PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Sonographic Evaluation of the Mechanism of Active Labor (SonoLabor study): observational study protocol regarding the implementation of the sonopartogram
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VERSION 1 – REVIEW

REVIEWER	Contag, Stephen University of Minnesota System, Obstetrics, Gynecology and Women's Health
REVIEW RETURNED	18-Jan-2021

GENERAL COMMENTS	Sonographic Evaluation of the Mechanism of Active Labor (SonoLabor study): observational study protocol regarding the implementation of the sonopartogram Summary: This is a protocol for the SonoLabor Study a prospectively collected trial of 168 deliveries collected in 2016. The project was suspended for lack of resources. The authors are now publishing the study protocol in advance of continuing the project as a component of a funded PhD project. It is proposed as a multicenter prospective trial and the authors have presented an introduction to justify the project, the study objectives, the methods and the statistical analysis to be performed. A power analysis is presented but it is not clear what information was used for the calculation. Strengths: 1. A large prospective multicenter trial would compare ultrasound assessment of progression of labor with clinical assessments. The outcome variable needs to be better defined. 2. The clinical predictor variables will be the currently used clinical assessments of cervical length, dilation, station and fetal head position. The ultrasound predictors include fetal head position based on transabdominal and infrapubic transverse scans. The fetal progression in labor will include sagittal infrapubic, and trans labial to measure progression angle, progression distance and head angle with progression, as well as trans labial transverse scan to determine head to perineum distance. The authors plan to create standards for progression variables. It is not clear how position variables will be accounted for. Limitations:

	1. The authors will need to clearly define the population. The primary and secondary aims/objectives are somewhat in conflict. If progression of labor varies according to parity, the ultrasound curves should also be divided according to parity. Furthermore, if it is well known that OP positions progress at different rates compared with OA positions, some study design adjustments need to be made to account for these differences, or, they should be treated as two different subpopulations. 2. The authors have recommended using the Friedman labor curve as a reference to define active labor. They also acknowledge that newer curves have demonstrated that active labor is not always evident until beyond 6 cm dilation. Using a contemporary reference to build a reference would allow broader applicability of the data. 3. The power analysis would benefit from clarification based on a better definition of the primary study population. 4. The protocol should be written in future tense, as such the study has not been carried out. Allusion to the pilot study should be in past tense. Section comments: Page 2 1. Abstract line 14-16: “are to assess the particularities of the sonopartogram in occiput posterior deliveries and to develop standard deviations based on the US pilot study findings. Finally, we will investigate the capability of the US labor monitoring to predict the outcome of delivery.” Please define what is meant by “particularities” and “outcome of delivery”. 2. Line 35: imagistic is not a word in English 3. Line 37-38: the authors use various criteria for study inclusion. In some sections it is limited to OA position, in others it does not limit study to OA position. 4. Line 53: “are poorly reproducible, and therefore unreliable”. This is central to management of labor and delivery. Please be more specific as to why the current form of management is unreliable. 5. Line 56-57: “Severe complications may occur secondary to failed instrumental delivery and Caesarean extraction with the fetal head deeply impacted in the maternal pelvis.” Need to determine whether this study is designed or capable o resolving this question. 6. Line 58: “head descend”, English. Page 4 7. Line 7-9: “our group concluded that the development of a sonopartogram, as an adjuvant to or a replacement of traditional labor monitoring, may be the answer to many of decision problems on the mode of delivery.” Needs to be determined. 8. Line 19-22: “Our study is the first to present a multicentre longitudinal assessment of the mechanism of both stages of active labor, in a representative population using concomitant blinded clinical and sonographic evaluations in unselected low-risk parturients at term. The aim of this paper is to describe the protocol of the current study.” Is this a study or protocol description? Is this really an assessment of the mechanisms of both stages of labor? Are both assessments blinded? 9. Line 26-27: If this is the primary objective then other positions should not be included in primary analysis. This might be best seen as an inclusion criterion. 10. “Line 36: to compare and correlate the US findings (sonopartogram data) with the classical clinical partogram parameters.” How will you compare these?

	11. Line 56: " The study aims to record almost simultaneously blinded US and clinical features of low-risk women in labor at term, with singleton eutrophic cephalic presentation pregnancies." Please specify what is blinded and what is meant by eutrophic singleton pregnancy. Page 4 1. Line 16: "Women are defined as being in labor in the presence of regular uterine contractions occurring at a frequency of at least 2 every 10 minutes associated with a cervical dilatation of 3-4 cm or more". Recommend incorporating current definitions of active labor endorsed by ACOG or other governing bodies. 2. Line 20: Define what is meant by early ultrasound dating. 3. Line 31: What are the potential benefits of this study to the participants? 4. Page 4 line 49 to Page 5 Line 40: Please organize data so that it is easier for th reader to grasp. Page 5 1. Lines 37-38 remove figure references 2. Lines 50-53: "The sonographer and the clinician are blinded to each other's findings (except FHPo) as the specific measurements are performed afterwards, offline and labor management is conducted by the Labor and Delivery department personnel." How is this accomplished? The clinical findings are being used for clinical management of labor. Definition of second stage is clinical. Sonographer cannot be blind to clinical findings, but clinician can be blind to ultrasound findings. 3. Labor characteristics are recorded: mode and time of delivery, neonatal Apgar score and birth weight, whether labor was spontaneous or induced, use of oxytocin or epidural anaesthesia, occipital position at delivery. Maternal characteristics are retrieved from the hospital records: age, height, weight, ethnicity, parity, gestational age. Who and how will the data be recorded. How will the ultrasound images be stored and who and when will the images be reviewed? Page 6 1. Line 6: If the study has already started, then please clarify. 2. Line 21-22: These are all progression markers, what about position? The study reported that inclusion would be limited to OA positions. If a fetus moves to OP, how will that be documented? 3. Line 30-41: Secondary outcomes: "to compare the labor clinical trend from our study data with the Friedman studies and other recent research on the partogram. to compare and correlate the US findings (sonopartogram data) with the classical clinical partogram parameters." How are these two outcomes different? 4. Line 37-39: "to analyse the temporal variation of the sonographic measurements in spontaneous vaginal delivery versus obstructed labor in primiparae versus multiparae and in fetuses with occiput anterior versus those with persistent occiput posterior." Needs to be more specific 5. Line 40: "to evaluate the capability of the US technique to predict the outcome of delivery." Which outcome? Page 7 1. Line 24-30: "According to previously published studies the overall rate of occiput posterior deliveries in nulliparous is around 7.2%, whereas for the multiparous deliveries the rate is around 4%. A suitable statistical power (two-tailed type of null hypothesis with default statistical power goals and type I error level of significance) can be P≥95% α=0.05 achieved if we have at least 102 patients in the case of nulliparous deliveries, and 57 multiparous deliveries, respectively, with occiput anterior

	positions." This requires some explanation: the authors discussed the power analysis in terms of rates of OP presentations and then discusses numbers of cases of OA presentations required to develop reference standards. It might help to define the study population and limit to either nulliparous or multiparous women, and only include women who enter labor in OA as initially stated. Also confusing, that if the 3 centers have a combined number of deliveries that is close to 4000 per year, why it would not be possible to collect data on 102 nulliparous and 57 multiparous women? 2. Lines 42-44: Not sure if this data can be presented as mean and SD, rather it should be broken down into mean values at various points in the progression of labor, such as at admission, at the end of 1 stage and in second stage 3. Line 52: "between US and time to delivery and digital vaginal examination for various clinical situations" Exactly which parameters will be correlated between clinical assessment and ultrasound: station and PD? 4. Line 52-57: It is not clear what the x-axis variable will be, where it starts and where it ends, as well as time intervals between measurements. Previously authors reported performing ultrasound assessment every hour while in labor and every 15 minutes while in second stage. How will the second stage measurements be reported, will they also be on an hourly schedule for the purpose of creating this graph? Page 8: 1. Line 3: How are you defining obstructed labor? 2. Line 13: "The induction–delivery interval within 24 hours will be evaluated using Kaplan–Meier survival analyses and Cox regression analyses." What will you be comparing with this analysis? Page 10 1. Line 36-37: If this study I funded, please list the sources. If not currently funded, please state that is currently has no outside funding. 2. Line 55: "The SonoLabor study recruited patients during January - December 2016 for a pilot study of 168 deliveries." This data could be us for the power analysis. Images: Recommend using images with ultrasound probe covered with probe cover, and ultra sonographer wearing a glove.

REVIEWER	Delabaere, Amélie Centre Hospitalier Universitaire de Clermont-Ferrand, obstetrics and gynaecology
REVIEW RETURNED	04-Feb-2021

GENERAL COMMENTS	The primary objective differ to the the primary outcome and concerned only women with occiput anterior position of fetal head, thus doesn't concerned all population included. The funding and the duration of the study are not specified. The ultrasound methods could be more described with more didactic scheme. As the author points out, the size of the population studied to create a normogram must be much larger, especially on such a heterogeneous population. This study is conducted in 3 university centers with more than 4000 deliveries per year. It therefore presents opportunities for adequate recruitment to this type of study.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Stephen Contag, University of Minnesota System
Comments to the Author:
BMJ Open Manuscript 2020-047188
Sonographic Evaluation of the Mechanism of Active Labor (SonoLabor study): observational study protocol regarding the implementation of the sonopartogram

Summary: This is a protocol for the SonoLabor Study a prospectively collected trial of 168 deliveries collected in 2016. The project was suspended for lack of resources. The authors are now publishing the study protocol in advance of continuing the project as a component of a funded PhD project. It is proposed as a multicenter prospective trial and the authors have presented an introduction to justify the project, the study objectives, the methods and the statistical analysis to be performed. A power analysis is presented but it is not clear what information was used for the calculation.

Strengths:
1. A large prospective multicenter trial would compare ultrasound assessment of progression of labor with clinical assessments. The outcome variable needs to be better defined.
2. The clinical predictor variables will be the currently used clinical assessments of cervical length, dilation, station and fetal head position. The ultrasound predictors include fetal head position based on transabdominal and infrapubic transverse scans. The fetal progression in labor will include sagittal infrapubic, and trans labial to measure progression angle, progression distance and head angle with progression, as well as trans labial transverse scan to determine head to perineum distance. The authors plan to create standards for progression variables. It is not clear how position variables will be accounted for.

Limitations:
1. The authors will need to clearly define the population. The primary and secondary aims/objectives are somewhat in conflict. If progression of labor varies according to parity, the ultrasound curves should also be divided according to parity. Furthermore, if it is well known that OP positions progress at different rates compared with OA positions, some study design adjustments need to be made to account for these differences, or, they should be treated as two different subpopulations.
2. The authors have recommended using the Friedman labor curve as a reference to define active labor. They also acknowledge that newer curves have demonstrated that active labor is not always evident until beyond 6 cm dilation. Using a contemporary reference to build a reference would allow broader applicability of the data.
3. The power analysis would benefit from clarification based on a better definition of the primary study population.
4. The protocol should be written in future tense, as such the study has not been carried out. Allusion to the pilot study should be in past tense.

Section comments:
Page 2
#1. Abstract line 14-16: “are to assess the particularities of the sonopartogram in occiput posterior deliveries and to develop standard deviations based on the US pilot study findings. Finally, we will investigate the capability of the US labor monitoring to predict the outcome of delivery.” Please define what is meant by “particularities” and “outcome of delivery”.

Reply #1. The authors agree that the secondary aims should be better explained. By “particularities” we meant the sonopartogram differences determined by the persistent posterior position of the fetal occiput, and the “outcome of delivery” refers to the outcome of vaginal delivery.

The paragraph was changed and now reads: “The primary outcome is to develop nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous women with occiput anterior position of the fetal head. The secondary aims are to assess the sonopartogram differences in occiput anterior and posterior deliveries, to compare the labor trend from our research with the classic and other recent partogram models and to investigate the capability of the US labor monitoring to predict the outcome of vaginal delivery.”

Also, following this observation the sentence: “to evaluate the capability of the US technique to predict the outcome of delivery.” from Objectives section, page 3, was adjusted: “to evaluate the capability of the US technique to predict the outcome of vaginal delivery.”

#2. Line 35: imagistic is not a word in English
Reply #2. The observation is correct. We replaced the word “imagistic” with “ultrasound” and the paragraph now reads: “The multicenter design on representative population and the blinded clinical / ultrasound assessment aims to intercept the potential sources of bias.”
The authors also replaced the word “imagistic” with “sonographic” in Procedures section, Interventions, page 6.

#3. Line 37-38: the authors use various criteria for study inclusion. In some sections it is limited to OA position, in others it does not limit study to OA position.
Reply #3. Although the primary objective of the study is the development of sono-nomograms for nulliparous and multiparous women at term with occiput anterior position of the fetal head, we did not intend to limit the inclusion criteria to occiput anterior position in any of the sections. We thank the review for signaling this important issue that is not properly presented throughout the manuscript.
For a better understanding of the inclusion of the occiput posterior position cases, the following manuscript sections were re-examined and several modifications have been made:

Abstract – Methods:
-“~~The primary outcome is to develop nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous women with occiput anterior position of the fetal head~~.” The phrase was changed and now reads: “The primary outcome is to develop nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous women with fetal cephalic presentation.”
-“The secondary aims are to assess the differences of the sonopartogram in occiput anterior and posterior deliveries…”). This phrase was not changed.

Objectives:
-primary objective: “~~The primary objective of this study is the development of sono-nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous women at term with occiput anterior position of the fetal head~~” was changed as following: “The primary objective of this study is the development of sono-nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous women at term with fetal cephalic presentation”.
-secondary objectives: “to study the influence of occiput position […] on the mechanism of delivery evaluated by US”, “to analyse the temporal variation of the sonographic measurements in spontaneous vaginal delivery versus obstructed labor in primiparae versus multiparae and in fetuses with occiput anterior versus those with persistent occiput posterior”). These paragraphs were not changed.

Methods and analysis, Study design and setting, page 3: “The study aims to record almost simultaneously blinded US and clinical features of low-risk women in labor at term, with singleton cephalic presentation pregnancies.”. The paragraph remains unchanged.

Participants, page 4, first paragraph: “Cases […] with non-cephalic presentation […] will be excluded from the study.” The paragraph remains unchanged.

Participants, Procedures, Interventions, Clinical examination, page 4: “occiput position – to determine fetal head position (FHPo) and occiput rotation during labor. Occiput position was classified as occiput anterior (OA), occiput posterior (OP) […]” – remains unchanged.

The Ultrasound evaluation, from Participants section, Interventions, page 5 was modified for a better presentation of the sonographic evaluation, but the fetal head position assessment both in the first and second stage of labor were kept intact.

Outcome measures, Primary outcome: ”The primary objective of this study is the elaboration of nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous.” We added a clarification: “with cephalic presentation” and the paragraph now reads: “The primary objective of this study is the elaboration of nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous with fetal cephalic presentation.”

Secondary outcomes, page 7: “to study the influence of occiput position, body mass index, parturient age on the mechanism of delivery evaluated by US”, “to analyse the temporal variation of the sonographic measurements […] in fetuses with occiput anterior versus those with persistent occiput posterior.” – remains unchanged.
Statistical methods, statistical analysis, page 8: “Descriptive statistics will be produced for all study variables: […]occiput position […]” – remains unchanged.

#4. Line 53: “are poorly reproducible, and therefore unreliable”. This is central to management of labor and delivery. Please be more specific as to why the current form of management is unreliable.
Reply #4: The fact that clinical digital pelvic estimations regarding fetal head position and station are inexact and poorly reproducible was demonstrated in the cited studies (2-17).
Although clinical evaluation remains the general approach for the management of labor and delivery, many centers included ultrasound determinations during labor in standard practice to overcome these clinical failings, e.g., the determination of the occiput position before instrumental delivery.

We rephrased the paragraph to explain better the limitations of standard labor assessment and highlighted the challenging clinical situations presented in the cited studies:
”Over the last decades, a large body of literature have shown that clinical digital pelvic estimations of fetal head position, station and progression in the pelvic canal are not accurate during the first[2] and second stage of labor[2-7], poorly reproducible when compared to US[8-10], poorly reliable[11-13] and experience-dependent[2,5] and often inexact in challenging labor circumstances, such as: prolonged first stage of labor[14], cases with arrested cervical dilation[15], obstructed labor[16], fetal head engagement[11,17] posterior and transverse occiput locations[7,15], or caput[5].”

We adjusted the bibliography accordingly. No indices were added, but the citations were reordered according their mention in the paragraph.

#5. Line 56-57: “Severe complications may occur secondary to failed instrumental delivery and Caesarean extraction with the fetal head deeply impacted in the maternal pelvis.” Need to determine whether this study is designed or capable of resolving this question.
Reply #5: A more objective method to monitor the labor progression or arrest have the potential to signal the labor complications earlier, which subsequently should lower such unfortunate events.
Previous studies that used sonographic evaluation in prolonged labor cases have demonstrated the potential to decrease the rate of late Caesarian extractions, and the approach / measurements proposed by previous literature were taken into account by our design.
However, the reviewer addressed a good point, and we decided to change the phrase, as following: “Previous studies that used sonographic evaluation in prolonged labor cases have demonstrated the potential to decrease the rate of late Cesarean extractions, and the approaches proposed in the literature were taken into account by our study design.”

#6. Line 58: “head descend”, English.
Reply #6. We apologize for the misspelling. “descend” was replaced with “descent”.

Page 3
#7. Line 7-9: “our group concluded that the development of a sonopartogram, as an adjuvant to or a replacement of traditional labor monitoring, may be the answer to many of decision problems on the mode of delivery.” Needs to be determined.
Reply #7. The authors agree the reviewer opinion. The end of the paragraph was reworded and now reads: “our group concluded that the development of a sonopartogram, as an adjuvant to or a replacement of traditional labor monitoring, provides the setting for a more objective evaluation of labor progression, which could enable more rapid decisions regarding the mode of delivery.”

#8. Line 19-22: “Our study is the first to present a multicentre longitudinal assessment of the mechanism of both stages of active labor, in a representative population using concomitant blinded clinical and sonographic evaluations in unselected low-risk parturients at term. The aim of this paper is to describe the protocol of the current study.” Is this a study or protocol description? Is this really an assessment of the mechanisms of both stages of labor? Are both assessments blinded?
Reply #8. We noted the observations of the reviewer and reworded the paragraph for a better understanding.

The manuscript describes the protocol of the study.
Both stages of labor are involved, since the evaluation starts from the beginning of active labor.
The sonographer and the clinician are blinded to each other's findings (except fetal head position) as the specific measurements are performed afterwards, offline and labor management is conducted by the Labor and Delivery department personnel (Procedures, page 5). Fetal head position represents an exception from the blinded design because of ethical issues regarding the neonatal outcome - the attending obstetrician should be informed in case of clinical and US discordance when instrumental or operative delivery is attempted (Procedures, Interventions, page 7).
The following changes have been made to the manuscript, so that the information could be presented clearer:
Introduction, last paragraph: "This study is designed to produce an original multicentre longitudinal assessment of the mechanism of active labor, including both stages, in a representative population using concomitant blinded clinical and sonographic evaluations in unselected low-risk parturient women at term. The aim of this paper is to describe the protocol of the study."
Procedures, Interventions, page 6: "The sonographer and the clinician are blinded to each other's findings (except FHPo, during the circumstances mentioned above) […]"
(section) Ethics approval and consent to participate. The following phrase was added, for a better presentation of the interaction between clinical and sonographic assessments: "The only potential sonographic intervention in the clinical assessment of labor is due to the ethical issues regarding the neonatal outcome when instrumental delivery is attempted. Thus, the attending obstetrician will be informed in case of clinical and US discordance"

#9. Line 26-27: If this is the primary objective then other positions should not be included in primary analysis. This might be best seen as an inclusion criterion.
Reply #9: We did not intend to include only occiput anterior cases. We initially considered that this is the primary objective of the study, because it will represent the vast majority of the fetal presentations in labor, aiming to achieve the sample size for occiput posterior cases (that will be encountered in only 5% of the deliveries, according the statistics).
As presented above, we have no intention to limit the inclusion criteria to occiput anterior cases. We thank the reviewer for the observation that determined us to modify the paragraph that states the primary objective, from Objectives section: "The primary objective of this study is the development of sono-nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous women at term with fetal cephalic presentation."

#10. "Line 36: to compare and correlate the US findings (sonopartogram data) with the classical clinical partogram parameters." How will you compare these?
Reply #10. In our study, we meant to compare this two methods by analyzing the agreement between sonopartogram and clinical partogram in estimating fetal head position and fetal head station. We appreciate the reviewer's question and thereby we include a clear phrase on the *Statistical analysis* section of our manuscript:
"We will analyze the agreement between sonopatogram and clinical partogram in estimating fetal head position and fetal head station. For the fetal head position we will assess the level of agreement between US and digital VE using Cohen's kappa statistics. Correlation coefficient (Pearson's correlation or the Spearman rank correlation or Kendall's rank correlation if appropriate) and linear regression will be employed for analyzing the strength of association between the fetal head station estimated by digital vaginal examination and the ultrasound parameters (HPD, PA, PD and HDA)."

#11. Line 56: "The study aims to record almost simultaneously blinded US and clinical features of low-risk women in labor at term, with singleton eutrophic cephalic presentation pregnancies." Please specify what is blinded and what is meant by eutrophic singleton pregnancy.
Reply #11. We presented here and in the manuscript how we intend to blind the sonographer and the clinician from each other findings. The procedures used to blind the evaluations results are presented in the next section of the manuscript, therefore we excluded this aspect from this section.
By eutrophic, we meant a normally developed fetus, according the gestational age, but this is not common for English language. We excluded the word "eutrophic", as the low-risk pregnancies concept excludes anyway macrosomia and growth restricted fetuses. In the following paragraph is stated that "neonates weighting less than 2500g or more than 4000g will be excluded from the study".

We reworded the phrase from Methods and analysis, Study design and setting, page 3: “The study aims to record simultaneously the labor progress by clinical and US evaluations in low-risk women in labor at term, with singleton cephalic presentation”

Page 4

#1. Line 16: “Women are defined as being in labor in the presence of regular uterine contractions occurring at a frequency of at least 2 every 10 minutes associated with a cervical dilatation of 3-4 cm or more”. Recommend incorporating current definitions of active labor endorsed by ACOG or other governing bodies.

Reply #1. We thank the reviewer for the observation regarding an endorsed definition for labor stages. We adjusted the paragraph and bibliography accordingly:

“Women will be admitted in first stage of labor when there are regular painful contractions and there is a progressive cervical dilatation from 4 cm, and the second stage will be established based on the finding of full dilatation of the cervix[39]”

(39).National Institute for Health and Care Excellence. Intrapartum care for healthy women and babies. London (UK): NICE; Published December 2014, Last updated: February 2017. https://www.nice.org.uk/guidance/cg190

#2. Line 20: Define what is meant by early ultrasound dating.

Reply #2. Pregnancy dating is best performed by the ultrasound assessment during the first trimester of pregnancy. However, we did not intend to limit the patient inclusion depending on the evidence of first trimester scan data. We agree that this aspect should be better explained and the paragraph was modified:

”Gestational age will be determined by the last menstrual period in women with regular menses, confirmed with US dating, preferably during the first trimester. If the first trimester biometry is not consistent with the menstrual dating by more than one week, gestational age will be established based on the sonographic evaluation alone. In women with irregular menses, the gestational age will be determined solely based on the first fetal biometry evaluation in pregnancy.”

#3. Line 31: What are the potential benefits of this study to the participants?

Reply #3. The authors meant that the patient was informed regarding the potential benefits of the sonopartogram after the completion of the study. The only direct benefit of the laboring women that participate in the study is represented by the communication between the obstetrician and sonographer regarding fetal head position before instrumental delivery. The respective phrase from Procedures / Recruitment section was rewritten for a better understanding of these aspects:

“The details of the study and the potential benefits that may result following the completion of the objectives will be explained thoroughly to the patient. The only direct benefit of the laboring women that participate in the study would be the communication between the obstetrician and sonographer regarding fetal head position when instrumental delivery is attempted, as presented in the Interventions section.”

#4. Page 4 line 49 to Page 5 Line 40: Please organize data so that it is easier for the reader to grasp.

Reply #4. We thank the reviewer for this observation. We restructured this section using the same information, but in a more clear and practical manner. We decided to use a Table format to link better the measured parameters to the acquisition planes and labor mechanism features that were investigated. The modifications are extensive (page 5 and 6) and highlighted in the text.

Clinical examinations will take place in women in active labor just before the US assessments (Figure 1). The clinician will note the observations on a specially designed partogram-like sheet that will be used for women in labor who agree to participate in the study. The following labor characteristics has to be noted before US assessment:

- ***cervical dilation*** in centimetres,
- ***fetal head descent or progression (FHPr)*** – determined by the evaluation of head station in relation to the ischial spines,
- ***fetal head position (FHPo)*** – the evaluation of occiput position in both stages and rotation in the second stage. Occiput position will be classified as occiput anterior (OA), occiput posterior (OP), left or right occiput transverse (LOT or ROT), left or right occiput anterior (LOA or ROA), or left or right occiput posterior (LOP or ROP)39,40.
- Presence of ***caput*** and / or ***molding***, with the approximate diameter.

Clinical examination will be followed by transabdominal and transperineal **ultrasound evaluations** conducted by obstetricians with appropriate training in US in labor, with minimum 1 year of experience in the field. Mobile and compact US machines will be used: Logic e (GE Healthcare, China), GE Voluson P6, Samsung R7, BenQ T3300and ALOKA f31 equipped with 2–5 and 2-6 MHz 2D convex transducers. The objectives of US evaluations are like those of clinical assessment, and aimed to record the mechanism of labor by specific measurements. In Table 1 we present the sonographic measurements, in relation to the acquisition planes and the features of labor mechanism that are involved. The respective images will be stored on the system's hard disk drive for off-line analysis and measurements that will be performed according to the techniques described in the literature, by the sonographer who performed the evaluation.

Table 1. Acquisition of US planes, and ultrasound measurements performed offline, according previous literature

Labor mechanism feature	Acquisition plane	Ultrasound measurements
Fetal head position (FHPo) in the first stage of labor	Transabdominal suprapubic transverse plane	• Occiput position6 (Figure 2) Both clinical and US findings of the FHPo are recorded on a data sheet depicting a circle, like a clock, divided into 24 sections, each of 15o, and the position of the occiput is assigned as anterior (OA), posterior (OP), left anterior (LOA), right anterior (ROA), left posterior (LOP), right posterior (ROP), right transverse (ROT), left transverse (LOT)6
Fetal head position (FHPo) in the second stage of labor, evaluation of head rotation	Transperineal infrapubic transverse plane (Figure 3), with visualization of the cerebral midline	• Occiput position • Midline angle (MLA) (Figure 3) The position of the occiput (OA, OP, LOA, ROA, LOP, ROP) is determined in a similar fashion transperineally in the 2nd stage of labor. Midline angle (MLA) is calculated26 based on the visualization of the cerebral midline in relation to the antero-posterior axis of the maternal pelvis - rotation angle or midline angle (MLA).
Fetal head descent / progression (FHPr)	Transperineal translabial sagittal plane	• Progression angle (PA)27,28, • Progression distance (PD)23, • Head direction angle (HDA)23,25 (Figure 4).
	Transperineal translabial transverse plane, at the level of the ischial tuberosity, applying firm pressure without creating discomfort, and the transducer moved and angled	• Head to perineum distance (HPD)41 (Figure 4).

	until the shortest distance to the fetal skull is visualized	
Caput and molding	Transperineal sagittal and transverse plane	• Caput (Figure 5) is measured as the maximum distance between the leading part of the skull and the fetal skin in the sagittal or transverse planes. • Molding (Figure 5) is diagnosed when the skull bones were seen overlapping in the sagittal or transverse planes.

Because of ethical issues, the design of the study states that the attending obstetrician should be informed in case of clinical and US discordance when instrumental or operative delivery is attempted.

Page 5

#1. Lines 37-38 remove figure references

Reply #1. The lines were removed.

#2. Lines 50-53: "The sonographer and the clinician are blinded to each other's findings (except FHPo) as the specific measurements are performed afterwards, offline and labor management is conducted by the Labor and Delivery department personnel." How is this accomplished? The clinical findings are being used for clinical management of labor. Definition of second stage is clinical. Sonographer cannot be blind to clinical findings, but clinician can be blind to ultrasound findings.

Reply #2. The observation is correct. During labor, the sonographer cannot be not completely blinded to clinical findings, as he/she perform the scans at certain time intervals, depending on the stage of labor. However, the sonographer only records the images and will perform later (offline) the measurements. The clinician will note the observations on a partogram-like sheet, that is not available for the sonographer.

We decided to add these explanations into the manuscript: "During labor, the available sonographer cannot be not completely blinded to clinical findings, as he/she will perform the scans at certain time intervals, depending on the labor stage, that is established by the clinician's cervical dilatation assessment. However, the sonographer will only record the images. The clinician will note the observations on a partogram-like sheet, that is not available for the sonographer, who in turn, will perform the measurements offline, after birth"

#3. Labor characteristics are recorded: mode and time of delivery, neonatal Apgar score and birth weight, whether labor was spontaneous or induced, use of oxytocin or epidural anaesthesia, occipital position at delivery. Maternal characteristics are retrieved from the hospital records: age, height, weight, ethnicity, parity, gestational age. Who and how the data will be recorded. How will the ultrasound images be stored and who and when will the images be reviewed?

Reply #3. The labor characteristics will be recorded by the clinician and noted on the clinical datasheet. The maternal characteristics will be retrieved from the hospital records (patient files) by the personnel involved in data centralization (DG, DR, CP, ZL, NR and RD).

Ultrasound images will be saved and stored on ultrasound hard drives during labor, then transferred by the sonographer to a designated PC storage unit after birth.

The images will be reviewed during the following week, by the same sonographer, who will also input the results into the center database.

The comment resulted in clarifications that were added to the following sections:

- Procedures, Interventions section, Clinical examination paragraph, page 4-5: "The clinician will note the observations on a partogram-like sheet, along labor characteristics"
- Procedures, Interventions section, page 7: "Labor characteristics will be recorded by the clinician on the study datasheet: mode and time of delivery, neonatal Apgar score and birth weight, whether labor was spontaneous or induced, use of oxytocin or epidural anaesthesia, occipital position at delivery. Maternal characteristics will be retrieved from the hospital records (patient files) by the personnel involved in data centralization: age, height, weight, ethnicity, parity, gestational age."
- Procedures, Interventions section, Ultrasound evaluation, page 6: "Ultrasound images will be saved and stored on ultrasound hard disk during labor, then transferred by the sonographer to a designated PC storage unit after birth. The images will be reviewed during the following week,

by the same sonographer, who will also input the offline measurements results into the database."

- Authors' contribution section, where the record / review activity was addressed: "IDG and AP conceived and designed the study and supervise the study implementation. ID drafted the protocol of the study. DL, DG, CM, DR, PC, ZL, NM and DR revised and refined the study protocol for an optimal implementation and provided final approval of the version to be published. CM, SB, RS provided methodological and statistical expertise and conducts the statistical analysis. IDG and DR drafted a PhD salary grant proposal for a previous approved pilot study. DG, DR, CP, ZL, NR and RD are responsible for study management, staff training and supervision and data centralization. IDG, AP and TG are the directors of the sites and provide clinical expertise and on-site management of the study. All authors critically reviewed and approved the final version of the manuscript."

Page 6

#1. Line 6: If the study has already started, then please clarify.

Reply #1. The study has not started, only a pilot study has been carried out, that included the respective workshop and group supervision sessions.

We rephrased the paragraph, that now reads (page 7): "To ensure protocol fidelity, the sonographers will have completed a one-day workshop and will participate in group supervision sessions, programmed weekly in the first month of the study. This approach proved to be successful during the previous pilot study conducted in our center."

We rewritten the entire manuscript in future tense, while the allusions to the pilot study were made in past tense.

#2. Line 21-22: These are all progression markers, what about position? The study reported that inclusion would be limited to OA positions. If a fetus moves to OP, how will that be documented?

Reply #2. The inclusion of parturient women will not be limited to OA position, as presented above.

The protocol states that the position of the fetal occiput will be documented during each evaluation. In the end, we will develop standards / labor curves for OA and OP deliveries. As the WHO partogram curve presents the descent of the fetal head in relation with time and cervical dilatation, we aimed for a similar presentation of the sonopartogram, where the head descent is evaluated objectively, using the US progression markers.

No changes were made to the manuscript.

#3. Line 30-41: Secondary outcomes: "to compare the labor clinical trend from our study data with the Friedman studies and other recent research on the partogram. to compare and correlate the US findings (sonopartogram data) with the classical clinical partogram parameters." How are these two outcomes different?

Reply #3. We apologize for the formulation of the phrases, that gives the impression of similar outcomes / objectives.

- The third secondary outcome of our study refers to the investigation of the potential differences between the labor clinical pattern, compared with the original labor curve created by Friedman and with the modern cohort studies, cited in the end of the sentence: "to compare the labor trend from our study with the Friedman studies[35,36] and ~~another~~ other recent research on the partogram[1]".
- The fourth secondary outcome aims to investigate the correlation between the clinical and US findings regarding fetal head position and descent during active labor in our study: "to compare and correlate the US findings (sonopartogram data) with the classical clinical partogram parameters".

Practically, we will compare the FHPo determined by US with FHPo evaluated digitally (clinically). Also, we will analyze the correlations between the US FHPr parameters and between US and clinical head descent / progression measurements.

- The last secondary outcome aims to evaluate the possibility to use the trend of US parameters in conjunction with clinical data involved by the study (cervical dilatation) to develop predictions for the outcome of labor (vaginal delivery or Cesarean section).

The following changes have been made in the manuscript:

- Three explanatory subpoints were added to the fourth point of the Secondary outcomes, that now reads: "to compare and correlate the US findings (sonopartogram data) with the classical clinical partogram parameters, regarding the fetal head position and descent during active labor:

    - correlation of the FHPo determined by US with FHPo clinically estimated (by digital vaginal evaluation);
    - correlations between the US FHPr parameters and between US and clinical (head station) FHPr parameters;
    - the concordance between the fetal head station evaluations determined by US and clinical digital exam."
- The last point of the Secondary outcomes now reads: "to evaluate the capability of the US technique to predict the labor outcome (vaginal or Cesarean birth) in both nulliparous and multiparous"
- In *Statistical analysis* section, the sentence "The maternal, labor, and neonatal characteristics of women will be compared using χ2, Fisher exact test, and the Wilcoxon rank sum test where applicable" was modified and it results in "Clinical obtained data from our study will be compared with similar data from other partograms. The results between groups (maternal, labor and neonatal characteristics of women assessed by classical clinical partograms or a more recent partogram and our sonopartogram) will be compared using Chi-square test or Fisher exact test (for categorical variables), and Student t-test or Mann Whitney test where applicable (for continuous variables) with a statistical significance level set at $p < 0.05$".

#4. Line 37-39: "to analyse the temporal variation of the sonographic measurements in spontaneous vaginal delivery versus obstructed labor in primiparae versus multiparae and in fetuses with occiput anterior versus those with persistent occiput posterior." Needs to be more specific
Reply #4. What we meant was to analyse the evolution of sonographic measurements according the outcome of vaginal delivery.
The sentence was modified and now reads (Secondary oucomes, page 7): "to analyse the evolution of the sonographic measurements in spontaneous vaginal delivery versus obstructed labor cases, in primiparae versus multiparae and in occiput anterior deliveries versus those with persistent occiput posterior."

#5. Line 40: "to evaluate the capability of the US technique to predict the outcome of delivery." Which outcome?
Reply #5. The authors refer to the outcome of labor – vaginal or Cesarean delivery. The sentence was modified accordingly: "to evaluate the capability of the US technique to predict the labor outcome (vaginal or Cesarean birth)."

Page 7
#1. Line 24-30: "According to previously published studies the overall rate of occiput posterior deliveries in nulliparous is around 7.2%, whereas for the multiparous deliveries the rate is around 4%. A suitable statistical power (two-tailed type of null hypothesis with default statistical power goals and type I error level of significance) can be P≥95% α=0.05 achieved if we have at least 102 patients in the case of nulliparous deliveries, and 57 multiparous deliveries, respectively, with occiput anterior positions." This requires some explanation: the authors discussed the power analysis in terms of rates of OP presentations and then discusses numbers of cases of OA presentations required to develop reference standards. It might help to define the study population and limit to either nulliparous or multiparous women, and only include women who enter labor in OA as initially stated. Also confusing, that if the 3 centers have a combined number of deliveries that is close to 4000 per year, why it would not be possible to collect data on 102 nulliparous and 57 multiparous women?
Reply #1. Thank you for your comment. Indeed, in the original manuscript, there is a mistake. We have mended it and change the phrases as such:

In the Statistical methods section / Sample size estimation, we have deleted:

~~"Our statistical goal was that the sample size should be large enough to yield precise estimates predictions of extreme centiles. We estimate the sample size in relation to the precision and accuracy of a single centile and regression based reference limits.[45,46]~~."

~~"Such population groups are not achievable during our present research. However, we hope that the publication of our protocol and the preliminary results with preliminary standard deviation results will trigger and help similar studies and a meta-analysis that will achieve the necessary size for this purpose~~."

And added: “An important challenge of our study is to achieve a sufficient number of OP cases in both nulliparous and multiparous women. According to the Central Limit Theorem and the Large Enough Sample Condition, a sample size of at least 30 items is sufficient for describing a ‘normal’ behaviour of the sample, even if it is not governed by the Gaussian distribution. By looking at the t-table we can see that when using around 30 degrees of freedom, the value of t become approximately equal to the value of the z statistics [Altman, D.G., Practical statistics for medical research, Chapman and Hall, 1991]. Taking into account previously published studies, the overall rate of occiput posterior deliveries in nulliparous is around 7.2%, whereas for the multiparous deliveries is around 4%. Only in 65% of these cases, the outcome is vaginal birth. This implies that the corresponding sample size is 642 primiparous women, and 1154 multiparous women with both OP and AP who give their consent to participate in the study. Using this sample size, we achieve a suitable statistical power two-type of null hypothesis with default statistical power goals $P \geq 95\%$ and type I error $\alpha = 0.05$ level of significance.
In our pilot study, a cervical dilatation of more than 4 cm was noted in 16.34% of the primiparous and 37.5% of the multiparous that were admitted in the hospital with labor criteria. In such cases, data from the beginning of labor will not be available for calculation. In order to achieve the sample mentioned above with patients registered from the beginning of labor, we adjusted the study size to include 767 primiparous women and 1846 multiparous women.”

2. Lines 42-44: Not sure if this data can be presented as mean and SD, rather it should be broken down into mean values at various points in the progression of labor, such as at admission, at the end of 1 stage and in second stage
Reply #2. We apologize for any ambiguities that may have occurred in the text. We intended to refer not to US progression markers, but to continuous variables in general (like maternal age, gestational age, etc). We appreciate the advice and we will likewise present the ultrasound findings in our results.
We modified the sentence “Continuous variables will be presented as the mean and standard deviation (SD) or mean (95% confidence intervals)” and now reads as: “Continuous variables will be presented as the mean and standard deviation (SD) or median, if appropriate”

#3. Line 52: “between US and time to delivery and digital vaginal examination for various clinical situations” Exactly which parameters will be correlated between clinical assessment and ultrasound: station and PD?
Reply #3.
The analysis between ultrasound parameters and digital vaginal examination will aim to investigate the correlations between the ultrasound (PA, PD, HAD and HPD) and clinical parameters (head station) features used to evaluate fetal head progression. As we already mentioned, we will also analyze the agreement between the US and clinical findings regarding fetal head position.
The following changes have been made to the paragraph: “Pearson’s correlation and regressions will be used for the evaluation of correlation between ultrasound parameters (PA, PD, HAD and HPD) and between US and time to delivery and digital vaginal examination (head station) for various clinical situations (nulliparous and multiparous, fetuses with OA and those with persistent OP position)”.

4. Line 52-57: It is not clear what the x-axis variable will be, where it starts and where it ends, as well as time intervals between measurements. Previously authors reported performing ultrasound assessment every hour while in labor and every 15 minutes while in second stage. How will the second stage measurements be reported, will they also be on an hourly schedule for the purpose of creating this graph?
Reply #3 Indeed our measurement will be done hourly in the first stage of labor and every 15 minutes in second stage as we mentioned in our manuscript. In order to emphasize the evolution of each US parameters from the beginning of the first stage of labor until delivery, the X - Axis will be time, having the granularity of the smallest measurement time unit (not minute because otherwise the graphic may be skewed).

Page 8:
#1. Line 3: How are you defining obstructed labor?
Reply #1. Labor is considered obstructed when the presenting part of the fetus cannot progress into the birth canal, despite strong uterine contractions. We agree that the phrasing should be improved, and the paragraph was modified: “In order to identify factors that predict vaginal birth, for each subgroup population (nulliparous and multiparous) […]”.

2. Line 13: “The induction–delivery interval within 24 hours will be evaluated using Kaplan–Meier survival analyses and Cox regression analyses.” What will you be comparing with this analysis?
Reply #2 Data from our pilot study suggested that, especially in primiparas, occiput posterior fetal head position determined by ultrasound could be associated with prolonged first stage of labor or prolonged second stage which will result in delivery by Cesarean section. We intend to evaluate the duration of active phase of labor in women with spontaneous beginning of labor with those with induced labor, both for primiparas and for multiparas.
We thank the reviewer for his remark and we rewrite this part of the *Statistical analysis* section to become clearer.
“The time from the ultrasound examination at the beginning of active phase of labor to vaginal delivery will be evaluated with Kaplan–Meier and Cox regression analysis. Data for women with Cesarean section will be censored. In the Cox regression analyses, fetal head position and fetal head station parameters will be tested as possible predictive factors. In additional analyses, we will adjust for maternal age, BMI, gestational age and parity as possible confounders.”

Page 10
#1. Line 36-37: If this study I funded, please list the sources. If not currently funded, please state that is currently has no outside funding.
Reply #1. The paragraph was changed to provide all proper clarifications in Funding section, page 11: “A funded PhD project provided the resources for a previous pilot study. Currently, the study has no outside funding. The project will take place as part of PhD and postdoctoral studies, and we will use the opportunities to apply for future research funding.”

2. Line 55: “The SonoLabor study recruited patients during January - December 2016 for a pilot study of 168 deliveries.” This data could be us for the power analysis.
Data from the pilot study was used to adjust the study size (Statistic analysis section) and estimate the time period necessary to complete the study (Current study status section).
The acceptability in our group was high - 98%, but was evaluated in one center only.
The following paragraph were added in the manuscript:
Statistical methods / Sample size estimation: “In our pilot study, a cervical dilatation of more than 4 cm was noted in 16.34% of the primiparous and 37.5% of the multiparous that were admitted in the hospital with labor criteria. In such cases, data from the beginning of labor will not be available for calculation. In order to achieve the sample mentioned above with patients registered from the beginning of labor, we adjusted the study size to include 767 primiparous women and 1846 multiparous women.”
Current study status: “Given the birth flow in the centres involved, the sample size required, the acceptability previously recorded and the disponible sonographers for intrapartum US evaluations, we should expect that the study should be completed during a two-years period of time”.

Images:
Recommend using images with ultrasound probe covered with probe cover, and ultra sonographer wearing a glove.
Reply #Images. The figures have been adjusted accordingly and also, for a clearer presentation of the ultrasound procedures.

Reviewer: 2
Dr. Amélie Delabaere, Centre Hospitalier Universitaire de Clermont-Ferrand
Comments to the Author:

#1. The primary objective differ to the primary outcome and concerned only women with occiput anterior position of fetal head, thus doesn't concerned all population included.
Reply #1. The reviewer is correct.
This observation resulted in rewriting Objective and Outcome sections:
-Objective section, first paragraph: “The primary objective of this study is the elaboration of nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous” now reads: “The primary objective of this study is the elaboration of sono-nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous at term with fetal cephalic presentation”.
-Outcome measures section, Primary outcome: “The primary objective of this study is the elaboration of nomograms for the longitudinal US assessment of labor in unselected nulliparous and multiparous with fetal cephalic presentation.”

#*2.* The funding and the duration of the study are not specified.
Reply #2. Funding resources are not available at the moment. We will apply for research project funding and for the moment the project will take place as part of PhD and postdoctoral studies.
The Funding section, page 10, was reconsidered and now reads: “The potential funding sources will play no role in data collection, analysis and interpretation, in the writing of the reports, or the decision to submit the paper for publication. A funded PhD project provided the resources for a previous pilot study. Currently, the study has no outside funding. The project will take place as part of PhD and postdoctoral studies, and we will use the opportunities to apply for future research funding.”
We approximated the duration of the study, based on the birth flow in the centres involved in the study, the sample size that is required and the acceptability previously recorded in our center (reference 43). The prediction was added in Current study status section, final paragraph: “Given the birth flow in the centres involved, the sample size required, the acceptability previously recorded and the disponible sonographers for intrapartum US evaluations, we should expect that the study should be completed during a two-years period of time”.

#3. The ultrasound methods could be more described with more didactic scheme.
Reply #3. We extensively modified the Procedures section - Interventions and Figures presentation, for a more didactic presentation of the ultrasound evaluation. The information remained the same, but is now better structured and understandable for readers. We decided to present the ultrasound procedures using a Table format, where we describe the sonographic measurements, in relation to the acquisition planes and labor mechanism features involved. The modifications are extensive (pages 5, 6), presented in the reply to Reviewer 1, Point “page 4, #4”, and highlighted in the manuscript.

#4. As the author points out, the size of the population studied to create a normogram must be much larger, especially on such a heterogeneous population. This study is conducted in 3 university centers with more than 4000 deliveries per year. It therefore presents opportunities for adequate recruitment to this type of study.
Reply #4. We thank the reviewer for the appreciation.

VERSION 2 – REVIEW

REVIEWER	Contag, Stephen University of Minnesota System, Obstetrics, Gynecology and Women's Health
REVIEW RETURNED	10-May-2021

GENERAL COMMENTS	- The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

VERSION 2 – AUTHOR RESPONSE

Comment SC1, page 2: Define this acronym at first use

The acronym US was defined as ultrasound.

Comment SC2, page 3: Has shown

The mistake pointed out by the reviewer has been corrected.

Comment SC3, page 3: How will ultrasound impact these conditions? May not be situations which will improve with ultrasound evaluation.

We agree with the reviewer. Therefore, we reworded the sentence which now reads: “Intrapartum sonographic evaluation may not provide a solution for all these conditions mentioned above, but previous studies have demonstrated the potential to decrease the rate of late Cesarean extractions in prolonged labor cases, and the various approaches proposed in the literature were considered by our study design”.

Comment SC4, page 3: Some statement regarding how exactly US will be used to improve labour management would be preferable.

The authors agree that a further explanation should be provided. The following phrase was added: “Intrapartum US evaluation is not meant to change the standard principles for labor mechanism evaluation, but to provide accurate evaluation of the main parameters involved: fetal head position and rotation, fetal head progression and engagement.”

Comment SC5, page 3: In general, English usage should be improved.

We reworded the sentence: “There is few information in the literature regarding the ultrasonographic monitoring of the entire active labor”

Comment SC6, page 3: This should not be why we do things in medicine. Motivation should be based on improving maternal care. Recommend removing this statement as this study is not designed to address medico legal liability.

We agree with the reviewer’s opinion and we rephrased the paragraph by removing the statement that addressed medico-legal liability: “Nowadays, the use of ultrasound in labor is generally limited to research settings and a relatively small number of women has been studied. Therefore, efforts should be made to describe the value of an objective partogram in general practice.”

Comment SC7, page 3: This is not a term of common usage. Would recommend using nomograms of ultrasound measured variables or assessment.

We modified the sentence according to the recommendation: “The primary objective of this study is the development of nomograms for ultrasound measured variables during labor in unselected nulliparous and multiparous women at term with fetal cephalic presentation.”

Comment SC8, page 3: Are you addressing the mechanism of delivery or progression of labour?

The authors addressed this point by providing an adequate explanation: “to study the influence of occiput position, body mass index, parturient age on the labor progression evaluated by US.”

Comment SC9, page 3: Please describe better how these two objectives different.

The objectives address different issues: the first one aims at confirming a different labor trend in modern obstetrical settings by means of objective US measurements and the other objective is designed for comparing the findings of sonographic and clinical evaluations. We reworded the content, for a better understanding:

"- to compare the labor trend from our study with the Friedman studies[37,38] and other recent research on the partogram[39] regarding the progression of labor by means of objective US evaluation.

- to correlate the US and standard clinical findings regarding the mechanism of labor, e.g. fetal occiput position and head descent during active labor."

Comment SC10, page 4: These appear to be two different study objectives.

Indeed, the phrase contains two objectives that we put together because they are similar, but they refer to different populations. We separated the objectives in the new version of the manuscript:

- "to analyse the temporal variation of the sonographic measurements in spontaneous vaginal delivery versus obstructed labor in nulliparae versus multiparae;
- to analyse the evolution of the sonographic measurements in spontaneous vaginal delivery versus obstructed labor in fetuses with occiput anterior versus those with persistent occiput posterior."

Comment SC11, page 4: Wording should be improved. What is being used is a test to evaluate a specific outcome. The test is based on ultrasound measurements. The test characteristics that will be evaluated need to be better defined. The guidelines for reporting this information are in STARD or TRIPOD: https://www.equatornetwork.org/?post_type=eq_guidelines&eq_guidelines_study_design=diagnostic-prognosticstudies&eq_guidelines_clinical_specialty=0&eq_guidelines_report_section=0&s=

The authors agree that the objective should be better presented. We modified the phrase and it now reads: "to investigate the value of combined US measurements to predict the outcome of vaginal delivery."

Comment SC12, page 4: Please define low risk

We agree that low-risk pregnancy represents a general concept with different definitions. Still, the inclusion / exclusion criteria are presented in the Participants section, several paragraphs below.

We modified the sentence that now reads: "The study aims to record simultaneously the labor progress by clinical and US evaluations in women in labor at term, with singleton cephalic presentation. We will include low-risk pregnancies, according the criteria defined in the Participants section."

Comment SC13, page 4: Need to define who these are

The observation of the reviewer is correct. We modified the paragraph accordingly. The requirements for the sonographers experience and quality control evaluations are described in Procedures / Interventions section, "ultrasound evaluations" and "protocol fidelity" paragraphs. The paragraph now reads:

“They will be consecutively included in the study, depending on the availability of the US operators involved in the study. We will try to attract a large team of collaborators, in order to investigate as many eligible cases as possible.”

Comment SC14, page 4: Is this based on clinical assessment?

Yes, the diagnosis of the first and second stage of labor will be established exclusively by clinical evaluation. We clarified this aspect in the present version of the manuscript.

“Following the clinical evaluation, women will be admitted in the first stage of labor when there are regular painful contractions and there is a progressive cervical dilatation from 4 cm, and the second stage will be established based on the finding of full dilatation of the cervix[41] regardless of whether the parturients underwent artificial rupture of the membranes, Oxytocin augmentation or epidural anaesthesia.”

Comment SC15, page 4: Performed at what gestational age?

We clarified this aspect in the respective paragraph: “Gestational age will be determined by the last menstrual period in women with regular menses, confirmed with US dating, preferably during the first trimester. If the first trimester biometry is not consistent with the menstrual dating by more than one week, gestational age will be established based only on the sonographic evaluation. In women with irregular menses, the gestational age will be determined solely based on the first fetal biometry evaluation in the first half of pregnancy.”

Comment SC16, page 5: There only appears to be 1 direct potential benefit

By the “potential benefits that may result following the completion of the objectives” we meant the favorable implications of developing sonopartograms. The next sentence clearly states that “The only direct benefit of the laboring women that participate in the study would be the communication between the obstetrician and sonographer regarding fetal head position when instrumental delivery is attempted”

We clarified this aspect in the paragraph: “The details of the study and the potential benefits of the research will be thoroughly explained to the patient.”

Comment SC17, page 5: English

The reviewer’s observation is correct. We reworded the sentence: “The following labor parameters must be noted before US assessment:”

Comment SC18, page 5: Consider using the term station or at least stating its equivalence to station. Please limit to one term, either descent or progression.

The authors modified the manuscript accordingly: “ ”

Comment SC19, page 5: How are you documenting rotation? It appears that what you are consistently documenting is position.

This is true, as fetal head rotation refers to the evolution of the occiput position during the second stage of labor. The term rotation was removed.

Comment SC20, page 5: Need to define how what you mean by each and how you will document each.

The reviewer's opinion regarding the missing information is correct.

Caput succedaneum is noted, if present, along with its diameter.

Regarding molding, we are currently using the clinical definition in relation to bone overlap: grade 1 is closure of sutures with no overlap; grade 2 is reducible overlap and grade 3 irreducible overlap. We document molding grades, because grades 2 and 3 are associated with risk of cephalopelvic disproportion and increased risk in operative vaginal deliveries, and fetal complications including cerebral palsy, intracranial hemorrhage and fetal death.

The following changes have been made to the manuscript: caput and molding clinical evaluations were described separately in the text:

"- Presence of caput, with the approximate diameter,

-Presence of molding and grading: closure of sutures with no overlap (grade 1), reducible bones overlap (grade 2) and irreducible overlap (grade 3)."

Comment SC21, page 5: Are you documenting the mechanism or the progression of labour?

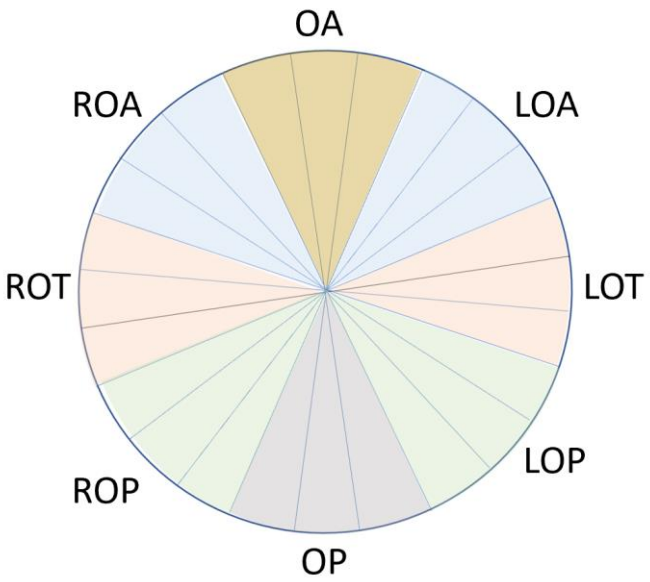
We apologize for the unfortunate wording of the sentence. The purpose of US evaluations is to document the progression of labor using objective measurements for the main parameters involved by the mechanism of labor. We modified the phrase accordingly: "The objectives of US evaluations are similar to those of standard clinical assessment. The purpose of US evaluations is to document the progression of labor using objective measurements for the main parameters involved in the mechanism of labor."

Comment SC22, page 5: References need for this statement.

The references are provided in Table 1. We adjusted the paragraph, that now reads: "The images will be stored on the hard disk drive of the system for off-line analysis and the measurements will be performed by the sonographer who evaluated the case, according to the techniques described in the literature[5,22-27,42,43] (Table 1)"

Comment SC23, page 6: You have described eight 30 degree sections

The reviewer observation is correct, we describe eight occiput positions: OA, OP, ORT, OLT, LOA, LOP, ROA, ROP. Each position consists of 45-degree (8 x 45 = 360). Our protocol with 24 divisions is not singular, and many other studies and textbooks proposed a similar approach to define occiput position, as 15-degree sections of the circle can be used to define 45-degree or different definitions for occiput positions.



Some examples:

- S Akmal, E Tsoi, N Kametas, R Howard, K H Nicolaides. Intrapartum sonography to determine fetal head position. J Matern Fetal Neonatal Med. 2002 Sep;12(3):172-7.
- Akmal S, Tsoi E, Nicolaides KH. Intrapartum sonography to determine fetal occipital position: interobserver agreement. Ultrasound Obstet Gynecol 2004; 24: 421–424
- Cunningham FG, MacDonald PC, Gant NF, Leveno KJ, Gilstrap LC, Hankins GDV, Clark SL. Mechanisms of normal labor in occiput presentation. In Cunningham FG, MacDonald PC, Gant NF, Leveno KJ, Gilstrap LC, Hankins GDV, Clark SL, eds. Williams Obstetrics, 20th edn. Stamford: Appleton & Lange, 1997: 319–25.
- Rane SM, Guirgis RR, Higgins B, Nicolaides KH. The value of ultrasound in the prediction of successful induction of labor. Ultrasound Obstet Gynecol. 2004 Oct;24(5):538-49.

No changes have been made in the manuscript.

Comment SC24, page 6: See comments regarding rotation above.

We opted to evaluate and separately present the fetal head rotation during the second stage US evaluation because of the following reasons:

-the evaluation of this feature in combination with other US parameters proved to be useful in previous studies (reference 25);

-the assessment plane is different – subpubic, and not suprapubic, as is for the head position determination during the first stage of labor.

We will document the head rotation by measuring the rotation angle, or midline angle (MLA), presented in Table 1, as in the study of Ghi et al. Ultrasound Obstet Gynecol. 2009;33(3):331-6, (reference 25).

No changes have been made to the manuscript.

Comment SC25: These sections need to be defined clearly in the text and not only referenced.

We agree with the reviewer's observation and we modified accordingly the manuscript:

"-Progression angle (PA)[26,27] (Figure 4),

as the angle between the longitudinal axis of the pubic symphysis and the line running from the anterior edge of the pubic symphysis tangentially to the leading edge of the fetal skull.

-Progression distance (PD)[22] (Figure 4),

as the minimal distance between a vertical line from inferior apex of the symphysis (infrapubic line) and the leading edge of the fetal skull.

-Head direction angle (HDA)[23,24] (Figure 4),

as the direction of the line perpendicular to the widest diameter of the fetal head, with respect to the infrapubic line."

Comment SC26: These sections need to be defined clearly in the text and not only referenced.

We agree with the reviewer's observation and we modified accordingly the manuscript:

"-Head to perineum distance (HPD)[43]

as the shortest distance from the outer bony limit of the fetal skull to the skin surface of the perineum (Figure 4)."

Comment SC27: These have been defined in the table but not in the text.

The reviewer is correct. We added the following paragraph in the Procedures section, ultrasound evaluation:

"-fetal head position (FHPo), by determining occiput position,

-fetal head rotation in the second stage of labor, by measuring the midline angle (MLA),

-fetal head descent or progression (*FHPr*), by evaluating the relation between the fetal head and maternal landmarks, using specific measurements: progression angle (PA), progression distance (PD), head direction angle (HDA), head to perineum distance (HPD),

-caput measurement, if present,

-molding notation, if present."

Comment SC28: Technically, these are not clinical partogram parameters but pelvic examination parameters. Partograms assess dilation and descent (station) of the presenting part.

We agree with the reviewers' opinion. The respective paragraph was modified according to the response to Comment 9 (Objectives section) and it now reads:

"to correlate the US and standard clinical findings regarding the mechanism of labor, e.g. fetal occiput position and head descent during active labor:"

Comment SC29: See comments above under objectives. Here it would b helpful to define how these secondary outcomes will be analysed i.e. statistical analysis.

We appreciate the reviewer for pointing this out. We addressed the statistical analysis for each of the secondary outcomes in the Statistical analysis section.

Comment SC30: Define frequency

The meetings will be held monthly and supplementary meetings will be announced if necessary. These clarifications were added to the manuscript:

“Monthly meetings will take place between study site personnel to discuss issues related to the conduct of the study and supplementary convocations will be announced whenever necessary”

Comment SC31: This was a function of population characteristics as much as it was of numbers of cases. Friedman did not perform a power analysis. The study published by Zhang et al did provide a power analysis for clinical assessment which is the only reference to use for calculating number of assessments that will be required. There are references that can be used to estimate number of women required to created reliable nomograms for progression of labour.

We did not use Friedman's study for the computation of the power analysis. We have mentioned it in the text just as a reference for how the procedure went 50 years ago.

Comment SC32: I’m not sure I understand this, but I think the authors are stating that they would require 642 nulliparous women to identify around 30-40 women in OP for study inclusion. This is true, but does not specify how many would be required to power the differences expected from hour to hour for each variable that will be evaluated clinically and ultrasound. Please use either nulliparous as primiparous are women with one prior delivery.

The term primiparous was replaced with nulliparous throughout the manuscript.

The same size was computed taking into account only the women who had hourly differences, hence giving birth vaginally. The women who needed caesarean were not taken into account. We have already stated this is the manuscript.

In the respective paragraph we deleted “with both OP and OA”. This explanation may be confusing, our intention was to state that the pregnant women will be included indifferently the fetal occiput position.

Comment SC33: Not statistically appropriate, Kappa is used to assess agreement between two operators for similar assessment. Here you are comparing two different methodologies for same outcome. Correlation coefficients should be strong since you are comparing the same outcomes using two different methodologies. Seems that it would be more appropriate to use a method that would compare the differences between the assessments for each assessment performed to determine the variability around the assessments

We thank the reviewer for his suggestion. While we appreciate the reviewer’s feedback, we think that kappa statistics will work out here if treating fetal head position as nominal categorical data as described above (OA, OP, LOT, ROT, LOA, ROA, LOP, ROP).

Other researchers had the same approach for emphasize the between-methods agreement (ultrasound and clinical vaginal examination) for fetal head position:

Wiafe YA, Whitehead B, Venables H, Nakua EK. The effectiveness of intrapartum ultrasonography in assessing cervical dilatation, head station and position: A systematic review and meta-analysis. Ultrasound. 2016; 24(4):222-232.

Shetty J, Aahir V, Pandey D, et al. Fetal head position during the first stage of labor: comparison between vaginal examination and transabdominal ultrasound. ISRN Obstet Gynecol 2014; 2014: 314617–314617.

Eggebo TM, Hassan WA, Salvesen KA, et al. Prediction of delivery mode with ultrasound assessed fetal position in nulliparous women with prolonged first stage of labor. Ultrasound Obstet Gynecol 2015; 46: 606–610.

Wiafe YA, Whitehead B, Venables H, Dassah T: Comparing intrapartum ultrasound and clinical examination in the assessment of fetal head position in African women. J Ultrason 2019; 19: 249–254. doi: 10.15557/JoU.2019.0037

No changes have been made in the manuscript.

Comment SC34: Since this is a study protocol. It seems that this should go under the introductory section

The observation is correct. We distributed the content of the Discussions section between the Introduction and Strengths and Limitations sections and highlighted the new content. The last paragraph of the Discussions was removed, along with the citations 47 and 48.