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Updated Bladder Cancer Imaging Techniques and Use of T2-Weighted Sequence High-Resolution Magnetic Resonance

Ayman Fathy Ahmed Amer [1], Engy Fathy Tantawy [2], Al Shaimaa Fathi Mohammed [3], and Saber Moftah Abdulrrazaiq Albakoush [4]

[1] Professor of Radiodiagnosis, Faculty of Medicine, Zagazig University.

[2] Assistant Professor of Radiodiagnosis, Faculty of Medicine, Zagazig University.

[3] Lecturer of Radiodiagnosis, Faculty of Medicine, Zagazig University.

[4] M.B.B.CH, Faculty of Medicine – Benghazi University - Libya.

Correspondingauthor:Saber Moftah Abdulrrazaiq Albakoush

Email:saberalbakoush68@gmail.com

Abstract

Background:Bladder cancer (BC) is the sixth most common disease in men and the seventeenth most common in women. Its incidence ranks first among malignant cancers of the urinary system and second only to prostate cancer in Western countries. Bladder cancers and those in the proximal urethra are commonly considered lower urinary tract tumors to distinguish them from ureteral, renal pelvic, and calyceal urothelial tumors, which are collectively referred to as upper urinary tract tumors. Imaging characteristics such as enhancement are helpful for characterization. For staging, cystoscopy and biopsy are used for stages Ta–T3a disease, confined to the bladder. Cross-sectional imaging is useful at stage T3b or later stages, after the tumor has escaped beyond the bladder wall. The multiplanar capability of MRI allows image acquisition in different planes to minimize partial volume averaging and optimize imaging when evaluating the depth of bladder wall invasion. T2 Weighted Imaging (T2WI) provides information on tumor depth and extravesical disease spread. On T2WI, urine has high SI, BC has intermediate to high SI, and the normal detrusor muscle appears as a hypointense line. Diffusion Weighted Imaging (DWI) does not require gadolinium administration and provides both qualitative and quantitative information that reflects changes at the cellular level concerning tumor cellularity and cell membrane integrity

Keywords: Bladder cancer (BC), T2-Weighted Sequence High-Resolution Magnetic Resonance.

Bladder Cancer:

Bladder cancers and those in the proximal urethra are commonly considered lower urinary tract tumors to distinguish them from ureteral, renal pelvic, and calyceal urothelial tumors, which are collectively referred to as upper urinary tract tumors**(1).**Transitional cell carcinoma (TCC) accounts for approximately 90% of all bladder tumors. The second most common cell type is squamous cell cancer (8%), followed by adenocarcinoma, arising in the urachus. Other rare subtypes such as small cell carcinoma account for less than 1% of the cases**(1).**

TCCs are characterized by a high recurrence rate and multiplicity. They involve any part of the urothelium in a random manner. This observation suggests that the entire mucosa is primed to become malignant, known as the "field defect" theory**(1).**

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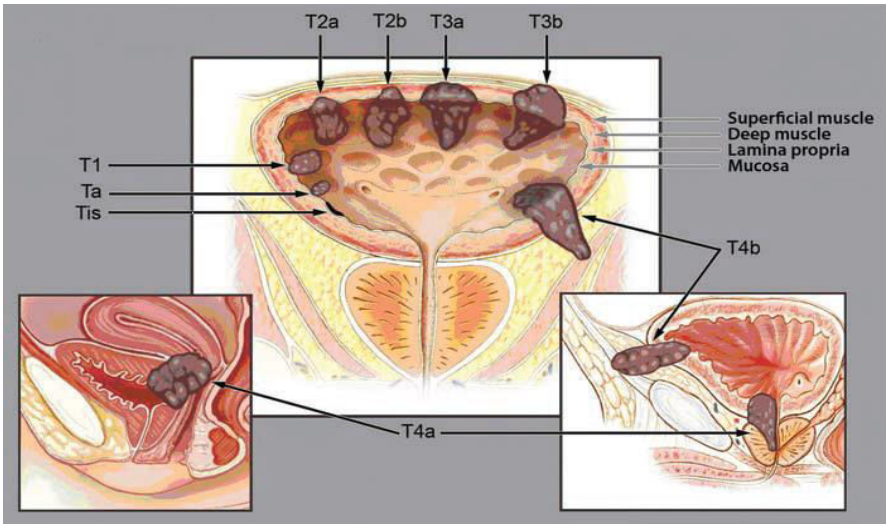
Staging of Bladder Cancer

The TNM and the Jewett-Strong-Marshall classification systems are used in classifying bladder tumors. The TNM staging system has become the system of choice primarily because it is more detailed, comprehensive, showing nodal involvement and distant metastasis. The TNM system, is identical to the American Joint Committee on Cancer system **(1).**



(Figure 1): Schematic diagram of T staging of bladder tumor**(1).**

Clinical presentation of bladder cancer

Local Symptoms

Over 80% of patients with bladder cancer have hematuria, which is typically macroscopic and painless**(2).**According to the American Urological Association guidelines, patients with asymptomatic microscopic hematuria who have no evidence of primary renal disease and in whom benign causes such as menstruation, exercise, trauma, and infection have been excluded require urologic work-up**(3).** Urgency pelvic heaviness are also may be presented**(2).**

Metastatic Symptoms

Hematogenous metastasis most commonly occurs to the lung, bones, liver, and adrenal glands**(1).** Metastatic symptoms include weight loss and loss of appetite; bone pain, with or without pathologic fracture; and lower extremity pain and edema due to obstruction of venous and lymphatic tributaries by nodal metastasis. Uremic symptoms can occur from ureteral obstruction caused by local tumor growth or retroperitoneal adenopathy secondary to nodal metastasis**(4).**

Table (1):Cancer bladder TNM classification system(1).

Stage	Characteristics of TNM classification system
Primary tumor (T)	
Tis	Carcinoma in situ: flat tumor
Ta	Noninvasive papillary carcinoma
T1	Tumor invades subepithelial connective tissue
T2	Tumor invades muscle layer
T2a	Tumor invades superficial muscle (inner half)
T2b	Tumor invades deep muscle (outer half)
T3	Tumor invades perivesical tissue
T3a	Tumor invades perivesical tissue microscopically

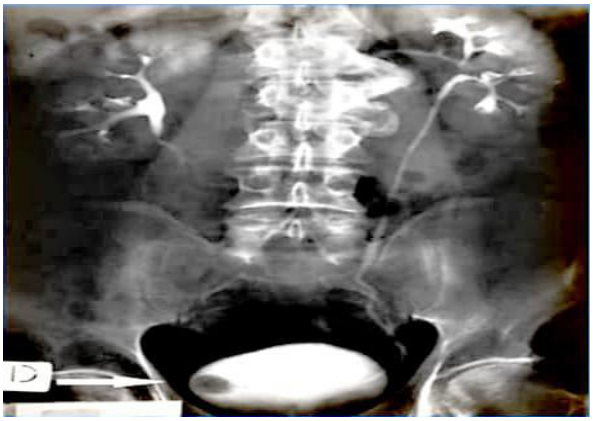
T3b	Tumor invades perivesical tissue macroscopically (extravesical mass)
T4	Tumor invades the adjacent organs
T4a	Tumor invades prostate, uterus, or vagina
T4b	Tumor invades pelvic wall or abdominal wall
Lymph nodes (N)	
N0	No regional lymph node metastasis
N1	Metastasis in a single lymph node ≤ 2 cm in greatest dimension
N2	Metastasis in a single lymph node > 2 cm but ≤ 5 cm in greatest dimension or metastases in multiple lymph nodes, none > 5 cm.
N3	Metastasis in a lymph node > 5 cm in greatest dimension
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

Imaging of bladder cancer

Radiologists may encounter bladder cancer as a mass found on routine imaging, staging, or follow-up after therapy. In the first instance, an incidentally noted mass in the bladder has a broad differential diagnosis, including benign (papilloma, hamartoma, leiomyoma) or malignant neoplasm, hematoma, calculus, fungus ball, cystitis cystica, foreign body, and endometriosis**(5).** Imaging characteristics such as enhancement are helpful for characterization. For staging, cystoscopy and biopsy are used for stages Ta–T3a disease, confined to the bladder. Cross-sectional imaging is useful at stage T3b or later stages, after the tumor has escaped beyond the bladder wall**(5).**

1-Excretory Urography

It involves injection of iodinated intravenous contrast medium and subsequent radiographs to demonstrate excretion of contrast into the kidneys, collecting systems, ureters and bladder. The primary bladder tumor may appear as a small capacity thick walled bladder or as a focal mass, which appears as a filling defect. If the tumor is multifocal, lesions may also be identified in the ureters or in the pelvicalyceal system. These lesions may appear as filling defects or as distortion of the pelvicalyceal or as ureteric strictures. The main limitation of excretory urography is that superficial or small tumors may not be identified, and if a tumor is identified there is no indication of the degree of invasion **(5) and(6).**



(Figure 2): Intravenous urography demonstrates a nodular filling defect (arrow) at the right urinary bladder wall; denoting underling bladder mass**(6).**

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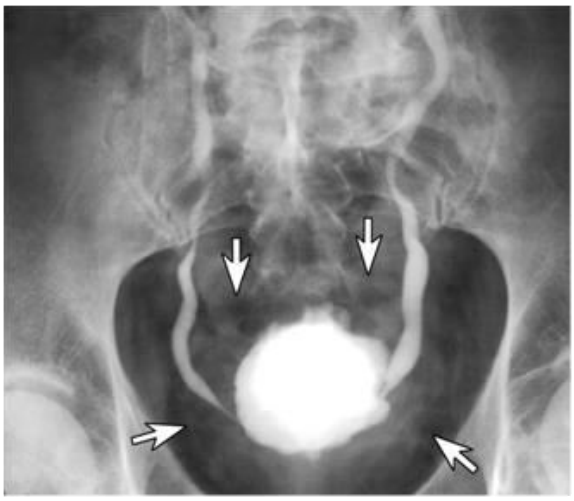
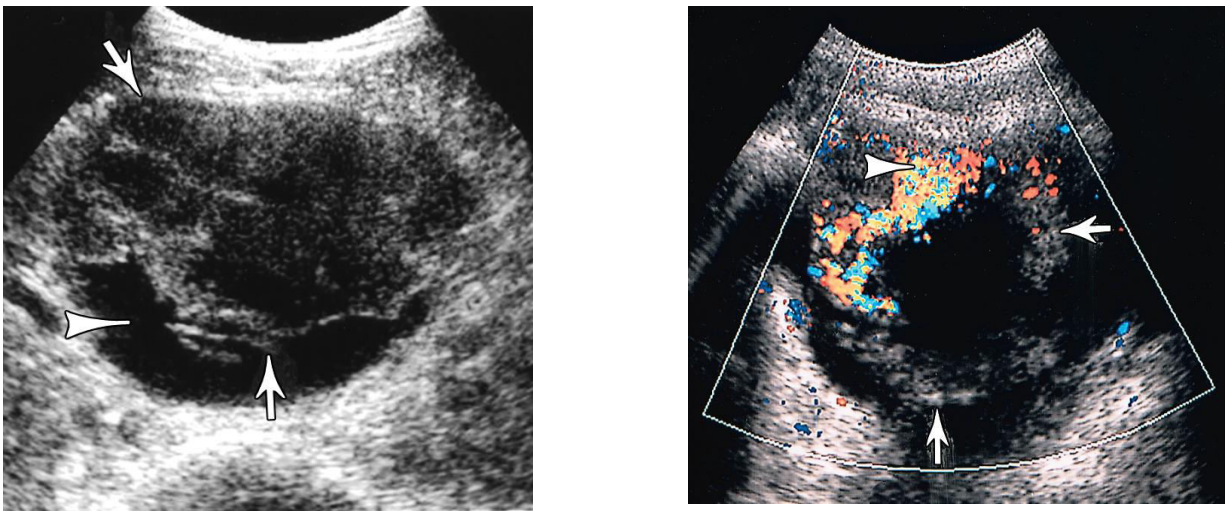


(Figure 3): Excretory urogram shows low capacity bladder and irregular wall thickening (arrows), consistent with infiltrating bladder tumor**(5).**

2. Sonography

Transabdominal, transurethral, transvaginal, and transrectal sonographic approaches have been used for assessment of bladder cancer. Transabdominal sonography is used to detect bladder tumors although it is poor prognosis. Moreover, accurate tumor staging using sonography is not possible because of the limited resolution of the different layers of the bladder wall. However, If the tumor is found incidentally on transabdominal sonography, it often appears as a polypoid or plaquelike, hypoechoic lesion that may project into the bladder. Moreover, blood flow can be shown in tumors on Doppler sonography **(5) and(6).**

Intravesical sonography is reported to be superior to transabdominal sonography with an accuracy ranging from 62% to 92%. However, its role in detecting and staging locally aggressive tumors is limited because of poor visualization of extravesical structures. Transvaginal and transrectal approaches may have advantages for tumors in specific locations close to the vagina and the rectum**(7).**



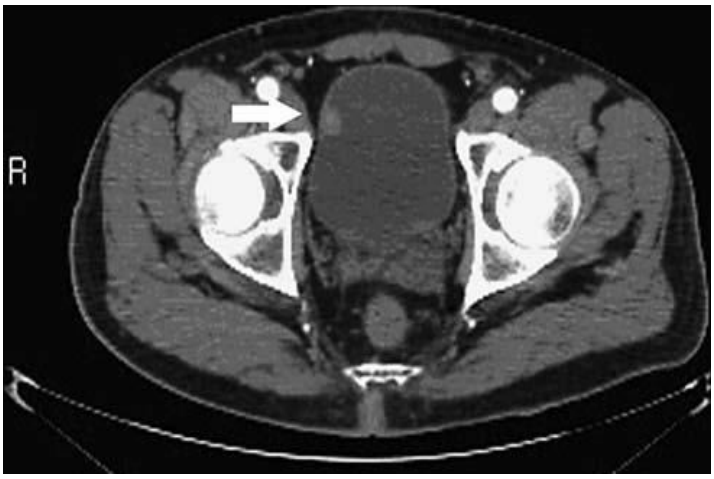
(Figure 4): (a). Ultrasonography for bladder tumor; obtained in sagittal plane reveals a

heterogeneous mass (arrows) at the anti-dependent aspect of bladder. anechoic material within bladder represents urine (arrowhead). (b). color doppler ultrasonography for bladder tumor; obtained in transverse plane shows blood flow (arrowhead) within the tumor (arrows)**(5).**

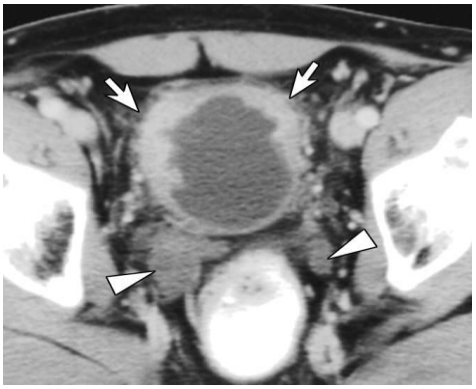
3. Computed Tomography (CT)

Bladder cancer may manifest with various patterns of tumor growth along thebladder wall, includingpapillary, sessile, infiltrating,mixed or flat lesions. T1-stage tumors appear as pedunculated lesions or asymmetrical thickening of the bladder. Hematoma andmuscle trabeculations are potential mimics of these tumors. T2-stage lesions arecharacteristically sessile tumors. CT cannot determine the depth of bladder wall invasion; it can however distinguish T3a from T3b or higher stage tumors**(5).**

T3b tumors produce an irregular outer bladder wall or soft tissue infiltration or stranding into the perivesical fat in the region of the tumor. Adjacent organ invasion can be excluded if a clear plane of separation is preserved, although the presence or absence of the fat plane is not completely reliable for determination of microscopic invasion. The tumor tissue within the invaded organ enhances similar to the bladder tumor with associated enlargement of the invaded organ. The reportedaccuracy in local staging of bladder cancer varies widely. The overall accuracy of CT for staging has been variously reported as 55-92%witha tendency to overstaging**(6) and(8).**



(Figure 5): Contrast enhanced CT image demonstrates a bladder mass; seen at the right lateral wall (arrow) with homogeneous enhancement**(6).**



(Figure 6): Contrast enhanced CT image demonstrates infiltrating bladder mass, manifested with irregular enhancing polypoid bladder wall thickening; sparing the posterior wall (arrow) with another focal mass at the distal right ureter and bilateral hydroureter (arrowheads)**(5).**

4- Magnetic Resonance Imaging (MRI)Technique

A dedicated bladder multi-parametric MRI (mp-MRI) protocol should include at least anatomic T2WI with a small field of view (FOV) in three planes (axial, sagittal, and coronal), a large FOV axial T1WI, DWI, and DCEI. The study of the bladder requires high spatial resolution that can be achieved with the use of a phased-array external surface coil (such as a cardiac coil) to increase signal-to-noise ratio, thin sections (3 mm), no interslice gaps, and a large matrix size**(9).**

The multiplanar capability of MRI allows image acquisition in different planes to minimize partial volume averaging and optimize imaging when evaluating the depth of bladder wall invasion. Coronal reformats are useful for delineating tumors located in the lateral bladder wall and dome, whereas sagittal images better depict lesions of the anterior and posterior wall and dome. These planes also help with local node detection**(10).**

T1-weighted and T2-weighted imaging

T1WI is used for identifying intraluminal extension of the tumor, extravesical fat infiltration, pelvic lymphadenopathy, and bone metastases. Differentiation of the BC from the detrusor muscle is problematic on T1WI because both have intermediate SI**(9).**

T2WI provides information on tumor depth and extravesical disease spread. On T2WI, urine has high SI, BC has intermediate to high SI, and the normal detrusor muscle appears as a hypointense line. BC lesions, which can be superficial or papillary, appear as hypo- to isointense filling defects compared with the urine. In cases of non-muscle invasive bladder cancer (NMIBC), the low-SI detrusor lining adjacent to the tumor is preserved whereas an interrupted irregular detrusor lining is observed in muscle invasive bladder cancer (MIBC) **(9).**

Findings suggestive of NMIBC tumors are muscle layer tenting of the bladder wall, fernlike vasculature, and uninterrupted submucosal enhancement. Findings suggestive of invasive tumors are an irregular wall at the base of the tumor, focal wall enhancement, and wall thickening around the tumor**(6).**

Tumor invasion into adjacent organs (prostate, uterus, and vagina) can also be better evaluated on T2WI compared with T1WI. The overall local staging accuracy of T2WI for BC has been reported to be 40–67% in reports published in the past 10 years**(11).**

Finally, the very strong urine signal on conventional T2WI can hamper assessment of the extent of bladder wall involvement. Fluid attenuation inversion recovery (FLAIR) sequences selectively suppress the urine signal in the bladder and enable superior and fast T2-weighted assessment of bladder tumors**(12).**

Dynamic contrast-enhanced imaging

Three-dimensional fat-suppressed fast spoiled gradient recalled echo T1-weighted images are obtained before and after intravenous paramagnetic agent administration and enable in-vivo assessment of tumor blood flow and permeability. The contrast agent is taken up more readily by tumor than surrounding normal tissue because the tumor has abnormal vasculature including vascular dilatation, vascular hyperpermeability, and increased vascular density.

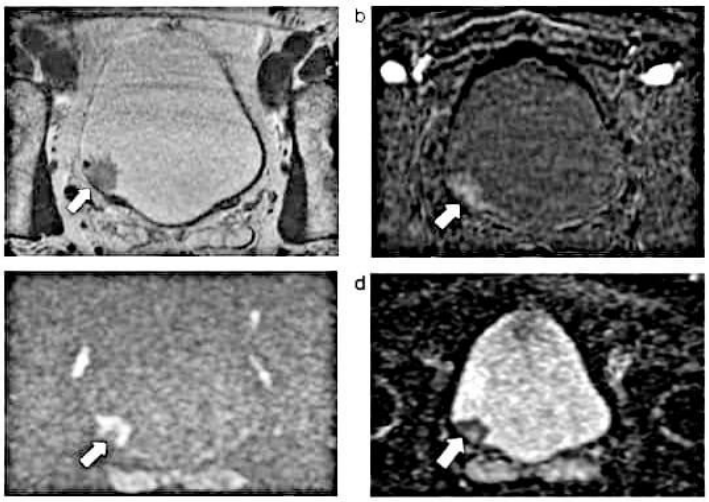
Although the bladder cancer, mucosa, and submucosa enhance early (at 20 s after contrast material injection), the muscle layer maintains its hypointensity and enhances late (at 60 s) **(12) and (9).** on delayed (>5 min) imaging, urine has high SI, thereby clearly showing the intraluminal portion of the bladder tumor, although small bladder wall tumors are obscure**(13).**

Diffusion-weighted imaging (DWI)

DWI does not require gadolinium administration and provides both qualitative and quantitative information that reflects changes at the cellular level concerning tumor cellularity and cell membrane integrity**(14) and (15).**

For most bladder tumors, increased cellular density manifests as increased SI on DW images with a reduced apparent diffusion coefficient (ADC) at quantitative analysis. A single-shot spin-echo echoplanar sequence performed with chemical shift–selective fat-suppression techniques at b values of 0 and 800 -1000 s/mm2 is used**(12).**

The stalk of a papillary tumor, which consists of submucosa with edema and fibrosis, generally shows low SI in contrast to the various SIs on T2WI, and the tumor covering the stalk shows very high SI**(14).** DWI is also useful for staging sessile tumors. DWI could differentiate thickened submucosa from inflammatory change or fibrosis occurring beneath the tumor, which mimics muscle invasion on T2WI or DCE-MRI. Inflammatory change or fibrosis beneath the tumor shows lower SI than that of the tumor. In such a case DWI could reduce the false-positive diagnosis of muscle invasion**(14) and (15).**



(Figure 7): A 70-yr-old man with microhematuria. (a) High-resolution T2WI, the right posterolateral aspect of the bladder wall showing a non–muscle-invasive papillary lesion preserving the hypointense detrusor lining underneath (arrow). (b) Dynamic contrast-enhanced imaging subtracted image displaying the enhancement of the lesion, confined to the mucosal layer (arrow). (c) Diffusion-weighted image and (d) apparent diffusion coefficient map showing highly restricted diffusion of the mass with low signal intensity of the submucosal stalk. There is no invasion of the muscle layer**(6).**

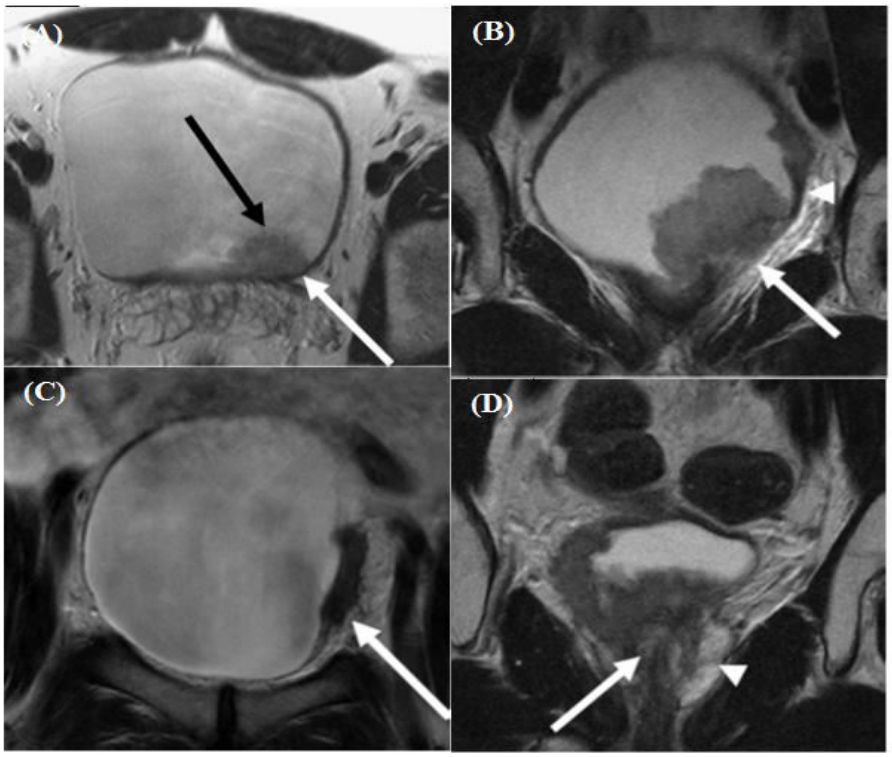
Bladder cancer staging using conventional MRI and functional MRI

The soft-tissue contrast resolution of MRI makes it the optimal imaging exam for determining bladder cancer T stage. The manifestation of each T stage depends on the MRI sequence, with

different features for T2W images, DCE images, and DWI. Multiple studies suggest that the accuracy of MRI for determining bladder cancer T stage is optimized when using all three of these sequences together (mp-MRI)**(16).**

A. Bladder cancer staging using T2 WI:-

On T2W images, the normal detrusor muscle appears as a T2 hypointense band outlining the bladder lumen**(17).** An intact T2 hypointense band suggests stage Ta, Tis, or T1bladder cancer. An irregular inner margin at the junction of the bladder tumor and the T2 hypointense band is consideredT2a disease, while disruption of the T2 hypointense band, without invasion of the adjacent peri-vesical fat, is consideredT2b. Tumor signal extending into the fat is considered T3b, and extension into the adjacent organs or the pelvic wall is T4 **disease (17).**



(Figure8): (A) Axial T2-weightedMRI image of the bladder showing a tumor on the left side (black arrow). White arrow depicts an uninterrupted detrusor muscle layer. This was staged as T1 on MRI and at histopathology. (B) Coronal T2-weighted MRI image of the bladder showing a large solid tumor on the left side. White arrow depicts interruption of the detrusor muscle layer, and the white arrowhead shows normal detrusor muscle. This was staged as T2 on MRI and at histopathology. (C) Axial T2-weighted MRI image of the bladder showing a tumor on the left side. White arrow depicts an extravesical mass. This was staged as T3b on MRI and at histopathology. (D) Coronal T2-weighted MRI image of the bladder showing a large solid tumor on the right side. White arrow depicts invasion of the prostate gland on the right. The white arrowhead shows a normal hyperintense peripheral zone of the prostate gland on the left side. This was staged as T4 on MRI. Initial TURBT staged this as T2;however, subsequent cystectomy confirmed a T4 tumor**(18).**

B. Bladder cancer staging using DCE-MRI(53)

• **Stage T1:** Intact muscle layer at the base of the tumor that shows low signal intensity on T2-weighted MRI and no early enhancement on DCE-MRI.

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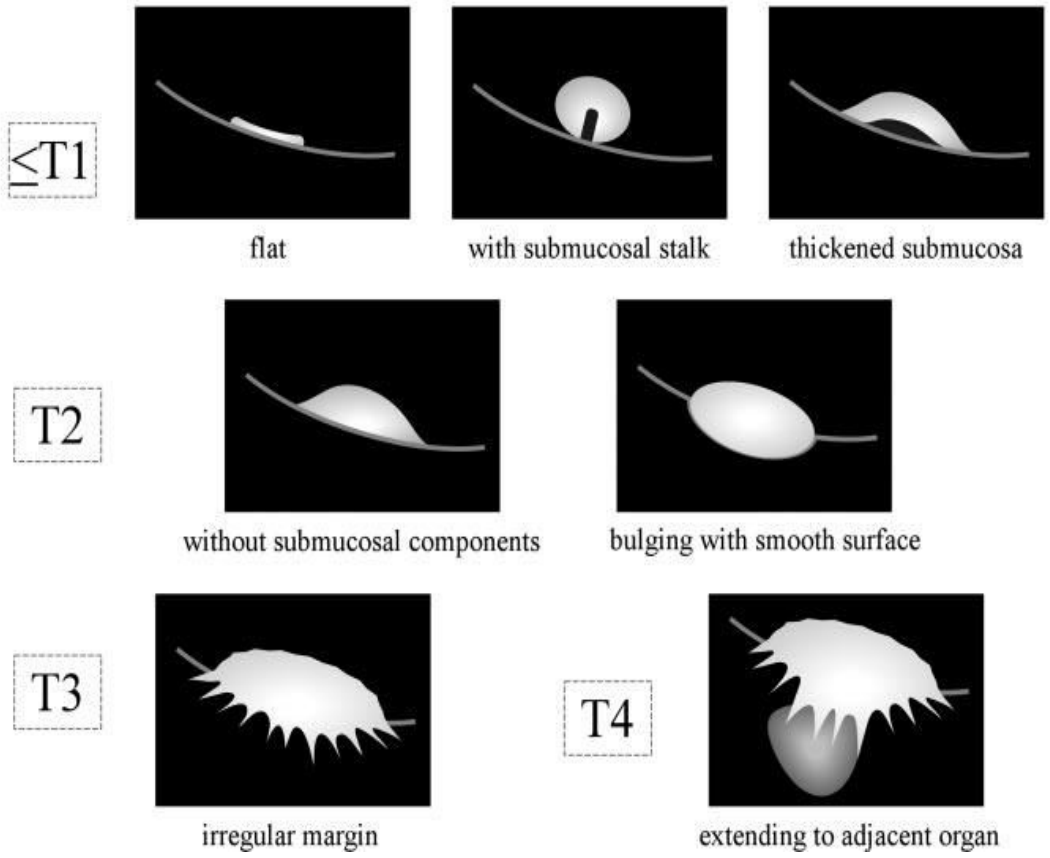
• **Stage T2a:** Irregular inner margin of the bladder wall muscle's hypointense line with or without enhancement difference.
• **Stage T2b:** Disrupted hypointense line and early enhancement without perivesical fat infiltration.
• **Stage T3:** Lesion with an irregular shaggy outer border and streaky areas in perivesical fat of the same signal intensity as the tumor.
• **Stage T4:** Lesion extending into an adjacent organ or abdominal and pelvic side walls with the same signal intensity of the primary tumor.

Bladder Cancer Staging Using DWI

A thin, flat, high SI area corresponding to the tumor or a high SI tumor with a low SI submucosal stalk or a thickened submucosa indicates stage T1 or lower; a high SI tumor without a submucosal stalk and with a smooth tumor margin indicates stage T2; extension into the perivesical fat with an irregular margin indicates stage T3; and extension into adjacent organs indicates stage T4 **(19).**

On DWI, a significant proportion of T1 or lower-stage bladder cancers have an archlike shape of high SI with a low SI submucosa stalk, called the inchworm sign. This sign provides useful information for differentiating T2 or higher-stage tumors**(19).**

The inchworm sign might reflect the micro-morphological features of Ta, T1, and T2 and provide information on the degree of microinvasion into the muscularis propria**(20).**



(Figure 9): Scheme showing diagnostic criteria for using DW imaging for staging bladder cancer. Cancer component, muscle layer, and submucosa show high, intermediate, and low SI, respectively. Submucosal stalk or thickened submucosa indicates T1 or lower stage; smooth tumor margin without submucosal components, T2; irregular margin toward the perivesical fat tissue,

T3; and extension into adjacent organs, T4**(19).**

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