

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

Variant 1: Initial staging of pretreatment ovarian cancer.

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

Variant 2: Extent of disease in suspected or known recurrence of ovarian cancer.

Procedure	Appropriateness Category	Relative Radiation Level
CT abdomen and pelvis with IV contrast	Usually Appropriate	⊕⊕⊕⊕
CT chest abdomen 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	O
CT abdomen and pelvis without IV contrast	May Be Appropriate	⊕⊕⊕⊕
CT chest abdomen pelvis without IV contrast	May Be Appropriate	⊕⊕⊕⊕
MRI abdomen and pelvis without IV contrast	May Be Appropriate	O
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	⊕⊕⊕⊕
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	⊕⊕⊕⊕
US abdomen and pelvis transabdominal	Usually Not Appropriate	O
US pelvis transvaginal	Usually Not Appropriate	O
X-ray contrast enema	Usually Not Appropriate	⊕⊕⊕
X-ray intravenous urography	Usually Not Appropriate	⊕⊕⊕

STAGING AND FOLLOW-UP OF OVARIAN CANCER

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Summary of Literature Review

Introduction/Background

Ovarian cancer is the fifth most common cause of cancer death in women in the United States behind lung, breast, colorectal, and pancreatic cancers, accounting for more than 3% of all cancers in women and causing more deaths than any other gynecologic malignancy [1]. Most of the information in this narrative regarding imaging use for staging and evaluation of recurrence applies to epithelial ovarian cancers. Two major subtypes of epithelial ovarian cancers are distinguished by molecular, genetic, and morphologic characteristics: type 1 being the relatively indolent low-grade serous, low-grade endometrioid, mucinous tumors, transitional (Brenner), and clear cell carcinomas; and type 2 being aggressive neoplasms, including high-grade serous or endometrioid, and undifferentiated cancer [2]. The aggressive (type 2) ovarian cancers most often present in advanced stages, stage III-IV, after the disease has spread widely out of the pelvis [3,4]. This document is mostly reflective of staging and follow-up for type 2 ovarian cancers. The major roles of diagnostic imaging have been to characterize the ovarian mass, determine the extent of preoperative disease, predict tumor resectability, and evaluate response to chemotherapy [4-11]. Surgical staging is both diagnostic and therapeutic, and an experienced gynecologic surgeon (a gynecologic oncologist, specifically) is critical in optimum debulking of this tumor [9,12,13]. However, up to 40% of patients may be understaged at laparotomy [14], and prognosis is tied to the presence of residual tumor after surgery.

CA-125 Levels

The preoperative evaluation of patients with suspected ovarian carcinoma usually includes a serum (cancer antigen) CA-125 determination. Only about 50% of all patients with stage I ovarian cancer have a true-positive result [4,15-17]. Thus, this test alone is inadequate when used in isolation as a screening tool. This is especially true in menstruating females, since false-positive results have been reported with endometriosis, benign ovarian cysts, pregnancy, and pelvic inflammatory disease. Pancreatic cancer and cirrhosis may also result in elevated CA-125 levels [18]. However, with stage II or greater ovarian cancer, the true-positive rate is as high as 80% [16]. There is a very high correlation between CA-125 levels and the clinical course of the patient during chemotherapy. CA-125 levels also can be used to predict tumor recurrence in patients who are clinically tumor free [19]. Oftentimes, other epithelial and nonepithelial tumor markers are ordered to differentiate tumor histology preoperatively. CA19-9 and carcinoembryogenic antigen (CEA) can also be elevated with epithelial ovarian neoplasms, but have limited specificity individually, and a high CA125-to-CEA ratio has been shown to optimize specificity for ovarian versus gastrointestinal primary neoplasms [20,21].

Overview of Imaging Modalities

Imaging is used to detect and characterize adnexal masses and to stage ovarian cancer both prior to and following initial treatment. Thus far, no imaging method has achieved a sufficiently high positive predictive value to be recommended for screening women of average risk [4]; please see the ACR Appropriateness Criteria[®] "[Ovarian](#)

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[Cancer Screening](#)” [22] for further discussion. In patients at increased risk for ovarian carcinoma based on hereditary factors or serum markers, transvaginal ultrasound (US) may be used for ovarian cancer screening, although determinations of outcome-based benefits are still preliminary at best [4,22-28]. Characterization of adnexal masses is not in the scope of this topic, please see the ACR Appropriateness Criteria® “[Clinically Suspected Adnexal Mass](#)” [29] for further discussion. Briefly, transvaginal US is also useful for determining the site of origin of a pelvic mass and to characterize the lesion [30]. A combination of morphology on transvaginal US and Doppler waveform analysis may provide an accurate risk assessment for adnexal lesions [8,23]. Magnetic resonance imaging (MRI) is excellent for characterizing adnexal masses that are indeterminate by US [6-8,31-33]. Positron emission tomography (PET) using the tracer fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG), particularly when combined with computed tomography (CT), has improved the accuracy of staging ovarian carcinoma [10,32,34-37]. PET combined with MRI is a newer modality, for which a specific role has not yet been established [38].

The decision regarding initial treatment for ovarian cancer depends on accurate staging. CT, FDG-PET/CT, and MRI have been used to assess the resectability of tumors, the candidacy of patients for effective cytoreductive surgery, the need for postoperative chemotherapy if debulking is suboptimal, and the need for referral to a gynecologic oncologist [5,34-36,39-45]. Referral to a gynecologic oncologist for optimal staging and debulking is the second most important determinant for survival after tumor stage in patients with ovarian carcinoma. The International Federation of Gynecologists and Obstetricians revised the criteria for ovarian cancer staging in 2014 [46]. The updated system recognizes the morphologic and molecular similarities between fallopian tube, primary peritoneal carcinomas, and ovarian malignancy [47]. Stage I disease includes tumor limited to 1 or both ovaries or fallopian tubes, stage II disease has spread to the surface of other pelvic organs, stage III indicates spread to retroperitoneal lymph nodes (IIIA1) or abdominal peritoneal surfaces (IIIA2 if microscopic disease, IIIB or C with macroscopic nodules), and stage IV is advanced disease with distant metastases to solid organs or a malignant pleural effusion [5,6,46]. When there is a contraindication to administration of iodinated contrast, CT without intravenous contrast offers limited evaluation of extent of disease in initial evaluation or follow-up; for more information on the imaging of patients with end-stage renal failure, please see the ACR Manual on Contrast Media [48].

Cytoreductive surgery is the standard initial treatment for ovarian cancer. Imaging is used to define the extent of disease, assess the likelihood of optimal primary cytoreduction [14], and select patients who may benefit from neoadjuvant chemotherapy [49,50]. The radiographic techniques for preoperative staging of ovarian cancer called for by the International Federation of Gynecology and Obstetrics—such as chest radiograph, barium enema, and excretory urography—have been replaced by more advanced cross-sectional imaging techniques such as CT [51-53] in the United States and many other countries. The accuracy of imaging for prediction of suboptimal debulking, and therefore patient selection for surgical versus neoadjuvant treatment, remains controversial [54-56].

Discussion of Procedures by Variant

Variant 1: Initial staging of pretreatment ovarian cancer.

CT Abdomen and Pelvis

Contrast-enhanced CT (with oral contrast) is the current imaging modality of choice in the preoperative evaluation of ovarian cancer and is an accurate method for identifying sites of abdominopelvic disease that predict successful surgical cytoreduction [57]. CT has been useful to detect local tumor involvement of the pelvic ureter and uterine serosa (although uterine serosal involvement is less important in ovarian cancer than it is for endometrial cancer), as well as metastases to the peritoneum, omentum, mesentery, liver, spleen, lymph nodes, and lung parenchyma [5,39,40,52]. CT has a reported accuracy for ovarian cancer staging of up to 94% [14]. The sensitivity varies by anatomic site, however, and the most important limitation of CT in staging ovarian cancer is its inability to reliably detect bowel surface, mesenteric, or peritoneal tumor implants <5 mm, especially in the absence of ascites [5,43,58,59]. CT is also useful for guiding biopsy of the omentum, or other abdominal tumor, a procedure that can increase the accuracy of preoperative diagnosis, if indicated [60-63].

For assessment of the resectability of ovarian cancer, cross-sectional imaging (CT or MRI) plays a critically important role in finding significant lesions (>2 cm) at the root of the mesentery, gastrosplenic ligament, omentum of the lesser sac, porta hepatis, intersegmental fissure of the liver, diaphragm, liver dome, and lung parenchyma, and also in detecting lymphadenopathy at or above the celiac axis, presacral extraperitoneal disease, and pelvic sidewall invasion [5,14,40,52,64-68]. Incomplete resection (residual tumor >1 cm) of primary tumor

yields little survival benefit while subjecting patients to substantial perioperative morbidity. To date, imaging and prediction models that are based on imaging, demographic characteristics, and tumor markers have not been shown to provide sufficiently high accuracy for prediction of suboptimal debulking to guide the decision regarding surgery [55,69]. Unresectable disease can be managed by needle or laparoscopic biopsy, followed by chemotherapy, and possibly by a later attempt at interval debulking, resulting in improved survival by virtue of response to chemotherapy and optimal resection [9,34,60-63].

Noncontrast-enhanced CT of the abdomen and pelvis offers limited ability to differentiate small peritoneal or mesenteric implants, or lymphadenopathy, from bowel or other adjacent organs.

CT Chest

CT of the chest is useful for detecting pleural and pulmonary metastases during primary staging. Although CT is not sensitive for detecting pleural metastases, these can be verified by video-assisted thoracoscopy, if needed [70]. Preoperative detection by CT of a moderate-to-large pleural effusion helps predict poor post-treatment outcome [71]. For postsurgical surveillance, the yield of chest CT is low if the chest radiograph shows no abnormalities, CT shows no abdominal or pelvic disease, and there is no rising serum CA-125 [72,73]. If PET using tracer FDG is used and includes chest, abdomen, and pelvis, the added value of diagnostic-quality chest CT is probably even lower.

MRI

MRI is an excellent problem-solving technique by virtue of its ability to define common conditions such as fibroids, dermoid cysts, endometriomas, and other benign lesions [6-8,31,44]. A multivariable analysis showed that the accuracy of MRI with gadolinium enhancement in separating ovarian malignancy from other types of adnexal masses was 93% [74]. Gadolinium enhancement and diffusion-weighted imaging offer improved diagnostic confidence and tissue characterization [31,74]. In staging, MRI has been shown to provide equivalent accuracy to CT and to predict peritoneal tumor volume comparable with surgery, with sensitivity of 0.88, specificity of 0.74, and accuracy of 0.84 [75,76]. However, the role of MRI in staging has been limited because 1) the use of intraluminal gastrointestinal contrast agents with MRI is not routine as it is with CT, and 2) patient motion is a greater problem for MRI than for CT. Although CT is currently the modality of choice for staging ovarian cancer, MRI is recommended for patients with borderline tumors or ovarian cancers that have been previously staged with fertility preservation (to minimize ionizing radiation exposure), or for some patients whose CT findings are inconclusive [68,77]. Higher-field MRI scans may improve the accuracy of MRI for staging ovarian cancer pending further investigation [78].

Intravenous contrast is preferable for detection and characterization of lesions suspected to represent tumor deposits. MRI without contrast may be considered for staging if contrast cannot be given and may offer improved soft-tissue contrast than noncontrast CT for staging in the pelvis; however, to our knowledge, there are no known studies on the comparative performance of MRI without contrast and CT without contrast for staging.

FDG-PET/CT

The use of FDG-PET imaging in the primary diagnosis and tissue characterization of ovarian cancer is unsupported to date. Specificity has been reported to be as low as 54%, while sensitivity has been as high as 86% [33,79,80]. Also, false-negative results have been reported with borderline tumors, mucinous tumors, early carcinomas, and other low-grade types of tumors [81,82]. False-positive results have been reported with fibromas, dermoid cysts, hydrosalpinges, and endometriosis [68,80].

However, FDG-PET, especially when combined with CT, is a valuable tool for diagnosing and staging advanced disease [32,34-37,79]. For staging, fusion FDG-PET/CT has higher reported accuracy than either CT or FDG-PET alone in multiple studies [32,35,36,79,83]. Improved detection of peritoneal disease may stem from metabolic activity in small deposits or lymph nodes that may be difficult to identify and characterize with CT alone. Thus, although CT with contrast is the modality of choice for initial staging, PET or FDG-PET/CT may be a useful adjunct test, particularly when CT is indeterminate.

Contrast Enema

Contrast enema is not routinely used for pretreatment staging of ovarian cancer. An exception may occur when there is concern about the possibility of a colonic primary versus ovarian primary malignancy based on preoperative CT findings, signs, symptoms, and CA-125 and CEA tumor marker ratio.

IVU

Intravenous urography (IVU) is not routinely used for pretreatment staging of ovarian cancer.

US

There is no evidence to support a role for US in initial staging evaluation of ovarian cancer. Transvaginal US is mainly useful for determining the site of origin of a pelvic mass and to characterize the lesion [30].

Variant 2: Extent of disease in suspected or known recurrence of ovarian cancer.

Imaging of the chest, abdomen, and pelvis plays a key role in evaluation for recurrence and the extent of disease. Rising CA-125, symptoms, or other clinical suspicion for relapse after treatment prompts imaging evaluation for recurrence. If imaging or clinical examination confirms a recurrent tumor, the extent of disease and timing of disease recurrence then determines the choice(s) of treatments, including surgery, chemotherapy, and radiation therapy. The choices for treatment depend upon the time that has passed since chemotherapy was completed. In general, surgical resection of the recurrent tumor is an option when chemotherapy was completed more than 6 months before recurrence and with the option for additional radiation therapy or chemotherapy after surgery.

The role for routine surveillance with imaging is unclear in patients considered to be in clinical remission. Imaging has been shown to have limited sensitivity for detection of small tumor deposits in the abdomen and pelvis, with or without monitoring of CA-125 [3,84]. Furthermore, the MRC OV05/EORTC trial did not show a difference in overall survival when patients were treated based on elevated CA-125 versus clinical evidence of recurrence (including imaging findings) [85], despite recognition that CA-125 is generally elevated in cases of recurrence before clinical or imaging signs become evident. The National Comprehensive Cancer Network guidelines for follow-up of primary chemotherapy with complete response include imaging tests as needed, using CT, FDG-PET, FDG-PET/CT, MRI, or chest radiographs [11].

CT

Contrast-enhanced CT (also using oral contrast) is the modality of choice for detecting recurrence in the chest, abdomen, or pelvis. Contrast-enhanced CT has a reported sensitivity ranging from 58% to 84% and specificity in the range of 59% to 100% in identifying tumor recurrence [52,86,87]. Recurrent disease usually manifests as peritoneal implants; within the peritoneal cavity and on the surface of the visceral organs. CT is used to identify tumor deposits in the root of the mesentery, gastrosplenic ligament, omentum of the lesser sac, porta hepatis, intersegmental fissure of the liver, diaphragm, liver dome, and lung parenchyma, and also in detecting lymphadenopathy. However, identification of small (<5 mm) tumor deposits in the mesentery, on bowel wall, or along the peritoneum may be limited [5,43,58,59].

Noncontrast-enhanced CT of the abdomen and pelvis offers limited ability to identify small peritoneal or mesenteric implants, or lymphadenopathy among bowel loops and other adjacent organs.

MRI

The reported accuracy of MRI for detecting lesions >2 cm in recurrent disease is comparable to that of CT at 93% to 95% [14]. However, MRI demonstrated a significantly lower area under the receiver operator characteristic curve than CT, FDG-PET, FDG-PET/CT, or CA-125 for overall detection of recurrent ovarian cancer in a meta-analysis [88]. CT remains the most widely used imaging method for detecting recurrence, and, despite some advantages, the role of MRI in follow-up imaging has been limited because 1) the use of intraluminal gastrointestinal contrast agents with MRI is not routine as it is with CT and 2) patient motion is a greater problem for MRI than for CT. Although CT is currently the modality of choice for suspected recurrence of ovarian cancer, MRI is recommended for borderline tumors or ovarian cancers that have been previously staged with fertility preservation (to minimize ionizing radiation exposure), or for some patients whose CT findings are inconclusive.

Intravenous contrast is preferable for detection and characterization of lesions suspected to represent tumor deposits. MRI without contrast may be considered for staging if contrast cannot be given and may offer improved soft-tissue contrast than noncontrast CT for staging in the pelvis. However, to our knowledge, there are no known studies on the comparative performance of MRI without contrast and CT without contrast for staging.

FDG-PET/CT

For suspected recurrent ovarian cancer, FDG-PET/CT has recently shown similar or higher accuracy for tumor detection than contrast-enhanced CT or PET alone [10,19,34,89,90], with a sensitivity of 95% to 97% and specificity of 80% to 100% [86,89,91]. The spatial resolution of PET limits sensitivity for subcentimeter metastases, and metabolic activity on or between bowel loops, particularly after surgery when adhesions or

inflammation are present, may be difficult to assess. For such reasons, PET or FDG-PET/CT has not uniformly shown improved sensitivity or specificity of recurrence compared with CT alone [88]. Still, the combined metabolic activity and anatomic localization of FDG-PET/CT have been shown to improve disease detection in small lymph nodes and unresectable sites, which can alter management [87,91]. Notably, the performance of FDG-PET/CT in the literature reflects a predominance of serous papillary carcinomas, and false-negative results have been reported with mucinous adenocarcinomas, and cystic, necrotic, low-grade or small-volume (<7 mm) deposits [82]. Thus, either CT or FDG-PET/CT may be used to evaluate suspected recurrence, and FDG-PET/CT may also be a useful adjunct when CT is indeterminate with persistent clinical concern [92].

Contrast Enema

Contrast enema is not routinely used for detecting recurrence of ovarian cancer.

IVU

IVU is not routinely used for detecting recurrence of ovarian cancer.

Laparotomy

Second-look laparotomy is no longer routinely performed because the noninvasive diagnosis of recurrence obviates the need for unnecessary surgery, and generally may be reserved for patients in which the second-look findings might change treatment planning or clinical trial protocols [93]. The decision for secondary debulking surgery is guided by a chemotherapy-free interval, patient performance status, and extent and resectability of disease at time of recurrence. Imaging therefore plays a critical role in the decision-making process for secondary debulking [94].

US

US is not routinely used for detection of recurrent ovarian cancer after surgery. In cases of borderline ovarian tumors (or invasive malignancies) in which fertility-sparing surgery has been performed, transvaginal US has been used in surveillance of the adnexa for recurrent lesions [95].

Summary of Recommendations

- For the initial staging of ovarian cancer, contrast-enhanced CT (with oral contrast) of the abdomen and pelvis is the imaging modality of choice, with inclusion of the chest where indicated. These examinations are complementary and should be performed together.
- Contrast-enhanced CT of the abdomen and pelvis (with oral contrast), or CT of the chest, abdomen, and pelvis are the modalities of choice for the extent of disease in suspected recurrence, and FDG-PET/CT is also usually appropriate as it can provide management-changing information about unresectable sites of tumor or small lymph nodes. CT and FDG-PET/CT are considered equivalent alternatives.

Summary of Evidence

Of the 96 references cited in the *ACR Appropriateness Criteria® Staging and Follow-up of Ovarian Cancer* document, 5 are categorized as therapeutic references including 4 good-quality studies. Additionally, 88 references are categorized as diagnostic references including 1 well-designed study, 25 good-quality studies, and 35 quality studies that may have design limitations. There are 28 references that may not be useful as primary evidence. There are 3 references that are meta-analysis studies.

The 96 references cited in the *ACR Appropriateness Criteria® Staging and Follow-up of Ovarian Cancer* document were published from 1986-2017.

Although there are references that report on studies with design limitations, 30 well-designed or good-quality studies provide good evidence.

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, both because of 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 to 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 [96].

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 (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies".

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

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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.