

Current Strategies and Recent Advances in Gynaecological Oncology Imaging

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ABSTRACT

Imaging is now a crucial tool in the management of gynaecological cancers to optimise clinical outcomes. This review provides an update on the current role and future trends of imaging in cervical, endometrial, and ovarian cancers. Modern imaging protocols, post-processing techniques, functional imaging modalities and reporting systems are discussed in the setting of staging and guiding of treatment decisions.

Key Words: Endometrial neoplasms; Genital neoplasms, female; Ovarian neoplasms; Uterine cervical neoplasm

中文摘要

婦科腫瘤影像學的當前策略和最新進展

黃文鳳、黎爾德、李燕蘋

影像學是現時婦科腫瘤治療優化臨床轉歸的關鍵工具。本文描述當前子宮頸癌、子宮內膜癌和卵巢癌影像學的角色和未來趨勢。從腫瘤分期及指導治療決策的角度討論現代影像學的掃描方案、後處理技術、功能性影像學方法和報告系統。

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INTRODUCTION

Imaging in gynaecological oncology has been revolutionised due to the advances in magnetic resonance imaging (MRI) and functional imaging in the past decades. Imaging methodologies have been integrated into disease diagnosis, staging, and treatment. The aim of this review is to provide an update on the current role and future trends of imaging in cervical, endometrial and ovarian cancers. Modern imaging protocols, post-processing techniques, functional imaging modalities and reporting systems are discussed in the setting of staging and guiding of treatment decisions.

CERVICAL CANCER

Cervical cancer is the seventh most common cancer in Hong Kong with about 500 new diagnoses every year. As there is no territory-wide screening programme in Hong Kong and the free human papillomavirus vaccination programme started only in 2019, the prevalence of cervical cancer is not expected to fall until a decade later. More than half of the patients present with disease stage II or above.¹ Precise staging at diagnosis is essential in order to optimise treatment. Early cervical cancer (International Federation of Gynecology and Obstetrics [FIGO] stage IIA or below) can be treated with radical hysterectomy with or without pelvic lymphadenectomy. For selected cases of early cancer, fertility-sparing surgery can be offered to patients who have not yet completed their families.^{2,3} Locally advanced disease is treated by chemoradiotherapy.^{4,5}

The 2018 FIGO revised staging incorporated imaging findings into the staging system for the first time. Prior to the revision, FIGO staging for cervical cancer was entirely based on clinical and surgical findings. The revised system stated that imaging and pathology findings can be used to supplement tumour size and extent at all stages. In addition, there was a newly introduced “stage IIIC” for lymph node involvement, which is further subdivided to IIIC1 (pelvic lymph node) and IIIC2 (para-aortic lymph node). A small letter “r” for imaging and a “p” for pathology is used as a suffix to the stage to denote the method of lymph node detection.⁶

MRI is the imaging modality of choice in evaluating local disease extent given its exquisite soft tissue resolution.⁶ The presence of parametrial invasion, which upstages disease to at least FIGO IIB and classifies the disease as locally advanced, is best identified by MRI, with sensitivity and specificity of 73% and 93%, respectively.⁷ T1-weighted images (T1WI) can be useful to visualise

haematometra, lymphadenopathy, and bone metastases, and should be incorporated in the MRI protocol (Table 1).⁸

To optimise the assessment of the parametrium, oblique axial images perpendicular to the long axis of the cervix are essential (Figure 1).⁸ An intact hypointense fibrous stromal ring on T2-weighted images (T2WI) has high negative predictive value for parametrial invasion. Signs of parametrial invasion include T2 intermediate signal in the parametrium with spiculated borders and encasement of periuterine vessels (Figure 2).^{9,10} Local invasion is well depicted on MRI. Abnormality of the urinary bladder on MRI is not uncommon.¹¹ Bullous oedema of the urinary bladder, which is seen on T2WI as markedly hyperintense thickening of the urinary mucosa, cannot be distinguished from mucosal involvement (Figure 3).¹² Cystoscopy and biopsy are needed to confirm mucosal involvement.

Endovaginal ultrasound is an inexpensive method for visualisation of the vaginal wall and outer contour of the cervix.^{13,14} Intravenous contrast gives no significant improvement in diagnostic accuracy.¹⁵

The presence of metastatic pelvic lymphadenopathy is an important adverse prognostic indicator¹⁶ and has been revised in the latest FIGO 2018 staging system.⁶ Compared to the 2014 staging system, the presence of pelvic and paraaortic lymphadenopathy now upgrades the disease to stage IIIC1 and IIIC2, respectively. Conventionally, size and shape criteria were used to differentiate metastatic from benign nodes. Morphology indicators such as lobulated or spiculated borders are highly specific but not sensitive. Size criteria vary in accuracy, sensitivity and specificity depending on the cut-off thresholds.¹⁷ Diffusion-weighted imaging (DWI) in conjunction with T2WI increases the ability of MRI to differentiate benign from malignant nodes (Figure 4). A meta-analysis by Shen et al¹⁸ involving 15 studies found a pooled sensitivity and specificity of 85% and 84% for DWI. The analysed studies were, however, heterogeneous due to a lack of optimal standardised DWI protocol among studies. Metabolic imaging based on 18-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) adds to the diagnostic accuracy of nodal involvement. Meta-analysis showed that FDG-PET/CT had a pooled sensitivity and specificity of 82% and 95% in determining pelvic lymph node involvement, compared to 56% and 91% respectively by MRI.¹⁹ With

Table 1. Sample scanning protocol for common gynaecological malignancy.*

Sequence	Plane	Technical aspects	Comments
Cervical cancer			
T1	Axial	Include whole pelvis, large FOV (e.g., 330 × 330), ST 5 mm	Assessment of pelvic side wall, lymph node and metastasis
T2 FS	Axial	Include whole pelvis, large FOV (e.g., 330 × 330), ST 5 mm	Assessment of pelvic side wall, lymph node and metastasis
T2	Sagittal Oblique axial and coronal with respect to long axis of cervix	Small FOV (e.g., 200 × 200), ST 3 mm	For assessment of parametrial invasion
DWI	Sagittal	With at least two b-values, from 0-2000 (e.g., b = 50, 500, 1000), ST 5 mm	
Endometrial cancer			
T1	Axial	Include whole pelvis, large FOV (e.g., 330 × 330), ST 5 mm	Assessment of pelvic side wall, lymph node and metastasis
T2 FS	Axial	Include whole pelvis, large FOV (e.g., 330 × 330), ST 5 mm	Assessment of pelvic side wall, lymph node and metastasis
T2	Sagittal Oblique axial and coronal with reference to long axis of uterus	Small FOV (e.g., 200 × 200), ST 3 mm	Oblique axial and coronal images for assessment of depth of myometrial invasion
DWI	Sagittal	With at least two b-values, from 0-2000 (e.g., 50, 500, 1000), ST 5 mm	
3D T1 post-contrast FS	Axial	50 s, 2.5 min and 5 min 1 mm × 1 mm in-plane resolution	
Ovarian mass characterisation			
T1 in/out phases	Axial	Include whole pelvis, large FOV (e.g., 330 × 330), ST 5 mm	Assessment of fat content
T2 FS	Axial	Include whole pelvis, large FOV (e.g., 330 × 330), ST 5 mm	Assessment of pelvic side wall, lymph node and metastasis
T2	Axial plus choice of sagittal or coronal	Small FOV (e.g., 200 × 200), ST 3 mm	
DWI	Axial	With at least two b-values, from 0-2000 (e.g., 50, 500, 1000), ST 5 mm	
T1 post-contrast FS	Axial	3D T1 FS with 1 mm × 1 mm in-plane resolution	

Abbreviations: 3D = three-dimensional; DWI = diffusion-weighted imaging; FOV = field of view; FS = fat-saturated; ST = slice thickness; T1 = T1-weighted; T2 = T2-weighted.

* Preparation: Fasting for at least 4 hours. Antiperistaltic agent immediately before examination (e.g., 1 mg glucagon). Moderately filled bladder.

these, FDG-PET/CT offers higher specificity while DWI-MRI is more sensitive in identifying nodal involvement in cervical cancer.²⁰

Fertility Preservation

Fertility sparing treatment such as conisation and trachelectomy can be alternatives to radical surgery in disease of FIGO 1B1 or below. Selection of cases requires a multidisciplinary approach and MRI plays a key role in this.^{21,22}

In addition to parametrial assessment, preoperative MRI gives accurate delineation of the craniocaudal extent of tumour, especially with endocervical cancer and its relationship to the internal os. Measurement on MRI correlates well with pathological measurement.

A distance of 5 mm to 10 mm between the tumour and the internal os puts the patient at high risk for local recurrence after surgery.^{23,24} Other factors to consider include a maximum tumour size of <2 cm with sufficient cervical length after resection (at least 1 cm), absence of deep cervical stromal invasion, and absence of lymph node involvement.²⁵

Image-guided Brachytherapy

The GEC-ESTRO (The Groupe Européen de Curiothérapie and the European Society for Radiotherapy & Oncology) guidelines recommend MRI-guided brachytherapy as a component of the radiotherapy in locally advanced cervical cancer treated with chemoradiotherapy (FIGO IB-IVA).²⁶ Studies showed that it improved local control and overall survival

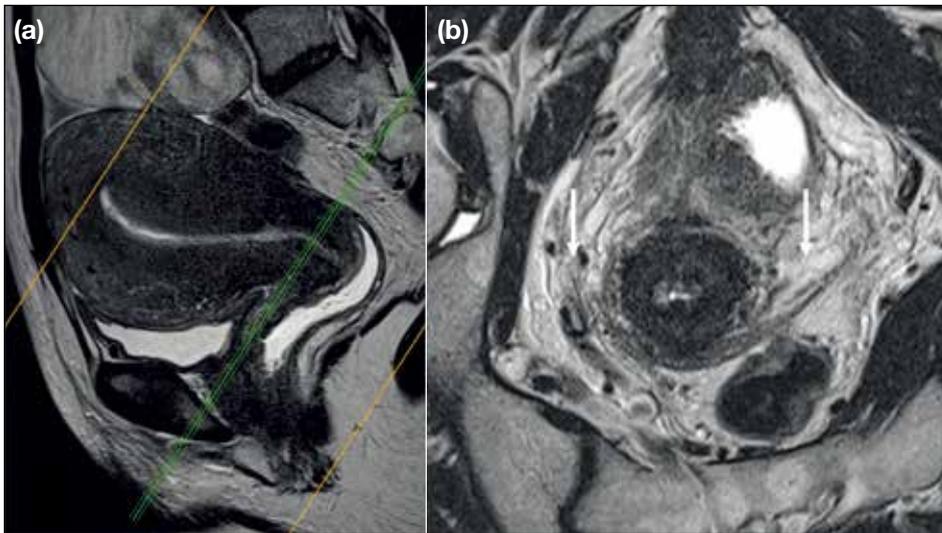


Figure 1. (a) Midline T2-weighted sagittal scan. Green line denotes the plane of oblique axial. (b) T2-weighted oblique axial scans. Normal parametrium (arrows).

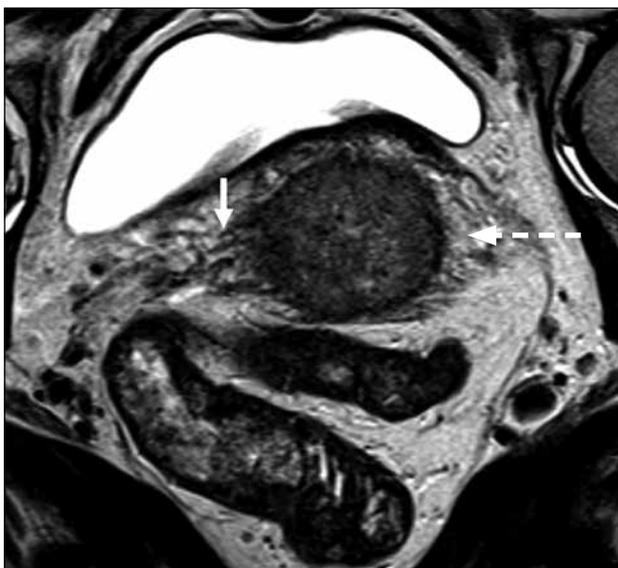


Figure 2. Spiculated soft tissue on the right side suggestive of parametrial invasion (solid arrow). Normal left parametrium with intact stromal line for comparison (dotted arrow).

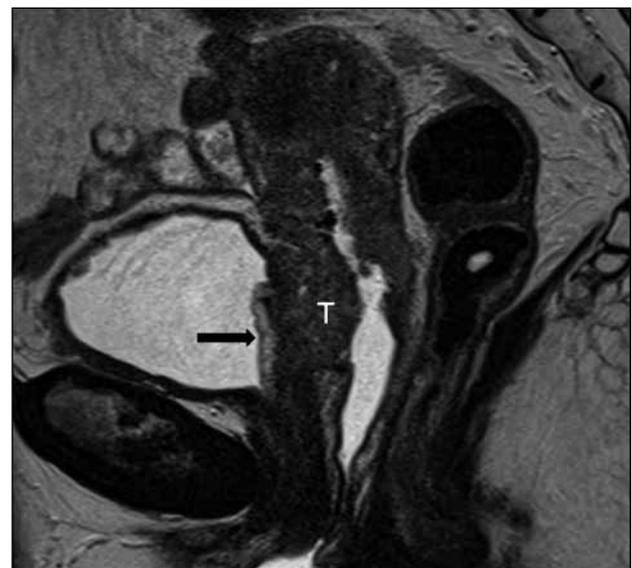


Figure 3. Sagittal T2-weighted magnetic resonance imaging for staging. Cervical tumour (T) centred at the anterior lip. Bullous oedema of the urinary bladder (arrow). This should not be taken as mucosal invasion of bladder unless proven by biopsy.

as compared with two-dimensional radiation planning of previous generation^{27,28} Brachytherapy was historically planned using orthogonal radiographs. From then it evolved to CT-based three-dimensional planning in the 1990's. Compared with traditional CT/X-ray-guided approaches, MRI gives superior contrast delineation and thus makes better tumour delineation from normal tissue.^{29,30} Three-dimensional contouring allows dose escalation to residual disease while sparing the organs at risk, hence improves local control and reduces complication rate (Figure 5).

Brachytherapy is performed following whole pelvis irradiation. The regimen of brachytherapy varies. Planning MRI for brachytherapy is performed immediately after applicator insertion. Logistics on how to minimise transfer time between operating theatre and MRI suite, and to the radiation suite have to be worked out, in addition to the appointment booking and coordination among different units.³¹

Scanning time is an important factor to consider with the applicator in situ. Shorter scanning time minimises

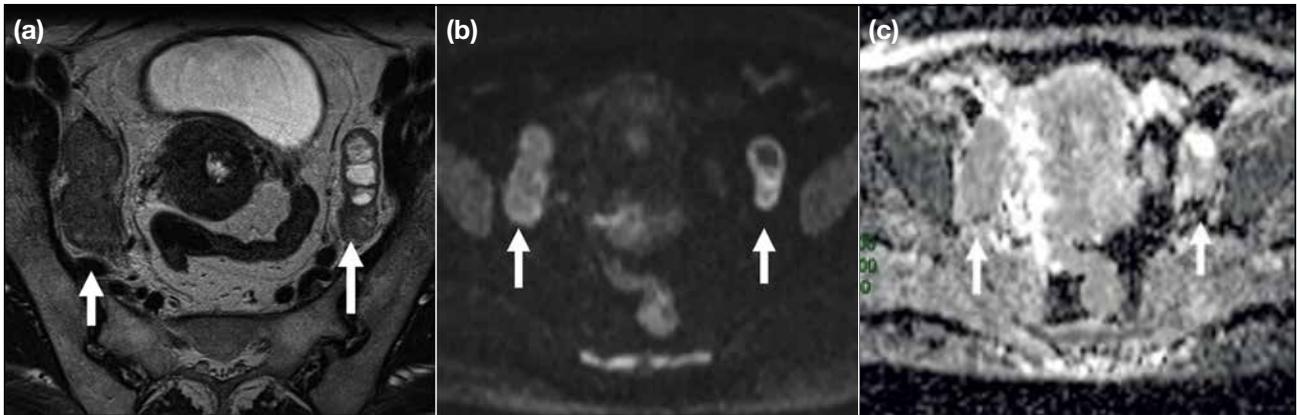


Figure 4. Case of cervical cancer with bilateral lymphadenopathy. (a) T2-weighted images showing bilateral pelvic side wall lymphadenopathy (arrows). (b) A lymph node showing heterogeneous signal (arrows) on the left side. (c) The lymph nodes are hyperintense (arrows) on diffusion-weighted imaging ($b = 1000$) and hypointense on apparent diffusion coefficient.

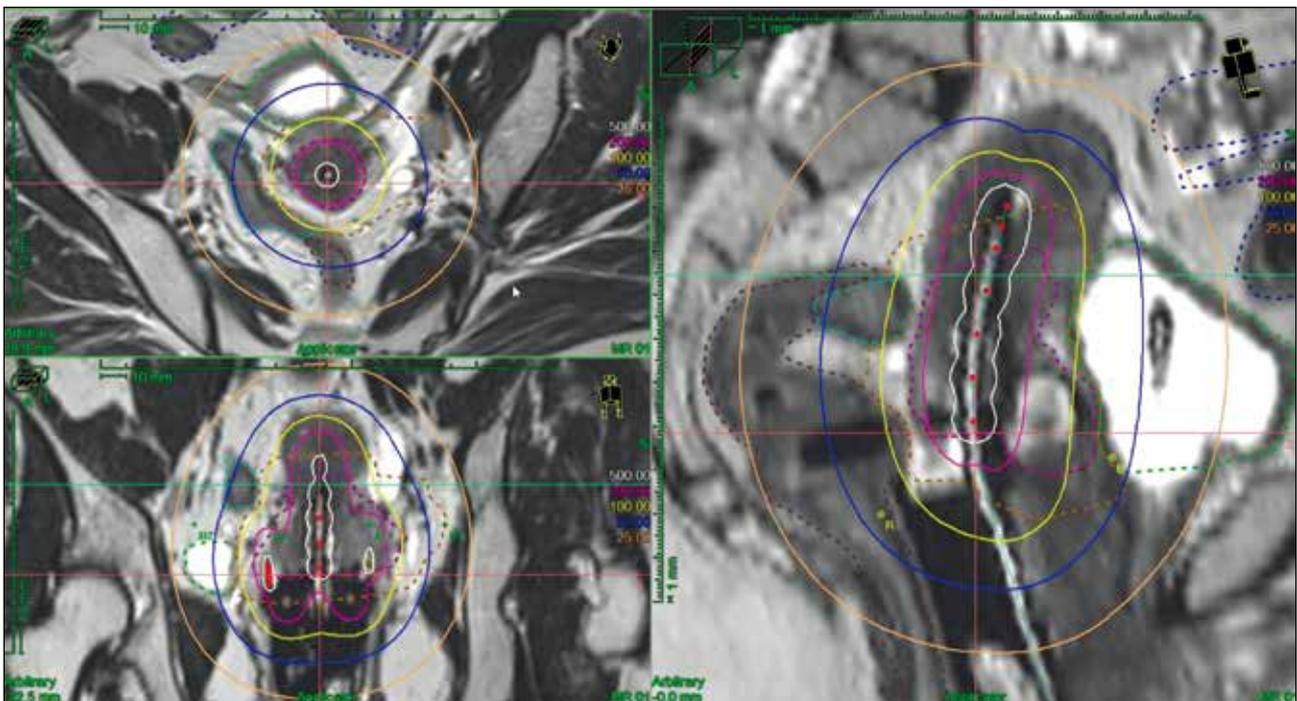


Figure 5. Contour line drawn with magnetic resonance image guidance for radiotherapy planning. (Image courtesy of Dr Amy TY Chang and Dr Rebecca MW Yeung, Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital)

patient discomfort and facilitates appointment booking in a busy radiology unit. According to GEC-ESTRO recommendations, mandatory sequences with an applicator are T2WI acquired in axial, coronal and sagittal planes through the cervix (Figure 6) to delineate the urinary bladder, uterus, and rectum.²⁹ T2WI orthogonal to the MRI table can be added if required for treatment planning.³² DWI and post-contrast sequences are non-essential for this purpose.

ENDOMETRIAL CANCER

The global incidence of endometrial cancer is on the rise, with a postulated association with increased exogenous hormones use, endogenous hormone exposure, and obesity.³³

The presence of deep myometrial invasion, defined by tumour invasion beyond half of the myometrial thickness, is positively correlated with pelvic lymphadenopathy and

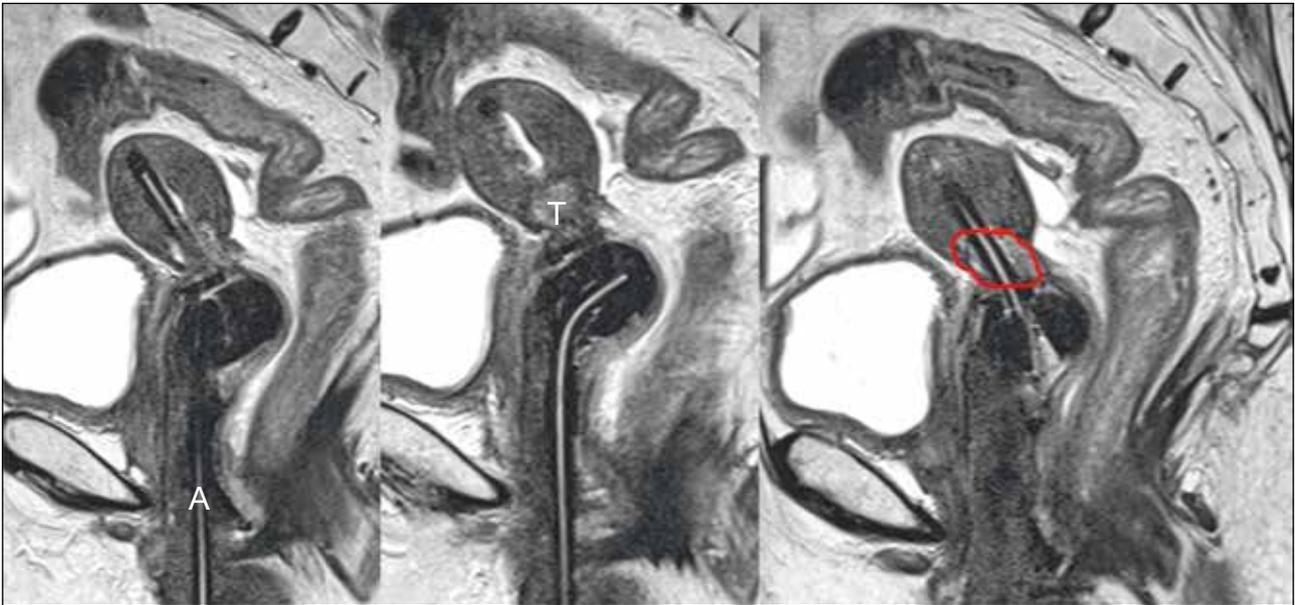


Figure 6. Magnetic resonance imaging–based image-guided brachytherapy. Applicators in situ (A) and residual tumour signal (T). Region of interest drawn around residual tumour signal for radiation planning.

adverse disease prognosis.^{34,35} The FIGO staging divides stage I disease into IA and IB, for superficial (<50% thickness of myometrium) and deep (>50% thickness of myometrium) invasion, respectively.³⁶

Lymphadenectomy in early endometrial cancer (stage I) is controversial and may bear no survival benefit.^{37,38} However, intermediate- and high-risk groups may benefit from pelvic and paraaortic lymphadenectomy.³⁹ The presence of deep myometrial invasion or unfavourable histology (non-endometrioid adenocarcinoma) results in an upgrade from low risk to intermediate/high risk. Cervical stromal invasion is associated with increased likelihood of pelvic lymphadenopathy^{40,41} and an adverse prognosis.^{42,43}

Scanning Protocol and Standard of Measurement

Most modern protocols incorporate T2, DWI, and post-gadolinium images, either by multiphase or dynamic contrast-enhanced (DCE) MRI. Intravenous contrast aids tumour visualisation through increased contrast of the tumour with normal myometrium. The endometrial tumour shows less enhancement than normal myometrium. Depiction of myometrial invasion is at equilibrium phase (2 min 30 s after contrast injection). The cervical stroma enhances later than myometrium. Thus, invasion of cervical stroma is best assessed in delayed phase (3–5 min after contrast injection).^{15,44}

DWI has also been used to depict deep myometrial invasion. Evidence suggested that DWI was at least equivalent to DCE, in detecting deep myometrial invasion (Figure 7).^{45,46} DWI has the potential to be an alternative to DCE in assessment of myometrial invasion, especially when intravenous contrast injection is contraindicated.

Methods of measuring depth of myometrial invasion vary, both in radiology and histology. This is further confounded when endometrial contour is distorted, as commonly occurs in the presence of benign pathology such as fibroids and adenomyosis causing irregular endometrial-myometrial junction, and in the presence of exophytic tumour.^{47,48} Measurement by subtraction might be a more reliable method.⁴⁹ The thickness of adjacent uninvolved myometrium is first obtained. Then the distance between the serosa and outermost tumour-free myometrium is obtained. The depth of invasion is obtained by subtraction of the two numbers (Figure 8). This method attenuates the effect of endometrial distortion from irregular endometrial-myometrial junction and excludes exophytic areas from calculation.

Nodal Staging

Surgical staging remains the gold standard in determining nodal status in endometrial cancer.^{50,51} MRI with DWI showed higher sensitivity but lower specificity than FDG-PET/CT (83% vs. 39% and 51% vs. 96%, respectively).⁵² In a meta-analysis of seven studies, the

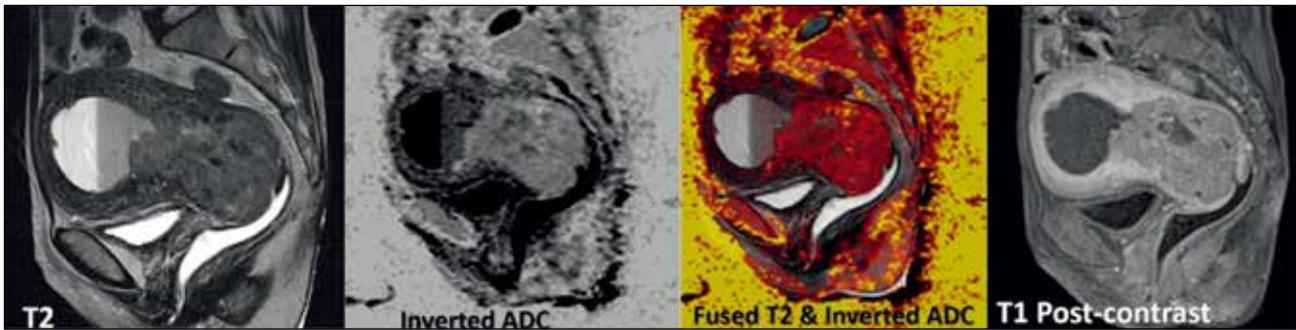


Figure 7. T2-weighted sagittal image showing a tumour at the lower segment of the uterus with cervical stromal invasion. Obstructive hydrometra with fluid-fluid level. Apparent diffusion coefficient (ADC) signal inverted fields on T2-weighted and post-contrast images of the same plane for comparison.

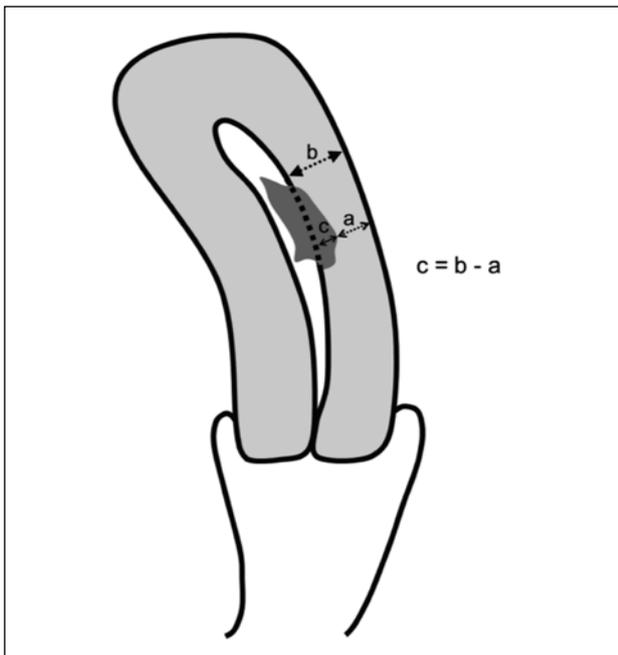


Figure 8. Schematic diagram illustrating the method of myometrial invasion depth. a = distance between serosa and outermost tumour-free myometrium, b = thickness of adjacent normal myometrium, the depth of myometrial invasion, c is obtained by subtraction of two numbers.

sensitivity and specificity of FDG-PET/CT in detecting pelvic and/or paraaortic nodal metastasis were 63% and 95%, respectively, with overall accuracy of 90%.⁵³ The authors concluded that FDG-PET/CT was highly specific but only moderately sensitive, and thus cannot replace lymphadenectomy. Surgical staging remains important and the decision to perform lymphadenectomy or nodal sampling should be determined by pathological risk factors.

OVARIAN CANCER Adnexal Mass Characterisation

Endovaginal ultrasonography (USG) is usually the first line of investigation for pelvic masses. Terminology and measurements on endovaginal USG have been standardised by the International Ovarian Tumor Analysis group.⁵⁴ The ROMA (Risk of Ovarian Malignancy Algorithm) score that incorporates ultrasound findings, CA125 and HE4 levels, is useful for prediction of the likelihood of malignancy of an adnexal mass.⁵⁵

Adnexal lesions with benign USG features, for example, simple anechoic cysts <5 cm in premenopausal women, can be safely dismissed. Depending on the USG features, some cases are safe to be followed up.⁵⁶ However, with frankly malignant adnexal mass or a patient with a high ROMA score, CT can be performed for disease staging and assessment of extrapelvic spread. The vast diversity of ovarian masses, and the wide overlap of benign and malignant imaging features, make specific radiological diagnosis difficult. Methods to risk stratify adnexal lesions with quantitative and qualitative measures have been put forward.^{57,58} MRI is useful in indeterminate adnexal masses for further characterisation.⁵⁹ T1WI (with and without fat saturation) is useful to detect fatty components, mucin, and haemorrhage. Post-contrast T1WI is important in further lesion characterisation. T2WI detects cystic components and detailed anatomical characteristics. Morphological features favouring malignancy include diameter >4 cm, a complex cystic mass with thick internal septations, thickness of the wall >3 mm, lobulated contour, tiny amorphous calcifications, necrosis, papillary projections, and tumour vascularity (Figure 9).^{60,61}

The apparent diffusion coefficient (ADC) value of the solid portion of an adnexal mass is lower in malignant than in benign lesions. With an ADC cut-off threshold value, malignant lesions can be excluded with high confidence. The ADC value could be a tool to streamline management strategies; however, inter-vendor and intersystem variability of ADC measurements render cross-centre validation difficult and thus limit the applicability of the method.⁶²

In a retrospective analysis of 37 pre-operative DCE-MRI performed for ovarian epithelial tumour, a Type 3 curve, defined by an initial rise in signal in the solid portion of an ovarian mass steeper than the myometrium, was present in malignant lesions and not in benign or borderline lesions.⁶⁰ Other semi-quantitative DCE parameters offer useful information in that the absolute and relative maximum contrast enhancement could identify malignant lesions with 100% sensitivity and specificity, the but studied cohort was small (n = 26).⁶³ A subsequent large-scale study with 102 patients also suggested the usefulness of DCE-MRI in differentiating benign from borderline and malignant tumours.⁶⁴ Contrast enhancement can thus be considered a tool to identify lesions that are safe to follow-up.

The role of FDG-PET/CT in ovarian lesion characterisation is not clearly established. It has been suggested that FDG-PET/CT could assist in differentiating malignant from benign ovarian masses when DCE-MRI is indeterminate.⁶⁵

Peritoneal Disease

Ovarian malignancies often present late with disseminated peritoneal disease. Cytoreductive surgery followed by systemic chemotherapy is the treatment of choice for advanced disease. The ability to achieve complete cytoreduction is related to improved survival rate.⁶⁶⁻⁶⁸

The volume of residual disease after cytoreductive surgery is one of the most important prognostic indicators.^{66,69} Optimal cytoreduction is defined as the largest residual disease of <1 cm.⁷⁰ In recent years, there has been a shift in the surgical paradigm in pursuit of a cytoreductive goal of no gross residual disease, which has been shown to be associated with improved progression-free and overall survival.⁷¹ Extensive surgical procedures are often required to achieve complete cytoreduction or minimal residual disease, and these can be technically challenging in patients with disseminated tumours. Neoadjuvant

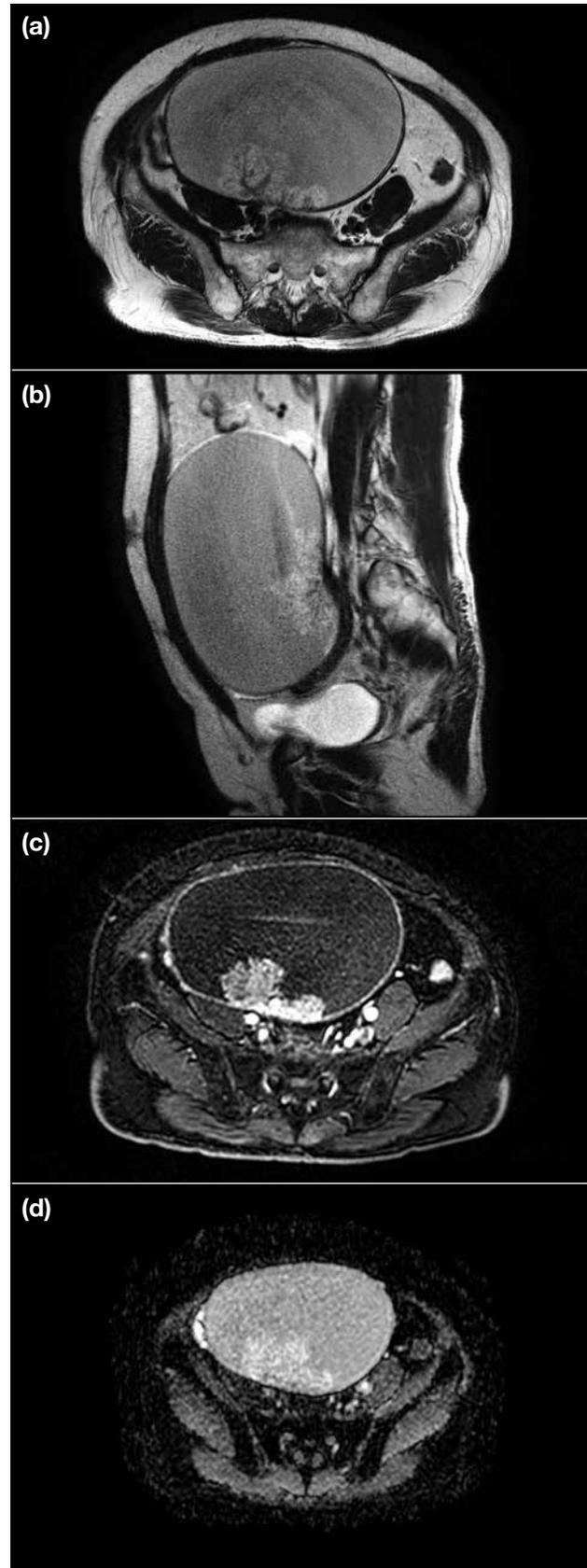


Figure 9. Serous borderline tumour. (a and b) T2-weighted axial and sagittal images showing a cystic lesion with enhancing solid component (c) but no restricted diffusion (d).

chemotherapy followed by debulking surgery is an alternative to primary cytoreductive surgery, yielding similar outcomes.⁷² Resectability criteria differ across centres. In general, disease in the upper abdomen might require more complex surgical procedures, including splenectomy and diaphragmatic resection, and likely involvement of more than one surgical specialty. The European Society of Urogenital Radiology guidelines suggest several negative prognostic factors for complete cytoreduction, including deposits >2 cm in the upper abdomen, parenchymal or subcapsular involvement of the liver and spleen, involvement of small bowel mesentery, and lymph node involvement above the renal hila.⁷³

Contrast-enhanced CT of the abdomen and pelvis is currently the first-line radiological investigation for detection of peritoneal disease. Its reported sensitivity in detecting peritoneal metastasis in ovarian cancer ranges

from 85% to 93%, but this substantially drops to 25% to 50% for subcentimetre peritoneal implants.⁷⁴

Techniques such as FDG-PET/CT and DWI enhance the visibility of peritoneal metastases (Figures 10 and 11).^{75,76}

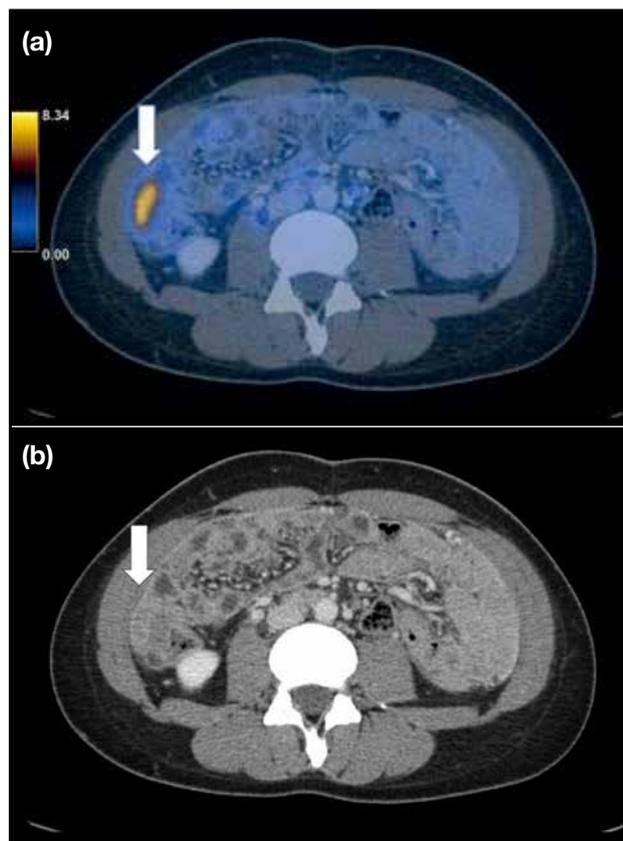


Figure 10. (a) 18-fluorodeoxyglucose positron emission tomography/computed tomography. Uptake in peritoneal deposits in the right paracolic gutter (arrows) which is subtle on contrast-enhanced computed tomography (b).

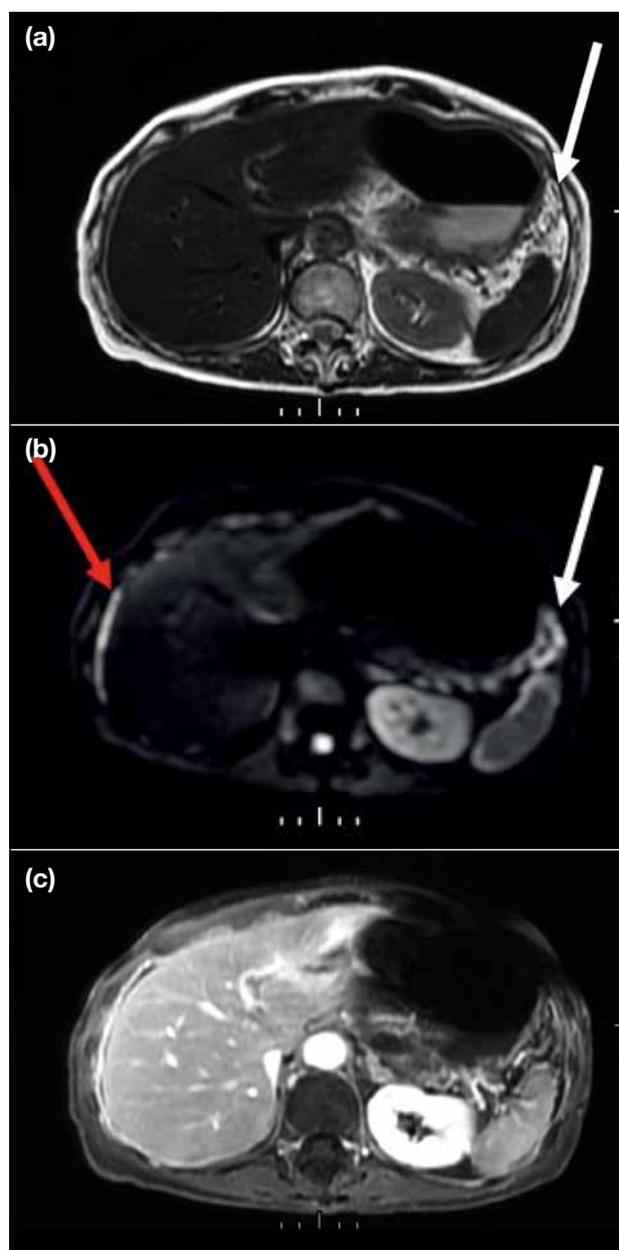


Figure 11. Ovarian cancer with peritoneal carcinomatosis. (a) T2-weighted axial image showing fat stranding along the lienogastric ligament (white arrow). (b) Diffusion-weighted imaging (b = 800) demonstrates hyperintense signal over left upper abdomen corresponding to the stranding along the lienogastric ligament (white arrow) and additional perihepatic disease, which is not visible on T2-weighted axial image (red arrow). (c) Corresponding post-contrast image confirming these findings.

Table 2. Summary of literature comparing the diagnostic power of conventional CT, FDG-PET/CT and MRI in detection of peritoneal disease in ovarian cancer.

Study	Cohort size	Modalities compared	Endpoint	Accuracy figures			Conclusions	
Schmidt et al ⁷⁹	15	CT, MRI, FDG-PET/CT	Peritoneal carcinomatosis	MRI	FDG-PET/CT	CT	CT, MRI and FDG-PET/CT are of similar diagnostic accuracies	
				Sensitivity	98	95		96
				Specificity	84	96		92
				NPV	96	92		94
				Accuracy	93	96		95
Low et al ⁸⁰	22	CT and MRI	CT and MRI predicted peritoneal carcinomatosis index (PCI)	Accuracy	MRI	CT	MRI is more accurate than CT to predict PCI score	
					91	50		
Lopez-Lopez et al ⁸¹	59	CT and FDG-PET/CT	PCI	FDG-PET/CT	CT	CT shows better diagnostic result as compared to FDG-PET/CT in detection of peritoneal disease		
				Sensitivity	24		35	
				Specificity	93		98	
				PPV	66		90	
				NPV	68		72	
Kim et al ⁸²	46	CT and FDG-PET/CT	Presence of peritoneal carcinomatosis	FDG-PET/CT	CT	FDG-PET/CT is more accurate than CT		
				Sensitivity	96		89	
				Specificity	90		65	
				PPV	93		77	
				NPV	95		81	
Rubini et al ⁸³	51	CT and FDG-PET/CT	Presence of peritoneal carcinomatosis	FDG-PET/CT	CT	FDG-PET/CT is more accurate than CT in detection of peritoneal metastasis		
				Sensitivity	79		54	
				Specificity	91		61	
				PPV	92		62	
				NPV	78		51	
Low et al ⁷⁶	34	MRI and DWI	Detection by site	DWI	Conventional MRI	Combined	Adding DWI to routine MRI improves accuracy	
				Sensitivity	100	97		100
				Specificity	75	57		71
				Accuracy	86	88		94

Abbreviations: CT = computed tomography; DWI = diffusion-weighted imaging; FDG-PET/CT = 18-fluorodeoxyglucose positron emission tomography/computed tomography; MRI = magnetic resonance imaging; NPV = negative predictive values; PCI = peritoneal cancer index; PPV = positive predictive values.

DWI can detect peritoneal deposits with the additional advantage of no intravenous contrast administration. It has reported sensitivity and specificity of up to 95% and 95%, respectively.⁷⁷ False positives from bowel content can be reduced by using high b-value images such as 800 s/mm². The high signal of peritoneal deposits on high b-value DWI-MRI adds to lesion conspicuity.

FDG-PET/CT has been suggested to be more sensitive and specific in predicting disease resectability as compared with conventional contrast-enhanced CT alone.⁷⁸ Table 2^{76,79-83} summarises current evidence of the use of FDG-PET/CT and MRI in detection of peritoneal disease in ovarian cancer.

CONCLUSION

Imaging plays a crucial role in gynaecological oncology,

from diagnosis to treatment stratification. The revised 2018 FIGO incorporates radiological findings in cervical cancer staging. Use of MRI planning in image-guided brachytherapy for cervical cancer improves treatment outcome. MRI is highly accurate in depicting myometrial invasion and cervical stromal invasion in endometrial cancer. Functional imaging is effective for detecting peritoneal carcinomatosis.

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