

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

Clinical Condition:

Staging of Invasive Cancer of the Cervix

Variant 1:

FIGO stage 1b1, tumor size <4 cm.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI pelvis without and with contrast	8	Appropriateness can depend on clinical circumstances, availability, and expertise. See statement regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body with concurrent diagnostic CT abdomen and pelvis	8	Appropriateness can depend on clinical circumstances, availability, and expertise.	High
CT abdomen and pelvis with contrast	5	Performed without concurrent whole-body PET.	High
X-ray chest	4		Min
US abdomen	2		None
US pelvis transabdominal	2		None
US pelvis transvaginal	2		None
X-ray contrast enema	1		Med
X-ray intravenous urography	1		Med
Tc-99m bone scan whole body	1		Med
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 2:

FIGO stage 1b2, tumor size >4 cm.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI pelvis without and with contrast	9	Appropriateness can depend on clinical circumstances, availability, and expertise. See statement regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body with concurrent diagnostic CT abdomen and pelvis	9	Appropriateness can depend on clinical circumstances, availability, and expertise.	High
X-ray chest	5		Min
CT abdomen and pelvis with contrast	5	Performed without concurrent whole-body PET.	High
US pelvis transvaginal	2		None
US pelvis transabdominal	2		None
US abdomen	2		None
X-ray contrast enema	1		Med
X-ray intravenous urography	1		Med
Tc-99m bone scan whole body	1		Med
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Clinical Condition:**Staging of Invasive Cancer of the Cervix****Variant 3:****FIGO stage greater than Ib.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI pelvis without and with contrast	9	Appropriateness can depend on clinical circumstances, availability, and expertise. See statement regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body with concurrent diagnostic CT abdomen and pelvis	9	Appropriateness can depend on clinical circumstances, availability, and expertise.	High
CT abdomen and pelvis with contrast	7	Performed without concurrent whole-body PET.	High
CT chest with contrast	7		Med
X-ray chest	2		Min
US pelvis transabdominal	2		None
US abdomen	2		None
Tc-99m bone scan whole body	2	Greater than stage II. Symptoms of bone metastases.	Med
US pelvis transvaginal	2		None
X-ray intravenous urography	1		Med
X-ray contrast enema	1		Med
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

STAGING OF INVASIVE CANCER OF THE CERVIX

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Summary of Literature Review

Cervical cancer is the third most common gynecological malignancy in the United States. It is estimated that during 2007 there were approximately 11,150 new cases of cervical cancer and 3,670 deaths from this disease in the United States [1]. Between 1959-61 and 1989-91, there has been a 63% decrease in the mortality of cervical cancer [2,3]. Furthermore, the American Cancer Society reports that the death rate from cervical cancer decreased 29% from 1991 to 2003 [4]. This improvement in mortality has been attributed to a significant increase in detection of early-stage, small cancers due to the development of the Papanicolaou smear. However, only minor improvement has been achieved in the survival rate for invasive cervical cancer [5]. Established risk factors for cervical cancer include early sexual activity, especially with multiple partners, cigarette smoking, immunosuppression, and infection with human papilloma viruses 16 and 18 [6].

The prognosis of cervical carcinoma is primarily determined by whether lymph nodes are involved by tumor [7]. This in turn is predicted clinically and pathologically by the stage of disease, the volume of the primary tumor, and the histologic grade [8-15]. The current staging system for cervical cancer is based on the International Federation of Gynecology and Obstetrics (FIGO) classification [16]. It defines the clinical staging system for cervical carcinoma based on clinical assessment, including physical examination under anesthesia, colposcopy, endocervical curettage, hysteroscopy, cystoscopy, proctoscopy, intravenous urography, barium enema (BE), and x-rays of lungs and skeleton [17]. Errors in clinical FIGO staging have been consistently reported. When compared with surgical findings, FIGO staging errors are 28% in stage Ib disease and 50%-64% in stage IIA-IIb disease [18-23]. Clinical evaluation underestimates the surgical stage in 15%-36%

of patients [18-23]. In clinically staged Ib disease, underestimation of tumor extent occurs in 21% and overestimation in 6% of patients [18-23].

Inaccuracy in clinical staging is predominantly due to difficulties in evaluating parametrial and pelvic sidewall invasion, bladder or rectal wall invasion, metastatic spread, in evaluating primary endocervical (endophytic) tumors, and in estimating primary tumor size [18-23]. Aside from the inaccuracies of clinical staging, evaluation of lymph node metastasis, which is an important prognostic factor and a determinant in treatment planning, is not included in the clinical staging system [17]. In surgically treated stages Ib and IIA cervical cancer, survival rates decline from 85%-90% to 50%-55%, respectively, in the presence of metastatic lymph nodes [12,24]. In spite of these limitations of clinical FIGO staging, modern cross-sectional imaging modalities such as ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) have not been incorporated into clinical staging. Among the most common arguments against the use of CT or MRI as staging tools are their high cost, interobserver variability, and lack of availability, especially in the underdeveloped regions of the world where invasive cervical cancer is the most prevalent [17].

Current Role of Imaging

The most important issue in staging cervical cancer is to distinguish early disease (stages IA and IB) that can be treated with surgery or combined chemo-radiation therapy from advanced disease that must be treated with radiation alone or radiation combined with chemotherapy [25]. Imaging modalities must be directed to solve this clinically important question. Conventional radiological studies such as excretory urography, BE, and lymphangiography are less commonly used today. However, there has been an increase in the use of cross-sectional imaging, particularly CT and MRI [26].

Radiographs

Chest radiographs are obtained as a staging procedure to identify pleural effusion or pulmonary metastasis, which occur in the late stages of cervical cancer. However, chest CT is superior to plain film in both cases.

Excretory Urography

Excretory urography is a sensitive test for detecting urinary obstruction. However, a low incidence (2.4%) of urinary obstruction in stage Ib disease argues against the routine use of this test [27,28]. Discontinuation of the routine use of BE, cystoscopy, and sigmoidoscopy has been suggested previously [27-29].

Ultrasound

Transabdominal US is a sensitive noninvasive means of detecting hydronephrosis but has a limited role in evaluating the local extent of cervical cancer. Transrectal and transvaginal US have been used in assessing local disease but are limited in the detection of parametrial

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disease and pelvic side wall involvement due to poor soft-tissue contrast, small field of view, and operator dependence [30,31].

Computed Tomography

CT has staging accuracy ranging from 32%-80% in cervical cancer [30,32-44]. The sensitivity for parametrial invasion ranges from 17%-100%, with an average of 64% [34-37,39-41,44]. Specificity ranges from 50%-100%, with an average of 81% [34-37,39-41,44]. There is a consensus in the literature that the value of CT increases with higher stages of disease, and that it has limited value (a positive predictive value of 58%) in evaluating early parametrial invasion [34-37,39-41,44]. CT has been reported to have an accuracy of 92% in depicting advanced disease [44]. However, a recent ACRIN® trial reported that CT had sensitivity of only 42% for detecting advanced disease, with sensitivity and specificity for detecting parametrial invasion ranging from 14%-38% and from 84%-100%, respectively [26,45]. The major limitation of CT in local staging is its inadequate differentiation between tumor and normal cervical stroma or parametrial structures [46]. Therefore, CT is mainly used in advanced disease and in the assessment of lymph nodes. The positive predictive value of CT for nodal involvement ranges from 50.8%-65%, with negative predictive value ranging from 86%-96% [32,33,35-44,47,48], with sensitivities reported recently to range from 31%-65% [26,47]. The reliance on size criterion alone (>1 cm) for diagnosing malignant lymphadenopathy on CT is believed to account for the low sensitivity, as microscopic metastases will be missed. CT is also performed to detect distant metastases, for radiotherapy planning, and for guiding interventional procedures [49].

Magnetic Resonance Imaging

MRI is very accurate in determining tumor size and location (exophytic or endocervical), the depth of stromal invasion, and the local extension of the tumor. MRI is superior to clinical evaluation in assessing tumor size, and MRI measurements are within 0.5 cm of the surgical size in 70%-94% of cases [13,40,46,50-53]. However, a recent ACRIN® trial reported that neither MRI nor CT was accurate for evaluating the cervical stroma [46]. The use of an endovaginal coil has been reported to be helpful in assessing small-volume disease [54]. The staging accuracy of MRI ranges from 75%-96% [34-37,40,51,53,55-60]. The sensitivity of MRI in evaluating parametrial invasion ranging from 40%-57% and the specificity from 77%-80% [34-37,40,45,51,53,55-60]. In studies that compare MRI and CT for evaluating parametrial invasion, MRI was superior to CT [34-37,40,51,53,55-57,59,60]. In evaluating nodal disease, the sensitivity and specificity ranges of MRI, 30%-73% and 93%-95%, respectively, are similar to those of CT [34-37,40,47,51,53,55-66]. Similar to CT, MRI relies on size criteria for assessing lymph nodes and thus will miss microscopic disease [67]. In assessing local tumor invasion, T2-weighted images are superior to contrast-enhanced T1-weighted images [68].

MRI can be a cost-effective staging technique. In a study of patients with cervical cancer, those who underwent MRI as the initial imaging procedure for staging required fewer tests and procedures compared with those who underwent standard clinical imaging [69]. Tumor size >4 cm, parametrial invasion, and extension are related to the likelihood of a positive lymph node, which significantly affects patient management and prognosis for survival [13,47,54]. Since these predictive criteria of the primary tumor are best evaluated radiologically, routine use of MRI has been recommended.

Lymphangiography

Although lymphangiography has been routinely used in the past for the pretreatment evaluation of lymph node metastases, it has been mostly replaced in this role by CT and MRI. Single studies that have compared lymphangiography and CT [70-72] have shown similar accuracy (72%-91% and 71%-88%, respectively) for both modalities. CT may have a slightly higher specificity than lymphangiography (88%-95% vs 59%-93%), but lymphangiography is more sensitive than CT (63%-88% vs 53%-72%), especially in early stages (I-II) of disease [70-72]. In a meta-analysis comparing the utility of lymphangiography, CT, and MRI in patients with cervical cancer, summary-receiver-operator characteristics revealed no significant differences in their overall performance, although MRI tended to perform better [73].

Positron Emission Tomography

Although the current use of positron emission tomography (PET) in the initial evaluation of cervical cancer is still under investigation, PET can be used to assess nodal disease and tumor recurrence. In the detection of metastatic lymph nodes in patients with cervical cancer, PET has been reported to have a sensitivity ranging from 79%-91% and a specificity ranging from 95%-100%, which are higher than those for MRI and CT [74,75] although microscopic metastases may still be missed [76]. Accuracy rates are reportedly higher for PET than MRI (78% vs 67%) [64]. Another study demonstrated that prognosis was best when patients had both PET-negative and CT-negative lymph node status and that the presence of PET-positive para-aortic lymph nodes was the most significant negative prognostic factor for progression-free survival [7]. Hybrid PET/CT represents a potentially significant advance in imaging of metastatic lymph nodes, combining the functional, metabolic imaging capabilities of PET with the spatial resolution of CT. Recent studies report sensitivity ranges of 58%-72%, specificity ranges of 93%-99%, and accuracy ranges of 85%-99% for PET/CT in detecting metastatic lymph nodes from cervical cancer [62,77]. Another study showed that when abdominal CT is negative, PET has a sensitivity of 85.7%, a specificity of 94.4%, and an accuracy of 92% for detecting para-aortic lymph node metastasis in patients with advanced cervical cancer [78], prompting some to advocate routine PET imaging in such cases [79]. For detecting recurrence, PET has been reported to have sensitivity and specificity ranges of 85.7%-90.3% and 76.1%-86.7%, respectively

[80-82]. PET has added value in patients with recurrent cervical cancer who undergo salvage therapy, as it can provide precise restaging information [83,84]. A recent study suggests that abnormal PET findings were the most significant prognostic factor for developing metastasis and death from cervical cancer [85].

Nuclear Medicine Bone Scan

Bone scans do not seem warranted for initial screening in asymptomatic patients with stage 0, I, or II cervical carcinoma [86,87], but may be useful in patients with advanced disease (stage III and IV) who are symptomatic for bone metastases, such as with pain or hypercalcemia. Future research will determine if PET/CT will replace bone scans.

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/1.73m²), 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/1.73m². For more information, please see the [ACR Manual on Contrast Media](#) [88].

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[®] [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[®] 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.