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FEMALE GENITOURINARY ONCOLOGY SPECIAL FEATURE: REVIEW ARTICLE

Implications of the new FIGO staging and the role of imaging in cervical cancer

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ABSTRACT

International Federation of Gynecology and Obstetrics (FIGO) staging, which is the fundamentally important cancer staging system for cervical cancer, has changed in 2018. New FIGO staging includes considerable progress in the incorporation of imaging findings for tumour size measurement and evaluating lymph node (LN) metastasis in addition to tumour extent evaluation. MRI with high spatial resolution is expected for tumour size measurements and the high accuracy of positron emission tomography/CT for LN evaluation. The purpose of this review is firstly review the diagnostic ability of each imaging modality with the clinical background of those two factors newly added and the current state for LN evaluation. Secondly, we overview the fundamental imaging findings with characteristics of modalities and sequences in MRI for accurate diagnosis depending on the focus to be evaluated and for early detection of recurrent tumour. In addition, the role of images in treatment response and prognosis prediction is given with the development of recent technique of image analysis including radiomics and deep learning.

BACKGROUND

Cervical cancer is the fourth most common cancer in females, following breast cancer, colorectal cancer, and lung cancer.¹ However, its incidence is the most frequent in underdeveloped regions.² This fact might explain that the International Federation of Gynecology and Obstetrics (FIGO) staging of cervical cancer is made according to results of clinical examination, without reliance on surgical pathological findings. Moreover, it explains why CT and MRI were not included as staging tools: they have high costs and low availability, especially in those countries.³ It had been recognised that the preceding FIGO system included several shortcomings, rendering them as unsuitable to actual clinical results. Clinical FIGO staging differs from final surgical staging in up to 32% of patients with Stage IB disease and in up to 65% of patients with Stage III disease.^{4,5} In FIGO 2018, as described by Bhatla et al,⁶ “Recent developments in imaging and increased use of minimally invasive surgery have changed the paradigm for management”. Accordingly, incorporation of imaging findings such as those from ultrasound, CT, MRI, and PET examinations for the assessment of tumour staging has been approved for all stages in addition to clinical examination where available. Therefore, the role of images in staging before treatment has increased, and more accurate imaging

diagnosis has been required. It is important to know what modality and which sequence in MRI should be used for accurate diagnosis depending on the focus to be evaluated and for early detection of the tumour. In addition, the role of images in treatment response and prognosis prediction is also expected with the development of recent technique like deep learning. This article aimed to review key imaging findings with diagnostic ability of each imaging modality emphasis on implications of the new FIGO staging and the role of images before and after treatment.

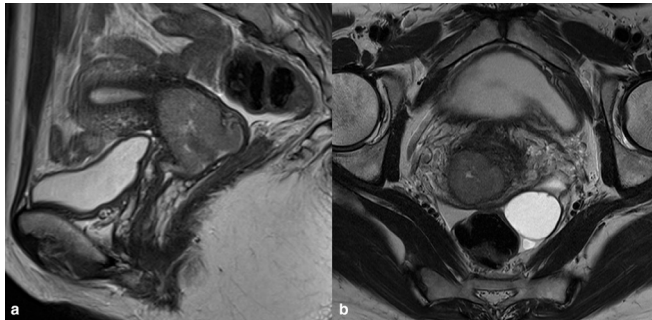
What’s new in 2018 FIGO?

From a radiological perspective, two main points of emphasis can be made of the revised FIGO stage: tumour size measurement and the assessment of lymph node (LN) metastasis.

Tumour size measurements

Regarding tumour diameter criteria in IB1 tumour, the new cut-off value of 2 cm has been added to 4 cm for stage Ib tumours, which is invasive carcinoma limited to the cervix. Therefore, IB tumours are now divided into three substages: Stage IB1 includes tumours smaller than 2 cm; IB2 includes those equal to or larger than 2 cm, but smaller

Figure 1. 45 y.o. female, Cervical cancer Stage Ib3. (a) A quite large tumour larger than 4cm involving the whole cervical stroma and extending beyond the internal os. The tumour also extends exophytically by expanding the vaginal fornix. (b) Oblique axial image shows the tumour is located within the vagina. Then the stage was inferred as Stage IB3 on MRI. Left ovarian cyst is observed.

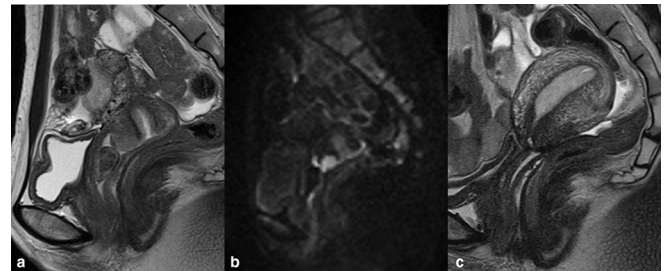


than 4 cm; and IB3 includes tumours equal to or larger than 4 cm (Figure 1).

Two major reasons exist for the addition of the new cut-off value, one of which is the relation between the diameter of the main tumour and the prognosis. A recent large multicenter study demonstrated that tumour size of greater than 2 cm is associated with increased frequency of parametrial involvement, LN metastases, and the depth of stromal invasion.⁷ Horn et al⁸ also reported lower frequency of pelvic LN involvement (13.3%) with tumours smaller than 2 cm than with those having largest diameter of 2–4 cm (23.4%) and over 4 cm (43.5%). In addition, both recurrence-free survival and overall survival are longer in cases of tumours of less than 2 cm diameter than in those with diameter greater than 2 cm.⁷ Another reason for the 2 cm cut-off is related with the increase of minimally invasive surgery, *i.e.* fertility-sparing surgery. Trachelectomy is representative of minimally invasive surgery. It includes removal of the uterine cervix and vaginal cuff, and parametrial resection, followed by the creation of an isthmic vaginal anastomosis.⁹ The current National Comprehensive Cancer Network (NCCN) recommendation for fertility-sparing trachelectomy is Stage IB1 tumour.¹⁰ Tumour size of less than 2 cm is also included as eligibility criteria for fertility-sparing management of cervical cancer, along with histology (squamous cell carcinoma (SCC), adenocarcinoma and adenosquamous carcinoma), tumour-to-internal os distance of more than 1 cm, cervical stromal invasion less than 50%, lack of parametrial invasion, and lack of LN metastasis (Figure 2).¹¹

Therefore, the accuracy of tumour size assessment using images is important to patients' care before the primary treatment. As the American College of Radiology Imaging Network (ACRIN) study indicated, MR showed the greatest agreement with pathological measurements, followed by CT and clinical assessment by a gynaecologist.¹² In addition, measurements by diffusion-weighted images (DWI) was almost equal with that by T_2 weighted images (WI).¹³ A recent report described close agreement between pathologic and MR imaging (T_2 WI) tumour sizes in ICC of 0.84–0.86, with good inter-reader agreement of two

Figure 2. Cervical cancer stage Ib1. (a) Cervical tumour observed at the surface of anterior to posterior lip of the cervix as slightly increased signal intensity on T_2 WI. (b) DWI clearly shows the tumour margin of less than 2 cm maximum diameter. The distance between the tumour to internal os was greater 1 cm. Trachelectomy was considered. (c) Patient received laparoscopic radical trachelectomy. Patients had two deliveries and have been disease-free more than ten years since surgery. DWI, diffusion-weighted imaging.



readers (ICC = 0.87).¹⁴ In other report, MR measurements has reported 3 mm smaller than macroscopic measurements by the pathologist.¹⁵ Note that in the study comparing MR measurement and histopathology of hysterectomy uterus, 10 mm margin was recommended to sufficiently cover invisible microscopic extension of the tumour delineated on MRI.¹⁵

Lymphnode metastasis

LN metastasis has been incorporated as a new FIGO stage. In Stages I through Stage III, allowing assessment of retroperitoneal LNs by imaging and/or pathological findings. If metastasis is suspected, the case is regarded as Stage IIIC (with notation of method used for stage allocation).¹⁶ Pelvic LN involvement is allocated to Stage IIIC1 and para-aortic LN to IIIC2.¹⁶

As a background, a certain percentage of LN metastases are present even in early stages of tumours, such as 12–38% in Stage I, 10–45% in Stage IIA, and 26–62% in Stage IIB of the previous FIGO.^{17–20} Additionally, the prognosis of cervical carcinoma has been recognised as linked strongly to LN involvement.²¹ The 5-year survival for LN-positive patients is 39–54%, compared with 67–92% in patients without nodal involvement.^{22,23} Accordingly, LN assessment using imaging was to be incorporated into staging.¹⁶

Among several imaging modalities, the role of PET-CT to detect lymph nodal metastasis has been emphasised in the FIGO committee report.¹⁶ As for transvaginal ultrasound, it will not give additional information on lymph node status due to operator dependent and the narrow field of view. In recent meta-analysis comparing CT, MRI and PET/CT sensitivity, specificity positive likelihood ratio (LR) and negative LR were 0.57, 0.91, 6.4 and 0.47 in CT, 0.54, 0.93, 8.2 and 0.50 in MRI and 0.66, 0.97, 19.3 and 0.35 in PET or PET/CT.²⁴ In several other meta-analyses have also indicated that PET shows better diagnostic ability, sensitivity of 78–91%, and specificity of 94–100%, which are higher than those for MRI and CT.^{25–28} Gouy et al suggested that high specificity and positive LR suggests that surgical staging is unnecessary when uptake is noted in the para-aortic area.²⁹

Nonetheless, there are non-detectable node mainly due to the small size of less than 5 mm.²⁹

Size criteria of the short axis of 10 mm for LN metastasis are well known to have limitations. These criteria lead to high specificity, but low sensitivity.³⁰ More than 80% of metastatic LNs were smaller than 10 mm; more than 50% were smaller than 5 mm.³¹ As Yamanoi et al showed, when the 5 mm cut-off was used, the sensitivity and negative predictive value (NPV) were both high: 70 and 96%, respectively.³² However, the detection of small size LN might produce many false positive cases and result in low specificity of 79%. Then, ¹⁸F-fludeoxyglucose (FDG) uptake in addition to LNs larger than 5 mm along the short-axis lead to high diagnostic values of 100% sensitivity, 99.6% specificity, 81% PPV, 100% NPV, and 99.6% accuracy.³³ Addition of ADC values to the size criteria might also be useful to detecting the LN metastasis as similar AUC with PET/CT of over 90%.²⁴

The most frequent site of metastasis is the obturator LNs, as suggested as sentinel LNs of cervical carcinoma.³⁴ Lymphatic spread from cervical carcinoma occurs initially to the parametrial nodes followed by the pelvic nodes, and then para-aortic nodes.³⁵ Therefore, as Kidd et al showed, all patients with para-aortic nodal involvement had pelvic LN disease, and all patients with supraclavicular metastasis had para-aortic and pelvic disease.¹⁷ Risk factors for pelvic LN metastases are deep cervical stromal invasion and lymph vascular space invasion (LVSI) of the primary tumour.³⁴

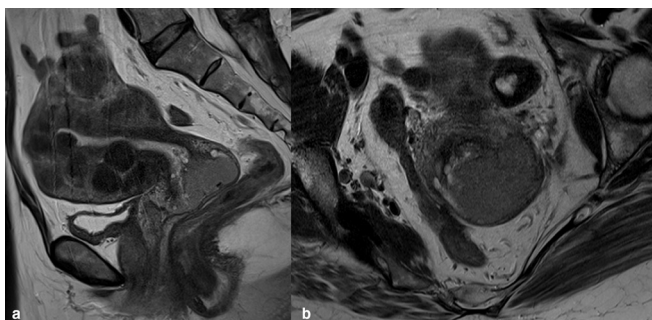
Key point for pre-treatment imaging diagnosis

The following six points are key evaluation items in pre-operative cervical cancer staging. Fundamental imaging findings along with diagnostic ability and pearls and pitfalls are reviewed.

1. Stromal invasion

Stromal invasion is an evaluation point in IB1, and is also important from the perspective of determining the indication for fertility-sparing surgery. The patients with stromal invasion deeper than 1 cm or two-thirds of the cervical stroma are relative contraindication to fertility sparing surgery depending on

Figure 3. Cervical cancer Stage IB2. (a) The tumour grows exophytically to vaginal cavity. Vaginal fornix was expanded by the tumour, but the tumour is confined within the cervix as observed by oblique axial image perpendicular to cervical long axis (b). The maximum tumour size was 33 mm. The tumour stage was inferred as IB2 under the new FIGO staging.



the institution.³⁶ On MR images, it is suspected by disruption of the low-signal-intensity “stromal ring” on T_2 WI (Figure 3).³⁷ Oblique axial T_2 WI perpendicular to the cervical axis is necessary to visualise the whole lesion of the “stromal ring” and for proper assessment of stromal invasion.³⁸ Diagnostic performance for stromal invasion on MR is quite high, *i.e.* pooled sensitivity of 87% and pooled specificity of 91%.³⁶ When deep stromal invasion is defined as tumour invasion to outer third of the cervical stroma in considering fertility sparing surgery, sensitivity decreased to 50–75%, but specificity was 90–94%.¹⁴ Lakhman et al¹⁴ reported the difficulty of detecting deep cervical stromal invasion by post-procedural inflammation and recommended performance of MR before conisation.

2. Vaginal invasion

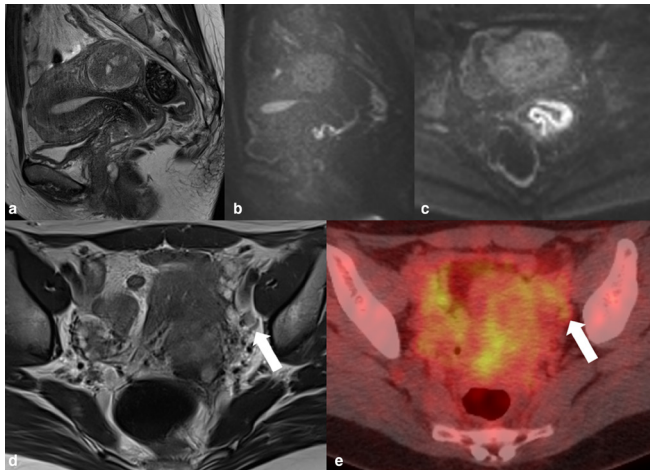
Vaginal involvement is related both Stage IIA and IIIA. Stage IIA indicate when the tumor is limited to the upper two-thirds of the vagina without parametrial involvement. In Stage IIIA, the main tumour involves the lower third of the vagina with no extension to the pelvic wall.¹⁶

Involvement of the vagina is suggested by disruption of the normal low-signal-intensity wall on T_2 WI (Figure 4).³⁹ Overall accuracy for vaginal invasion is 86–93%.^{37,40} The tumour on anterior fornix is tend to be over diagnosed.³⁷ In cases of bulky tumour expanding vaginal fornix, it might be difficult to identify vaginal wall invasion because it was stretched by the tumour.^{41,42} Therefore, we should note that it might be intact even if the normal vaginal wall cannot be recognised in case of that position.

3. Parametrial invasion

Parametrial invasion is the key factor for Stage IIB and might indicate the treatment strategy as concurrent chemoradiotherapy (CCRT) in the presence of parametrial invasion.¹⁰ On ultrasound, tumour is recognised as hypoechoic tumour with irregular margin extending into adjacent paracervical regions.⁴³ In ultrasound, it shows high diagnostic value, sensitivity of 77% and specificity of 98%.⁴⁴ On MR imaging, recent meta-analysis including 14 papers showed the pooled sensitivity as 0.76 (95% CI 0.67–0.84) and specificity as 0.94 (95% CI 0.91–0.95).⁴⁵ T_2 WI is the fundamental sequence to diagnosis and the addition of CE- T_1 WI images with or without fat suppression did not improve the accuracy obtained using T_2 WI alone, though tumour in CE- T_1 WI is better visualisation of tumour margins than T_2 WI.^{46,47} On T_2 WI, parametrial invasion is visualised as full-thickness cervical stromal involvement and one of the following additional findings: spiculated or nodular tumour-to-parametrial interface and/or parametrial vessels encased by the tumour.^{48,49} For evaluating these finding, oblique axial T_2 WI perpendicular to cervical axis, possibly with a smaller field of view (FOV) is important for the recognition of exact anatomical position (Figure 5).^{38,50} DWI may give additional value for the diagnosis, especially in combination with T_2 WI.^{45,51} Park et al showed that a fused image of high b-value diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) on T_2 WI improved the diagnostic capability of parametrial invasion from sensitivity of 75.7–78.4, specificity of 85.7–88.7 by T_2 WI alone to sensitivity of 67.6–70.3, specificity of

Figure 4. 43 y.o. female. The tumour crawls on the surface of the anterior lip of the cervix to anterior fornix of vagina. (b) Sagittal and (c) axial DWI clearly show tumour extension to the anterior vaginal fornix. Vaginal wall invasion was suspected at anterior fornix by irregularity. This case was diagnosed as Stage IIA in 2017 under the previous FIGO stage system. (d) Round lymph node about 8 mm diameter was observed at the left obturator node (arrow). (e) FDG-PET/CT showed mild uptake, with suspected lymph node metastasis. At operation, lymph node metastasis was confirmed. Therefore, this case is Stage IIIC1 at the present FIGO stage. DWI, diffusion-weighted imaging; PET, positron emission tomography.



95.7–97.4.⁵² The strong point of DWI is differentiation of tumour from peritumoral oedema or inflammation that can be a cause of false-positive findings on T_2 WI especially in cases of full thickness of cervical stromal invasion.⁵² DWI can be a new standard sequence for evaluating parametrial invasion on MRI.

4. Pelvic wall invasion

The presence of pelvic wall invasion become Stage IIIB.¹⁶ Pelvic wall involvement can be correctly diagnosed by T_2 WI on MRI and is diagnosed when a tumour located at less than 3 mm from the pelvic wall, those are the internal obturator, levator ani, or pyri-formis muscles.⁵³ Furthermore, iliac vessel encasement, ureteral

Figure 5. 53 y.o. female with abnormal genital bleeding. (a) Sagittal T_2 WI shows diffuse infiltration of the tumour from the uterine cervix to the uterine body. (b) On axial T_2 WI, parametrial invasion is observed in all directions and diagnosed as Stage IIB. Low signal tumour extension along the uterosacral ligament in both directions (arrows).

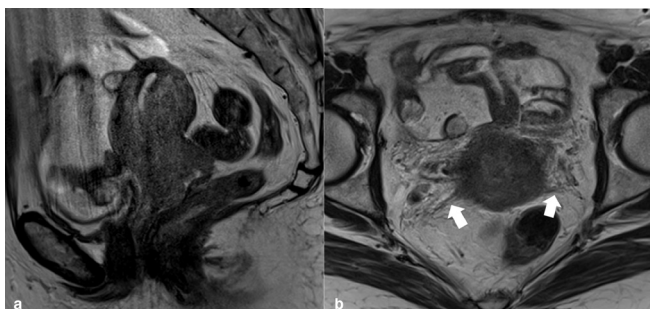
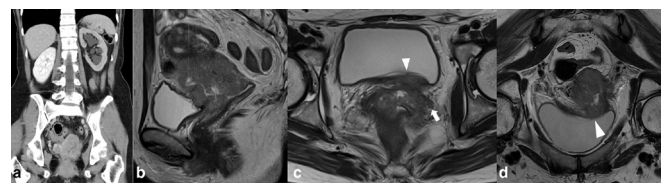


Figure 6. 47 y.o. female with abnormal genital bleeding and lower abdominal pain. (a) On CT, left hydronephrosis is observed. (b) Sagittal T_2 WI showed a large irregular shaped tumour involve cervix and extend along the vaginal wall and uterine body. The tumour also extends anteriorly to the bladder. No intact fat tissue was observed between the tumour and bladder wall. (c) Axial T_2 WI showed parametrial invasion to anterior and left side-of the cervix. The tumour involved the left ureter (arrow). Disruption of the low-signal intensity bladder wall (arrowhead) by the tumour was suspected. Mucosal oedema is also observed. (d) Oblique axial T_2 WI showed no disruption of the bladder wall (arrowhead), but only oedema. Cystoscopy revealed mucosal oedema as prominent, and the left ureteral orifice was not observed. Tumour invasion to the mucosa of bladder wall was not recognised. The case was designated as Stage IIIB.



infiltration with upstream hydronephrosis, and infiltration of muscles with increased signal intensity of adjacent muscles on T_2 WI are positive MR findings for pelvic wall involvement.^{54–56}

5. Bladder/rectal invasion

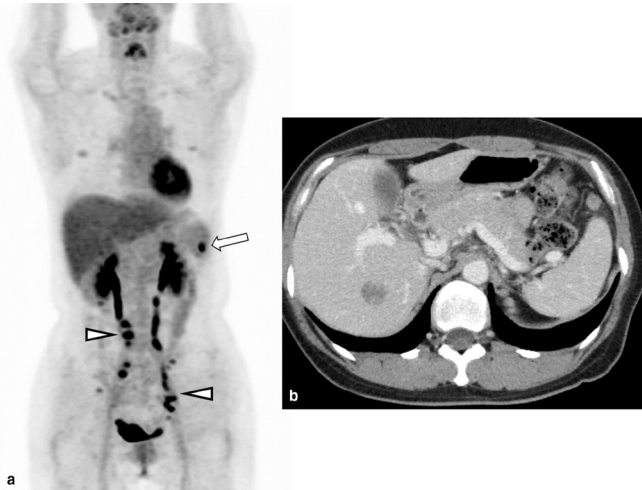
Bladder and rectal invasion are regarded as Stage IV. Regarding the imaging diagnostic value of bladder or rectal invasion, absence of bladder or rectal invasion can be diagnosed with sufficient confidence using an MRI. An early MRI study found the accuracy of bladder or rectal invasion to have an NPV of 100%.³⁷ The following reports present similar results, *i.e.* high specificity of 86–88% and high NPV of 96–100% as evaluated by MRI.^{57,58} These results lead to elimination of invasive cystoscopic or endoscopic staging for tumour staging.⁵⁸

Bladder/Rectal invasion is suspected when the disruption of the low-signal intensity wall on T_2 WI, with invasion of the mucosal layer by tumour.⁴⁸ Mucosal oedema alone in association with bladder muscle wall invasion was insufficient for Stage IV tumour diagnosis (Figure 6).¹⁶ Bladder muscle and/or serosal invasion is suspected when MRI findings of wall irregularity with heterogeneous signal and nodularity or loss of a fat plane are observed.⁵⁹ Tumour involvement of bladder mucosa is significantly associated with poor disease specific survival and disease-free survival ($p < 0.05$), but bladder muscle involvement alone is not associated with poor survival.⁵⁹ Additionally, the prognosis for patients with evidence of muscle and/or serosal invasion of the bladder on MRI might not differ from that for patients without abnormality on MRI.⁶⁰ Therefore, the differentiation of bladder mucosal invasion from muscle/serosal invasion is important both for tumour staging and prognosis.

6. Distant metastasis

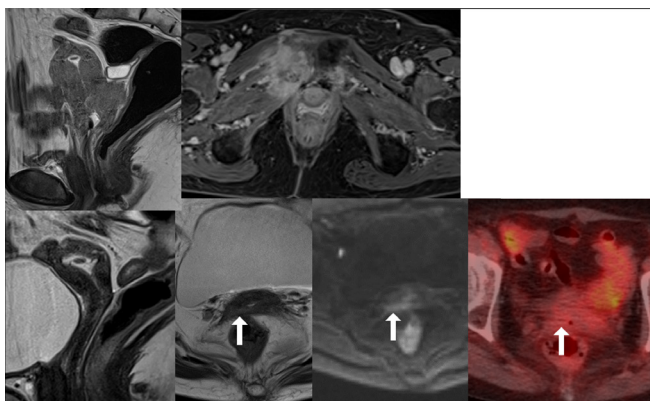
A multicentre study for detecting the distant metastasis of advanced cervical cancer (IB2 (FIGO2009) <) revealed that

Figure 7. The same patients as those for Figure 4 after 6 months of total hysterectomy, salpingo-ophorectomy and pelvic lymph node resection. (a) PET/CT clarified the dissemination at upper left abdomen (arrow) and multiple lymph node metastases (arrowheads) at paraaortic and pelvic region. (b) Dissemination was located anterior of the spleen. Liver metastasis was also found on CT, but not on PET. PET, positron emission tomography.



13.7% (21/153) of patients showed distant metastasis; the most frequent sites were lung (5.2%) followed by peritoneum (4.6%) and supraclavicular LN (3.3%).⁶¹ To find metastatic disease involving distant organs, whole body PET/CT is recommended for evaluation of metastatic disease by the NCCN guideline (Figure 7).⁶² Tumour detection by PET/CT demonstrated high

Figure 8. 68 y.o. female with abnormal genital bleeding. (a) A large tumour involving the entire cervix and extend along vaginal wall. The tumour margin was irregular at the posterior vaginal wall, with suspected parametrial invasion. (b) Axial contrast-enhanced T_1 WI shows irregularly enhanced lesion at the right pubic bone, diagnosed as bone metastasis and Stage IVB. (c) After the patient received chemotherapy, the tumour decreased dramatically (d) Slightly high signal intensity was found at right posterior lip both on axial T_2 WI (d) and DWI (e). FDG-PET/CT showed no uptake at local lesion. It was diagnosed as no residual tumour. High signal intensity area on MRI was oedema after chemotherapy.



specificity (97.7%) and PPV (79.3%), but limited sensitivity of 54.8%.⁶¹ The most recent report suggested quite high diagnostic value of PET/MRI in all 100% of sensitivity, specificity and accuracy.⁶³ PET / MRI is not yet widespread, but the combination of functional information of PET and anatomical images may be effective in diagnosing distant metastases.

Tumour recurrence after complete response/ following surgery

Recurrence rate have been reported to occur in 15–40% in females with FIGO stage IB2 to IIB LACC.⁶⁴ Approximately, two-thirds of cases show recurrence within the first 2 years following initial treatment; 90% of cases show recurrence by 5 years.^{65–68} Recurrent cervical cancer is defined as local tumour regrowth or the development of distant metastases at least 6 months after the lesion has regressed.⁶⁹ The most commonly involved lesion of recurrence is local recurrence of cervix, followed by that of the pelvic wall, which is central or non-central.^{67,70} Central diseases include tumours limited to the vagina, bladder, rectum, and/or parametrium, whereas non-central disease involves the pelvic wall, muscles, and/or vasculature of the lateral pelvic wall.⁷¹ Survival rates after tumour recurrence are reported as 6–77%, but patients with central recurrence have better prognoses than those with pelvic wall recurrence.⁷² Because larger tumours are known to have poorer prognosis, early detection of recurrence might increase the long-term survival probability.^{66,72}

For the surveillance of recurrent disease, the NCCN guideline offers imaging surveillance including PET/CT, and/or MRI depending on the initial tumour stage and symptoms or examination findings by gynaecologists.⁶² CT is useful for the rapid detection of lymphadenopathy from the neck to pelvic cavity, but has limited applicability for differentiating recurrent tumour at the vaginal stump from post-radiation fibrosis.^{73,74} MRI can contribute to evaluate local tumour extension with its excellent soft tissue contrast. PET/CT can provide high detectability for local recurrence in sensitivity of 93%, specificity of 93% and accuracy of 93% and for distant metastasis in sensitivity of 96%, specificity of 95% and accuracy of 95%.⁷⁵ In recent examination using whole body PET/MRI, all the recurrent pelvic tumours from gynaecological cancers were correctly identified, compared with 84% of patients by MRI alone.⁷⁶

On MRI, tumour recurrence appears as a region of intermediate to high signal intensity on T_2 WI compared with low signal intensity of the radiation fibrosis tissues and adjacent pelvic sidewall muscle.⁷⁷ Nonetheless, it can be indeterminate, particularly within the first 6 months following treatment.⁷⁸ Because of increased T2 signal caused by oedema, inflammation, necrosis etc., T_2 WI has low specificity (22%–38%) to detect recurrent disease (Figure 8).^{79,80} The additional value of DWI and dynamic contrast-enhanced (DCE)-MRI has been proposed. Kinkel et al showed optimal tumour enhancement time of 45–90 s on DCE-MRI.⁷⁹ Lucas et al compared the appropriate sequences for detection of local recurrence among T_2 WI alone, DCE-MRI alone, a combination of T_2 WI/DWI, and a combination of T_2 WI/DCE-MRI.⁸⁰ Results show that T_2 WI/DWI provides the best accuracy of 92%, followed by T_2 WI/DCE and DCE-MRI alone

of 80%, and T_2 WI of 73%.⁸⁰ Considering the convenience and less invasiveness to the patients, DWI will be recommended for the detection of tumour surveillance.

The patterns of recurrence of cervical cancer have changed in this decade since integrating novel radiotherapy with high precision (image-guide radiotherapy and brachytherapy). RetroEMBRACE multi institutional study of image guided adaptive brachytherapy (IGABT) for cervical cancer shows that the predominant failure of patients treated with IGABT is systemic, whereas the predominant failure with conventional brachytherapy is in the pelvis.⁸¹ Para-aortic irradiation based on number or location of LNs on imaging (CT, MR, or PET/CT) can also favourably improve para-aortic control.⁸² The current problem is distant failures owing to a lack of effective biomarkers to guide adjuvant chemotherapy or bevacizumab. Future radiogenomic researches may help improve prediction of distant failures and guide treatment for patients with cervical cancer.

Tumour response after chemoradiation therapy/surgery

The knowledge of predicting factor of treatment response and the risk factor of tumour recurrence may affect the patients' treatment and follow-up after initial therapy. One of the predictor of tumour recurrence is the presence of residual tumour after therapy. In early-stage cancer following radical hysterectomy, the predictor of recurrence is the presence of residual tumour at final pathology and tumour size over 2 cm.⁸³ Also in locally advanced cervical cancer (LACC) patients with CCRT, patients with good tumour response for the CCRT were found to have a significantly lower rate of para-aortic recurrence and distant metastasis than non-responsive patients.⁸⁴

DWI, which may represent tumour cellularity, extracellular space or the size of nuclei, can be used for monitoring treatment response. In meta-analysis of LACC patients, an increase of ADC values more than $0.62 \times 10^{-3} \text{ mm}^2/\text{s}$ after CCRT can be considered a complete response and less than $0.31 \times 10^{-3} \text{ mm}^2/\text{s}$ as no response.⁸⁵ More early response are expected by the change in ADC values at 2 weeks and 4 weeks after the start of the therapy, but its results are heterogeneous. Valentini showed tumour volume measured early after treatment could predict pathological response in LACC, but ADC did not.⁸⁶ On the other hand, Harry and Kim showed the significance of δ ADC.^{87,88} Therefore, more number of large studies are required to be confident with this results.⁸⁵ Gladwish et al⁸⁹ showed improvement of estimation of disease-free survival (DFS) in combination of DWI and clinical factors. The addition of ADC value to clinical factors including large tumour size and nodal involvement increased AUC for estimation of DFS from 0.55 to 0.71 in LACC patients.⁸⁹ Strong and fast enhancement tumour at dynamic contrast-enhanced MR imaging (DCE-MRI) also associated with early recurrence and also presence of residual tumour after CCRT.⁹⁰ Prognosis and

therapeutic effects are predicted based on various quantitative values obtained from MRI, but the results are not constant. Evaluation by more robust methods such as autosegmentation can be lead to more reliable prognosis prediction.

Future directions

Artificial intelligence (AI), which include convolutional neural networks (CNNs), have shown great development for medical imaging analysis and affect the diagnosis and predicting prognosis.^{91,92} At present, fully automatic uterine segmentation with modified U-net was developed irrespective of the presence of major uterine disorders such as uterine fibroid.⁹³ First-order radiomics features extracted from auto tumour segmentation of ADC map were robust and reproducible.⁹⁴ If such automatic extraction is applied to other MR sequences, more quantitative values will be automatically obtained and the results may be more reliable. A deep learning model developed using pre-treatment ¹⁸F-FDG PET/CT radiomics and tumour recurrence and metastasis were successfully predicted in accuracy of 89 and 87%, respectively.⁹⁵ Texture analysis, as a part of radiomics, can merge quantitative CT/MRI/PET imaging and clinical information and engender development of new biomarkers for diagnosis and prognosis.⁹⁶ Several texture analysis has been applied for the prediction of LN metastasis, LVSI and histological grade in cervical cancer.⁹⁷⁻⁹⁹ Decision trees incorporating a radiomic model for LN metastasis or radiomic nomogram predicting LVSI are also being developed.^{97,98} Pre-treatment images may automatically determine treatment strategy and prognosis. When genomic data are merged with imaging features, it is designated as radiogenomics.¹⁰⁰ For ovarian cancer, radiogenomic methods have been developed with the capability of revealing a relation between the histology of high-grade serous carcinomas and genetic levels.¹⁰¹ These radiogenomics research efforts are expected to be applicable also to cervical cancer to support personalised management and to provide benefits to patients.

CONCLUSION

Revised FIGO staging allow to use imaging modalities including CT, MRI, and PET/CT more specifically than before, based on the fact that those imaging evaluation are indispensable for pre-operative staging and post-operative follow of cervical cancer. The measurement of tumour diameter and LN assessments, which are newly added to the stage evaluation in 2018, are particularly image-dependent and resulted in increase of responsibility of diagnostic imaging. At present, PET/CT is recommended for LN assessment, but size criteria is still in discussion. Then, well designed and a large number of studies will be needed. High diagnostic ability of MRI is expected for evaluation of local tumour evaluation, and PET/CT is expected for detection of distant metastasis/recurrence. The usefulness of PET/MRI is also expected, but it will be required to accumulate the data as the equipment becomes more widespread. In addition, more reliable data is expected for the prediction of therapeutic effect and prognosis by the progress of image analysis methods.

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