform to international recommendations, the self (patient) - administered questionnaire should be used for outcome research.

PO-Gyn 03.07

Surgical treatment of complications with alloplastic slings and meshes

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Objective: This was an analysis of 350 consecutive patients within the last 5 years referred to the department of Obstetrics & Gynaecology of the Helios-Clinics in Schwerin.

Materials and methods: 350 patients have been examined pre- and intraoperatively by history, ultrasound, photo documentation, gynaecological and cystoscopic examination. The complications observed included abscess formation, hematoma, penetration of the urogenital tract, defect healing, voiding dysfunction and overactive bladder.

Results: The most frequent problem was wrong technique (46%) either not staying “tension-free” provoking obstruction or wrong placement of the sling at the bladder neck or even bladder base of extending the mesh to the suburethral area. 42% demonstrated a marked paravaginal defect with nearly complete disruption of the vaginal fixation to the pelvic side wall, which apparently is better cured by colposuspension rather than a distal sling. Obesity, nicotine abuse, multiple previous surgeries and urogenital aging are factors predisposing for penetration of the organs or defect healing. Transobturator slings or meshes have an increasing frequency of dyspareunia and pain in the legs or groin which is difficult to treat because if the non-accessible parts behind the obturator fascia. Multiple slings and meshes in failures were apparently no solution; we have even seen women with up to 4 slings.

Conclusions: We reviewed 350 patients with complications after sling and mesh implantation. Reasons were mostly wrong technique (46%), wrong indication (42%) and wrong patient selection. Alloplastic slings and meshes are a real innovative strategy but, definitively not the solution for all pelvic floor problems.

PO-Gyn 03.08

Only women who are aware of the pelvic floor are able to train it

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Objective: Anatomy and function of the pelvic floor (PF) play an important role as possible causes of female urinary incontinence. Pelvic floor muscles (PFM) training is the most commonly used physical therapy treatment for women with stress and urge urinary incontinence.

Materials and methods: In the geriatric department of the Hochzirl Hospital (Austria), 704 female geriatric patients with symptoms of

urinary incontinence were investigated according to a standard Geriatric Basis Assessment. Age, body-mass-index, functional status, number of child births, absolved PFM training in the past and history of hysterectomy were evaluated. The ability to contract PFM was examined by a digital vaginal palpation. Possible correlations between the different parameters were evaluated.

Results: More than 85% of the patients were unaware of their PF and unable to voluntarily contract the PFM. No squeezing action under the examining finger and no elevation of the PF were noted (“absent” or “weak” PFM contraction according to the ICS). A positive correlation was observed between the cognitive function, mobility, an absolved PFM training in the past and the ability to contract the PFM. The correlation between age and ability to contract the PFM was negative. Body-mass-index, number of child births and history of hysterectomy did not influence the PFM function.

Conclusions: The high percentage of female geriatric patients lacking an understanding about the position and function of their PF and who are unable to voluntarily contract the PFM has to be considered in the planning of conservative treatment strategies. PFM function has to be routinely examined before PFM training starts as well as during therapy control. We further recommend interdisciplinary examinations to prove whether the lack of awareness about the PF in older women is just a result of aging, or whether these patients have never learned to use their PF actively during their lives.

PO-Gyn 03.09

Laparoscopic paravaginal repair and colposuspension as alternative minimal invasive methods in surgical treatment of pelvic floor disorders - relaunch of a method

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Objective: Meshes are widely used in surgical treatment of pelvic floor disorders. Despite of promising results, complications remains high. We describe laparoscopic approaches for “active” women to prevent mesh caused complaints (i.e. erosions, dyspareunia). The indications for laparoscopic paravaginal repair and colposuspension is the same as in open surgery (paravaginal defect, stress incontinence).

Materials and methods: We perform the approaches as routine laparoscopy. For paravaginal repair and colposuspension peritoneal incision is made on the pelvic sidewall, retroperitoneum is opened and obliterated umbilical ligament is visualized, isolated and pushed medially. The paravesical space is opened. Pubic ramus, Cooper’s ligament and arcus tendinous fascia pelvis are visualized. The anterior vagina is identified and cleared from fatty tissue. If paravaginal wall defects are present, lateral margins of the detached pubocervical fascia and the broken edge of arcus tendinous can be visualized. Paravaginal repair: After defect identification, the surgeon’s no dominant hand inserting into vagina and elevate the vaginal wall along the arcus tendineus. 2–0 no absorbable suture is used further. The first suture is placed about 2 cm proximal to the urethrovesical junction. We use a series of 3–4 sutures on one side for repair of the defect. No suture bridges! Colposuspension: The surgeon’s no dominant hand inserting into vagina and elevate the vaginal wall. No. 0 no absorbable suture is used further. The first suture is placed 2 cm lateral to the midurethra and the suture is then passed through Cooper’s ligament. 2 stitches are used on one side. We leave a suture bridge of 2 cm.

Conclusions: Our initial results in 10 patients suggest that these techniques are safe and effective to traditional but also to mesh surgery. Future trials may establish the approach as a minimally invasive method for successful mesh free anterior vaginal prolapse and stress incontinence treatment.

PO-Gyn 03.10**Pelvic floor ultrasonography: a new ultrasound technique for reconstructive surgery of pelvic organ prolapse and incontinence, which allows purpose and goal-oriented surgical interventions both in first line therapy and in handling of complications**Jacek Kociszewski¹, *Sebastian Kolben¹,¹Ev. Krankenhaus Hagen-Haspe, Department of Gynecology and Obstetrics, Hagen, Germany

Objective: Due to the variety of surgical methods using prostheses to treat pelvic floor prolapse and incontinence, there is a need to objectify the surgical outcome and individualise treatment for post-operative recurrences and complications. Utilising pelvic floor ultrasonography enables new insights regarding the position of the graft, its shape and their relation to adjacent structures and organs.

Materials and methods: Pelvic floor ultrasonography is a new ultrasound concept which combines introital, vaginal and abdominal ultrasonography. With this combination it is possible to gain a three-dimensional image of all pelvic floor compartments, offering a good view on both the anatomical structures and the implanted prostheses as well at rest as during movement.

Results: The technique allows distinguishing between an urethrocele with and without funnelling and differentiation between tractions- and pulsion cystoceles, all implying different therapeutic strategies. A latent incontinence can be diagnosed preoperative to counsel the patient accordingly. Furthermore, it is possible to differentiate between rectocele and enterocele in posterior vaginal wall prolapse which allows the surgeon to get all necessary information whether an operation with or without an implant will be more successfully. After implantation of a sling or a mesh, the material can be examined and documented in size, shape and position. An essential benefit is to evaluate the relation between the anatomical structures and the implant in vivo, as this may offer a possible prediction of long term surgical success. Complications with the implant can often be fixed in a minimally invasive fashion, as ultrasound can identify exactly the possible causes of the underlying problem.

Conclusions: The pelvic floor sonography presents a method to gain objective and reproducible diagnoses in an uncomplicated and fast way. It allows the development of therapeutic concepts for the treatment of pelvic floor disorders as well as the goal-oriented interventions of postoperative complications.

PO-Gyn 03.11**Pelvic floor ultrasound to evaluate TVT-O biomechanics and optimize its positioning: the one-half rule**Jacek Kociszewski¹, Grzegorz Surkont², Edyta Wlazlak², Aldona Dunicz-Sokolowska², Volker Viereck³, Jacek Suzin², *Sebastian Kolben¹,¹Ev. Krankenhaus Hagen-Haspe, Department of Gynecology and Obstetrics, Hagen, Germany, ²Medical University of Łódź, Madurowicz Hospital, 1st Department of Obstetrics and Gynecology, Łódź, Poland, ³Cantonal Hospital Frauenfeld, Department of Gynecology and Obstetrics, Frauenfeld, Switzerland

Objective: The transobturator tape (TVT-O) was developed to reduce the risk of complications observed with the retropubic tape (TVT). Differences in biomechanics (except for the less acute angle of the TVT-O) between both tapes are well known. This study evaluated TVT-O biomechanics by ultrasound to identify possible reasons for failure.

Materials and methods: TVT-O surgery was performed in 63 incontinent women. The first 29 operations were performed according to the 1/3 rule—incision starting at 1/3 of the ultrasonographically measured urethral length (standard TVT placement technique at our departments). Due to unsatisfying results, we then switched to start the incision at 1/2 of the urethral length, hypothesizing that better results should be achieved with the tape placed closer to the high pressure zone. Ultrasonographically assessed TVT-O biomechanics showed reduced tape mobility during straining compared with TVT. Pelvic floor ultrasound was performed using a 5–9 MHz vaginal probe. The parameters explored included urethral length, linear urethral dorsocaudal movement (LUDM), longitudinal urethral tape localization (LUTL), and distance between hypochoic urethra and tape (DHUT). Success was assessed 6 months after surgery. For this analysis patients were divided into 2 groups: cured versus not cured. **Results:** TVT-O placement according to the 1/3 rule showed 34.5% failures versus 11.8% according to the 1/2 rule. Low urethral mobility and high fixation of the urethra negatively affected the cure result. DHUT >5 mm also had negative impact on continence. We found no correlation between maximal urethral closure pressure (MUCP) ≤20 cm H₂O and cure rate.

Conclusions: To obtain similar results as with TVT, the incision for TVT-O placement should be started according to the 1/2 rule. Women with a less mobile urethra and high urethral fixation have a higher risk of TVT-O failure.

PO-Gyn 03.12**The use of the single port system for benign adnexial surgery: a pilot study***Felix Neis¹, Bernd Holthaus¹¹Krankenhaus St. Elisabeth, Gynecology and Obstetrics, Damme, Germany

Objective: The Laparo-Endoscopic Single-Site (LESS) surgery is a technique, which only needs a single incision in the umbilicus to perform an operative laparoscopy. There is no need for further incisions for working trocars. The aim was to evaluate the indications, the options and the limitations of the LESS surgery.

Materials and methods: 25 patients with benign adnexial tumors were treated with this operative technique and the data was analyzed.

Results: All surgeries were performed in an analog way as in the conventional minimal invasive surgery (MIS). Neither additional incisions nor a conversion to a laparotomy was necessary. The use of the instruments, which were built especially for this technique, is easy to learn. Because of this the duration of the surgery is not extended.

Conclusions: The LESS surgery is a technically feasible and save procedure with a very good cosmetic outcome. It is, in the adnexial surgery, an alternative solution to the conventional MIS. To make a final statement, the other indications for the LESS surgery, have to be verified.

PO-Gyn 03.13**Complications, reoperation rate and functional results after laparoscopic sacropexy: a cohort study**Carolin Banerjee¹, *Heiko Leufgen¹, Wolfgang Hatzmann², Karl-Guenter Noe¹¹KKH Dormagen, Gynecology, Dormagen, Germany, ²University Witten, Gynecology, Witten, Germany

Objective: Deep laparoscopic sacropexy is a modern method for genital prolapse. The aim of this study was to evaluate the

intermediate-term outcome after laparoscopic sacropepy with regard to complication rate, repropulse rate and patient's contentedness.

Materials and methods: 287 patients suffering from genital prolapse higher than I° and laparoscopic sacropepy were included. LASH was performed in case of pre-existing uterus ($n = 171$). Anterior and posterior colporrhaphia, lateral repair and anti-incontinence operations were performed simultaneously if necessary. All patients were asked in a questionnaire about de novo symptoms and subsequent operations. Patients were asked to evaluate their operative contentedness in a rating scale (0 = worst result, not content, 10 = best result, maximum content). Additionally medical records and the electronic data base were analysed.

Results: Mean age was 62.4 years (31–91 years). Mean follow up interval was 28 month. 84% filled in the questionnaire. No severe intraoperative complication was found. Infections of the lower urinary tract were found in 11.4%, wound infections and stump-infection after LASH in 6.6%. 18.6% (45/242) patients underwent subsequent operations. Four patients developed a mechanical ileus. 16 patients reported de novo stress-incontinence and eight patients de novo urgency. Re-prolapses rate was 7.8%. Mesh-erosion was seen in two cases. Mean operative contentedness was 8.3.

Conclusions: Laparoscopic sacropepy shows good intermediate-term results respectively repropulse rate, complication rates and contentedness of patients. Infections of the lower urinary tract constitute a problem after gynaecological surgery. The preoperative risk and benefits information should include accurate advices concerning de novo incontinence and re-prolapse rate.

PO-Gyn 03.14

Robot-assisted surgery in gynecology: early experience with the daVinci surgical system

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Objective: To present our preliminary data on the feasibility, safety, advantages, and disadvantages along the learning curve with robotic surgery in general gynecology.

Materials and methods: The daVinci robotic system (dVS) with a port set-up for 3 operating arms was used in all cases. Before we performed the first operations in Dresden, 2 experienced surgeons, 2 younger physicians, and 2 nurses participated in a training course at the IRCAD in Strassbourg/France for 3 days, followed by 2 days of robotic surgery under supervision at our department.

Results: Benign robot-assisted surgery was started in August 2009 and until now 16 patients were treated with hysterectomy ± salpingo-oophorectomy. Mean patient's age was 48 years (22–73 years). The mean 185 min operative time ranged from 140 to 253 min. Mean assembly time of the dVS lasted 20 min and disassembly needed about 8 min. None of our daVinci operations had to be converted to laparotomy. No mayor complications occurred intra- or postoperatively and no patient required blood transfusion. The length of the patient's hospital stay averaged 4.5 days. Additional costs of 1.500€ for each daVinci operation have to be considered.

Conclusions: Our first data show that experienced surgeons, doing mainly open surgery, can use the dVS with success and safety after a training of only 1 week. This seems to be a great advantage of the robot system. However, additional costs for each operation means a great disadvantage especially in the context of our health system.

PO-Geb 03.15

Endoscopic intracorporal knotting and suture techniques: talent or experience?

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Objective: Endoscopic intracorporal knotting and suture techniques demand sophisticated surgical skill. Young surgeons can be trained to perform endoscopic intracorporal techniques using dummies. This study examines whether talent or practice is more likely to predict how well an endoscopic surgeon performs endoscopic intracorporal techniques. Coexisting factors including sinistrality and myopia were sub-analysed.

Materials and methods: 25 medical students participated in an endoscopic suture teaching program (ESTP). The program included two three-hour sessions of intensive training at the pelvic trainer. In the first session, each student executed three complete knots followed by one continuous suture that starts and ends with a knot. During the second session (one week later) the students completed a single knot followed by two continuous sutures (two knots). Each complete knot consists of a double knot in one direction and a single knot in the reverse direction. Each student's skill level was determined by measuring their knotting times. Individual factors such as size, weight, length, gender, age, myopia, sinistrality etc., and education, including previous hours of laparoscopic assistance, industrial arts and co-factors (sports, music, were accounted for with a self-administered questionnaire.

Results: No correlation between individual and co-factors was found and there was no significant difference between the performance of right and left handed individuals. Students with more than 20 h of experience assisting endoscopic operations had significantly faster knotting times for the first three knots than students who had less than 20 h or no experience assisting endoscopic operations.

Conclusions: The development of the skills required to perform endoscopic knotting and suture techniques can be attributed to experience rather than talent.

PO-Geb 03.16

Port site and abdominal wall metastases after laparoscopy and laparotomy in advanced ovarian cancer: a retrospective long-run analysis of incidence and impact on survival

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Objective: In the field of gynecological oncology the laparoscopic surgery becomes more and more impact. The Disadvantage of laparoscopic surgery in cancer is the risk of port site or abdominal wall metastases. We analyzed a group of patients with advanced ovarian cancer to investigate the incidence of port site metastases and the impact on survival.

Materials and methods: Patients with ovarian cancer who got neoadjuvant chemotherapy after diagnostic laparoscopy or laparotomy were subject of our study. 30 patients got a laparoscopy before starting neoadjuvant chemotherapy, 17 patients got a laparotomy. The time of first operation has been between 1997 and 2001. This analysis was retrospective by using a database of our patients with ovarian

cancer. All patients have an advanced ovarian cancer beginning at stadium FIGO IIIB.

Results: All 47 patients were followed up after the primary therapy until now. The occurrence of abdominal wall metastasis after laparotomic staging is 13% versus 12%; the difference is not significant. The median overall survival of all patients is 36.5 months; the median overall survival in the group of laparotomy is 49.5 months, in the group of laparoscopy 32.5 months. The difference between median overall survival in both groups is not significant (using *t* test). The observed value of expected survival in both groups correlates to the normal distribution.

Conclusions: Port site metastases are a potential complication of laparoscopic cancer surgery. The highest observed incidence is in ovarian cancer with 9–16%. In our retrospective analysis the occurrence of port site metastasis was correlates with the data in the literature. Reflecting the data of survival the diagnostic operation procedure before neoadjuvant chemotherapy has no impact on median survival thus port site metastases also do not influence the survival in our group.

PO-Geb 03.17

Well-leg compartment syndrome after surgery for gynecologic cancer: a case report

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Objective: Acute compartment syndrome (ACS) is a life-threatening process induced by abnormally high pressure between muscles and enveloping fasciae. There are few reports in combination with gynecologic surgery.

Materials and methods: A 38 year old underwent extended surgery for a malignant yolk sac tumor of the ovary. The operating time was 6 h, anesthesia time and time in lithotomy position almost 7 h. On the first postoperative day the patient reported pain and swelling in the lower left leg and ACS was diagnosed. An immediate fasciotomy with necrectomy of the soleus muscle was performed. The patient subsequently required repeated debridements on the 4th and 6th postoperative days. Five months postoperatively, after physical therapy, the patient was well and mobile but foot drop persisted.

Conclusions: ACS is a clinical diagnosis confirmed by laboratory findings. It is well known to trauma and plastic surgeons, but the well-leg variant is rare and may not be familiar to gynaecologic surgeons. Gynecologic surgeons need to be aware of this potential problem in patients at risk.

PO-Geb 03.18

Acellular dermal matrix used for breast reconstruction after mastectomy

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Objective: Mastectomy can be a harming procedure for mental well-being of affected women, which underlines the importance of reconstructive surgery. There are several strategies. At first the use of autologous material like tram flap, latissimus dorsi flap or deep inferior epigastric perforator flap (diep), associated with the

disadvantage of long operation durations, the risk of flap necrosis as well as scars in areas outside the breast or thorax. At second the expander/implant approach, that sometimes leads to a cranial position of implants, less natural form of the breast, dislocation of the implant and the need for a two stage procedure. A single stage reconstruction with good cosmetic outcome and no risk of flap necrosis would certainly mean progress. Acellular dermal matrix (ADM) has been popularized in other countries as an adjunct to tissue expander or implant breast reconstruction given its utility in providing additional coverage and support for the inferior pole. In Germany there is no government approval for alloderm® (acellular cadaveric dermis) therefore other materials like acellular dermal matrix based on pig skin (Strattice®) have to be used.

Materials and methods: We have used ADM for reconstructive surgery after radical, skin sparing or subcutaneous mastectomy. The subpectoral pocket is opened laterally at the insertion of the pectoralis muscle. The submuscular and ADM pocket is subsequently formed. The acellular dermal matrix is used to create a nice submammary fold which helps to give the permanent prosthesis a more caudal and therefore more natural position. The tissue expander (when necessary) or permanent prosthesis is then placed in the pocket and the pectoralis muscle is connected through interrupted stitches to the ADM. Without the use of ADM lower pole expansion is rather restricted.

Conclusions: Encouraged by the good cosmetic results we will further use this technique, although longer follow up is needed.

PO-Geb 03.19

A survey of the application of sentinel lymph node biopsy versus complete inguinofemoral lymphadenectomy in patients with vulvar cancer in Germany

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Vulvar cancer is a rare disease with an incidence of 2.5/100,000 and a mortality of 1.3/100,000 patients per year, whereas squamous cell carcinomas are the vast majority. One of the most important prognostic factors in vulvar carcinoma patients is the presence of lymph node metastases. The surgical therapy of vulvar carcinoma patients includes radical local excision or a partial/complete vulvectomy accompanied by uni- or bilateral inguinofemoral lymphadenectomy depending on the tumour infiltration depth. Although complete inguinofemoral lymph node dissection is accompanied by a high morbidity, the evaluation of the diagnostic accuracy of the sentinel lymph node biopsy as an alternative method with less side effects is not yet complete. In a multicenter survey, we asked gynecological surgeons of 41 hospitals about their experience with the sentinel lymph node biopsy. The majority of these surgeons are fully adapted to perform this technique in patients with vulvar carcinoma (73%, *n* = 30). Among our survey hospitals, 27% (*n* = 11) perform inguinofemoral lymphadenectomy as a standard procedure, 10% (*n* = 3) of them apply the sentinel lymph node technique alone, and in 63% (*n* = 26) of the hospitals both procedures are used in combination. Only 20% (*n* = 6) of the surveyed institutions apply the sentinel lymph node biopsy in patients with vulvar carcinoma according to the consensus criteria/S2 guideline. Moreover, in our survey we further asked, whether the surgeons always complete the sentinel lymph node biopsy in patients with vulvar cancer by complete inguinofemoral lymphadenectomy in addition: This was standard in 24% (*n* = 10) of the hospitals. We are planning a prospective randomised multicenter study in patients with vulvar cancer to compare the effectiveness of

sentinel lymph node biopsy alone versus complete inguino-femoral lymphadenectomy. Of the survey hospitals, 73% ($n = 30$) of them would take part in a randomised study to address this question.

PO-Geb 03.20

Subcutaneous mastectomy in female-to-male transsexuals (FTMTS)

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Objective: Breasts caused the most gender identity conflict, therefore subcutaneous mastectomy is the first surgical procedure in FTMTS. The aims of subcutaneous mastectomy are removal of the breast tissue and excess skin as well as the adequate positioning and sizing of the nipple-areola complex. For a good cosmetic outcome scars are to be minimized.

Materials and methods: From January 2005 to March 2010, a total of 50 subcutaneous mastectomies were performed in 25 female-to-male transsexuals. The technique used depended on the breast size, the skin elasticity, and the position of the nipple-areola complex. The concentric circular technique (19 of 25, 76%) was used for small to medium-sized breasts, the free nipple graft technique (6 of 25, 24%) for large-volume breasts. A retrospective review of patient charts was undertaken, and a questionnaire was used to rate the overall aesthetic result of the subcutaneous mastectomy.

Results: The overall postoperative complication rate was 12.0% (6 of 50 subcutaneous mastectomies), and in 4 of these patients (16.0%), an additional operative intervention was required because of hematoma, wound dehiscence, and/or partial necrosis of the nipple-areola complex. Additional procedures for improving aesthetic results (e.g. wrinkling) were performed on 2 patients (8.0%). The highest patient satisfaction rating was found among the concentric circular group.

Conclusions: We introduced two operative procedures for subcutaneous mastectomy in FTMTS. Skin excess and skin elasticity are the key factors in choosing the appropriate technique. For breasts with small to moderate breast size the concentric circular technique is suitable, whereas large-volume breasts will likely require the free nipple graft technique. There is a high rate of overall satisfaction as well as a low rate of postoperative complications.

PO-Geb 03.21

Comparison of a reusable with a disposable vessel sealing device in a sheep model: efficacy and cost analysis

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Objective: During the past few years, a variety of high frequency sealing devices for vessel ligation has been introduced. So far, the vast majority of these devices are disposable. The purpose of this study was an in-vivo comparison of efficacy of the new reusable vessel sealing device MarSeal[®] (MS) with the conventional standard disposable LigaSure[®] (LS) device in an animal model.

Materials and methods: In 13 sheep, the carotid and femoral arteries were dissected bilaterally and sealed randomly with MS unilaterally and consecutively with LS contralaterally in-vivo. Afterwards the burst pressure was determined for each artery. Study endpoints included sealing time, failure rate, and burst pressure. Students *t* test for continuous and chi-square test for categorical variables were used and $p < 0.05$ was considered statistically significant.

Results: The mean diameter of all arteries sealed did not differ significantly between both groups (MS 5.40 mm vs. LS 5.35 mm, $p = 0.79$). The mean sealing time was significantly shorter using the reusable device (MS 5.2 s vs. LS 9.1 s, $p < 0.0001$). With respect to sealing failure rate, we did not find a significant difference between both groups (MS 7.0% vs. LS 9.1%, $p = 0.28$). In addition, analysis of mean burst pressure did not reveal a significant difference between the different devices (MS 429 mmHg vs. LS 484 mmHg, $p = 0.16$).

Conclusions: In our in-vivo animal study, the new reusable MS device appears to be equivalent effective for vessel sealing when compared to the conventional disposable LS device.

Oncology

PO-Onko 03.01

A device for real-time, intraoperative margin assessment in breast-conservation surgery (BCS) of ductal carcinoma in situ (DCIS)

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Objective: A sufficient margin assessment when excising a DCIS of the breast is difficult. Frozen section is unreliable and intraoperative radiography of the specimen gives only information about the size of the noticed lesion or the microcalcifications. This trial was conducted to study the benefit of a novel device (MarginProbe[®], Dune Medical Devices, Ltd.) in intraoperative margin assessment for BCS of DCIS and the associated reduction in re-operations.

Materials and methods: A multi center, single arm study was conducted to determine the added benefit of the device use. The device was used as an adjunctive tool to the current practice. The surgeon received real time device output and reacted surgically intraoperatively. Based on the permanent histology report outcome, the added benefit of device use is demonstrated. Analyzed were the first 16 pts. enrolled in our institution (Sept. 2009–March 2010). This preliminary analysis was done because of the excellent results. The final analysis might be presented at 58th DGGG meeting.

Results: Patients who benefit from MarginProbe[®] were analyzed (9/16). Device use was associated with improved correct surgical reaction, defined as patients in which all histologically detected positive margins on the main specimen were identified by the device and resected intraoperatively. In 55% (5/9, 55%) a repeat operation was avoided, in 2 pts. the device did not detect all positive margins (2/9, 22%) and two patients turned out to have invasive cancer (2/9 22%).

Conclusions: Intraoperative use of the MarginProbe[®] for positive margin detection is safe, fast and effective in BCS and decreases the rate of repeat operations by 55%.

PO-Onko 03.02**Germline mutations in the PALB2 gene are population specific and occur with low frequencies in familial and sporadic breast cancer**

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Objective: Screening of more than 7000 German breast and ovarian cancer families by PCR based techniques revealed mutation frequencies in the two known BRCA genes between 35–50%. In contrast, mutations in other predisposing genes like CHEK2 and ATM were detected with very low prevalence. As a still significant proportion of our families are lacking mutations in these known genes, we decided to screen them for mutations in another predisposing gene for breast cancer, called PALB2. In addition, we included sporadic cases.

Materials and methods: We performed a comprehensive mutation screening of PALB2 in 818 familial and 820 sporadic cases of breast cancer from Germany. All affected index patients had been screened for small nucleotide alterations in BRCA1 and BRCA2 by dHPLC and/or by direct DNA-sequencing and tested negative for pathogenic mutations. Eight out of 13 PALB2 exons were analysed, covering 100% of the mutations previously reported in PALB2 positive breast cancer families.

Results: We found eight truncating mutations (seven of them novel), five in 818 BRCA1/2-mutation-negative families with familial breast cancer and three in 820 sporadic cases. Moreover, three novels potentially disease causing missense mutations were found. In contrast, none of the previously published deleterious mutations found in other populations, except one, were identified.

Conclusions: Our observations indicate firstly, low prevalence of deleterious PALB2 mutations and secondly, a distinct mutation profile within the German population. More intriguing however, our data indicate that mutations in PALB2 are not restricted to familial, but can rarely occur, like CHEK2 gene mutations, in sporadic cases.

PO-Onko 03.03**Prediction of disease-free nipple-areola complex in patients with extended DCIS by computer-assisted detection in breast MRI**

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Objective: Important preoperative information to decide for skin-sparing mastectomy (SSM), a surgical option in selected patients with extended ductal carcinoma in situ (DCIS), is a disease-free nipple-areola complex (NAC). Breast MRI can be used to detect patients with disease in ductal tissue behind the NAC. The purpose of this study was to evaluate the impact of computer-assisted detection (CAD) with breast MRI as an additional diagnostic tool in the prediction of preoperative tumor extension with respect to the NAC.

Materials and methods: A routine case series of 28 patients with extended DCIS underwent 3D (Gd)-enhanced 1.5T MR mammography preoperatively using a T1-w FLASH pulse sequence. Two radiologists assessed the images in consensus reading. According to the enhancement distance towards the NAC 3 groups were defined: Group (1): NAC reached; (2): ≥ 4 –6 mm (intraoperative assessment of surgical margins required) and (3): ≥ 6 mm (disease-free). Histopathological analysis served as standard of reference.

Results: Contrast uptake was in 84% ductal and in 16% segmental. Without CAD $n = 2$ false-positive cases for retroareolar tumor involvement were found in group (1), a marginal disease-free NAC of $n = 9/28$ was in group (2); $n = 17/28$ were categorized disease-free in group (3). With additional CAD $n = 20/28$ were now classified (2) (+32.1%), $n = 1$ re-classified from (1) to (2) and $n = 10$ re-classified from (3) to (2). The CAD-supported findings confirmed a more accurate tumor extension and diameters in correlation with microscopic margins of resection.

Conclusions: Preoperative CAD-assisted MRI enables detailed evaluation of the subnipple ductal tissue and prediction of disease-free NAC. This breast imaging modality is important for the preoperative decision making process between prophylactic mastectomy and SSM in patients with extended DCIS. For the oncological safety of SSM breast MRI with additional CAD can show NAC involvement, an important information for preoperative surgical planning in extended DCIS patients.

PO-Onko 03.04**Prophylactic bilateral mastectomy in BRCA-1 and BRCA-2: unreasonable difference of 1,534.22 € in reimbursement for similar operations with same costs and effort**

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Objective: Due to the exploding expenditures in the health system accompanied by decreasing reimbursement for medical performances, economic thinking and acting in hospitals becomes more and more significant. Target-aimed hospital controlling means being aware of clinic-individual costs of every last medical procedure in addition to optimized coding. Issuing cost-coverage for bilateral, subcutaneous and nipple-sparing mastectomy with immediate breast-reconstruction in case of BRCA-1 or BRCA-2 gene mutation carriers, a comparison of costs and proceeds has been made.

Materials and methods: Restriction of the main diagnosis Z80.3 and Z40.00 and according OPS-codes (ICPM) 870.0, 872.1, 876.2 and 876.3 in 2009. Precise retrospective cost-analysis of consecutive cases ($n = 9$) in 2009 in due consideration on basis of actual labour costs, material costs and overheads in the OB/GYN department of the University Hospital of Cologne on database of the controlling departure. Furthermore comparison of generated revenues for DRGs J24B and Z01Z.

Results: The costs for a prophylactic mastectomy add up to 4,093.93 € in total for each in-patient treated. Deficient cost-coverage of 1,707.84€/case (=41.72%) in the event of assignment to DRG Z01Z. At analogical expended effort and cost-structure, the cost-coverage of DRG J24B averages 95.76%, which equals a difference of 1,534.22 € in reimbursement for same effort and expenses on the part of the clinic.

Conclusions: The variation in refunds do not seem reasonable. According to the German coding-guideline, a subcutaneous mastectomy requires coding in Z80. A skin-sparing mastectomy does not equal a subcutaneous mastectomy though and needs to be sharply divided also in regard of the OP-documentation by the medical staff.

In case of skin-sparing mastectomy (OPS 5–872.–) due to high risk of familial breast cancer, an assignment to ICD-Code Z40 is strictly recommended in order to gain appropriate reimbursement for actual costs.

PO-Onko 03.05

Influence of breast cancer on sexuality

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Objective: We examine the sexuality of women who have received treatment for breast cancer. We investigate differences pertaining in the sample by age, type of operation and metastases. Our research sheds light on the ways women are affected in their sexuality after breast cancer treatment.

Materials and methods: 1217 breast cancer patients treated in the department of gynaecology and obstetrics at the University of Schleswig-Holstein, Campus Lübeck during the last 5 years received a questionnaire regarding their sexuality.

Results: Of the 318 patients who filled in the questionnaire 85% informed us of their age, 98% gave us details about the type of operation, where 71.15% were treated with BCT and 28.85% received a mastectomy. In the subgroup that received a mastectomy there was a significantly higher rate of metastases, which corresponds to the fact that in more advanced breast cancer a higher rate of mastectomies is performed. There was no significant correlation between age and the kind of operation or the mastectomy rate. The self-perceived physical wellbeing did not differ between the age groups. Women who were suffering from metastases generally reported a lower level of psychological wellbeing. The desire of sexuality was overall much lower than the desire of closeness. Interestingly there was no correlation between the operation method and the desire of sexuality. 36% of 266 reported an increased fear of sexual intercourse, especially regarding pain and loss of attractiveness.

Conclusions: Overall, we observe some significant differences in sexuality and wellbeing depending on the method of treatment, age and prevalence of metastases. Further research is needed to confirm and specify these influences. The large amount of personal comments in the questionnaires shows the importance of this topic.

PO-Onko 03.06

Obesity and tumor characteristics in nodal positive early stage breast cancer: results of the German ADEBAR study

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Objective: Overweight and obesity are often associated with an increased risk of dying from breast cancer and poor outcomes of therapy. Tumor characteristics are relevant in prognosis and treatment

of breast cancer and potentially strongly associated with the body mass index.

Materials and methods: The ADEBAR study is a German multicenter phase III trial ($n = 1502$) with the goal to evaluate whether breast cancer (BC) pts with > 3 axillary lymph node metastases benefit from a sequential anthracycline-docetaxel regimen (EC-Doc) compared to dose-intensive anthracycline-containing polychemotherapy (FEC). For our evaluation Adebar-Patients were grouped according to the WHO global database on body mass index (BMI).

Results: There is a strong correlation between BMI, age and menopausal status at clinical diagnosis of breast cancer. This analysis shows no connection of tumor localisation (unilateral left or right and bilateral breast cancer) and BMI. The tumor size at clinical diagnosis was strongly associated to the patient's weight (< 0.0001). In underweight, normal, overweight as well as obese patients there was no sign for a significant difference in the number of positive lymph nodes ($p = 0.2890$), tumor histology ($p = 0.9750$) and grading ($p = 0.9520$). Breast Cancer Positivity for ER and PR hormone receptors (ER $p = 0.9708$, PR $p = 0.7785$) and the expression of HER-2 at the tumor surface ($p = 0.1710$) were not significant associated to overweight and obesity in study patients.

Conclusions: Our analysis shows a highly significant coherence between BMI and tumor size in patients with early stage node positive breast cancer. This finding is in line with current publications which show that overweight and obese woman's have often been diagnosed at a more advanced stage of disease and the treatment in this patients being less effective as a consequence. Weight reduction might be an additional approach on breast cancer therapy and prevention.

PO-Onko 03.07

Assessing the efficacy of targeted therapy using Circulating Epithelial Tumor Cells (CETC): the example of SERM therapy monitoring as a unique tool to individualize therapy

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Objective: In malignant tumors predictive markers have been developed with respect to targeted therapies. One of the first targeted therapies was hormone blocking treatment of tumors of the male and female reproductive system. A typical therapy in breast cancer is the use of the selective estrogen receptor modulator (SERM) tamoxifen. However, only part of the patients, positive for the target molecules, responds to the selected therapy. It would, therefore, be highly desirable to have a tool to timely assess the therapeutic efficacy of the applied agent in the individual patient.

Materials and methods: We, here, report on the successful use of CETC as a unique tool to monitor therapy response in 178 breast cancer patients followed prospectively during hormone therapy. Requiring only 1 ml of peripheral blood using a fluorochrome-labelled antibody against surface-epithelial antigen and image analysis allowed calculation of CETC numbers with relation to blood volume and monitoring over the course of treatment.

Results: An increase of more than tenfold in CETC during therapy was a strong indicator of looming relapse ($p = 0.0001$ hazard ratio 5.5; 95% confidence interval 1,297–23,626) and a cox regression analysis of age, tumor size, receptor expression, nodal status and previous treatment resulted in a regression model in which CETC

behavior was the parameter with the highest independent correlation to relapse-free survival.

Conclusions: Thus the change in the number of CETC (increase or decrease) can be used in the future to guide therapy in order to change in good time to other available treatment options.

PO-Onko 03.08

Metastatic breast cancer during pregnancy: critical aspects of treatment and materno-fetal implications

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Objective: Breast cancer (BC) is the most frequently diagnosed malignancy during pregnancy. Important treatment considerations include counseling abortion, surgery and chemotherapy during pregnancy or delayed treatment after pregnancy. The objective of this case report is to describe the challenges faced in the treatment of a patient with metastatic BC during pregnancy.

Materials and methods: Case report and review of the literature.

Results: A 34-year-old woman, G4P3 at 24 weeks of gestation presented with a palpable mass in the right breast and enlarged axillary and supraclavicular lymph nodes. Biopsy revealed an invasive ductal carcinoma with negative hormone receptor status. The past medical history is significant for invasive breast cancer of the left breast (G3 pT2 pN1 (2/9) M0 L1) which was treated elsewhere with anthracycline-based chemotherapy, radiation and endocrine therapy with tamoxifen 6 years ago. Staging by non-contrast MRI revealed advanced bone metastases without other metastatic loci. Five applications of paclitaxel weekly induced severe hematologic toxicity making transfusion necessary and led to treatment discontinuation due to thrombocytopenia. Due to the onset of an atypical pneumonia a cesarian section was performed at 33 weeks of gestation with the birth of a healthy newborn. Postoperatively the patient was transferred to the intensive care unit due to progressive respiratory distress and progression of disease. The patient died 19 days postpartum. Several points of caution with respect to the clinical management are discussed: the use of supportive therapy (steroid type and dose, 5HT3-serotonin antagonists, G-CSF) during pregnancy; the use of analgetics (neonatal abstinence syndrome), response evaluation criteria (validity of tumor markers, imaging) as well as reevaluation of hormone receptor status post-partum (down regulation during pregnancy).

Conclusions: Weighting the impact on maternal prognosis and perinatal outcome, treatment of metastatic BC poses a significant challenge. The lack of evidence, different symptoms and patterns of disease require individualized treatment.

PO-Onko 03.09

The effects of classical massage therapy on stress perception and cortisol in breast cancer patients

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Objective: We conducted a randomized, controlled trial to investigate the efficacy of classical massage treatment in reducing stress perception, cortisol and mood disturbances.

Materials and methods: Women diagnosed with primary breast cancer were randomized into an intervention group and control group. The intervention group received a 30 min classical massage of back and head-neck-area, twice a week, for a period of 5 weeks. The control group received no additional treatment to their routine health care. For evaluating treatment efficacy the questionnaires: Perceived Stress Questionnaire (PSQ) and Berlin Mood Questionnaire (BSF) were administered and the patient's blood was collected at baseline (t1), at the end of intervention (t2) and to follow up after 11 weeks (t3).

Conclusions: Thirty-four eligible women (mean age 59 years, $n = 17$ each group) were enrolled. Compared with control group, women in the intervention group reported significantly lower mood disturbances, especially for anger ($p = 0.048$) and anxious depression ($p = 0.03$) at t2, and tiredness at t3 ($p = 0.01$). Perceived stress and cortisol serum levels ($p = 0.03$) were significantly reduced after massage therapy only in the intervention group. However, the intervention group exhibited no different serotonin levels. Further research is needed to validate our findings.

PO-Onko 03.10

Intraoperative boost irradiation (Intrabeam[®]) for breast cancer: what's important for patients versus physicians

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Objective: We examined the reasons for patients versus physicians to decide on intraoperative radiotherapy (IORT) as boost irradiation for invasive breast cancer. Furthermore, the grade of satisfaction with IORT of patients and physicians has been investigated.

Materials and methods: Patients for IORT were carefully selected. Only patients with unifocal, ductal-invasive breast cancer, without a DCIS-component in the preoperative core biopsy were considered for IORT treatment. This retrospective study included all consecutive patients who underwent IORT in our hospital from 5/2009 till 4/2010 and is based on a voluntary questionnaire. The same questionnaire was also given to the treating physicians of the patients. Main outcome parameters were reasons for decision to undergo IORT and satisfaction with this new method. Data analysis was conducted with SPSS.

Results: The main reasons for patients and physician to decide on IORT are different. Saving time is a very important reason for patients, whereas for physicians, local tumour control plays a decisive role. Further it is demonstrated that IORT is well accepted both by patients and physicians.

Conclusions: Both patients and physicians are satisfied with IORT (intrabeam[®]), the estimation of benefits differs.

PO-Onko 03.11

Training of assistant doctors in gynecological training

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Objective: The residency period of young doctors has been the subject of numerous debates in Germany. The present online study aims at assessing working conditions and subjective satisfaction of assistant doctors in gynecologic training.

Materials and methods: Residents from 62 German hospitals were invited via email to participate in an online survey. The anonymous questionnaire included demographic data and information on the curriculum of training as well as different aspects of subjective satisfaction with the training.

Results: Of the 424 doctors contacted, 186 responded from 48 hospitals in the online questionnaire. Respondents were mainly dissatisfied with the instruction for the first operations and with the limited availability of time to practice. The satisfaction of training related to the satisfaction preparation before the first surgery and an opposite relation to the average training necessary for specialisation. The feedback from medical colleagues and superiors or rather the availability of mentors had also an effect on the training satisfaction.

Conclusions: The results indicate that physicians in gynecologic education want in particular more technical expertise and more time in practical training. The results of the study can contribute to the evaluation of the quality of gynecologic training.

PO-Onko 03.12

Granulomatous mastitis attributed to tuberculosis infection: a case report

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Breast tuberculosis is a very rare disease and commonly misdiagnosed either as a non-specific abscess, granulomatous mastitis or carcinoma. We report the case of a 51 year old Chinese woman with a breast abscess initially and recurrently diagnosed as granulomatous mastitis but finally proven to be tuberculosis of the breast. She presented with a mass in her right breast associated with pain and ulceration. In the last 12 months 3 incision biopsies had been performed. We decided to perform a complete excision of the mass and a reconstruction with a thoracoepigastric flap. The histology of necrosis with giant cell granulomatous infection with a negative Ziehl–Neelsen-reaction and the exclusion of a malignant disease raised the suspicion of culture negative breast tuberculosis. PCR was performed showing a product characteristic of subtypes of mycobacterium tuberculosis complex (*M. bovis*, *M. africanum*, *M. canetti*, *M. microti*). We performed a complete staging that showed no other sites of tuberculosis. A tuberculostatic therapy with Rifampicin, Pyrazinamid, and Isoniacid was commenced. There has been no recurrence until now with follow-up of 7 months. This case report highlights the diagnostic dilemma differentiating granulomatous mastitis, inflammatory breast cancer (IBC) from granulomatous inflammatory conditions attributed to tuberculosis infection.

PO-Onko 03.13

HPV awareness and knowledge among Swiss students: a nationwide web-based survey

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Objective: To investigate the knowledge of human papillomavirus (HPV) as a sexually transmitted disease, its relation to the development of cervical cancer and the attitudes to HPV vaccination among Swiss students.

Materials and methods: A web based questionnaire comprising 38 questions on risk factors, mode of transmission, screening and vaccination for HPV was composed. Female and male students from 5 universities in Switzerland were included in this cross-sectional survey conducted 2008 prior to the introduction of the HPV vaccine program.

Results: Out of total 3728 female and 1380 male participants responding to the survey, 48.3 and 39.9%, respectively, had previously heard about HPV. 33.8% of the female and 28.7% of male participants indicated to have a good knowledge, 17.9 and 31.4%, respectively, indicated to have never heard of HPV. Participants achieving high HPV-knowledge scores reported the gynaecologist (MS: 14.53, SD 2.90), the general practitioner (MS: 14.43, SD 2.78) and press/media (MS: 14.20, SD 3.12) as main source of knowledge, whereas family (MS: 12.93, SD 2.8) and friends as sources achieved significantly lower scores (MS: 13.25 SD 2.59, $p < 0.0001$). Women with past history of abnormal smear or HPV infection achieved higher HPV knowledge scores (MS: 14.87; SD: 3.01). The knowledge on cervical cancer (MS 6.51, SD: 3.78), HPV-testing (MS: 1.79, SD: 0.40) and HPV-vaccination (MS: 4.21, SD 1.94) was better among women compared to men (all $p < 0.05$). 52.9% of the participants would accept vaccination for themselves, whereas 30.6% were not sure and 12.9% refused vaccination. At the time of survey 3.7% were already vaccinated.

Conclusions: Although almost half of Swiss students had already heard about HPV, accurate knowledge was not high. Information obtained through gynaecological visits and general practitioners led to significantly better HPV education, which underlines the importance for careful medical education and counselling of patients in daily clinical practice.

PO-Onko 03.14

64 year old women with ovarian cancer and a cutaneous involvement of the vulva

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Objective: Ovarian cancer is one of the cancer diseases with the highest mortality rate. The 5 year over all survival is approximately 30% and the diagnosis is often determined in an advanced stage. Although aggressive cytoreductive surgery and adjuvant chemotherapy have contributed to improved local tumor control and prolonged survival, these therapeutic measures have limited success in preventing the development in distant metastases. Cutaneous involvement of ovarian carcinoma is unusual. Although the intraperitoneal route is considered the most common way of dissemination, ovarian cancer may also metastasize through the lymphatic channels and the hematogenous route. Distant metastases may occur at the time of ovarian cancer diagnosis or can arise during the evolution of the disease. Ovarian cancer rarely metastasizes to the vagina or vulva.

Materials and methods: We present a 64 year-old women who had applied adjuvant chemotherapy with carboplatin and taxol following cytoreductive surgery because of a stage 3C ovarian cancer in the year 2004. Several relapses like a progress of the lymphatic deposits occur in the period from 2006 until 2009. Therefore a long period of treatment with several chemotherapies followed. A supraclavicular lymph node metastasis and a metastatic deposit in the vulva were detected in the year 2009. A punch biopsy verified the histology of an ovarian cancer. Finally she died in the same year in a very poor condition after radiotherapy of the vulva which could not repress the proliferation.

Conclusions: Our case shows that after a long period of effective surgery and different types of chemotherapeutic treatment a skin metastasis of the vulva is very difficult to treat and repress.

PO-Onko 03.15**Dissiminated, genito-peritoneal tuberculosis mimicking advanced ovarian cancer. Diagnosis and treatment of a rare disease in Western Europe***Sonja Christ¹, Ingrid. C. Jarutat², Anton Hartinger³, Dieter Grab⁴¹Krankenhaus Harlaching, Obstetrics and Gynaecology, Munich, Germany, ²Krankenhaus Harlaching, Pathology, Munich, Germany, ³Krankenhaus Harlaching, Microbiology, Munich, Germany, ⁴Krankenhaus Harlaching, Obstetrics and Gynaecology, Munich, Germany

Objective: Genito-peritoneal tuberculosis is often confused with advanced-stage epithelial carcinoma due to similar clinical, radiologic, and laboratory findings. To establish more sensitivity for genital tuberculosis as a differential diagnosis to advanced stage ovarian cancer. Showing diagnostic procedures to identify the characteristic features and the treatment of choice.

Materials and methods: Case report about a 41 year old, postmenopausal Philippine woman presenting massive ascites and elevated CA125 levels who underwent diagnostic laparoscopy for ovarian cancer and found to have genito-peritoneal tuberculosis.

Results: Despite similarities in clinical, radiologic and laboratory findings, a genito-peritoneal tuberculosis may not be confused with advanced ovarian cancer. Bleeding disorders and the patients country of origin can substantiate suspicion. Tissue samples confirm the diagnosis. Treatment of choice is multiple antibiotic therapy.

Conclusions: Peritoneal tuberculosis with abdomino-pelvic mass is difficult to differentiate from ovarian cancer. Abdomino-pelvic tuberculosis should be considered in all cases with pelvic mass, ascites and high levels of CA125, although clinical features and laboratory results specifically indicate neither ovarian malignancy nor abdomino-pelvic tuberculosis. Bleeding disorders such as early menopause, infertility and specific countries of origin can substantiate suspicion. Diagnostic laparoscopy as well as laparotomy is a direct and safe method for taking tissue samples. Antitubercular drugs are the treatment of choice and complete surgery being difficult and hazardous should be avoided.

PO-Onko 03.16**Granular-cell tumour of female breast: a rarity***Beate Richter¹, Regine Rathmann², Maren Krohn³, Peter Landwehr⁴, Klaus Richter¹¹Pathologie Hannover Zentrum, Hannover, Germany, ²Mammographiescreening Hannover, Hannover, Germany, ³Diakoniekrankenhaus Rotenburg (Wümme), Frauenklinik, Rotenburg, Germany, ⁴Diakoniekrankenhaus Henriettenstiftung, Klinik für Diagnostische und Interventionelle Radiologie, Hannover, Germany

Objective: Occurrence of granular-cell tumours in the female mammary gland tissue indeed represents a rarity. What is special about these tumours is that, in the imaging process, they usually appear malignant, but are histologically usually benign. We report observations made on such a tumour which proved to be a challenge for all the disciplines involved.

Materials and methods: In the upper inner quadrant of the right breast of a 69-year-old patient a compact, pressure-painful, readily displaceable resistance on the thoracic wall with plateau phenomenon was felt. The patient was otherwise clinically healthy. All laboratory values were normal. Sonography, mammography, pre-operative minimal-invasive diagnosis and operative removal of the tumour were undertaken.

Results: Sonography: at 2 o'clock, 6 cm from the right nipple, a low echo; lengthwise oval focus, interruption of the bordering structure of the

connective tissue of 12 × 9 × 10 mm. Dorsal echo extinction. Mammography: 10 cm behind and 4.5 cm medial to the nipple in a specially set-up latero-medial shot, a 7 mm radio-dense focus. No microcalcification. Under strong suspicion of invasive carcinoma, application of sonographic-controlled high-speed punches that held parts of a granular-cell tumour without histological criteria of malignancy. Then complete operative removal of tumour. Histological identical tumour tissue as in the high-speed punching. Immunohistological reactions: S100 protein, vimentin, pan-cytokeratin, oestrogen and progesterone receptors, Her2-neu, p53, Mib1, LCA, neurofilaments, neurone-specific enolase and actin. Apart from this PAS. Normal post-operative course. Tumour- and symptom-free follow-up over 2 6/12 years.

Conclusions: The rare granular-cell tumours of the female breast give indications during imaging of being malignant, but are usually histological benign and thus constitute a considerable diagnostic challenge. The triad: patient age, touch detectable, compact nodes with localization in the upper (inner) quadrant, no microcalcification, can be a vague indication of a benign granular-cell tumour.

PO-Onko 03.18**Detection of lymphovascular invasion in endometrial cancer by D2-40 (podoplanin) as a predictor for lymph node metastasis***Sarah Kristin Weber¹, Axel Sauerwald¹, Martin Pölcher¹, Michael Braun¹, Manuel Debal¹, Nuran Serge¹, Walter Kuhn¹, Christian Rudlowski¹¹University Hospital Bonn, Department of Obstetrics and Gynecology, Bonn, Germany

Objective: Lymph node involvement plays a major role in the spread of endometrial cancer and predicts prognosis. In tumors confined to the uterus lymph node metastasis is observed in up to 30%. For clinical application evaluation of lymph vessel invasion (LVI) as marker for lymph node metastasis is of important value. D2-40, a monoclonal immunohistochemical marker might be able to increase the detection rate of LVI compared to conventional Haematoxylin–Eosin (H.E.) staining. The aim of the study was to evaluate the eligibility of D2-40 for the prediction of lymph node metastases.

Materials and methods: Immunohistochemical staining with D2-40 was performed on paraffin-embedded tissue sections of 182 patients with endometrioid adenocarcinoma. Slides were screened for the presence of lymphatic vessel invasion. Correlation with clinicopathological features including LVI as retrieved by routine haematoxylin and eosin (H.E.) stained sections was assessed. Treatment modalities and patients follow-up were available.

Results: Immunostaining with D2-40 significantly ($p = 0.001$) increased the frequency of detection of lymphatic invasion compared to conventional H.E. staining. LVI was identified by D2-40 (D2-40-LVI+) in 53/182 (29.1%) of tumor specimen as compared to 34/182 (18.3%) by routine HE staining (H.E. + LVI). D2-40-LVI+ in tumor tissue was detectable in 90% of the nodal positive tumors and ($p = 0.001$) predicted significantly lymph node metastases. Furthermore, D2-40 was the only independent prognostic factor for patients overall survival ($p < 0.01$) considering tumor stage, lymph node involvement, H.E.-LVI and tumor differentiation.

Conclusions: Immunostaining with D2-40 significantly increased the frequency of detection of lymphatic invasion compared to conventional H.E. staining in endometrial cancer. D2-40 + LVI was a strong predictor for lymph node metastases and a prognostic relevant parameter. Further studies on large patients group a required to evaluate the clinical role of D2-40 + LVI in endometrial cancer. These studies have to be focused on patients in which lymph node dissection could be omitted without worsening patients outcome.

PO-Onko 03.19**Human endogenous retroviral over expression in endometrial carcinoma is due to hypomethylation of the 5'LTR**

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Human endogenous retroviruses (HERV) embody over 8% of the human genome and are derived from ancestral germ line retroviral infection. Some HERV envelope (env) proteins are essential for mediating cell-cell-fusion of cytotrophoblasts to the syncytiotrophoblast in human placentogenesis, but are also implicated in tumorigenesis. Hypomethylated 5'Long-Terminal-Repeats (5'LTR) of HERVs correlating with increased expression have been shown for HERV-W and HERV-K in different human carcinomas. Previously, we demonstrated a significant step-wise increase of the Syncytin-1 HERV-W env gene at both mRNA and protein levels for EnCa and prestages compared to controls. The purpose of this study was to determine expression of five HERV envelope genes in Endometrial Carcinomas (EnCa) and correlation with CpG-methylation of the 5'LTR of HERV-W in EnCa and prestages compared to matched control tissues. We established methods for absolute quantification (qPCR) for five different HERV-env genes and methylation-specific-PCR (MSP) using bisulfite treated genomic DNA. Methylated CpGs were verified by cloning and sequencing. Gene expression of benign and malignant endometrial tissues (EnCa $n = 44$, polyps $n = 21$, hyperplasia $n = 12$) compared to control postmenopausal endometrium ($n = 33$) showed that the HERV-env genes Syncytin-1, HERV-K, ERV-3, HERV-P(b) and Syncytin-2 were significantly up-regulated. In control and benign prestages ERV3 was the highest expressed HERV-env, whereas in EnCa Syncytin-1 was the most prominent. Methylation studies of the HERV-W 5'LTR of Syncytin-1 showed that seven out of 20 CpGs were significantly hypomethylated in EnCa compared to control endometrial tissue from the same patient ($n = 7$). These sites correlated with transcription factor binding sites. Studies using the demethylation agent 5'Aza-2'Cytidine with EnCa cell lines resulted in a 2.5-fold increase of Syncytin-1 gene expression. In conclusion, up-regulation of Syncytin-1 in EnCa is due to specific hypomethylation of the 5'LTR. Understanding epigenetic regulation of HERV-env genes will contribute to the molecular etiology of EnCa and stepwise induction from benign prestages.

PO-Onko 03.20**Estrogen receptor β 2 is associated with expression of growth regulatory genes p21/WAF1, SCUBE2 and MYBL2 in endometrial adenocarcinoma**

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Objective: Endometrial cancer is known to be a hormone-dependent neoplasia which is caused by a stepwise accumulation of molecular alterations in cellular pathways regarding proliferation and differentiation. Several studies have discussed a possible tumor suppressor role for ER β in the carcinogenesis of hormone-dependent target tissues. In this study, we examined the association between expression of the three ER β isoforms ER β 1, ER β 2 and ER β 5 and expression of eleven cancer-associated genes to further approach the function of ER β in endometrial cancer.

Materials and methods: We analyzed expression of steroid hormone receptors ER β 1, ER β 2, ER β 5, ER α and PR and of eleven candidate genes (proliferation genes or cancer biomarkers) in 76 human endometrium samples and endometrial cancer specimens by means of real time RT-PCR and tested their association by means of a Spearman correlation.

Results: ER β splice variants were differentially expressed in endometrial cancer and exhibited an isoform-specific co-expression with marker genes. While ER β 1 expression was not altered in endometrial cancer but was weakly associated with HER2 mRNA levels, ER β 2 expression was significantly weaker in endometrial cancer than in normal tissue and was associated with expression of the growth-inhibitory genes SCUBE2 and p21/WAF1 and with cell cycle gene MYBL2. In contrast, ER β 5 transcript levels were significantly elevated in the endometrial cancer group and also were weakly associated with MYBL2. ER α expression, while being decreased in the G3 subgroup, was not only strongly associated with PR, but also with expression of SCUBE2 ($p < 0.001$). Furthermore, we identified a highly significant co-expression pattern of aurora kinase A, Ki-67, cyclin B1 and MYBL2 in endometrial cancer.

Conclusions: The differential expression of ER β splice variants 1, 2 and 5 as well as their specific association with marker genes supports their distinct role in endometrial carcinogenesis. The obtained co-expression data will allow further studies on its functional relevance in endometrial cancer.

PO-Onko 03.21**Paclitaxel has apoptotic as well as non-apoptotic effects on different endometrial carcinoma cells**

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Objective: Taxanes are important substances in gynaecological oncology. Their classical effects are to interfere with microtubules, which are important for cell division, and to induce apoptosis. However, they also have non-apoptotic effects. Because importance of a systemic approach in the therapy of endometrial cancer is unclear, this work deals with the effect of Paclitaxel on endometrial carcinoma cells in vitro.

Materials and methods: The endometrial carcinoma cell lines ECC-1, RL95-2 and AN3 CA were incubated with Paclitaxel. The rate of apoptosis, cell cycle analysis and proliferation were detected using flow cytometry and viability assays. The activation of the signaling pathways p44/42-, p38-MAPK (mitogen activated protein kinase), JNK (c-jun N-terminal kinase) and NF (nuclear factor)- κ B was measured via in-cell western assay. The secretion of chemokines was quantified using ELISAs.

Results: Paclitaxel mediated a dose-dependent inhibition of proliferation in all three cell lines. This effect was accompanied by an accumulation of the cells in the G2/M-phase and an increased rate of apoptotic cells. The extent of these effects varied between the different cell lines. In contrast to p38-MAPK, JNK and NF- κ B, the p44/42-MAPK signaling pathway was highly activated upon Paclitaxel stimulation. In addition, Paclitaxel caused a differential regulation of the chemokines IL (interleukin)-8, MCP (monocyte chemo attractant protein)-1 and RANTES (regulated and activated normal T-cell expressed and secreted) in the different cell lines.

Conclusions: Paclitaxel inhibits proliferation and induces apoptosis in endometrial carcinoma cells. Moreover this taxane has regulatory effects on main signaling pathways as well as the secretion of chemokines, dependent on the differentiation level of the cells. From a clinical point of view these results extend the knowledge of the

spectrum of taxane activity, arising new options for these substances in the therapy of endometrial cancer.

PO-Onko 03.22

MR-imaging of endometrial cancer using an endorectal surface coil

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Objective: The aim is to evaluate the preoperative staging preciseness of clinical examination and MR-Imaging using an endorectal surface coil (eMRI) comparing the histopathological outcome in patients with endometrial cancer.

Materials and methods: 10 consecutive patients with biopsy-proven endometrial cancer were clinically staged according to the FIGO-classification and underwent eMRI prior to surgery. MR-Imaging was performed with 4–10 mm slice thickness using T2-weighted turbo spin-echo (tse) sequences in sagittal, coronal and transversal orientation and T1-weighted spin-echo (SE) sequences (transversal) with fat-saturation (fs) and additional contrast medium on a 1.5T MRI. Dynamic MR-Imaging in sagittal orientation was carried out after 25 s and 60 s with a 3 mm slice thickness.

Results: Regarding tumor size 5 patients were staged correctly according to the FIGO-classification, one was overstaged and one understaged comparing the histopathological outcome. In 3 patients the myometrial infiltration was not mentioned in which case a comparison was not possible. With endorectal coil MRI all tumors were depicted. Four patients were staged correctly regarding tumor size and myometrial invasion, 5 were overstaged regarding myometrial invasion and one was understaged. In terms of lymph-node diagnostics the eMRI staged correctly in 9 patients and overstaged one patient. Cervical tumor invasion was described by the pathologist in two cases. One patient was evaluated correctly by the radiologist.

Conclusions: In this study eMRI could detect and describe the endometrial cancer nearly as precise as did the FIGO-staging in terms of size and myometrial invasion. Lymph-nodes were shown accurately on eMR-images and were excluded in cases with limited tumors. Concluding, the eMRI showed high quality images of the female pelvis and easily depicted the cancer. At this point of practice tumor staging in patients with endometrial cancer with help of eMRI seems to be promising imaging modality and needs to be assessed in larger studies.

PO-Onko 03.23

Pilot study for pretherapeutical evaluation of the axillary lymph node status (ax LNS) in primary breast cancer patients by ultrasound compared to interventional assessment by fine needle aspiration (FNA)

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Objective: The axillary lymph-node status (LNS) is considered to be the most important prognostic factor in breast cancer. Therefore identification of the LNS is important for the determination of the overall therapeutical concept. However, an appraisal of the axillary lymph node status that is solely based on clinical and/or image-based judgement

would lead to an overtreatment of 40% of the patients. In order to reduce the rate of unnecessary axillary dissection (AD), a pretherapeutical interventional clarification is necessary, which provides closer information about the histological condition of the lymph node.

Materials and methods: In a pilot study 27 primary breast cancer patients have been evaluated by sonographic assessment of the axillary lymph nodes' dignity, following preoperative interventional clarification by fine needle aspiration (FNA).

Results: Results of the FNA and the postoperative histological staging were compared to pretherapeutical clinical/sonographical evaluation of lymph node dignity. An adequate sonographic assessment on the basis of standardized sonomorphological criteria is crucial for further interventional clarification. In 37% of cases with pN0 we could identify normal lymph nodes by FNA, although clinical nodal status presented to be suspect. Therefore an overtreatment with unnecessary rate of ADs could be avoided by preoperative clarification with FNA. This implicates the fact, that FNA should be included in the preoperative evaluation of the lymph node status, beside the existing clinical/ sonographical examination. Our findings will be further investigated in prospective studies.

PO-Onko 03.24

Postoperative infections due to bladder catheters after anterior colporrhaphy: a prospective, randomized three-arm study

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Objective: Different forms of urinary drainage are applied after anterior colporrhaphy. Suprapubic (SUC) and indwelling urinary catheters (IUC) for 2–96 h are preferred. If there is no difference in symptomatic urinary tract infection (SUTI) or complications between IUCs for 96 and 24 h, the latter will be considered sufficient. If IUCs have no higher rate of infections or complications compared to SUC for 96 h, the former could be considered sufficient.

Materials and methods: It was a three-arm prospective, randomized study including 257 patients. The three arms were: IUCs for 24 h, IUCs for 96 h and SUCs for 96 h. Mann-Whitney-test was used for statistical analyses.

Results: We found no significant difference in SUTIs between all three groups. Although the SUC arm showed no SUTIs, a significant higher rate of complications was seen.

Conclusions: The optimal bladder catheter after anterior colporrhaphy was in our trial the IUC for 24 h.

PO-Onko 03.25

Contraception and benign breast disease: a retrospective cohort study in women younger than 40 years

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Objective: Benign breast disease (BBD) association with exogenous hormones assumption is still doubtful. Our study aims to determine contraception prevalence in young women affected by BBD and its eventual correlation with BBD features.

Materials and methods: We collected data about contraception use in all women younger than 40 with a diagnose of BBD who applied the Senology Outpatients during 2008, focusing on hormonal type and dosage, exposure time, and eventual influence on the BBD. We analysed data by R (version 2.8.0), considering significant $p < 0.05$. Also multivariate analysis was performed.

Results: Among 355 women affected by BBD, 105 are younger than 40, 60% of which have ever used contraception. BBD is represented by fibroadenoma (55.24%), fibrocystic mastopathy (19.05%), mastodynia (10.48%), galattorrhoea (5.71%), and mastitis (4.76%).

Conclusions: Contraception may negatively influence BBD development in predisposed young women.

PO-Onko 03.27

Prevalence of hypoactive sexual desire disorder (HSDD) in women after five different hysterectomy procedures

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Objective: The advantages and disadvantages of the different surgical methods of hysterectomy are currently a topic of debate, and there is particular controversy over leaving the cervix in situ in the laparoscopic supracervical hysterectomy (LASH) procedure. The aim of this study was to compare the prevalence hypoactive sexual desire disorder (HSDD) after five different hysterectomy procedures.

Materials and methods: The Brief Profile of Female Sexual Function (B-PFSF) score was used to evaluate postoperative prevalence of HSDD in women after different hysterectomy procedures. The questionnaire was sent to 590 women who had undergone a hysterectomy between 2002 and 2007 for benign conditions at the Department of Obstetrics and Gynecology of the University Hospital of Erlangen. The following procedures were performed during the study time: abdominal hysterectomy (AH), vaginal hysterectomy (VH), laparoscopic assisted vaginal hysterectomy (LAVH), laparoscopic supracervical hysterectomy (LASH) and total laparoscopic hysterectomy (TLH).

Results: 304 questionnaires were returned and 258 were adequate answered to be used for statistical analysis. The mean follow-up interval was 2 years for women after LASH and TLH and 3 years for women after AH, VH, and LAVH. The women of the AH group were significant older than women of the LASH group and women of the VH group were significant older than women of the LASH or TLH group. The mean B-PFSF score was 24.4 in women after LASH, 23.3 in women after TLH, 22.5 in women after LAVH, 22.2 in women after VH and 21.1 in women after AH. The differences were statistically not different between the five groups.

Conclusions: Women after LASH showed the highest B-PFSF score in comparison with women after other hysterectomy procedures. However this difference was statistically not significant. Using the B-PFSF there were no differences in prevalence of HSDD after hysterectomy, irrespective of the used surgical technique.

PO-Onko 03.28

Is there a time for a structured residency training in obstetrics and gynecology in Germany?

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Objective: The learning aims of German residents in Obstetrics and Gynaecology are well defined by the German medical association and specified in a mandatory logbook. However, structured training

programs have not been established, leading to a heterogeneous variety in quality and quantity of residency training. The purpose of this study was to examine the feasibility of a structured perennial postgraduate training program in Obstetrics and Gynaecology.

Materials and methods: A structured 3-year residency training program with theoretical and practical courses in Obstetrics and Gynaecology was inaugurated in 2006. Courses were held on a weekly basis. Acquired knowledge was assessed by written tests. Evaluations of the quality of the course were obtained on a weekly basis. At the end of the 3-year program a questionnaire was administered to the residents to obtain the overall impression. Questions were asked about the impact of the program on their working satisfaction, motivation, gain of knowledge and skills. Moreover the feasibility of the program in a university hospital setting was assessed.

Results: Residents participating in a structured residency training program in Obstetrics and Gynaecology felt better prepared for daily clinical work. The improvement of knowledge enhanced the working motivation and was incentive to participate at the courses. Lack of time was the most common reason for non-attendance.

Conclusions: Structured residency training is feasible in a German university setting to improve work satisfaction and knowledge among residents. Yet, a shortage of staff due to the workload makes regular attendance difficult. So, is there a time for a structured residency training program?

PO-Onko 03.29

QuaSiMa: optimization of quality management at certified and not-yet-certified breast centres and an introduction to the Senopedia.org knowledge base: preliminary results from a health services research study

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Objective: The introduction of certification into medicine has had considerable impact on improving the quality of care provided by German breast centres. Substantial investments (in staff, software, working time, etc.) are necessary to establish and maintain a quality management system (ISO 9001:2000) and to generate the key performance data required for certification, to conduct audits, etc. IT-based systems greatly facilitate the implementation and maintenance of QM systems in oncology and generate learning and synergy effects. QmMed.net enables the creation, via the QmMed.net internet portal, of an internet-based digital QM manual (QMM) based on ISO 9001:2000 as well as the adaptation of existing certified QM contents generated by academic certified breast centres. In addition, certification procedures according to the OnkoZert requirements are supported by means of document management, document control as well as document versioning. Senopedia.org is based on experience and designed as a knowledge portal. As of the fourth quarter of 2010, the portal will be made available free of charge to all breast centres by the German Society of Obstetrics and Gynaecology (DGGG) beyond the study period.

Study objectives:

- To evaluate the status quo of medical quality assurance processes by implementing internet-based QM systems at breast centres and conducting functional analysis

- To analyse the use of web-based tumour boards
- To improve the quality of cancer care
- To determine and compile the resources necessary for the process of (re)certification
- To promote the centres' internal and external communication
- To provide standard operating procedures (SOPs) and system processes on the Senopedia.org portal

The implementation questionnaire addressed important aspects such as time saving during QMM implementation, the use of resources for QMM transfer to the QMMed.net platform, the update status of the tumour board software at the various centres and the potential for optimization and evaluation of curricular continued education.

Conclusions: QuaSiMa and Senopedia.org enable breast centres to establish their own certification-relevant quality assurance and quality systems by providing:

- Access to a complete library of procedural instructions and quality-related documents for breast centres and gynaecological cancer centres
- Intuitive integration of in-house contents and adaptation of centre-specific processes
- Introduction and support during initiation by participation in training courses and video conferences
- Participation in the evaluation programme for (re-)certified centres.

PO-Onko 03.30

A perivascular epitheloid cell neoplasm of the uterus, arising from the right ovarian vein to the right atrium of the heart causing acute bilateral lung embolism

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Objective: Perivascular epitheloid cell tumor (PEComa) is a very rare mesenchymal tumor, however the uterus is one of the most frequently affected organs. Therefore we want to report the rare case of an angioleiomyolipoma of the uterus presenting as thrombosis and pulmonary embolism in a woman.

Materials and methods: A 52 year old woman was hospitalized in the department of vascular surgery in November 2009 because of an acute pulmonary embolism and a thrombosis of the right atrium of the heart, the inferior vena cava, the left vena iliaca communis, the left vena iliaca interna and the left vena ovarica. A CT-scan of the abdomen displayed a large conglomerate in the field of the uterus and the right ovary with a diameter of 8 cm in addition to the extended thrombosis. At first a fractional excision of the thrombosis in the right atrium and the inferior vena cava was performed and the histological examination revealed a myxoma. Thereafter excision of the residual thrombosis and hysterectomy with removal of both ovaries in collaboration with vascular surgery were performed in January 2010. Histological staining showed an uterine angioleiomyolipoma, a tumor of the perivascular epitheloid cell neoplasm (PEComa) family. Follow-up visits of the patient including CT scans performed on a monthly basis have shown normal findings so far.

Conclusions: Despite the fact, that PEComa is a very rare finding, the uterus is one of the most frequently reported anatomic location of its origin. Thus physicians should have in mind, that enlargement of the uterus in conjunction with thrombosis of the inferior vena cava or pulmonary embolism could be caused by a perivascular epitheloid cell neoplasm of the uterus.

PO-Onko 03.31

First results from the Patient's Anastrozole Compliance to Therapy Program (PACT) evaluating the influence of a standardized information service on compliance in postmenopausal women with early breast cancer (EBC)

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Objective: Retrospective data demonstrate that compliance to adjuvant endocrine therapy for early breast cancer (EBC) may drop below 80% after 1 year and as low as 50% by year 4. The PACT program aims to increase treatment adherence in postmenopausal women assigned for adjuvant anastrozole via a standardized information service.

Materials and methods: PACT is a prospective, randomised, two-arm, parallel group trial with a primary study phase of 12 months and subsequent 60 months follow-up. The program is sponsored by AstraZeneca Germany and supported by breast cancer advocates. Postmenopausal women on anastrozole for hormone-receptor positive (HR+) EBC were randomized to routine clinical care alone or additional standardized information for the first 12 months of adjuvant therapy. Primary endpoint is the compliance rate after 12 months. Secondary endpoints include reasons for non-compliance, influence of baseline characteristics, and clinical outcome parameters. Compliance is evaluated via patient questionnaires, prescription data and physician recall. **Results:** Recruitment was completed with 4,924 women in November 2008 with an average age of 64.7 years. Bilateral tumours occurred in 3.13% of patients, 25% had pTcIN0M0 disease, 3,141 (66.7%) had G2 tumours. 74.5% had received breast preserving surgery, 23.5% a mastectomy. 38.8% of patients had had adjuvant chemotherapy, 6.4% neo-adjuvant chemotherapy and 85.4% received adjuvant radiation therapy. 97.7% were ER+ (IRS), 8.4% HER2+ and approx. 4.9% received trastuzumab. Data on the primary endpoint of compliance at 12 months will be presented.

Conclusions: PACT is the largest prospective trial ever on compliance in patients with HR + EBC to clarify whether standardized information services throughout year one of adjuvant therapy may improve compliance to endocrine treatment and influence outcomes in postmenopausal women with HR + EBC.

PO-Onko 03.32

Effective chemotherapy free treatment of triple negative breast cancers with GHRH-Antagonist JMR-132 in combination with Avastin

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Objective: Triple negative breast cancers (TNBC) represent a subtype of breast cancers lacking the expression of estrogen receptor (ER), progesterone receptor (PR) and HER2neu. TNBC are associated with a poor prognosis and limited therapy options. In this study we evaluated *in vivo* the effect of GHRH-Antagonist JMR-132 in combination with Avastin on tumour growth inhibition in the triple negative doxorubicin resistant human breast cancer cell line MX1.

Materials and methods: The mRNA expression of pGHRH-R and the splice variant SV1 was detected by RT-PCR. For proliferation Assays cells were treated with different concentrations of JMR-132 and cell viability was assessed after 72 h using an MTS proliferation assay. For *in vivo* experiments MX1 tumours were xenotransplanted subcutaneously into nude mice. The animals were randomized into 4 groups receiving solvent only (Control), JMR-132 (10 mg/day s.c.), Avastin (10 mg/kg i.p. twice weekly) or the combination of both substances, respectively.

Results: The cell line MX1 expressed the pGHRH-R and the splice variant SV1. In the proliferation assays JMR-132 showed a significant inhibition of cell viability compared to control. In the *in vivo* experiment JMR-132 and Avastin showed a significant inhibition of tumour growth compared to control. The combination of JMR-132 and Avastin showed a significant tumour growth inhibition compared to all other groups.

Conclusions: The GHRH-Antagonist JMR-132 demonstrated an effective tumour growth inhibition in TNBC. This effect was increased in the combination with Avastin and represents a potential chemotherapy free treatment option for triple negative breast cancers.

PO-Onko 03.33

Aesthetic and functional outcome after breast conserving therapy: development and interaction with quality of life over time

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Objective: Functional and aesthetic outcome after breast cancer surgery are important correlates of the patient's quality of life. Therefore the interaction and development of functional and aesthetic outcome and overall quality of life over time is of special interest.

Material and methods: This prospective cohort study examines the correlation between the functional and aesthetic outcome with the quality of life and addresses the influence of the time of assessment. 138 patients treated with breast conserving surgery at the Heidelberg Breast Unit were included. The patients answered the BCTOS (Breast Cancer Treatment Outcome Scale) and the EORTC C30-BR23 questionnaires postoperatively and one year after surgery to measure function, aesthetics and breast sensitivity as well as overall and specific dimensions of quality of life.

Results: The results indicate that functional and aesthetic outcome keep an equally strong impact on overall quality of life over the course of time. Spaerman's Rho was 0.28 shortly and 0.45 one year after surgery for the interaction of functional and global health status and 0.36 and 0.32 for aesthetic and global health status, respectively. We observed the functional and aesthetic status to stay relatively stable on temporal progress with score means 1.38 shortly and 1.38 one year after surgery for the functional status and 1.82 versus 1.90 for the aesthetic status respectively. However, the breast sensitivity status improved with time (2.10 shortly versus 1.84 one year after

surgery; $p < 0.0001$) and tend to be stronger correlated to the global health status postoperatively than on the one year follow-up control (Spaerman's Rho = 0.4 shortly and 0.28 one year after surgery, $p = 0.29$).

Conclusions: Breast sensitivity is an increasingly important prognostic factor for quality of life with respect to temporal progress. Functional and aesthetic results do not change significantly within one year but remain important covariates.

PO-Onko 03.34

Inhibition of proliferation and induction of apoptosis of different breast carcinoma cell lines with anti-Mucin 1 antibody PankoMab

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Objective: Therapeutic antibodies gain more and more importance in cancer treatment. Tumor specific Mucin 1 is expressed in squamous cell carcinomas, but not in normal adult tissue. Beside its carrier function for onco-fetal carbohydrates Mucin 1 acts as a membrane receptor tyrosine kinase involved in cell adhesion and signal transduction. The anti-Mucin 1 antibody PankoMab only ligates tumor specific and active Mucin 1.

Materials and methods: The breast carcinoma cell lines MCF7, T47D, CAMA, MDA-MB-435, ZR75-1 and MDA-MB-231 were incubated in 96-well plates and in chamber slides with increasing concentrations of the PankoMab for 48 h. Proliferation was determined by a BrdU-uptake. Rates of apoptosis were defined by immunohistochemistry with the M30-antibody in the early phase and by nick-translation in the late phase. Every cell line without antibody incubation served as reference. Each approach was done five times.

Results: The cell lines MCF7, T47D, CAMA, MDA-MB-435 showed decreasing proliferation rates by increasing antibody concentrations. The lines ZR75-1 and MDA-MB-231 remained unimpressed. Apoptosis was induced in antibody treated cells of the cell lines MCF7, CAMA-1 and T74D.

Conclusions: *In vitro* the anti Mucin 1-antibody PankoMab is able to inhibit proliferation and to induce apoptosis of different breast carcinoma cell lines according to antibody concentration. Because Mucin-1 is a qualified tumor specific target and because PankoMab only binds tumor specific and membrane bound Mucin 1, we suppose an entry in a new antibody based therapy for patients with breast carcinoma.

PO-Onko 03.35

Acceptance of oral chemotherapy within metastatic breast cancer patients: a prospective questionnaire study

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Objective: Oral (p.o.) chemotherapy treatments have gained increasing importance in the palliative treatment of metastatic breast cancer.

The acceptance of p.o. compared to i.v. chemotherapy is not clearly evaluated. The aim of this survey was to study the reasons why patients would decide for a p.o. treatment and to objectify their individual attitudes to oral therapy.

Materials and methods: A specific questionnaire with 14 items was designed. Patients under a newly launched p.o. or i.v. chemotherapy treatment were prospectively evaluated within an observation period of 4 months. A total of 224 questionnaires using descriptive statistics, chi-square test, Spearman correlation were evaluated.

Results: The median age of patients was 54 years, 164 patients received i.v. therapy, 60 patients were on oral therapy. 89% of patients with p.o. chemotherapy (50/56) and 67% with i.v. regimens (106/158) would choose p.o. over i.v. therapy, if equal efficacy is guaranteed. Significant differences between the two treatment groups were found in terms of personal benefit (28% versus 58% by i.v./p.o.), reduced malaise under p.o. treatment (26% i.v., 64% p.o.), better disease coping by oral chemotherapy (36% i.v., 68% p.o.). A reduction of side effects due to p.o. regimens is seen by 18% of i.v. versus 52% of p.o. patients.

Conclusions: The p.o. chemotherapy has a major role in the palliative treatment of metastatic breast cancer and shows a high acceptance in patients under therapy. Prerequisite for successful treatment remains compliance, which can be achieved in particular through a differentiated indication, patient education and competent support along a p.o. treatment.

PO-Onko 03.36

COMpliance and Arthralgias in Clinical Therapy (COMPACT): assessment of the incidence of arthralgia, therapy costs and compliance within the first year of adjuvant anastrozole therapy

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Objective: Aromatase inhibitors (AI) are well established as adjuvant endocrine treatment for postmenopausal women with hormone receptor-positive (HR +) early breast cancer (EBC). However, AI are more frequently associated with arthralgia than tamoxifen. Prospective data are lacking on the effects of AI-associated arthralgia on patient compliance and patient outcomes as well as treatment costs of arthralgia in routine clinical practice.

Materials and methods: COMPACT is an open, prospective, non-interventional study assessing the incidence of arthralgia, therapy costs, and compliance within the first year of adjuvant anastrozole therapy in postmenopausal patients with HR + EBC. The study is sponsored by AstraZeneca and supported by German health insurance funds [GWQ ServicePlus AG, DAK]. Starting in April 2009, approx. 3,212 patients who have been on anastrozole for 3–6 months will be

enrolled at 700 breast centres and practices throughout Germany. Patients will be stratified to initial adjuvant anastrozole or switch from tamoxifen. All patients will receive regular standardized information about breast cancer from baseline through to week 20 after study start to support treatment compliance. Data on demographics, arthralgias, therapy of arthralgia, and quality of life will be collected at baseline, 3, 6 and 9 months. Primary endpoints are scaled data on arthralgia and compliance within the first year of anastrozole therapy. Secondary endpoints include the incidence of arthralgias, therapy costs, reasons for non-compliance, and influence of arthralgias on clinical outcome. For a subgroup of patients data on arthralgia therapy and compliance will be validated with corresponding accounting data of participating health insurance funds.

Results: NA.

Conclusions: COMPACT aims to provide valid data on AI-associated arthralgias, treatment, and treatment costs. This may help to better inform patients and health care providers about these clinically important issues with the aim to improve adherence to anastrozole treatment, breast cancer outcomes, and therapy costs.

PO-Onko 03.37

Influence of Galectin-1 on apoptosis, proliferation and the expression of receptor tyrosine kinases in breast cancer cell lines

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Objective: The Thomsen–Friedenreich (TF) epitope is a highly tumor specific carbohydrate antigen. Breast cancer patients expressing TF showed higher survival rates compared to TF negative breast cancer patients. Galectin-1 (Gal-1) is known to bind TF in choriocarcinoma patients and induces signal transduction in these cells. The aim of this study was to investigate role of Gal-1 in TF positive/negative breast cancer cells in vitro.

Materials and methods: Breast cancer cell lines CAMA1 with high expression and MDA-MB-231 with no expression of TF were used for the study. The cell lines were incubated with 60 µg/ml recombinant Gal-1 in DMEM for 48 h. Apoptosis rates were determined by nick translation, immunocytochemistry with a M30 Cytodeath antibody and a cell death detection ELISA. Proliferation was measured by a BrdU cell proliferation ELISA. Receptor tyrosine kinase-expression patterns were analyzed by a Phosphor-RTK Array and quantified with the “Quantikine” software.

Results: Gal-1 inhibited the proliferation and induced apoptosis of the CAMA1 cell line. MDA-MB-231 cell lines showed a higher proliferation rate and an unaffected apoptosis rate after Gal-1 stimulation. The Phosphor-RTK-Array resulted in a down regulation of ErbB2 and an up regulation of ErbB4 after stimulation of CAMA1. Stimulated MDA-MB-231 had a lower expression for EGFR and a highly elevated Axl.

Conclusions: TF high expressing breast cancer cells showed low proliferation rate and higher amount of apoptotic cells, compared to breast cancer cells with no expression of this antigen. In addition, signal transduction processes were completely different in both cell lines. Therefore we speculate that Gal-1 induced signal transduction via TF is one factor responsible for high survival rates of TF positive patients.

PO-Onko 03.38**Underfunding of 90.3% of implant costs for prostheses and expanders in DRGs for mastectomy with immediate breast reconstruction**

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Objective: Economic patient care requires comparison and adjustment of costs and reimbursement for all medical service from clinics' point of view. Due to flat-rate payment the reimbursement equals target costs for diagnostic and therapy. To verify cost coverage for implants in uni- and bilateral mastectomy with immediate reconstruction, DRGs J06Z and J16Z, a comprehensive cost-reimbursement analysis was performed.

Materials and methods: Retrospective analysis of calculated DRG-revenues for material expenses for implants from DRG-Browser 2007/2009HA, issued by InEK, and comparison with actual costs of the OB/GYN department for implants in 2009 from annual report and eisTIK-data base of the controlling department. Calculation of relative cost-coverage for implants by number of DRGs J06Z or J16Z performed multiplied with DRG-calculated material expenses for implants divided by implant costs for 2009.

Results: At our institution $n = 98$ J06Z and $n = 18$ J16Z were performed in 2009. DRG-calculated material expenses for implants were 69.65€ for each J06Z and 123.07€ for each J16Z, a total of 9,040.96€. Actual costs for all implants ($n = 190$) were 121,645.60€, 0699.11€ (404.94–1,171.44€). The percentage of immediate breast reconstruction for all patients results in calculatory implant costs of 77.0%, 93,679.28€. Implants are underfunded by –90.3%, ranging from –82.8% for least costly prosthesis in unilateral mastectomy to –94.7% for most expensive expanders in bilateral mastectomy. Subvention for implant expenses necessary from clinic's budget ranges 335.29–2,219.81€/case.

Conclusions: Immediate breast reconstruction with implants after mastectomy is even 6 years after introduction of DRGs not adequately cost-covering calculated, since actual implant costs exceed calculated revenues by far. At present time our institution subsidizes these implants with 090.3%. If economic patient care is mandatory, a maximum of only 1 in 10 patients with mastectomy can be offered immediate breast reconstruction with implants in Germany.

PO-Onko 03.39**Clinically relevant gene signatures in triple negative and basal like breast cancer**

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Objective: Prognostic and predictive gene expression profiles in breast cancer mainly reflect ER, PgR, HER2 status, and proliferation. Triple

negative breast cancers (TNBC) seem to constitute a heterogenous group of and their relationship to basal-like breast cancers (BLBC) is not fully clear. Further understanding of TNBC is important since new treatments are needed.

Materials and methods: We assembled an Affymetrix dataset of $n = 579$ TNBC (finding cohort $n = 394$, validation cohort $n = 185$). Unsupervised methods identified principal metagenes differing among TNBC in this clean cohort. Clinical data were correlated to these metagenes for the basal-like phenotype, the apocrine phenotype, different types of immune cells, a stromal signature, the claudin-CD24 signature, markers of blood and adipocytes, as well as an angiogenesis signature and an inflammatory signature.

Results: 73% of TNBC displayed a basal-like phenotype which correlates with poor histological grading and younger age. However, no effect of basal-like phenotype on survival was observed. A good prognosis was obtained for expression of immune cell metagenes and a poor prognosis was associated with metagenes for inflammation, angiogenesis and stromal cells. A combination of high B-cell metagene and low inflammation metagene expression identified 27% of TNBC with a good prognosis (HR 4.0, 95% CI 2.1–8.0; $P < 0.001$) remaining the only significant factor in multivariate analysis with standard parameters.

Conclusions: All available clinical parameters and genomic signatures assign TNBC to a poor prognosis group. Use of a subtype-specific dataset not confounded by the main variables of breast cancer allowed the identification of prognostic signature for TNBC.

PO-Onko 03.40**Shear Wave Elastography: results on 1000 cases in the Breast Elastography (BE1) investigators multicenter study**

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Objective: ShearWave™ Elastography (SWE) offers a new and independent method of investigating tissue characteristics. The BE1 study tested its ability to refine breast mass diagnosis with conventional BI-RADS ultrasound by adding SWE features. To evaluate specificity without reducing sensitivity.

Materials and methods: Patients scheduled for a breast ultrasound were recruited to the BE1 study which was approved by the IRB of each center. B-mode-US were performed on the institution's own system and on the new system, followed by a SWE scan. 1000 lesions from 17 sites were entered. 910 had proven pathology, 90 are being followed-up. The reproducibility of SWE images and measurements was assessed on 3 consecutive acquisitions. The best three-variable model, including the BI-RADS score and 2 SWE features, was determined using multivariate regression analysis and used for reclassification.

Results: Weighted kappa test demonstrated very good agreement between the BI-RADS classification on the home and SWE systems (0.89). The low rate (1.3%) of cases with very dissimilar acquisitions demonstrated qualitative reproducibility; intra-operator reproducibility of 0.95 and 0.91 demonstrated good reproducibility of size and elasticity measures, respectively. The home and new systems were equivalent (kappa = 0.89) and the SWE images proved to be reproducible. All SWE features improved the area under the ROC curve of the conventional BI-RADS test (0.72). Adding SWE Homogeneity

and mean elasticity value or ratio gave the best models (AUC 0.89 and 0.88). Both increased the specificity of the test by over 20%; its sensitivity and NPV decreased by <4%. For BI-RADS 3 and 4 lesions showing 2 SWE signs of benignity/malignity, Model 2 correctly regraded 80.7% of 197 lesions.

Conclusions: SWE is highly reproducible. Adding two SWE features to BI-RADS test significantly improved ROC curves.

PO-Onko 03.41

Conization of the cervix during pregnancy:

a retrospective study

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Objective: The aim of this study was the evaluation of the efficacy and clinical outcome of patients who underwent conization during pregnancy. We compared the preoperative cytological and histological results with the postoperative results. Prenatal and peripartal complications were evaluated.

Materials and methods: We performed a file review and found 27 patients who underwent conization during pregnancy between 2003 and 2009. Suspect cytological or histological findings (colposcopic assisted biopsy) lead to LLETZ conization. Furthermore, the data collection contains HPV-testing, intraoperative and postoperative complications and affection of the margins. Additionally, a questionnaire was created to get further information about the mode of delivery, postpartum cytological results and procedures.

Results: Three patients showed an invasive cancer, in 22 patients a CIN3 and one CIN2 lesion were found histologically. In one case the histological result could not be evaluated. 24 of 25 were tested positive for high-risk HPV DNA (13 HPV16, 1 HPV18, 1 HPV31, 1 HPV39 + 51, 1 HPV52). In 8 patients HPV could not be subtyped. No intraoperative complications were observed. One patient showed a postoperative missed abortion. In 15 patients we found positive microscopic resection margins. In 10 cases colposcopy and biopsy and in 11 cases colposcopy and conization revealed identical results, respectively. Histological results of the biopsy and the conization matched in 9 cases. All cases of cervical cancer were classified as no more than Pap IV or CIN3 before conization.

Conclusions: The performance of a conization during pregnancy is important in patients where invasive cancer cannot be excluded. We showed a rate of 11.1% of invasive cancer that could not be detected prior to conization. LLETZ conization can be performed as curative therapeutic option in pregnancy with a low intraoperative, postoperative and peripartal complication rate.

PO-Onko 03.42

Public awareness and practice of cervical cancer prevention in Greece

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Objective: The aim of the present study was to investigate the awareness of Greek women on cervical cancer prevention, HPV

infection and preventive vaccination against HPV, as well as their participation in cervical cancer screening.

Materials and methods: This is a prospective, cross-sectional study, including women from various geographical regions of Greece. Between October 2005 and June 2009, 4,373 Greek women completed the study questionnaire, which included questions about the demographic characteristics of participants, their personal history, knowledge about the natural history of HPV infection and cervical cancer, and methods currently used for primary and secondary prevention of cervical cancer. The following inclusion criteria were used: female participants only; age 18–65 years; Greek as native language and residency in Greece.

Results: The largest age group among the 4,373 participants was that of women aged 30–39 years (26.5%). Whereas 66.5% of women were well-informed about cervical cytology (Pap-test), 32% were not. Only 40.8% of women answered that they have had a Pap-test at least three times; 33% had only one Pap-test, while 26% answered that they have never had a Pap-test. Forty four per cent of women were aware that cervical cancer can be prevented, 46% have heard about HPV, but 76% were not aware of the etiological association between HPV-infection and cervical cancer. Only 29% of women knew how HPV can be transmitted. Regarding HPV-testing, 42% of participants were aware of, while 40% have never heard of HPV-testing. The majority of women (59%) would be vaccinated against HPV, while 9.5% would not accept to be vaccinated.

Conclusions: Greek women are poorly informed about cervical cancer prevention, HPV infection and HPV-testing. Acceptability of preventive vaccination against HPV, and participation in cervical cancer screening are currently far from ideal.

PO-Onko 03.43

SPECT/CT improved intraoperative detection of sentinel lymph nodes in vaginal and cervical cancer

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Objective: Pelvic and paraaortic sentinel lymph nodes (SLN) in cervical and vaginal cancer are detected by lymphoscintigraphy and intraoperative by gamma probe. In this study we evaluated the value of single photon emission computed tomography combined with computed tomography (SPECT/CT) for the detection of SLN in cervical/vaginal cancer.

Materials and methods: Between August 2008 and March 2010 the SLN of 28 women with cervical cancer and 2 women with vaginal cancer were marked pre-operatively using peri-tumoral injections of 10 MBq technetium-99 m-nanocolloid (4 × 2.5 MBq; 0.5 ml each). After 45 min p.i. planar lymphoscintigraphy was performed followed by SPECT/CT and surgery. Intra-operatively the SLN were searched using a gamma probe. We analyzed the following information's: number and anatomical location of SLN on lymphoscintigraphy as well as on SPECT/CT. In addition SLN in non-typical anatomic locations were recorded.

Results: The planar lymphoscintigraphy alone detected SLN in 25 of 30 patients. SPECT/CT detected SLN in 28 of 30 patients. In 7 patients the SPECT/CT showed 1 to 3 lymph nodes more the planar mapping. On the one hand these additional lymph nodes were really SLNs located near the injection places; on the other hand lymph nodes that impressed as one in the planar images identified themselves as multiple SLNs in the SPECT/CT. In 27 of 28 patients the lymph nodes detected in SPECT/CT could be found and removed

intraoperatively. Five patients had one or more SLN metastasis; 1 of them had more non-SLN metastases. In one patient non-SLN metastasis were found with non-affected SLN.

Conclusions: With use of SPECT/CT in patients with vaginal and cervical cancer a higher number of SLNs can be detected compared to conventional lymphoscintigraphy. Furthermore this method permits a more accurate anatomical correlation of SLN and improved the intraoperative detection. This may prevent large tissue damage during searching and removal of SLN.

PO-Onko 03.44

Development of a cervical organ culture model to identify the HPV target cell capable of driving viral persistence

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Objective: Crucial factors determining persistent HPV-infection and development of precancerous and cancerous lesions are largely unknown. We previously identified a putative stem cell population within the cervical epithelium which preferentially binds virus-like particles. This study aimed to develop a 3D organotypic culture system to monitor HPV-infection.

Materials and methods: Organotypic cervical explant models were designed based on a modified raft culture system using fragments of human uterine cervix. HPV-16 pseudoviruses (PsV), GFP-coupled and packaged with RFP reporter plasmids, were used to assess virus binding and infection of cervical epithelial cells. Fluorescence microscopy and FACS-analysis were employed to monitor integration of encapsidated plasmids into the host cell genome and to define the phenotype of the respective epithelial target cells.

Results: We report on the successful development of a cervical organ culture model maintaining original organ architecture, tissue heterogeneity and expression of cellular markers for up to 4 weeks. These cervical explants provided the basis for monitoring virus binding and the course of infection within the regenerating epithelium after exposure to HPV-16 PsV. Long term infection was detected in only a small number of cells within the basal cell layer. These cells possess characteristics and functional properties of stem cells, thus suggesting that stem cells are the targeted cell type to achieve viral persistence.

Conclusions: Our studies describe the development of the first cervical organ culture system maintaining all cell types of squamous epithelium over a 4-week period, permitting monitoring high risk HPV-infection. This explant model is a valuable in-vitro system to study mechanisms and time course of epithelial regeneration and viral infection. Our data indicate that infection of stem cells within the cervical epithelium is indeed necessary to establish long term infection. These findings represent an important step forward to define the role of stem cells in HPV-associated carcinogenesis.

PO-Onko 03.45

Detection of high-risk HPV mRNA in liquid based cytology (LBC) specimens with the APTIMA[®] HPV assay

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Objective: The objective of this study was to compare the APTIMA HPV assay (AHPV; Gen-Probe Inc.) that detects E6/E7 mRNA from 14 high-risk types and the Hybrid Capture 2 HPV DNA test (HC2; Qiagen Inc.) for their ability to detect high-grade cervical lesions (CIN 2+) in women referred to colposcopy.

Materials and methods: A total of 424 clinical specimens were included in this study, stored in liquid based cytology (LBC) vials at room temperature for up to 3 years and then tested by both AHPV and HC2. Specimens processed with the HC2 test that yielded no pellet after centrifugation and were HC2 negative were excluded to avoid bias against HC2. Assay results were compared to each other and to cytology and histology.

Results: The overall agreement between AHPV and HC2 was 88.4%. The sensitivity (specificity) of AHPV, HC2, and cytology for the detection of CIN2+ was 92.0% (75.1%), 91.2% (60.7%), and 85.3% (67.1%), and for the detection of CIN3+ 98.1% (56.1%), 96.7% (45.8%), and 94.4% (55.0%), respectively. Most of the disease positive specimens missed by AHPV were HPV negative or only contained low-risk HPV, making it unlikely that those specimens were truly disease positive.

Conclusions: Thus, AHPV is able to detect high-risk HPV mRNA in LBC specimens stored at room temperature for up to three years with strong correlation to high-grade lesions. AHPV had a similar sensitivity, but a considerably higher specificity than HC2. AHPV was both more sensitive and specific than cytology.

PO-Onko 03.46

Feasibility of simultaneous radio-chemotherapy in cervical cancer: implementation of standards in daily routine in a tertiary gynecologic oncology unit

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Objective: Simultaneous radio-chemotherapy (SRCT) is standard of care for locally advanced cervical cancer. Achieving adequate dose intensity as established in several studies is essential for treatment success. Our aim was to evaluate compliance with study driven standards in clinical reality in a general patient population.

Materials and methods: Retrospective analysis of all patients with cervical cancer in our tumor registry between 2000 and 2007, treated at our institution with SRCT. Patients with FIGO IB2-IIIb (primary) or FIGO IA1-IB1 with adjuvant therapy due to postoperative up-staging, positive lymph nodes, lymphangiosis or G3 adenocarcinomas were included.

Results: 77 Patients, scheduled for SRCT were included. 31 of these patients were planned for primary, 46 patients for adjuvant radio-chemotherapy (RCT). 74%, respective 76% of patients in both cohorts (primary/ adjuvant) received full planned dose-intensity. 6 patients never started and 14 patients discontinued RCT: 10 for medical, 4 for personal reasons. Out of these 14 patients, 11 patients achieved full radiation dose and 2 of them received at least 34.2 Gy; 13 patients completed at least 2 cycles of chemotherapy. After 52 months of median follow-up we observed 8 recurrences in the adjuvant group: 2 (25%) of them with incomplete primary therapy. 11 recurrences of whom 3 (27%) had incomplete therapy in the primary treatment group. 5-year-survival after adjuvant treatment was 75% and 45% after primary RCT.

Conclusions: SRCT can be completed in most patients as scheduled. In our cohort, prior surgery had no negative impact on patients' compliance with RCT.

PO-Onko 03.47

Prognostic value of perineural invasion (PNI) in carcinoma of the cervix uteri

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Objective: Limited information exists about the frequency and the prognostic impact of perineural invasion (PNI) in patients with cervical carcinoma (CX).

Materials and methods: The original histologic slides from patients primarily treated by radical hysterectomy and systematic pelvic lymphonodectomy were re-examined regarding the occurrence of PNI. PNI was correlated to recurrence free (RFS) and overall survival (OS).

Results: 35.1% of all patients (68/194) represented perineural invasion (=PNI 1). Patients with PNI showed significant reduced RFS-rate at 5-years, when compared to patients without PNI (5-year RFS of 69.5% [95% CI: 57.2–81.8%] for PNI 1 and of 78.3% [95% CI: 70.9–85.7%] for PNI 0 but without statistical significance ($p = 0.3$). The 5-year-overall-survival-rate was significantly decreased in patients with PNI 1 (PNI 1: 51.1% [95% CI: 38.0–64.2] versus PNI 0: 75.6% [95% CI: 67.8–83.4]; $p = 0.001$). In a separate analysis the prognostic impact persisted in the node negative, but disappeared in the node positive cases. In multivariate analysis, pelvic lymph node involvement and PNI were independent prognostic factors for overall survival.

Conclusions: A reliable number of patients with CX show perineural invasion (PNI). PNI might represent a prognostic factor but, its clinical implication is unclear at time. Further studies are required to get a deeper insight about the clinical impact and the pathogenetic mechanisms of PNI in CX.

PO-Onko 03.48

Expression of sialyl Lewis A (SLeA) in cervical dysplasia and invasive cervical cancer

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Objective: SLeA is a carbohydrate motif that mediates adhesion between tumour cells and endothelium. It is usually not expressed in non-malignant tissue. Malignant transformation is associated with abnormal glycosylation, resulting in synthesis and expression of altered carbohydrate determinants, including SLeA. Aim of this study was to investigate the expression of SLeA in normal cervical squamous epithelium, cervical dysplasia grade 1–3 (CIN I–III), carcinoma in situ and invasive cervical squamous cancer.

Materials and methods: Tissue was collected from conisation specimen, fixed and embedded in paraffin. Slides were fixed and incubated with monoclonal antibodies against SLeA (IgM). Staining reaction was performed with ABC reagent. The intensity of immuno-histochemical reaction was analyzed using the Remmele-Score. We evaluated 10 samples each of normal squamous epithelium, CIN I,

CIN II, CIN III, carcinoma in situ and invasive squamous cancer which had been classified before by standard pathological examination. Evaluation was done by two independent observers including a pathologist.

Results: Median Score for normal squamous epithelium was 7, for CIN I was 10, for CIN II was 7; for CIN III was 9, for Carcinoma in situ was 7 and for invasive squamous cancer was 3. There was no measurable difference between the non-invasive cervical dysplasias and normal squamous epithelium. Comparing non-invasive to invasive samples there was a measurable loss of staining in invasive squamous cancer. In cancer specimen there were totally unstained tumours. Tumours with loss of differentiation and/or necrosis showed strong staining of SLeA

Conclusions: Expression of SLeA in normal cervical squamous epithelium can be explained by physiological function in human reproduction. Loss of expression in invasive cancer may resemble the loss of differentiation according to physiological function. Positive staining in above described tumour areas may refer to higher potential for hematogen metastasis via selectin mediated binding to blood vessels or other unexplained mechanism.

PO-Onko 03.49

Establishing a highly sensitive and specific assay for quantifying circulating tumour cells in patients with cervical carcinoma

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Objective: There is mounting evidence that the detection of circulating tumour cells (CTC) in the blood of cancer patients may be useful for therapy monitoring and for the prediction of early relapse. We aim to establish a highly sensitive and specific assay for quantifying CTC in the blood of cervical carcinoma patients.

Materials and methods: Our assay is based on HPV oncogene transcripts which are characteristic molecular markers for cervical cancer cells. Therefore we have designed a real-time one-step-RT-PCR for the detection of cells expressing spliced HPV16/18-E6 mRNA. By combining Ficoll-separation and ThinPrep-fixation of mononuclear blood cells (MNBC) with digital RT-PCR it is possible to detect individual CTCs independent of the viral transcript levels of individual tumour cells.

Results: Experiments with cultured HPV-positive cells in a background of HPV-negative cells demonstrated the high sensitivity of our assay (detection of one HPV16/18—positive cultured cell in 100,000 up to 500,000 HPV-negative cells). Furthermore by performing spike-in experiments with 10 HPV-positive cells per 1 ml EDTA-blood we obtained concordant positive results in PCR experiments and immunocytochemical analyses using MNBCs equivalent to 100 µl blood. At present we are analyzing blood samples of patients with cervical carcinomas of FIGO stage III/IV.

Conclusions: Using a highly sensitive one-step RT-PCR in combination with intact, fixed cells we could quantify low numbers of HPV16/18-E6 expressing cells even in a high background of HPV-negative cells. This practicable method for the detection of circulating tumour cells in whole blood of cervical carcinoma patients seems to be very promising and might become a valuable tool for the early detection of relapse and response to systemic chemotherapy.

PO-Onko 03.50**Age at menarche and menstrual cycle attitudes in a population of high school girls**

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Objective: Menarche is one of the most important biologic signals in the life of a woman. The first cycles tend to be anovulatory and vary widely in length. Menarche occurs between the ages of 10 and 16 years in most girls in developed countries. The aim of this study is to examine the association between the menarcheal age and menstrual cycle abnormalities.

Materials and methods: In this survey-based study, college-aged Medicin and Pedagogic-girls University of Alexandroupolis ($n = 85$) were screened by completing a questionnaire concerning their menarcheal and menstrual attitudes experiences. The results of detail endocrinologic workup were appropriate. A transvaginal sonographic examination, accompanied if necessary by a transabdominal examination was performed on all participants.

Results: The average age at menarche for the girls was 11.6 ± 1.3 . Girls who had extremely early menarche (Group A = 40) or extremely late menarche (Group B = 45) returned to complete questionnaires concerning current menstrual attitudes experiences. Girls in the group B reported more menstrual cycle abnormalities. (Group A = 15/45 vs. Group B = 9/40) respectively. The levels of hormonal parameters and endometrial thickness were normal in all cases. In the Group A the teenagers with menstrual cycle abnormalities reported about irregular bleeding in 66% and prolonged bleeding in the remaining cases. In the Group B the teenagers with menstrual cycle abnormalities had complaint of amenorrhoea in 29.5% cases, 34.5% had infrequent and 26% frequent bleeding.

Conclusions: The diagnosis and management of menstrual disorders in adolescent girls is a particular challenge. A detailed and confidential medical and psychosocial history are necessary.

PO-Onko 03.51**Unusual complication after core needle biopsy of the breast: therapy resistant mastitis after core needle biopsy of a phyllodes tumour**

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Objective: Percutaneous US-guided core needle biopsy (CNB) is a safe standard procedure in the work-up of suspicious breast lesions with a low complication rate.

Materials and methods: A 48 year-old patient presented to our department in 8/2009 because of a routine mammography (BIRADS IV bilaterally). Ultrasonographically, numerous lesions suspect of fibroadenoma were seen (BIRADS IV). CNB was performed and histology revealed a cyst (right breast) and a benign phyllodes tumour (left breast). She had no significant past medical history, but was status post open biopsy of the right breast (1981) and two reduction surgeries bilaterally (1991, 2005). Ten days after biopsy, the patient developed a diffuse mastitis. Despite intensive therapeutic measures such as oral and intravenous antibiotics as well as conservative measures the mastitis had not shown relevant improvement over months. The

infection was extensive (ca. 15×12 cm) with signs of fluid necrosis of the fatty tissue. At no time an abscess had developed.

Results: We recommended excision of the phyllodes tumour of the left breast. Because of her past surgical history and with the risk of subsequent operations the patient refused a breast-conserving surgery. She preferred bilateral mastectomy which was performed seven months after the CNB with following adequate wound healing. Histology revealed a phyllodes tumour 3 cm in size (left breast) and a benign phyllodes tumour of 1 cm as well as a fibroadenoma (right breast).

Conclusions: Percutaneous US-guided CNB is a standard procedure in the work-up of suspicious breast lesions with a low complication rate. The most common complications are haematoma and infection with each less than 1:1000. In this case, the prolonged course of breast infection after CNB was not as expected. Possibly due to her previous surgeries, the impaired tissue of the breast resulted in a mastitis that was resistant to conservative therapies.

PO-Onko 03.52**Comparison of conventional Papanicolaou smear and liquid-based cytology taken from the vaginal cuff after gynecological malignoma and radiation therapy**

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Objective: The conventional Papanicolaou (CP) smear and liquid-based cytology (LBC) are today's available cytological methods for the preventive gynecological examination. Literature about an advantage of one method is inconsistent. This study evaluates the difference between these two methods in terms of unclear results in an oncologic follow-up care setting.

Materials and methods: We examined 81 patients in the context of follow-up care after therapy of gynecological malignoma in our oncological ambulance. All patients underwent hysterectomy and radiation therapy (\pm chemotherapy). We performed a CP smear and a LBC taken from the vaginal cuff in every patient switching the order after every patient. The samples were fixated in a standard procedure and were stained using the Papanicolaou protocol. The evaluation was performed by one experienced gynecological cytologist using the Munich II nomenclature.

Results: All 162 samples were evaluable. There were no results in the group Pap III D or higher. In the LBC group we found a Pap II in 74 cases and a Pap III in 7 cases. In the CP group there were 66 cases of Pap II and 15 cases of Pap III. That means that inconclusive results were more than double as high in the CP group than in the LBC group.

Conclusions: Even though the advantage of one of the discussed methods as a standard procedure in the preventive gynecological examination is disputed, we found in our small group of patients a surprisingly high difference concerning Pap III results with much less unclear results in the LBC group.

PO-Onko 03.53**Quality of life and sexual functioning in endometrial cancer survivors**

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Objective: Recent evidence suggests equivalent efficacy in terms of local control for adjuvant vaginal brachytherapy (VBT) compared to external beam radiotherapy after surgery in patients with

intermediate-high endometrial cancer. The objective of this study is to compare the quality of life (QoL) and sexual function of women with endometrial cancer that were treated with either surgery alone or surgery in combination with postoperative VBT.

Materials and methods: Women were interviewed at least 5 years after initial treatment for endometrial cancer. QoL was evaluated by using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 and the cervical cancer module, CX-24. Sexual function was evaluated by using the Female Sexual Function Index (FSFI). Eligible women had early stage disease, were currently disease-free, and had undergone surgery and adjuvant VBT, but neither external beam radiotherapy nor systemic treatment. This study group were then compared using univariate and multivariate analyses with an age-matched control group comprising of endometrial cancer patients without adjuvant VBT.

Results: Fifty-five patients (29 surgery + VBT and 26 surgical controls without VBT) were included for analysis. With respect to QoL including physical, role, cognitive, emotional, and social functioning in the C30 questionnaire or symptom experience and body image in the CX24 questionnaire, univariate and multivariate analyses did not show significant differences between the study group and controls. Likewise, in terms of sexual function statistical analyses did not show significant differences between patients with VBT and controls on any of the outcome measures in the FSFI questionnaire.

Conclusions: Adjuvant VBT after surgery does not seem to have a significant impact on quality of life and sexual function in endometrial cancer survivors.

PO-Onko 03.54

Effect of antiretroviral drugs on mitochondrial DNA in HIV-infected pregnant women and their newborns

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Objective: Nucleoside Reverse Transcriptase Inhibitors (NRTIs) can reduce the risk of mother to child HIV transmission. Besides their effect on viral reverse transcriptase, NRTIs can influence the mitochondrial DNA replication. To analyse the toxic effect of NRTIs on maternal and fetal mitochondria the amount of mitochondrial DNA (mtDNA) was detected.

Materials and methods: HIV-infected NRTI-treated pregnant women and healthy controls were included in the study. The amount of mtDNA (copies/cell) in maternal and fetal (umbilical cord blood) peripheral mononuclear cells (PBMCs) was detected by Taqman-PCR. The mtDNA value in PBMCs of newborns was followed up after 3 months.

Results: Compared to their HIV- and NRTI-exposed children and the healthy controls, PBMCs of HIV-infected NRTI-treated women showed a significant reduction in mtDNA copies per cell. No significant effect could be detected in mtDNA value of healthy controls. In HIV- and NRTI-exposed newborns no significant mtDNA depletion could be measured compared to newborns of healthy controls at birth and after 3 months.

Conclusions: The use of antiretroviral drugs, in particular NRTIs, in HIV-infected pregnant women can induce mitochondrial toxicity. In their newborns no matchable reduction in mtDNA at the time of birth and after 3 months could be detected compared to healthy controls. Furthermore a toxic time dependent effect in NRTI-exposed HIV-negative newborns is unclear.

PO-Onko 03.55

Chromosome segregation control pathway of Aurora kinases correlates with tumor grade in breast cancer and ovarian cancer

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Objective: Cells of solid tumors frequently show unbalanced chromosome distributions. The deficient segregation is accompanied by upregulated expression of the aurora kinases pathway involving AURKa, AURKb and STK6. Here we are able to show that the expression of these genes correlates with the tumour grade in ovarian cancer and breast cancer like proliferation markers do.

Materials and methods: The expression pattern of AURKa, AURKb, STK6, Ki67, CDC2 and CDK2 were examined on paraffin embedded tissue sections of 21 normal breast and 42 breast cancer samples by immunohistochemistry. In addition 89 ovarian cancer specimens were stained for AURKa, AURKb, STK6 and Ki67. For statistical analysis Pearson's correlation coefficient and Jonkheere-Terpstra-Test were performed. Clinical Data was obtained from the hospitals own data base.

Results: As expected expression levels for all proteins were raised in tumor cells compared to benign tissue. In all explored specimens AURKa, AURKb and STK6 significantly correlate among each other ($p < 0.001$) and also with established proliferation markers like Ki67, CDC2 and CDK2 ($p < 0.001$). Expression of Aurka, Aurkb and STK6 was significantly increased in higher grade tumors compared to that in lower grade tumours ($p < 0.001$). Reduced recurrence free survival for breast cancer and ovarian cancer patients is detected if the aurora kinase pathway is upregulated.

Conclusions: Apart from well known proliferation markers like Ki67, CDC2 and CCK2, tumorproliferation is also represented by the upregulation of the aurora kinase pathway. The increased expression of these proteins which regulate chromosome segregation is also associated with the tumor grade and reduced progression free survival. We conclude that there is a causal correlation between incorrect chromosome segregation and carcinogenesis, whereas the question arises, whether the incorrect chromosome segregation leads to carcinogenesis or average tumor cell proliferation always gives rise to deficient chromosome segregation.

PO-Onko 03.56

Lymphedema following surgical treatment for gynecological malignancies: prevalence and risk factors

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Objective: Lymphedema is a major cause of morbidity following surgical treatment that involves lymph node dissection in cancer patients. However, the impact of lymph node removal on the prevalence of lower extremity lymphedema in patients with gynecological malignancies is largely unknown. The aim of this study was to determine prevalence of such lymphedema, its relationship to the extension of lymphadenectomy, and risk factors for its occurrence.

Materials and methods: A retrospective analysis of all patients undergoing lymphadenectomy in newly diagnosed gynecological malignancies at the University Hospital of Zurich 2000–2007 was performed. Patients with lower limb lymphedema were identified through any medical records available. Cases of lymphedema diagnosed prior to surgery or related to other causes were excluded.

Results: 313 patients receiving treatment for gynecological malignancies which involved initial lymphadenectomy were evaluated. 37% of patients were diagnosed with lymphedema within 1 year after surgery. Incidence of lymphedema correlated positively with the number of lymph nodes dissected. Patients suffering from wound infections and lymphocysts had a significant increased risk to develop lymphedema. Association with TNM-classification, chemo-/radiotherapy, age, BMI, history of previous abdominal surgery and venous insufficiency/thrombosis is under current statistical analysis and will be presented at the DGGG meeting.

Conclusions: Lymphedema is a frequent complication after treatment of gynecological cancers. Our data stress the need for prospective evaluations of lower limb lymphedema after surgery involving lymphadenectomy. These results will not only guide the physician in identifying high-risk patients but also provide the basis to sufficiently inform the patient about such complications that potentially have a significant impact on postoperative quality of life. Furthermore, the risk for post-treatment prevalence of lower body lymphedema must be taken into consideration during treatment planning as we gain increasing knowledge about the therapeutic benefit of systematic lymphadenectomy in patients with different stages of gynecological malignancies.

PO-Onko 03.57

A rare presentation of an isolated stromal compartment endometriosis of the lung: a variation that may mimic metastases of a low malignant stromal sarcoma

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Objective: Endometriosis is thought to affect 30% of women in reproductive age. Most commonly, the pelvic organs are involved. The manifestation of extragenital endometriosis is still rarely presented. In addition, there are just a few cases that report on the manifestations of thoracic endometriosis, defined by the presence of endometrial tissue in the lungs or pleura. Furthermore, histological findings of thoracic endometriosis with a solitary stromal component have barely been described so far. Histologically, endometriosis resembles endometrium consisting of both stroma and glands with cuboidal to cylindrical epithelium in different proportions.

Materials and methods: We report an unusual case of a 38 year old female who was referred to our hospital with a medical history of recurrent pneumothoraces from 2001 to 2008 primarily caused by unknown origin. In the later histological findings thoracic endometriosis was suspected. The patient was seen by consultants from the pulmonary, thoracic surgery and obstetrics/gynecology departments. The CT scan showed a cystic transformation of the lung in both sides. Physical examinations and laboratory investigations were unremarkable. Thoracoscopic procedures with biopsy, pleurodesis and partial wedge resection of the lung were performed on both sides. The histological findings according to the morphology and the immunohistochemical expression patterns showed endometrial stroma cells. Further investigations like a hysteroscopy with fractional curettage and diagnostic pelviscopy with peritoneal and ovarian biopsies were demonstrated without detection of intraperitoneal

endometriosis. Finally, in synopsis of all results a thoracic endometriosis with an isolated stromal component in the absence of epithelial cells was suspected. Differential diagnosis of this entity included benign metastasing leiomyoma and metastatic low-grade-endometrial stromal sarcoma.

Conclusions: We report on recurrent pneumothoraces caused by thoracic stroma cell endometriosis, which is still rarely described. The diagnosis of this variation of thoracic endometriosis is difficult and extensive histopathological and immunohistochemical analysis is needed.

PO-Onko 03.58

Role of the new estrogen receptor GPR30 in endometrial pathology after tamoxifen for breast cancer

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Objective: This study was undertaken to evaluate the potential role of G-protein-coupled estrogen receptor, GPR30, in endometrial pathology associated with tamoxifen treatment of breast cancer patients.

Materials and methods: We investigated whether the GPR30 plays a role in mediating proliferating effect of tamoxifen in endometrial carcinoma cell lines. These results were compared to the GPR30 expression pattern in endometrial tissue from a cohort of 95 breast cancer patients, who received tamoxifen or another adjuvant therapy. **Results:** In vitro tamoxifen significantly stimulated the mitogen-activated protein kinase (MAPK) phosphorylation and cell proliferation of endometrial cell lines. This effect was blocked by knocking down GPR30 by specific anti-sense oligonucleotides. In vivo, there was a significant correlation between GPR30 expression and the tamoxifen-induced endometrial pathology ($p = 0.006$). Tamoxifen-associated endometrial pathology was observed in 40 of 58 (69%) specimens positive for GPR30 and in only 13 of 38 (24.5%) tissues immunostained negatively for GPR30. Moreover, GPR30 positivity was predictive of an earlier development of symptoms, such as bleeding or suspect endometrial thickness, induced by tamoxifen therapy ($p = 0.019$).

Conclusions: GPR30 is more possibly an important player of tamoxifen-induced endometrial abnormalities.

PO-Onko 03.59

Ovarian teratoma associated with Anti-N-Methyl D-Aspartate (NMDA) antibodies and severe encephalitis

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It has been shown that patients suffering from paraneoplastic encephalitis associated with ovarian teratoma display antibodies for NMDA receptors in CSF or plasma. Most of concerned patients are young women. This syndrome appears in the majority of cases with

headache or a non-specific viral-like illness and continues with psychiatric and severe neurological symptoms.

Objective: Confirmation of suspected diagnoses in anti-NMDA antibody positive encephalitis and teratoma as a possible cause and consideration of surgical treatment in this respect of the radical ovariectomy on both sides.

Materials and methods: (1) A 1 Gravida/1 Para patient of 33 years with no history of gynecological disease. She was admitted in intensive care unit through the emergency department with sudden onset of neurological and psychiatric symptoms. Intubation and ventilation were necessary. Ultrasound showed ovaries with echogenic structure. We performed a laparoscopy with left ovariectomy and biopsy of the right ovary. The histology confirmed the diagnosis of a mature teratoma of the left ovary.

(2): A 34 years IG/IP. A diagnosis of meningoencephalitis with detection of NMDA antibodies led to a gynecological consultation. In sonography the right ovary showed an echogenic structure compatible with a teratoma. We also performed a laparoscopy with right ovariectomy and a wedge biopsy of the left ovary. Histologically an ovarian teratoma was confirmed.

Conclusions: The suspected diagnoses of an Anti-NMDA Encephalitis is in association with an ovarian teratoma in these two cases were ratified. After the surgery with ovariectomy the recovery of the patients could be observed.

PO-Onko 03.60

Discriminative power in adnexal masses: value of diagnostic tools in the pre-operative work-up

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Objective: The discrimination between malignant and benign adnexal masses prior to laparoscopic exploration is important for the optimal therapeutic management. We compared the discriminative power of the most commonly used preoperative diagnostic strategies.

Materials and methods: We analyzed all cases from 2002 to 2005 with the diagnosis of an adnexal mass and subsequent laparoscopic exploration at our institution. 1302 women were included (870 premenopausal, 432 postmenopausal). Sensitivity, specificity, the diagnostic odds ratio (DOR) and Cohen's kappa were calculated for CA 125, expert sonography, the combination of both and the RMI by Jacobs and applied to all cases and to postmenopausal patients only.

Results: A total of 49 malignant lesions were found, including 19 borderline lesions. Sensitivity for CA 125 was 0.48, specificity yielded 0.83. DOR yielded 4.51 and kappa was 0.1. For postmenopausal women, sensitivity was 0.59 and specificity was 0.84; DOR was 7.59 and kappa yielded 0.22. Sonography reached a sensitivity of 0.67 and a specificity of 0.96. Values increased to 0.78 for sensitivity and 0.92 for specificity in the postmenopause. DOR yielded 47.9 overall and 39.3 in the postmenopause; kappa yielded 0.46 overall and 0.48 for the postmenopause. By combining both methods, DOR increased to 72 and kappa to 0.6 in the postmenopause. RMI achieved a sensitivity of 0.3 and a specificity of 0.97, DOR yielded 13.29 and kappa 0.35. In the postmenopause an increase of discriminative power was observed, DOR yielded 19.6 and kappa 0.41.

Conclusions: Expert sonographic examination proved itself to be the gold standard in classification of an adnexal mass with a high specificity in pre- and postmenopausal women. For the postmenopause, adding a measurement CA125 lead to an increase of discriminative power. RMI as a diagnostic strategy did not show a satisfying discriminative values.

PO-Onko 03.61

Neuroendocrine carcinoma in situ of the vagina with merkel cell phenotype: a case report

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Objective: Primary neuroendocrine carcinoma of the vagina is extremely rare. It occurs mostly in elder patients. Because of its rareness there is no evidenced based therapy.

Materials and methods: We report on a 71 year old woman who had breast cancer in 1995. Five years later she was suspected to have a metastasis of the breast cancer in the vagina and so a partial colpectomy was performed. Because of a very early relapse—diagnosed by punch biopsy—after 6 months a radiation was done and the patient was treated by an antihormonal therapy. In 2007 and 2008 the patient had repeated conspicuous smears without any macroscopic lesion. A MRI scan of the pelvis showed no signs of a relapse. In June 2008 a punch biopsy was done again and the histological investigation showed a neuroendocrine carcinoma in situ of the vagina with merkel cell phenotype. Retrospectively it can be assumed that the vaginal neoplasia detected in 2000 was also a neuroendocrine tumor rather than a metastasis of the breast cancer. The tumor cells were positive for cytokeratin 20. As there was no macroscopically visible tumor and neither operation nor radiation was possible, a vaporisation of the residual vagina with argon beamer was performed. Until now there are no signs of a relapse.

Conclusions: Positive expression of CK 20 in neuroendocrine carcinoma of the vagina might represent a Merkel cell carcinoma subtype. The occurrence in the vagina is very rare. Surgery, radiation and vaporisation might be a treatment option.

PO-Onko 03.62

Case report: primary angiosarcoma of the breast in a 39 year old woman

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Objective: Angiosarcoma of the breast is a rare malignant neoplasm which accounts for <0.04% of all primary malignant breast tumors and approximately 8% of mammary sarcomas. Compared to other angiosarcomas, the angiosarcoma of the breast affects younger women between the age of 30 and 40 years.

Materials and methods: A 39 year old woman presented with a self-discovered, rapidly enlarging angiomatous and angiolipomatous tumor of the left breast, initially showing no signs of malignancy in a core needle biopsy. Ultrasound, mammography and magnetic resonance imaging merely displayed a heterogeneously hypoechoic mass with cystic lesions. A resection in toto was recommended. Breast conserving therapy lead to an initial R1 resection, resulting in a skin sparing mastectomy and the implantation of an expander. Axillary lymph node dissection was not necessary due to the predominant hematogenous metastatic spread of the tumor entity.

Results: 7 cm Angiosarcoma pT3, pNx, G3 (FNCLCC)/G2(NCI),R0,M0. Due to the extent of the tumor, the decision for adjuvant radiotherapy was made (total dose 55.8 Gy–1.8 Gy 5×/week). Adjuvant chemotherapy has no proven effect. A postoperative CT scan (thorax/abdomen), performed due to the special at-risk situation of the patient, showed a lesion in the right middle lung lobe,

measuring 1 mm. A second suspicious lesion in the left breast was examined via jet biopsy and showed no signs of recurring disease. Continuous follow-up examinations are planned in close cooperation with the department of Internal Medicine.

Conclusions: Angiosarcoma is an aggressive malignancy with a poor prognosis. Recently, an increase in incidence has been reported in the form of secondary angiosarcomas following breast conserving surgery and radiotherapy. Mammograms and cored needle biopsies may be deceptively normal and early adequate biopsy is needed to confirm the diagnosis and start treatment. New findings suggest Taxanes/Trabectedin as a possible treatment option in the future.

PO-Onko 03.63

Myofibroblastom: or what? A case report

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Objective: A 46 years old patient has been referred because of an actually increasing finding of approximately 6 cm in the right mamma, existing since 2 years. The patient for more than 20 years takes HRT, currently with Activelle (R). The patient also has a positive family history of breast cancer (mother with 66 years).

Materials and methods: First of all an ultrasonography as well as a mammography has been done. After that a Tru-cut biopsy and finally the excision has been done as well. The postoperative developing was without any problems.

Results: The imaging shows a 6 × 6 cm wide, complex soft tissue tumor with displacing growth and with inhomogenic density. The expansion is between the subcutaneous tissue and the fascia of the pectoral muscle. Doppler sonography shows a strong perfusion. Diagnosis: mixed tumor, hamartoma, giant adenoma, atypical giant fibroma, phylloid tumor. No typical appearance of a lipoma. Density ACR:I, classification BIRADS:4. The Tru-cut biopsy only showed fibrolipomateous soft tissue with focal fibrosis and with hyaline aspect. In the final histology myofibroblastoma with typical character was confirmed: A sharply bounded tumor, characterised by dumpy collagenous connective tissue with small lesions of partial fascicular or reticulated spindle cells. Mitosis are rare. Necrosis are absent. Typical immunohistochemical markers like Vimentin, Aktin, Desmin, CD 34 and oestrogenreceptors shows positive results.

Conclusions: In this patient with a palpable tumor, positive family history of breast cancer, longtime hormone replacement therapy and a mammography with classification of BIRADS 4, the suspicion of breast cancer is high. Nevertheless the radiological image is very untypical. Only the final histology examination brings clarity. This case demonstrates that the numbers of possible diagnosis in senology are very complex and inexhaustible big. Those differential diagnosis often provide for surprising results and only could be clarified with a histological examination and sometimes needs specific immunohistology.

PO-Onko 03.64

Psychological distress in breast and gynecological cancer patients at different stages of oncological treatment

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Objective: It is unclear whether there are differences of psychological distress in cancer patients during the initial phase of treatment. This study investigates levels of psychological distress in patients of a breast cancer centre and a gynaecological cancer centre at different stages in the beginning of treatment.

Materials and methods: Psychological distress was measured using the Hornheider Screening Inventory (HSI). Data were obtained during acute care hospital stay, i.e. condition 1 ($n_1 = 30$), and at the first and second appointments for ambulant chemotherapy, i.e. condition 2 ($n_2 = 31$) and condition 3 ($n_3 = 23$), respectively. Condition 1 was compared to conditions 2 and 3 using the Mann–Whitney-*U*-Test for independent samples. Within-subject comparisons between conditions 2 and 3 were calculated using the Wilcoxon-Ranks-Test. Additionally, patients of the two cancer centres were compared using the Whitney-*U*-Test.

Results: Highest levels of psychological impairment were found in condition 1, i.e. during the acute hospital stay. The HSI scores of conditions 1 and 2 were significantly higher than the score assessed in condition 3 during ambulant chemotherapy (both $p < 0.05$). In condition 1, patients of the gynaecological cancer centre were significantly more distressed than breast cancer patients ($p < 0.01$).

Conclusions: Patients were most distressed during oncological in-house treatment and the initial phase of ambulant chemotherapy. By the time of second chemotherapy treatment, which was 3 weeks after first chemotherapy, psychological distress was reduced significantly and to a level below indication of psychooncological support needs. Hence, psychological support for cancer patients is particularly important during the initial stages of treatment. Differences of distress levels within this time frame can be identified using a brief screening inventory. Future research is required to explore levels of distress at further phases of oncological treatment and to investigate specific needs for psychooncological interventions in these phases.

PO-Onko 03.65

Cooperation between breast centers and private practice: the Cologne model

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Objective: The certification of breast centers (BC) in North Rhine Westphalia (NRW) is based on the implementation of a close cooperation between gynecologists working in private practice in an outpatient setting (OBGYN) and the team in the breast center to fulfill the needs of patients and the certification criteria. In densely populated areas such as NRW, OBGYN often work in cooperation with several BCs.

Materials and methods: To improve the quality of cooperation between OBGYN and BC, a project was started together with private practice physicians (OBGYN), the medical association (Ärzttekammer Westphalen-Lippe) and members of the BCs, to develop a certified cooperation model, named the Zertifizierung als Kooperationspartner der Brustzentren in NRW nach dem Kölner Modell. The certification is based on three elements: 1. Medical qualification: participation in an interdisciplinary and case-oriented curriculum with final theory examination, tumorboard participation and observational rotation in the BC. 2. Certification of the outpatient practice within the Cologne model as an interface between outpatient care and BC (by

ÄK Zert). The interface has been pre-defined for both partners in an obligatory and reviewable fashion. 3. Optional certification of the outpatient practice concerning quality management structures (if no other QM system available) (by ÄK Zert). Both partners apply for certification at the medical association, the certificate is then valid for 3 years.

Conclusions: In January 2010 the first certification round started with more than 80 participants from the private practice setting and from the three Cologne BCs with the aim to improve and standardize cooperative care for breast cancer patients. The model can be transferred to other BCs and regions in NRW and beyond. We will report first experiences in development and implementation of the model. Further information is available: www.aekwl.de, Stichwort Zertifizierung Kooperationspartner.

PO-Onko 03.66

New tissue acquisition tools for translational research in gynecology

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Objective: Histological and molecular examinations are a prerequisite to understand diseases, determine optimal individualized care, and identify targets for potential novel therapies. Despite this key role of tissue based research the act of biopsy still remains troublesome for senological and gynecological applications.

Materials and methods: For the breast, the tru-cut and vacuum-assisted biopsy requires more than one sample resulting in increased contamination. Contamination with non-target tissue or blood makes quantitative analysis unreliable. For cervical tissues both mucosa and underlying stroma need to be present. Punch biopsy forceps harvest almost entirely epithelial parts.

Results: New direct and frontal biopsy technologies are emerging with the aim to alleviate the bottleneck of inappropriate minimal invasive interventions. Their recent availability provides a good occasion to look into the subject of tissue acquisition problem, i.e. not enough high quality tumor tissue in sufficient quantity. Recent literature provides evidence that macrobiopsies, like Spirotome and Coramate, give tissue samples between 150 and 300 mg of highly specified parts of the diseased area in a way very similar to open surgery. In addition, the biopsy procedures are increasingly more patient friendly with appropriate comfort and safety. The new macrobiopsies are less expensive, making molecular biology at reach for every gynecological patient, company and health care provider.

Conclusions: Direct and frontal macrobiopsies open new avenues for future bio-banking, pharmacogenomics and personalized medicine. It is anticipated that drug discovery and clinical implementation will be highly facilitated and that clinical research time will be significantly shortened.

PO-Onko 03.67

Recurrent epithelioid vulva sarcoma in a 19-year-old woman

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Objective: Epithelioid sarcoma of the vulva is an extremely rare and aggressive tumor, accounting for approx. 1% of all vulvar malignancies. Symptoms and growth are usually asymptomatic, therefore lesions are often mistaken for benign processes, leading to diagnosis

at later stages. A case report with therapy including recurrence and follow up is presented.

Materials and methods: Case report of a recurrent epithelioid vulva sarcoma from a university gynecological cancer center with follow up of 16 months.

Results: A 19-year-old patient was admitted with a slowly growing, slightly painful tumor at the left labium that developed over previous 2 years before resected in 11/2008. Proximal type of an epithelioid sarcoma was diagnosed by immunohistology. Staging by CT of thorax and abdomen showed no metastases. Since R0 status was unconfirmed in first procedure e.m., second surgery was done in 02/2009 and a residual tumor of 1.5 cm was removed. The diagnosis of vulva-sarcoma pT1b, pN0, M0, G3, R0 with close margins was confirmed. Subsequently, adjuvant radiation with 54 + 9 Gy in the tumor region was administered from 5–7/2009. Re-staging in 7/ and 10/2009 showed no evidence of disease. In 11/2009 a suspect left inguinal lymph node was detected by ultrasound. Biopsy proved relapse of sarcoma and patient underwent inguinal and pelvic lymph node dissection with only $n = 1/53$ positive lymph node. Radiation of left groin was recommended but refused by patient. In 1/2010 CT revealed inguinal lymph nodes suspicious for second relapse but another biopsy performed was benign. Recent follow up in 3/2010 was uneventful.

Conclusions: Complete operative resection according to guidelines is crucial for therapy of vulva-sarcomas. Surgery combined with radiotherapy offer better local control and should be considered for G3-tumors or too close surgical margins. Chemotherapy can be administered in metastatic disease with unconfirmed success. Therefore follow-ups should be done in short intervals.

PO-Onko 03.68

Hyperthermia abrogates the Y-box binding protein-1 (YB-1) expression

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Objective: The application of hyperthermia as a therapy against various types of cancer started more than 100 years ago. Nowadays, in the clinic, hyperthermia can be used concomitant to chemotherapy or radiotherapy and may improve the effect of those classical treatments. In previous projects, we investigated the expression of different splicing factors, such as YB-1, in malignancies. Overexpression of YB-1 in malignant cells has been described in various studies and YB-1 seemed to play an important role in the development of tumors as well as in the occurrence of resistances to chemotherapies. In the present study we focussed on the effect of hyperthermia at a molecular level, specifically its impact on the expression YB-1 in cancers.

Materials and methods: Various gynaecological cancer cell lines were cultured under hyperthermia (2 h, 42°C) followed by maintenance under normal conditions (4 h, 37°C). RNA and protein were isolated using TRIzol[®] method and expression levels were subsequently analysed by RT-PCR and Western Blot.

Results: The analyses revealed a markedly decreased level of YB-1 RNA and protein in the breast, cervical, endometrial as well as ovarian cancer cell lines treated with hyperthermia compared to the cell lines treated under normal condition.

Conclusions: Our results suggest that hyperthermia could have an impact on the expression of splicing factors such as YB-1. Thus, hyperthermia might be a way to influence the progression of malignancies and could improve the response to chemotherapeutical treatments.

PO-Onko 03.69**Sorafenib-mediated downregulation of mcl-1 induces chemosensitization of gynecological cancer cells**

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Objective: Overexpression of the anti-apoptotic mitochondrial membrane protein mcl-1 is an often cause of acquired or pre-existing resistance of cancer cells against chemotherapeutic drugs. We tested the effect of the multikinase inhibitor sorafenib on signaling pathways that contribute to the upregulation of mcl-1 in gynecological cancer cells.

Materials and methods: A variety of breast, ovarian, and cervical cancer cells was treated with sorafenib and analyzed for mcl-1 expression, MAP-Kinase signaling pathways, mitochondrial membrane potential, and overall cell survival.

Results: Pretreatment of gynecological cancer cells with sorafenib induced a significant downregulation of mcl-1 expression, associated with an inhibition of the ERK1/2 phosphorylation cascade, subsequently resulting in a mitochondrial membrane disruption. Sorafenib could effectively be combined with other chemotherapeutic drugs, especially those which itself did not sufficiently induce a disruption of the mitochondrial membrane potential.

Conclusions: Sorafenib, an already approved drug for the treatment of renal cancer, reveals a high efficacy and good combination potential for the use in gynecological cancer.

PO-Onko 03.70**Paraneoplastic cerebellar degeneration as presenting symptom of recurrent endometrial stromal sarcoma with sex-cord elements**

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ESS are rare (6–20% of uterine sarcomas), may contain sex-cord elements, have a metastasis- and recurrence-potential (36–56%, 3 months–23 years), so that long-term follow-up is mandatory (5-year survival 62–93%). Clinical manifestations: vaginal bleeding, abdominal pain, enlarged uterus (often misinterpreted as fibroid uterus). Recurrence in pelvis, intraperitoneal, distant metastases (lungs, bones). Treatment guidelines do not exist. Total hysterectomy, BSO without routine pelvic/periaortic lymphonodectomy is the standard operating procedure. In case of recurrences, surgeries are an option. ESS express oestrogen and progesterone receptors, therefore an adjuvant hormonal treatment (progestins—medroxyprogesterone, megestrol—or aromatase inhibitors—letrozole, anastrozole) can reduce recurrence rates. Adjuvant chemotherapy (cisplatin/adriamycin, ifosfamide, ifosfamide/epirubicin/cisplatinum or doxorubicin/ifosfamide) is reserved for hormone receptor negative cases, progression/recurrence under hormonal treatment or high grade malignancy. We report a case in which paraneoplastic cerebellar atrophy (PCA) was preceding the diagnosis of multifocal recurrent ESS with sex-cord elements 16 years after diagnosis and surgery (abdominal hysterectomy and BSO without adjuvant therapy). The

patient presented with gait ataxia, truncal imbalance, blurred vision, horizontal and vertical gaze-evoked nystagm and dysarthria. MRI/CT revealed cerebellar atrophy mainly involving the upper vermis, bilateral pulmonary metastases infiltrating thoracic vertebrae without evidence of local recurrence. Histologically that lesions were metastases of the formerly diagnosed ESS, containing sex-cord elements. 80% of the cells expressed ER and 10% PR. The slight progression of the metastases within four months and the unlikely response to chemotherapy due to low proliferation index, led us to perform debulking surgery (lobectomy-10 metastases, mediastinal lymphonodectomy, vertebra-metastasis removal requiring post-operative focal radiation). Anastrozole was administrated with the intention to delay further recurrence. After 3 months she is without evidence of tumor. Neurological examination showed a virtually complete resolution of ataxia by persisting oculomotor abnormalities. **Conclusions:** We show that PCA can also occur in combination with late recurrent ESS.

PO-Onko 03.71**Specific antibody microarray tool for the early detection of invasive breast cancer**

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Objective: Breast cancer is one of the leading causes worldwide for women mortality. Although the survival rate has increased, many patients die from metastatic relapse. One of crucial factors for breast cancer healing is its early detection. At the present time, no suggested biomarkers for breast cancer have been established for the use in clinical assays as a putative diagnostic tool. The aim of our study was a comparison of protein expression in sera of breast cancer patients and control group.

Materials and methods: We involved in our study 100 participants including 50 women with primary diagnosed breast carcinoma without metastasis and another 50 healthy age-matched women without known malignancies. We constructed an antibody microarray tool to compare the regulation different acute phase proteins, interleukins and complement factors in both groups. For that purpose, we incubated selected antibodies on nitrocellulose microarray slides with sera of test persons and compared the reaction intensities with different statistical algorithms.

Results: We obtained a panel of significantly different regulated proteins in breast cancer patients. The neural network could distinguish cancer patients from the control group with sensitivity of % and the specificity of %. The area under curve (AUC) of 0.xy was obtained. The most significant regulation differences were shown by acute-phase proteins like heat-shock proteins HSP60, 27 and 90 and complement factor c3/3a.

Conclusions: In this study with the use of antibody microarrays we were able to compare the regulation of different proteins in sera of cancer patients and healthy controls. Also we generated a panel of putative serum protein biomarkers which could distinguish the cancer group from the controls with a high specificity and sensitivity. Our next aim will be the prospective validation of obtained biomarkers in an independent clinical study. Moreover, our findings could contribute to a development of a clinically useful biomarker assay.

PO-Onko 03.72**Realtime-sonoelastography: a tool for improvement of the BIRADS classification, that means improvement of patients treatment and earlier breast cancer detection**

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Objective: Realtime-sonoelastography is an ultrasound technique that enables a highly depiction of tissue elasticity distribution. Malignant breast lesions tend to be harder than benign ones. The usage of elastography in combination with B- Mode and Doppler-ultrasound could lead to more accurate differential diagnosis of breast lesions. The risk of malignancy of BIRADS 4 lesions ranges from 3–90%. Accordingly the optimal treatment recommendation is hard to find. The purpose of this study is to improve the patient's treatment. On the one hand, to avoid unnecessary biopsies and on the other hand to clarify suspect lesions earlier.

Materials and methods: Prospective study of BIRADS 3 and BIRADS 4 lesions with realtime-elastography which have been performed with B- mode and Doppler ultrasound before. The elasticity is visually evaluated using a predefined scale of colours. Hard tissue areas appear blue, intermediate hard tissue appears green to yellow and soft areas red. According to this scale BIRADS classifications are corrected and afterwards correlated to the results of biopsy.

Results: 70 BIRADS 3 lesions und 34 BIRADS 4 lesions were examined with realtime elastography. 28% of the BIRADS classifications were changed after realtime-elastography. With upgrading to BIRADS 5 category the sensivity could not be improved. The results of the tissue biopsy confirm in 83% the adjusted BIRADS classification after realtime-elastography.

Conclusions: Sonoelastography is a tool to improve in combination with B- mode- and Doppler-ultrasound the BIRADS classification of breast lesions, but cannot replace the usual examination tools. Further studies for the significance of realtime-elastography have to be performed.

PO-Onko 03.73**Expression of cancer testis antigens (CTA) in primary breast cancer and their prognostic significance**

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Objective: Cancer-testis antigens (CTA) are a family of proteins normally expressed in the human germ cells such as in the testis or placenta. They also have been found in various types of malignant tumors including breast cancer. Because of their restricted expression pattern they are frequently able to elicit T-cell immune responses, and therefore they are considered as ideal targets for cancer immunotherapy. Breast differentiation antigen NY-BR-1 has also immunogenic properties. The aim of this study was to explore the CTA expression in breast cancer and detect possible clinical correlations.

Materials and methods: The expression patterns of 6 CTAs (MAGE A1-MA454, MAGE A3-M3H67, MAGE A4-57B, NY-ESO-1-E978, GAGE, MAGE A-6C1) and NY-BR-1 were examined by immuno-

histochemistry in a series of 210 non-selected patients with primary invasive breast cancer using the tissue microarray technique. The intensity of the stain was scored semi-quantitatively in a scale 0 to +3. The expression of the antigens was correlated to established clinicopathological parameters as well as disease-free and overall survival. **Results:** CTA expression exhibited a predominantly cytoplasmic and occasionally nuclear localization. At least one CTA was identified in 37.2% of cases with expression of each antigen varying from 4.5 to 15%. NY-BR-1 was positive in 46.6% of tumors, with the well differentiated tumors showing more frequent expression. MAGE A4-57B ($p = 0.048$ and 0.015) and MAGE A3-M3H67 ($p = 0.001$ and 0.004 , respectively) positive staining was significantly correlated to shorter overall and disease-free survival. Additionally, the mortality rate increased substantially if co-expression of 3 or more CTAs was observed.

Conclusions: Our findings suggest that CTAs could serve as potential prognostic markers in primary breast cancer patients. The exclusive expression of CTAs in tumor tissues as well as the frequent expression of NY-BR-1 could define potential new targets for specific breast cancer therapies.

PO-Onko 03.74**Additive effects of trastuzumab and genistein on human breast cancer cells**

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Objective: Women with HER2-overexpressing breast cancer are treated with trastuzumab. Genistein is a phytoestrogen and natural tyrosine kinase inhibitor that can inhibit growth of breast cancer cells. Genistein is an agonist of estrogen receptor β (ER β), which is able to exert antitumoral functions. Considering these pleiotropic effects on breast cancer cells, a combined treatment with genistein and trastuzumab could be a promising therapeutic approach. In this in vitro study, we tested to what extent genistein would be able to enhance the antitumoral action of trastuzumab.

Materials and methods: First we characterized the HER2-, ER β 1-, ER β 2-, ER β 5- and ER α -expression in the three breast cancer cell lines SK-BR-3, BT-474 and MDA-MB-231 by real time RT-PCR. With a proliferation assay, we measured the influence of combinations of ER α -agonist (PPT), ER β -agonist (DPN) or genistein with trastuzumab on the growth of these cell lines over a time span of six days. Relevant gene changes were measured by PCR.

Results: Treatment with genistein (10 μ M) significantly increased the growth-inhibitory effect of trastuzumab on HER2-overexpressing, ER α / β -positive BT-474 breast cancer cells, but not on ER α -negative SK-BR-3 cells. ER β agonist DPN exerted similar effects on trastuzumab-treated BT-474 cells. In contrast, neither addition of 17- β estradiol, ER α agonist PPT nor tamoxifen did affect the antiproliferative action of trastuzumab. On the molecular level, treatment with genistein reduced HER2 transcript levels and inhibited trastuzumab-triggered upregulation of ER α - and c-fos expression. Though both drugs inhibited expression of proliferation genes Ki-67 and MYBL2, no additive effect was observed. Both drugs notably increased ER β 2 transcript levels, and their combination further elevated mRNA levels of this receptor variant.

Conclusions: Our data suggest, that the antiproliferative effect is triggered by genistein binding to ER β and is dependent on presence of ER α . Particularly women with HER2-overexpressing and ER α / β positive breast cancer might benefit from such combinatory treatment.

PO-Onko 03.75**Spontaneous tumor-specific immune responses in breast cancer patients: generation, regulation and prognostic impact**

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Objective: Tumor-specific memory T-cells (TCs) are detectable in the bone marrow (BM) of a majority of breast cancer patients. The clinical relevance, however, and the conditions for their generation remain unclear yet. In this study, we characterized conditions that determine immune responses in primary breast cancer patients and evaluated their potential prognostic implications.

Materials and methods: We used ex vivo IFN- γ EliSpot assays and ELISA in 207 untreated patients to evaluate tumor-specific TCs in the BM or MUC1-specific antibodies in the peripheral blood. In this context, 27 intratumoral cytokines, chemokines, and growth factors were quantified by multiplex analysis. Results were compared with multiple pathologic and clinical parameters and correlated to the general patients' prognosis by Adjuvant! Online calculation.

Results: In 45% of patients we detected tumor-specific memory TCs in the BM. The presence of type-I memory TCs correlated significantly to primary tumors with high differentiation, estrogen receptor expression, low proliferative activity and reduced cancer mortality risk. High tumor cell differentiation correlated with increased concentrations of IFN- α and reduced levels of transforming growth factor TGF β 1 in the primary tumor tissue. In 50% of patients we found tumor-specific B cell responses in the peripheral blood mainly in form of IgM isotype. Dichotomically, B cell responses correlated with increased TGF β 1 and reduced IFN- α in the primary tumor tissue as well as with advanced tumor stage and the absence of TC responses in BM.

Conclusions: For the first time we can show a strong correlation of cellular tumor-immune responses with prognosis-relevant parameters in tumor pathobiology. We were able to define specific intratumoral cytokine microenvironments that are dichotomically linked to distinct immune responses in the individual patient. These findings shed light on the relation between immune response and cancer prognosis.

PO-Onko 03.76**Role of GPR30 in the mechanisms of tamoxifen resistance in breast cancer MCF-7 cells**

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Objective: Tamoxifen is the most frequently used anti-hormonal drug for treatment of women with hormone-dependent breast cancer. The aim of this study was to investigate the mechanism of tamoxifen resistance and the impact of the new estrogen G-protein coupled receptor (GPR30).

Materials and methods: MCF-7 cells were continuously exposed to tamoxifen for 6 months to induce resistance to the inhibitory effect of tamoxifen.

Results: These tamoxifen resistant cells (TAM-R) exhibited enhanced sensitivity to 17- β -estradiol and GPR30 agonist, G1, compared to the parental cells. In TAM-R cells, tamoxifen was able to stimulate the cell growth and MAPK phosphorylation. These effects were abolished by EGFR inhibitor AG1478, GPR30 anti-sense oligonucleotide, and the selective c-Src inhibitor PP2. Only EGFR basal expression was slightly elevated in the TAM-R cells, whereas GPR30 expression and the basal phosphorylation of Akt and MAPK remained unchanged compared to the parental cells. Interestingly, estrogen treatment significantly increased GPR30 translocation to the cell surface, which was stronger in TAM-R cells. Continuous treatment of MCF-7 cells with GPR30 agonist G1 mimics the long-term treatment with tamoxifen and increases drastically its agonistic activity.

Conclusions: This data suggests the important role of GPR30/EGFR receptor signaling in the development of tamoxifen resistance. The inhibition of this pathway is a valid option to improve anti-hormone response in breast cancer.

PO-Onko 03.77**ERBB2 induces an anti-apoptotic expression pattern of Bcl-2 family members in node negative breast cancer**

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Objective: Members of the Bcl-2 family act as master regulators of mitochondrial homeostasis and apoptosis. We analyzed whether ERBB2 influences prognosis of breast cancer by influencing the pro-versus anti-apoptotic balance of Bcl-2 family members.

Materials and methods: ERBB2 regulated Bcl-2 family members were identified by inducible expression of ERBB2 in MCF-7 breast cancer cells and by correlation analysis with ERBB2 expression in breast carcinomas. The prognostic relevance of ERBB2-regulated and all additional Bcl-2 family members was determined in 782 untreated node-negative breast cancer patients. The biologic relevance of ERBB2-induced inhibition of apoptosis was validated in a murine tumor model allowing conditional ERBB2 expression.

Results: ERBB2 caused an anti-apoptotic phenotype by upregulation of MCL-1, TEGT, BAG1, BNIP1 and BCL2L13 as well as downregulation of BAX, BMF, BNIPL, CLU and BCL2L13. Upregulation of the anti-apoptotic MCL-1 ($P = 0.001$, HR = 1.5) and BNIP3 ($P = 0.024$, HR = 1.4) was associated with worse prognosis considering metastasis-free interval, whereas clusterin ($P = 0.008$, HR = 0.88) and the pro-apoptotic BCL2L13 ($P = 0.019$, HR = 0.45) were associated with better prognosis. This indicates that ERBB2 alters expression of Bcl-2 family members in a way that leads to adverse prognosis. Analysis of apoptosis and tumor remission in a murine tumor model confirmed that the prototypic Bcl-2 family member Bcl-xL can partially substitute for ERBB2 to antagonize tumor remission. **Conclusions:** Our results support the concept that ERBB2 influences expression of Bcl-2 family members to induce an anti-apoptotic phenotype. Antagonization of anti-apoptotic Bcl-2 family members may improve breast cancer therapy, whereby MCL-1 and BNIP3 represent promising targets.

PO-Onko 03.78**Expression patterns of microtubule associated proteins RHAMM and AURKA in undifferentiated sporadic and hereditary breast cancers**

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Objective: There is recent evidence that BRCA1 is required for terminal differentiation of mammary epithelial cells in vitro and in vivo probably due to direct impact on mammary stem or progenitor cell fate. Loss of apico-basal orientation and cell-cell contacts which are dependent on non-centrosomal microtubule (MT) nucleation are important step in malignant progression. Moreover, BRCA associated breast cancers show an undifferentiated “basal-like” phenotype suggesting that MT nucleation which requires an orchestrated interplay of MT-associated proteins is disturbed in BRCA1 tumors. We aimed to investigate the expression pattern of the MT-associated proteins phosphorylated hyaluronan receptor (pT703RHAMM) and its activating kinase aurora (AURKA) in undifferentiated breast cancers with or without inactivating BRCA1 mutations.

Materials and methods: Paraffin embedded specimen from sporadic differentiated and undifferentiated breast cancers and control tissue from reduction mammoplasties were subjected to immunohistochemistry with primary antibodies targeted against pT703RHAMM and AURKA. Stained slides were scored by two blinded investigators.

Results: Tumor specimen showed a homogenous cytoplasmic staining pattern of AURKA. RHAMM-phosphorylation occurred at the nuclear envelope of some nuclei, but mitotic chromosomes in pro- and meta- but not in ana- or telophase showed a strong pT703RHAMM staining.

Conclusions: Whereas AURKA distribution appears to be more or less homogenous RHAMM phosphorylation occurs at the nuclear envelope in interphase nuclei, and at mitotic chromosomes in pro- and anaphase in breast cancer tissues. Differences in staining intensity and pattern between different subsets of tumours are subject to ongoing analyses.

PO-Onko 03.79**The unfavorable prognostic effect among patients with TNBC is conserved among stratification for patient age**

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Objective: Patients with triple negative breast cancer (TNBC) carry a particularly unfavorable prognosis compared to patients with other breast cancer subtypes (Perou et al., Nature 2000). Young age at diagnosis is a significant unfavorable prognostic factor for patients with breast cancer. We examine the correlation between TNBC and age at diagnosis.

Materials and methods: We combined publicly available gene expression datasets (Affymetrix U133A) of 1772 patients with breast cancer into a single database. Patients were stratified into three

distinct age groups according to Anders et al. (J Clin Oncol 2008). Molecular subgroups were defined using the method of Hugh et al. (J Clin Oncol 2008).

Results: Patients with TNBC had a low mean event-free survival (EFS) of only 85 months (95% confidence interval (CI) 80–92) compared to patients with luminal A breast cancer (104 months (95% CI 101–107)). Patients <46 years carried a significantly worse prognosis (87 months, 95% CI 82–93) compared to patients of 46–64 or >64 years of age (94 months, 95% CI 91–98 and 93 months, 95% CI 89–98, respectively; $p = 0.025$). Patients <46 years were more often diagnosed with TNBC compared to patients 46–64 or 64 years (28.5% vs. 22.0% vs. 13.5%, respectively). Interestingly, there was only a modest prognostic impact of age at diagnosis after stratification for molecular breast cancer subgroups. Whereas among patients with ER positive (luminal A and B) breast cancer a continuous increase in estrogen receptor (ESR1_205225_at) expression with patient age was observed, no such phenomenon occurred for the expression of progesterone receptor (PGR_208305_at) or HER2 (ERBB2_216836_at). **Conclusions:** The unfavorable prognostic effect among patients with TNBC is conserved among subgroups stratified for patient age. TNBC, however, is diagnosed among distinct age groups with varying frequency. Prognostic differences between distinct patient subgroups may thereby result in part from these differences.

PO-Onko 03.80**Bevacizumab and carboplatin as neoadjuvant second line treatment for triple negative inflammatory breast cancer recurrence**

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Objective: Recurrent breast cancer is a therapeutical dilemma in cases where the recurrent disease is presenting as an inflammatory breast cancer and especially if the tumor is triple negative. On one hand there are no data about the value of systemic therapy in recurrent disease, on the other hand the situation requires neoadjuvant treatment and endocrine therapy is no option. Bevacizumab as well as Carboplatin has shown activity in triple negative breast cancer.

Materials and methods: We are reporting the case of a patient who had her first diagnosis of breast cancer in the left breast in 1991 at the age of 42. She had BCT with axillary dissection, radiation and 5 y tamoxifen as a primary therapy. 2005 she developed breast cancer in her right breast, was treated with MRM with SLNB and refused any adjuvant therapy. In July 2008 she presented with an inflammatory triple negative recurrence in her left breast, the tumor diameter was 5 cm, no distant metastases were found. We started neoadjuvant chemotherapy with TAC, after 2 cycles we stopped the therapy because of progressive disease. In this desperate situation we discussed off-label therapy with the patient and started 6 cycles of Bevacizumab/Carboplatin. Clinically we saw a complete remission, the pathologic report after MRM in December 2008 showed a ypTmic, with residual disease of 1 mm. We decided to continue Bevacizumab mono up to 1 year and discontinued therapy in August 2009. The patient still shows no signs of disease in March 2010 (FU 15 months).

Conclusions: Therapy of triple negative inflammatory breast cancer with Bevacizumab and Carboplatin is far from being a standard. But in the desperate case of recurrent disease not responding to standard chemotherapy it may be an option and should be more thoroughly evaluated.

PO-Onko 03.81**MicroRNAs and their target messenger RNAs associated with progression of breast cancer**

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Background: Based on own results using laser micro dissected cells of invasive ductal (IDC) and ductal in situ (DCIS) breast cancer of the same tumor combined with Affymetrix microarray technology 445 differentially transcribed candidate genes have been identified (Schütz et al., 2006). In this project differential expression of miRNAs and mRNAs was investigated in the same DCIS/IDC breast cancers and pure DCIS fixed in formalin and embedded in paraffin (FFPE).

Objective: (1) Identification of miRNAs and their target mRNAs differentially expressed between DCIS and IDC; (2) Identification of a miRNA/mRNA set to characterize aggressive DCIS with a high invasive potential.

Materials and methods: Bioinformatic analysis using support vector machine and principle component analyses was applied to extract a prognostic gene set from the set of differentially expressed genes and qRT-PCR validation was carried out on micro-dissected FFPE epithelial cells. Additionally, microarray technology was applied for mRNA/miRNA expression analysis.

Results: We obtained a 9-gene progression set which is able to correctly classify DCIS and IDC in 23 out of 24 cases (95.8%). Eight of the 9 possible marker genes were correctly validated in FFPE tissues. Further, expression of these genes also varied between pure DCIS and DCIS areas of DCIS/IDC mixed tumors—expression validation is currently done with qRT-PCR. Nineteen miRNAs were differentially expressed between DCIS and IDC, of which 4 had already been described in tumors. These 4 miRNAs have binding sites on 5 of the 9 candidate genes.

Conclusions: A small gene set of potential progression markers obtained by microarray analysis of native breast carcinomas was successfully validated on FFPE tissues. In addition, a set of targeting miRNAs was identified that might thus serve as prognostic markers. Further analyses are still ongoing.

PO-Onko 03.82**Simultaneous breast reconstruction following mastectomy: multidisciplinary approach improves both, aesthetic result and tumour control**

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The timing of breast reconstruction following mastectomy has been an area of controversy. Immediate breast reconstruction

allows the patient to adjust to the loss of a breast by restoring her body image. However, simultaneous reconstruction has not been widely accepted due to concerns about interference with locoregional recurrence control and possible delay in adjuvant chemotherapy or radiation. A video presentation of a Deep Inferior Epigastric Artery Perforator (DIEP) Flap will serve as introduction of an approach, where all cases with local advanced breast cancer are considered for skin or nipple sparing mastectomy and simultaneous breast reconstruction. Every case has been discussed in a multidisciplinary breast team including pathologists, radiologists, gynecologists, reconstructive plastic surgeons, and medical and radiation oncologists. Special attention has been given to the main factors involved in the decision making process, such as type, stage, and location of the tumour, the necessity for adjuvant therapy, the techniques used for breast reconstruction and follow up data. All patients with local advanced invasive or in situ breast cancer, where mastectomy is indicated to obtain optimal tumour control should be considered for immediate breast reconstruction after individual multidisciplinary discussion and counselling. With an multidisciplinary approach, immediate breast reconstruction is the method of choice without loss of locoregional recurrence control or delay in adjuvant therapy in the majority of cases.

PO-Onko 03.83**Neoadjuvant chemotherapy in BRCA positive breast cancer patients-state of the art: case report and review of literature**

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Objective: A selective targeting and individual predictive assessment is aimed for with future chemotherapies. Genetic characteristics define tumor biology among others and open options for an in vivo response measure in a neoadjuvant setting.

Materials and methods: We present a case of a 39-year old woman with bilateral breast cancer under neoadjuvant chemotherapy and reviewed literature to work out state of the art and data on neoadjuvant chemotherapy in BRCA mutation carriers.

Conclusions: In 25–40% with patients under age of 35 years breast cancer originates hereditary. 50% of family cases are due to hereditary breast cancer genes, BRCA1 or BRCA2, that normally go along with a worse prognosis. Several in vitro, in vivo as well as clinical analysis have shown differences in chemosensitivity between BRCA1/2 derived tumors in comparison to sporadic variants but there has been no clear guidelines for mutation carriers. Neoadjuvant chemotherapy has its place in non-metastatic situations in order to decrease tumor bulk ideally to a complete pathological response. An in vivo response to chemotherapy in a neoadjuvant setting is monitored due to regular clinical as well as imaging appearance and could allow an individual chemotherapeutic adaptation depended on response in future. The knowledge of mutation status and its difference in chemosensitivity has not yet influenced chemotherapy protocols.

PO-Onko 03.84**A pooled analysis of efficacy with trabectedin as 2nd/3rd line single agent in Relapsed Ovarian Cancer (ROC) patients (pts) with a Platinum-Free Interval (PFI) of 6–12 months**

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Objective: 295 ROC pts demonstrated a median time to progression (TTP) of 4.6 months (McMeekin, ASCO 2007). Pts sensitive to platinum with a PFI >6 m (PS), reached a TTP of 6.0 months, and an overall response rate (ORR) of 36.4% (45.5% in pts with >2 prior lines). This subanalysis is focused in ROC pts with partially platinum sensitive (PPS) disease, i.e. relapsing between 6 and 12 m after the end of last prior platinum regimen (PFI: 6–12 months).

Materials and methods: Of the 295 pts, 103 were PPS. Three trabectedin schedules were studied: 0.58 mg/m² 3-h weekly 3xq4w, 1.3 mg/m² 3-h and 1.5 mg/m² 24-h q3 weeks, administered to 41, 34 and 25% patients, respectively. Efficacy and safety of patients are reported.

Results: Baseline characteristics: median age 58 years (35–80), ECOG PS0/1: 72%/27%; papillary/serous histology 76%; histology grade 1-2/3: 28%/58%; liver involvement 35%. Treatment with trabectedin induced 4% complete responses (CR), 26% partial responses (PR), and 40% stable disease (SD); median response duration (RD:PR + CR) 5.2 months (95% CI: 3.9–5.8). Median TTP was 5.3 months (95% CI: 3.8–6.2); 43% pts were progression free at 6 months (95% CI: 32.6–52.7%). In pts with liver metastases CR + PR was 36% with median TTP 5.5 months (95% CI: 2.9–7.3). The most common adverse events were neutropenia and transaminase elevations, which were manageable and without serious clinical consequences.

Conclusions: Trabectedin monotherapy is active in patients with ROC, including patients with PPS disease (PFI: 6–12 months), with a 30% ORR plus 40% SD, with a median TTP of 5.3 months. Activity was retained in pts with liver metastasis, with 36% ORR and almost identical TTP. These single-agent results support the findings of the randomized phase III trial OVA-301 where trabectedin + PLD demonstrated superior clinical benefit over PLD alone in the overall population with particularly pronounced efficacy in the PPS cohort.

PO-Onko 03.85**Identification of biomarkers in resistant ovarian cancer cell lines stimulated with the targeted drug enzastaurin**

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Objective: Aim of the study was to identify novel biomarkers, which may be useful for the stratification of patients with ovarian cancer in responder and non-responder subgroups with respect to platinum-based chemotherapies in combination with gemcitabine, pemetrexed and enzastaurin.

Materials and methods: We investigated the RNA expression of a panel of 73 candidate genes and further panel of 54,000 human transcripts using Affymetrix GeneChip analysis in the ovarian cancer cell line HEY and its drug-resistant subclones against cisplatin, etoposide, docetaxel, paclitaxel, pemetrexed, gemcitabine, TRAIL and enzastaurin that had been stimulated with 10 μM enzastaurin for 1 and 24 h, respectively. First, unstimulated naïve HEY cells were compared to each of the other chemoresistant HEY cell types in order to get possible insight into resistance mechanisms. Second, gene expression were analyzed before and after the treatment time with enzastaurin at 1 and 24 h for each chemoresistant HEY cell type, in order to identify genes that are differentially expressed under enzastaurin stimulation.

Results: Interestingly, treatment with enzastaurin for 24 h led to remarkable change of differential gene expression in the most enzastaurin-sensitive cisplatin-resistant HEY subclone, but also in the enzastaurin-resistant HEYs compared to the parental and other drug-resistant HEY cell lines (24 genes (39 probe-sets) and more than 30 genes (64 probe-sets)).

Conclusions: These findings indicate that (i) enzastaurin may be synergistic to cisplatin and (ii) enzastaurin could be used as a second line treatment to overcome enzastaurin resistance and (iii) the newly identified genes may be used as a biomarker kit for clinical trials in ovarian cancer using enzastaurin and cisplatin. Further investigations are necessary to confirm which subset of these potential markers is best suited as accompanying biomarker for the respective drugs in clinical trials.

PO-Onko 03.87**Clinical outcome of tertiary surgical cytoreduction in epithelial ovarian cancer relapse**

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Objective: The impact of tertiary cytoreductive surgery (TCS) on the overall survival (OS) of patients with relapsed epithelial ovarian cancer (ROC) remains controversial considering the associated morbidity of the heavily pre-treated patients. Aim of the present study was to evaluate the operative and clinical outcome after TCS.

Materials and methods: We systematically evaluated all consecutive patients undergoing TCS. Tumor-dissemination-pattern, operative-morbidity, tumor-residuals and survival are described based on a validated intraoperative documentation-tool. Predictors of survival and complete tumor-resection are analyzed with Cox-regression or logistic-regression-models.

Results: Between 10/2000 and 12/2008, 135 patients (median-age: 51 years; range: 22–80) of mainly initial FIGO-stage ≥III (106 patients;78.5%) were evaluated. In 53 (39.3%) patients a complete tumor resection was obtained. One-month-operative-mortality was 6% (8 patients). During a median follow-up-period of 9.6 months (range: 0.1–75) 78 (57.8%) patients died, while 52 (38.5%) patients experienced a further relapse. Median-OS was 19.1 months for the total collective (95% CI: 14.84–23.35), 37.8 months (95% CI: 12.7–62.7) for patients without tumor-residuals, 19.0 month (95% CI: 9.8–28.2) for tumor-residuals ≤1 cm and 6.9 month (95% CI: 3.05–10.7) for tumor-residuals >1 cm ($p < 0.001$). The presence of peritoneal carcinomatosis did not seem to significantly affect OS. Complete tumor-resection was identified as the strongest predictor of OS. Other independent predictors of survival were interval to primary diagnosis ≥3 years (HR: 0.28; 95% CI: 0.14–0.59) and serous-papillary-histology (HR: 0.23; 95% CI: 0.09–0.56). Forty-two patients (31.1%) presented at least one major complication.

Multivariate analysis identified tumor involvement of the middle abdomen and peritoneal carcinomatosis as independent predictors of complete tumor-resection.

Conclusions: Postoperative tumor-residual-disease remains the strongest predictor of survival even in TCS-setting. To identify the optimal candidates for TCS, the predictive value of ascites and peritoneal carcinomatosis should be confirmed by future prospective trials.

PO-Onko 03.88

Immunohistochemical analysis for expression of Calpain 1, Calpain 2 and calpastatin in ovarian cancer

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Objective: Calpains, are intracellular, non-lysosomal cytoplasmic cysteine endopeptidases. Their endogenous specific inhibitor is cilastatin. The calpain system plays an important role in many processes including apoptosis, necrosis, ischemia formation and exocytosis. So far, there exist many reports on studies about the influence of calpains in different tumors (skin, breast, renal cell or prostate cancers), but there are no studies on calpains being involved in the pathogenesis of ovarian cancer. This was the goal of this work.

Materials and methods: The tissue samples consisted of 21 ovarian cancers and 15 non-cancerous tissue samples. The tissue was embedded in paraffin blocks. For representation of Calpain 1 and Calpastatin monoclonal antibodies were used, which were obtained from ascites fluid of mice. Calpain 2 has been shown with polyclonal antibodies, which were obtained from antiserum of rabbits.

Results: We evaluated the correlation between enzyme expression in malign and benign ovarian tissues. In malignant ovarian tissue, we found a decreased expression, staining intensity and immunoreactive score of cilastatin. With higher grading of the ovarian carcinoma, staining intensity and immunoreactive score of Calpain 1 decreased. Staining intensity of Calpain 2 in ovarian carcinoma was decreased with increasing lymph node status. We clearly demonstrated differences between enzyme expressions in malign and benign tissue.

Conclusions: This study could not find any specific function of calpains in patients with ovarian cancer. Only few studies in literature have been found to deal with calpain evaluation of ovarian cancer. Additional studies including more patients are required to elucidate the functional role and impact of calpain in tumors.

PO-Onko 03.89

Treg attracting chemokine CCL22 is produced by ovarian carcinoma-infiltrating monocytes

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Objective: Intratumoral regulatory T cells (Treg) correlate with reduced overall-survival in patients with ovarian carcinoma. Intratumoral expression of the chemokine CCL22 serves as a mechanism for

the attraction of Treg to the tumor site. In the present study we investigated which cells in the tumor are responsible for the production of CCL22 and thus for the attraction of Treg.

Materials and methods: Tumor-infiltrating immune cells were isolated from freshly resected human epithelial ovarian cancers and cultured in vitro for three days followed by measurement of CCL22 in the supernatants. Furthermore CCL22 levels were determined in the supernatants of different ovarian cancer cell lines.

Results: We detected high levels of CCL22 in the supernatants of tumor-infiltrating immune cells. In contrast, no secretion of CCL22 was observed by any of the analyzed tumor cell lines (OVCAR-3, COV18, CaoV-3, OV-1). The supernatants from tumor-infiltrating immune cells were capable to attract Treg in vitro, showing that tumor-infiltrating immune cells rather than the cancer cells themselves may be involved in the attraction of Treg to the tumor tissue. To determine which population of immune cells is responsible for CCL22 secretion we isolated CD14+ monocytes from freshly resected tumors. Interestingly, CCL22 was detected in the supernatants of the intratumoral CD14+ monocytes, but not in the CD14-depleted fraction of tumor-infiltrating immune cells. By staining CCL22 histologically, we could show high levels of CCL22 in ovarian carcinoma tissue. Serum of ovarian carcinoma patients also contained an elevated level of CCL22.

Conclusions: We thus conclude, that tumor-infiltrating monocytes play a crucial role in secreting CCL22 and in attracting Treg to human ovarian cancer.

PO-Onko 03.90

A single center experience of interval debulking surgery (IDS) in patients with FIGO stage IIIC–IV ovarian, fallopian tube and peritoneal cancer (OVCA) with large volume ascites from 2002–2008

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Objective: The EORTC-GCG/NCIC-CTG trial shows non inferiority of IDS with lower morbidity compared to treatment with primary debulking surgery in FIGO IIIC–IV OVCA patients. Our objective was to evaluate a single center experience of IDS in patients with stage IIIC–IV OVCA, using the presence of ≥ 500 ml ascites as predictor of poor prognosis for stratification.

Materials and methods: Patients with stage IIIC–IV OVCA presenting with ≥ 500 ml ascites underwent laparoscopy for biopsy to receive IDS ($n = 74$) after 2–3 courses of platinum-based chemotherapy (CT), completing courses to a total of 6 after surgery. Clinical outcomes were noted.

Results: 61 patients were staged FIGO IIIC, 13 FIGO IV. Median follow up was 22 months (range 3–67 months). PFS was 16 months (95% CI 11–21 months). OS was 34 months (95% CI 21–46) (FIGO IIIC: 17 and 37 months respectively). Median age was 63 years. Macroscopically residual free status was achieved in 35.1%, optimal debulking (no and < 1 cm of residual tumor) in 82.4% of cases. Pretherapeutic median CA125 was 946U/ml. 23% of patients were ASA III and IV, 95.9% were serous OVCA. Median operation time was 380 min (range 165–580 min). 48.6% of patients underwent at least one bowel resection, and rate of upper abdominal surgery was 28.4%. The median blood transfusion rate was 4 units (range 0–28 units) per patient. Perioperative mortality rate was 1.4%. Median stay in ICU was 1 day (range 0–13 days) and patients were discharged after 14 days (range 9–63 days). 90.5% of patients received a platinum/taxane CT, 6.8% were treated with platinum alone. 23% failed to

complete the schedule with full dose intensity or discontinued prematurely.

Conclusions: Our experience with IDS in stage FIGO IIIC–IV patients with large volume ascites OVCA underlines the results of the EORTC trial. IDS after neoadjuvant CT is a suitable procedure in poor prognosis OVCA patients.

PO-Onko 03.91

Long time results of 1131 women with ovarian cancer: results of the multicenter tumour register of the tumour centre of Berlin

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We report on the first analysis of epidemiological and outcome data derived from the clinical cancer register of the Tumour Center Berlin consisting of eight centers in Berlin. All together 1131 patients have been evaluated. The median age of the patients with ovarian cancer was 61 years (range 15–94). FIGO stage III and IV was found in 83.6%. Grading II or III was present in 91.1%. About 30% of the ovarian cancer patients received cytoreductive surgery within one month after primary diagnosis. The median follow-up was 15 months (range 0–52). During the observation period 241 patients died. The 3-year survival was 60%, the median overall survival was not reached yet. The survival rates correlated significantly with the FIGO stage and pathological tumor stage.

PO-Onko 03.92

Prognostic value of FSH and LH receptor expression in ovarian cancer

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Objective: An influence of gonadotropines on the course of ovarian cancer has been discussed controversially over years. Therefore, we quantified the FSH- and LH-receptor expression in ovarian cancer tissue and analyzed their relation to relapse and survival of ovarian cancer patients.

Materials and methods: Patients had been primary diagnosed and treated for ovarian cancer at our institution between 1990 and 2002.

Patient characteristics and histological data including histological subtype, tumor stage and grading and follow-up data were available. Immunohistological staining was performed to determine LH and FSH receptor expression. Correlation analysis for the receptor expression was applied for histological subtype, tumor stage, grading and clinical data. Statistical significance was assumed at $p < 0.05$.

Results: Paraffin embedded tissue of 156 ovarian cancer patients was available. Most patients had presented with progressive disease at primary diagnosis [FIGO I: $n = 35$ (22.6%), FIGO II: $n = 9$ (5.8%), FIGO III: $n = 109$ (70.3%), FIGO IV: $n = 2$ (1.3%)]. Median follow-up time was 7.3 years (range 0.3–16.8) with 26 documented relapses and 91 deaths. Ovarian cancer tissue showed LH- and FSH-receptor expression in 64.3% and 63.1%, respectively. Only slight differences in the LH- and FSH-receptor expression could be identified for the histological subtype, grading or tumor staging. Kaplan Meier analysis revealed a poor prognosis for sole FSH-receptor but a good survival rate for sole LH-receptor expression ($p = 0.03$). Cox-regression analysis showed the LH- and FSH-receptor to be independent prognostic markers for patient survival [LH-R: $p = 0.026$, 95% CI 0.349–0.937, FSH-R: $p = 0.015$, 95% CI 1.139–3.286].

Conclusions: The LH and FSH receptor are often expressed in ovarian cancer tissue. Both receptors have prognostic significance and can be used for the choice of adjuvant treatment. Since they are specific for ovarian tissue, they may serve as targets for new cancer therapies.

PO-Onko 03.93

Natural HLA-ligands provide novel T-cell antigens for immunotherapy of ovarian carcinoma

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Objective: Development of resistance to chemotherapy is a main factor for the high mortality among women suffering from ovarian cancer. Here, immunotherapy represents a promising strategy to circumvent drug resistance. In clinical trials, peptide-based vaccines based on well characterized tumor antigens have induced specific cytotoxic T-cell (CTL) responses with minimal side effects—yet clear clinical responses remain rare. Aim: This study aims to identify new targets for peptide-based immunotherapy by identification of HLA class I-ligands presented on ovarian tumor samples and the confirmation of their immunity.

Materials and methods: HLA class I-ligands were eluted from two tumor samples, separated by HPLC (high performance liquid chromatography) and fragmented by MS/MS (mass spectrometry). Among the 83 identified HLA-ligands were several peptides derived from established tumor antigens or proteins linked to tumorigenesis. Peptides corresponding to these sequences were synthesized, loaded onto dendritic cells and B cells and used to stimulate peripheral blood mononuclear cells (PBMC) of healthy donors. After 4–6 rounds of stimulation, peptide-specific CD8+ T-cells were identified by intracellular cytokine staining.

Results: So far, five HLA-ligands induced peptide-specific interferon-gamma production, suggesting they represent novel T-cell epitopes. CD8+ T-cells specific for two novel epitopes (Tho complex 4 (THOC4) and HLA-B associated transcript 3 (BAT3)) were multifunctional, expressing also TNF-alpha as well as CD107a.

Conclusions: These results suggest that analysis of HLA-ligands from tumor samples may represent a promising approach for the discovery of peptide-vaccine candidates for ovarian cancer patients.

PO-Onko 03.94**What do primary and recurrent ovarian cancer (OC) patients expect from their doctors? Final results of a German survey in 676 patients.**

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Objective: To explore the information needs and preferences of OC patients with special focus on doctor–patient communication we conducted the following survey in Germany.

Materials and methods: A questionnaire was developed and validated in a phase-I study and was then administered to OC patients via internet (online) or as a print-version.

Results: A total of 676 patients were interviewed (201 online, 475 print version). In the online group 97% had an own internet access 49% in the print group. The median age of the online group was 49 years (range 19–73), for the print group 62 years (26–92). 39% of the patients had recurrent OC. The most effective and “patient-relevant” source of information and explanation of treatment options was the consultation with their physician (88%). All patients judged the therapeutic consultation by their physician on a likert scale (1: very bad, 10: very well): Completeness: 8; understanding: 8; response to questions: 9; competence of physician: 10; shared decision: 9 and involvement of relatives into therapy decision: 8. When asked to suggest areas for improvement, most frequent answers were: doctors should have more time for explanations (46%); no alopecia under treatment (35%); therapy should be made to be more effective (31%). The most stated answers to “How do you measure the success of a therapy?” were: based on my current well-being (55%); response of the tumour marker CA 125 (45%); based on the feedback that I receive from my doctor (38%). An independent second opinion centre was desired by 70% of the patients, but only 20% know such an institution. **Conclusions:** This study underlines the high need of ovarian cancer patients to discuss all details about treatment options and clinical management.

PO-Onko 03.95**Cervical manifestation of a borderline type ovarian cancer with pseudomyxoma peritonei: a case report and review of the literature**

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Borderline tumours of the ovary (BOT) are rare tumour entities that—even though they can display characteristics of malignant tumours—do not show any destructive or invasive growth in the majority of cases. BOT represent about 8–10% of all ovarian tumours, but the differential diagnosis remains difficult. The mucinous subtype can also originate from the appendix, and ovarian metastases can mimic primary ovarian BOT, often accompanied by peritoneal manifestation

in terms of pseudomyxoma peritonei. In cases where a concomitant appendiceal tumour is present, it may prove difficult to determine the primary tumour. Therefore in most guidelines involving a mucinous borderline tumour an additional appendectomy is recommended as a routine surgical procedure. We present a special case with a concrete example for the complexity of the differential diagnosis of pseudomyxoma peritonei, especially if a case is simultaneously linked to appendiceal and ovarian cancer. Moreover, this case is exceptional for its unusual manifestation of BOT in the cervix. According to our information, only one other case of endocervical manifestation of a BOT has been reported so far. The fact that borderline cells were found in the endocervix indicates the ability of this tumour to form metastases outside of the abdominal cavity. Until now the widely accepted opinion is that this tumour can only spread by direct seeding. Irrespective of the place of origin, whether it is the ovary or the appendix, this mode and site of metastatic dispersal is uncommon and might indeed be capable of indicating a sign of increased metastatic activity and thus malignancy.

PO-Onko 03.96**Prognostic and predictive impact of CA-125 at primary surgery of ovarian cancer patients**

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Objective: Despite radical surgery and chemotherapy at primary diagnosis, most patients with ovarian cancer develop recurrence and die due to progressive disease. To stratify patients for optimal therapy, prognostic and predictive factors are needed. We therefore examined the role of CA-125 in this context.

Materials and methods: A total of 233 patients with primary ovarian cancer who presented for surgery at our institution between 1996 and 2004 were included in this study (25% stage I/II and 75% stage III/IV). The prognostic and predictive significance of CA-125 serum concentrations before and after surgery and correlation with clinicopathological variables were analyzed.

Results: Median preoperative CA-125 in stage I/II was 61.6 kU/l (9–1867 kU/l) and 533.15 kU/l in stage III/IV (10–22617 kU/l). 67% of FIGO I/II patients had elevated CA-125 levels (>35 kU/l) before surgery and 96% of FIGO III/IV patients. There was a significant decrease of CA-125 after surgery (61.6 vs. 43.4 kU/l, $p = 0.001$ and 533.15 vs. 92.3 kU/l, $p < 0.001$, respectively). Neither preoperative and postoperative CA-125 concentration nor its decrease had prognostic relevance for recurrence and survival in any stage.

Conclusions: Although CA-125 serum levels differ significantly before and after surgery in early and advanced stage ovarian cancer patients we could not find a prognostic or predictive value for this marker.

PO-Onko 03.97**The clinical relevance of certain cytokines, steroid hormones and oxalate in mamma carcinoma patients**

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Objective: Possible parameters for the biochemical monitoring of breast tumors are reactive C1- and C2-molecules, that are generated

during tumor development (e.g. oxalate). Moreover, IL 6 seems to be associated with the progression of the disease. IL 8, 18, 20 and 21 could also show a correlation with respect to the amount of metastasis. The steroid hormones estrogen, testosterone, androstendione, DHEA and DHEA-S are known substances with involvement in tumorigenesis. We aim to reveal a possible clinical relevance of the above mentioned biochemical markers in breast cancer patients, taking into consideration the clinical status and the established tumor marker CA 15-3.

Materials and methods: The samples of serum were taken from 54 patients of our clinic. The detection of the tumor marker CA 15-3 was done using the LIA-methode. Oxalate was detected via a chemiluminescence method. The detection of the cytokines was performed with the ELISA method. DHEA, DHEA-S, androstendione and testosterone were detected with a radioimmunoassay, estrogen with a chemiluminescence immunoassay.

Results: Oxalate: The tumor free group (mean = 20.88 $\mu\text{mol/l}$) showed a significant difference compared with the group of 3 to 4 metastasis localizations (mean = 16.24 mol/l) (mean difference = 4.64 mol/l/ $p = 0.033$). IL 6: The tumor free group (mean = 0.13 pg/ml) showed a significant difference compared with the group of 1 to 2 metastasis localisations (mean = 6.97 pg/ml) ($p < 0.0005$) and the group with 3 to 4 metastasis localisations (mean = 10.00 pg/ml) ($p < 0.0005$). A statistical difference between the groups of different amounts of metastasis localizations could also be observed ($p = 0.087$) (Mann–Whitney-Test).

Conclusions: Oxalate showed during progression of the disease an inverse correlation compared to CA 15-3. Independent of inflammatory conditions the serum concentration of IL 6 increased during tumor progression.

PO-Onko 03.98

Clinical examination, ultrasound and magnetic-resonance-imaging are sufficient for diagnosing the Mayer–Rokitansky–Küster–Hauser-Syndrome

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Objective: For the identification of genital malformations in patients with Mayer–Rokitansky–Küster–Hauser-Syndrome (MRKH-syndrome) there are the following means of diagnosis: clinical examination, ultrasound imaging, magnetic-resonance-imaging (MRI) and laparoscopy. This study compared the different diagnostic means in order to classify the genital malformations in the best way.

Materials and methods: The assessment of the genital malformations was based on the VCUAM-classification. For the individual organs the following reference methods were settled: vagina—clinical examination, cervix, uterus and adnexa—laparoscopy, kidney—MRI. The study analysed the concordance of the different diagnostic methods with the reference methods in 138 patients with MRKH-syndrome.

Results: The MRI did not turn out to be an ideal method for assessing the vagina when compared with the reference method of diagnosing the vagina ($\kappa = 0.74$). It was not possible to make any substantial findings regarding the vagina using Ultrasound and laparoscopy. Because the examination results rarely mentioned the cervix separately, it was also not possible to assess the best classification of the cervix. MRI was a very good means in terms of classifying the uterus ($\kappa = 0.93$) but also ultrasound imaging showed a high rate of agreement ($\kappa = 0.83$). None of the imaging methods was able to

achieve a sufficient classification of the adnexa. Ultrasound imaging was held to be a good method to find renal malformations in comparison with the reference method ($\kappa = 0.87$).

Conclusions: Mainly clinical examination, MRI and ultrasound are sufficient for the assessment of genital malformations in MRKH-patients. However malformations of the adnexa were not sufficiently diagnosed using both imaging techniques. In order to correctly assess the adnexa it is compulsory to perform laparoscopy which all patients receive when creating a neovagina.

PO-Onko 03.99

Results of the AGO studies on the operative approaches in the care of endometrial cancer in Germany from 2006 and 2009

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Objective: In 2006 and 2009 the AGO explored reality of common therapeutic approaches of endometrial carcinoma (EC) in Germany. Here we present crucial operative features like the use of laparoscopy (LSC), pelvic and paraaortic lymphadenectomy (LNE) and frozen section (FS). **Materials and methods:** A questionnaire was sent to 500 German gynaecological departments in 2006 (775 in 2009). The results of 2006 and 2009 were compared using Fisher's exact test. The results were correlated with the departments' number of beds (NB) and number of cases of EC (NC) calculating quartiles and Pearson's chi-square test. The results concerning LNE were compared to the guideline of AGO.

Results: 258/775 (33.3%) responses in 2009 and 179/500 (35.8%) in 2006 were available. LSC was performed more often in 2009 as in 2006 (21.1% vs. 11.4%, $p = 0.012$). LSC is more often used by NB > 69 and NC > 29 as by NB < 40 and NC < 16 (2006: 8.1% (NB < 40) vs. 34.7% (NB > 69), $p = 0.01$). Pelvic LNE was performed independently of NB and NC according to guideline in 2009 and 2006. In 2009 paraaortic LNE was conducted roughly according to guideline independently of NB and NC. Paraaortic LNE was not conducted according to guideline in NB < 40 and NC < 16 in 2006 (69.5% (NB < 40) vs. 95.5% (NB > 69), $p = 0.011$; 85.2% (NC < 16) vs. 97.1% (NC > 29), $p = 0.004$). The decision to conduct a LNE was taken intraoperatively in 62.4% independently of NB or NC in 2009 (65.7% in 2006). 69.5% used FS to estimate myometrial infiltration in 2009 (66.5% in 2006). FS was used less frequently in NC < 16 as in NC > 29 (2009: 57.3% vs. 77.1%, $p = 0.008$; 2006: 48.8% vs. 83.8%, $p = 0.001$).

Conclusions: LNE was roughly conducted in accordance to guideline in 2009 independently to NB and NC. LNE in 2006, LSC and FS depend on NB and NC. Further studies are warranted to determine an impact on patients' outcome.

PO-Onko 03.100

Laparoscopic diagnosis of chlamydial salpingitis

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Objective: Salpingitis has a complex aetiology dominated by Chlamydia trachomatis (C.t.), however, results from the lower genital tract do not always correlate with those from tubal swab samples.

Materials and methods: The microbiological results of tubal swab specimens are compared with those from cervical swabs of patients with laparoscopically diagnosed salpingitis. C.t. was identified by means of PCR and/or LCR.

Results: Between 1/94 and 12/09 342 patients out of 1188 with suspected PID were laparoscopically diagnosed to suffer of acute salpingitis, 95 due to C.t. ($n = 342$): cervix 46 + 4*, tubes 66, tubes only 27 + 18**, all 95 (*cervix specimen only; **tubes specimen only).

Conclusions: The difficulty in gaining access to the fallopian tubes is the major obstacle in microbiologic evaluation of salpingitis, however, a large proportion of C.t. positive cases would be missed not performing laparoscopy.

PO-Onko 03.101

A comparison of dequalinium chloride vaginal tablets (Fluomizin®) and clindamycin vaginal cream in local treatment of bacterial vaginosis

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Objective: To evaluate whether vaginal application of non-absorbable dequalinium chloride (dequalinium) is as efficient as vaginal clindamycin in women with bacterial vaginosis (BV).

Materials and methods: International, multicentre, single blind randomized treatment trial of 321 women with BV, comparing vaginal use of 6 days of 10 mg dequalinium chloride tablets (Fluomizin®) with 7 days clindamycin 2% cream. The study was registered at EudraCT (2006-004398-89) and was conducted in 15 centres in Belgium, Czech Republic, Germany, Slovakia and Switzerland in accordance with the Declaration of Helsinki and the Guidelines on Good Clinical Practice. Clinical cure based on the Amsel's criteria (absence of clue cells and a negative result for at least 2 other criteria) was the primary outcome variable at one week and one month after treatment. Secondary outcome variables included among others rate of treatment failures and recurrence, incidence of vulvovaginal candidosis (VVC), lactobacillary grade (LBG), and Total Symptom Score (TSC).

Results: Treatment with dequalinium chloride had equal efficacy as clindamycin cream at 1 week after treatment, with higher cure rates. After 1 month, cure rates with dequalinium chloride and clindamycin cream were also comparable. Total failure rates were about 24% in both groups. A trend to less common post-treatment VVC in the dequalinium chloride group as compared to the clindamycin group was observed. No serious adverse events and mainly local events were observed.

Conclusions: This new treatment with vaginal tablets containing 10 mg dequalinium chloride (Fluomizin) shows equal efficacy as clindamycin 2% cream, is well tolerated, and is a valid alternative treatment for women with BV, even in pregnancy as dequalinium chloride absorption is negligible. The broad antimicrobial spectrum of dequalinium chloride can offer a stronger benefit for patient, particularly as there is no defined causative microorganism and no microbiological diagnosis for BV. Also there is a decreased likelihood for Candida infection after treatment when compared with clindamycin.

PO-Onko 03.102

Influence of protein-isolates on the proliferation and cytotoxicity of mammary carcinoma-cells and healthy cells

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Objectives: Lupin flour has high nutritional qualities (e.g. high protein concentration) and is therefore used by many food manufacturers. The aim of this study was to find out whether proteins from the lupin seed flour of 3 different types of *Lupinus angustifolius* (Boregine, Probor, Vitabor) have a proliferative or cytotoxic effect on different cell lines (2 mammary carcinoma cell lines: BT20 and MCF7, 2 healthy cell lines: fibroblasts and hepatocytes).

Materials and methods: We used 2 proliferative tests (MTT and BrdU by Roche) and 1 cytotoxicity test (LDH by Roche). Additionally we measured the pH before and after applying the lupin-extract. Each test was repeated 3 times with each 4 samples per different concentration. The lupin seeds were floured and afterwards solubilized in 1 M Tris-buffer. From each lupin seed we tested the following concentrations: 70, 35, 3.5, 1.75, 0.875 and 0.7 µg/µl.

Results: Hepatocytes: LDH-test: no cytotoxicity in all concentrations of all 3 lupin seed-extracts, pH did not differ after applying the extracts. Fibroblasts: LDH-test: no cytotoxicity. MTT-test: proliferating effects (about 20%) at 70 and 35 µg/µl (Vitabor). BrdU-test: high proliferating (70–200%) effect of all 3 lupin types (at 70, 35 µg/µl). Lower concentrations: 0–20% proliferation pH did not change MCF-7: LDH-test: no cytotoxicity MTT-test: about 15–25% proliferation at 35 and 70 µg/µl, inhibition up to 20% at lower concentrations. BrdU-test: low proliferative effects (Probor: about 5%), pH did not change. BT20: LDH-test: 8–17% cytotoxicity at 70 µg/µl, lower concentrations: no cytotoxicity MTT-test: lupin Boregine: at 70 µg/µl about 10% proliferation, lower concentrations up to 30% inhibition. BrdU-test: 60–150% proliferation at 70 and 35 µg/µl pH stayed the same.

Conclusions: Interesting for patients with connective tissue-softness (alternatively to HRT). Further researches necessary if in vivo high concentrations of lupin seed flour have the same proliferating effects as in vitro.

PO-Onko 03.103

Primary hyperparathyroidism with parathyroidectomy in the third trimester: a case report

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Objective: Primary Hyperparathyroidism (pHPT) is a rare disease in gravidity which entails considerable maternal and fetal risks. Beyond pregnancy, parathyroidectomy is the therapy to be chosen. In case of affection during gravidity there are no evidence-based therapy guidelines available, because of a lack of randomized studies and few cases. Based on a case of pHPT in the third trimester at our hospital, this article discusses the diagnostic and therapeutic approaches.

Materials and methods: A 36 year old Gravida II Para I with an hitherto inconspicuously developing gravidity was hospitalized in week 28 of gestation with premature contractions (without cervical shortening). A lung maturation was induced. Kidney pains and normal urinalysis led to a renal sonography. It showed a renal calcinosis. On enquiry the patient complained about fatigue, polydipsia and polyuria. The clinical pattern revealed hypercalcaemia, hypophosphataemia, calciuria and anaemia with increased levels of parathyroid hormone (PTH). Sonography stated an adenoma-suspect finding parapharyngeal, possibly explaining the pHPT. Different therapy-options were discussed on an interdisciplinary level with the patient. Due to the risks of a severe neonatal hypocalcaemia as a consequence of a postpartal secondary hypoparathyroidism of the infant, an operative exploration of the parathyroid glands was indicated. An adenoma of the parathyroid gland was removed without any complications. Operative the PTH normalized. Serum calcium regularized with oral calcium- and vitaminD3-substitution. Nine days after surgery the patient was released into ambulant care.

Conclusions: The therapeutic options of pHPT during gravidity are limited. Conservative treatment is confined to hydration and calcium restriction with frequent clinical follow-ups, medicinal therapy is limited: relatively contra-indicated are diuretics, contra-indicated are bisphosphonates, not approved during gravidity are Cinacalcet and Calcitonin. Few case studies show that PTE, done in the second, but also in the third trimester often seems to have less complications than the conservative management of pHPT.

PO-Onko 03.104

Ileal conduit and continent Ileo-cecal pouch for patients undergoing pelvic exenteration

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Objective: Over the last years creating a continent urinary pouch has become an alternative to the ileal conduit for patients undergoing exenteration for advanced gynecologic malignancies.

Materials and methods: In this study we compared intra- and post-operative complications and Quality of Life scores for the modified ileo-cecal-pouch and the ileal conduit in anterior or total pelvic exenteration.

Results: In 31 out of 85 patients an ileal pouch (IP) was created, the other 54 were treated by an ileal conduit (IC). Creating and IP prolonged the exenterative procedure by 88 min. compared to fashioning an IP (IC = 462 min. vs. IP = 550 min.; $p = 0.009$). Overall complication rate was similar but patients with an IP suffered significantly more complications of urinary diversion ($n = 15$; 48.4%) than patients with an IC ($n = 15$; 27.7%; $p = 0.03$). The SF 12 score estimating quality of life was significantly better in the IP group (IC: median 56 vs. IP median 81; $p = 0.01$).

Conclusions: A continent IP is an alternative to the IC in cases of pelvic exenteration. Early complications are less frequent than with an IC but quality of life is better with an IP.

PO-Onko 03.105

The effects of a TVTR and the TVTO on the pelvic floor and the musculoskeletal system

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Objective: According to current studies approximately 10–41% of the female population suffers from stress incontinence (SUI). After exhausting all conservative measures for treatment and clear indication the TVTR or TVTO are the preferred operative interventions. Current publications frequently compare the two surgical options and also describe the occurrence of postoperative pain in the adductor muscles. None of the investigations looked at pre- and postoperative functional status of the musculoskeletal system.

Question: What are the effects of the TVT and the TVTO on the musculoskeletal system regarding the quality of life (QoL), the strength of the pelvic floor muscles and the musculoskeletal system in general?

Materials and methods: The study was prospective and randomized with $N = 70$ of which 37 patients received a TVTO and 33 patients a TVT. Pre-surgery diagnostic was done. On the day of pre-medication for the surgery and six weeks post operatively a physical therapy evaluation was done which included the following: evaluation of posture and mobility of the spine, diaphragmatic breathing, strength testing of the pelvic floor muscles and manual tests of the pelvic girdle. All patients suffered from a verified dominant 2nd degree SUI. In addition a visual analog scale (VAS) was used for measuring the QoL. A perineal sonography was done the digital grading of pelvic floor strength using the Oxford and Laycock grading scale.

Conclusions: The results 6 weeks post surgery was as follows: Significant improvement of pelvic floor muscle strength and QoL. No pain unless it was present prior to the surgery. The improved motor control of the pelvic floor muscles can be explained through the phenomenon of muscular neurodynamics and improved mechanosensitivity of the muscles. After evaluation of the outcomes of both surgeries, they can be equally considered as positive intervention if done with clear indications and by an experienced surgeon.

PO-Onko 03.106

Vaginal sacrospinal uteropexy in surgery for genital prolapse

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Objective: Vaginal sacrospinal uteropexy is supposed to be a secure, time sparing and effective option in prolapse surgery.

Materials and methods: Retrospective analysis of 35 patients with at least stage II genital prolapse (according to ICS classification). Patients were operated with vaginal sacrospinal uteropexy, accompanying cystoceles and rectoceles were corrected simultaneously by using traditional techniques. Postoperative prolapse and clinical examination were classified by the Pelvic organ prolapse quantification system (POP-Q), approved by the International Continence Society (ICS) and the American Urogynecology Society (AUGS). In addition, patients completed a standardised questionnaire about urinary and anal incontinence, sexuality and quality of life.

Results: More than 50% of the patients have been examined in this ongoing study postoperatively up till now. Objective results are promising, patients satisfaction is very high. Exact data concerning prolaps stage before and after surgery and subjective outcome will be presented later.

Conclusions: Clinical outcome and patients satisfaction after vaginal sacrospinal uteropexy are very promising. Thus hysterectomy needs its own indication during prolapse surgery. Vaginal sacrospinal uteropexy is a valuable less invasive and cost effective alternative procedure compared with traditional abdominal or laparoscopic uteropexy.

PO-Onko 03.107**An interdisciplinary approach in the operative therapy of severe pelvic floor insufficiency: a follow up of 36 months***Imke Mebes¹, Markus Grebe¹¹University of Hamburg, Department of Gynecology, Hamburg, Germany

Objective: The intussusception of the rectal and/or sidmoidealmucosa represents a longitudinal descensus of the rectosigmoid (inner rectal mucosal prolapse). The unidisciplinary correction of only one of these combined defects often ends in unsatisfactory or insufficient results, which include residual problems or recurrent prolapse. The combination of rectal mucosa intussusceptions and vaginal prolapsed particularly favours an interdisciplinary approach

Materials and methods: 18 patients were operated on rectosigmoidal intussusceptions symptomatic with stool outlet obstruction and vaginal prolapse grade III-IV or recurrent prolapse grade II (POP-Q/ICS). Median age was 62 years. The resection rectopexy is conducted by laparoscopy. The vaginal mesh-colposuspension (Prolift[®], Ethicon Gynecare) is carried out according to the technique which has been developed by the French TVM Group. Postoperative follow up was done at 12 and 36 months.

Results: Outcome: 15/15 patients after 36 months were healed from vaginal descensus following the anatomical criterias (POP-Q grade 0-I°). 2 patients reported local discomforts. 1 patient had a current rectocele as reported at the follow up trial after 12 months showed a reduction to POP-Q Grad I° after 36 months. 14/15 Patientinnen were without symptomatical intussusception or defecal obstructions. 1 patients complained discomforts, declaiming optional surgery. 1 patient showed tissue erosion at the vaginal ending after discontinuing hormone therapy after 6 months with spontaneous remission after refreshing local therapy. 2 patients are lost to follow up.

Conclusions: Interdisciplinary approach by abdominal surgeons and gynecologists does not involve a higher peri-operative risk for the patient. In this small treatment sequence there was no infection that required surgical intervention nor any insufficient anastomosis. The success rate of 93% is an encouragement for positive long-term results over 36 months.

Reproductive medicine**PO-Repro 03.01****Advanced procedures for the analysis of follicular fluids**Stefan Neubeck¹, Ines Hoppe², Claudia Holzhauser³, Marianna Alunni-Fabbroni³, Ferdinand von Eggeling⁴, Karin Görner³, Wolfgang Starker², *Udo Markert¹,¹Universitätsklinikum Jena, Abteilung für Geburtshilfe, Jena, Germany, ²Universitätsklinikum Jena, Abteilung für Gynäkologie, Jena, Germany, ³Beckman Coulter Biomedical, Munich, Germany, ⁴Universitätsklinikum Jena, Institut für Humangenetik, Jena, Germany

Objective: The analysis of oocytes before fertilization is restricted to morphological aspects. Therefore, we aimed to establish new methods for the analysis of follicular fluids (FF) and granulosa cells (GC).

Materials and methods: We analyzed 112 FF and 18 serum samples by Surface Enhanced Laser Desorption Ionisation-Time Of Flight (SELDI-TOF) mass spectrometry is a further advanced method to reduce overlapping signals from different substances. Furthermore, we analyzed more than 60 GC immediately after isolation or after up to 10 days of culture by multiplex single cell PCR plus several

samples of 2 or more GC for the expression of inhibin A, inhibin B, insulin-like growth factor binding protein 1 (IGFBP1), IGFBP4, IGFBP5, anti-Müllerian hormone (AMH), AMH receptor (AMHR) and CD45 (control for lymphocyte exclusion).

Results: By using IMAC copper protein chips for SELDI-TOF, 28 high signal proteins (>10 µA) were detected exclusively in serum and 16 exclusively in FF. Further 4 proteins have been detected in almost all FF, but in only 13–35% of sera samples. Approximately 80% of GC expressed IGFBP5. The other genes were expressed less frequently. After 10 days of culture GC expressed up to 5 out of the analyzed genes, while GC from short term culture did not express more than 2 genes. The combination of expressed genes was very variable and no preferential pattern could be detected yet.

Conclusions: FF specific proteins may serve as a new tool for prognostic evaluation of follicle and oocyte quality with respect to fertilization and implantation. Presence of proteins which should be absent in FF may be used for blood contamination control or may indicate pathologic processes. Gene expression in individual GC is very inhomogenous. The level of variability or the dominance of specific patterns may become an indicator for follicle and oocyte quality.

PO-Repro 03.02**AKT phosphorylation and insulin/growth factors I–II receptors gene expression modulation in decidualized endometrial stromal cells and the potential effect of metformin**Edison Capp¹, Julia Jauckus², Helena von Eye Corleta¹, Thomas Strowitzki², *Ariane Germeyer²,¹Universidade Federal do Rio Grande do Sul, Obstetrics and Gynecology, Porto Alegre, Brazil, ²University of Heidelberg, Gynecological Endocrinology and Reproductive Medicine, Heidelberg, Germany

Objective: Insulin and the insulin growth factors I and II play an important role in the fetomaternal interaction during implantation. Through their paracrine signalling pathways decisive signals for nidation are exchange between the embryo and the maternal cells. Metformin, an anti-diabetes drug, can potentially influence this mechanism and is often used in anovulatory women with polycystic ovaries. To assess the local metformin effect on AKT phosphorylation and insulin/IGF1/IGF II receptors expression in decidualized endometrial stromal cells (ESC) after stimulation with insulin, IGF I and II.

Materials and methods: ESC were obtained and isolated from healthy, regularly cycling women ($n = 5$). After two passages cells were decidualized with estrogen and progesterone with or without metformin. Then cells were incubated with insulin, IGF I or IGF II for 5, 10 and 20 min to assess AKT-phosphorylation by Western blot. In order to assess insulin, IGF I and IGF II receptor gene expression in ESC realtime PCR was performed after stimulation with insulin, IGF I and IGF II for 6 and 24 h.

Results: We demonstrated statistical significant phosphorylation of AKT after 5 min insulin, IGF I and IGF II stimulation in ESC in both control (control 0.0819 ± 0.031 vs insulin 0.737 ± 0.189 , IGF1 0.678 ± 0.220 , IGF2 0.526 ± 0.132 , $p < 0.05$) and metformin (control 0.035 ± 0.013 vs insulin 0.747 ± 0.111 , IGF1 0.738 ± 0.146 , IGF2 0.673 ± 0.094 , $p < 0.05$) cells. However, there was no difference between ESC treated with or without metformin. Each receptor gene expression changed significantly after addition of insulin, IGF I and IGF II in control with minimal changes after metformin pretreatment.

Conclusions: Insulin, IGF I and IGF II induce AKT phosphorylation and lead to changes in the gene expression of their receptors in ESC.

PO-Repro 03.03**Association of thyroid autoimmunopathy with lower life-birth rate and risk of miscarriage**

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Objective: The thyroid gland has a key position in the complex endocrine system, which itself is intimately associated with the body's immune function. Autoimmune thyroid disorders, which may result in an abnormal/damaged thyroid follicular structure, are characterized by the presence of anti-thyroid antibodies (Ab). A potential relationship with impaired fertility and increased pregnancy loss has been suggested, but results of most trials are inconclusive.

Materials and methods: A total of 222 women who presented for the first time in our outpatient endocrine clinic with (pre/post-)menopausal complaints (median age 49 years) were screened for thyroid function (TSH, T3, T4), and for thyroglobulin(TG), thyroid peroxidase(TPO)- and TSH receptor(TR)-Ab using standard serum assays. The same day all patients were interviewed for previous obstet./gyn. events as part of a complete medical history.

Results: Thyroid autoimmunity was detected in 22.5% (50/222) women: TG-Ab in 20.7% (46/222), TPO-Ab in 12.6% (28/222), with a significant relationship between both parameters ($p < 0.0001$), TR-Ab in 1.4%. Less patients with elevated TG-Ab levels had given birth to at least one child: 47.8% (22/46) compared to 65.3% of women without TG-Ab ($p < 0.03$), and 46.4% of individuals with TPO-Ab (13/28) compared to 63.9%. Significantly more women with pathological TG-Ab levels reported on previous abortions: in 21.7% compared to 9.7% in the group without TG Ab ($p < 0.03$), and in 25.0% in case of elevated TPO-Ab compared to 10.4%. The prevalence of these Ab was without difference in patients $< > 49$ years, but TPO-Ab were more frequent in women > 56 years (75% age perc.) ($p < 0.05$), no relationship was found with the BMI.

Conclusions: The results demonstrate that thyroid autoimmunity is very frequent in peri/post-menopausal women (TG-and/or TPO-Ab in 22.5%), and that this autoimmunologic reaction is significantly associated with a higher risk of abortion and a lower life-birth rate on retrospective analysis.

PO-Repro 03.04**Increase of the intrauterine pressure after administration of human seminal plasma in a uterus perfusion model**

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Objective: Uterine contractility is important not only for labor, but also for the transport of semen and gametes, and successful embryo implantation. Uterine activity is regulated by complex and mutual interactions among sex-steroids, neurohypophysial-hormones, and neurotransmitters. It also involves the integration of many signal-transducing events, resulting in precise coordination of myometrial contractile activity. There are many uterotonic agents and also many intracellular effectors that are known to be crucial for efficient uterine smooth-muscle contraction—such as oxytocin, various prostaglandins, and muscarinic receptor-agonists. Some of these compounds are also present in seminal plasma. It has been known since the 1930s that seminal plasma can induce contractions and even cramps in humans. The aim of this study was to test an experimental uterus perfusion

model as to whether it can be used to analyze uterine contraction patterns after the administration of human seminal plasma.

Materials and methods: Each swine uterus was perfused in a perfusion system with Krebs–Ringer solution. After 45 min with rhythmical spontaneous contractions present, human seminal plasma was administered via a catheter intrauterine and the intrauterine pressure was recorded.

Results: An increase in intrauterine pressure (IUP) in the isthmus uteri and corpus uteri was observed after the administration of seminal plasma or buffer solution. The direct comparison of the intrauterine pressure over time after administration of seminal plasma or buffer solution shows a significant pressure rise with seminal plasma.

Conclusions: This study demonstrates that seminal plasma has an effect in these preliminary experiments in that it stimulates uterine contractions and may enhance sperm transport. The clinical implication of the results of our pilot study would be that the application of seminal plasma in artificial insemination could increase the chance of conception also in humans, due to the increase of uterine contractility.

PO-Repro 03.05**The 5-methyltetrahydrofolate-homocysteine methyltransferase reductase 66A>G/I22 M mutation is associated with decreased anti-Müllerian hormone concentrations and lower number of retrieved oocytes after controlled ovarian hyperstimulation**

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Objective: The one-carbon metabolism is an essential process in the biological network that regulates the biosynthesis of nucleosides and the methylation of proteins, lipids, and DNA. Epidemiological evidence suggests that genetic variants of enzymes in the one-carbon metabolism pathway as well as folate intake influence ovarian function. We have shown that A.R.T patients carrying the T allele of the 5,10-methylenetetrahydrofolate reductase (MTHFR) 677C>T mutation require more FSH for controlled ovarian hyperstimulation and produce fewer oocytes. To study this association more closely, we investigated the 66A>G/I22 M mutation of the MTRR enzyme which is also involved in one-carbon metabolism.

Materials and methods: This study included 235 patients undergoing IVF/ICSI for male factor ($n = 171$) or tubal factor infertility ($n = 64$). AMH as a marker of ovarian reserve was measured after ten days of gonadotropin-releasing hormone super agonist treatment and prior to COH. Oocytes were collected following ovulation induction and counted microscopically after follicle puncture. The MTRR 66A>G genotype was characterized by a TaqMan 5' nuclease assay.

Results: The MTRR 66A>G/I22 M genotype distribution (AA: $n = 46$; AG: $n = 119$; GG: $n = 70$) was in Hardy–Weinberg equilibrium ($\chi^2 = 0.129$; $p = 0.719$). Average AMH levels and number of oocytes retrieved (NOR) of MTRR 66GG patients (AMH: 1.87 ± 1.55 ng/ml; NOR: 9.28 ± 5.95) were significantly lower than those of individuals homozygous for the MTRR 66A allele (AMH: 2.53 ± 1.68 ng/ml; $p = 0.014$; NOR: 12.73 ± 7.58 ; $p = 0.017$). Heterozygous patients had intermediate values (AMH: 2.22 ± 2.26 ng/ml; NOR: 11.75 ± 7.99).

Conclusions: We report for the first time that homozygous carriers of the MTRR 66G allele have significantly lower NOR and AMH serum concentrations compared to wild-type. Our findings support the notion, that enzymes involved in one-carbon metabolism may be involved in ovarian function.

PO-Repro 03.06

Changes in AMH levels following ovarian cortex removal: implications for fertility preservation

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Objective: One option of fertility-preservation is cryopreservation of ovarian cortex before chemotherapy. However, not all chemotherapies result in a complete eradication of the follicular-reserve, thus the biopsy itself may impair fertility after chemotherapy. Therefore, we aimed to establish a model assessing the relative change in Anti-Müllerian-Hormone following ovarian biopsies of varying sizes.

Materials and methods: Participants of this longitudinal, prospective, interventional study underwent caesarean-section. AMH was measured by ELISA, 2–15 h before section (d0), as well as 70–75 h (d3) and 3 month (m3) after. At section, cortical pieces from one ovary were removed. Controls had blood sampling at the same time-points but no biopsy. The follicular-density was determined in HE-stained slides. Assessed were absolute and relative short-term (d0–d3), long-term AMH-changes (d0–m3) and correlation between cortex weight, follicular-density and relative AMH-change.

Results: Interim-analysis of 12 women with biopsy und 2 controls: In the study-group an absolute and relative median short-term AMH-change of -0.16 ng/ml (-0.61 to 0.01) and -18.45% , were observed, 0.27 ng/ml (0.03 – 0.50) and 171.21% , respectively in the controls ($p = 0.028$). The long-term AMH-changes in the study-group were 0.84 ng/ml (0.06 – 3.03) and 131.9% , 0.67 ng/ml (0.44 – 0.90) and 283.03% , respectively in the controls ($p = 0.27$). A correlation between the weight of the biopsy and the relative short-term AMH-change could not be established with statistical significance as well as a correlation between follicular density and AMH d0 or absolute and relative changes.

Conclusions: This study shows that even small ovarian biopsies (36 – 230 μg) result in a short-term AMH-change of -18% . An unexpected finding was the long-term increase in AMH in contrast to a previous study. Thus, AMH behaviour during pregnancy and puerperium needs a re-assessment. The interim-analysis was underpowered to show significant correlations. This is the first study in healthy women estimating the follicular-reserve reduction caused by cortex biopsies.

PO-Repro 03.07

Case report: ovarian pregnancy after IVF

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Objective: Ovarian pregnancy is a rare condition of ectopic pregnancy. The risk of ectopic pregnancy after in vitro fertilization is increased. Due to the increasing number of assisted reproduction the incidence of ectopic pregnancies has risen. The precise etiology of ovarian pregnancy after IVF is still unknown.

Materials and methods: We report on a 33-year old primipara, who underwent IVF because of a male factor. During the second IVF-cycle the patient was stimulated with recombinant FSH and GnRH-

antagonist. After transvaginal oocyte pickup the patient was admitted to our unit because of OHSS where she has been treated symptomatically. Two embryos were replaced in utero under ultrasound guidance. At gestational age of 8 weeks +1 the patient was admitted again as a result of no ultrasonic sign of intra- or extrauterine viable pregnancy. At this time the patient was asymptomatic. Serum β -hCG level was 2018 mU/ml, 48 h later β -hCG was 1892 mU/ml. The asymptomatic patient insisted in expecting management. At 8 weeks +3 days she developed lower abdominal pain and got hemodynamically instable. Ultrasound revealed an ectopic pregnancy with positive heart action and free echogenic fluid. On laparoscopy there was blood in the upper and lower abdomen. The right ovary showed a ruptured ovarian pregnancy. Placental tissue and a gestational sac could be removed. Bleeding was stanching and the ovary could be preserved. Both tubes were normal and separated from the ovaries. The post-operative period was uneventful. Pathology report confirmed an ovarian pregnancy.

Conclusions: Ovarian pregnancy is infrequent and difficult to diagnose. Increasing number of assisted reproduction and therefore increasing risk of ectopic pregnancies demands intensive monitoring (β -hCG levels, ultrasound). Laparoscopy is the traditional treating method whereas methotrexat therapy can be considered at early diagnosis.

Our case fulfills Spielberg criteria for ovarian pregnancy.

PO-Repro 03.08

Slow-freezing vs. vitrification in ovarian tissue preservation

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Objective: Cancer patients benefit from advanced treatments by chemo- and radiotherapy. Gonadotoxic treatments, however, often result in infertility and premature ovarian failure. Slow-cooling is currently the standard for cryopreservation of ovarian tissue prior to chemotherapy. Vitrification could be an effective alternative, however the data on the efficacy of the procedure are still conflicting. We therefore performed a systematic comparison of cryodamage after vitrification versus slow-freezing of human ovarian tissue.

Materials and methods: This study was performed at the Department of Obstetrics and Gynecology, University of Lübeck. Ovarian tissue biopsies were collected from 17 patients undergoing Caesarean sections. The tissue was cut to pieces, which were randomly frozen using either slow-freezing or vitrification. Vitrification was performed according to the protocol described by Hasegawa (2004) and Wang (2008). An acupuncture-needle was used as a carrier. Slow-freezing was performed according to the protocol described by Gosden (1994) and Donnez (2008). After incubation in the cryoprotectant the samples were cooled to minus 150°C following a multiple step freezing-protocol. Vitrification and slow-freezing samples were stored for at least 2 weeks in liquid-N₂. After thawing, the number of viable and damaged follicles was counted, and the proportion of primordial and primary follicles of high-morphological-quality was assessed according to Maltaris (2007).

Results: 277 primordial and primary follicles (137 slow-freezing; 140 vitrification) were counted and analyzed. 23.5% of the samples in the slow-cooling-group showed no high-morphology follicles as compared to 5.8% in the vitrification-group (Fisher's Exact test, $p = 0.17$). Vitrification resulted in a mean 25.6% increase of primordial and primary follicles with high-morphological-quality (t test for paired samples, $p = 0.08$).

Conclusions: Vitrification shows a trend towards better morphological integrity as compared to slow freezing. Inferiority of vitrification for this outcome is thus unlikely. Taking the ease of vitrification into account, this procedure might become a first choice option for freezing ovarian tissue.

PO-Repro 03.09

Oocyte retrieval as an option for fertility preservation of female-to-male transexual patients: a case report

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Objective: Transexual people have to undergo hormonal and surgical treatments before transition to their desired gender, leading to loss of their reproductive potential. We report a case of a female-to-male-transsexual patient, who underwent oocyte retrieval.

Materials and methods: A 30-year-old female-to-male transsexual patient underwent hormonal treatment for over 2 years. The patient received 11.25 mg of Leuprorelin acetate (Trenantone[®], Takeda Pharma, Germany) for pituitary suppression subcutaneously (s.c.) every 3 months under simultaneous transdermal daily application of 50 mg testosterone (Testogel[®], Bayer Vital, Germany). A bilateral mastectomy has already been performed, the patient wished to undergo fertility preservation measures before hysterectomy and oophorectomy. After pausing testosterone treatment, the patient received 225 IU highly purified urinary FSH (Altermon[®], IBSA, Greece) s.c. daily for ten days, followed by 300 IU s.c. daily for three days according to the step-up protocol without pausing leuprorelin treatment. On stimulation day 14 the patient received 250 µg recombinant Choriongonadotropin alfa s.c. (Ovitrelle[®], Merck Serono, Greece) for ovulation induction, 36 h before oocyte retrieval. Estradiol level on this day reached 4210 pg/ml. Donor sperm (Cryos International, Denmark) was used for in vitro fertilization.

Results: 11 of 14 metaphase-II retrieved oocytes were fertilized after ICSI procedure, achieving a fertilization rate of 78.6%. On day 2 after follicle retrieval six 4-cell embryos were vitrified (Medicult Vitrification Cooling[®], Medicult Denmark).

Conclusions: This is the first transexual patient undergoing oocyte retrieval in our clinic. Long-term testosterone application could have a positive impact on oocyte production and oocyte quality, as shown by high number of retrieved oocytes and high fertilization rate. Despite ethical aspects concerning the attitude of medical world, legislation and society towards this group of patients, fertility preservation measures, such as in vitro fertilization, sperm, oocyte or ovarian tissue banking, should be discussed and offered to transexual people undergoing gender reassignment therapy.

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Ongoing pregnancy after hMG stimulation/timed-intercourse in a 40 year old woman with undetectable AMH levels

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Objective: In adult women, Anti-Müllerian hormone (AMH) is synthesized by granulosa cells in primary to early antral follicles. Serum levels of AMH correlate closely with the antral follicular count and predict oocyte yield in ovarian stimulation cycles. Furthermore, AMH serves as a marker of ovarian reserve, and the gradual decline in the primordial follicle pool is best represented by decreasing levels of AMH. Women with an extremely low AMH level have a severely diminished ovarian reserve and have a severely reduced prospect for clinical pregnancy using IVF.

Materials and methods: This is a case report of a 40 year old female patient with AMH levels below the detection limit (<0.05 ng/ml) measured by active MIS/AMH ELISA (Beckman Coulter). The patient had a history of secondary infertility for 2 years. Two pregnancies were achieved in a previous relationship resulting in live births in 1997 and 2005. In 2004 the diagnosis of premature ovarian failure had already been established by her gynecologist. Despite this diagnosis, the patient underwent a treatment trial with clomifene 50 mg at a different gynecologic department and she conceived by timed intercourse in 2004. In a new relationship in 2007 she tried to conceive again spontaneously, without success. In 2009 she came to our department with childish and oligomenorrhea. The evaluation of early follicular phase hormone levels revealed a FSH of 26mIU/ml and AMH <0.05 ng/ml.

Results: Before treatment was started the antral follicular count was 2. Early follicular phase hormone levels were measured: Progesterone 0.7 ng/ml, E2 42 pg/ml, LH 8.2 mIU/ml, FSH 26 mIU/ml, prolactin 7.6 ng/ml, testosterone 2.49 nmol/l, DHEA-sulfate 1.9 µg/ml. The semen analysis showed teratozoospermia. The first cycle was stimulated with clomifene 50 mg as performed previously (resulting in live birth in 2005), but E2 remained low (peak level 18 pg/ml) and no follicular development was observed. A second treatment cycle was performed with daily 75 IU of menopausal gonadotrophin stimulation. Two follicles developed with a pre-ovulatory E2 level of 174 pg/ml, and ovulation induction was performed with 5,000 IU of hCG subcutaneously on cycle day 10. The couple had timed intercourse resulting in a pregnancy which is at 23 + 6 weeks at the time writing.

Conclusions: Two pregnancies were achieved by a patient despite of undetectable AMH levels, a low antral follicle count, elevated FSH and oligomenorrhoea. This leads to the conclusion that low AMH levels should be interpreted with caution when predicting the chance of pregnancy for individual cases. Further investigations of low or undetectable AMH levels and spontaneous pregnancies are needed to evaluate the incidence.