

Learning Objectives

- To describe the role of MRI and PET/CT for initial treatment selection, planning, and response assessment in uterine malignancies
- To explain eligibility criteria for fertility preservation in cervical cancer
- To highlight combined MR features that may distinguish uterine sarcoma from atypical leiomyoma (LM)

18.1 Cervical Cancer

18.1.1 Epidemiology and Diagnosis

Cervical cancer is the fourth most common malignancy among women worldwide [1, 2]. Most cases and deaths occur in developing countries, whereas in developed countries widespread cytology-based screening has led to a sharp decline in incidence [1, 3].

The main risk factor is chronic human papillomavirus (HPV) infection [1, 3]. Thus, cervical cancer can be effectively prevented with HPV vaccines and HPV DNA-based screening [1]. Abnormal cytology or positive high-risk HPV test should prompt colposcopy and cervical biopsy. Squamous cell carcinoma comprises 70–80% and adenocarcinoma 20–25% of cases [1].

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18.1.2 Initial Staging and Management

Cervical cancer is staged using the International Federation of Gynecology and Obstetrics (FIGO) classification [4]. It is the only gynecologic malignancy staged clinically owing to high prevalence in developing countries. Lymph node (LN) status, a major prognostic factor, is excluded from FIGO staging as clinical detection is not possible [1]. Cross-sectional imaging is not accepted for formal assignment of FIGO stage but is used routinely in developed countries to guide treatment decisions [1, 5]. Treatment selection is determined by tumor stage and presence/location of LN metastases (Fig. 18.1).

18.1.3 MRI and Initial Staging

MRI is the method of choice to evaluate locoregional extent (Table 18.1) [6, 7]. Small field-of-view T2-weighted imaging in the sagittal and short-axis planes is the mainstay of staging MRI (Fig. 18.2) [6]. Diffusion-weighted imaging (DWI) in conjunction with T2-weighted imaging improves delineation of tumor margins. Dynamic contrast-enhanced imaging (DCE) is used largely in research for prognosis and response assessment.

18.1.3.1 Stage I: Cervix-Confined Disease

Stage IA is microscopic in size. Stage IB is visible clinically and is divided based on size into IB1 (≤ 4 cm) and IB2 (>4 cm). The tumor has intermediate signal intensity (SI) on T2-weighted imaging and shows diffusion restriction. Intact rim of low-SI fibrous cervical stroma around the tumor indicates cervix-confined disease (Fig. 18.3) [6]. Fertility preservation (LN assessment + cone/trachelectomy) is possible for patients with \leq Stage IB1 (Table 18.2) [8, 9].

Fig. 18.1 Diagram (adapted from [6]) highlights the role of MRI and PET/CT to assess disease extent and guide treatment decisions in patients with new diagnosis of cervical cancer

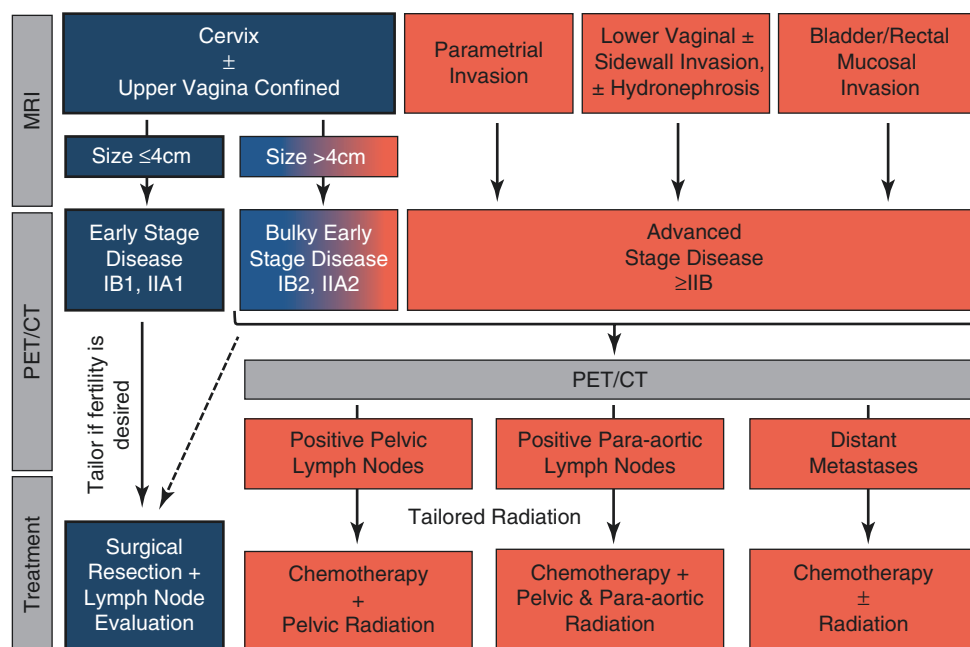


Table 18.1 Suggested MRI protocol to stage cervical and endometrial cancer [7]

Sequences	Planes	Field of view (FOV)	Assessment/detection of
T1-weighted imaging	Axial	Large FOV, Kidneys to pubic symphysis	<ul style="list-style-type: none"> • Pelvic and para-aortic LNs • Bones
T2-weighted imaging	Axial	Pelvis, small FOV	<ul style="list-style-type: none"> • Hydroureter • Pelvic sidewall invasion • Adnexal involvement
	Sagittal	Pelvis, small FOV	<ul style="list-style-type: none"> • Cervical cancer • Endocervical extent • Endometrial cancer • Depth of myometrial invasion • Both • Cervical stromal invasion • Vaginal involvement
	Short-axis plane perpendicular to cervix (cervical cancer) or endometrium (endometrial cancer)	Pelvis, small FOV	<ul style="list-style-type: none"> • Endometrial cancer • Depth of myometrial invasion • Both • Cervical stromal invasion • Parametrial invasion
DWI $B = 0, \geq 800$	Sagittal	Pelvis, small FOV	<ul style="list-style-type: none"> • Adjunct to T2-weighted imaging to assess tumor extent
	Short-axis plane (as above)	Pelvis, small FOV	<ul style="list-style-type: none"> • Adjunct to T2-weighted imaging to assess tumor extent • Increase in LN conspicuity
Optional for cervical cancer	<ul style="list-style-type: none"> • Vaginal gel: Upper vaginal invasion • Endovaginal coil: Small tumors prior to fertility preservation • Long-axis plane T2-weighted imaging + DWI (parallel to cervix) <ul style="list-style-type: none"> – Endocervical extent – Cervical stromal invasion – Parametrial invasion 		
Optional for endometrial cancer	<ul style="list-style-type: none"> • Long-axis plane T2-weighted imaging + DWI (parallel to endometrium) <ul style="list-style-type: none"> – Depth of myometrial invasion – Cervical stromal invasion 		

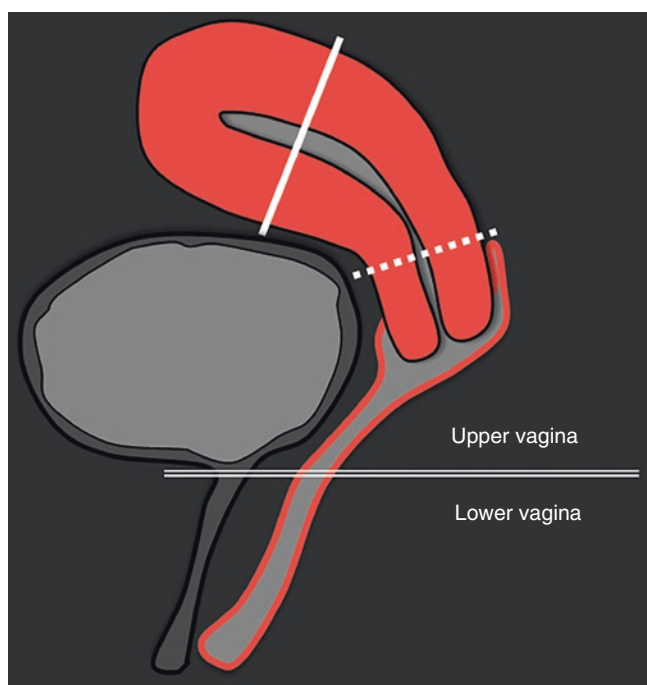


Fig. 18.2 Drawing illustrates orientations of short-axis planes to stage endometrial cancer (solid line oriented perpendicular to endometrium) and cervical cancer (dashed line oriented perpendicular to endocervical canal). Double line is drawn at the bladder base/urethral junction and divides the vagina into upper and lower portions

18.1.3.2 Stage II: Cervical + Upper Vaginal Disease ± Parametrial Invasion

Stage IIA invades the upper vagina (upper two-thirds) but not the parametrium. Similar to Stage IB, it is divided into IIA1 (≤ 4 cm) and IIA2 (> 4 cm). Vaginal invasion is diagnosed when intermediate-SI tumor disrupts low-SI vagina on T2-weighted imaging. A horizontal line drawn at the bladder base on sagittal T2-weighted imaging divides the vagina into upper and lower portions (Fig. 18.2).

Stage IIB invades the parametrium. Complete loss of low-T2 SI stromal ring does not always indicate parametrial invasion. Parametrial invasion is present if tumor disrupts low-SI stroma *AND* causes spiculated/nodular tumor-parametrial interface ± encases parametrial vessels (Fig. 18.4) [6]. DWI + T2-weighted imaging improve specificity for detecting parametrial invasion [10]. Accurate diagnosis is important as parametrial invasion indicates concurrent chemotherapy and radiation (CCRT) as treatment of choice (Fig. 18.1).

18.1.3.3 Stage III: Pelvic Sidewall Invasion, Lower Vaginal Involvement, Hydronephrosis, or Nonfunctional Kidney

Stage IIIA invades the lower vagina. Stage IIIB extends to the pelvic sidewall ± causes hydronephrosis. Tumor

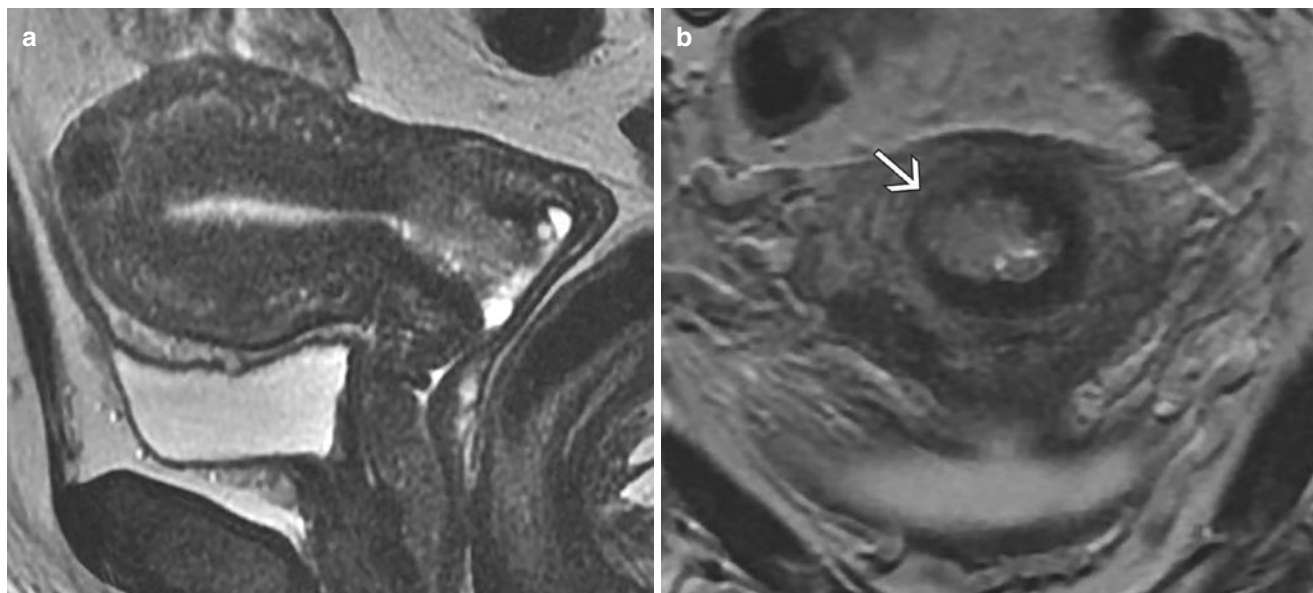


Fig. 18.3 52-year-old woman with Stage IB1 cervical adenocarcinoma. Sagittal T2-weighted imaging (a) and short-axis T2-weighted imaging (b) demonstrate 1.8 cm tumor with intermediate SI on

T2-weighted imaging. Tumor involves partial thickness of cervical stroma with intact low-SI stromal ring (arrow) ruling out parametrial invasion

Table 18.2 Selection criteria for conservative management of women with ≤ Stage IB1 lesions and desire for fertility

Eligibility criteria
• Squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma
• Tumor size ≤2 cm
– Some centers ≤4 cm
• Tumor-to-internal os distance ≥1 cm
– Some centers ≥0.5 cm
• Cervical stromal invasion <50%
– Some centers, any depth
• Cervix-confined disease
– Absence of parametrial invasion or LN metastases

within 3 mm of iliac vessels or obturator internus, piriformis, or levator ani muscles indicates sidewall invasion [6].

18.1.3.4 Stage IV: Bladder/Rectal Mucosal Invasion or Extension Beyond the Pelvis

Stage IVA invades the bladder/rectal mucosa; invasion is present when intermediate-SI tumor disrupts low-SI muscle wall and extends into the mucosa on T2-weighted imaging. Bullous edema alone (high-SI mucosa) does not mean Stage IVA [6]. Stage IVB is indicated by the presence of

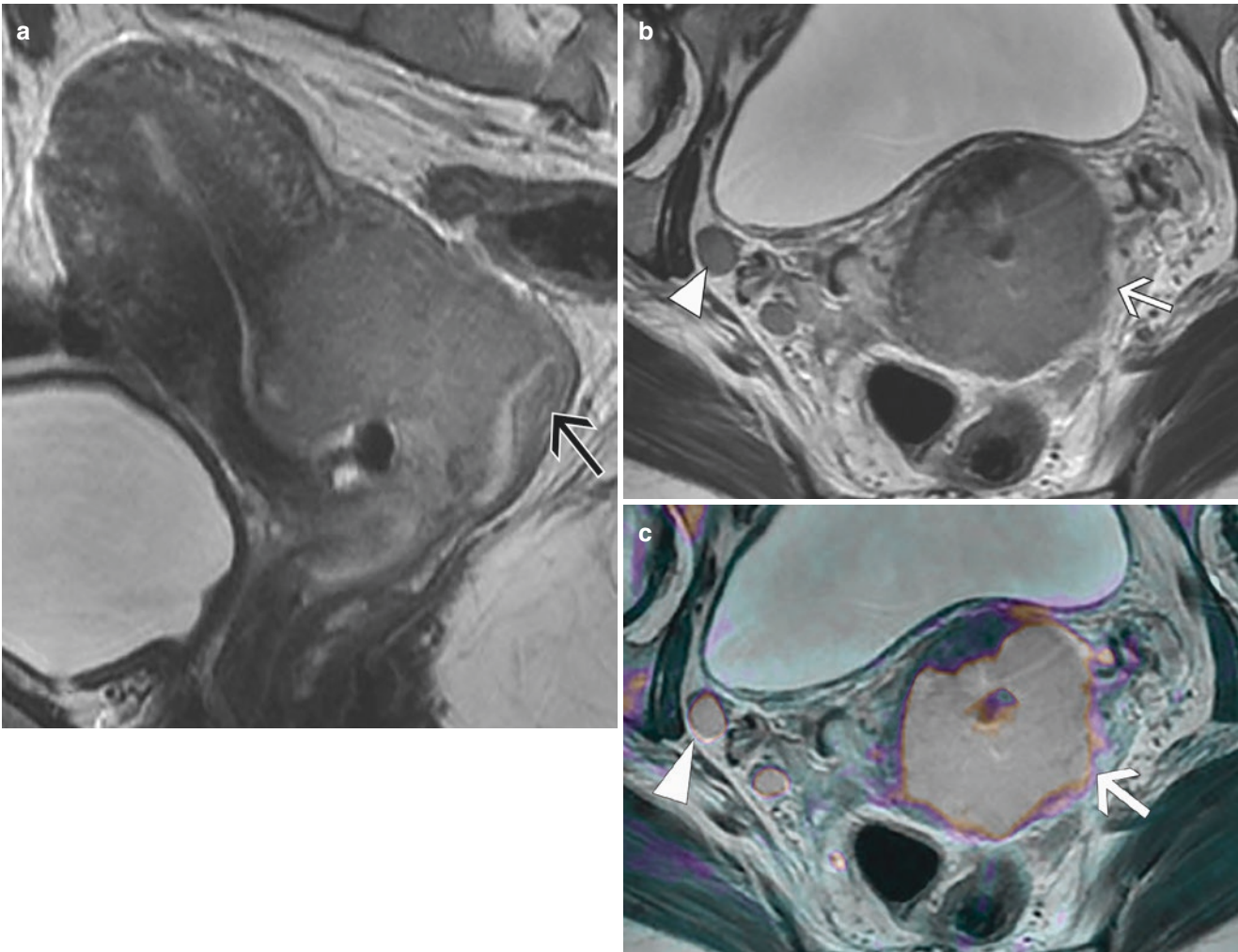


Fig. 18.4 35-year-old woman with Stage IIB cervical squamous cell carcinoma. Sagittal T2-weighted imaging (a), short-axis T2-weighted imaging (b), and fused T2-weighted imaging + DWI (c) demonstrate

5.2 cm tumor involving the lower uterus, upper vagina (arrow), and parametrial regions. There is nodular interface between the tumor and parametrium (arrow). Also note right internal iliac LNs (arrowhead)

distant metastases (including LN metastases beyond the pelvis).

18.1.4 PET/CT and Initial Staging

LN metastases impact prognosis and treatment. On MRI (and CT) short-axis diameter ≥ 1 cm is a main diagnostic criterion but yields low-to-moderate sensitivity because metastases to normal-sized LNs remain undetected (Fig. 18.5) [11]. LNs show high SI on DWI, increasing their conspicuity (Fig. 18.4); however, DWI is not used to distinguish benign from malignant LNs due to overlap in ADC values [10]. PET/CT improves N and M staging and is recommended for Stage \geq IB2 disease (Fig. 18.5) [5, 12].

18.1.5 Evaluation During and After Initial Treatment

After radical hysterectomy, imaging is obtained if recurrence is suspected clinically [1, 5]. After fertility-sparing surgery, MRI is recommended at 6 months and annually thereafter [5].

MRI and PET/CT are useful for radiotherapy (RT) planning. For example, RT field is extended to para-aortic regions if para-aortic LN metastases are present on pretreatment PET/CT (Figs. 18.1 and 18.5) [1, 5], and mid-treatment MRI allows adjustment of brachytherapy dose based on volume/location of residual tumor [13, 14].

Low-SI stroma on T2-weighted imaging indicates tumor-free cervix, but an abnormal signal may persist up to

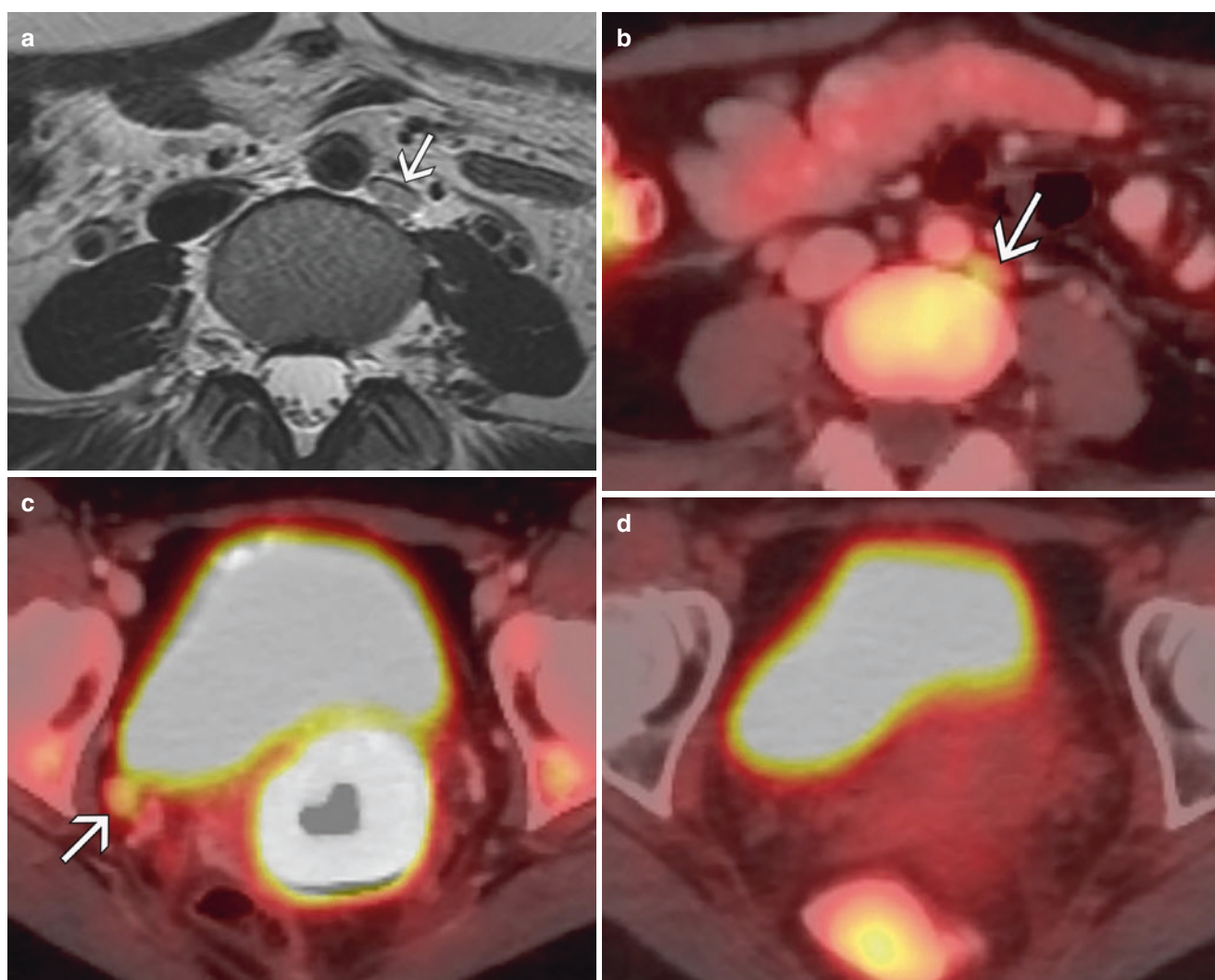


Fig. 18.5 Same patient as in Fig. 18.4. Axial T2-weighted imaging and PET/CT images show 0.5 cm short-axis FDG-avid left para-aortic LN (a, b). (c) Baseline axial PET/CT image through the pelvis demon-

strates FDG-avid cervical tumor and right internal iliac LN (arrow). (d) Complete resolution of FDG avidity after CCRT

6 months after CCRT [6]. Thus, PET/CT obtained 3–6 months after CCRT is useful. Absent FDG avidity indicates low risk of recurrence; diminished FDG avidity signifies moderate risk; and unchanged, increased, or new FDG-avid foci indicate persistent disease (Fig. 18.5) [15]. The role of DWI and DCE to assess response is an area of active research [10, 13].

18.1.6 Evaluation of Recurrence

Recurrent cervical cancer has similar imaging features as primary lesions [6]. In the absence of prior pelvic RT, localized recurrence may be approached with CCRT. Radical surgery is the only potential cure in previously irradiated pelvis. MRI and PET/CT are essential to determine eligibility and tailor the extent of surgery [16].

18.1.7 Future Directions

PET/MRI may offer a “one-stop-shop” approach to the evaluation of cervical cancer in both primary and recurrent settings [17].

18.2 Endometrial Cancer

18.2.1 Epidemiology and Diagnosis

Endometrial cancer is the sixth most common malignancy among women worldwide and the most common gynecological cancer in developed countries [2]. Incidence has steadily increased, primarily due to increased longevity and obesity in developed countries. Approximately 75% of cases occur in postmenopausal women and >90% present with postmenopausal bleeding. As such, most patients are diagnosed at an early stage with 5-year survival rates >90% in this subgroup [18].

Initial evaluation includes pelvic ultrasound (US) and pipelle endometrial biopsy or dilatation and curettage. Thresholds of endometrial thickness of 4–5 mm in postmenopausal women detect endometrial cancer with a sensitivity of up to 95% and a specificity of 77% [19]. Endometrial cancer is traditionally subdivided into two types based on biological behavior: *type 1* tumors are estrogen-dependent and include FIGO grades 1 and 2 endometrioid adenocarcinomas, while *type 2* tumors include serous papillary carcinomas, clear cell adenocarcinomas, carcinosarcomas, and FIGO grade 3 endometrioid adenocarcinomas [18]. *Type 2* tumors are not estrogen dependent, present at a higher stage, and behave more aggressively.

18.2.2 Initial Staging and Management

Endometrial cancer is staged surgically using the FIGO system [4]. The standard surgical staging procedure consists of total abdominal hysterectomy, bilateral salpingo-oophorectomy, LN dissection, peritoneal washing, and omental biopsies. FIGO stage correlates well with prognosis, but preoperative staging remains important, since early-stage/low-grade tumors may be treated with minimally invasive surgery and may not require LN dissection [20, 21].

18.2.3 MRI and Initial Staging

MR imaging is the modality of choice to determine the depth of myometrial invasion, which correlates with tumor grade, LN metastases, and 5-year survival (Table 18.1) [22]. Small field-of-view high-resolution imaging in the sagittal and short-axis planes is the mainstay of MRI staging (Fig. 18.2) [6]. The combination of T2-weighted imaging, DCE, and DWI offers the best diagnostic accuracy [23, 24].

MRI with its high-spatial resolution and larger field of view has a particular advantage over endovaginal US in the setting of bulky tumors, advanced stage, and concomitant benign disease, i.e., adenomyosis and LMs.

18.2.3.1 Stage I: Uterine-Confined Disease

Stage IA is confined to the endometrium or inner half of the myometrium, i.e., <50% myometrial thickness involvement (Fig. 18.6). Stage IB extends to the outer half of the myometrium (≥50%) (Fig. 18.7). The tumor has intermediate-to-low SI on T2-weighted imaging, is hypointense to myometrium on later phases of DCE, and shows restricted diffusion. However, small tumors may be iso- or only minimally hypointense relative to the normal endometrium and may be hypervascular relative to the endometrium early on after contrast administration. A partially intact, low-SI junctional zone around the tumor indicates the absence of deep myometrial invasion.

18.2.3.2 Stage II: Cervical Stromal Invasion

Stage II invades and disrupts the low-SI cervical stroma on T2-weighted imaging. Polypoid extension of the tumor into the endocervical canal or endocervical mucosal invasion is not sufficient to assign Stage II. Tumor extension beyond the cervix into the parametrium requires a radical hysterectomy.

18.2.3.3 Stage III: Invasion of Uterine Serosa, Adnexa, Vagina, and/or Pelvic or Para-Aortic Lymph Nodes

Stage IIIA invades the uterine serosa appearing as an area of intermediate SI on T2-weighted imaging with loss of normal rim enhancement of the outer myometrium on DCE. Direct

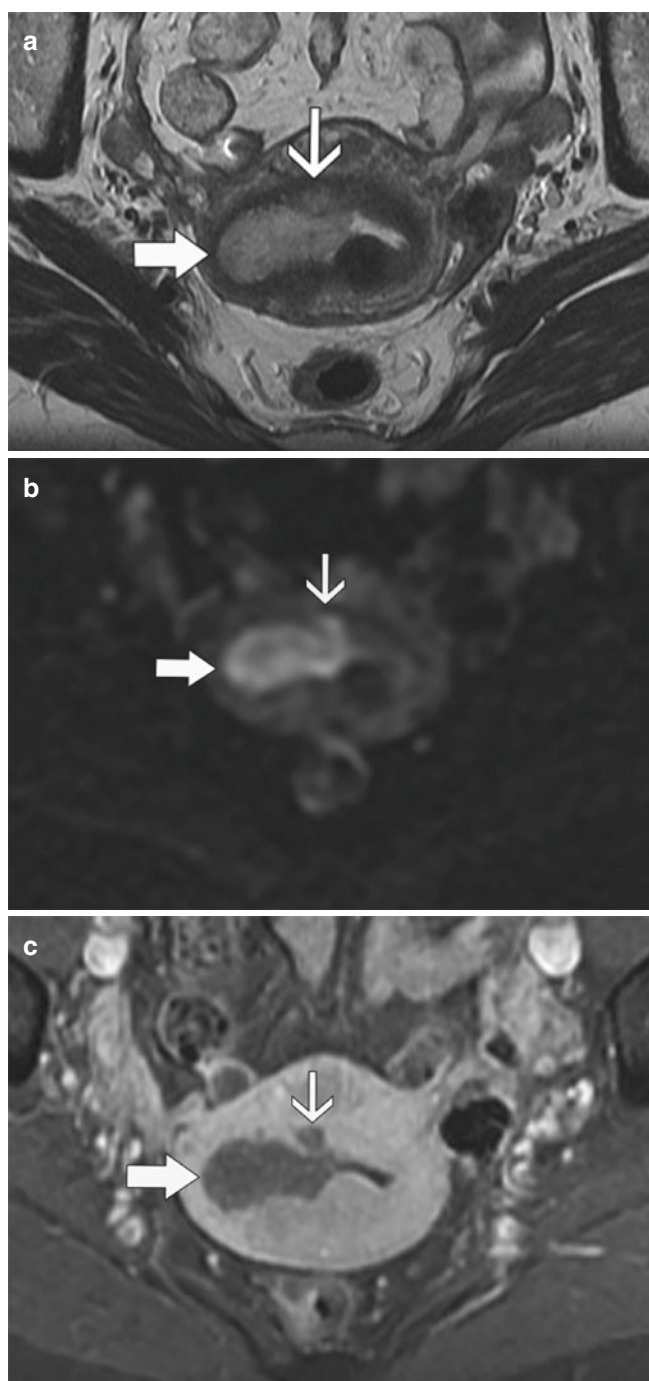


Fig. 18.6 62-year-old woman with Stage IA endometrioid adenocarcinoma (grade 2) of the endometrium. Short-axis (a) T2-weighted imaging, (b) B1000 DWI, and (c) delayed post gadolinium 3D T1-weighted imaging demonstrate an endometrial-based tumor (thick arrow) at the level of the fundus and right cornua. There is partial invasion of the inner half of the myometrium with a thin rim of junctional zone (thin arrow) remaining intact

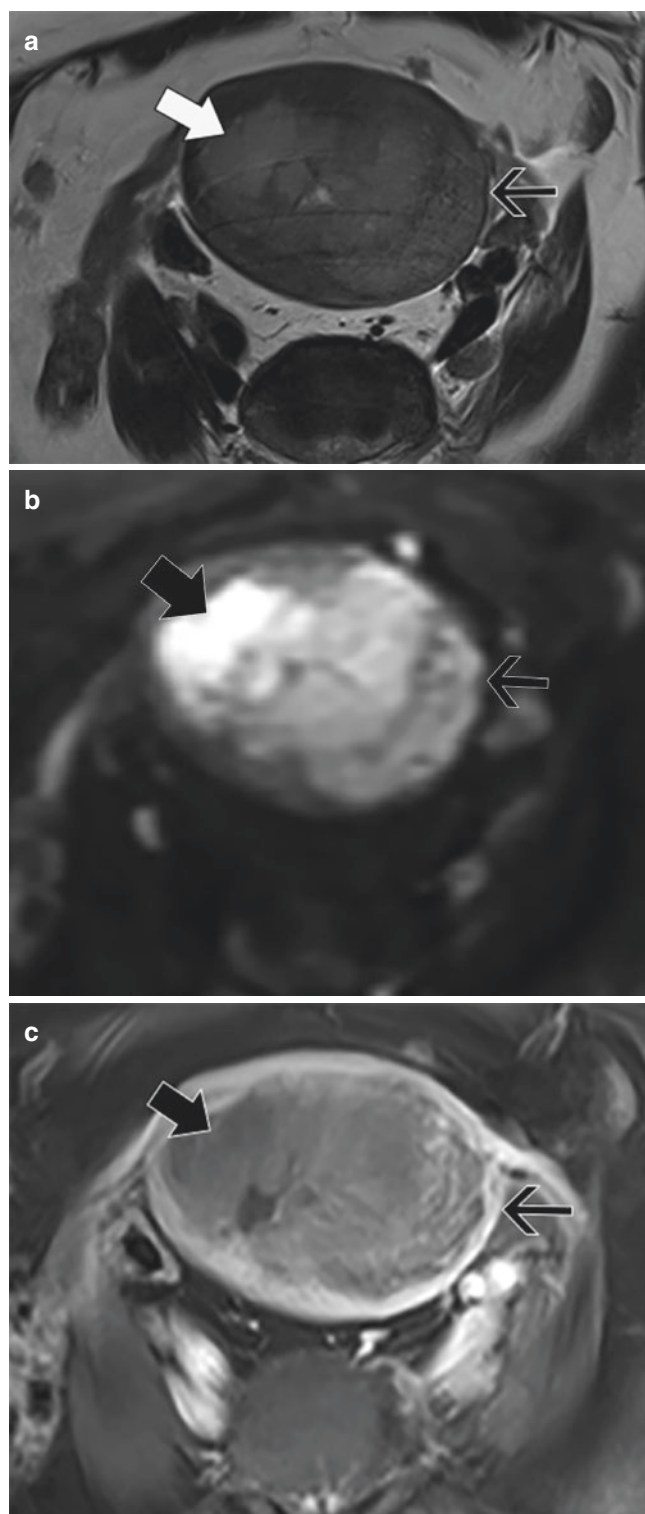


Fig. 18.7 76-year-old woman with Stage IB endometrioid adenocarcinoma (grade 3) of the endometrium. Short-axis (a) T2-weighted imaging, (b) B1000 DWI, and (c) delayed post gadolinium 3D T1-weighted imaging demonstrate a large tumor (thick arrow) invading the deep myometrium. There is a thin rim of intact outer myometrium (thin arrow) along the left aspect of the uterus excluding serosal involvement

tumor spread to the adnexa or ovarian metastases is considered Stage IIIA disease. It is important but challenging to differentiate synchronous ovarian lesions from metastases to the ovaries. *Type 2* tumors have a higher pretest probability of advanced disease, and therefore a meticulous search for advanced tumor extent is required in this subgroup.

Stage IIIB involves the vagina either by contiguous spread or metastatic involvement.

Stage IIIC is diagnosed when there is pelvic (Stage IIIC1) and/or para-aortic (Stage IIIC2) LN metastatic involvement. The use of a 1 cm short-axis cutoff value results in a high specificity but poor sensitivity (range, 36–89.5%) for predicting LN metastases [6]. A cutoff value of 0.8 cm increases the sensitivity albeit at the cost of specificity. In practice, given that endometrial carcinoma is staged surgically, it is important to provide the size and detail the location of LNs exceeding 0.5–0.6 cm in short-axis. The role of DWI and ADC to assess LNs is the same as described for cervical cancer [10]. PET/CT improves N and M staging; however, PET/CT is currently not part of standard of care for initial staging of endometrial cancer.

18.2.3.4 Stage IV: Bladder/Rectal Mucosal Invasion or Extension Beyond the Pelvis

Please refer to section “MRI and Initial Staging of Cervical Carcinoma,” as the findings are the same for endometrial and cervical carcinoma.

18.2.4 Evaluation of Recurrence

Recurrent endometrial cancer has a similar imaging appearance as the primary tumor. Risk factors for recurrence include advanced stage at presentation, high-grade disease, and lymphovascular invasion. More than 80% of recurrences occur within 3 years of initial treatment with LNs (46%) and the vaginal vault (42%) being the most common sites. MRI is useful to evaluate surgical resectability of pelvis-confined recurrent disease, while PET/CT is helpful to exclude distant and LN metastases [6, 16].

18.3 Uterine Sarcomas

18.3.1 Epidemiology and Presentation

Uterine sarcomas are rare aggressive tumors originating from mesenchyme and comprising <3% of uterine corpus tumors [6, 21]. Leiomyosarcoma (LMS) is the most common histologic subtype, followed by endometrial stromal sarcoma (ESS) and undifferentiated uterine sarcoma. ESS is subdivided into low- and high-grade ESS based on differences in histopathology and clinical outcomes [21]. Carcinosarcoma

was previously categorized as uterine sarcoma but is now classified as high-grade endometrial carcinoma [6, 21].

Uterine sarcomas arise *de novo* and have no biologic link to LM [25]. Prompt radical surgery is the standard of care for uterine sarcomas [21]. In contrast, symptomatic LM can be approached with traditional surgery (hysterectomy, myomectomy) or newer minimally/noninvasive strategies (embolization, ablation, medical therapy). The latter do not yield histologic diagnosis, highlighting the need for precise initial diagnosis [26].

Uterine sarcoma and LM manifest with similar symptoms. Large size and rapid growth are unreliable signs of malignancy [25]. Growth of uterine mass after menopause and elevated LDH, particularly LDH isozyme type 3, should be viewed as suspicious for LMS [25]. Endometrial sampling may aid diagnosis of uterine sarcoma, but sensitivity is limited due to myometrial origin [21, 25].

18.3.2 Role of Imaging

MRI is the imaging method of choice if uterine sarcoma is suspected clinically or if intervention is planned for symptomatic LM (to map tumors and exclude sarcoma) [26].

No single MR feature can reliably distinguish uterine sarcoma (including LMS) from atypical LM (degeneration or histologic variants). Combined MR features may suggest correct diagnosis including a single large uterine mass with hemorrhage (high SI on T1-weighted imaging), heterogeneous high SI on T2-weighted imaging, infiltrative/nodular borders on T2-weighted imaging, and central necrosis [27]. Uterine sarcoma also demonstrates rapid early enhancement of solid components on DCE and restricted diffusion (Fig. 18.8) [27]. Diffusion restriction alone is insufficient for diagnosis because it may be observed with LM, especially cellular LM [27].

ESS often demonstrates distinct MR features that aid diagnosis including an ill-defined myometrial mass with endometrial component, wormlike low-SI bands on T2-weighted imaging (normal myometrium compressed by tumor), and contiguous extension along the fallopian tubes, periuterine vessels, and pelvic ligaments [6].

Key Points

- MRI excels at locoregional staging of cervical and endometrial cancer for treatment stratification, while PET/CT improves N and M staging in uterine malignancies.
- MRI facilitates patient selection prior to fertility preservation for early stage cervical and endometrial cancers.
- MRI aids the characterization of clinically suspected uterine sarcoma.

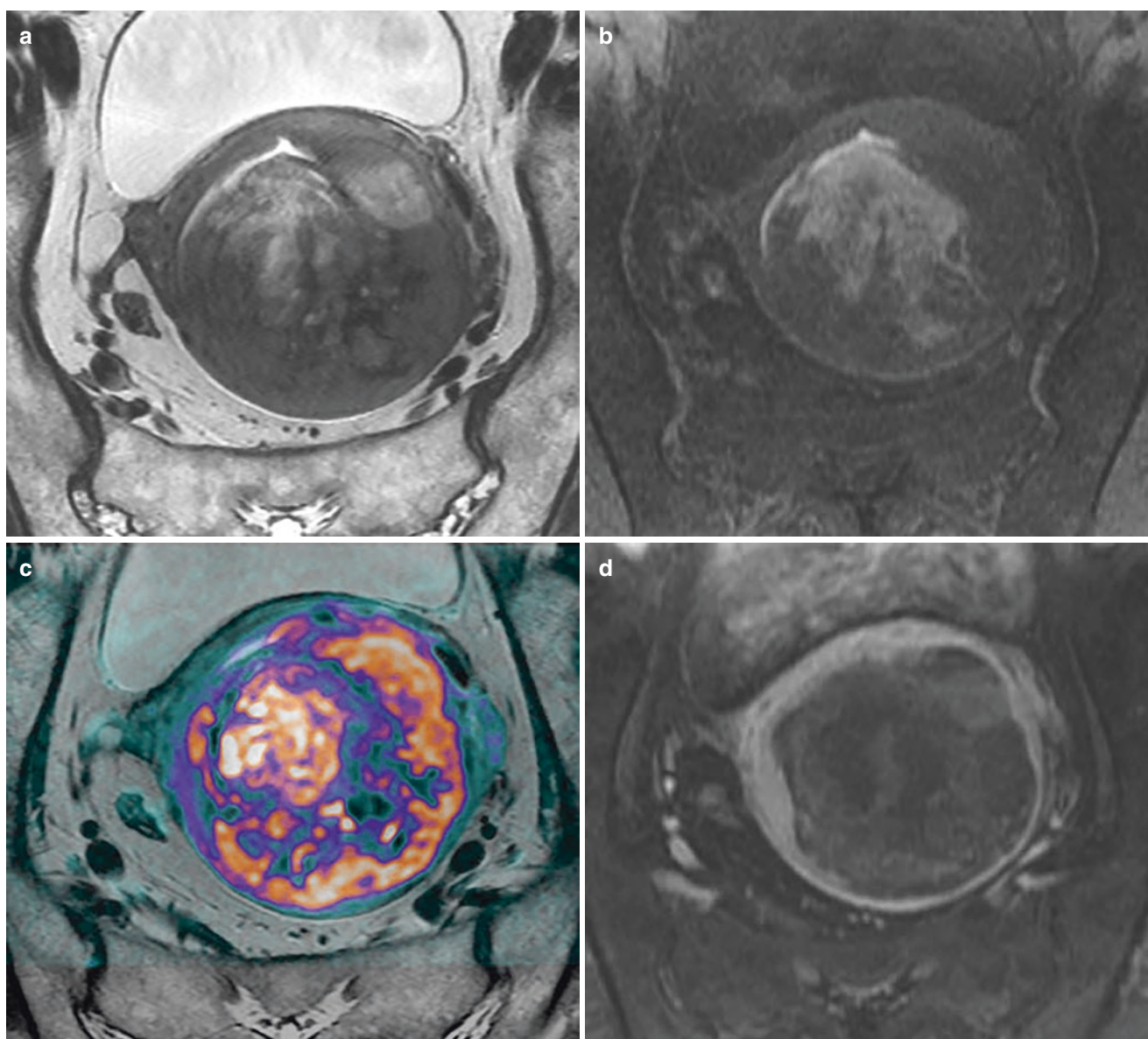


Fig. 18.8 69-year-old woman with uterine sarcoma. Short-axis images show ill-defined myometrial mass with heterogeneous high SI on T2-weighted imaging (a), hemorrhage on fat-saturated T1-weighted

imaging (b), diffusion restriction on fused T2-weighted imaging +DWI (c), and central necrosis on DCE (d)

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