

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:** Endometrial Cancer of the Uterus

**Variant 1:** Newly diagnosed endometrial cancer; diagnostic work-up and staging.

Radiologic Procedure	Rating	Comments	<a href="#">RRL*</a>
MRI pelvis with contrast	8	See statement regarding contrast in text under "Anticipated Exceptions."	None
X-ray chest	6		Min
MRI abdomen with contrast	4	See statement regarding contrast in text under "Anticipated Exceptions."	None
CT abdomen with contrast	4		Med
CT pelvis with contrast	4		Med
US pelvis transvaginal	4		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Variant 2:** Assessing the depth of myometrial invasion.

Radiologic Procedure	Rating	Comments	<a href="#">RRL*</a>
MRI pelvis with contrast	9	See statement regarding contrast in text under "Anticipated Exceptions."	None
MRI pelvis without contrast	6		None
CT pelvis with contrast	4		Med
US pelvis transvaginal	4		None
US hysterosonogram	1	Very low risk of malignant cell dissemination into peritoneal cavity.	None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Variant 3:** Lymph node evaluation.

Radiologic Procedure	Rating	Comments	<a href="#">RRL*</a>
CT pelvis with contrast	8	Either CT or MRI is appropriate.	Med
MRI pelvis with contrast	8	Either CT or MRI is appropriate. See statement regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body	5	Applies to stand-alone PET without CT or MRI on all endometrial cancer including grade I. Fusion PET/CT under investigation.	High
US pelvis transvaginal	2		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Clinical Condition:****Endometrial Cancer of the Uterus****Variant 4:****Assessing endocervical tumor extent.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
MRI pelvis with or without contrast	8	See statement regarding contrast in text under "Anticipated Exceptions."	None
US pelvis transvaginal	4		None
CT pelvis with contrast	4		Med
<b><u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate</b>			<b>*Relative Radiation Level</b>

# ENDOMETRIAL CANCER OF THE UTERUS

Expert Panel on Women's Imaging: Susanna I. Lee MD, PhD<sup>1</sup>; Rochelle F. Andreotti, MD<sup>2</sup>; Teresita L. Angtuaco, MD<sup>3</sup>; Arthur C. Fleischer, MD<sup>4</sup>; Mindy M. Horrow, MD<sup>5</sup>; Marcia C. Javitt, MD<sup>6</sup>; Anna S. Lev-Toaff, MD<sup>7</sup>; Leslie M. Scoutt, MD<sup>8</sup>; Carolyn Zelop, MD.<sup>9</sup>

## **Summary of Literature Review**

Cross-sectional imaging in the pretreatment evaluation of gynecologic cancer patients can play an important role. In cancer of the uterus, it offers an assessment of morphologic prognostic factors, including tumor size, depth of penetration, stage of disease, and lymph node status. Imaging should be viewed as a complementary tool rather than competitive with the other methods of tumor evaluation (eg, clinical or surgical assessment).

### **Clinical Background and Prognostic Factors**

Endometrial carcinoma is the fourth most common cancer in women and the leading invasive malignancy in the female genital tract. About 39,080 new cases and 7,400 deaths were expected in the United States in 2007 [1]. Endometrial cancer primarily presents at stage I (80% of cases), and the recommended treatment is total abdominal hysterectomy and bilateral salpingo-oophorectomy. Depending on prognostic factors such as depth of myometrial invasion and tumor grade, lymphadenectomy may also be indicated. The major diagnostic factors necessary for the preoperative evaluation of endometrial cancer are:

1. Determination of the risk of lymph node metastasis in order to have subspecialist surgical consultation available.
2. Diagnosis of gross cervical invasion, which requires preoperative radiation therapy or a different treatment plan, (ie, radical hysterectomy instead of total abdominal hysterectomy).
3. Detection of advanced disease.

The most important prognostic variables for carcinoma of the uterus are the histologic grade and the stage of tumor (Appendix 1), including depth of myometrial invasion and lymph node metastasis [2,3]. In a study of 1,566 patients with adenocarcinoma of the uterus, the depth of

myometrial invasion was found to be the single most important prognostic factor. In stage IA and IB disease, when the tumor is confined to the endometrium or to the superficial myometrium, the incidence of para-aortic lymph node metastases is <2.5%. Conversely, in stage IC disease, when there is deep myometrial invasion, para-aortic lymph node metastases occur in 15%-45% [3,4].

The International Federation of Gynecology and Obstetrics (FIGO) staging is not accurate to assess the depth of myometrial invasion or the presence of lymphadenopathy. Because clinical staging carries an overall error in understaging of about 13%-22%, FIGO has recommended routine surgical staging since 1988 [2]. Preoperative imaging of endometrial carcinoma can define the extent of disease in order to tailor treatment and indicate referral to a subspecialist if deep myometrial invasion, cervical extension, or lymphadenopathy is suspected. Diagnostic imaging may also be helpful in a primarily obese, elderly population in which radiation therapy rather than surgery might be advocated as a primary treatment or as a preoperative adjuvant to surgery.

### **Use of Imaging in Clinical Guidelines**

#### *Transabdominal and Transvaginal Ultrasound*

Transabdominal ultrasound (US) is considered unreliable in staging endometrial cancer. The use of transvaginal US has shown some promise in the evaluation of myometrial invasion. Reported accuracies for myometrial invasion in stage I range from 69%-93% in differentiating deep invasion (stage IC) from absent or superficial invasion (stages IA and IB) [5-10], and from 68%-69% in differentiating stage IA from stage IB from stage IC [11,12]. A study using high-frequency transvaginal US showed a similar accuracy of 73% in assessing myometrial invasion [13]. However, studies directly comparing the accuracy of transvaginal US to that of contrast-enhanced magnetic resonance imaging (MRI) for staging have consistently demonstrated that the latter performs with greater accuracy [6,12].

In addition, there are insufficient reports about the value of transvaginal US in predicting cervical extension, parametrial invasion, or lymphadenopathy. In one study, transvaginal US showed cervical involvement in only 7 of 10 patients with cervical extension [14].

Hysterosonography, (ie, transvaginal US evaluation of the uterus after intracavitary saline infusion), has been considered as a imaging modality for evaluating deep myometrial invasion with accuracy of 89% (17/19) in one series [15]. However, recent reports indicate that the procedure disseminates malignant cells into the peritoneal cavity in 6%-7% of patients with an established diagnosis of endometrial cancer [16,17]. Although there is no evidence that this dissemination increases rates of intraperitoneal metastases, these results imply that hysterosonograms have the potential to upstage a patient from disease confined to the uterus (stage I or II) to stage

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III thereby altering postsurgical treatment and follow-up algorithms. While use of hypertonic saline has been proposed to induce cell lysis and potentially decrease or eliminate the risk of peritoneal spread, this has not yet been practically demonstrated in the literature.

#### *Computed Tomography*

Computed tomography (CT) has been used for evaluating endometrial carcinoma, with emphasis on evaluating the depth of myometrial invasion and assessing lymph node status. In studies comparing CT with US or MRI, the accuracy of CT for myometrial invasion is reported to be from 58%-61% versus 68%-69% in US and 88%-89% in MRI [6,10]. One study found no significant difference between helical CT and US for diagnosing deep myometrial invasion [6]. The value of CT in diagnosing cervical extension is not evident, because an easy identification of the margin between the cervix and the uterine corpus is difficult on axial imaging planes. Moreover, most reports suffer from having a few patients with stage II, which may prevent valid conclusions to be drawn. Preoperative evaluation of multidetector CT (MDCT) for staging endometrial carcinoma has not as yet been evaluated in randomized prospective controlled trials.

#### *Magnetic Resonance Imaging*

MRI is significantly superior to US in the evaluation of both tumor extension into the cervix and myometrial invasion [6,11-13]. A meta-analysis study showed that the efficacy of contrast-enhanced MRI is significantly better than that of US, CT, or noncontrast MRI in evaluating the depths of myometrial invasion in patients with endometrial cancer [18]. Contrast-enhanced MRI performs significantly better than unenhanced MRI for evaluation of the depth of myometrial invasion [18]. The superiority of MRI compared to CT and clinical staging has also been documented [6,10]. MRI provides the most accurate and consistent evaluation of patients with endometrial cancer. The overall staging accuracy of MRI has been reported to be between 85%-93% [6,10,12,19,20]. The efficacy of MRI is improved with the use of dynamic contrast-enhanced imaging. The assessment of the depth of myometrial invasion shows significant improvement with the use of dynamic scanning (accuracy of 55%-77% for noncontrast images versus 85%-91% for contrast-enhanced images) [21-25]. Compared with T2-weighted images, the use of contrast media will reduce both overestimation as well as underestimation of depth of myometrial invasion. An erroneous MRI assessment of the depth of myometrial invasion can sometimes be ascribed to as large polypoid endometrial cancer, which distends the uterus so that the thin rim of myometrium is stretched over it rather than deeply infiltrated [12]. Cervical extension can be diagnosed reliably with accuracy ranging from 86%-95% [22,26,27]. One study comparing MRI with fractional curettage and hysteroscopy showed that MR imaging had the highest sensitivity (91%) and specificity (96%) for diagnosing cervical involvement in endometrial cancer [26]. A recent meta-analysis showed that use of contrast-

enhanced MRI significantly affects the post-test probability of deep myometrial invasion in patients with all grades of endometrial cancer and could be used to select patients for specialist referral [28].

#### *Lymphangiography*

Lymphangiography is not recommended for evaluating cancer of the endometrium. Not only because it is invasive (and very few imaging centers offer this service) but also, because of the difficulties in the evaluation of pelvic nodes, its performance is not reproducible and, even performed optimally, slightly inferior to that of CT and MRI.

#### *Positron Emission Tomography*

The role of positron emission tomography (PET) in endometrial cancer imaging is still under investigation. In detecting lymph node involvement by tumor, PET performs with accuracy (95%) comparable to that of CT or MRI [29,30]. However, because 45% of endometrial cancer is stage I and not FDG-avid, the reported improved sensitivity of PET (60%-86%) is only true for nodes >1 cm. This limitation, coupled with the limitations of PET in assessing intraperitoneal tumor implants and parenchymal metastases makes CT and MRI preferable in detecting extrauterine disease. PET was reported to be useful in the post-therapy surveillance, both for localizing suspected recurrences and for detecting asymptomatic recurrent disease [31]. A study showed that in the detection of recurrence and the evaluation of treatment response, FDG-PET, with help by CT and/or MRI, performed better (sensitivity 100%, specificity 88.2%, and accuracy 93.3%) compared with CT and/or MRI (sensitivity 84.6%, specificity 85.7%, and accuracy 85%) and tumor markers, ie CA125, CA19-9, CEA, and sialyl TN antigen, (sensitivity 100%, specificity 70.6%, and accuracy 83.3%). The results of FDG-PET correlated well with the clinical outcome of the patients, with patients having negative PET results tending to show disease-free courses [32].

#### **Recommended Imaging Approach**

Because contrast-enhanced MRI demonstrates the highest accuracy for overall staging of endometrial cancer, it should be used, when available, as the preferred modality for treatment planning. Transvaginal US can be used to assess the depth of myometrial invasion and cervical involvement, albeit with less accuracy than MRI. CT and MRI perform equivalently for assessing nodal involvement. PET is promising in the post-treatment surveillance of endometrial cancer patients. However, there are no outcome studies or cost-effectiveness analyses on imaging evaluation of endometrial cancer.

#### **Summary**

Patients with endometrial carcinoma should undergo diagnostic imaging only in cases of clinical staging difficulties, including those with medical comorbidities that preclude surgery, large tumors, high histologic tumor grade, or possible cervical involvement. If imaging is needed, MRI is the most accurate technique and should be the preferred modality.

## Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie, <30 mL/min/1.73m<sup>2</sup>), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73m<sup>2</sup>. For more information, please see the [ACR Manual on Contrast Media](#) [33].

## Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria<sup>®</sup> [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

## Supporting Document(s)

- [ACR Appropriateness Criteria<sup>®</sup> Overview](#)
- Evidence table under review

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

### Appendix 1. Revised Surgical FIGO Staging of Endometrial Carcinoma [2]

Stage	Definition
0	Carcinoma in situ
I	Tumor confined to corpus
	IA tumor limited to endometrium
	IB invasion smaller than 50% of myometrium
II	IC invasion equal to or greater than 50% of myometrium
	Tumor invades cervix but does not extend beyond uterus
	IIA invasion of endocervix
III	IIB cervical stromal invasion
	Tumor extends beyond uterus but not outside pelvis.
	IIIA invasion of serosa, adnexa, or positive peritoneal cytology
	IIIB invasion of vagina
IV	IIIC pelvic and/or para-aortic lymphadenopathy
	Tumor extends outside pelvis and/or invades bladder or rectal mucosa
	IVA invasion of bladder or rectal mucosa
	IVB distant metastasis (includes intra-abdominal or inguinal lymphadenopathy)