

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

Clinical Condition: **Pretreatment Staging of Invasive Bladder Cancer**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
X-ray chest	9	Effective screen of site of most common hematogenous metastasis.	☼
CT abdomen and pelvis without and with contrast (CT urography)	8	Precontrast and postcontrast with excretory phase.	☼ ☼ ☼ ☼
MRI pelvis without and with contrast	8	Appropriate for local staging if CT is not performed or is inconclusive, and depending on institutional expertise or preference. See statement regarding contrast in text under “Anticipated Exceptions.”	O
X-ray intravenous urography	5		☼ ☼ ☼
CT abdomen and pelvis with contrast	5	May be appropriate if done in combination with IVU.	☼ ☼ ☼ ☼
Tc-99m bone scan whole body	3	Probably not indicated unless bone pain is present.	☼ ☼ ☼
MRI abdomen without and with contrast	3	Probably not indicated unless CT is inconclusive.	O
CT chest with contrast	3	Probably not indicated unless chest radiograph is suspicious.	☼ ☼ ☼
US pelvis (bladder)	3	Limited visualization beyond the bladder wall.	O
CT pelvis with contrast	2	Optimized with a variety of intraluminal contrast agents (eg, CO ₂ , dilute iodinated contrast, etc) for application of 3D rendering techniques (virtual cystoscopy) when conventional cystoscopy is not possible or advisable.	☼ ☼ ☼
FDG-PET whole body	2		☼ ☼ ☼ ☼
CT pelvis without contrast	2		☼ ☼ ☼
MRI pelvis without contrast	2		O
MRI head with or without contrast	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

PRETREATMENT STAGING OF INVASIVE BLADDER CANCER

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Summary of Literature Review

The National Cancer Institute estimates that in 2009 there will be 70,980 new cases of bladder cancer and 14,300 deaths from the disease in the U.S. [1]. Bladder cancer has a high tendency toward multifocality at presentation and recurrence after treatment [2]. Transitional cell carcinoma of the bladder (TCCB) is the most common cell type, accounting for more than 90% of all cases of bladder cancer [3]. The average age of patients with TCCB in the U.S. is 65 at diagnosis. Almost 85% of patients with TCCB present with hematuria, which is either gross or microscopic and is usually painless and intermittent [4].

TCCB spreads by local extension through the basement membrane into the muscular layer, then to the perivesical fat. Progressive extension into the muscular layer allows vascular and lymphatic invasion and more distant spread. The most common sites of hematogenous spread are lung, bone, liver, and brain [2,5]. Superficial lesions do not metastasize until they invade deeply and may remain indolent for many years. It has been estimated that 70%-85% of TCCB is superficial at presentation, confined to the mucosa or submucosa, without muscle invasion [3]. However, a recent population-based study from the northeastern United States reported that only 7.6% of bladder tumors identified through the New Hampshire state cancer registry were staged T2 or higher [6]. Only invasive tumors will be considered here. The imaging workup begins after the bladder tumor has been identified

or confirmed cystoscopically and has been proven by biopsy.

TCCB is staged by its extension at presentation and graded according to microscopic (pathologic) criteria of aggressiveness [4]. The standard staging system for bladder cancer is now the Tumor, Node, Metastasis (TNM) system [4,7]. The TNM system encompasses the status of the primary tumor (T), the lymph nodes (N), and any metastases (M) ([Appendix 1](#)).

Tumor grade relates directly to depth of invasion but inversely to curability. In a multi-institutional study from Japan, patients with pT1 (p = pathologic) or lower stage pT2, pT3, and pT4 disease without lymph node metastases had 5-year overall survival rates of 81%, 74%, 47%, and 38%, respectively [8]. Another study of 507 patients who underwent radical cystectomy without neoadjuvant therapy had 5-year recurrence-free and overall survival rates of 73% and 62% for organ-confined, node-negative tumors and 56% and 49% for non-organ-confined, node-negative tumors [9]. In a study of 300 cystectomy patients, there was a clear dichotomy in disease-specific survival rates between organ-confined disease (67%) and non-organ-confined disease (31%) [10]. Differentiating between microscopic (pT3a) and gross (pT3b) extravesical TCCB does not have prognostic significance for patients undergoing radical cystectomy [11]. In such patients, recurrence-free and overall survival is significantly better in patients with lymph-node-negative disease irrespective of the extent (microscopic or gross) of extravesical involvement [8,9,11].

Treatment ranges from cystoscopic local excision or segmental bladder resection with pelvic lymphadenectomy for early tumors to irradiation, chemotherapy, and/or radical extirpation for deep invasion [3,12,13]. Radical cystectomy with pelvic lymphadenectomy remains the standard treatment for muscle-invasive urothelial tumors of the bladder [14,15].

Since clinical staging by cystoscopy and bimanual examination under anesthesia is inaccurate in more than 50% of patients, imaging is vital to the proper treatment of these patients [16]. The principal task is to identify muscle invasion, extravesical spread, and nodal metastases [16]. Unfortunately, none of the imaging modalities can identify microscopic spread to muscle layer, perivesical fat, lymph nodes, or other organs.

Cystography, pelvic angiography, lymphangiography (LAG) with or without percutaneous fine-needle aspiration (FNA) biopsy, and radiographic whole-lung laminography are no longer routinely used in staging TCCB since the advent of cross-sectional imaging.

Intravenous Urography

Intravenous urography (IVU) was once the best screening examination for upper-tract disease and was the most sensitive test in detecting small urothelial lesions [17]. With widespread use of computed tomography (CT)

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urography, the role of IVU in evaluating the renal collecting system and ureter is declining [18]. Although only 60% of known bladder tumors are visualized by IVU, obstruction of a ureteral orifice at the level of the ureterovesical junction is usually due to invasive bladder tumor, if urolithiasis is excluded [19,20]. Any degree of ureteric obstruction is significantly associated with both decreased overall survival rates and decreased tumor-free interval [21]. Ureteral obstruction can also be clearly demonstrated by CT urography.

Yousem et al [17] found synchronous TCC above the bladder in 14 of 597 (2.3%) patients with TCCB, 8 (1.3%) with ureteral TCC, and 6 (1.0%) with renal TCC. They reported a range of incidence of synchronous upper-urinary-tract lesions between 0% and 6.4% and stated that IVU “must be performed” when TCCB is first diagnosed. It is important to note that this recommendation predates the widespread availability of CT urography. Retrograde ureteropyelography is also excellent for detailed study of the urothelium, especially when IVU is contraindicated or the results are equivocal [17]. However, recent studies have reported an incidence of upper-tract urothelium tumors was 1.1% in which IVU was able to diagnose only 66% of these cases [22].

Chest Radiograph and Computed Tomography of the Chest

All patients with invasive TCCB need pulmonary evaluation. The chest radiograph is an effective, inexpensive, low-morbidity screen [5]. Patients with equivocal chest radiograph and those thought to be at high risk should have standard chest CT.

Radionuclide Bone Scan

The incidence of metastases in TCCB patients increases with tumor stage at time of diagnosis [5]. A 4.6% positive rate was found in 458 bone scan studies [23]. Since therapy was affected in only 0.9%, the conclusion was that scintigraphy has “no place in the routine preoperative staging of bladder carcinoma” [23]. Another study of 91 patients with precystectomy bone scan concluded that “the findings of a routine preoperative bone scan are usually unable to identify patients with bladder cancer of stage \geq T2 who will not be cured by total cystectomy” [24]. Bone scanning may be limited to patients with bone pain and/or elevated levels of serum alkaline phosphatase. Further evaluation with radiographs and/or magnetic resonance imaging (MRI) can be helpful, and, if necessary, guided needle biopsy can be definitive.

MRI of the Head

Neurologic complications directly related to TCCB are rare and usually the result of local extension rather than brain metastases. Therefore, MRI of the head is not recommended for asymptomatic patients [25].

Ultrasound: Transabdominal, Transrectal, and Transurethral

The distended bladder is a superb acoustic window. Size and location of the tumor affect detectability with ultrasound (US) [26]. Lesions smaller than 0.5 cm that are

flat and/or near the bladder neck can be easily missed [26]. A study by Ozden et al [27] of 214 bladder tumors in 85 patients showed the lowest detection rate for US for tumors located at the inferior region of the anterior wall (47%). In this same study, detection rates were significantly lower for tumors $<$ 5 mm. US is limited in visualization beyond the bladder wall and cannot reliably detect nodal enlargement [28]. Some investigators have correlated sonographically determined contact length and height-to-length ratio with depth of tumor invasion [29]. Color Doppler with transrectal US (TRUS) adds nothing to evaluation of stage or grade [30].

TRUS is excellent for evaluating the prostate and seminal vesicles. Transurethral US (TUUS) is more sensitive than transabdominal US (TAUS), and TRUS is more accurate in staging depth of wall involvement but is not widely available [30]. TRUS provides local staging information with 62%-100% accuracy, highest for superficial tumors [28,31]. TRUS staging is unreliable for tumors \geq 3 cm and tumors with calcifications, largely because of acoustic shadowing [28]. It is poor (70%) for evaluating extravesical spread [31]. Three-dimensional US rendering is yet another new diagnostic tool with potential to aid in discriminating superficial from muscle-invasive tumors [32]. The use of transabdominal 3D US to detect bladder tumors was recently assessed. The combination of gray-scale US, multiplanar reconstruction, and 3D virtual US had a sensitivity of 96.4%, specificity of 88.8%, positive predictive value (PPV) of 97.6%, and negative predictive value (NPV) of 84.2% for bladder tumor detection [33].

Endoluminal US (ELUS), also known as intravesical US (IVUS), uses a miniature, high-frequency transducer introduced by a rigid cystoscope for intravesical evaluation [34,35]. ELUS is both sensitive and specific in detecting muscle invasion in bladder cancer, with rates comparable to those of TUUS, and it provides greater bladder wall detail. Limitations include difficulty in depicting the tumor base in certain locations and in depicting the depth of invasion in tumors $>$ 2 cm with broad bases [34,36].

With progression from TAUS to TRUS to TUUS and ELUS, the diagnostic accuracy of US has improved. In 214 new cases of TCCB with pathological correlation, Fang et al [37] reported overall accuracy of 78.6% in local staging with TAUS. They had 9.8% overstaging and 11.7% understaging. Their accuracy was 87% for stage A, 60.5% for stage B, 41.2% for stage C, and 83.3% for stage D. Akdas et al [38] reported an overall accuracy of 96.5% in diagnosing and staging bladder tumors with TUUS in 104 patients: 96.2% for stage Ta-T1 lesions, 100.0% for T2 lesions, 91.7% for T3 lesions, and 100.0% for T4 lesions. There was no discussion of N or M staging.

Studies have shown ELUS to be 100% sensitive, 75% specific, and 84% accurate in detecting muscle invasion in bladder cancer, with both a PPV and NPV of 100% [34,35]. 3-D rendering had a 66% staging accuracy for

pTa tumors, 83% for pT1 tumors, and 100% for >pT1 or muscle-invasive tumors [32].

Computed Tomography of the Pelvis and Abdomen

The primary contribution of conventional CT is distinguishing tumors that are organ-confined from those with extravesical extension [2]. It demonstrates bulky thickening of the bladder wall, perivesical extension, lymph node enlargement, and distant metastases very well [12,39,40]. As with US, tumor location affects detection rates by CT. Identification of the primary lesion can be difficult in the areas of the anterior wall, bladder neck, and dome [27,39]. CT cannot distinguish inflammatory postoperative or postradiation edema or fibrosis from tumor and cannot assess depth of invasion of the bladder wall [12,39]. CT is also unable to detect microscopic or small-volume extravesical tumor extension and metastases in nonenlarged lymph nodes [41]. The detection of peritoneal metastases from bladder cancer with CT has recently been described [42]. In this study, CT findings of peritoneal metastases were found in eight of 105 patients and were indicative of a poor prognosis [42].

Voges et al [40] found an accuracy of 50% in CT staging of pT2(B1) and pT3a(B2) lesions, understaging of 29.5% of cases, and overstaging of 20.5% of cases. Staging of pT3b(C) lesions was 46.2% accurate, with 53.8% understaged. Of 16 pT4 lesions, one (6.3%) was correctly diagnosed and 15 were understaged. All had infiltration into prostate or seminal vesicle.

Barentsz et al [28] reviewed 437 cases in the literature using CT to stage TCCB. Overall accuracy ranged from 40%-85%, with correct staging of nodes and metastases ranging from 82%-97%. For extravesical extension, accuracy ranged from 40%-92% with a mean of 74%. Paik et al found overall accuracy of 54.9%, with 39% understaging and 20.7% false negative for extravesical spread. Preoperative CT staging altered planned surgical management in only 3.7% of cases [41]. Multi-detector row helical CT with intravenous (IV) contrast and 60-second delayed images is a highly sensitive and specific method for detecting bladder cancer and associated perivesical invasion, particularly when there more than a 7-day time interval between intervention and CT. Its sensitivity and specificity are up to 92% and 98%, respectively, in this setting [43].

Various methods for bladder distension have been studied to increase the accuracy of detecting muscle invasion in bladder cancer on CT imaging. These include evaluating the bladder filled with urine, urine opacified with iodinated contrast material, and air [44]. These methods have accuracies of approximately 84%, 89% and 93%, respectively, with overstaging and understaging percentages comparable, ranging from 4%-7% for overstaging and 2%-4% for understaging [44].

In addition to conventional CT, helical and multi-detector CT with multiplanar reformation, 3D reconstruction, and creation of images mimicking traditional cystoscopy (a technique often referred to as virtual cystoscopy or

CTVC) have been described in the literature. Using helical CT and multiplanar reformation, Wang et al [45] found an overall accuracy of 87.7% in CT staging of all stages of bladder cancer and, more specifically, 76.9% for Ta-T2 lesions and 94.7% for T3-T4 lesions. Pathologic lymph nodes were confirmed in six of seven cases. Multiplanar reformation was shown to be useful in evaluating the origin and extent of extravesical invasion, as well as the tumor's relationship to the ureter. A study by Browne et al [46] found that the sensitivity of 3D reconstruction in detecting bladder carcinomas of all stages was 76.9%. CT traditional cystography and CTVC may find use in patients unable to tolerate traditional cystoscopy, in those for whom traditional cystoscopy failed, or in those with narrow-necked bladder diverticula that may contain lesions [46]. Tsampoulas et al [47] detected 96% of bladder tumors found at conventional cystoscopy with MDCT using multiplanar reformation and CTVC, including 18 of 20 tumors ≤ 5 mm in size. Kishore et al [48] detected all but two of 14 bladder tumors in 11 patients using CTVC performed by instilling dilute contrast medium into the bladder. Both tumors missed in this study were 7 mm. CTVC provides comparable views to traditional cystoscopy but may not add additional diagnostic data in patients able to tolerate traditional cystoscopy [46,49].

Multidetector CT urography (which includes thin-section imaging of the collecting systems, ureters, and bladder during the excretory phase) provides collecting system opacification comparable to that of IVU [50]. As upper tracts are increasingly evaluated by CT for hematuria, the addition of lower-tract evaluation adds negligible cost and avoids the discomfort that may be associated with traditional cystoscopy, thereby streamlining the evaluation of patients with hematuria [51]. In a study by Tsili et al [52] MDCT urography detected 20 urinary bladder tumors in 75 patients being evaluated for hematuria. In this study, there were two false-positive cases of bladder tumor and a false-negative case of a small (<5 mm) bladder tumor obscured by blood clot.

A 200-patient study conducted at a fast-track hematuria clinic demonstrated 93% sensitivity and 99% specificity for bladder cancer detection by CT urography, rates similar to those of traditional cystoscopy [51]. More recently, Sadow et al [53] found an overall sensitivity and specificity of 79% and 94%, respectively for bladder cancer detection with CT urography in a group of 779 patients. Absolute degree of contrast enhancement of tumor may correlate with histologic grade in TCCB, as demonstrated in a study of 65 patients. Although interesting, this finding may find greater application in research on tumor angiogenesis and regression postantiangiogenesis therapy [54].

Magnetic Resonance Imaging

MRI is superior to CT in demonstrating the lower pelvic anatomy. There is striking inherent contrast between the bright perivesical fat and the intermediate-signal-intensity bladder wall on T1-weighted images. Multiplanar imaging and gadolinium enhancement improve

visualization of tumors on T1-weighted images [2,28,55-58]. Fat suppression techniques can help identify perivesical extension [2]. Deep-muscle invasion presents as disruption of the low-signal-intensity bladder wall by tumor, which usually is of higher signal intensity on enhanced T1-weighted images [39,56,59]. After intravenous gadolinium chelates, TCCB shows earlier and greater enhancement than normal bladder or nonmalignant tissue [55,56].

Most recently, Tekes et al [60] demonstrated staging accuracies of 85% and 82% in differentiating superficial from muscle invasive tumors and organ-confined from non-organ-confined tumors, respectively. Additionally, the accuracy of pathologic lymph node detection was 96%. Overstaging occurred in 32% of cases. The length of time between transurethral resection and MRI did not affect staging accuracy [60]. Barentsz et al [28] reviewed 340 cases using MRI. The T staging of tumor was accurate in 73%-96% of cases, and the staging of nodes and metastases was accurate in 73%-98% of cases. The best staging results were with gadolinium-enhanced T1-weighted fast spin-echo sequences 14 seconds after injection. These authors suggest that following cystoscopic identification of tumor, MRI should be used as the initial imaging modality to stage the tumor. Hayashi et al [14] reviewed 71 patients using gadolinium-enhanced endorectal surface coil and reported an 83% overall staging accuracy. Muscle invasion was diagnosed with 87% accuracy, 91% sensitivity, and 87% specificity. More recently, Røe et al [61] have demonstrated that the normalized area between tumor and muscle contrast uptake curves generated with dynamic gadolinium-enhanced MRI correlates with T stage for bladder cancer. Deserno et al [62] found that MRI performed with ferumoxtran-10 (ultrasmall superparamagnetic iron oxide) contrast demonstrated an accuracy in pathologic lymph node detection of up to 92% and a sensitivity of up to 96%.

There has also been interest in 3D rendering techniques with MR data sets (including multiplanar reconstructions and creation of cystoscopic-like images) as a replacement for traditional cystoscopy and to assist in staging. High diagnostic accuracy has been demonstrated, with sensitivity of 90.7% and specificity of 94.0% using combined cystoscopic-like views created from MR data sets and multiplanar reconstructions. These results are comparable to those of CT, and MR cystography is especially promising in special cases where traditional cystoscopy may be contraindicated (urethral stricture), or suboptimal (narrow-necked bladder diverticula) [63]. Similar conclusions were previously drawn by Lammler et al [64].

Recently, investigators have demonstrated that diffusion-weighted MRI (DWI) can differentiate between bladder carcinoma and surrounding structures and that bladder carcinoma has a lower apparent diffusion coefficient (ADC) value than surrounding, nonneoplastic structures [65]. Further study is needed to determine if DWI can improve staging accuracy of MRI.

Computed Tomography versus Magnetic Resonance Imaging

CT urography offers the potential for a one-stop-shop examination to assess local disease, lymph nodes, distant metastases, and the upper urinary tracts, while MRI may offer advantages over CT for local staging [2]. Noting that MRI appears to have slightly better sensitivity and specificity than CT for local staging, Klein and Pollack [66] stated that MRI and CT have similar accuracy for detecting perivesical fat invasion and that the most notable advantage of MRI is its apparent ability to differentiate between superficial and deep invasion of the bladder wall. Barentz et al [28] concluded that MRI is the best technique for staging invasive tumors, as it was slightly better than or equal to CT at differentiating T3a from T3b lesions and superior to CT detecting for tumors at the bladder dome or base. In deeply infiltrating tumors (stages T3b-T4b), they asserted that MRI “is generally agreed to be the most accurate staging technique,” and “when MRI is available, CT is no longer needed.” MacVicar [12] in a review article stated that MRI is the investigation of choice for local staging and is the preferred technique in postcystectomy and radiation therapy follow-up. A more recent review by Beyersdorff et al [16] contends that “MRI is superior [to CT] for evaluation of the depth of invasion in the bladder wall.” These authors go on to say that “both modalities continue to have difficulties in determining whether perivesical changes are related to tumor or inflammation from the previous transurethral biopsy.” Robinson et al [67] in a review of 143 patients prior to radiotherapy confirmed that MRI is superior to clinical staging and provided additional prognostic information.

Both CT and MRI rely on enlargement of lymph nodes as a criterion for metastasis, but they are limited in detecting metastases to normal-sized nodes. This may change if further studies corroborate the early results of using lymphotropic nanoparticle-enhanced MRI for detecting micrometastasis in nonenlarged lymph nodes [68]. Lymph node metastasis in patients with superficial tumors (less than T3) is rare, but if deep muscle layers are involved (T2b) or if extravesical invasion is seen, the incidence of lymph node metastasis rises to 20%-30% and 50%-60%, respectively. If a lymph node is considered to contain metastasis, a fine-needle aspiration biopsy should be considered. Both CT and MRI are equivalent in their ability to detect nodal enlargement [69].

Positron Emission Tomography and Radioimmunosintigraphy

Recently, Bouchelouche and Oehr [70] reviewed the use of positron emission tomography (PET) and PET/CT for imaging of urothelial malignancies, concluding that despite advances in these techniques, larger clinical trials are needed to establish the role of these techniques for imaging urological malignancies. Conventional PET using fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) is limited for imaging bladder tumors because of its high urinary excretion, although it may have a role in detecting recurrent or metastatic disease [71]. Preliminary results suggest that images obtained after intravenous

administration of diuretic and oral hydration can improve results of FDG-PET/CT for detecting locally recurrent or residual bladder tumors [72]. FDG-PET is 67% sensitive, 86% specific, and 80% accurate in detecting pathologic lymph nodes in patients with bladder cancer, which exceeds both CT and MRI [73]. A study correlating FDG-PET and CT results in the same patients reported sensitivity, specificity, and accuracy of 60%, 88%, and 78%, respectively, in nodal and metastasis staging, suggesting improved distant metastatic and locoregional node staging [74]. PET imaging with FDG may be more limited in detecting metastatic disease once a patient has received chemotherapy, with sensitivity for proven metastases of only 50% in one small series [75].

¹¹C-choline PET when compared with CT promises slightly increased accuracy of lymph node staging (63.0% vs 88.9%, $P < 0.01$) and may avoid false-positive results for lymph nodes due to reactive hyperplasia when compared with CT, although further evaluation with this agent is needed to confirm these findings [76]. Gofrit et al [77] studied ¹¹C-choline PET for preoperative staging of transitional cell carcinomas in 18 patients (17 bladder tumors), finding that uptake was present in all primary TCCs and that ¹¹C-choline PET was “highly positive for primary and metastatic bladder cancer.”

The experimental modality of radioimmunoscintigraphy using anti-MUC1 mucin monoclonal antibody C595 labeled with various radiotracers has been shown to be up to 90% sensitive in detecting invasive cancer and 88% sensitive in detecting distant metastases in sites such as lymph node, bone, and lung. [78,79].

Optical Coherence Tomography

Optical coherence tomography (OCT) is a new method of imaging biological tissues *in vivo* with exceptional spatial resolution (10-15 μm) [80]. OCT uses light generated by a superluminescent diode to image tissue in a manner analogous to B-mode US. OCT has been used to evaluate superficial bladder carcinoma with encouraging but very preliminary results [80]. At this time, the depth and width of the scanning field are severely limited, and OCT remains experimental.

Summary

- With the increasingly widespread use of CT urography, the role of IVU is declining. CT urography not only is effective for local staging but also provides information for evaluating the upper urinary tracts, the liver, and the nodal status.
- Chest CT can be limited to those with equivocal chest radiographs.
- Radionuclide bone scan is not indicated without bone pain and/or elevated serum alkaline phosphatase levels.
- Radiographs can be limited to sites of increased uptake and/or bone pain.
- US is useful for local tumor (T) staging; TUUS and ELUS appear to be equally effective in this regard.

- Contrast-enhanced MRI is preferred over CT for local staging and is equivalent in assessing regional lymph nodes.
- CT or MRI supplemented with 3D rendering techniques may be used in specific cases such as evaluation of narrow-necked bladder diverticula, which may be poorly evaluated by traditional cystoscopy, but they are not indicated in the majority of patients.
- CT and MRI supplemented with 3D rendering techniques may also be of use in patients unable to tolerate traditional cystoscopy and may be considered to streamline evaluation of hematuria, combining staging and screening.
- MRI of the head is needed only if neurological symptoms are present.
- PET studies to date are not proven to enhance pretreatment local staging and are not indicated until further validation and studies are completed.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie, $< 30 \text{ mL/min/1.73m}^2$), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates $< 30 \text{ mL/min/1.73m}^2$. For more information, please see the [ACR Manual on Contrast Media](#) [81].

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

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	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 NS (not specified).

Supporting Document(s)

- [ACR Appropriateness Criteria® Overview](#)
- [Procedure Information](#)
- [Evidence Table](#)

References

1. National Cancer Institute. *Comprehensive Cancer Information*. <http://www.cancer.gov/cancertopics/types/bladder/>. Accessed July 2009.
2. Zhang J, Gerst S, Lefkowitz RA, Bach A. Imaging of bladder cancer. *Radiol Clin North Am* 2007; 45(1):183-205.
3. Amling CL. Diagnosis and management of superficial bladder cancer. *Curr Probl Cancer* 2001; 25(4):219-278.
4. Kirkali Z, Chan T, Manoharan M, et al. Bladder cancer: epidemiology, staging and grading, and diagnosis. *Urology* 2005; 66(6 Suppl 1):4-34.
5. Kuroda M, Meguro N, Maeda O, et al. Stage specific follow-up strategy after cystectomy for carcinoma of the bladder. *Int J Urol* 2002; 9(3):129-133.
6. Schned AR, Andrew AS, Marsit CJ, Kelsey KT, Zens MS, Karagas MR. Histological classification and stage of newly diagnosed bladder cancer in a population-based study from the Northeastern United States. *Scand J Urol Nephrol* 2008; 42(3):237-242.
7. Pavone-Macaluso M, Lopez-Beltran A, Aragona F, Bassi P, Fitzpatrick JM. The pathology of bladder cancer: An update on selected issues. *BJU Int* 2006; 98(6):1161-1165.
8. Takahashi A, Tsukamoto T, Tobisu K, et al. Radical cystectomy for invasive bladder cancer: results of multi-institutional pooled analysis. *Jpn J Clin Oncol* 2004; 34(1):14-19.
9. Madersbacher S, Hochreiter W, Burkhard F, et al. Radical cystectomy for bladder cancer today--a homogeneous series without neoadjuvant therapy. *J Clin Oncol* 2003; 21(4):690-696.
10. Dalbagni G, Genega E, Hashibe M, et al. Cystectomy for bladder cancer: a contemporary series. *J Urol* 2001; 165(4):1111-1116.
11. Quek ML, Stein JP, Clark PE, et al. Microscopic and gross extravesical extension in pathological staging of bladder cancer. *J Urol* 2004; 171(2 Pt 1):640-645.
12. MacVicar AD. Bladder cancer staging. *BJU Int* 2000; 86 Suppl 1:111-122.
13. Barocas DA, Clark PE. Bladder cancer. *Curr Opin Oncol* 2008; 20(3):307-314.
14. Hayashi N, Tochigi H, Shiraishi T, Takeda K, Kawamura J. A new staging criterion for bladder carcinoma using gadolinium-enhanced

magnetic resonance imaging with an endorectal surface coil: a comparison with ultrasonography. *BJU Int* 2000; 85(1):32-36.

15. Malkowicz SB, van Poppel H, Mickisch G, et al. Muscle-invasive urothelial carcinoma of the bladder. *Urology* 2007; 69(1 Suppl):3-16.
16. Beyersdorff D, Zhang J, Schoder H, Bochner B, Hricak H. Bladder cancer: can imaging change patient management? *Curr Opin Urol* 2008; 18(1):98-104.
17. Yousem DM, Gatewood OM, Goldman SM, Marshall FF. Synchronous and metachronous transitional cell carcinoma of the urinary tract: prevalence, incidence, and radiographic detection. *Radiology* 1988; 167(3):613-618.
18. Kawashima A, Vrtiska TJ, LeRoy AJ, Hartman RP, McCollough CH, King BF, Jr. CT urography. *Radiographics* 2004; 24 Suppl 1:S35-54; discussion S55-38.
19. Hatch TR, Barry JM. The value of excretory urography in staging bladder cancer. *J Urol* 1986; 135(1):49.
20. Hillman BJ, Silvert M, Cook G, et al. Recognition of bladder tumors by excretory urography. *Radiology* 1981; 138(2):319-323.
21. Golding RP, van Zanten TE, Tierie AH, Batterman JJ, Hart G. Intravenous urography as a prognostic indicator in vesical carcinoma. *Cancer* 1987; 60(4):883-886.
22. Herranz-Amo F, Diez-Cordero JM, Verdu-Tartajo F, Bueno-Chomon G, Leal-Hernandez F, Bielsa-Carrillo A. Need for intravenous urography in patients with primary transitional carcinoma of the bladder? *Eur Urol* 1999; 36(3):221-224.
23. Brismar J, Gustafson T. Bone scintigraphy in staging of bladder carcinoma. *Acta Radiol* 1988; 29(2):251-252.
24. Braendengen M, Winderen M, Fossa SD. Clinical significance of routine pre-cystectomy bone scans in patients with muscle-invasive bladder cancer. *Br J Urol* 1996; 77(1):36-40.
25. Anderson TS, Regine WF, Kryscio R, Patchell RA. Neurologic complications of bladder carcinoma: a review of 359 cases. *Cancer* 2003; 97(9):2267-2272.
26. Itzchak Y, Singer D, Fischelovitch Y. Ultrasonographic assessment of bladder tumors. I. Tumor detection. *J Urol* 1981; 126(1):31-33.
27. Ozden E, Turgut AT, Turkolmez K, Resorlu B, Safak M. Effect of bladder carcinoma location on detection rates by ultrasonography and computed tomography. *Urology* 2007; 69(5):889-892.
28. Barentsz JO, Ruijs SH, Strijk SP. The role of MR imaging in carcinoma of the urinary bladder. *AJR* 1993; 160(5):937-947.
29. Ozden E, Turgut AT, Yesil M, Gogus C, Gogus O. A new parameter for staging bladder carcinoma: ultrasonographic contact length and height-to-length ratio. *J Ultrasound Med* 2007; 26(9):1137-1142.
30. Horstman WG, McFarland RM, Gorman JD. Color Doppler sonographic findings in patients with transitional cell carcinoma of the bladder and renal pelvis. *J Ultrasound Med* 1995; 14(2):129-133.
31. Koraitim M, Kamal B, Metwalli N, Zaky Y. Transurethral ultrasonographic assessment of bladder carcinoma: its value and limitation. *J Urol* 1995; 154(2 Pt 1):375-378.
32. Wagner B, Nessler T, Bartsch G, Jr., Hautmann RE, Gottfried HW. Staging bladder carcinoma by three-dimensional ultrasound rendering. *Ultrasound Med Biol* 2005; 31(3):301-305.
33. Kocakoc E, Kiris A, Orhan I, Poyraz AK, Artas H, Firdolas F. Detection of bladder tumors with 3-dimensional sonography and virtual sonographic cystoscopy. *J Ultrasound Med* 2008; 27(1):45-53.
34. Saga Y, Numata A, Tokumitsu M, et al. Comparative study of novel endoluminal ultrasonography and conventional transurethral ultrasonography in staging of bladder cancer. *Int J Urol* 2004; 11(8):597-601.
35. Tomita Y, Kobayashi K, Saito T, Tanikawa T, Kimura M, Takahashi K. Use of miniature ultrasonic probe system for intravesical ultrasonography for transitional cell cancer of the urinary tract. *Scand J Urol Nephrol* 2000; 34(5):313-316.
36. Horiuchi K, Tsuboi N, Shimizu H, et al. High-frequency endoluminal ultrasonography for staging transitional cell carcinoma of the bladder. *Urology* 2000; 56(3):404-407.
37. Fang YC, Chou YH, Hsu CC, Chang T. Staging of bladder cancer by transabdominal real-time ultrasound. *Zhonghua Yi Xue Za Zhi (Taipei)* 1993; 52(1):21-25.
38. Akdas A, Turkeri L, Ersev D, Ersev A, Kullu S. Transurethral ultrasonography, fiberoptic cystoscopy and bladder washout

- cytology in the evaluation of bladder tumours. *Int Urol Nephrol* 1992; 24(5):503-508.
39. Husband JE, Olliff JF, Williams MP, Heron CW, Cherryman GR. Bladder cancer: staging with CT and MR imaging. *Radiology* 1989; 173(2):435-440.
 40. Voges GE, Tauschke E, Stockle M, Alken P, Hohenfellner R. Computerized tomography: an unreliable method for accurate staging of bladder tumors in patients who are candidates for radical cystectomy. *J Urol* 1989; 142(4):972-974.
 41. Paik ML, Scolieri MJ, Brown SL, Spirnak JP, Resnick MI. Limitations of computerized tomography in staging invasive bladder cancer before radical cystectomy. *J Urol* 2000; 163(6):1693-1696.
 42. Turkbey B, Basaran C, Karcaaltincaba M, et al. Peritoneal carcinomatosis in urinary bladder cancer. *Clin Imaging* 2008; 32(3):192-195.
 43. Kim JK, Park SY, Ahn HJ, Kim CS, Cho KS. Bladder cancer: analysis of multi-detector row helical CT enhancement pattern and accuracy in tumor detection and perivesical staging. *Radiology* 2004; 231(3):725-731.
 44. Caterino M, Giunta S, Finocchi V, et al. Primary cancer of the urinary bladder: CT evaluation of the T parameter with different techniques. *Abdom Imaging* 2001; 26(4):433-438.
 45. Wang D, Zhang WS, Xiong MH, Yu M, Xu JX. Bladder tumors: dynamic contrast-enhanced axial imaging, multiplanar reformation, three-dimensional reconstruction and virtual cystoscopy using helical CT. *Chin Med J (Engl)* 2004; 117(1):62-66.
 46. Browne RF, Murphy SM, Grainger R, Hamilton S. CT cystography and virtual cystoscopy in the assessment of new and recurrent bladder neoplasms. *Eur J Radiol* 2005; 53(1):147-153.
 47. Tsampoulas C, Tsili AC, Giannakis D, Alamanos Y, Sofikitis N, Efremidis SC. 16-MDCT cystoscopy in the evaluation of neoplasms of the urinary bladder. *AJR* 2008; 190(3):729-735.
 48. Kishore TA, George GK, Bhat S. Virtual cystoscopy by intravesical instillation of dilute contrast medium: preliminary experience. *J Urol* 2006; 175(3 Pt 1):870-874.
 49. Arslan H, Ceylan K, Harman M, Yilmaz Y, Temizoz O, Can S. Virtual computed tomography cystoscopy in bladder pathologies. *Int Braz J Urol* 2006; 32(2):147-154; discussion 154.
 50. McNicholas MM, Raptopoulos VD, Schwartz RK, et al. Excretory phase CT urography for opacification of the urinary collecting system. *AJR* 1998; 170(5):1261-1267.
 51. Turney BW, Willatt JM, Nixon D, Crew JP, Cowan NC. Computed tomography urography for diagnosing bladder cancer. *BJU Int* 2006; 98(2):345-348.
 52. Tsili AC, Efremidis SC, Kalef-Ezra J, et al. Multi-detector row CT urography on a 16-row CT scanner in the evaluation of urothelial tumors. *Eur Radiol* 2007; 17(4):1046-1054.
 53. Sadow CA, Silverman SG, O'Leary MP, Signorovitch JE. Bladder cancer detection with CT urography in an Academic Medical Center. *Radiology* 2008; 249(1):195-202.
 54. Xie Q, Zhang J, Wu PH, et al. Bladder transitional cell carcinoma: correlation of contrast enhancement on computed tomography with histological grade and tumour angiogenesis. *Clin Radiol* 2005; 60(2):215-223.
 55. Barentsz JO, Jager GJ, van Vierzen PB, et al. Staging urinary bladder cancer after transurethral biopsy: value of fast dynamic contrast-enhanced MR imaging. *Radiology* 1996; 201(1):185-193.
 56. Barentsz JO, Witjes JA, Ruijs JH. What is new in bladder cancer imaging. *Urol Clin North Am* 1997; 24(3):583-602.
 57. Sohn M, Neuerburg J, Teuffl F, Bohndorf K. Gadolinium-enhanced magnetic resonance imaging in the staging of urinary bladder neoplasms. *Urol Int* 1990; 45(3):142-147.
 58. Tanimoto A, Yuasa Y, Imai Y, et al. Bladder tumor staging: comparison of conventional and gadolinium-enhanced dynamic MR imaging and CT. *Radiology* 1992; 185(3):741-747.
 59. Buy JN, Moss AA, Guinet C, et al. MR staging of bladder carcinoma: correlation with pathologic findings. *Radiology* 1988; 169(3):695-700.
 60. Tekes A, Kamel I, Imam K, et al. Dynamic MRI of bladder cancer: evaluation of staging accuracy. *AJR* 2005; 184(1):121-127.
 61. Roe K, Muren LP, Rorvik J, et al. Dynamic contrast enhanced magnetic resonance imaging of bladder cancer and implications for biological image-adapted radiotherapy. *Acta Oncol* 2008; 47(7):1257-1264.
 62. Deserno WM, Harisinghani MG, Taupitz M, et al. Urinary bladder cancer: preoperative nodal staging with ferumoxtran-10-enhanced MR imaging. *Radiology* 2004; 233(2):449-456.
 63. Beer A, Saar B, Zantl N, et al. MR cystography for bladder tumor detection. *Eur Radiol* 2004; 14(12):2311-2319.
 64. Lammle M, Beer A, Settles M, Hannig C, Schwaibold H, Drews C. Reliability of MR imaging-based virtual cystoscopy in the diagnosis of cancer of the urinary bladder. *AJR* 2002; 178(6):1483-1488.
 65. Matsuki M, Inada Y, Tatsugami F, Tanikake M, Narabayashi I, Katsuoka Y. Diffusion-weighted MR imaging for urinary bladder carcinoma: initial results. *Eur Radiol* 2007; 17(1):201-204.
 66. Klein L, Pollack HM. Computed tomography and magnetic resonance imaging of the female lower urinary tract. *Radiol Clin North Am* 1992; 30(4):843-860.
 67. Robinson P, Collins CD, Ryder WD, et al. Relationship of MRI and clinical staging to outcome in invasive bladder cancer treated by radiotherapy. *Clin Radiol* 2000; 55(4):301-306.
 68. Saksena MA, Dahl DM, Harisinghani MG. New imaging modalities in bladder cancer. *World J Urol* 2006; 24(5):473-480.
 69. Jager GJ, Barentsz JO, Oosterhof GO, Witjes JA, Ruijs SJ. Pelvic adenopathy in prostatic and urinary bladder carcinoma: MR imaging with a three-dimensional T1-weighted magnetization-prepared-rapid gradient-echo sequence. *AJR* 1996; 167(6):1503-1507.
 70. Bouchelouche K, Oehr P. Positron emission tomography and positron emission tomography/computerized tomography of urological malignancies: an update review. *J Urol* 2008; 179(1):34-45.
 71. Schoder H, Larson SM. Positron emission tomography for prostate, bladder, and renal cancer. *Semin Nucl Med* 2004; 34(4):274-292.
 72. Anjos DA, Etchebehere EC, Ramos CD, Santos AO, Albertotti C, Camargo EE. 18F-FDG PET/CT delayed images after diuretic for restaging invasive bladder cancer. *J Nucl Med* 2007; 48(5):764-770.
 73. Hain SF, Maisey MN. Positron emission tomography for urological tumours. *BJU Int* 2003; 92(2):159-164.
 74. Driessens O, Oyen R, Van Poppel H, Vankan Y, Flamen P, Mortelmans L. FDG-PET for preoperative staging of bladder cancer. *Eur J Nucl Med Mol Imaging* 2005; 32(12):1412-1417.
 75. Liu IJ, Lai YH, Espiritu JI, et al. Evaluation of fluorodeoxyglucose positron emission tomography imaging in metastatic transitional cell carcinoma with and without prior chemotherapy. *Urol Int* 2006; 77(1):69-75.
 76. Picchio M, Treiber U, Beer AJ, et al. Value of 11C-choline PET and contrast-enhanced CT for staging of bladder cancer: correlation with histopathologic findings. *J Nucl Med* 2006; 47(6):938-944.
 77. Gofrit ON, Mishani E, Orevi M, et al. Contribution of 11C-choline positron emission tomography/computerized tomography to preoperative staging of advanced transitional cell carcinoma. *J Urol* 2006; 176(3):940-944; discussion 944.
 78. Hughes OD, Perkins AC, Frier M, et al. Imaging for staging bladder cancer: a clinical study of intravenous 111indium-labelled anti-MUC1 mucin monoclonal antibody C595. *BJU Int* 2001; 87(1):39-46.
 79. Simms MS, Perkins AC, Price MR, Scholfield DP, Bishop MC. 99mTechnetium-C595 radioimmunoscintigraphy: a potential staging tool for bladder cancer. *BJU Int* 2001; 88(7):686-691.
 80. Manyak MJ, Gladkova ND, Makari JH, et al. Evaluation of superficial bladder transitional-cell carcinoma by optical coherence tomography. *J Endourol* 2005; 19(5):570-574.
 81. American College of Radiology. *Manual on Contrast Media*. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/contrast_manual.aspx.
 82. Greene FL, Page DL, Fleming ID, et al, eds, for the American Joint Committee on Cancer. *AJCC Cancer Staging Manual*. 6th ed. New York, NY: Springer-Verlag; 2002.

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

Appendix 1. Staging of Bladder Cancer [82]

Primary tumor (T)

Stage	Sub-Stage	Definition
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Ta		Noninvasive papillary carcinoma
Tis		Carcinoma in situ (ie, flat tumor)
T1		Tumor invades subepithelial connective tissue
T2		Tumor invades muscle
	pT2a	Tumor invades superficial muscle (inner half)
	pT2b	Tumor invades deep muscle (outer half)
T3		Tumor invades perivesical tissue
	pT3a	Microscopically
	pT3b	Macroscopically (extravesical mass)
T4		Tumor invades any of the following: prostate, uterus, vagina, pelvic wall, or abdominal wall
	T4a	Tumor invades the prostate, uterus, vagina
	T4b	Tumor invades the pelvic wall, abdominal wall

[Note: The suffix "m" should be added to the appropriate T category to indicate multiple lesions. The suffix "is" may be added to any T to indicate the presence of associated carcinoma in situ.]

Regional lymph nodes (N)

Stage	Sub-Stage	Definition
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single lymph node, ≤ 2 cm in greatest dimension
N2		Metastasis in a single lymph node, > 2 cm but ≤ 5 cm in greatest dimension; or multiple lymph nodes, ≤ 5 cm in greatest dimension
N3		Metastasis in a lymph node, > 5 cm in greatest dimension

Distant metastasis (M)

Stage	Sub-Stage	Definition
MX		Distant metastasis cannot be assessed
M0		No distant metastasis
M1		Distant metastasis

Appendix 2. Stage Grouping [82]

Stage 0a	Ta, N0, M0
Stage 0is	Tis, N0, M0
Stage I	T1, N0, M0
Stage II	T2a, N0, M0
	T2b, N0, M0
Stage III	T3a, N0, M0
	T3b, N0, M0
	T4a, N0, M0
Stage IV	T4b, N0, M0
	Any T, N1, M0
	Any T, N2, M0
	Any T, N3, M0
	Any T, Any N, M1