Magnetic Resonance Imaging in Endometrial Cancer

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Introduction

Magnetic resonance imaging (MRI) has been widely accepted as the most reliable and accurate modality for diagnosis, staging, treatment planning, and follow-up of endometrial carcinoma. MRI is the best modality to assess the uterus given its excellent soft tissue resolution and direct multiplanar capabilities. It is the only modality that demonstrates the zonal anatomy of the uterus and therefore is essential for the preoperative staging of endometrial carcinoma. The depth of myometrial invasion is the most important morphologic prognostic factor and can only be accurately assessed with MRI [1].

Diffusion-weighted MRI and dynamic contrast-enhanced MRI are also useful adjuncts for evaluation of the uterus and pelvis in endometrial cancer.

Technique

Optimal MRI of the female pelvis should be performed on a high-field strength MRI system (1.5 T or 3 T systems) using local phased array coils. These surface coils provide increased signal to noise ratio which allows a small field of view image with high spatial resolution. An endoluminal coil (such as endo-vaginal/endorectal coil) has less patient acceptance and additionally causes local artifact; this is hence not used.

Imaging Protocols

It is recommended that prior to the MRI scan, the patient fasts for about 4 h to reduce artifact from bowel motion. Alternatively, an antiperistaltic agent such as hyoscine butyl bromide/glucagon can be administered. Vaginal gel, such as ultrasound gel, is inserted to distend the vagina.

Imaging is performed in sagittal, coronal, and axial planes and most importantly in an axial oblique plane perpendicular to the endometrial cavity. These high-resolution images obtained perpendicular to the uterus are important when assessing for myometrial invasion.

Diffusion-weighted images are obtained. Dynamic contrast images may also be obtained using a three-dimensional GRE T1-weighted LAVA acquisition after administration of gadolinium (at the rate of around 2 ml/s). Post-contrast images are obtained at around 25 s, 1 min, and 2 min and after 4 min [1]. This is done as the different zones of the uterus enhance at different

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times, and this is helpful to assess for the depth of myometrial invasion in endometrial carcinoma.

(Note: Gadolinium is generally avoided in women with renal impairment.)

Normal Uterine Anatomy

On T1-weighted images, the uterus is similar in signal intensity to the muscle, and the zonal anatomy is not displayed.

On T2-weighted images, however, zonal anatomy is excellently demonstrated [2] with the uterus showing three distinct zones (Figs. 8.1 and 8.2) as follows:

1. The central high-signal intensity endometrium
2. The middle low-signal junctional zone, i.e., the inner myometrium
3. The intermediate-signal outer myometrium

The central endometrium has a high T2 signal due to the endometrium and secretions. The endometrium varies in thickness with the menstrual cycle and menopausal status. It can measure up to 14 mm in the secretory phase but is thinned in the follicular phase. Postmenopausal women should have a homogenous endometrium with a width less than 5 mm [3].

The myometrium is separated into (1) the inner myometrium, also known as the junctional zone which appears like a low-signal band on T2-weighted images, and (2) the outer myometrium which has an intermediate T2 signal.

When using oral contraceptives, the endometrium becomes thinned and the junctional zone less prominent.

After menopause, the junctional zone is thinned and not visualized consistently.

Post-contrast, the junctional zone shows the earliest enhancement, the outer myometrium enhances slightly later, and the endometrium enhances last.

The cervix shows four distinct zones on T2-weighted images:

1. Central hyperintense-signal mucus.
2. High-signal endocervical mucosa and glands.
3. Hypointense fibrous stroma; this is continuous with the junctional zone of the uterus.
4. Outer intermediate-signal loose stroma.

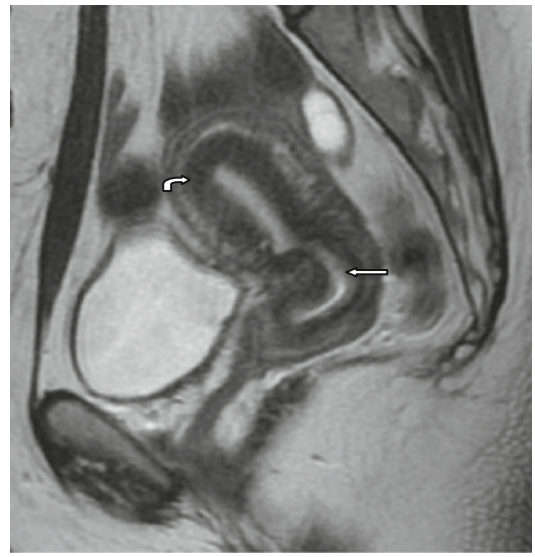

Fig. 8.1 Normal uterus; sagittal T2-weighted MRI clearly depicting the zonal anatomy of the uterus with the three zones displayed: intermediate signal of the endometrial lining (*straight arrow*), low signal of the junctional zone, i.e., the inner myometrium (*curved arrow*), and intermediate signal of the outer myometrium

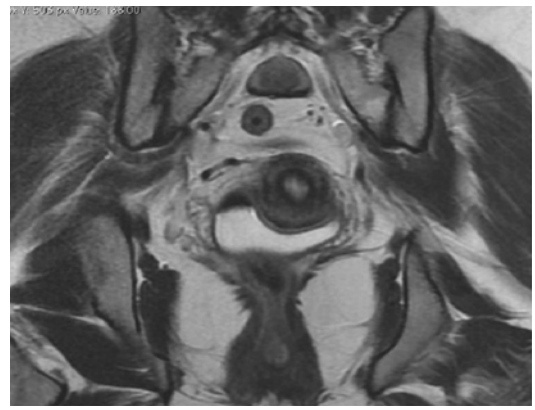

Fig. 8.2 Axial T2-weighted MRI showing three distinct zones of the uterus

MRI in Endometrial Carcinoma

MRI is essential for preoperative staging because it demonstrates the depth of myometrial invasion which is the most important morphologic prognostic factor. The depth of myometrial invasion and histological grade correlate strongly with the presence of lymph node metastases and patient survival. Lymph node metastases prevalence increases from 3 % with superficial myometrial invasion to 46 % with deep myometrial invasion [4, 5].

Evaluation of the extent of myometrial invasion by gross inspection at surgery or at frozen section remains inaccurate in a significant number of patients [6]. Though the majority of patients present with Stage 1A where the standard treatment is total abdominal hysterectomy with bilateral salpingo-oophorectomy, the challenge is to identify patients at risk for recurrence who would require more radical surgery or adjuvant therapy and avoid overtreating low-risk patients [6]. Preoperative MRI hence helps in this decision making between lymph node sampling for Stage 1A disease and radical lymph node resection for Stage 1B disease.

MRI also assesses more advanced disease such as cervical stromal involvement. Gross cervical invasion could require preoperative radiation therapy or a different surgical approach such as a radical hysterectomy rather than a total abdominal hysterectomy. Adnexal involvement, uterine tumor size/volume, and the presence of ascites or nodal disease can also be assessed. These can help determine the surgical approach such as transabdominal, transvaginal, or laparoscopic.

Full assessment of the abdomen can be done to assess for lymph nodal involvement/ hepatic or peritoneal disease. In high-risk patients for surgery due to comorbidities, MRI is helpful in planning alternative therapy such as radiation or hormonal therapy for Stage 1 disease. *Depth of myometrial invasion which is the most important morphologic prognostic factor can only be evaluated with MRI, as MRI is the only modality which demonstrates the zonal anatomy of the uterus.*

The FIGO staging system was updated in 2009 with three important changes which are relevant to MRI.

Tumors confined to the endometrium (previous Stage 1A) and those involving the inner half of the myometrium (previous Stage 1B) are now combined together in *Stage 1A*. This actually improves the accuracy of MRI, as with the old system distinguishing between the two was difficult in some patients due to thinning/loss of the junctional zone or poor tumor to myometrium contrast.

One of the important changes in the FIGO staging system (2009) is the clubbing together of tumors confined to the endometrium (previous Stage 1A) and those involving the inner half of the myometrium (previous Stage 1B); both come under Stage 1A. This improves the accuracy of MRI (Figs. 8.3 and 8.4).

The other change is in **Stage II**. IIA tumors were those with endocervical glandular invasion, and IIB tumors were those with cervical stromal invasion. In the new system, endocervical glandular invasion is included in Stage 1 disease and those with cervical stromal invasion, **Stage II** disease.

Stage IIIA disease invades the serosa or adnexa (Figs. 8.5 and 8.6).

Stage IIIB disease involves the vagina or parametrium. Vaginal invasion is shown as segmental loss of the low-signal line of the vaginal wall. Parametrial involvement appears as disruption of the serosa with direct extension into the surrounding parametrium.

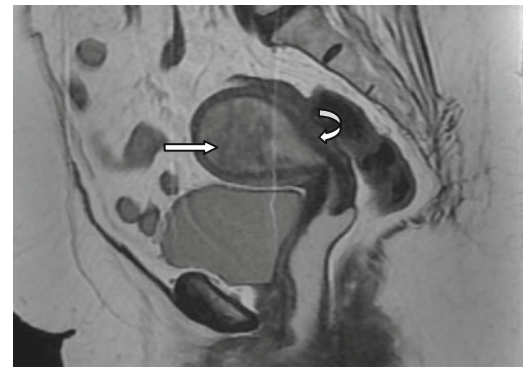

Fig. 8.3 81-year-old lady with postmenopausal bleed. Sagittal T2-weighted MRI showing a large mass filling the endometrial cavity (*straight arrow*). Intact junctional zone clearly demonstrated (*curved arrow*) with no extension of mass into the myometrium. No extension to the vagina

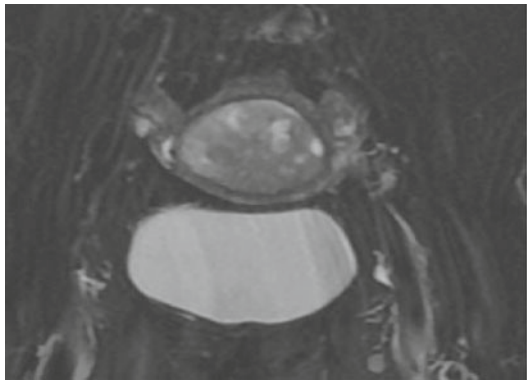

Fig. 8.4 Axial T2-weighted MRI showing the large mass filling the endometrial cavity. Intact junctional zone clearly demonstrated with no extension of mass into the myometrium

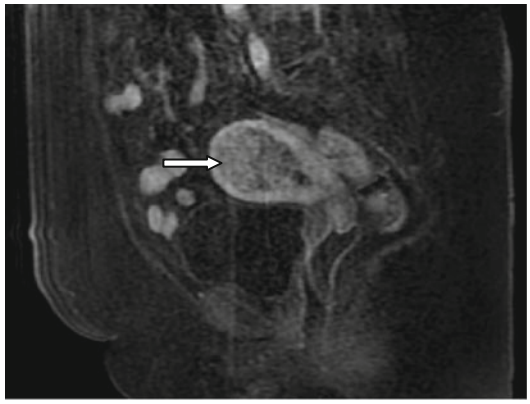

Fig. 8.5 Post-contrast sagittal T1 fat-suppressed image showing the mass in the endometrial cavity (*straight arrow*), enhancing less than the adjacent myometrium

MRI Appearances

Endometrial carcinoma shows heterogeneous intermediate-signal intensity on T2-weighted images when compared to the normal hyperintense endometrium.

It is mildly hyperintense on T2-weighted images when compared to the myometrium. The depth of myometrial penetration with extension beyond/breach of the junctional zone is well seen on the high-resolution T2 images in the sagittal plane and axial oblique plane obtained perpendicular to the endometrial cavity except where there is thinning of the junctional zone or poor tumor to myometrium contrast.

In a postmenopausal woman, in addition, there is often an overall thinning of the myometrium due to uterine involution which can render accurate assessment of myometrial invasion difficult.

Other pitfalls which make accurate assessment difficult include extension into the cornua, compression of the myometrium by a large polypoid tumor/tumor filling the endometrial cavity with compression of the overlying myometrium, and presence of leiomyomas or adenomyosis.

In these cases, additional imaging such as dynamic contrast or diffusion-weighted imaging is of help. The depth of myometrial penetration with extension beyond/breach of the junctional zone is well seen on the high-resolution T2

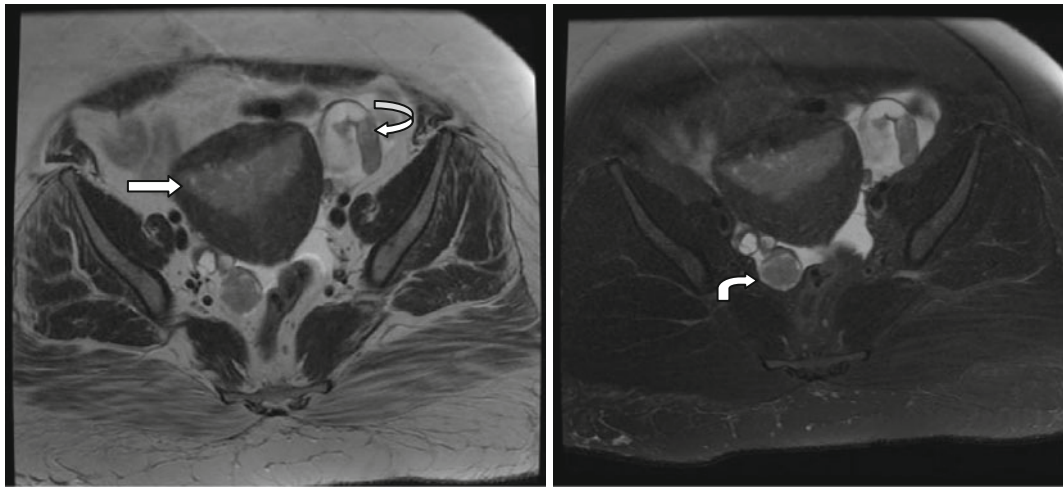

Fig. 8.6 39-year-old lady with biopsy-proven endometrial carcinoma, axial T2 and T2 fat-suppressed images showing mass in the endometrial cavity (*straight arrows*) and extension to the bilateral fallopian tubes (*curved arrows*) – Stage IIIA disease

images in the sagittal plane and most importantly in the axial oblique plane which is obtained perpendicular to the endometrial cavity.

Dynamic Contrast-Enhanced MRI

This has been shown to improve the diagnostic accuracy of MRI from 55 % to 77 % for routine non-contrast MRI to 85–91 % for dynamic contrast-enhanced images [6].

Differential enhancement of the tumor allows the tumor to be distinguished from non-enhancing blood products/debris.

In general, endometrial tumors enhance earlier than the normal endometrium and later than the adjacent myometrium. This helps in defining small tumors confined to the endometrium and also myometrial infiltration.

The early enhancement phase (0–1 min) allows identification of the junctional zone which enhances earlier than the rest of the myometrium. This is useful in detecting early myometrial invasion especially in postmenopausal women who have thinned junctional zones which make identification of this difficult on routine T2-weighted images. An intact junctional zone as indicated by a band of sub-myometrial enhancement excludes deep myometrial invasion.

The equilibrium phase (2–3 min after injection) allows better evaluation of deep myometrial invasion (maximum contrast between the myometrium and the endometrium is between 50 and 120 s).

Differential enhancement of the tumor allows the tumor to be distinguished from non-enhancing blood products/debris. Different zones of the uterus enhance at different times, and this is helpful to assess for the depth of myometrial invasion in endometrial carcinoma.

The delayed phase (3–4 min) helps in the evaluation of cervical stromal involvement.

Diffusion-Weighted Imaging

Diffusion-weighted imaging has recently proved to be able to distinguish between normal and endometrial disease. As endometrial tumors have high cellularity, they appear bright on diffusion-weighted images. T2 images and contrast-enhanced images have traditionally been used to determine the depth of myometrial invasion. Dynamic contrast images are helpful to detect depth of myometrial penetration as most of the tumors are hypovascular relative to the vascular myometrium and hence stand out well. However, a significant number of tumors are iso- or hypervascular relative to the myometrium, and hence, these tumors are not well delineated on contrast-enhanced imaging. Diffusion is however independent of differences in vascularity and hence can be very useful for detecting myometrial invasion [7]. It has been found to depict tumor foci that are not appreciated on T2 or contrast images in the uterus or even peritoneal spread. It is also very useful when contrast administration is not possible such as in renal failure. As endometrial tumors have high cellularity, they appear bright on diffusion-weighted images, and this can be a useful adjunct to determine the depth of myometrial invasion (Figs. 8.7–8.15).

The only drawback of diffusion-weighted images is reduced anatomic detail and decreased signal intensity. To overcome the morphologic deterioration of diffusion-weighted images, fusion of the T2-weighted images with diffusion-weighted images has been performed to assess for myometrial invasion [8].

Diffusion-Weighted Imaging of Nodal Disease

Both benign and malignant nodes appear bright on diffusion with low ADC values. Necrotic areas in nodes can be misleading. Comparison of the signal intensity of the primary tumor with the nodes can be helpful. Diffusion-weighted imaging can be used for node mapping, especially in patients with ascites or paucity of intra-abdominal fat.

Lymph Node Disease

MRI and CT both rely on size criteria, both having a comparable accuracy in detecting lymph nodal metastases, 83–90 % for CT and 86–90 % for MRI [6]. Relying on size criteria results in a low sensitivity (43–73 % for MRI) as metastasis in normal-sized nodes is not detected.

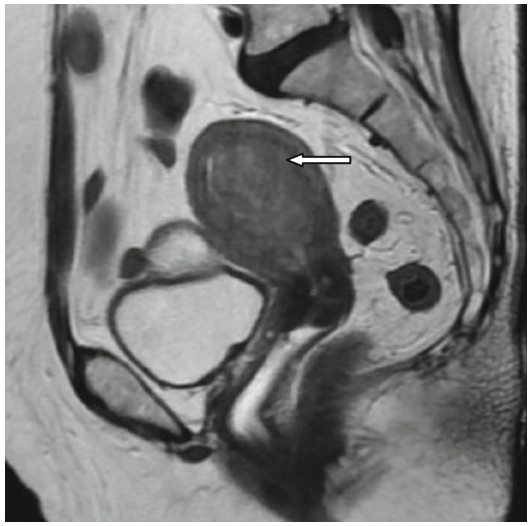

Fig. 8.7 83-year-old lady with history of postmenopausal bleed; T2 sagittal MRI showing mass filling the endometrial cavity (*straight arrow*). Poor tumor to myometrial differentiation is noted, making accurate assessment of myometrial infiltration difficult

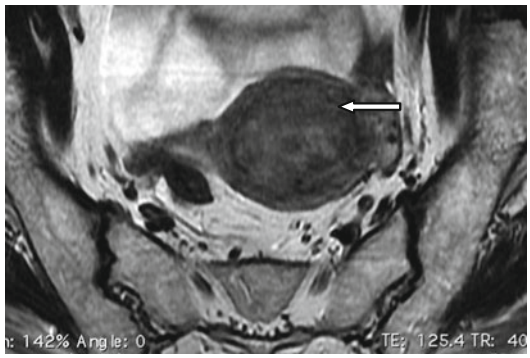

Fig. 8.8 Axial T2 weighted image with history of postmenopausal bleed; T2 axial MRI showing mass filling the endometrial cavity (*straight arrow*). Poor tumor to myometrial differentiation is noted, making accurate assessment of myometrial infiltration difficult

The use of lymph node-specific MRI contrast agents such as ultrasmall super-paramagnetic iron oxide (USPIO) particles has been shown to improve the sensitivity and specificity of detection [9]. Rockall et al. [9] showed an increase in sensitivity from 29 % to 93 % when using USPIO on a node to node basis and an increase from 27 % to 100 % on a patient to patient basis.

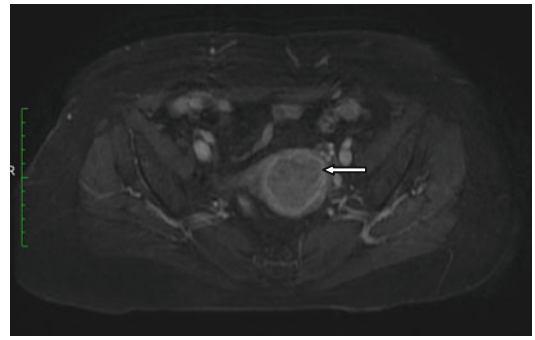

Fig. 8.9 Post-contrast axial T1-weighted fat-suppressed image showing mass in the endometrial cavity surrounded by intact early and brightly enhancing junctional zone (*straight arrow)*; early contrast phase allowing easy distinction of the endometrial mass from the junctional zone

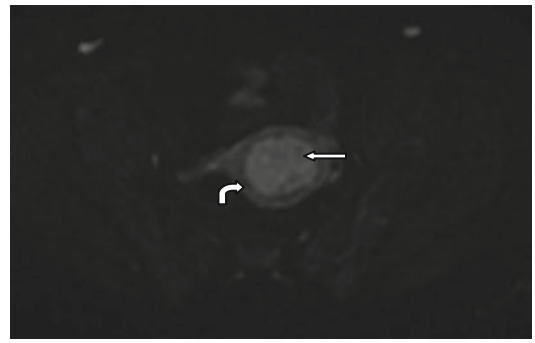

Fig. 8.10 Diffusion-weighted image showing restricted diffusion (bright signal) in the endometrial mass confined to the endometrial cavity (*straight arrow)*. Low-signal intact junctional zone (*curved arrow*) clearly depicted surrounding the mass with no extension of mass into the myometrium

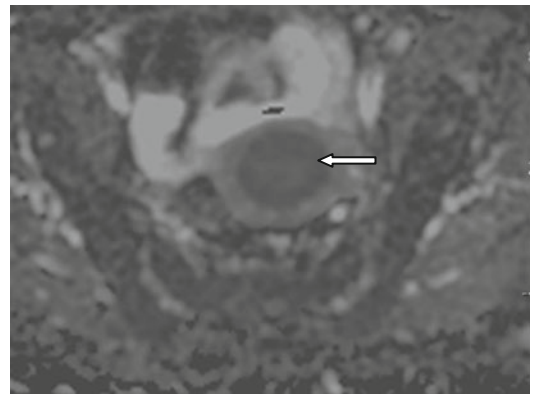

Fig. 8.11 ADC map at the same level showing low signal in the corresponding region (*straight arrow*), confirming restricted diffusion

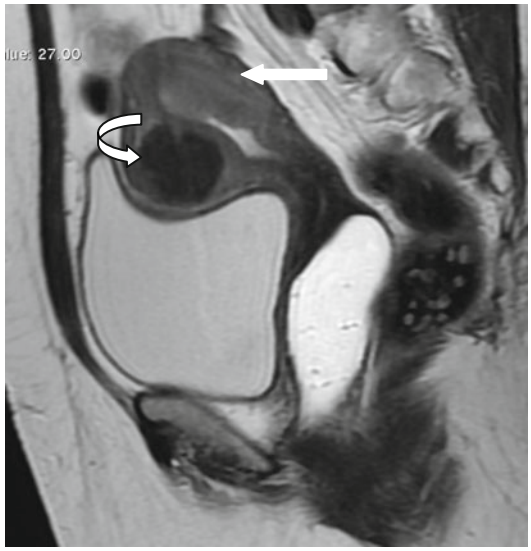

Fig. 8.12 63-year-old lady with postmenopausal bleed, T2 sagittal and axial MRI showing mass in the endometrial cavity infiltrating the myometrium (*straight arrow*). An anterior wall fibroid is also noted (*curved arrow*)

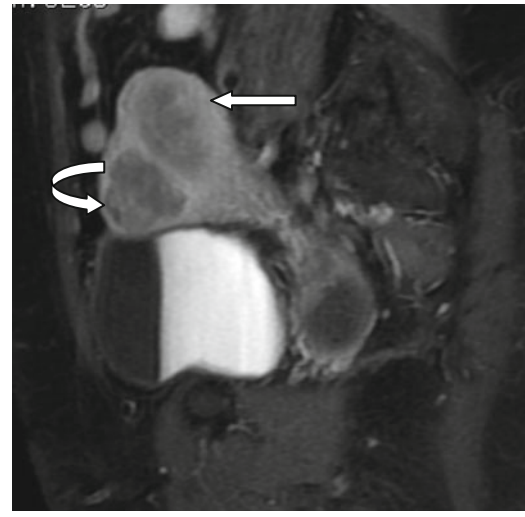

Fig. 8.14 63-year-old lady with postmenopausal bleed, T1 sagittal and axial MRI showing mass in the endometrial cavity infiltrating the myometrium, more than 50 % thickness (*straight arrow*). An anterior wall fibroid (*curved arrow*) is also noted

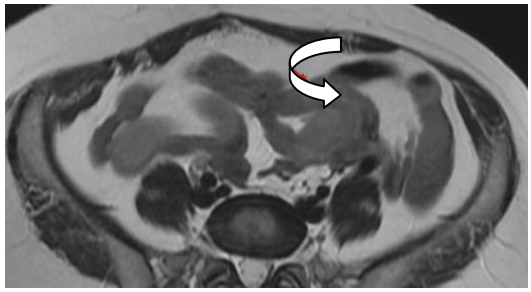

Fig. 8.13 63-year-old lady with postmenopausal bleed, T2 sagittal and axial MRI showing mass in the endometrial cavity infiltrating the myometrium (*curved arrow*)

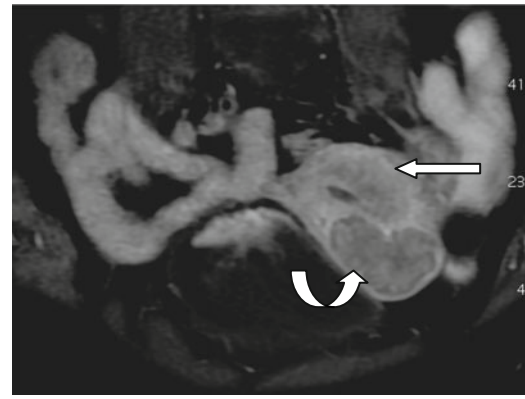

Fig. 8.15 63-year-old lady with postmenopausal bleed, T1 sagittal and axial MRI showing mass in the endometrial cavity infiltrating the myometrium, more than 50 % thickness (*straight arrow*). An anterior wall fibroid (*curved arrow*) is also noted

Recurrent Disease

Most recurrence occurs within 2 years of therapy, and the most common sites include the vaginal vault. Other sites include the perirectal fascia, pelvic and retroperitoneal lymph node, and the pelvic side wall. Distant metastases such as liver, bone, and peritoneal metastases are also seen.

Vaginal vault recurrence after surgery is indicated by the loss of the low-signal intensity linear configuration and replacement by a high-signal intensity soft tissue mass, similar in signal to the initial primary tumor. When a patient has had radiation, distinguishing between recurrent disease and postradiation changes is critical. Recurrent disease appears as a heterogeneous soft tissue mass of similar signal to the initial tumor, while fibrosis has a low T2 signal [6].

Note is made, soon after radiation, due to inflammation and edema in the adjacent soft tissues; parametrial invasion can be overestimated due to edema showing high T2 signal similar to the primary tumor [2].

Delayed enhancement is not specific and can be seen in recurrent tumors/postradiation fibrosis/inflammation/radiation necrosis.

On dynamic contrast scans, however, recurrent mass shows earlier enhancement than fibrosis (maximum enhancement at around 45–90 s). Contrast scans are also helpful in assessing parametrial and side wall recurrence.

When not clear, serial imaging, imaging-guided biopsy, or PET may be required for clarification.

Sarcomas of the Uterus

These are rare and account for 3–5 % of all uterine cancers. MRI can provide information about their size and extent preoperatively. Uterine sarcomas are broadly divided into three groups: smooth muscle tumors, endometrial stromal tumors, and tumors with both smooth and epithelial components. The primary modality for imaging the uterus is MRI in view of its ability to demonstrate local spread well. CT is however commonly used for staging, assessment of metastases, and follow-up.

1. Carcinosarcomas are the most common uterine sarcomas. They generally appear as large broad-based bulky masses replacing the endometrial cavity and can prolapse through the endocervical canal. They may have a stalk-based attachment or multifocality. Hemorrhage and necrosis are prominent features. Though they can spread hematogenously, local lymphatic spread and intraperitoneal seedling are more common. These tumors are staged using the same FIGO staging as for endometrial carcinoma.
2. Leiomyosarcomas may arise de novo from the uterine musculature or connective tissue of a blood vessel or in a previously existing leiomyoma. They usually present as massive uterine enlargement with extensive necrosis and hemorrhage. Spread occurs to the myometrium, lymph nodes, and contiguous pelvic structures and distantly to the lungs. An irregular margin has been suggested as a finding to suggest sarcomatous transformation of a leiomyoma, but the specificity of this finding has not been proven yet [10].
3. Low-grade endometrial stromal sarcomas tend to invade the myometrium and adjacent structures. They can have a variable appearance appearing as a polypoid endometrial mass to a myometrial mass mimicking a leiomyoma with cystic degeneration. A high-grade endometrial sarcoma has a more aggressive appearance with infiltration of the myometrium in a destructive manner and areas of hemorrhage and necrosis. On MRI, they often appear as a large polypoid markedly heterogeneous mass showing contiguous extension into adjacent structures because of marked vascular and lymphatic involvement of the tumor [10].

Conclusion

MRI is superior to CT in the staging of uterine malignancies, in particular with regard to endometrial carcinoma. In addition, it may aid in differentiating radiation fibrosis from recurrent tumor. MRI has been shown to be a "one-stop shop" minimizing the costs in some clinical settings and obviating the need for more expensive invasive diagnostic tests or surgical procedures.

Key Points

1. Depth of myometrial invasion is the most important morphologic prognostic factor that can only be evaluated with MRI. MRI is the only modality which demonstrates the zonal anatomy of the uterus.

2. One of the important changes in the FIGO staging system (2009) is the clubbing of tumors confined to the endometrium (previous Stage 1A) and those involving the inner half of the myometrium (previous Stage 1B); both now come under Stage 1A. This improves the accuracy of MRI.
3. The depth of myometrial penetration with extension beyond/breach of the junctional zone is well seen on the high-resolution T2 images in the sagittal plane and most importantly in the axial oblique plane which is obtained perpendicular to the endometrial cavity.
4. Differential enhancement of the tumor allows the tumor to be distinguished from non-enhancing blood products/debris. Different zones of the uterus enhance at different times, and this is helpful to assess for depth of myometrial invasion in endometrial carcinoma.
5. As endometrial tumors have high cellularity, they appear bright on diffusion-weighted images, and this can be a useful adjunct to determine depth of myometrial invasion.

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