

American College of Radiology ACR Appropriateness Criteria®

Clinical Condition: Post-Treatment Surveillance of Bladder Cancer

Variant 1: Superficial TCC; no invasion or risk factors.

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis without and with contrast	3	Consider this procedure if metastatic disease is suspected, although this will be rare. CT urography is preferred (includes high-resolution excretory phase images of the kidneys, ureters, and bladder).	☢ ☢ ☢ ☢
X-ray intravenous urography	3	Use of intravenous urography has continued to decline with the increasing widespread use of CT urography.	☢ ☢ ☢
MRI abdomen and pelvis without and with contrast	3	MR urography is preferred. See statement regarding contrast in text under "Anticipated Exceptions."	O
X-ray chest	2		☢
FDG-PET/CT whole body	1		☢ ☢ ☢ ☢
US pelvis (bladder)	1		O
MRI abdomen and pelvis without contrast	1		O
CT chest with contrast	1		☢ ☢ ☢
CT chest without contrast	1		☢ ☢ ☢
CT chest without and with contrast	1		☢ ☢ ☢
CT abdomen and pelvis with contrast	1		☢ ☢ ☢ ☢
CT abdomen and pelvis without contrast	1		☢ ☢ ☢ ☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition: **Post-Treatment Surveillance of Bladder Cancer****Variant 2:** **Superficial TCC; no invasion; with risk factors.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
CT abdomen and pelvis without and with contrast	8	CT urography is preferred (includes high-resolution excretory phase images of the kidneys, ureters, and bladder).	☢ ☢ ☢ ☢
MRI abdomen and pelvis without and with contrast	6	MR urography is preferred. See statement regarding contrast in text under “Anticipated Exceptions.”	O
X-ray chest	5		☢
X-ray intravenous urography	3		☢ ☢ ☢
FDG-PET/CT whole body	3		☢ ☢ ☢ ☢
MRI abdomen and pelvis without contrast	3		O
CT abdomen and pelvis with contrast	3	The visceral/nodal status is evaluated during CT urography.	☢ ☢ ☢ ☢
CT abdomen and pelvis without contrast	1		☢ ☢ ☢ ☢
US pelvis (bladder)	1		O
CT chest with contrast	1		☢ ☢ ☢
CT chest without contrast	1		☢ ☢ ☢
CT chest without and with contrast	1		☢ ☢ ☢
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition: Post-Treatment Surveillance of Bladder Cancer**Variant 3:** Invasive TCC with or without cystectomy.

Radiologic Procedure	Rating	Comments	RRL*
X-ray chest	9		☢
CT abdomen and pelvis without and with contrast	8	CT urography is preferred (includes high-resolution excretory phase images of the kidneys, ureters, and bladder).	☢ ☢ ☢ ☢
X-ray abdomen loopogram	8	Consider this procedure in patients with an ileal loop postcystectomy.	☢ ☢ ☢
CT abdomen and pelvis with contrast	7	CT urography is preferred (includes high-resolution excretory phase images of the kidneys, ureters, and bladder).	☢ ☢ ☢ ☢
MRI abdomen and pelvis without and with contrast	7	MR urography is preferred. See statement regarding contrast in text under “Anticipated Exceptions.”	O
MRI abdomen and pelvis without contrast	5		O
FDG-PET/CT whole body	5		☢ ☢ ☢ ☢
X-ray intravenous urography	3		☢ ☢ ☢
CT abdomen and pelvis without contrast	3		☢ ☢ ☢ ☢
CT chest with contrast	3	This procedure is performed if chest x-ray is equivocal.	☢ ☢ ☢
CT chest without contrast	3		☢ ☢ ☢
US pelvis (bladder)	3		O
CT chest without and with contrast	1		☢ ☢ ☢
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

POST-TREATMENT SURVEILLANCE OF BLADDER CANCER

Expert Panel on Urologic Imaging: John R. Leyendecker, MD¹; Mary Jennings Clingan, MD²; Steven C. Eberhardt, MD³; Barak Friedman, MD⁴; Pat F. Fulgham, MD⁵; Matthew S. Hartman, MD⁶; Keyanoosh Hosseinzadeh, MD⁷; Elizabeth Lazarus, MD⁸; Mark E. Lockhart, MD, MPH⁹; Aytekin Oto, MD¹⁰; Christopher Porter, MD¹¹; Gary S. Sudakoff, MD¹²; Sadhna Verma, MD¹³; Erick M. Remer, MD.¹⁴

Summary of Literature Review

Introduction/Background

Transitional cell carcinoma (TCC) of the bladder accounts for more than 90% of all bladder cancer in the United States [1]. It is 3 times more common in men than in women and is estimated to be the third leading cause of cancer death related to the genitourinary tract [1]. The American Cancer Society estimated that there would be 73,510 new cases in the United States in 2012 and that 14,880 people would die of the disease. For all stages combined, the 5-year relative survival rate is 78% [1]. When the cancer is diagnosed at a localized stage (0 and I), the 5-year survival rate is 98% and 88%, respectively; 75% of cancers are detected at this early stage [2]. For advanced stages such as III and IV, 5-year relative survival rates are 46% and 15%, respectively [2]. Patients who have been diagnosed and treated for TCC of the bladder require follow-up evaluation, which is usually based on the type of treatment as well as accurate initial grading and staging of the tumor.

The purposes of surveillance imaging are to detect new or previously undetected tumors in the bladder, to detect recurrent or metastatic disease, and to monitor the effects and/or complications following urinary diversion surgery. Recommendations for tumor surveillance can be based on the classification of patients into 3 groups: 1) those with superficial bladder cancer but no additional risk factors who are treated by local therapy; 2) those with superficial bladder cancer and with additional risk factors but still treated by local therapy; and 3) those with invasive bladder cancer usually treated with cystectomy [3]. It should be noted that at least one study has questioned the efficacy of surveillance for recurrence after radical cystectomy for bladder cancer and advocated a symptoms-based approach to imaging [4]. However, particularly in light of constantly improving imaging techniques and therapeutic regimens, further study is required before imaging surveillance can be considered unnecessary.

In patients with newly diagnosed superficial TCC of the bladder, the median time to the first recurrence is 23 months [5]. Subsequent recurrences present with increasing frequency [5]. Stage T1, higher grades, and Ki-67 stain positivity have been associated with the first recurrence [5]. Additionally, “p53 stain positivity” might be used to identify patients at high risk for a second recurrence [5]. As for muscle-invasive bladder cancer, a study of 1,054 patients treated with radical cystectomy and lymph node dissection showed the median time to recurrence to be 12 months among patients in whom the cancer recurred. In 22% there was a distant recurrence, and in 7% there was a local (pelvic) recurrence [6]. In a review of muscle-invasive bladder cancer by Malkowicz et al [7] the authors assert that “contemporary cystectomy series demonstrate a 5%–15% chance of local disease recurrence that is associated with nodal status (25%–50%) at the time of surgery and clinical stage of disease (15%–50%). Most recurrences manifest during the first 24 months, and many are concentrated within 6–18 months after surgery. In all, 50%–70% of these local recurrences are noted to occur without concomitant distant disease.”

Distant recurrence most often occurs within 2 years but can occur beyond 5 years. In a study by Ghoneim et al [8], radical cystectomy for muscle-invasive bladder cancer was associated with a 55.5% 5-year disease-free survival. Tumor stage, histological grade, and lymph node status had a significant and independent impact on survival. Herrmann et al [9] determined that although survival of patients with \geq pT3 (p = pathologic) bladder cancer was adversely affected by the presence of lymph node metastases, the same was not true for patients with

¹Principal Author and Panel Vice-chair, Wake Forest University School of Medicine, Winston Salem, North Carolina. ²Research Author, Wake Forest University School of Medicine, Winston Salem, North Carolina. ³University of New Mexico, Albuquerque, New Mexico. ⁴Long Island Jewish Medical Center, New Hyde Park, New York. ⁵Urology Clinics of North Texas, Dallas, Texas, American Urological Association. ⁶Allegheny General Hospital, Pittsburgh, Pennsylvania. ⁷University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania. ⁸Alpert Medical School of Brown University, Providence, Rhode Island. ⁹University of Alabama at Birmingham, Birmingham, Alabama. ¹⁰The University of Chicago, Chicago, Illinois. ¹¹Virginia Mason Medical Center, Seattle, Washington, American Urological Association. ¹²Medical College of Wisconsin, Milwaukee, Wisconsin. ¹³Johns Hopkins Hospital, Baltimore, Maryland. ¹⁴Panel Chair, Cleveland Clinic, Cleveland, Ohio.

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≤pT2 disease. In this same study, lymphovascular invasion was associated with impaired survival regardless of T stage.

The likelihood of recurrent, progressive, or metastatic disease increases with the presence of one or more of the following risk factors:

1. *Depth of invasion:* Most TCCs of the bladder (75%–85%) are superficial, although this represents a heterogeneous group consisting of pTa (70%), pT1 (20%), and carcinoma in situ (CIS) (10%) lesions [3,10,11]. Although the risk of recurrence is high, most superficial tumors remain superficial, with a minority of such tumors progressing to invasive carcinoma. Patients with CIS are more likely to progress to invasive disease [10]. There is evidence to indicate that cancers that invade the lamina propria (stage T1) should not be regarded as superficial; they are associated with a higher rate of progression [10]. Up to 50% of patients who are treated locally for invasive cancer manifest distant metastases, and they usually die of their disease within 2 years [11].
2. *Tumor size:* Various studies have shown that tumors >3 cm have up to a 35% chance of progression, and tumors >10 grams are also associated with a poor prognosis [12–14].
3. *Grade:* Progression from grade I to III in patients without interval intravesical chemotherapy, cystectomy, or radiation therapy has been associated with an increased incidence of invasive disease and a decrease in 5-year survival rates [15,16]. Even stage Ta tumors, which are limited to the mucosa, are associated with a nearly 50% recurrence rate and a 25% rate of progression to invasive disease when classified as grade III [16].
4. *Adjacent or remote bladder mucosal changes:* If there are adjacent or distant changes of atypia or dysplasia, there is a significant chance of progression to muscle invasion (more than 30% within 4 years of diagnosis). CIS in patients with low-grade, low-stage lesions may be associated with progression to muscle invasion (greater than 80% within 4 years of diagnosis) [12,17].
5. *Multiplicity of foci:* A finding of multiple tumors is seen in approximately 30% of cases and is associated with a recurrence rate that is almost one-third higher than it is in patients with single lesions. This finding is generally associated with a shortening of the average time until recurrence [13,14]. Two of 3 patients with single lesions but 9 of 10 with multiple lesions develop recurrent carcinoma [12,18]. In patients with initial T1G3 bladder cancer, the presence of multifocality, along with a tumor size of >3cm and concomitant CIS, predicted an adverse oncological outcome in those undergoing a bladder sparing approach [19].
6. *Upper-tract obstruction:* Upper-tract obstruction has been associated with a decreased 5-year survival rate. Patients with bilateral hydronephrosis had a 5-year survival rate of 31%, compared with 45% for those who had unilateral involvement and 63% for those with no hydronephrosis [20].
7. *Lymphatic invasion:* Invasion of the lamina propria is a very poor prognostic sign [21], and most patients so affected die within 6 years [14]. Solid (nonpapillary) lesions have a greater tendency for lymphatic invasion [17].
8. *TCC involvement of the prostate:* When TCC of the bladder is associated with involvement of the prostate (such involvement has been observed in 29%–43% of cystectomy specimens), particularly with stromal invasion, there is a substantially increased risk of urethral recurrence. Sixty-seven percent of men with urethral recurrence had prostatic TCC in cystectomy specimens. Urethral recurrence can be expected in only 1%–4% of cases when there is no TCC in the prostate. Those patients who are not candidates for cystoprostatectomy with urethrectomy are best followed up with urethral washings. Urethroscopy is performed in those having positive cytologic results [18,22,23].

Laboratory Tests and Chromosomal Abnormalities

There has been interest in developing quantitative tests to complement or even replace urinary cytology in surveillance of bladder carcinoma. Kumar et al [24] demonstrated 85% sensitivity in detecting recurrent bladder cancer using the nuclear matrix protein 22 (NMP22) marker detection device versus 41% sensitivity for traditional cytology, suggesting that it may substitute for urinary cytology. Additional studies demonstrate similar sensitivities for detecting bladder cancer with various molecular markers, and Messing et al [25], Varella-Garcia et al [26], and Bhuiyan et al [27] suggest that, due to its sensitivity, immunohistochemical testing may increase the time period between cystoscopies or even replace cystoscopy. Van Rhijn et al [28] evaluated the literature regarding the use of urine tumor markers for urothelial carcinoma surveillance, concluding that in their view “Microsatellite analysis, ImmunoCyt, NMP22, CYFRA21-1, LewisX, and FISH (fluorescence in situ hybridization) are the most promising markers for surveillance at this time. Nevertheless, clinical evidence is

insufficient to warrant the substitution of the cystoscopic follow-up scheme by any of the currently available urine marker tests.” In other words, no biomarker assays replace or eliminate the need for cystoscopy at the present time [11,29]. Specific problems among these tests include high false-positive rates for some, limited clinical experience, and a need for more prospective clinical trials [30]. In addition, not all tumor markers are FDA-approved for clinical use.

Cystoscopic and Virtual Cystoscopic Surveillance

One recommended surveillance program for patients treated for superficial bladder TCC includes cystoscopy every 3 months for 2 years, then every 6 months for 2 to 3 years, and yearly thereafter [3,31]. Recently published European guidelines recommend that patients with low-risk nonmuscle-invasive tumors should have a cystoscopy at 3 months and, if negative, surveillance cystoscopy at 9 months and then yearly for 5 years [29,32,33]. For high-risk tumors, the first postoperative cystoscopy should be at 3 months [29,32,33]. If cystoscopic findings and cytology are negative, follow-up cystoscopies should be continued every 3 months for a period of 2 years, every 6 months thereafter until 5 years, and yearly thereafter [29,32,33]. Annual lifelong imaging of the upper urinary tract should also be performed for muscle-invasive disease and patients who have high-risk nonmuscle invasive bladder cancer [29,33].

There has been interest in developing virtual cystoscopic or cystographic techniques using magnetic resonance imaging (MRI) and computed tomography (CT) both for problem-solving in cases that are suboptimal for standard cystoscopy (narrow-necked diverticula) and as a way to avoid the patient discomfort associated with standard cystoscopy. Browne et al [34] demonstrated CT cystography to have a 100% sensitivity in identifying 0.5 cm masses and a sensitivity of 95% for all patients in detecting neoplasm with an accuracy of 88%. Kishore et al [35] examined 11 patients with 14 bladder tumors with virtual CT cystoscopy using intravesical instillation of dilute contrast media and found that this technique missed only 2 tumors, both measuring 7 mm. Tsampoulas et al [36] found 16-channel multidetector CT to be 96% sensitive for detecting bladder lesions ranging in size from 3 mm to 9.7 cm, including 18 lesions ≤ 5 mm in size. Beer et al [37] examined MR cystography (multiplanar reconstructions) with virtual MR cystoscopy and found that they demonstrated a combined sensitivity and specificity of 90.7% and 94.0%, respectively. Both CT and MR cystoscopy provide views comparable to those of standard cystoscopy.

Urinalysis and cytologic evaluation should be performed at the time of each cystoscopy. Positive cytologic findings are followed by examination of the remaining bladder and upper tracts [29,38].

Intravenous Urography

Intravenous urography (IVU) was once the most common imaging modality used to evaluate the urothelium of the upper collecting system [39]. In a recent study of 322 patients who underwent cystectomy and urinary tract diversion for urothelial carcinoma followed by routine surveillance with excretory urography, only half of subsequent tumors of the upper urinary tract were detected on 8 of 1,064 studies [40]. In this study, patients with positive distal ureteral resection margins or a history of upper urinary tract tumors had up to a 10-fold higher risk for recurrence in the upper urinary tract.

Now in widespread use, CT urography has supplanted IVU for assessment of the upper urinary tract [41,42]. Although protocols vary, CT urography is essentially a precontrast and postcontrast CT of the abdomen and pelvis that includes high-resolution images of the kidneys, ureters, and bladder during the excretory phase. Advantages of a cross-sectional technique, such as CT urography, include the ability to directly visualize small masses, which may be obscured by contrast material or overlying bowel gas on excretory urography, and to identify focal wall thickening. CT urography can also better distinguish between filling defects such as enhancing tumor versus nonenhancing calculi and blood clots [43,44]. CT also offers limited assessment of a nonfunctioning/obstructed kidney that would not excrete the contrast medium required for excretory urography [43,44]. These strengths led Jinzaki et al [43] to conclude that “CT urography should be considered as the initial examination for the evaluation of patients at high risk for upper urinary tract urothelial carcinoma.” Furthermore, Cohan et al [45] in their review conclude “the consensus is that CT urography can detect many more bladder cancers than excretory urography.”

Computed Tomography

Cross-sectional imaging surveillance is important in patients with invasive bladder cancer or risk factors. In their study, Giannarini et al [46] found that 36.3% of the 479 patients followed after radical cystectomy with ileal orthotopic bladder substitution recurred; however, only half of these patients were symptomatic. The remaining

metastases and recurrences were only detected by routine surveillance and were mainly comprised of lung and urethral recurrences. Among symptomatic patients, bone metastases were more common [46]. Of note, the asymptomatic patients diagnosed with recurrence after routine surveillance had a higher survival probability than symptomatic patients with recurrence [46].

CT is recommended at 6, 12, and 24 months for surveillance of patients with minimal muscle invasion (T2) who elect either cystectomy or other types of therapy without cystectomy, since most recurrences become evident within the first 2 years after surgery [29,47]. There is a different recommendation for surveillance of patients treated with bladder-preserving surgery. In these patients with transurethral resection of localized muscle-invasive TCC and surveillance combined with neoadjuvant chemotherapy and radiation therapy, CT scans of the abdomen and pelvis should be performed at 3 months after completion of radiation therapy and then every 6 months or “as otherwise indicated” [48].

When CT is used to evaluate patients following cystectomy, the pelvis is the most common site of recurrence. In these cases, the CT examination should include evaluation of the abdomen and perineum so that unsuspected, isolated abdominal metastases and recurrent perineal tumors will not be missed. Most metastases are detected within the first 18–24 months following surgery. The most common sites of metastatic TCC are lymph nodes, liver, lung, bone, peritoneum, and adrenal glands [7,29,49]. The upper urinary tract is the most common site of late recurrence [29]. The mean interval between initial treatment of bladder tumor and detection of subsequent upper urinary tract cancer is 40–80 months [38,50].

Many believe that, in the absence of risk factors, urine cytologic evaluation and cystoscopy are sufficiently accurate, especially since the risk of upper urinary tract TCC in all patients treated for bladder carcinoma is only about 2%–5% [2,38,50–54]. This low risk may not be sufficient to justify routine upper urinary tract screening [52,55] despite the fact that not all recurrences give positive cytologic results or are associated with symptoms such as hematuria.

At the present time, surveillance of the upper urinary tract is appropriate in patients with positive urine cytology results, symptoms of hematuria, muscle-invasive bladder cancer or annually in nonmuscle invasive patients with the following risk factors (usually postcystectomy) [56]:

1. *Carcinoma in situ (CIS)*: When found in the cystectomy specimen, patients had a 9%–13% incidence of upper urinary tract TCC, with a correlation between the extent of the CIS and the risk of upper tract TCC [38,50–53]. Up to 24% of patients with CIS developed upper tract tumors during a mean follow-up of 94 months, and 32.2% of these patients had bilateral disease [29].
2. *Urethral CIS*: When present, the likelihood of upper urinary tract TCC increases to 20%–30% [18,50,51,53].
3. *Multiple tumors*
4. *Recurrent tumors*
5. *Tumors involving the trigone or ureteral orifices* [29,50–53,56]
6. *Tumors arising in bladder diverticula*: This can be as a result of later detection and earlier transmural tumor extension [57].
7. *Higher tumor grade, stage, and vesicoureteral reflux* [29]

If a documented recurrence is invasive, the patient is then staged [58].

CT urography is now the preferred noninvasive imaging method for screening the upper tracts and can easily be incorporated into CT protocols for metastatic disease surveillance. A recent study comparing the accuracy of detection and localization of upper urinary tract urothelial carcinoma with CT urography versus excretory urography favored CT urography with a per-patient sensitivity, specificity, and overall accuracy of 93.5%, 94.8%, and 94.2%, respectively, compared to 80.4%, 81.0%, and 80.8%, respectively, for excretory urography [43].

If CT urography cannot be done or if there is incomplete visualization or nonvisualization of the collecting structures, evaluation can be supplemented with retrograde pyelography or, in those patients with ileal conduits, replaced by loopogram. CT urography is also promising in those patients with urinary diversions and may provide additional diagnostic information, as it provides examination of the entire abdomen and pelvis unlike a standard loopogram. A study by Sudakoff et al [59] demonstrated that CT urography with 3-D rendering depicted both normal and abnormal postoperative findings in patients with urinary diversions. The addition of digital radiography enhanced visualization of the urinary collecting system to a statistically significant degree [59].

Antegrade pyelography is uncommon but occasionally performed for diagnosis when the above techniques fail or if the collecting system is directly accessed to perform urine cytology or nephroscopy [56].

In addition to evaluating the upper tracts, CT urography also detects bladder tumors. Turney et al [60] reported a 93% sensitivity and 99% specificity for CT urography in detecting bladder cancer in patients presenting with macroscopic hematuria. In a larger population of 779 patients with hematuria or a history of urothelial cancer, CT urography had a sensitivity of 79%, specificity of 94%, and accuracy of 91% detecting bladder cancer [61]. In this study, the negative predictive value (NPV) rose from 95% for all patients to 98% for patients evaluated for hematuria alone, but the accuracy dropped to 78% for patients with a prior urothelial malignancy [61].

Magnetic Resonance Imaging

MRI of the bladder may be used to evaluate superficial and invasive bladder tumors. CT provides limited visualization of the depth of tumor invasion within the bladder wall [23,62,63]. MRI, because of its high soft-tissue contrast resolution, has been noted to be “superior to clinical staging” even in the absence of intravenous contrast-enhanced sequences. MRI allows distinction between bladder wall layers and also between advanced T3a tumors and the less invasive T1, T2, and early T3a lesions [11,64,65]. Tekes et al [66] 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%. However, overstaging occurred in 32% of cases. [66]. In addition to superior contrast resolution, multiplanar capabilities also help MRI detect adjacent organ involvement [67].

Preliminary evidence suggests that dynamic contrast-enhanced MRI may also be useful to assess treatment response after chemotherapy [68]. A study looking at neoadjuvant chemotherapy and chemoradiation therapy found no significant difference in accuracy of staging by MRI between a group receiving neoadjuvant chemotherapy following biopsy and preoperative staging biopsy alone (75.0% versus 77.8%, respectively) [67]. However, given the inflammatory infiltration and/or fibrous changes caused by chemoradiation, the accuracy of MRI staging in this group was lower (30%) [67].

Newer MR technologies in pelvic imaging, such as diffusion-weighted imaging (DWI), when used as a marker of tumor cellularity, may prove useful in the diagnosis and surveillance of patients with bladder tumors [69]. Mean apparent diffusion coefficients (ADC) in patients with bladder tumors were significantly lower than ADC values of normal bladder [69]. In a recent study comparing DWI-MRI with cystoscopy in the diagnosis and follow-up of patients with bladder carcinoma, DWI was found to have a sensitivity of 90%, a specificity of 93%, and an accuracy of 91% compared with cystoscopy [70].

El-Assmy et al [71] recently compared staging accuracy of DWI to T2-weighted sequences, finding superior performance of DWI in staging organ-confined tumors less than or equal to T2 disease. Likewise, Takeuchi et al [72] found that DWI added information when evaluating the T stage of bladder cancer, significantly improving accuracy, specificity, and area under the receiver operating curves, with best results from combining T2-weighted images, contrast-enhanced images, and DWI. DWI has also been suggested to improve specificity and accuracy in assessing therapeutic response to induction chemoradiotherapy in patients with muscle invasive bladder cancer, thereby predicting complete response and optimizing patient selection for bladder-sparing protocols as well as monitoring recurrence [73].

Although more costly than CT, MRI has no ionizing radiation and is more accurate in differentiating between stages T3b and T4a, between stages T4a and T4b, and between marrow and no-marrow infiltration [11,64,65,74]. Although not widely available, MRI performed with ferumoxtran-10 (ultrasmall superparamagnetic iron oxide) contrast demonstrated accuracies in pathologic lymph node detection of up to 92% and sensitivities of up to 96% [75]. These improved techniques for detecting new, recurrent, or metastatic tumors in patients with proven invasive TCC [47] have sometimes been associated with decreased morbidity, although not with increased curability [56].

As with CT, urographic sequences can be added to routine abdominal and pelvic MR sequences to combine upper tract screening with a metastatic survey. There are relatively few studies evaluating the sensitivity, specificity, and accuracy of MR urography (MRU) for upper urinary tract malignancy. Most MRU protocols utilize a combination of T2-weighted hydrographic sequences and diuretic augmented, excretory T1-weighted sequences using a gadolinium-based contrast agent to visualize the upper tracts [76]. Takahashi et al [77] found that MRU had a sensitivity, specificity, and accuracy of 72.4%–86.2%, 97.9%–99.5%, and 94.6%–97.7%, respectively, for upper tract malignancy. Lee et al [78] compared MRU with retrograde pyelography and ureteroscopy, finding that the

NPV of MRU was comparable (92%) to retrograde assessment (88%). However, the sensitivities for detection of upper tract malignancy for both techniques were lower than that typically reported for CT urography.

Ultrasonography

Modern transabdominal ultrasonographic techniques have been found to have a sensitivity of 78.5%, a specificity of 100%, a positive predictive value (PPV) of 100%, and a NPV of 86.9% for diagnosing bladder cancer recurrence in patients with a history of superficial bladder cancer [79]. However, transabdominal ultrasound (US) has “important limitations” for bladder cancer detection, particularly for tumors that are flat, <5 mm, or near the bladder neck or dome [17,79]. Transrectal ultrasound can improve detection and may be effective for monitoring tumor response or recurrence following neoadjuvant chemotherapy or cystectomy [80,81]. Newer technology may also improve the performance of US for detection of bladder cancer. Kocakoc et al [82] reported a sensitivity of 96.4%, a specificity of 88.8%, a PPV of 97.6%, and a NPV of 84.2% for bladder tumor detection using a combination of grayscale sonography, multiplanar reconstruction, and 3-D virtual sonography.

Chest Radiography

Periodic chest radiography (posteroanterior and lateral) to search for occult metastases is recommended at 6-month intervals for the first 2–3 years and subsequent yearly radiographs following cystectomy for early T-stage disease. For more advanced disease ($\geq T3$), more frequent surveillance may be considered [83,84]. Although the relative values of chest CT versus radiography for surveillance in the setting of bladder cancer have not been clearly established, a lung lesion suspected on chest radiography may be appropriately followed by a CT scan of the chest for improved characterization.

Positron Emission Tomography

Currently, there is a growing role for positron emission tomography (PET) imaging in the assessment and surveillance of bladder cancer. According to Shvarts et al [85], “It has a high PPV and can be used for problem-solving in patients with indeterminate findings on conventional imaging.” A review by Bouchelouche and Oehr [86] stated that for bladder cancer, fluorine-18-2-fluoro-2-deoxy-D-glucose PET (FDG-PET) is useful for identifying distant metastases but is limited for detecting primary tumors due to the urinary excretion of FDG. The role of ^{11}C -choline and ^{11}C -methionine, they added, remains to be evaluated further in clinical studies.

Kosuda et al [87] used PET in 12 patients with histologically proven bladder cancer. Their study demonstrated a true-positive rate of 66.7% and a false-negative rate of 33.3%. PET was able to identify 100% (17/17) of distant metastases (lung, bone, and remote lymph node) as well as 66.7% (two-thirds) of local pelvic lymph nodes [85]. Therefore, they concluded FDG-PET might be useful in detecting perivesical tumor growth or distant metastasis in patients with advanced bladder cancer and for the early detection of recurrent cancer following therapy, although a major pitfall remains the intense FDG accumulation in the urine [87].

Likewise, a review of PET imaging in patients with bladder, prostate, and renal cancer concluded that FDG is unsuitable for imaging bladder tumors because of its high urinary excretion, although there may be a role for it in detection of recurrent disease [88]. A more recent study, however, suggests that detection of locally recurrent or residual bladder tumors can be dramatically improved using FDG-PET/CT with delayed images after a diuretic and oral hydration [89]. Investigators in a study correlating FDG-PET and CT results in the same patients reported sensitivity, specificity, and accuracies of 60%, 88%, and 78%, respectively, in nodal and metastasis staging, suggesting improved distant metastatic and locoregional node staging [90].

Evidence that the combination of FDG-PET/CT also outperforms conventional imaging such as CT alone was found by Kibel et al [91], who prospectively evaluated FDG-PET/CT for the staging of muscle-invasive bladder carcinoma in patients with no evidence of metastatic disease by conventional staging methods, reporting a sensitivity of 70%, specificity of 94%, PPV of 78%, and NPV of 91% for PET/CT amongst this population. Of note, FDG-PET/CT detected occult metastatic disease in 7 of 42 patients with negative conventional preoperative evaluations including CT and bone scan. In this study, treatment approach was altered in 2 patients, one receiving neoadjuvant chemotherapy and a second with widespread metastatic disease resorting to palliative chemotherapy.

Looking at muscle-invasive urothelial carcinoma before radical cystectomy, after radical cystectomy, and after systemic chemotherapy, Lodde et al [92] found FDG-PET/CT to be more sensitive, although less specific, than CT in detecting the primary urothelial bladder cancer. Although CT and FDG-PET/CT had similar specificity for lymph node metastasis, FDG-PET/CT demonstrated almost twice the sensitivity of CT. FDG-PET/CT was also useful in detecting metastatic disease outside of the pelvis and was in agreement with bone scans for all patients

with bone metastasis, except in one patient in which 2 additional lesions were detected by FDG-PET/CT but not appreciated at scintigraphy. These results led Lodde et [92] to conclude “FDG-PET/CT could replace standard CT and bone scintigraphy in the presurgical staging and monitoring of patients with urothelial carcinoma after surgery or chemotherapy” as a cost-effective single method of staging and surveillance.

PET imaging after initial treatment of bladder cancer is impacting patient management. Recent results from the national oncologic PET registry were published on the impact of FDG-PET used after initial treatment of cancer. In restaging patients 65 years and older with bladder cancer, the intended management was changed in approximately 35%, with 29.4 % changing from nontreatment to treatment and 5.9% changing from intended treatment to nontreatment in the 2009 cohort [93]. The impact of PET on intended management during chemotherapy monitoring was also evaluated for the 2009 cohort with 42.9% continuing therapy, 27.0% switching therapy, 5.8% adjusting therapy, and 19.7% stopping therapy [93].

Preliminary studies show that ^{11}C -choline PET, when compared with CT, promises slightly increased accuracy of lymph node staging (63.0% versus 88.9%, $P<0.01$) and may avoid false-positive lymph nodes due to reactivity when compared with CT. In addition there is negligible urinary excretion of ^{11}C -choline [94].

Summary

- Routine imaging surveillance is not indicated for patients with low-grade superficial TCC of the bladder and no invasion of the lamina propria or additional risk factors.
- Patients with superficial TCC of the bladder require careful observation and upper-tract assessment with CT urography, MRU, or, if CT/MRU is not available, IVU every 1–2 years **IF** any of the following risk factors for recurrent tumor are present: 1) tumor size >3 cm or 10 grams, 2) higher than grade I tumor; or 3) adjacent or remote bladder mucosal changes of dysplasia or CIS.
- Additional imaging may be necessary if there are positive urine cytologic findings, hematuria, or abnormal cystoscopy.
- Patients with invasive TCC of the bladder—especially those with evidence of: 1) lymphatic or 2) hematogenous invasion; those with associated 3) dysplasia or 4) CIS in the cystectomy specimen; those with associated 5) urethral TCC, 6) multifocal bladder tumors, 7) recurrent bladder tumors, and 8) tumors in bladder diverticula; or 9) involving the ureterovesical junctions—should have CT or MRU every 1–2 years. IVU, urography, loopogram, or pyelography (retrograde or antegrade) can be used as a substitute or supplement.
- For patients requiring cystectomy for invasive bladder cancer, suggested surveillance protocol includes an MRI or a CT scan at 6, 12, and 24 months and a chest radiograph at least every 6 months for the first 2–3 years and yearly chest radiography thereafter.
- There is growing evidence as to the increased sensitivity of FDG-PET/CT in detecting metastatic disease outside of the pelvis in patients with muscle-invasive bladder cancer. This modality also has a greater sensitivity of detecting lymph node metastasis and may change management in restaging patients and monitoring response to chemotherapy.
- If recurrent bladder cancer is found and considered invasive, new staging may be required (see the ACR Appropriateness Criteria® “[Pretreatment Staging of Invasive Bladder Cancer](#)”) [58].

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie, <30 mL/min/1.73m²), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73m². For more information, please see the [ACR Manual on Contrast Media](#) [95].

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with

different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

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 “Varies”.		

Supporting Documents

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

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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.