

**American College of Radiology
ACR Appropriateness Criteria®
Staging and Follow-up of Primary Vaginal Cancer**

Variant: 1 Vaginal cancer. Pretreatment staging. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	○
CT abdomen and pelvis with IV contrast	Usually Appropriate	☼☼☼
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☼☼☼☼
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	○
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
MRI pelvis without IV contrast	May Be Appropriate	○
CT chest with IV contrast	May Be Appropriate	☼☼☼
CT chest without IV contrast	May Be Appropriate	☼☼☼
US abdomen and pelvis transabdominal	Usually Not Appropriate	○
US pelvis transvaginal	Usually Not Appropriate	○
Fluoroscopy contrast enema	Usually Not Appropriate	☼☼☼
Radiography intravenous urography	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼

Variant: 2 Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	○
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☼☼☼☼
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	○
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
MRI pelvis without IV contrast	May Be Appropriate	○
CT abdomen and pelvis with IV contrast	May Be Appropriate	☼☼☼
CT chest with IV contrast	May Be Appropriate	☼☼☼
CT chest without IV contrast	May Be Appropriate	☼☼☼
US abdomen and pelvis transabdominal	Usually Not Appropriate	○
US pelvis transvaginal	Usually Not Appropriate	○
Fluoroscopy contrast enema	Usually Not Appropriate	☼☼☼
Radiography intravenous urography	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼

Variant: 3 Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	○
CT abdomen and pelvis with IV contrast	Usually Appropriate	☼☼☼
CT chest with IV contrast	Usually Appropriate	☼☼☼
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☼☼☼☼
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	○
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
MRI pelvis without IV contrast	May Be Appropriate	○
CT chest without IV contrast	May Be Appropriate	☼☼☼
US abdomen and pelvis transabdominal	Usually Not Appropriate	○
US pelvis transvaginal	Usually Not Appropriate	○
Fluoroscopy contrast enema	Usually Not Appropriate	☼☼☼
Radiography intravenous urography	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼

Panel Members

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Summary of Literature Review

Introduction/Background

Primary vaginal cancer is rare, comprising 1% to 2% of gynecologic malignancies and 20% of all malignancies involving the vagina [1,2]. More frequently, the vagina is involved secondarily either by direct invasion from malignancies originating in adjacent organs, most commonly the cervix or vulva, or by metastases from other pelvic or extrapelvic primary malignancies [1,2]. Additionally, any vaginal tumor involving the cervix or vulva, whether or not the lesion is centered in the vagina, is classified by the International Federation of Gynecology and Obstetrics (FIGO) system as a primary cervical or vulvar cancer, respectively. Squamous cell carcinoma is the most common underlying histology in primary vaginal cancer, representing 80% to 90% of primary vaginal cancer [3] and occurs most frequently in postmenopausal women, with adenocarcinoma representing around 5% to 10% of cases and even rarer histologies such as sarcoma, melanoma, and lymphoma accounting for the remainder [1,2].

Primary vaginal cancer is staged according to two systems, FIGO and the American Joint Committee on Cancer (AJCC). FIGO stipulates a clinical staging paradigm, whereby features derived from bimanual and/or rectovaginal examination, cystoscopy, proctoscopy, and radiography are permissible for incorporation into staging [4]. Although FIGO encourages the use of advanced imaging modalities such as CT, MRI, and PET to guide management, information derived from these examinations does not alter the formal clinical FIGO stage [4]. Given the rarity of primary

vaginal cancer, treatment principles are derived from retrospective data in addition to extrapolation from more established management paradigms for cervical and anal squamous cell cancers. Surgical management for vaginal cancer is limited primarily to small (<2 cm) early stage lesions, with larger lesions posing greater difficulty for achieving negative surgical margins. Although surgical options exist for locally advanced disease, they often involve a degree of pelvic exenteration and therefore confer substantial morbidity. For this reason, the management paradigm for locally advanced disease has largely trended toward definitive radiation therapy with concurrent chemotherapy [1,5]. Though data on the use of imaging in vaginal cancer are sparse, insights derived from the study of imaging in cervical cancer have reasonable generalizability to vaginal cancer because of similar tumor biology. Moreover, given the trend toward definitive chemoradiation for both cancers in all but early stage lesions, principles of postchemoradiation tumor response evaluation are largely analogous. Accordingly, many of the recommendations outlined in this document are informed by principles translated from the literature on cervical cancer.

Special Imaging Considerations

Radiation Therapy Planning

CT and MRI are fundamental to radiation therapy planning for gynecologic malignancies, during which precise delineation of the target volume and at-risk organs optimizes tumor control while minimizing treatment-related toxicity [6,7]. The evolving trend of adaptive image-guided external beam radiation therapy and brachytherapy for cervical and vaginal cancer—whereby target volumes and dose curves are dynamically modified over the course of therapy based on changes in tumor volume—has further expanded the role of advanced imaging [8,9]. The use of imaging in initial and adaptive radiation planning for vaginal cancer is not specifically addressed in this document, and analogous principles for cervical cancer are covered in extensive detail elsewhere [6].

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously wherein each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

Although the 2009 FIGO staging system for vaginal cancer indicates that findings on advanced imaging (CT, MRI, PET/CT) should not modify stage designation [4], such imaging findings are

routinely employed in clinical practice to prognosticate and guide management decisions in patients with vaginal cancer. Recent updates to the FIGO staging system for cervical cancer, which incorporate advanced imaging results into staging [10], reflect the wide recognition that cross-sectional imaging provides actionable staging information not readily obtained by physical examination or conventional radiography. Moreover, the increasing use of definitive radiotherapy across all stages of vaginal cancer obligates the incorporation of advanced imaging into pretreatment evaluation, because it is essential for treatment planning.

The rationale for optimizing staging accuracy in vaginal cancer, in part via the inclusion of cross-sectional imaging, is multifold. First, accurate initial staging is fundamental to prognostication [11], facilitating incorporation of expectations of treatment efficacy into goals of care. Second, proper initial staging permits selection of the most appropriate treatment based on extent of disease. Regarding local extent, for vaginal lesions deemed likely confined to the vaginal wall (stage I) based on clinical examination, exclusion of extravaginal invasion with further testing is essential for ensuring that planned definitive surgery is likely to achieve a disease-free margin or that a radiation field properly incorporates the tumor volume. Regional nodal metastases include pelvic nodal metastases, which are primarily detected with cross-sectional imaging, and inguinal nodes (in lower vaginal cancers), a subset of which can be identified on clinical examination. Pretreatment knowledge of suspicious nodes may impact the decision to pursue surgery versus radiation. In addition, the distribution of suspicious nodes has the potential to influence radiation-specific factors such as field and dose planning, including possible node-directed boost doses as employed in cervical cancer [12]. Regarding distant metastases, detection of extraregional nodal or solid organ lesions can obviate unnecessarily morbid radical pelvic surgery and instead direct care toward palliative regimens or radiotherapy with an extended field. Finally, the ability to accurately stage noninvasively can avoid the need for invasive staging procedures such as cystoscopy (for bladder mucosal invasion) and proctoscopy (for rectal mucosal invasion), both of which are historical components of the FIGO clinical staging system [1].

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

A. CT Chest

Although thoracic metastases are known to occur in vaginal cancer, no studies specifically address their incidence or the incremental value of chest CT for initial staging. Pulmonary metastases have been studied to a limited degree in cervical cancer, occurring in approximately 5% to 10% of patients at diagnosis [13,14]. Pulmonary metastases appear to occur slightly more frequently as a site of recurrent disease, with one large study of recurrent cervical cancer indicating an overall incidence of 13%, and the lungs representing the only site of recurrence in 6% of cases [15]. In studies evaluating pulmonary metastases from cervical cancer, chest CT was the most frequent diagnostic modality employed, with the vast majority of patients asymptomatic at the time of imaging [16,17]. These findings support the use of chest CT with or without intravenous (IV) contrast in the early posttreatment evaluation of cervical cancer, as endorsed by the National Comprehensive Cancer Network (NCCN) guidelines, and suggest that a similar strategy would be useful for vaginal cancer.

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

B. CT Abdomen and Pelvis

Data on the diagnostic performance of CT in primary vaginal cancer staging are very limited. A small retrospective study evaluating fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT in 23 patients with primary vaginal cancer found that CT and FDG-PET detected pelvic nodal metastases

in 17% (4 of 23) and 35% (8 of 23) of patients, respectively, suggesting inferior sensitivity of CT alone [18].

CT has been studied more extensively in cervical cancer staging, with available data comparing CT to MRI for local staging and CT (with or without IV contrast) to PET for regional and distant staging. For local staging, the ACRIN 6651 study showed that CT and MRI had sensitivity of 42% and 53%, respectively, and specificity of 82% and 75%, respectively, for classifying disease as stage IIB (parametrial invasion) or higher, with none of these differences reaching statistical significance [19]. However, a more recent meta-analysis suggested improved performance of MRI for parametrial invasion with modern hardware (sensitivity 76%, specificity 94%), particularly when the field strength was 3T and diffusion-weighted imaging was included [20], whereas a recent study of multidetector CT showed only 50% sensitivity for parametrial invasion [21].

Although older literature suggested lower sensitivity of CT compared with FDG-PET/CT for nodal metastases [22], the more recent ACRIN 6671/Gynecology Oncology Group (GOG) 0233 trial demonstrated a more modest difference in sensitivity for abdominal nodes (42% versus 50%, respectively) [23]. Likewise, in a recent meta-analysis, CT had only modestly lower area under the curve (AUC) (0.83) compared with PET/CT (0.90) for detection of nodal metastases from cervical cancer [24]. For distant metastases from cervical cancer, CT is inferior in the detection of osseous metastases (sensitivity 66%) compared with FDG-PET/CT (sensitivity 96%) [25].

These findings, if applied to vaginal cancer, suggest that modern multidetector CT abdomen and pelvis is a reasonable staging tool for regional and distant metastases, although is likely inferior to MRI for local staging, modestly inferior to FDG-PET/CT for nodal metastases, and inferior to FDG-PET/CT for osseous metastases. The use of IV contrast is strongly encouraged when possible, because the improved tissue contrast likely benefits primary tumor evaluation, delineation of lymph nodes from adjacent vessels, and detection of hepatic metastases. No studies have specifically evaluated the performance of CT of the abdomen and pelvis without IV contrast for vaginal cancer staging.

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

C. FDG-PET/CT Skull Base to Mid-Thigh

Data regarding the diagnostic performance of PET/CT for initial staging in patients with vaginal cancer are limited. Lamoignon et al [18], in a prospective study, evaluated the comparative performance of PET versus CT in 23 patients with primary vaginal cancer prior to treatment. PET identified suspicious pelvic and/or groin lymph nodes in 35% (8 of 23) of patients, whereas CT did so in only 17% (4 of 23) of patients, although a pathologic reference standard was present in only two sampled groin nodes. No patient had extrapelvic nodal or distant disease, limiting the applicability of this study to metastases outside of the pelvis.

A study of 50 patients (83 imaging examinations) enrolled in the National Oncologic PET Registry, which included 29 FDG-PET/CT studies from patients with known or suspected primary or recurrent vaginal cancer, found that FDG-PET/CT changed the treating physician's prognostic impression in 45% (13 of 29) of cases [26]. Additionally, a change in patient management occurred following 36% (30 of 83) of all FDG-PET/CT studies, including the 53 studies in vulvar cancer patients. However, conclusions regarding comparative performance of FDG-PET/CT versus conventional imaging (CT or MRI) on the basis of this study are limited, because only a minority of cases had comparison to conventional imaging (CT or MRI), and a majority of the lesions compared were incidental and not

pertinent to the primary malignancy.

Although data are limited for primary vaginal cancer staging, a growing body of literature supports the role of FDG-PET/CT in the initial staging of cervical cancer. Prospective data from the ACRIN 6671/GOG 0233 trial suggested, with borderline statistical significance, that FDG-PET/CT is more sensitive than CT alone for extrapelvic nodal metastases in cervical cancer (50% versus 42%, respectively), with similar specificity (85% versus 89%, respectively) [23], supporting prior retrospective data [22]. FDG-PET/CT is also more sensitive than conventional CT for osseous metastases [25], with sensitivity and specificity of 55% and 98%, respectively, for all distant metastases [13]. Accordingly, the NCCN guidelines endorse preference for whole-body FDG-PET/CT over conventional CT for initial staging of all cervical cancer designated stage II and above, with either FDG-PET/CT or conventional CT recommended in stage I disease [27].

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

D. Fluoroscopy Contrast Enema

There is no relevant literature regarding the use of fluoroscopic contrast enema in the modern imaging workup of vaginal cancer, and its use has largely been replaced by cross-sectional imaging techniques.

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

E. MRI Pelvis

Because of the rarity of vaginal cancer, the primary data regarding the use of MRI in initial staging of vaginal cancer are sparse. Taylor et al [28] retrospectively evaluated pelvic MRI for initial staging in 25 patients with primary vaginal cancer spanning all disease stages. MRI depicted the primary tumor in 96% (24 of 25) of patients, demonstrating hyperintense signal compared to muscle on T2-weighted images, and enabled assignment of a radiologic disease stage based on adaptation of FIGO clinical staging criteria. Because 80% (20 of 25) of patients received either radiation or palliative therapy, pathologic confirmation of imaging findings could be obtained in only 20% (5 of 25) of cases. Of these cases, MRI stage was concordant with pathologic stage in 40% (2 of 5) of the cases. More recent data in cervical cancer patients support the use of MRI for initial staging, with a meta-analysis suggesting high sensitivity (76%) and specificity (94%) of MRI for parametrial invasion [20].

Although MRI readily depicts lymph nodes, it has constraints similar to CT with regard to the limited sensitivity and specificity of size and morphologic criteria. No study has specifically evaluated the performance of MRI for pretreatment nodal staging in vaginal cancer. However, data from mixed cohorts of patients with recurrence of cervical, vaginal, and other gynecologic cancers have suggested superior sensitivity of FDG-PET/CT for pelvic nodal metastases compared with pelvic MRI and CT [29,30].

The use of IV contrast may improve tissue characterization but is not considered essential, with variable inclusion in published protocols for evaluation of vaginal [28,31] and cervical cancer [7,32-34]. No study has specifically compared the incremental utility of contrast-enhanced sequences over T2-weighted sequences for pelvic MRI in this context. Regarding the use of vaginal gel in MRI of the pelvis, there is insufficient primary data in the literature to support its routine use.

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

F. MRI Abdomen and Pelvis

Because of the rarity of vaginal cancer, the primary data regarding the use of MRI in initial staging of vaginal cancer are sparse. Taylor et al [28] retrospectively evaluated pelvic MRI for initial staging in 25 patients with primary vaginal cancer spanning all disease stages. MRI depicted the primary tumor in 96% (24 of 25) of patients, demonstrating hyperintense signal compared to muscle on T2-weighted images, and enabled assignment of a radiologic disease stage based on adaptation of FIGO clinical staging criteria. Because 80% (20 of 25) of patients received either radiation or palliative therapy, pathologic confirmation of imaging findings could be obtained in only 20% (5 of 25) of cases. Of these cases, MRI stage was concordant with pathologic stage in 40% (2 of 5). More recent data in cervical cancer patients support the use of MRI for initial staging, with a meta-analysis suggesting high sensitivity (76%) and specificity (94%) of MRI for parametrial invasion [20].

Although MRI readily depicts lymph nodes, it has constraints similar to CT with regard to the limited sensitivity and specificity of size and morphologic criteria. No study has specifically evaluated the performance of MRI for pretreatment nodal staging in vaginal cancer. However, data from mixed cohorts of patients with recurrence of cervical, vaginal, and other gynecologic cancers have suggested superior sensitivity of FDG-PET/CT for pelvic nodal metastases compared with pelvic MRI and CT [29,30].

If MRI of the abdomen and pelvis is used in place of CT of the abdomen and pelvis, the addition of chest CT is encouraged to evaluate for pulmonary metastases. The use of IV contrast may improve tissue characterization and is particularly beneficial when MRI of the abdomen is included, because it improves detection of hepatic metastases.

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

G. Radiography Intravenous Urography

There is no relevant literature regarding the use of radiographic IV urography in the modern imaging workup of vaginal cancer, and its use has largely been replaced by cross-sectional imaging techniques.

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

H. US Pelvis Transvaginal

Transvaginal (TV) pelvic ultrasound (US) has no established role in the initial staging of primary vaginal cancer, and no study to date has evaluated its utility in this setting. Multiple prospective studies have explored the role of TVUS in cervical cancer staging with variable results but suggestion of a similar general range of accuracy for detecting parametrial invasion compared to MRI [35,36]. Other retrospective data have suggested agreement between 3-D TVUS and MRI ranging from moderate ($k = 0.51$) to good ($k = 0.60$) for parametrial invasion, with very good ($k = 0.84$) agreement for bladder invasion [37,38]. Although these findings suggest some potential utility of 3-D TVUS for cervical cancer staging, the current NCCN guidelines do not endorse its use for staging. At present, the generalizability of these studies to vaginal cancer staging remains limited, although these data along with emerging techniques such as sonovaginography—the instillation of vaginal gel during TVUS to improve vaginal wall visualization—may prompt future investigation into the role of potential TVUS for local staging in vaginal cancer. For pelvic node evaluation, TVUS has limited utility [39].

Variant 1: Vaginal cancer. Pretreatment staging. Initial imaging.

I. US Abdomen and Pelvis Transabdominal

There is no relevant literature regarding the role of transabdominal abdominopelvic (TA) US in

vaginal cancer staging. TAUS is inferior for visualizing the female genital tract compared with TVUS, and neither technique has a role in the evaluation of regional or distant disease.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

As the use of definitive chemoradiation for the treatment of primary vaginal cancer has grown, so too has the role of cross-imaging for assessment of treatment response. In contrast to extirpative surgery, in which pathologic margin assessment can confirm removal of viable tumor, evaluation for tumor eradication following chemoradiation relies in part on imaging assessment. Much of the support for the value of early posttreatment imaging in primary vaginal cancer is extrapolated from the large body of literature on cervical cancer, for which the treatment paradigm and endpoints are analogous. Early posttreatment imaging is performed most commonly following a period of approximately 3 to 6 months after the completion of chemoradiation. Some centers also image during therapy for early response assessment and/or adaptive radiation planning [7].

The goals of early posttreatment imaging are multiple. First, imaging response after chemoradiation is a potent predictor of oncologic outcome, therefore providing crucial prognostic data [40-42]. Second, the degree of imaging response directly informs therapeutic decision-making, because persistent or progressive disease following chemoradiation requires salvage therapy [40]. For persistent pelvic disease, options include salvage radical surgery or less commonly reirradiation. Detection of new distant disease following initial treatment obviates curative surgery and may direct therapy toward chemotherapeutic and/or palliative options. Finally, the degree of response can influence the frequency of subsequent surveillance, with complete response enabling more conservative follow-up testing [42].

Following complete response, there is no formally established role for routine surveillance imaging in asymptomatic patients treated for vaginal cancer nor has a role been established for cervical cancer. Guidelines generally advocate for routine clinical examination for surveillance in asymptomatic patients, with imaging suggested in the setting of symptoms or abnormal physical examination findings [43].

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

A. CT Chest

Although thoracic metastases are known to occur in vaginal cancer, no studies specifically address their incidence or the incremental value of chest CT in early posttreatment evaluation. Pulmonary metastases have been studied to a limited degree in cervical cancer, occurring in approximately 5% to 10% of patients at diagnosis [13,14]. Pulmonary metastases appear to occur slightly more frequently as a site of recurrent disease, with one large study of recurrent cervical cancer indicating an overall incidence of 13%, and the lungs representing the only site of recurrence in 6% of cases [15]. Moreover, the lungs can uncommonly represent a site of distant disease that newly arises following definitive chemoradiation for disease that was initially locoregional [41]. In studies evaluating pulmonary metastases from cervical cancer, chest CT was the most frequent diagnostic modality employed, with the vast majority of patients asymptomatic at the time of imaging [16,17]. These findings support the use of chest CT with or without IV contrast in the early posttreatment evaluation of cervical cancer, as endorsed by the NCCN guidelines, and suggest that a similar strategy would be useful for vaginal cancer.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial

imaging.

B. CT Abdomen and Pelvis

For detection of residual primary tumor after chemoradiation, CT alone is likely inferior compared with FDG-PET/CT and pelvic MRI based on extrapolation from data on comparative imaging performance in the pretreatment evaluation of cervical cancer [21,44]. CT lacks the tissue contrast of MRI and the metabolic data of FDG-PET, both of which are useful in deciphering posttreatment changes from residual disease. Because CT relies primarily on size criteria for nodal evaluation, it has limitations similar to MRI with respect to sensitivity and specificity for nodal metastases. Therefore, although CT may depict size regression of nodal metastases following therapy, it is likely at least modestly inferior for detecting new or residual disease in subcentimeter lymph nodes compared with FDG-PET/CT [22,23,29,30].

CT of the abdomen and pelvis is not commonly performed in the absence of chest CT, given that the lungs are a potential site of distant disease that may newly arise in patients who have undergone definitive chemoradiation for disease that was initially locoregional [41]. Importantly, CT alone is inferior to FDG/PET-CT for evaluation of distant disease in the bones [25] and modestly inferior for nodal assessment [23,41].

The use of IV contrast is strongly encouraged when possible, because the improved tissue contrast likely benefits primary tumor evaluation, delineation of lymph nodes from adjacent vessels, and detection of hepatic metastases. No studies have specifically assessed the performance of CT of the abdomen and pelvis without IV contrast for posttreatment evaluation of primary vaginal cancer.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

C. FDG-PET/CT Skull Base to Mid-Thigh

Although data in primary vaginal cancer patients are limited, studies substantiating its treatment response assessment role in cervical cancer are numerous. In one prospective study in cervical cancer patients treated with definitive chemoradiation, FDG-PET/CT responses classified as complete metabolic response (absence of abnormal uptake at prior sites of disease), partial metabolic response and progressive disease at a mean of 3 months after therapy correlated closely with prognosis, with 3 year progression-free survival of 78%, 33%, and 0%, respectively [40]. In another prospective study, 9% (5 of 55) of patients developed new distant disease at the time of a posttreatment FDG-PET/CT scan, underscoring the value of whole-body imaging rather than pelvic-only imaging at the time of response evaluation [41]. Accordingly, the NCCN guidelines for cervical cancer recommend whole-body FDG-PET/CT at 3 to 6 months after completion of definitive therapy for disease stages II to IV, because it directly informs prognosis, therapy, and intensity of surveillance [27].

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

D. Fluoroscopy Contrast Enema

There is no relevant literature regarding the use of fluoroscopic contrast enema in the modern imaging workup of vaginal cancer, and its use has largely been replaced by cross-sectional imaging techniques.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial

imaging.

E. MRI Pelvis

Although no study has specifically evaluated pelvic MRI for treatment response assessment in vaginal cancer patients, multiple studies support its potential value in cervical cancer to which analogous principles apply. Following successful therapy with chemoradiation, the initially intermediate to high-signal-intensity tumor on T2-weighted images decreases in both size and signal intensity, with eventual conversion to low-signal-intensity fibrotic tissue [7,31]. However, the main limitation of MRI in the very early posttreatment period (<2 months after completion) is its difficulty distinguishing early postradiation change from residual tumor, both of which can demonstrate intermediate- to high-signal T2-weighted intensity and avid gadolinium enhancement [33,34].

One retrospective study evaluating pelvic MRI at a median of 5 weeks after completion of chemoradiation for cervical cancer found that 37% (16 of 44) of MRI examinations were considered indeterminate for discriminating residual disease and fibrosis [34]. Despite diagnostic confidence in the remainder of cases, sensitivity and specificity for residual disease were 80% and 55%, respectively, indicating a high false-positive rate because of posttreatment change. A more recent retrospective study in cervical cancer patients found better performance of pelvic MRI at a later postchemoradiation time point (median 9 weeks) with strict objective diagnostic criteria, achieving sensitivity and specificity of 91% and 85%, respectively, for residual disease [33]. Therefore, for cervical cancer, the suggested time interval for determining posttherapy treatment response with pelvic MRI is 3 to 6 months after completion of therapy [27], although earlier imaging is sometimes used for interim assessment of tumor regression for prognostication and/or adaptive radiation planning. Because MRI relies primarily on size criteria for nodal evaluation, it has limitations similar to CT with respect to sensitivity and specificity for nodal metastases. Therefore, although MRI may depict size regression of nodal metastases following therapy, it is likely at least modestly inferior for detecting new or residual disease in subcentimeter lymph nodes compared to FDG-PET/CT [22,23,29,30].

The use of IV contrast may improve tissue characterization but is not considered essential, with variable inclusion in published protocols for evaluation of vaginal [28,31] and cervical cancer [7,32-34]. No study has specifically compared the incremental utility of gadolinium-enhanced sequences over T2-weighted sequences for pelvic MRI in this context. Regarding the use of vaginal gel in MRI of the pelvis, there is insufficient primary data in the literature to support its routine use.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

F. MRI Abdomen and Pelvis

MRI of the abdomen and pelvis can be considered in the early posttreatment evaluation of primary vaginal cancer, although its main value is in the utility of pelvic MRI for primary tumor response assessment. MRI of the abdomen is not commonly included, given the availability of whole-body FDG-PET/CT or CT of the chest, abdomen, and pelvis for evaluation of distant disease. Although no study has specifically evaluated pelvic MRI for treatment response assessment in vaginal cancer patients, multiple studies support its potential value in cervical cancer to which analogous principles apply. Following successful therapy with chemoradiation, the initially intermediate- to high-signal-intensity tumor on T2-weighted images decreases in both size and signal intensity, with eventual conversion to low-signal-intensity fibrotic tissue [7,31]. However, the main limitation

of MRI in the very early posttreatment period (<2 months after completion) is its difficulty distinguishing early postradiation change from residual tumor, both of which can demonstrate intermediate- to high-signal T2-weighted intensity and avid gadolinium enhancement [33,34].

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If MRI of the abdomen and pelvis is used in place of CT of the abdomen and pelvis, the addition of chest CT is encouraged to evaluate for pulmonary metastases. The use of IV contrast may improve tissue characterization and should be used especially when MRI of the abdomen is included, because it improves detection of hepatic metastases.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

G. Radiography Intravenous Urography

There is no relevant literature regarding the use of radiographic IV urography in the modern imaging workup of vaginal cancer, and its use has largely been replaced by cross-sectional imaging techniques.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

H. US Abdomen and Pelvis Transabdominal

There is no relevant literature regarding the role of TAUS in vaginal cancer staging. TAUS is inferior for visualizing the female genital tract compared with TVUS, and neither technique has a role in nodal or distant evaluation.

Variant 2: Posttreatment evaluation of vaginal cancer. No suspected recurrence. Initial imaging.

I. US Pelvis Transvaginal

There is no relevant literature regarding the role of TVUS in the early posttreatment evaluation of primary vaginal cancer. Limited studies in cervical cancer patients have evaluated the use of color and/or power Doppler US for detecting changes in tumor vascularity as a marker of treatment response [45]. However, the applicability of these findings to clinical practice remains unclear. The NCCN guidelines do not currently endorse the use of TVUS for early posttreatment evaluation in

cervical cancer, and its role in vaginal cancer remains undefined. Additionally, TVUS has limited utility for pelvic nodal evaluation [39].

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

Cross-sectional imaging plays a crucial role in the evaluation of patients with known or suspected vaginal cancer recurrence, in which physical examination is of limited value in determining disease extent. In one retrospective study of patients with primary vaginal cancer who underwent definitive radiation and experienced recurrence, the mechanism of recurrence was locoregional alone in 56% for disease stages I and II and 71% for disease stages III to IVA, whereas the remainder of recurrences were distant [46]. Once locoregional recurrence is identified, the presence or absence of distant recurrence becomes a discriminating factor in eligibility for salvage pelvic exenteration. In the presence of distant recurrence, exenteration confers morbidity without significantly improving oncologic outcomes, whereas in the absence of distant recurrence, exenteration can potentially eradicate pelvic tumor burden. When distant disease has been excluded by imaging and a patient is deemed eligible for pelvic exenteration, the degree of local organ invasion determines whether partial (anterior or posterior) or total exenteration is indicated [32]. Therefore, imaging findings in patients with known or suspected vaginal cancer recurrence can influence both the appropriateness and type of salvage therapy, in addition to predicting prognosis.

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

A. CT Chest

Although thoracic metastases are known to occur in vaginal cancer, no studies specifically address their incidence or the incremental value of chest CT for suspected recurrence. Pulmonary metastases have been studied to a limited degree in cervical cancer, occurring in approximately 5% to 10% of patients at diagnosis [13,14]. Pulmonary metastases appear to occur slightly more frequently as a site of recurrent disease, with one large study of recurrent cervical cancer indicating an overall incidence of 13% and the lungs representing the only site of recurrence in 6% of cases [15]. In studies evaluating pulmonary metastases from cervical cancer, chest CT was the most frequent diagnostic modality employed, with the vast majority of patients asymptomatic at the time of imaging [16,17]. These findings support the use of chest CT with or without IV contrast in the early posttreatment evaluation of cervical cancer, as endorsed by the NCCN guidelines, and suggest that a similar strategy would be useful for vaginal cancer.

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

B. CT Abdomen and Pelvis

Data on the diagnostic performance of CT in known or suspected recurrence of vaginal cancer are very limited, requiring extrapolation from pretreatment vaginal cancer cohorts as well as cohorts of patients with other gynecologic malignancies.

Regarding local extent evaluation, the prospective ACRIN 6651 study of patients with cervical cancer prior to treatment, found that CT was insensitive for detection of rectal and bladder invasion, suggesting that performance would be similarly poor in the setting of recurrent disease prior to pelvic exenteration [19].

A small retrospective study evaluating FDG-PET/CT in 23 patients with primary vaginal cancer prior

to treatment found that CT and FDG-PET detected pelvic nodal metastases in 17% (4 of 23) and 35% (8 of 23) of patients, respectively, suggesting inferior sensitivity of CT alone for nodal metastases. Although older literature suggested that CT is less sensitive than PET/CT for nodal metastases [22], the more recent ACRIN 6671/GOG 0233 trial in cervical cancer patients prior to treatment showed a more modest difference in sensitivity for abdominal nodes (42% versus 50%, respectively), and no significant difference in sensitivity for pelvic nodes (79% versus 83%, respectively) [23]. Likewise, CT had only modestly lower AUC (0.83) compared with PET/CT (0.90) for detection of nodal metastases from cervical cancer in a recent meta-analysis [24]. For distant metastases from cervical cancer, CT is inferior in the detection of osseous metastases (sensitivity 66%) compared with FDG-PET/CT (sensitivity 96%) [25].

These findings, if applied to vaginal cancer, suggest that CT is a reasonable staging tool for known or suspected tumor recurrence in the abdomen and pelvis, although it is likely inferior to MRI for evaluating local tumor extent, modestly inferior to FDG-PET/CT for nodal metastases, and inferior to FDG-PET/CT for osseous metastases. The use of IV contrast is strongly encouraged when possible, because the improved tissue contrast likely benefits primary tumor evaluation, delineation of lymph nodes from adjacent vessels, and detection of hepatic metastases. No studies have specifically assessed the performance of CT of the abdomen and pelvis without IV contrast for evaluation of known or suspected vaginal cancer recurrence.

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

C. FDG-PET/CT Skull Base to Mid-Thigh

No study has evaluated FDG-PET/CT in a cohort limited to patients with recurrent vaginal cancer. Data on the utility of FDG-PET/CT in this setting is limited to mixed cohorts of patients with various gynecologic malignancies, including vaginal cancer, with cervical squamous cell carcinoma generally comprising the majority of patients. One such cohort of 27 patients with recurrent gynecologic malignancies prior to pelvic exenteration was studied prospectively to compare FDG-PET and CT. FDG-PET was 100% sensitive and 73% specific for identifying extrapelvic metastases, most notably outperforming CT in the detection of pelvic and para-aortic nodal metastases [29].

A retrospective study of 85 patients with recurrent gynecologic malignancies reached similar conclusions, identifying findings suspicious for extraregional recurrence in 28% (24 of 85) of patients by PET versus 9% (8 of 85) of patients by conventional imaging (CT and pelvic MRI), with nodal metastases accounting for many of the discrepancies [30]. Concordant with these findings, the NCCN guidelines recommend whole-body FDG-PET/CT in patients with suspected recurrence of cervical cancer [27], although no such formal guidelines exist for vaginal cancer.

FDG-PET/CT has also demonstrated the potential to evaluate bladder, rectal, and pelvic sidewall invasion with high accuracy (AUC 0.76–0.96) in patients with recurrent gynecologic malignancies [47]. Nonetheless, MRI remains the preferred modality for evaluating local tumor extent for known or suspected vaginal cancer recurrence [32].

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

D. Fluoroscopy Contrast Enema

There is no relevant literature regarding the use of fluoroscopic contrast enema in the modern imaging workup of vaginal cancer, and its use has largely been replaced by cross-sectional

imaging techniques.

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

E. MRI Pelvis

Given the rarity of vaginal cancer, primary data regarding the use of MRI in this setting are sparse. Donati et al [32] evaluated the utility of pelvic MRI in 50 patients with recurrent or persistent pelvic malignancies prior to pelvic exenteration, of which 12% (6 of 50) were vaginal cancer and 56% (28 of 50) were cervical cancer. They compared all imaging findings to a surgical and pathologic reference standard and found that for detection of bladder, rectum, and pelvic sidewall invasion, respectively, the AUC ranges for 2 readers were 0.95 to 0.96, 0.88 to 0.90, and 0.90 to 0.98; sensitivities were 87%, 75% to 81%, and 75% to 88%; and specificities were 93% to 100%, 97%, and 94% to 97%, with excellent interobserver agreement ($k = 0.81\text{--}0.85$). Although diagnostic performance in vaginal cancer was not specifically separated, 68% (34 of 50) of the patients had either vaginal or cervical cancer, therefore providing some degree of generalizability to vaginal cancer patients.

Although MRI readily depicts lymph nodes, it has constraints similar to CT with regard to the limited sensitivity and specificity of size and morphologic criteria. No study has evaluated the diagnostic performance of MRI for nodal staging isolated to a cohort of primary vaginal cancer patients with disease recurrence. However, data from mixed cohorts of patients with recurrence of cervical, vaginal, and other gynecologic cancers have suggested superior sensitivity of FDG-PET/CT for pelvic nodal metastases compared with pelvic MRI and CT [29,30].

The use of IV contrast may improve tissue characterization but is not considered essential, with variable inclusion in published protocols for evaluation of vaginal [28,31] and cervical cancer [7,32-34]. No study has specifically compared the incremental utility of gadolinium-enhanced sequences over T2-weighted sequences for pelvic MRI in this context. Regarding the use of vaginal gel in MRI of the pelvis, there is insufficient primary data in the literature to support its routine use.

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

F. MRI Abdomen and Pelvis

Given the rarity of vaginal cancer, primary data regarding the use of MRI in this setting are sparse. Donati et al [32] evaluated the utility of pelvic MRI in 50 patients with recurrent or persistent pelvic malignancies prior to pelvic exenteration, of which 12% (6 of 50) were vaginal cancer and 56% (28 of 50) were cervical cancer. They compared all imaging findings to a surgical and pathologic reference standard and found that for detection of bladder, rectum, and pelvic sidewall invasion, respectively, the AUC ranges for 2 readers were 0.95 to 0.96, 0.88 to 0.90, and 0.90 to 0.98; sensitivities were 87%, 75% to 81%, and 75% to 88%; and specificities were 93% to 100%, 97%, and 94% to 97%, with excellent interobserver agreement ($k = 0.81\text{--}0.85$). Although diagnostic performance in vaginal cancer was not specifically separated, 68% (34 of 50) of the patients had either vaginal or cervical cancer, therefore providing some degree of generalizability to vaginal cancer patients.

Although MRI readily depicts lymph nodes, it has constraints similar to CT with regard to the limited sensitivity and specificity of size and morphologic criteria. No study has evaluated the diagnostic performance of MRI for nodal staging isolated to a cohort of primary vaginal cancer

patients with disease recurrence. However, data from mixed cohorts of patients with recurrence of cervical, vaginal, and other gynecologic cancers have suggested superior sensitivity of FDG-PET/CT for pelvic nodal metastases compared with pelvic MRI and CT [29,30].

If MRI of the abdomen and pelvis is used in place of CT of the abdomen and pelvis, the addition of chest CT is encouraged to evaluate for pulmonary metastases. The use of IV contrast may improve tissue characterization and is particularly beneficial when MRI of the abdomen is included, because it improves detection of hepatic metastases.

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

G. Radiography Intravenous Urography

There is no relevant literature regarding the use of radiographic IV urography in the modern imaging workup of vaginal cancer, and its use has largely been replaced by cross-sectional imaging techniques.

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

H. US Pelvis Transvaginal

There is no relevant literature regarding the role of TVUS in the evaluation of known or suspected vaginal cancer recurrence nor is there any such literature for cervical cancer recurrence. Additionally, the potential applicability of TVUS for recurrent vaginal cancer would be limited to local recurrence, because TVUS has little to no utility for pelvic nodal evaluation [39].

Variant 3: Vaginal Cancer. Suspected or known recurrence. Evaluate extent of disease. Initial imaging.

I. US Abdomen and Pelvis Transabdominal

There is no relevant literature regarding the role of TAUS in vaginal cancer staging. TAUS is inferior for visualizing the female genital tract compared with TVUS, and neither technique has a role in nodal or distant evaluation.

Summary of Recommendations

- **Variant 1:** MRI pelvis without and with IV contrast or CT abdomen and pelvis with IV contrast or FDG-PET/CT skull base to mid-thigh is usually appropriate as the initial imaging for pretreatment staging of vaginal cancer. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 2:** MRI pelvis without and with IV contrast or FDG-PET/CT skull base to mid-thigh is usually appropriate as the initial imaging for posttreatment evaluation of vaginal cancer with no suspected recurrence. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 3:** MRI pelvis without and with IV contrast or CT abdomen and pelvis with IV contrast or CT chest with IV contrast or FDG-PET/CT skull base to mid-thigh is usually appropriate as the initial imaging of vaginal cancer to evaluate the extent of disease with suspected or known recurrence. These procedures are equivalent alternatives (ie, only one procedure will

be ordered to provide the clinical information to effectively manage the patient's care).

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at <https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria>.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

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. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). 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*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
○	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢ ☢	0.1-1 mSv	0.03-0.3 mSv
☢ ☢ ☢	1-10 mSv	0.3-3 mSv
☢ ☢ ☢ ☢	10-30 mSv	3-10 mSv
☢ ☢ ☢ ☢ ☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies.”

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Disclaimer

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.

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