

**American College of Radiology
ACR Appropriateness Criteria®
Staging of Renal Cell Carcinoma**

Variant 1: **Renal cell carcinoma. No contraindication to either iodinated CT contrast or gadolinium-based MR intravenous contrast. Staging.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen and pelvis without and with IV contrast	Usually Appropriate	○
MRI abdomen without and with IV contrast	Usually Appropriate	○
CT abdomen and pelvis with IV contrast	Usually Appropriate	⊕⊕⊕
CT abdomen with IV contrast	Usually Appropriate	⊕⊕⊕
CT chest with IV contrast	Usually Appropriate	⊕⊕⊕
Radiography chest	May Be Appropriate	⊕
Bone scan whole body with SPECT or SPECT/CT area of interest	May Be Appropriate	⊕⊕⊕
CT head with IV contrast	May Be Appropriate	⊕⊕⊕
CT abdomen and pelvis without and with IV contrast	May Be Appropriate (Disagreement)	⊕⊕⊕⊕
CT abdomen without and with IV contrast	May Be Appropriate (Disagreement)	⊕⊕⊕⊕
US abdomen	Usually Not Appropriate	○
US abdomen with IV contrast	Usually Not Appropriate	○
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	○
MRI abdomen without IV contrast	Usually Not Appropriate	○
MRI head without and with IV contrast	Usually Not Appropriate	○
MRI head without IV contrast	Usually Not Appropriate	○
MRU without and with IV contrast	Usually Not Appropriate	○
MRU without IV contrast	Usually Not Appropriate	○
Bone scan whole body	Usually Not Appropriate	⊕⊕⊕
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT head without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT head without IV contrast	Usually Not Appropriate	⊕⊕⊕
CTU without and with IV contrast	Usually Not Appropriate	⊕⊕⊕⊕
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕⊕
Fluoride PET/CT skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕

Variant 2:**Renal cell carcinoma. Contraindication to both iodinated CT and gadolinium-based MR intravenous contrast. Staging.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen and pelvis without IV contrast	Usually Appropriate	○
MRI abdomen without IV contrast	Usually Appropriate	○
CT chest without IV contrast	Usually Appropriate	☼☼☼
Radiography chest	May Be Appropriate	☼
MRI head without IV contrast	May Be Appropriate	○
Bone scan whole body	May Be Appropriate	☼☼☼
Bone scan whole body with SPECT or SPECT/CT area of interest	May Be Appropriate	☼☼☼
CT abdomen and pelvis without IV contrast	May Be Appropriate	☼☼☼
CT abdomen without IV contrast	May Be Appropriate (Disagreement)	☼☼☼
US abdomen	Usually Not Appropriate	○
US abdomen with IV contrast	Usually Not Appropriate	○
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	○
MRI abdomen without and with IV contrast	Usually Not Appropriate	○
MRI head without and with IV contrast	Usually Not Appropriate	○
MRU without and with IV contrast	Usually Not Appropriate	○
MRU without IV contrast	Usually Not Appropriate	○
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen with IV contrast	Usually Not Appropriate	☼☼☼
CT chest with IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
CT head with IV contrast	Usually Not Appropriate	☼☼☼
CT head without and with IV contrast	Usually Not Appropriate	☼☼☼
CT head without IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼
CT abdomen without and with IV contrast	Usually Not Appropriate	☼☼☼☼
CTU without and with IV contrast	Usually Not Appropriate	☼☼☼☼
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☼☼☼☼
Fluoride PET/CT skull base to mid-thigh	Usually Not Appropriate	☼☼☼

Variant 3:**Renal cell carcinoma. Contraindication only to iodinated CT intravenous contrast. Staging.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen and pelvis without and with IV contrast	Usually Appropriate	○
MRI abdomen without and with IV contrast	Usually Appropriate	○
CT chest without IV contrast	Usually Appropriate	☼☼☼
Radiography chest	May Be Appropriate	☼
Bone scan whole body with SPECT or SPECT/CT area of interest	May Be Appropriate	☼☼☼
CT abdomen and pelvis without IV contrast	May Be Appropriate	☼☼☼
CT abdomen without IV contrast	May Be Appropriate	☼☼☼
US abdomen	Usually Not Appropriate	○
US abdomen with IV contrast	Usually Not Appropriate	○
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	○
MRI abdomen without IV contrast	Usually Not Appropriate	○
MRI head without and with IV contrast	Usually Not Appropriate	○
MRI head without IV contrast	Usually Not Appropriate	○
MRU without and with IV contrast	Usually Not Appropriate	○
MRU without IV contrast	Usually Not Appropriate	○
Bone scan whole body	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen with IV contrast	Usually Not Appropriate	☼☼☼
CT chest with IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
CT head with IV contrast	Usually Not Appropriate	☼☼☼
CT head without and with IV contrast	Usually Not Appropriate	☼☼☼
CT head without IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼
CT abdomen without and with IV contrast	Usually Not Appropriate	☼☼☼☼
CTU without and with IV contrast	Usually Not Appropriate	☼☼☼☼
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☼☼☼☼
Fluoride PET/CT skull base to mid-thigh	Usually Not Appropriate	☼☼☼

STAGING OF RENAL CELL CARCINOMA

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Summary of Literature Review

Introduction/Background

Renal cancer is the third most common urologic cancer and accounts for 1% to 3% of all adult malignancies. Renal cell carcinoma (RCC) represents the vast majority (85%-90%) of all malignant renal tumors in adults. It is estimated that there will be approximately 76,080 new cases of renal cancers and more than 13,780 renal cancer-related deaths in the United States in 2021 [1,2].

The incidence of RCC is reported to be higher in men, with a 2.02% lifetime risk, compared with 1.03% in women. Various potential risk factors have been reported for RCC including smoking, obesity, high blood pressure, advanced renal disease, exposure to certain chemicals such as trichloroethylene, and a family history of renal cancer. African Americans are at a higher risk of developing renal malignancies, although the cause for this increased risk is not yet known. Although the vast majority of RCCs are sporadic, approximately 5% of these tumors are hereditary. There are numerous hereditary renal cancer syndromes, and several of these have autosomal dominant inheritance, including von Hippel-Lindau disease, hereditary leiomyomatosis and RCC, Birt-Hogg-Dubé syndrome, and hereditary papillary renal cancer. Among these, the most common hereditary renal cancer syndrome is von Hippel-Lindau disease, and the prevalence of RCC in these patients varies from 25% to 45%.

Recent advances in the molecular cytogenetics of RCC have significantly enhanced understanding of the pathogenesis, tumor biology, management, and prognosis of this highly heterogeneous malignancy. In 2016, the World Health Organization published the revised classification of renal tumors. There are more than 14 histological subtypes of RCC, but the majority of RCC belong to 3 histological variants, namely clear-cell RCC (75%), papillary RCC (10%-15%), and chromophobe RCC (4%-6%) [3].

Tumor stage is an extremely important prognostic factor in RCC. Patients with stage I localized RCC have an 81% 5-year survival rate compared with just an 8% 5-year survival rate for those with stage IV RCC. Staging of RCC is performed using the TNM staging system, which was developed by the American Joint Committee on Cancer (AJCC) [4].

T1 tumors measure ≤ 7 cm in greatest dimension and are limited to the kidney. T1 tumors are further subdivided into T1a (tumor ≤ 4 cm) and T1b (tumor >4 cm but ≤ 7 cm). T2 tumors measure >7 cm at the greatest dimension and are also limited to the kidney. Similar to T1 tumors, T2 tumors are subdivided based on size into T2a (tumor >7 cm but ≤ 10 cm) and T2b (tumor >10 cm). T3 tumors extend beyond the kidney and may extend into renal vein, inferior vena cava (IVC), or perirenal fat but not into the ipsilateral adrenal gland and not beyond Gerota fascia. T3 tumors are divided into T3a (involvement of renal vein, pelvicalyceal system, perirenal fat, renal sinus fat), T3b (involvement of the IVC below the diaphragm), and T3c (involvement of the IVC above the diaphragm or invasion of the wall of the IVC). T4 tumors are those that involve the ipsilateral adrenal gland and/ or extend beyond Gerota fascia. N0 indicates absence of nodal involvement, whereas N1 refers to presence of regional nodal involvement. M0 indicates absence of metastatic involvement, whereas M1 designation refers to presence of distant metastases. Stage I disease indicates T1N0M0, whereas stage II disease refers to the presence of T2N0M0. Stage III disease is

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presence of any nodal metastases (N1) and/ or T3 tumor. Stage IV disease is the presence of any distant metastases (M1) and/or presence of T4 tumor.

Curative treatment for RCC may be accomplished with surgical resection. Partial nephrectomy is the preferred treatment option for small T1 RCC, especially because it is associated with lower risk of renal failure and cardiovascular mortality compared to radical nephrectomy. However, it has been reported that incidence of complications such as postoperative bleeding and urinary leaks may be high in partial nephrectomy. Hence, urologists carefully select patients for partial nephrectomy using preoperative scoring systems, such as the Preoperative Aspects and Dimensions Used for Anatomic assessment score, Renal Nephrometry Score, and Centrality Index. Although a full description of these scoring systems is beyond the scope of this manuscript, urologists consider various factors for surgical planning including size of the tumor and the number of lesions (such as presence of multiple and/or bilateral tumors). The location of the tumor is another important criteria. Factors such as tumor location in the upper/mid/lower pole of the kidney, tumor location in the anterior versus posterior renal cortex, location in the medial or lateral rim, and presence of exophytic versus endophytic tumor may impact the decision to perform partial nephrectomy. Furthermore, tumor involvement of renal sinus and perinephric fat, involvement of renal vein and IVC, tumor extension into adjacent organs, and presence of nodal and distant metastases are critical information needed for treatment planning. Although partial nephrectomy may be the preferred curative option in many patients, active surveillance and local ablative therapies are being increasingly considered in carefully selected patients in the management of small localized T1 RCC [5].

Locally advanced T2 to T4 RCC and complex tumors not amenable for partial nephrectomy approach may benefit from radical nephrectomy. Metastatic disease at presentation varies with the patient series but typically occurs in approximately 1 in 10 patients [6,7]. The most common sites of distant metastases, in descending order, are the lungs, bone, retroperitoneal and mediastinal nodes, liver, brain, or multiple sites [8,9].

Radical nephrectomy with metastasectomy remains an option for carefully selected patients with oligo-metastases. Similarly, cytoreductive nephrectomy may be considered even in advanced stage RCC. However, many patients with advanced stage RCC present with multifocal metastatic disease, warranting a multidisciplinary approach. Better understanding of RCC tumor biology has paved the way for the development of numerous FDA-approved therapeutic options for advanced stage RCC including targeted therapy and immunotherapy.

Imaging plays an important role in the staging of RCC [10]. In this document, we provide an update on the appropriate use of imaging examinations for initial staging of known RCC.

Special Imaging Considerations

CT urography (CTU) is an imaging study that is tailored to improve visualization of both the upper and lower urinary tracts. There is variability in the specific parameters, but it usually involves unenhanced images followed by intravenous (IV) contrast-enhanced images, including nephrographic and excretory phases acquired at least 5 minutes after contrast injection. Alternatively, a split-bolus technique uses an initial loading dose of IV contrast and then obtains a combined nephrographic-excretory phase after a second IV contrast dose; some sites include arterial phase. CTU should use thin-slice acquisition. Reconstruction methods commonly include maximum intensity projection or 3-D volume rendering. For the purposes of this document, we make a distinction between CTU and CT abdomen and pelvis without and with IV contrast. CT abdomen and pelvis without and with IV contrast is defined as any protocol not specifically tailored for evaluation of the upper and lower urinary tracts and without both the precontrast and excretory phases.

MR urography (MRU) is also tailored to improve imaging of the urinary system. Unenhanced MRU relies upon heavily T2-weighted imaging of the intrinsic high signal intensity from urine for evaluation of the urinary tract. IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, focal lesions, and stones. A contrast-enhanced T1-weighted series should include corticomedullary, nephrographic, and excretory phases. Thin-slice acquisition and multiplanar imaging should be obtained. For the purposes of this document, we make a distinction between MRU and MRI abdomen and pelvis without and with IV contrast. MRI abdomen and pelvis without and with IV contrast is defined as any protocol not specifically tailored for evaluation of the upper and lower urinary tracts, without both the precontrast and excretory phases, and without heavily T2-weighted images of the urinary tract.

Discussion of Procedures by Variant

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Bone Scan Whole Body

The prevalence of osseous metastases for localized RCC has been shown to be low in patients without symptoms (ie, bone pain) or without laboratory abnormalities suggestive of osseous metastases (ie, elevated serum alkaline phosphatase level) [11,12]. Furthermore, the sites commonly involved by osseous metastases, such as the thoracolumbar spine and ribs, are located in areas covered by chest and abdominal imaging. Thus, even though bone scanning can be helpful to confirm clinically or radiographically suspected metastatic disease, current guidelines from the European Association of Urology (EAU) and National Comprehensive Cancer Network (NCCN) do not support its routine use in the initial staging of asymptomatic RCC [5,13]. However, in patients with RCC with symptoms suspicious for bone metastases, bone scan may be useful.

Bone Scan Whole Body with SPECT or SPECT/CT Area of Interest

The prevalence of osseous metastases for localized RCC has been shown to be low in patients without symptoms (ie, bone pain) or without laboratory abnormalities suggestive of osseous metastases (ie, elevated serum alkaline phosphatase level) [11,12]. Furthermore, the sites commonly involved by osseous metastases, such as the thoracolumbar spine and ribs, are located in areas covered by chest and abdominal imaging. Thus, even though bone scanning can be helpful to confirm clinically or radiographically suspected metastatic disease, current guidelines do not support its routine use in the initial staging of asymptomatic RCC [5,13].

In patients with RCC with symptoms suspicious for bone metastases, bone scan may be useful. If the bone scan shows areas of abnormal radiotracer uptake suspicious for osseous metastases, single-photon emission CT (SPECT) fused with CT can be used to provide detailed anatomic localization of the abnormal radiotracer uptake and further improve the characterization of the nature of the abnormality [14].

CT Abdomen

Preoperative imaging of RCC provides critical information on staging and serves as a roadmap to the surgeon. Both CT and MRI are comparable in staging of the primary tumor [15,16]. CT of the abdomen with IV contrast is considered in all major guidelines as an adequate method for staging of RCC, including the guidelines from the EAU and NCCN [5,13]. Use of IV contrast helps in the diagnosis and staging of the RCC [14,15,17-27]. Acquisition of nephrographic phase images is vital and most important in the detection and characterization of RCC. Corticomedullary phase images and excretory phase images are optional and may be helpful in differentiating RCC subtypes, distinguishing RCC from urothelial tumors and in providing complementary information on the vasculature and tumor extension into pelvicalyceal system.

As alluded to before, the size of the RCC, which is localized to the kidney, is important for the T stage classification in the AJCC TNM staging system because localized tumors measuring ≤ 7 cm in greatest dimension are classified as T1 compared with T2 tumors, which measure > 7 cm in greatest dimension. Numerous studies have reported that CT is accurate for evaluating the size of RCC and highly correlates with the tumor size on surgical pathology, although discrepancies may occur [28-30]. CT is also helpful in detecting T3 and T4 tumors, although it is acknowledged that accurate identification of features such as perinephric or renal sinus fat invasion may be difficult on imaging [3,31,32].

Extension into the perinephric fat is difficult to discriminate from nonspecific perinephric stranding due to edema, vascular engorgement, or fibrosis. High-resolution CT using thin sections appears to improve detection of perinephric infiltration, although false positives are common [15,16,33]. Various authors have reported 85% to 93% sensitivity and 32% to 96% specificity for the detection of perinephric invasion on IV contrast-enhanced CT abdomen [33-35]. In a study involving 117 patients, CT abdomen was reported to have a sensitivity of 59% to 88% and a specificity of 71% to 93% in detecting stage T3a RCC [36]. In particular, CT had a 71% to 88% sensitivity and 71% to 79% specificity for renal sinus fat invasion, a 68% to 83% sensitivity and a 72% to 76% specificity for perinephric fat invasion, and a 59% to 69% sensitivity and a 91% to 93% specificity for renal vein invasion [36]. In a more recent study, 96 patients with 100 pathologically proven RCC, CT was reported to have an 86% sensitivity and 88% specificity for renal sinus fat invasion and an approximately 86% sensitivity and 97% specificity for renal vein invasion [37]. However, CT only had a modest 77% sensitivity and 72% specificity for detecting perinephric fat invasion in this study, emphasizing the difficulties in differentiating nontumoral causes for perinephric soft tissue stranding, from true tumor perinephric fat invasion [37].

It has been reported that the presence of enhancing soft tissue nodule in the perinephric fat on CT may be a helpful sign for the assessment of perinephric fat invasion. Landman et al [38] reported that the presence of enhancing perinephric soft tissue nodule had an 87% accuracy in predicting perinephric fat invasion compared with the CT finding of perinephric soft tissue stranding, which only had a 56% accuracy. However, the sensitivity of enhancing perinephric soft tissue nodule in detection of perinephric fat invasion is relatively low (31%) [38].

CT has an excellent sensitivity for detecting ipsilateral adrenal involvement in RCC (T4 tumors), but the specificity varies from 76% to 95%. One study involving 229 patients with RCC reported that CT had a 100% sensitivity for ipsilateral adrenal involvement in RCC, but only a 76% specificity [39]. However, Blakely et al [40] reported a 100% sensitivity and a 94% specificity for CT in identifying adrenal involvement. Similar findings have been reported by other authors. In another study involving 579 patients, CT was reported to have a 100% negative predictive value, a 100% sensitivity, and a 95% specificity for identifying adrenal involvement [41].

Assessment of RCC nodal metastases on CT is limited [42]. This is due to the fact that CT uses size criteria for nodal metastasis (size >1 cm in short-axis), but this leads to underestimation of disease, resulting in false negatives in the presence of micrometastases in nodes <1 cm in size. Furthermore, false positives are also often seen because of presence of reactive adenopathy, with nodes >1 cm in size. CT is accurate in detecting distant metastases in the abdomen. RCC visceral metastases may occur at various organs including liver, pancreas, adrenals, and contralateral kidney. RCC metastases tend to be hypervascular, and some authors have suggested that arterial phase imaging can be useful to accurately detect the extent of distant metastases [43-46].

CT Abdomen and Pelvis

Preoperative imaging of RCC provides critical information on staging and serves as a roadmap to the surgeon. Both CT and MRI are comparable in staging of the primary tumor [15,16]. Advantages of CT include rapid acquisition time that may translate to better patient compliance and high spatial resolution. Hence, it is often the most commonly used modality for this indication. CT abdomen without and with IV contrast is typically performed for characterizing a renal mass as RCC and staging the tumor. Acquisition of nephrographic phase images is vital and most important in the detection and characterization of RCC. Corticomedullary phase images and excretory phase images are optional and may be helpful in differentiating RCC subtypes, distinguishing RCC from urothelial tumors and in providing complementary information on the vasculature and tumor extension into pelvicalyceal system.

As alluded to before, the size of the RCC that is localized to the kidney is important for the T stage classification in the AJCC TNM staging system because localized tumors measuring ≤ 7 cm in greatest dimension are classified as T1 compared with T2 tumors, which measure >7 cm in greatest dimension. Numerous studies have reported that CT is fairly accurate for evaluating the size of RCC and highly correlates with the tumor size on surgical pathology, although discrepancies may occur [28-30]. CT is also helpful in detecting T3 and T4 tumors, although it is acknowledged that accurate identification of features such as perinephric or renal sinus fat invasion may be difficult on imaging [3,31,32].

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Although CT of the abdomen with IV contrast is considered in all major guidelines as an adequate method for the staging of RCC, imaging of the pelvis for RCC staging is considered optional in the guidelines [5,13]. There is no relevant literature with high-quality evidence regarding the use of CT of the pelvis in the staging of RCC. Although it is likely that CT pelvis may not offer additional information in most patients with early stage RCC, pelvic imaging can be helpful in patients with more advanced RCC, in whom metastatic spread is suspected [47,48].

CT Chest

Chest imaging is indicated in the staging of RCC, given that lungs are one of the most common sites of metastases in RCC [5,13]. There is a lack of literature that have directly compared the accuracy of chest CT with chest radiography for detecting pulmonary metastases in the initial staging of RCC. However, limited data have demonstrated that CT is more sensitive than radiography for the detection of pulmonary metastases from RCC [49]. Hence, CT chest with IV contrast is recommended by the current NCCN guidelines [13].

Apart from identifying pulmonary metastases, chest CT has a high sensitivity for the detection of hilar and mediastinal nodal metastases from RCC [50]. Although it is generally accepted that CT has a high sensitivity for detecting pulmonary nodules, it should be noted that presence of small subcentimeter pulmonary nodules does not equate to pulmonary metastases. Most patients with small T1a RCCs are unlikely to have pulmonary metastases. Prior studies have reported that the risk of metastases is highly correlated with size of the tumor and is virtually nonexistent in tumors <2 cm in size, occurs <1% in tumors of 2 to 3 cm, and occurs approximately 1% to 2% for lesions 3 to 4 cm [51-53]. Hence, the presence of small subcentimeter pulmonary nodules in T1a RCCs is often likely to be a false-positive finding (ie, intrapulmonary lymph nodes and granulomas) but can lead to further unnecessary and potentially invasive investigations.

Larcher et al [54] evaluated the role of staging chest CT in 1,946 patients with RCC. Of the 1,946 patients, 119 had a positive chest CT (6%). Based on multivariable logistic regression model, the authors predicted that patients with RCCs >cT1b, cN1, and systemic symptoms of anemia and thrombocytopenia are more likely to benefit from preoperative chest CT rather than having it performed for all patients with RCC [54]. A more recent study involving 1,082 patients with RCC provided external validation of the Larcher nomogram and reported that the risk of positive chest was <1% in patients without any systemic symptoms and tumor size ≤4 cm [55]. Further large-scale prospective studies would be helpful in deciding when to perform CT chest versus chest radiography in the initial imaging of RCC.

CT Head

Most patients with metastases to the central nervous system are symptomatic. Thus, current guidelines from the EAU and NCCN do not support routine imaging of the brain to search for metastases in asymptomatic patients in the initial staging of RCC. Brain imaging should be performed only in cases with suggestive signs or symptoms [5,13]. Recent studies indicate that up to 4% of patients with advanced, metastatic RCC may harbor asymptomatic brain metastasis [56,57].

Hence, routine brain imaging with IV contrast may be considered in patients with advanced, metastatic RCC, even if they are asymptomatic [56,57].

CTU

There is no relevant literature suggesting that CTU offers any additional benefit over conventional CT of the abdomen in the initial staging of RCC, and thus, this method is not included in the guidelines from the EAU and NCCN [5,13].

FDG-PET/CT Skull Base to Mid-Thigh

Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT has a limited role in the diagnosis and local staging of RCC [58]. Differentiating renal tumor from background normal renal tissue can be difficult because of the renal excretion of FDG. Furthermore, RCC is reported to have variable FDG avidity, limiting its utility. Nakanishi et al [59] reported a 56% sensitivity, a 67% specificity, a 15% positive predictive value, a 57% negative predictive value, and a 65% accuracy for FDG-PET in the staging of RCC. A recent clinical trial from Turkey involving 62 patients with RCC reported an 84% accuracy for contrast-enhanced FDG-PET/CT in staging RCC [60]. However, further studies are warranted before PET/CT can be used in the routine initial staging of RCC. At present, given the paucity of literature to support the use of FDG-PET/CT, the guidelines from the EAU and NCCN do not recommend routine FDG-PET/CT in the initial staging of RCC [5,13].

Fluoride PET/CT Skull Base to Mid-Thigh

Preliminary results for other PET tracers are also becoming available. In a small prospective study of 10 patients with metastatic RCC, 18F-sodium fluoride (NaF) PET/CT was found to be significantly more sensitive for the detection of RCC skeletal metastases than Tc-99m bone scintigraphy or CT, with sensitivities of 100%, 29%, and 46%, respectively. CT and Tc-99m bone scintigraphy in this study identified only 65% of the metastases detected by fluoride PET/CT [61]. However, given the paucity of literature for utility of fluoride PET/CT in the initial staging of RCC, current guidelines from the EAU and NCCN do not support routine fluoride PET/CT to search for metastases in asymptomatic patients in the initial staging of RCC [5,13].

MRI Abdomen and Pelvis

MRI of the abdomen without and with IV contrast is considered a reliable method for the staging of RCC. Various MR sequences, including T2-weighted, chemical shift T1-weighted, contrast-enhanced T1-weighted, and diffusion-weighted images, are typically obtained for the staging of RCC. In a study involving 40 patients with RCC, MRI was reported to have an accuracy of 81% to 86% for T staging [62]. Breath-hold MRI showing a lack of perinephric fat involvement is reported to have a high negative predictive value for no perinephric tumor invasion [63].

In a study of 73 RCCs, Roy et al [64] showed that the presence of a pseudocapsule on MRI had an accuracy of 93% for clear-cell carcinomas in separating T1/T2 tumors from T3a tumors. Lal et al [65] performed a prospective observational study in 50 patients with RCC, comparing MRI with histopathological findings. In this study, MRI was reported to have a 90% agreement with histopathology for detecting perirenal extension and a 97% agreement with histopathology for detecting tumor extension beyond Gerota fascia [65]. Both contrast-enhanced multidetector CT and MRI are helpful in detecting venous involvement, particularly in the main renal vein and the IVC [33,66].

Increased diameter of the IVC and renal vein, presence of tumor signal both inside and outside the vessel wall, altered signal intensity in the vessel wall, presence of flow around the tumor thrombus, and mobility in different phases are some of the MRI features that are helpful in detecting venous involvement [67,68]. Bland thrombus featuring a uniform signal intensity and lack of enhancement after gadolinium can be distinguished from tumor thrombus, which exhibits intermediate or high signal intensity, heterogeneous intensity, and, more reliably, the presence of small vessels. In a recent study involving 81 patients with RCC, MRI was reported to have a 92% sensitivity, an 86% specificity, an 89% positive predictive value, and a 91% negative predictive value for identifying IVC wall invasion [69]. Pitfalls of MRI include the potential for large tumors to compress the vena cava and cause flow-related artifacts. Such artifacts can be reduced with appropriate saturation pulses.

Although MRI of the abdomen with IV contrast is considered in all major guidelines as an adequate method for the staging of RCC, imaging the pelvis for RCC staging is considered optional in the guidelines [5,13]. There is no relevant literature with high-quality evidence regarding the use of MRI of the pelvis in the staging of RCC. Although it is likely that MRI pelvis may not offer additional information in most patients with early stage RCC, pelvic imaging can be helpful in patients with more advanced RCC, in whom metastatic spread is suspected [47,48].

MRI Abdomen

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MRI Head

Most patients with metastases to the central nervous system are symptomatic. Thus, current guidelines do not support routine imaging of the brain to search for metastases in asymptomatic patients in the initial staging of RCC. Brain imaging with contrast should be performed only in cases with suggestive signs or symptoms [5,13].

Recent studies indicate that up to 4% of patients with advanced, metastatic RCC may harbor asymptomatic brain metastasis [56,57]. Hence, routine brain imaging with IV contrast may be considered in patients with advanced, metastatic RCC, even if they are asymptomatic [56,57].

MRU

There is no relevant literature suggesting that MRU offers any additional benefit over conventional MRI of the abdomen in the initial staging of RCC, and thus, this method is not included in the guidelines from the EAU and NCCN [5,13].

Radiography Chest

The lung is the most common site of metastases in patients with RCC presenting with synchronous metastases. Although the incidence of metastases in RCC <4 cm is low (approximately 1%-2%), it has been reported that 20% to 30% of T1a tumors may have potentially aggressive histologic features. Hence, chest radiography is usually performed in the staging of RCC [13]. However, CT is more sensitive than radiography for the detection of pulmonary metastases from RCC during staging. In addition to a high sensitivity for the detection of pulmonary metastases, chest CT has a high sensitivity for the detection of intrathoracic nodal metastases from RCC. Therefore, in patients with higher risk of pulmonary metastases (such as tumor >4 cm, cN1, presence of systemic symptoms), chest CT is preferred [54,55].

US Abdomen

Ultrasound (US) can be useful in the characterization of renal masses because it can help in differentiating solid and cystic renal masses. However, it is seldom used in the staging of RCC because of its relatively poor performance in evaluating local tumor spread and metastatic disease [70,71]. US can be challenging to perform in patients with a high body mass index. Additional challenges in the use of US may be related to incomplete visualization of the mass, acoustic shadowing from partially calcified cysts or masses, variability in echogenicity of hemorrhagic cysts, and poor sensitivity in diagnosing isoechoic small renal tumors. There is no relevant literature suggesting that US offers any additional benefit over conventional CT or MRI of the abdomen in the initial staging of RCC, and thus, this method is not included in the guidelines from the EAU and NCCN [5,13]. However, intraoperative US may be helpful in performing partial nephrectomy, especially in patients with endophytic renal tumors [72,73].

Variant 2: Renal cell carcinoma. Contraindication to both iodinated CT and gadolinium-based MR intravenous contrast. Staging.

Bone Scan Whole Body

The prevalence of osseous metastases for localized RCC has been shown to be low in patients without symptoms (ie, bone pain) or without laboratory abnormalities suggestive of osseous metastases (ie, elevated serum alkaline phosphatase level) [11,12]. Furthermore, the sites commonly involved by osseous metastases, such as the thoracolumbar spine and ribs, are located in areas covered by chest and abdominal imaging. Thus, even though bone scanning can be helpful to confirm clinically or radiographically suspected metastatic disease, current guidelines do not support its routine use in the initial staging of asymptomatic RCC [5,13].

Bone Scan Whole Body with SPECT or SPECT/CT Area of Interest

The prevalence of osseous metastases for localized RCC has been shown to be low in patients without symptoms (ie, bone pain) or without laboratory abnormalities suggestive of osseous metastases (ie, elevated serum alkaline phosphatase level) [11,12]. Furthermore, the sites commonly involved by osseous metastases, such as the thoracolumbar spine and ribs, are located in areas covered by chest and abdominal imaging. Thus, even though bone scanning can be helpful to confirm clinically or radiographically suspected metastatic disease, current guidelines do not support its routine use in the initial staging of asymptomatic RCC [5,13].

In patients with RCC with symptoms suspicious for bone metastases, bone scan may be useful. If the bone scan shows areas of abnormal radiotracer uptake suspicious for osseous metastases, SPECT fused with CT can be used to provide detailed anatomic localization of the abnormal radiotracer uptake and further improve the characterization of the nature of the abnormality [14].

CT Abdomen

Preoperative imaging of RCC provides critical information on staging and serves as a roadmap to the surgeon. Both CT and MRI are comparable in the staging of the primary tumor [15,16]. Advantages of CT include rapid acquisition time, which may translate to better patient compliance, and high spatial resolution. Hence it is often the most commonly used modality for this indication. CT abdomen without and with IV contrast is typically performed for characterizing a renal mass as RCC and staging the tumor. However, in patients with contraindications to iodinated contrast, only unenhanced CT may be possible, limiting the assessment. MRI abdomen may be useful in this setting, given the superior soft tissue resolution of MRI compared to unenhanced CT.

CT Abdomen and Pelvis

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There is no relevant literature with high-quality evidence regarding the use of CT of the pelvis in the staging of RCC. Although it is likely that CT pelvis may not offer additional information in most patients with early stage RCC, pelvic imaging can be helpful in patients with more advanced RCC, in whom metastatic spread is suspected [47,48]. If pelvic imaging is indicated in patients with contraindications to iodinated contrast, pelvic MRI may be preferred to unenhanced CT pelvis.

CT Chest

Chest imaging is indicated in the staging of RCC, given that lungs are one of the most common sites of metastases in RCC [5,13]. There is a lack of literature that have directly compared the accuracy of chest CT with chest radiography for detecting pulmonary metastases in the initial staging of RCC. However, limited data have demonstrated that CT is more sensitive than radiography for the detection of pulmonary metastases from RCC [49].

Current literature supports use of IV contrast-enhanced CT chest for detecting pulmonary metastases, especially in patients with large renal tumors [5,13,34,63,64,74,75]. However, in patients with contraindications to iodinated contrast, unenhanced CT chest may be performed because that would be able to detect pulmonary nodules, despite the lack of IV contrast.

CT Head

Most patients with metastases to the central nervous system are symptomatic. Thus, current guidelines do not support routine imaging of the brain to search for metastases in asymptomatic patients in the initial staging of RCC. Brain imaging should be performed only in cases with suggestive signs or symptoms [5,13]. In patients with contraindication to IV contrast, MRI brain may be more helpful.

CTU

There is no relevant literature suggesting that CTU offers any additional benefit over conventional CT of the abdomen in the initial staging of RCC, and thus, this method is not included in the guidelines from the EAU and NCCN [5,13].

FDG-PET/CT Skull Base to Mid-Thigh

FDG-PET/CT has a limited role in the diagnosis and the local staging of RCC [58]. Differentiating renal tumor from background normal renal tissue can be difficult because of renal excretion of FDG. Furthermore, RCC is reported to have variable FDG avidity, limiting its utility. Nakanishi et al [59] reported a 56% sensitivity, a 67% specificity, a 15% positive predictive value, a 57% negative predictive value, and a 65% accuracy for FDG-PET in the staging of RCC. A recent clinical trial from Turkey involving 62 patients with RCC reported an 84% accuracy for contrast-enhanced FDG-PET/CT in staging RCC [60]. However, further studies are warranted before PET/CT can be used in the routine initial staging of RCC. At present, given the paucity of literature to support the use of FDG-PET/CT, the guidelines from the EAU and NCCN do not recommend routine FDG-PET/CT in the initial staging of RCC [5,13].

Fluoride PET/CT Skull Base to Mid-Thigh

Preliminary results for other PET tracers are also becoming available. In a small prospective study of 10 patients with metastatic RCC, 18F-NaF PET/CT was found to be significantly more sensitive for the detection of RCC skeletal metastases than Tc-99m bone scintigraphy or CT, with sensitivities of 100%, 29%, and 46%, respectively. CT and Tc-99m bone scintigraphy in this study identified only 65% of the metastases detected by fluoride PET/CT [61]. However, given the paucity of literature for utility of fluoride PET/CT in the initial staging of RCC, current guidelines from the EAU and NCCN do not support routine fluoride PET/CT to search for metastases in asymptomatic patients in the initial staging of RCC [5,13].

MRI Abdomen and Pelvis

MRI of the abdomen without and with IV contrast is considered to be a reliable method for the staging of RCC. Various MRI sequences, including T2-weighted, chemical shift T1-weighted, contrast-enhanced T1-weighted, and diffusion-weighted images, are typically obtained for the staging of RCC.

Although MRI of the abdomen with IV contrast is considered in all major guidelines as an adequate method for the staging of RCC, imaging the pelvis for RCC staging is considered optional in the guidelines [5,13]. There is no relevant literature with high-quality evidence regarding the use of MRI of the pelvis in the staging of RCC. Although it is likely that MRI pelvis may not offer additional information in most patients with early stage RCC, pelvic imaging can be helpful in patients with more advanced RCC, in whom metastatic spread is suspected [47,48].

In patients with contraindications to both iodinated CT and gadolinium-based MRI IV contrast, unenhanced MRI may be preferred over noncontrast CT. This is due to the fact that unenhanced MRI has a superior soft tissue resolution compared to unenhanced CT, thereby increasing its diagnostic utility.

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Most patients with metastases to the central nervous system are symptomatic. Thus, current guidelines from the EAU and NCCN do not support routine imaging of the brain to search for metastases in asymptomatic patients in the initial staging of RCC. Brain imaging should be performed only in cases with suggestive signs or symptoms [5,13]. In symptomatic patients with contraindication to IV contrast, MRI brain without contrast may be helpful.

MRU

There is no relevant literature suggesting that MRU offers any additional benefit over conventional MRI of the abdomen in the initial staging of RCC, and thus, this method is not included in the guidelines from the EAU and NCCN [5,13].

Radiography Chest

The lung is the most common site of metastases in patients with RCC presenting with synchronous metastases. Although the incidence of metastases in RCC <4 cm is low (approximately 1%-2%), it has been reported that 20% to 30% of T1a tumors may have potentially aggressive histologic features. Hence, chest radiography is usually performed in the staging of RCC [13]. However, CT is more sensitive than radiography for the detection of pulmonary metastases from RCC during staging. In addition to a high sensitivity for the detection of pulmonary metastases, chest CT has a high sensitivity for the detection of intrathoracic nodal metastases from RCC. Therefore, in patients with higher risk of pulmonary metastases (such as tumor >4 cm, cN1, presence of systemic symptoms), chest CT is preferred [54,55].

US Abdomen

US can be useful in the characterization of renal masses as it can help in differentiating solid and cystic renal masses. However, it is seldom used in the staging of RCC because of its relatively poor performance in evaluating local tumor spread and metastatic disease [70,71]. Additional challenges in the use of US may be related to incomplete visualization of the mass, acoustic shadowing from partially calcified cysts or masses, variability in echogenicity of hemorrhagic cysts, and poor sensitivity in diagnosing isoechoic small renal tumors. There is no relevant literature suggesting that US offers any additional benefit over conventional CT or MRI of the abdomen in the initial staging of RCC, and thus, this method is not included in the guidelines [5,13]. However, intraoperative US may be helpful in performing partial nephrectomy, especially in patients with endophytic renal tumors [72,73].

Variant 3: Renal cell carcinoma. Contraindication only to iodinated CT intravenous contrast. Staging.

Bone Scan Whole Body

The prevalence of osseous metastases for localized RCC has been shown to be low in patients without symptoms (ie, bone pain) or without laboratory abnormalities suggestive of osseous metastases (ie, elevated serum alkaline phosphatase level) [11,12]. Furthermore, the sites commonly involved by osseous metastases, such as the thoracolumbar spine and ribs, are located in areas covered by chest and abdominal imaging. Thus, even though bone scanning can be helpful to confirm clinically or radiographically suspected metastatic disease, current guidelines from the EAU and NCCN do not support its routine use in the initial staging of asymptomatic RCC [5,13].

Bone Scan Whole Body with SPECT or SPECT/CT Area of Interest

The prevalence of osseous metastases for localized RCC has been shown to be low in patients without symptoms (ie, bone pain) or without laboratory abnormalities suggestive of osseous metastases (ie, elevated serum alkaline phosphatase level) [11,12]. Furthermore, the sites commonly involved by osseous metastases, such as the thoracolumbar spine and ribs, are located in areas covered by chest and abdominal imaging. Thus, even though bone scanning can be helpful to confirm clinically or radiographically suspected metastatic disease, current guidelines from the EAU and NCCN do not support its routine use in the initial staging of asymptomatic RCC [5,13].

In patients with RCC with symptoms suspicious for bone metastases, bone scan may be useful. If the bone scan shows areas of abnormal radiotracer uptake suspicious for osseous metastases, SPECT fused with CT can be used to provide detailed anatomic localization of the abnormal radiotracer uptake and further improve the characterization of the nature of the abnormality [14].

CT Abdomen

Preoperative imaging of RCC provides critical information on staging and serves as a roadmap to the surgeon. Both CT and MRI are comparable in the staging of the primary tumor [15,16]. Some of the advantages of CT include rapid acquisition time, and hence it is often the most commonly used modality for this indication. CT abdomen without and with IV contrast is typically performed for characterizing a renal mass as RCC and staging the tumor. However, in patients with contraindications to iodinated contrast, only unenhanced CT may be possible, limiting the assessment. MRI abdomen may be useful in this setting, given the superior soft tissue resolution of MRI compared to unenhanced CT.

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CT Chest

Chest imaging is indicated in the staging of RCC, given that lungs are one of the most common sites of metastases in RCC [5,13]. There is a lack of literature that have directly compared the accuracy of chest CT with chest radiography for detecting pulmonary metastases in the initial staging of RCC. However, limited data have demonstrated that CT is more sensitive than radiography for the detection of pulmonary metastases from RCC [49].

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MRI Abdomen and Pelvis

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MRI Head

Most patients with metastases to the central nervous system are symptomatic. Thus, current guidelines do not support routine imaging of the brain to search for metastases in asymptomatic patients in the initial staging of RCC.

Brain imaging should be performed only in cases with suggestive signs or symptoms [5,13]. In symptomatic patients with contraindication to IV contrast, MRI brain without contrast may be helpful.

MRU

There is no relevant literature suggesting that MRU offers any additional benefit over conventional MRI of the abdomen in the initial staging of RCC, and thus, this method is not included in the guidelines from the EAU and NCCN [5,13].

Radiography Chest

The lung is the most common site of metastases in patients with RCC presenting with synchronous metastases. Although the incidence of metastases in RCC <4 cm is low (approximately 1%-2%), it has been reported that 20% to 30% of T1a tumors may have potentially aggressive histologic features. Hence, chest radiography is usually performed in the staging of RCC [13]. However, CT is more sensitive than radiography for the detection of pulmonary metastases from RCC during staging. In addition to a high sensitivity for the detection of pulmonary metastases, chest CT has a high sensitivity for the detection of intrathoracic nodal metastases from RCC. Therefore, in patients with higher risk of pulmonary metastases (such as tumor >4 cm, cN1, presence of systemic symptoms), chest CT is preferred [54,55].

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Summary of Recommendations

- **Variation 1:** MRI abdomen and pelvis without and with IV contrast, or MRI abdomen without and with IV contrast, or CT abdomen and pelvis with IV contrast, or CT abdomen with IV contrast is usually appropriate for staging of RCC in patients without contraindications to either iodinated CT contrast or gadolinium-based MR IV contrast. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care) and are complemented by CT chest with IV contrast (ie, more than one procedure is ordered as a set or simultaneously in which each procedure provides unique clinical information to effectively manage the patient's care). Although the panel did not agree on recommending CT abdomen and pelvis without and with IV contrast or CT abdomen without and with IV contrast, because there is insufficient medical literature to conclude whether these patients would benefit from the procedures, their use may be appropriate.
- **Variation 2:** MRI abdomen and pelvis without and with IV contrast or MRI abdomen without and with IV contrast is usually appropriate for staging of RCC in patients with contraindications to both iodinated CT contrast or gadolinium-based MR IV contrast. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care) and are complemented by CT chest without IV contrast (ie, more than one procedure is ordered as a set or simultaneously in which each procedure provides unique clinical information to effectively manage the patient's care). Although the panel did not agree on recommending CT abdomen without IV contrast, because there is insufficient medical literature to conclude whether these patients would benefit from the procedure, its use may be appropriate.
- **Variation 3:** MRI abdomen and pelvis without and with IV contrast or MRI abdomen without and with IV contrast is usually appropriate for staging of RCC in patients with contraindication only to iodinated CT IV contrast. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care) and are complemented by CT chest without IV contrast (ie, more than one procedure is ordered as a set or simultaneously in which each procedure provides unique 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 go to www.acr.org/ac.

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 [76].

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.”

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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.