Pre-operative MRI of Endometrial Cancer: Clinically relevant findings and pitfalls to avoid.

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Objectives

- Overview of normal MRI uterine anatomy
- Describe MR imaging features and staging of endometrial cancer
- Learn to differentiate the appearance of endometrial cancer from endometrial hyperplasia, adenomyosis, fibroids, and polyps
- Highlight common pitfalls encountered in the MRI assessment of endometrial cancer
Introduction

- Endometrial cancer
  - 4th most common cancer in women
  - Most common gynecologic malignancy

- Peak incidence: 55 and 65 years

- Risk factors
  - Obesity
  - Nulliparity
  - Late menopause
  - Unopposed estrogen exposure
  - Tamoxifen
Over 80% of patients present with early stage disease due to symptoms of abnormal uterine bleeding, with an overall excellent prognosis.

Endometrial cancer is traditionally surgically staged and the treatment varies by stage, grade, regional guidelines, and expertise.

MRI is a valuable adjunct to pre-operative planning as it can accurately depict endometrial cancer. The goal of MRI is to identify patients pre-operatively who would benefit from abdominopelvic lymph node dissection and adjuvant therapy while avoiding overtreating early stage patients with unnecessary lymphadenectomies.
MRI Protocol

Preparation
- To minimize bowel motion consider
  - Fasting for 4-6 hours prior to the study
  - Anti-peristaltic medications prior to exam
- Empty bladder to avoid motion artifact

Basic Protocol
- Torso or Cardiac Coil
- Axial/Sagittal T1-pre and -post contrast images
- Axial/Sagittal T2-wt images with fat saturation
- Dynamic contrast enhanced images - 40 and 90 sec
- Axial and sagittal diffusion weighted images

Figure: Sagittal T2-wt, sagittal T1-post contrast, axial T1-wt, axial T2-wt, and diffusion weighted imaging of the pelvis. These images demonstrate a mass within the endometrial cavity ( ).
Normal MRI Uterine Anatomy

- Uterus has three distinct layers
  - Endometrium
  - Junctional zone
  - Myometrium

- Anatomy best delineated on T2-wt images

**Figure:** Sagittal T2-wt fat-saturated image demonstrates the normal trilaminar appearance of the uterus. The T2 hyperintense endometrium (e), the hypointense junctional zone (jz), and isointense myometrium (m) creates the trilaminar appearance. The cervix demonstrates a hyperintense endocervical canal and hypointense cervical (cs) stroma. Bladder (b), vagina (v), rectum (r).
Endometrial Cancer Staging and Grading

Risk stratification and treatment planning is based on tumor histology and tumor stage.

- **Tumor Histology**: pre-operative from endometrial biopsy
  - Tumor grade: I-III (well - poorly differentiated)
  - Tumor cell type: 90% adenocarcinoma with endometroid subtype. Clear cell and papillary serous carcinoma have a worse prognosis.

- **Tumor Stage**: surgically staged in the OR
  - Based on 2009 International Federation of Gynecologic and Obstetrics (FIGO) Surgical Staging System
  - Full staging consists of total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal washings, and retroperitoneal lymph node dissection
  - Key prognostic factors are depth of myometrial invasion (MI), cervical stromal invasion, and lymphovascular invasion (LVSI)

### FIGO 2009 Surgical Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Tumor confined to uterus, &lt;50% MI</td>
</tr>
<tr>
<td>IB</td>
<td>Tumor confined to uterus, ≥50% MI</td>
</tr>
<tr>
<td>II</td>
<td>Cervical stromal invasion</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumor invasion into serosa or adnexa</td>
</tr>
<tr>
<td>IIIB</td>
<td>Vaginal or parametrial involvement</td>
</tr>
<tr>
<td>IIIC1</td>
<td>Pelvic node involvement</td>
</tr>
<tr>
<td>IIIC2</td>
<td>Para-aortic node involvement</td>
</tr>
<tr>
<td>IVA</td>
<td>Tumor invasion into bladder/bowel mucosa</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

Figure modified from: Beddy et al. FIGO Staging System for Endometrial Cancer. RadioGraphics 2012
Goals of MRI

- Depict endometrial cancer origin (endometrial vs endocervical)
- Determine the depth of myometrial invasion (MI)
  - Most important morphologic prognostic factor
  - Prevalence of lymph node metastasis increases from 3% with superficial MI to 46% with deep MI
- Sensitivity/specificity of MRI for MI approaches 94%/100%
- Evaluate for cervical stromal involvement (CI) and extra-uterine spread
  - Sensitivity and specificity of MRI for CI approaches 96%/80% respectively
- Additional imaging features (uterine size, tumor volume, ascites and adnexal disease) may also determine surgical approach (open laparotomy vs transvaginal vs laparoscopic; +/- lymphadenectomy)
- Overall reported accuracy of MRI for endometrial cancer staging approaches 93%

Grade 1/2:
If there is greater than 50% MI, positive cervical or extrauterine spread, the risk of lymph node metastasis increases and lymphadenectomy is performed at some institutions.

Grade 3:
MRI gives the surgeon information about the extent of the spread of disease which can help with choosing the surgical approach.

### FIGO 2009: Management based on Stage

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<tr>
<td>IA</td>
<td>Tumor confined to uterus, &lt;50% myometrial invasion</td>
<td>Surgery</td>
</tr>
<tr>
<td>IB</td>
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<td>Surgery +/- vaginal brachytherapy</td>
</tr>
<tr>
<td>II</td>
<td>Cervical stromal invasion</td>
<td>Surgery + vaginal brachytherapy +/- pelvic radiotherapy</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>IIIB</td>
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<td>Surgery + pelvic radiotherapy +/- chemotherapy</td>
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<td>IIIC1</td>
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<td>Distant metastases</td>
<td>+ Hormonal Rx</td>
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Tumor on T2-wt images
- Intermediate signal intensity relative to the hyperintense endometrial lining
- Mildly hyperintense relative to isointense myometrial lining

Figure: Sagittal T2-wt fat-saturated images in two patients with endometrial cancer. In image A, there is diffuse intermediate signal intensity thickening (→) of the endometrium. No normal endometrium is identified. In image B, the intermediate signal intensity tumor (*) is well-differentiated from the surrounding normal hyperintense endometrium (→). Note the disruption of the junctional zone and extension into the myometrium inferiorly (→).
- **T1-pre contrast imaging**
  - Tumor isointense relative to hypointense normal endometrium on unenhanced images
  - Often difficult to discern on pre- contrast imaging, especially in small tumors

- **T1-post contrast images**
  - Dynamic contrast enhanced images are obtained
  - **Tumor enhances homogenously and more slowly with less avidity than adjacent myometrium**
  - Endometrial tumors enhance earlier than normal endometrium

**Figure**: Sagittal T2-wt and T1-post contrast images in a 55 year old female with endometrial cancer. The tumor demonstrates intermediate T2 signal intensity (→) as well as hypoenhancement (*) relative to the avidly enhancing myometrium (→). Note the irregular myometrial contour (→) consistent with myometrial invasion.
Endometrial cancer demonstrates diffusion restriction compared to surrounding tissue

Diffusion weighted imaging (DWI)
- B=0, B=500 and ADC maps
- The tumor will become progressively brighter from B=0 to B=500
- On the ADC map, the tumor is dark relative to the endometrium and myometrium, but can blend in with the junctional zone

Figure: Sagittal T2-wt, T1-post-contrast and diffusion weighted images. The tumor appears round, minimally hyperintense on T2-wt images (↑), hypointense compared to avidly enhancing myometrium on post contrast images (↑), and on DWI (↑) was gray on B=0, bright on B=500 and dark on ADC map. In this case there is greater than 50% myometrial invasion.
Depth of myometrial invasion is optimally seen on T2-wt images and DWI images

Figure: (A) Sagittal T2-weighted image of the deepest extent of myometrial invasion. Measure the depth of myometrial invasion by drawing a line along the expected inner edge of the myometrium. Then draw lines measuring the thickness of the entire myometrium and the extent of tumor invasion into the myometrium. The ratio of the black line over the white line is the percentage of MI. (B) B=0, B=500, and ADC map depicting the tumor. Use the DWI image to aid in your measurement and help find the deepest extent of MI.
Stage IA

- Stage 1 tumors account for over 80% of cases
- Abnormal signal intensity on T2-wt images confined to the endometrium as well as tumor that invades less than 50% of the myometrium

Figure: Sagittal T2-wt, T1-post contrast and diffusion weighted images in a 68 y/o female with Stage IA endometrial cancer. The abnormal signal intensity on the T2-wt image is confined to the endometrium (→). There is preservation of the junctional zone (→) and no evidence of myometrial invasion. The mass restricts diffusion (→) on the ADC map.

Figure: Sagittal T2-wt and T1-post contrast images in a 64 y/o female with Stage IA endometrial cancer. There is focal abnormal T2 signal intensity involving the endometrium (*). There is disruption of the junctional zone anteriorly and posteriorly in the region of the body with less than 50% myometrial invasion (→). No cervical invasion.
Figure: T2-wt and T1-post contrast images in a 59 year old female with Stage IB endometrial cancer. The abnormal signal intensity on the T2-wt images involves greater than 50% of the myometrium (→). T1-post contrast images provide tumor to myometrium contrast and demonstrates the hypoenhancement of the tumor (→) relative to the adjacent myometrium.
Direct invasion of the cervical stroma

Tumor demonstrates intermediate to high signal intensity on T2-wt images that disrupts the normal low signal intensity cervical stroma

Radical hysterectomy is required for these patients as opposed to total abdominal hysterectomy in earlier stage patients

Lymphadenectomy is also performed at many institutions in these patients

**Figure:** T2-wt and T1-post contrast images in a 51 year old female with Stage II endometrial cancer. There is a lobulated T2 hyperintense non-enhancing mass along the posterior uterine wall in the lower uterine segment (→). The mass splays open the endocervical canal (→) and extends into the hypointense cervical stroma (→).
Stage III and IV

- **IIIA**
  - Invasion of uterine serosa or adnexa

- **IIIB**
  - Invasion into upper vagina or parametrium

- **IIIC**
  - Enlarged regional lymph nodes
    - IIIC1-pelvic lymph node involvement
    - IIIC2-paraortic lymph node involvement

- **IVA**
  - Bladder or rectal wall invasion

- **IVB**
  - Distant metastasis
    - Lymphadenopathy above the renal vein, malignant ascites or peritoneal carcinomatosis

- **Imaging features of lymph node metastasis**
  - Size criteria > 1 cm in short axis diameter
  - Rounded or irregular contour
  - Multiplicity
  - Central necrosis
  - Diffusion restriction
  - Hypermetabolic activity on PET
  - However, metastasis can be present in normal sized lymph nodes!

**Figure:** Axial T2-wt and T1-post contrast images in a 56 year old female with stage IIIC1 endometrial cancer. There is an enlarged 1.5 cm rounded left external iliac lymph node present (→). Notice there is an area of intermediate signal in the endometrial canal on the T2-wt image (←), which is seen to subtly enhance on the T1-post image (→).
Benign mimics of Endometrial Cancer

- Fibroid
- Adenomyosis
- Polyp
- Endometrial hyperplasia
Figure: Sagittal T2-wt, T1-post contrast and diffusion weighted images demonstrating two large fibroids (→, ←), one of which is degenerating (→). Fibroids typically demonstrate low T1 and T2 signal and heterogeneous enhancement; however, degenerating fibroids demonstrate increased T2 signal intensity. Typical fibroids will be dark on B=0, B=500 and the ADC map. Degenerating fibroids will be bright on the B=0 and B=500, having a variable appearance on the ADC map.
Adenomyosis

Figure: Sagittal T2-wt and diffusion weighted images in a 45 year old female with adenomyosis (→) and concurrent endometrial cancer (→). Adenomyosis is defined as the presence of heterotopic endometrial glands and stroma in the myometrium with adjacent smooth muscle hyperplasia. MRI imaging features include diffuse widening of the junctional zone with bright T2 foci within the junctional zone (corresponds to heterotopic endometrial tissue); both of these findings are seen in this case. PITFALL: In patients with coexistent endometrial cancer and adenomyosis, myometrial invasion is often overestimated leading to staging errors. In this case, less than 50% myometrial invasion was called on MRI and pathology demonstrated no myometrial invasion.
Figure: Sagittal T2-wt, T1-post contrast and diffusion weighted imaging in a 55 year old female demonstrating a polyp in the endometrial canal. Polyps can demonstrate low T2 signal intensity secondary to the central fibrous core. However, polyps can also contain glandular secretions and cystic areas and therefore can also demonstrate high T2 signal. Polyps enhance briskly and sometimes have a “lace-like” appearance on the post-contrast images. When polyps are dark on the T2-wt images, they are dark or isointense on B=0, B=500 and ADC map compared with endometrium. When polyps display high signal on T2-weighted images, they will follow the endometrium on B=0, B=500 and ADC map. PEARL: Diffusion weighted imaging is key, polyps won’t restrict diffusion while endometrial cancer will.
Figure: Same case! There is concurrent endometrial hyperplasia (→) in the canal. PEARL: The appearance of the tissue surrounding the polyp (→) is T2 bright and is bright on B=0, B=500 and ADC map, typical of endometrial hyperplasia. Endometrial hyperplasia does not restrict diffusion.
Same patient…keep looking

Figure: Sagittal T2-wt, T1-post and diffusion weighted images again in the same patient, now to the right of midline. The patient also has concurrent endometrial cancer (➡️). The round area within the fundus demonstrates T2 hyperintensity, minimal enhancement, slight hypointensity compared to endometrium on B=0, becomes bright on B=500, and is dark on the ADC map. This is consistent with endometrial cancer. Adjacent hyperplastic endometrium is bright on B=0, B=500 and ADC (➡️). This was proven on surgical pathology.
Concurrent endometrial cancer, hyperplasia and polyp

Figure: Axial T2-wt, T1-post-contrast and diffusion weighted images depict all three entities in one plane. Endometrial hyperplasia (→) is hyperintense to myometrium on T2-wt images and is bright on all DWI images and the ADC map. Endometrial cancer (→) and the polyp (→) are isointense to myometrium on the T2-wt images and enhance on post contrast images. The endometrial cancer becomes brighter on the B=500 image and darker on the ADC map. The endometrial polyp remains dark on all DWI images and ADC map. These findings were confirmed on surgical pathology.
Summary

- MRI is excellent at depicting uterine anatomy and assessing endometrial cancer.
  - Tumor size and extension
  - Myometrial invasion
  - Parametrial/cervical invasion
  - Lymphadenopathy

- Although currently endometrial cancer is staged surgically, MRI does play a critical role in pre-operative planning.

- Differentiating endometrial cancer from co-existing endometrial hyperplasia, adenomyosis, fibroids, and polyps is important in the accurate assessment of endometrial cancer.
Sources

- Siegelman E. Body MRI. Saunders 2005
THANK YOU FOR YOUR ATTENTION!

Questions or Comments? Please feel free to contact us at KPatellipmann@uwhealth.org or ESadowski@uwhealth.org.