Original Article
Special Topic: Advances in Bladder Cancer Therapy
Current Urology
OPEN

Role of multiparametric magnetic resonance imaging in the diagnosis and staging of urinary bladder cancer

Essam A. Shalaby[a,*], Ahmed R. Mohamed[b], Tarek H. Elkammash[b], Rasha T. Abouelkheir[c], Ahmed M. Housseini[b]

[a]Department of Urology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt; [b]Department of Diagnostic Radiology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt; [c]Diagnostic Radiology, Urology and Nephrology Center, Mansura University, Mansura, Egypt

Abstract

Objectives: To assess the role of multiparametric magnetic resonance imaging (mp-MRI) in the diagnosis and staging of urinary bladder cancer (BC).

Materials and methods: Fifty patients diagnosed with bladder masses underwent mp-MRI study. The results of 3 image sets were analyzed and compared with the histopathological results as a reference standard: T2-weighted image (T2WI) plus dynamic contrast-enhanced (DCE), T2WI plus diffusion-weighted images (DWI), and mp-MRI, including T2WI plus DWI and DCE. The diagnostic accuracy of mp-MRI was evaluated using receiver operating characteristic curve analysis.

Results: The accuracy of T2WI plus DCE for detecting muscle invasion of BC was 79.5% with a fair agreement with histopathological examination ($\kappa = 0.59$); this percentage increased up to 88.6% using T2WI plus DWI, with good agreement with histopathological examination ($\kappa = 0.74$), whereas mp-MRI had the highest overall accuracy (95.4%) and excellent agreement with histopathological data ($\kappa = 0.83$). Multiparametric MRI can differentiate between low- and high-grade bladder tumors with a high sensitivity and specificity of 93.3% and 98.3%, respectively.

Conclusions: Multiparametric MRI is an acceptable method for the preoperative detection and accurate staging of BC, with reasonable accuracy in differentiating between low- and high-grade BC.

Keywords: Apparent diffusion coefficient; Bladder cancer; Diffusion-weighted imaging; Multiparametric magnetic resonance imaging; Transurethral resection of bladder tumor

1. Introduction

Bladder cancer (BC) is the 10th most common cancer worldwide (approximately 3.2% of all cancers), with an estimated 549,000 new cases and 200,000 deaths in 2018.[1] The estimated BC incidence worldwide is 8.2 per 100,000. However, the rates are higher in the Middle East (17.2 per 100,000), comparable to those in Europe (18 per 100,000) and the Americas (12.9 per 100,000).[2] Bladder cancer is classified into either non-muscle-invasive bladder cancer (NMIBC) or muscle-invasive bladder cancer (MIBC); the classification is important for making the correct treatment choice. Most NMIBC cases are indolent and are usually treated with transurethral resection with or without intravesical therapy. Approximately one-third of NMIBC cases are of high grade and can progress rapidly to MIBC and metastatic tumors. Muscle-invasive bladder cancer is the most aggressive disease and must be treated with radical cystectomy, radiation therapy, chemotherapy, or combination therapy.[3]

Bladder cancer staging depends on radiological, clinical, and pathological features. Although transurethral resection of bladder tumor (TURBT) is the cornerstone of staging, there are concerns regarding overstaging and understaging. Up to 30% to 60% of MIBC cases are initially staged as NMIBC, as the residual tumor rates following TURBT vary significantly.[3,4] Therefore, it has been recommended to conduct a second-look cystoscopy 2 to 6 weeks after the initial resection, which may change the treatment plan in approximately 25% of patients.[4,5] Ultrasonography (US) is valuable only in the initial evaluation of hematuria; however, it is not routinely used for detection or staging because it is operator-dependent and limited to the assessment of surrounding structures.[6] The overall accuracy of computed tomography (CT) for urinary BC staging is approximately 73%; however, magnetic resonance imaging (MRI) provided high soft tissue discrimination, especially in superficial and multiple tumors, compared with CT, resulting in a more accurate staging reaching 96%, which improves with the use of functional techniques.[7]

Multiparametric magnetic resonance imaging (mp-MRI) includes T2-weighted images (T2WIs) and functional techniques, such as dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and diffusion-weighted magnetic resonance imaging (DWI-MRI). The diagnosis of muscle wall invasiveness on T2WI depends on signal intensity (SI). The detrusor muscle appears to have a low SI and is preserved in NMIBC, but is interrupted in MIBC.[7] Diffusion-weighted imaging (DWI) is used for tumor localization and staging depending on cellularity and is also considered promising in the assessment of tumor aggressiveness, follow-up, and improvement of local lymph

* Corresponding Author: Essam A. Shalaby, Borg Elgandol, Shebeen Elkom St, flat no 206, Ismailia, 41511, Egypt. E-mail address: essamshalby1@hotmail.com (E. Shalaby).

Current Urology, (2022) 16, 3, 127–135
Received January 31, 2022; Accepted May 7, 2022.
http://dx.doi.org/10.1097/CU9.0000000000000128

nodal staging.[8–10] Dynamic contrast enhancement is useful for the assessment of tissue angiogenesis, as tumor enhancement is credited to neovascularization; therefore, malignant tumors show early contrast enhancement compared with healthy tissue, which presents as a rapid washin and washout of contrast.[11,12]

The aim of the current study was to assess the value of mp-MRI parameters in the diagnosis and local staging of urinary BC.

2. Materials and methods

2.1. Patients

Multiparametric MRI studies for patients with bladder masses were performed at Suez Canal University Hospital from January 2017 to October 2019. The study protocol was approved by our institutional medical ethics committee (approval no. 3385), and all the included patients provided signed informed consent before enrollment. This research was conducted in accordance with the World Medical Association's Declaration of Helsinki and its amendments (2004).

Adult patients with bladder masses detected by diagnostic office cystoscopy or other radiological investigations, such as US or CT, underwent full mp-MRI examinations, including T2WI, DWI, and DCE-MRI. Patients with impaired renal function, prior history of TURBT, intravesical therapy, previous pelvic irradiation, known history of gadolinium contrast agent allergy, contraindications to MRI (metallic prostheses and cardiac pacemakers), poor tumor visualization (≤5 mm) on MRI, and insufficient tumor specimens were excluded.

All patients underwent thorough medical evaluation, physical examination, laboratory investigation (including a complete blood count, bleeding profile, kidney function test, urine analysis, and urine cytology), and imaging studies in the form of abdominopelvic US or abdominal CT scans. Diagnostic office cystoscopy was performed in suspicious instances with a negative imaging study. Patients with masses in the urinary bladder underwent mp-MRI followed by standard traditional cystoscopy and examination under anesthesia. Transurethral resection of bladder tumor was performed, followed by tissue biopsy for histopathological evaluation. The clinical and invasive characteristics of malignancies determined the treatment provided to the patients.

2.2. MRI examination

All MRI examinations were performed on a 1.5-T system (Achieva; Philips Medical Systems, Best, the Netherlands) with a phased-array body coil. All patients were required to fast for 4 to 6 hours before undergoing the MRI examination. Next, 1 hour prior to the procedure, the patients were asked to drink a large amount of water to achieve moderate bladder distension (pelvic US examination was performed prior to MRI study to ensure moderate bladder distension). The patients were positioned supine with intravenous access. The pelvis was examined from the aortic bifurcation to the lower part of the symphysis pubis.

All patients underwent mp-MRI with the following parameters: T1W, high-resolution T2W, DWI, and DCE-MRI after gadolinium contrast injection (mp-MRI parameters) (Supplement 1, http://links.lww.com/CURRUROL/A14).

Magnevist contrast agent (gadopentetate dimeglumine; Bayer Schering Pharma, Berlin, Germany) was administered at a dose of 0.1 mL/kg, followed by injection of 20 mL of normal saline. Between 8 and 10 dynamic scans, each lasting 20 to 30 seconds, were performed sequentially for 5 minutes using the same parameters used in the unenhanced sequence.

T1-weighted image was used only to identify hemorrhage and clots in the bladder and bone metastases. T2-weighted image was used to localize bladder lesions and to look for a continuous low SI line in the bladder wall, which represents an intact muscularis propria, as well as to detect pelvic lymph nodes.

- Stage T1: uninterrupted low SI line representing the integrity of the muscularis propria
- Stage T2: interruption of the low SI line, suggesting an extension of tumor tissue to the muscularis propria
- Stage T3: extension of the intermediate SI tumor to the extravesical fat, representing invasion of the entire bladder wall and extravesical tissue
- Stage T4: extension of the intermediate SI tumor to extravesical pelvic organs or pelvic walls

T2-weighted image was used to evaluate the DWIs. On DWI, the tumor is hyperintense, but on the apparent diffusion coefficient (ADC) map, it is hypointense. On DWI, the muscularis propria may have an intermediate SI, whereas the stalk and inner layers have a low SI.[13]

- Stage T1: muscularis propria with intermediate continuous SI on DW images (lesion hyperintense on DW images and hypointense on ADC, with or without stalk and/or low SI thickened inner layer on DW images)
- Stage T2: high SI tumor on DW images and low SI tumor on ADC images extending focally to the muscularis propria
- Stage T3: high SI tumor on DW images and low SI tumor on ADC images extending to the entire bladder wall and extravesical fat
- Stage T4: tumor hyperintensity extending into adjacent organs and abdominal or pelvic wall

A region of interest (ROI) was carefully drawn around the greatest area of the mass observed at b = 800 s/mm^2. Diffusion-weighted imaging was used to determine the ADC value of a mass lesion, which was best visualized using high contrast to the surrounding tissues. A single observer performed the process thrice for each patient, and the mean ADC value was calculated as the average of the 3 readings.

The ROI for MRI enhancement was obtained from the region of maximum enhancement in the tumor that correlated with the areas of high vascularity with the generation of time-SI curves. The ROIs were between 1 and 2 cm^2. Three ROIs were placed within the masses for SI calculation, and the highest value was chosen. For SI calculation, 3 ROIs were positioned within the masses, and the highest value was chosen. The mean value was calculated as the average of 3 measurements.

Image analysis with DCE-MRI revealed that bladder tumors, mucosal and submucosal, were enhanced early, whereas the muscle layer maintained its hypointensity and was enhanced late. The following staging system was used according to Takeuchi et al.[14]

- Stage T1: no early enhancement of the muscularis propria
- Stage T2: tumor early enhancement extends focally to the muscularis propria
- Stage T3: early tumor enhancement extending to the entire bladder wall and extravesical fat
- Stage T4: tumor extending into an adjacent organ or abdominal and pelvic sidewalls

Time-SI curves were also constructed from SI values obtained from freely drawn ROIs selected based on optimal visualization of the lesion and the region of greatest enhancement.[15]

- Type I (ascending) curve: The time-SI curve shows enhancement followed by a slow increase.
- Type II (plateau) curve: The time-SI curve shows enhancement followed by a plateau.
- Type III (descending) curve: The time-SI curve shows enhancement followed by contrast washout.

Two radiologists (A.M.H and A.R.M., with 21 and 9 years of experience in MRI interpretation, respectively) independently assessed the MRI scans on a picture archiving and communication system workstation using a commercially available software system (Philips Medical Systems). Without knowledge of the surgical or histological data, the 3 image series (T2W plus DCE, T2W plus DW, and T2W plus DW and DCE) for each patient were qualitatively analyzed.

2.3. Surgical and endoscopic technique

All patients included in the study were evaluated under anesthesia. The initial features of diagnostic urethrocystoscopy and tumor characteristics were recorded, including the tumor shape, location, size, multiplicity, and associated carcinoma in situ (CIS). Transurethral resection of bladder tumor was performed based on the resection of all visible tumors with the underlying muscle layer. In the case of multiple bladder tumors, each specimen with underlying muscle layers was collected separately for histopathological evaluation and correlation with the mp-MRI results. A second TURBT was performed for all patients with T1, CIS, high-grade disease, and missing detrusor muscles in the initial sampling. Patients with NMIBC received an early single dose of epirubicin 50 mg within 6 hours of primary resection, followed by a standard regimen of 6-week induction course of bacillus Calmette-Guérin 2 weeks after TURBT in all patients with T1, CIS, and Ta high-grade tumors and maintenance bacillus Calmette-Guérin when appropriate. Patients with MIBC underwent radical cystectomy or chemotherapy plus or minus radiotherapy according to the standard guidelines, considering the patient's medical condition and surgical tolerability. The final diagnosis was confirmed based on the histopathology of the operated specimen, either by the initial TURBT confirmed by the second TURBT for NMIBC and biopsy or radical cystectomy for MIBC. Tumor staging and grading were analyzed and compared with mp-MRI results.

2.4. Statistical analysis

The data were analyzed using SPSS 22 for Windows (SPSS Inc, Chicago, IL). Quantitative data are expressed as the mean (SD), whereas qualitative data are expressed as number (%). Fisher exact test was used to compare quantitative variables. The sensitivity, specificity, positive predictive value, negative predictive value, and muscle invasion detection accuracy were calculated using receiver operating characteristic (ROC) curve analysis. Kappa statistics were calculated to determine the strength of agreement and harmony between the MRI stage of each image set and the histopathological results. The stage value of κ was defined as follows: <0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good, and 0.81–1.00 = almost perfect. An α error <0.05 was considered significant.

3. Results

Fifty-eight patients were evaluated for participation in the study. Eight patients were excluded from the final analysis for the following reasons: small tumor size in one patient, poor imaging quality, motion artifacts, or incomplete study in 3 patients, and claustrophobia and indefinable pathological results in 4 others. The remaining 50 patients were eligible for the study and final analysis. The mean age of the patients was 61.8±8.5 years, with 38 (76%) being males and 12 (24%) being females. Hematuria was the most common presenting symptom, seen in 38 patients (76%), followed by irritative lower urinary tract symptoms in 4 patients (8%). Bladder tumors were accidentally detected in 8 patients (16%) during routine pelvic ultrasound examination. According to diagnostic urethrocystoscopy and histopathological results, 22 patients (44%) with NMIBC underwent initial complete TURBT followed by second-look TURBT to confirm the initial pathology; we found missing lesions in 3 patients, with no significant difference in tumor stage or grade between the initial and second TURBT. Twenty patients (40%) with MIBC underwent radical cystectomy, and 8 patients (16%) underwent only biopsy (2 patients with advanced MIBC received chemotherapy, and 6 patients were diagnosed with cystitis histopathologically).

In terms of histological analysis, urothelial carcinoma (UC) was detected in 39 patients (78%), squamous cell carcinoma (SCC) was observed in 5 patients (10%), and cystitis was found in 6 patients (12%). T1 was found in 18 patients (36%; 15 had low-grade tumors, and 3 had high-grade tumors). T2 was found in 12 patients (24%) and T3b in 14 patients (28%); all of them were high-grade tumors. Six patients (12%) were diagnosed with cystitis (Table 1).

The diagnostic accuracy of T2WI combined with DCE images in detecting tumor staging compared with the histopathological examination was 75.5%, 80%, and 91% in T1 stage, T2 stage, and T3b stage, respectively. T2-weighted imaging combined with DWI showed an overall accuracy of 92%, 88%, and 94% in T1,

Table 1

Demographic data and pathological features.

Variables	n (%)
Age, mean (SD), yr	61.8 (8.5)
Sex	
Males	38 (76)
Females	12 (24)
Clinical presentation	
Hematuria	38 (76)
LUTS	4 (8)
Accidental discovery on US	8 (16)
Pathological results	
NMIBC post TURBT	22 (44)
MIBC radical cystectomy (T2–T3)	20 (22)
Biopsy only, 8 patients	
Advanced MIBC	2 (4)
Cystitis	6 (12)
Histopathology	
Urothelial carcinoma	39 (78)
Squamous cell carcinoma	5 (10)
Cystitis	6 (12)
Tumor number in MRI	
Single	41 (82)
Multiple	7 (14)
Diffuse wall thickness	2 (4)
Pathological stage	
T1	18 (36)
Low grade	15 (30)
High grade	3 (6)
T2 (high grade)	12 (24)
T3 (high grade)	14 (28)
Cystitis	6 (12)

NMIBC = non-muscle-invasive bladder cancer; MIBC = muscle invasive bladder cancer; MRI = magnetic resonance imaging; LUTS = lower urinary tract symptoms; TURBT = transurethral resection of bladder tumor; US = ultrasonography.

T2, and T3b stages, respectively. T2-weighted imaging, DWI, and DCE imaging, among other mp-MRI techniques, improved overall accuracy by 96%, 94%, and 96% in the T1, T2, and T3b stages, respectively (Table 2).

T2-weighted and DCE images had an overall accuracy of 79.5% in detecting muscle invasion by bladder mass, which increased to 88.6% when combined with T2W and DW images. However, mp-MRI, which includes T2W, DW, and DCE images, could accurately detect muscle invasion by 95.4% (Table 3).

Regarding staging, there was fair overall agreement ($\kappa = 0.59$) between T2WI plus DCE and histopathological results. As a rule of thumb, perfect agreement was 1, excellent agreement was 0.8 to 1, good agreement was 0.6 to 0.8, fair agreement was 0.4 to 0.6, poor agreement was >0 to 0.4, and agreement by chance alone was 0. The agreement between the staging of the T2W and DW images as well as the histologic staging was good ($\kappa = 0.74$). The overall agreement ($\kappa = 0.83$) between the mp-MRI and histological staging was excellent.

The ROC curve based on ADC values demonstrated an excellent area under the curve of 0.985. A cutoff ADC value of 1.03×10^3 mm^2/s was used to differentiate low-grade from high-grade bladder tumors, with a sensitivity of 93.3% and a specificity of 98.3% (Fig. 1).

The ADC values of urinary BCs were measured and compared with the tumor grades; the mean ADC value for high-grade tumors was 0.98×10^3 mm^2/s, whereas the mean ADC value for low-grade tumors was 1.57×10^3 mm^2/s. The ADC levels were considerably lower in high-grade tumors than in low-grade tumors ($p < 0.001$) (Fig. 2).

Muscle-invasive bladder cancer (stages T2 and T3) was significantly associated with a Type III curve ($p < 0.001$); however, a Type I curve was associated with low-grade tumors and cystitis. In contrast, the Type II curve showed no significant association with tumor stage or grade. In our study, all 6 cases of cystitis had ascending (Type I) time-intensity curves. Only 4 cases with low-grade tumors had Type I curves, whereas the other 11 had plateau (Type II) curves. The majority of high-grade tumors (23 patients) had washout (Type III) curves, with only 6 having plateau curves (Table 4).

According to the lymph node evaluation, the majority of the cases were diagnosed as N0 stage by mp-MRI (39 patients [78%]), 3 cases as stage N1, 4 cases as N2, and 4 cases as benign appearing lymph nodes. In 20 cases, pathology confirmed N0 stage, N1 stage in 5 cases, and N2 stage in 2 cases, with no nodal pathology collected in 23 cases. The mp-MRI detected nodal metastases with an overall accuracy of 85%, with 2 cases of overstaging and 2 cases of understaging. The T2WI, DWI, ADC, DCE, and time-intensity curves are shown for the representative cases in Figure 3, 4, 5.

Table 2

Diagnostic efficacy of different MRI techniques for detection of different pathological staging.

Pathological staging	Sensitivity	Specificity	PPV	NPV	Accuracy
Stage T1					
T2 + DCE	76.5%	81.5%	72.2%	84.6%	75.5%
T2 + DW	94.4%	90.6%	85%	96.7%	92%
T2 + DW + DCE	94.4%	96.9%	94.4%	96.9%	96%
Stage T2					
T2 + DCE	58.3%	86.8%	58.3%	86.8%	80%
T2 + DW	66.7%	94.7%	80%	90%	88%
T2 + DW + DCE	91.7%	94.7%	84.6%	97.3%	94%
Stage T3b					
T2 + DCE	89%	92.3%	89%	92.3%	91%
T2 + DW	92.9%	94.7%	86.7%	97.1%	94%
T2 + DW + DCE	92.9%	97.2%	92.9%	97.2%	96%

DCE = dynamic contrast enhanced; DW = diffusion-weighted; MRI = magnetic resonance imaging; NPV = negative predictive value; PPV = positive predictive value.

Table 3

Diagnostic accuracy of different MRI techniques for the detection of muscle layer invasion.

	NMIBC		MIBC			
	TP	FP	TP	FP	Total	Accuracy
T2 + DCE	13	5	22	4	35/44	79.5%
T2 + DW	16	2	23	3	39/44	88.6%
T2 + DW + DCE	17	1	25	1	42/44	95.4%
Pathology	Total = 18		Total = 26		Total = 44	

DCE = dynamic contrast enhanced; DW = diffusion-weighted; FP = false positive; MIBC = muscle-invasive bladder cancer; MRI = magnetic resonance imaging; NMIBC = non–muscle-invasive bladder cancer; TP = true positive.

4. Discussion

Bladder cancer is one of the most common tumors worldwide, accounting for 6% to 8% of all cancers in males and approximately 2% to 3% in females, with a peak age incidence of 50 to 70 years. Moreover, 90% of BCs are urothelial tumors, with the remainder being SCCs (approximately 6%–8%) and adenocarcinomas (2%).[1,2]

Histopathological examination was the reference gold standard in our study and was conducted in all 50 patients, either by initial TURBT followed by a second TURBT for NMIBC and cystoscopic biopsy, or after radical cystectomy for MIBC. Most of the patients (39 patients [78%]) were diagnosed with UC, whereas only 5 patients (10%) were diagnosed with SCC, and 6 (12%) were diagnosed with cystitis. In a study involving 106 patients, Abou El-Ghar et al.[16] made a similar observation in that 94.3% of the patients were diagnosed with UC, whereas only 5.7% had SCC, and 13.2% had cystitis.

Preoperative diagnosis of detrusor muscle invasion, whether non-muscle-invasive (stage T1 or lower) or muscle-invasive (stage T2 or higher), is critical for treatment planning. The initial TURBT and histopathological staging with biopsy may not be representative of the entire tumor, necessitating repeated evaluation. T4 tumors can be easily diagnosed using US, CT, or conventional MRI. However, the use of MRI to distinguish between T1, T2, and T3 cancers in detecting detrusor muscle invasion is challenging.[17]

Submucosal linear enhancement has been described as being useful for assessing detrusor muscle invasion immediately after intravenous contrast injection, and 60% of the tumors show an SI similar to that of the submucosa.[14] The accuracy of BC staging using DCE-MRI has been found to be 62%, with a 32% rate of overstaging.[18] The accuracy of using DCE-MRI scans in conjunction with T2WI to detect muscle invasion was 79.5% in our study, with a 16% rate of overstaging and a fair agreement with histopathological data ($\kappa = 0.59$). Similarly, Gupta et al.[19] discovered a 73.3% staging accuracy by DCE-MRI, with a considerable degree of concordance with the pathological data ($\kappa = 0.619$) and 20% overstaging. Moreover, Takeuchi et al.[20] reported accuracy values between 75% and 92%.

Diffusion-weighted imaging has been shown to be better than conventional imaging.[21] Because of the lower signal-to-noise ratio and lack of anatomical information, DWI should be interpreted in conjunction with T2WI to provide a clear basic anatomical structure

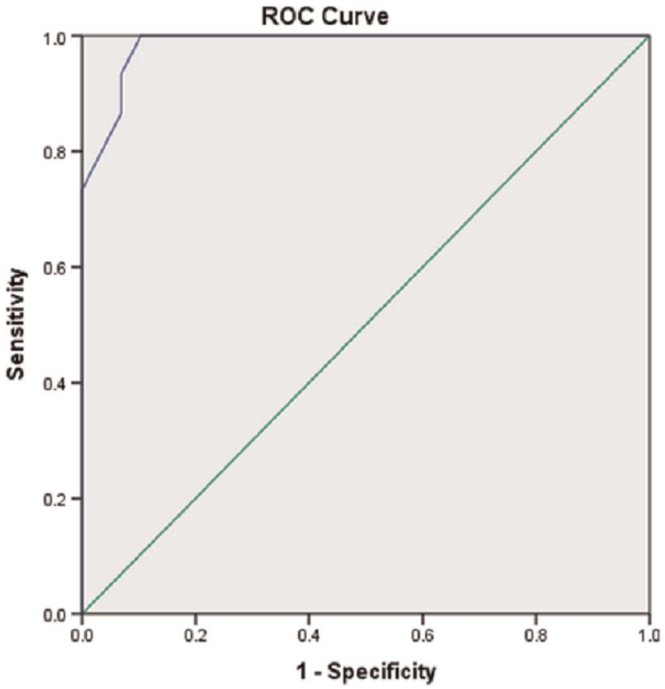

Figure 1. ROC, sensitivity, and specificity of the ADC value in detecting muscle invasion in bladder cancer. ADC = apparent diffusion coefficient; ROC = receiver operating characteristic curve.

of the bladder. In our study, DWI plus T2W had an overall accuracy of 88.6% in detecting muscle layer invasion, with overstaging in only 11.3% of patients and good agreement with histopathological findings ($\kappa = 0.74$). According to Kobayashi et al.,[22] the accuracy of differentiation between NMIBC and the MIBC was 78.8% to 81.7% for DWI, which is consistent with our findings. Gupta et al.[19] found that DWI staging was accurate in 76.7% of cases, the extent of agreement with pathological data was high ($\kappa = 0.669$), and overstaging occurred in only 16.7% of cases.

In our study, the mean ADC values in stage T1 tumors were 1.650.21 × 103 mm^2/s, 1.260.36 × 10^3 mm^2/s in stage T2 tumors, 0.990.24 × 10^3 mm^2/s in stage T3 tumors, and 1.750.45 × 10^3 mm^2/s in cystitis. The mean ADC value of high-grade tumors was much lower than that of low-grade tumors (0.98 × 10^3 mm^2/s vs. 1.57 × 10^3 mm^2/s). With a sensitivity of 93.3% and specificity of 98.3%, the ROC curve revealed a cutoff ADC value of 1.03 × 10^3 mm^2/s to differentiate high-grade from low-grade tumors (area under the curve = 0.985). In a study including 104 patients, Kobayashi et al.[22] found that the threshold ADC value was 0.86 × 10^3 mm^2/s and that ADC values were significantly lower in high-grade and high-stage cancers. In another study including 132 patients, Kobayashi et al.[23] found similar results; the threshold ADC value was 0.85 × 10^3 mm^2/s, and there was a substantial association between the ADC value and T stage.

In terms of time-intensity curves, Type III "washout" curves were related to high-grade tumors in our study, whereas Type I "ascending" curves were associated with low-grade tumors and

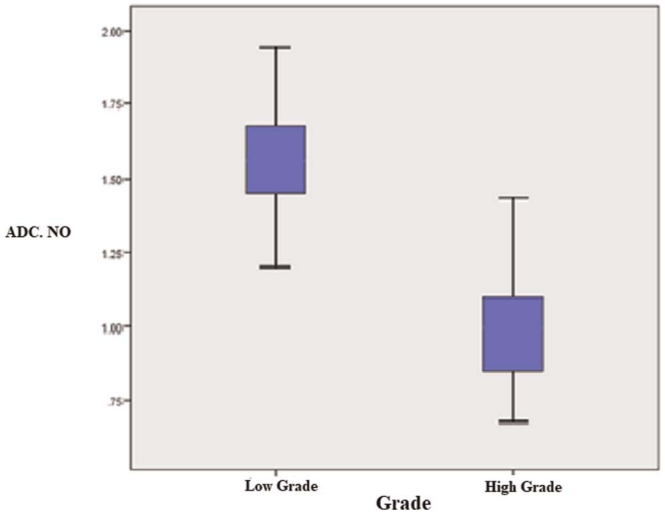

Figure 2. Box plots comparing measured ADC values and their corresponding pathological grades. ADC = apparent diffusion coefficient.

Table 4

Tumor grade and pathological staging of malignant lesions in relation to the time-intensity curve in dynamic DCE-MRI.

	Time-intensity curve		
Bladder tumor	**Type I ascending**	**Type II plateau**	**Type III washout**
Grade (50 points)			
Low grade	4	11	0
High grade	0	6	23
Benign (cystitis)	6	0	0
	Type I ascending n = 4 (%)	**Type II plateau n = 17 (%)**	**Type III washout n = 23 (%)**
Stage (44 points)			
NMIBC (T1), 18 (40.9%)	4 (100)	13 (76.5)	1 (4.3)
MIBC (T2 + T3), 26 (59.7%)	0 (0)	4 (23.5)	22 (95.7)
	$p < 0.001$*		

DCE-MRI = dynamic contrast-enhanced magnetic resonance imaging; MIBC = muscle-invasive bladder cancer; NMIBC = non-muscle-invasive bladder cancer.
*p values are based on Fisher exact test. Statistical significance <0.05.

cystitis. Gupta et al.[19] found a substantial association between time-intensity curves and tumor grade, which is consistent with our findings. However, our findings demonstrated no association between tumor grade and the Type II "plateau" time-intensity curve.

In our study, the overall accuracy of mp-MRI for distinguishing NMIBC from MIBC was 95.4%, with overstaging in only 2 patients (5%). The agreement between the histopathological examination and results was excellent (κ = 0.83). Takeuchi et al.[20] reported approximately 92% overall accuracy in BC staging in a trial study including 40 patients.

The diagnosis of the T3 stage by conventional MRI was accurate and showed a significant difference when compared with that using DWI and DCE images; however, the diagnosis of T1 and T2 stages by conventional MRI was more challenging in our study. The overall accuracy values for diagnosis of stage T3 tumors using DCE plus T2WI, DWI plus T2WI, and mp-MRI were 91%, 94%, and 96%, respectively; however, the overall accuracy values for diagnosing the T1 stage were 75.5%, 92%, and 96% using DCE plus T2W images, DW plus T2W images, and mp-MRI, respectively. In the diagnosis of stage T2 tumors, DCE-MRI plus T2WI, DWI plus T2WI, and mp-MRI had accuracy values of 80%, 88%, and 94%, respectively.

Diffusion-weighted imaging was found to minimize the overstaging ratio in our study, which is consistent with the results of previous studies.[14,17,21,24,25] Even small tumors (<0.5 cm) were detected on DCE-MRI scans but not on DW images, suggesting that DCE-MRI has no benefit in tumor staging. Lesions appearing as random spot-like areas with slight or no diffusion restriction on DWI have received relatively little attention, and all these lesions were pathologically proven as being category T1 or less. In addition, Type III time-intensity curves

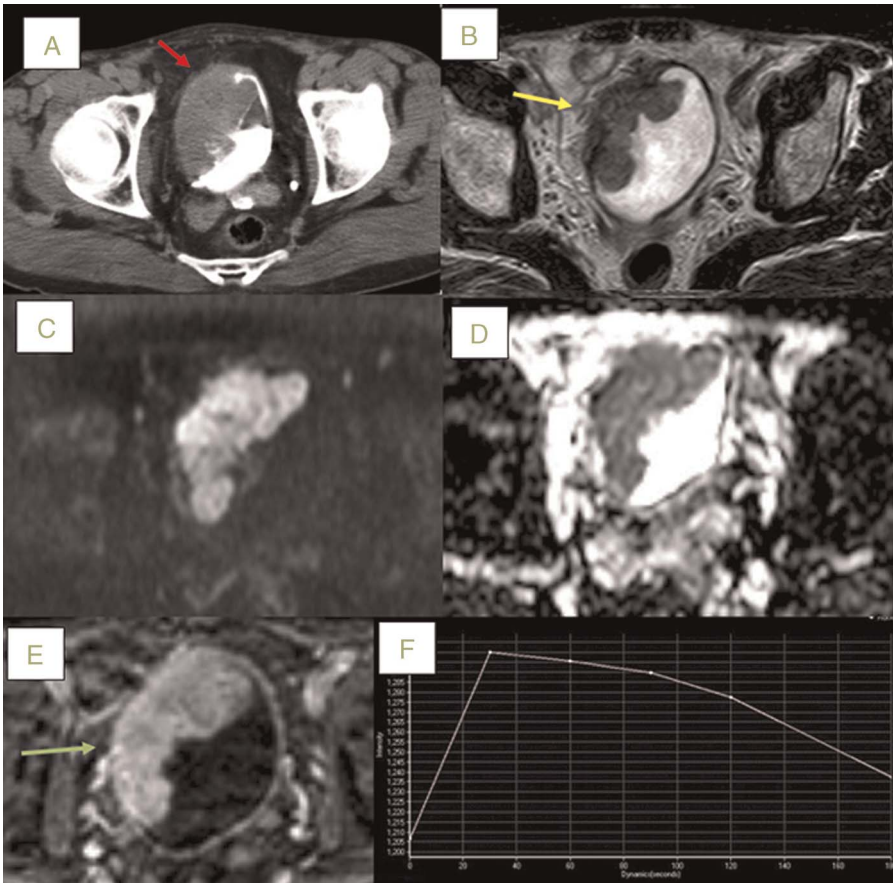

Figure 3. (A) Axial CT of the pelvis reveals a large bladder mass (red arrow). (B) Axial T2W MRI scan of the pelvis reveals a fungating intravesical mass with evidence of muscle layer and perivesical fat invasion (yellow arrows). (C) Axial diffusion-weighted image (b = 1000 s/mm^2). (D) ADC map of the pelvis reveals a bladder mass infiltrating the anterior wall and perivesical fat. ADC value = 1×10^3 mm^2/s. (E) Axial DCE. (F) Time-intensity curve showing an enhancing infiltrating bladder mass and evidence of wall infiltration (green arrow) and Type III curve "washout." ADC = apparent diffusion coefficient; CT = computed tomography; DCE = dynamic contrast enhanced; MRI = magnetic resonance imaging; T2W = T2-weighted. b value measures the degree of diffusion weighting applied, thereby indicating the amplitude (G), time of applied gradients (δ) and duration between the paired gradients ($\triangle$) and is calculated as: $b = \gamma^2 G^2 \delta^2 (\triangle - \delta/3)$.

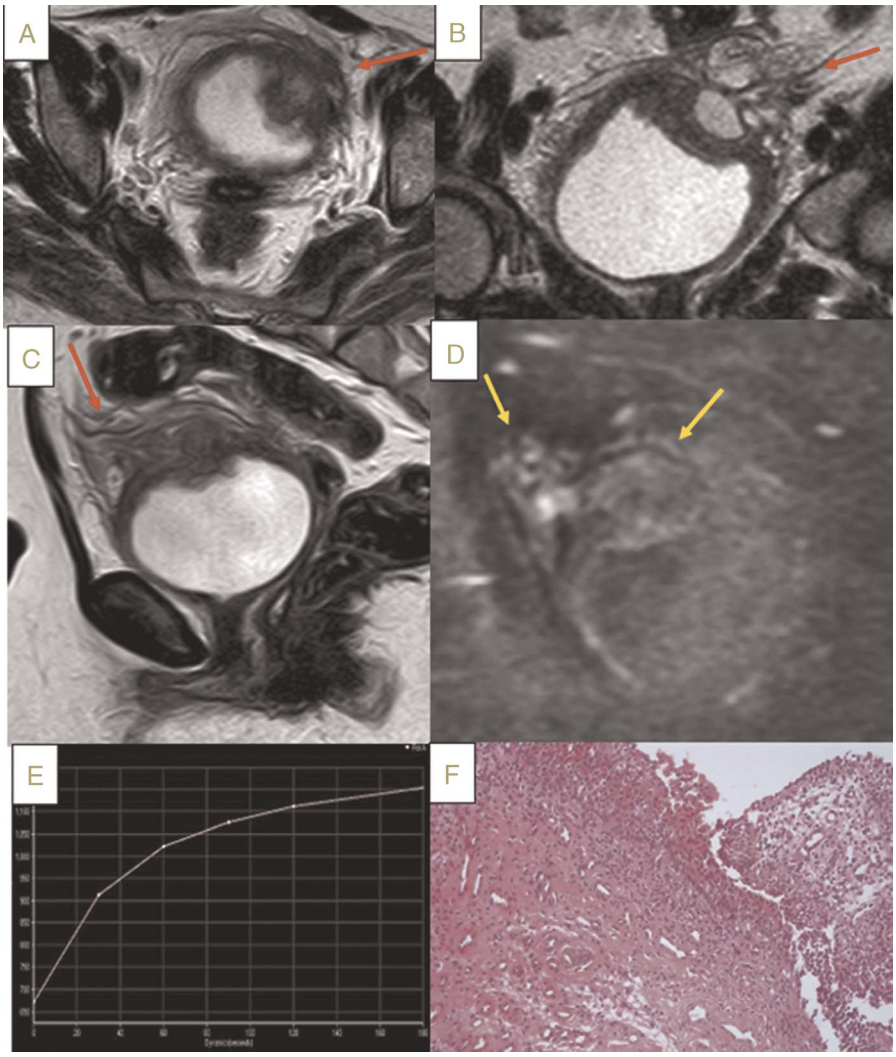

Figure 4. (A) Axial T2W MRI. (B) Coronal T2W. (C) Sagittal T2W MRI scans of the pelvis show diffuse wall thickening, a sessile mass lesion in the left lateral wall, and evidence of perivesical fat infiltration (red arrows). (D) Axial diffusion-weighted image (b = 1000 s/mm^2) of the pelvis reveals bladder mass showing no restricted diffusion "facilitated" (yellow arrows). ADC value = 2.4 × 10^3 mm^2/s. (E) Time-intensity curve showing a Type I curve "rising." (F) Hematoxylin-eosin-stained slide reveals follicular cystitis. ADC = apparent diffusion coefficient; MRI = magnetic resonance imaging; T2W = T2-weighted. b value measures the degree of diffusion weighting applied, thereby indicating the amplitude (G), time of applied gradients (δ) and duration between the paired gradients (Δ) and is calculated as: $b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$.

were strongly associated with high-grade tumors, whereas Type I time-intensity curves were associated with low-grade tumors and benign lesions. As a result, DCE-MRI demonstrated its potential benefits, in accordance with the findings of Wang et al.[26]

Overall, mp-MRI demonstrated an accuracy of 85% in detecting nodal metastases in this study, with 2 cases of overstaging and 2 cases of understaging; however, no nodal biopsy was performed in 23 cases (superficial bladder masses and cystitis).

Despite its prospective nature, this study has several limitations. First, there was a small number of cases with an uneven distribution of T-stages. Second, because no lymph node samples could be collected in NMIBC, it was impossible to correlate the radiological lymph node results with histopathological findings. Third, the exclusion of patients with impaired renal function may be a consequence of tumor invasion. Finally, although the Vesical Imaging-Reporting and Data System was proposed by the European Association of Urology in 2018 as a new reporting method for mp-MRI in assessing the possibility of detrusor muscle invasion through the 5-point scoring system,[13] it was not used in our study; therefore, further studies are recommended to validate and compare our results using the Vesical Imaging-Reporting and Data System.

5. Conclusions

Multiparametric MRI is a reliable approach for detecting and staging BC before surgery, with good sensitivity and specificity for distinguishing between low- and high-grade bladder tumors. Dynamic contrast-enhanced can detect BC tumors as small as 0.5 cm in diameter, and the Type III "washout" time-intensity curve is significantly associated with high-grade malignancies.

Acknowledgments

None.

Statement of ethics

The study protocol was approved by our institutional medical ethics committee (approval number: 3385), and all the included patients provided signed informed consent before enrollment. This research was conducted in accordance with the World Medical Association's Declaration of Helsinki and its amendments (2004).

Conflict of interest statement

No conflict of interest has been declared by the authors.

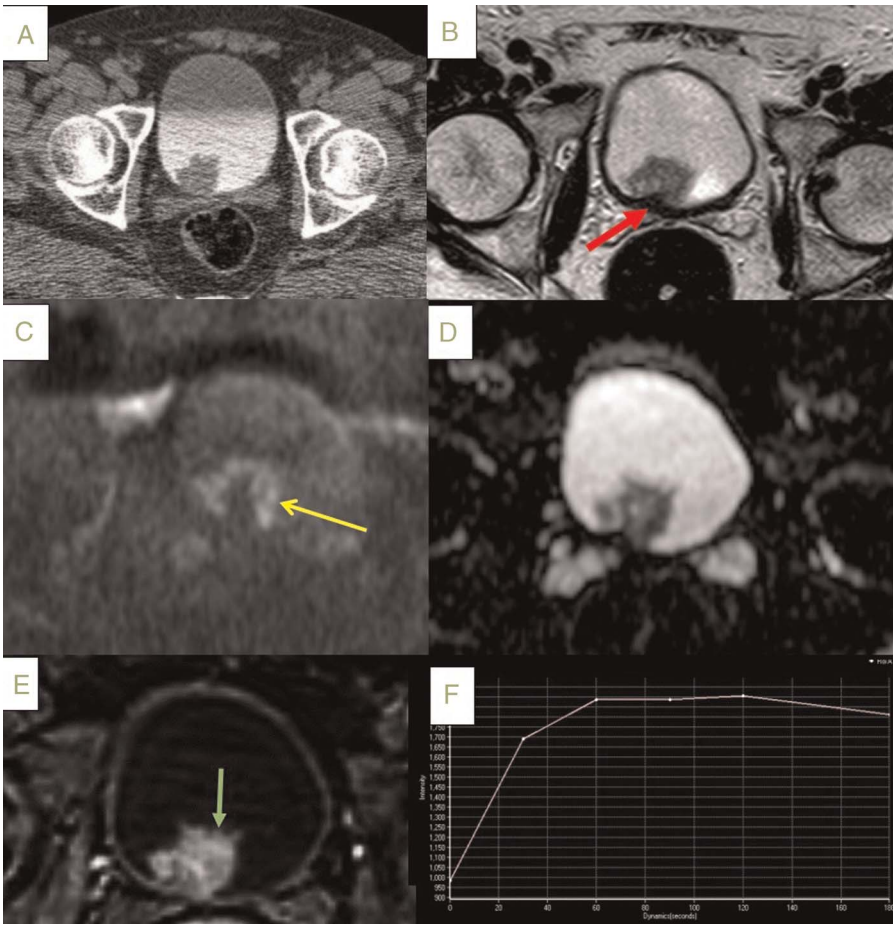

Figure 5. (A) Axial CT image of the pelvis shows a polypoidal mass lesion in the posterior wall. (B) Axial T2WI MRI of the pelvis reveals a polypoidal mass lesion with intact hypointense muscle layer (red arrow). (C) Axial diffusion-weighted image (b = 1000 s/mm^2). (D) ADC map of the pelvis reveals a bladder mass with an intact muscle layer and positive inchworm sign (yellow arrows). ADC value = 1.7 × 10^3 mm^2/s. (E) Sagittal DCE. (F) Time-intensity curve; shows early enhancing bladder mass (green arrow), no early bladder wall enhancement, and Type II curve "plateau." ADC = apparent diffusion coefficient; CT = computed tomography; DCE = dynamic contrast enhanced; MRI = magnetic resonance imaging; T2WI = T2-weighted image. b value measures the degree of diffusion weighting applied, thereby indicating the amplitude (G), time of applied gradients (δ) and duration between the paired gradients (Δ) and is calculated as: $b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$.

Funding source

None.

Author contributions

EAS, ARM, THE, RTA, AMH: Study concept; conduct, management, and collection of data; follow-up of the cases; methodology, data analysis, and article drafting; article and last revision; reading and approval of the final manuscript.

References

[1] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68(6):394–424.

[2] Adeloye D, Harhay MO, Ayepola OO, et al. Estimate of the incidence of bladder cancer in Africa: A systematic review and Bayesian meta-analysis. *Int J Urol* 2019;26(1):102–112.

[3] Babjuk M, Böhle A, Burger M, et al. EAU guidelines on non-muscle-invasive urothelial carcinoma of the bladder: Update 2016. *Eur Urol* 2017;71(3):447–461.

[4] Kulkarni GS, Hakenberg OW, Gschwend JE, et al. An updated critical analysis of the treatment strategy for newly diagnosed high-grade T1 (previously T1G3) bladder cancer. *Eur Urol* 2010;57(1):60–70.

[5] El-Barky E, Sebaey A, Eltabey M, Aboutaleb A, Hussein S, Kehinde EO. The importance of second-look transurethral resection for superficial bladder cancer. *J Clin Urol* 2015;8(5):299–305.

[6] Lee CH, Tan CH, Faria SC, Kundra V. Role of imaging in the local staging of urothelial carcinoma of the bladder. *AJR Am J Roentgenol* 2017;208(6):1193–1205.

[7] Rouprêt M.Tumours of the bladder: What does the urologist expect from imaging?*Diagn Interv Imaging* 2012;93(4):291–296.

[8] El-Assmy A, Abou-El-Ghar ME, Mosbah A, et al. Bladder tumour staging: Comparison of diffusion- and T2-weighted MR imaging. *Eur Radiol* 2009;19(7):1575–1581.

[9] Giannarini G, Petralia G, Thoeny HC. Potential and limitations of diffusion-weighted magnetic resonance imaging in kidney, prostate, and bladder cancer including pelvic lymph node staging: A critical analysis of the literature. *Eur Urol* 2012;61(2):326–340.

[10] Yoshida S, Takahara T, Kwee TC, Waseda Y, Kobayashi S, Fujii Y. DWI as an imaging biomarker for bladder cancer. *AJR Am J Roentgenol* 2017;208(6):1218–1228.

[11] Tuncbilek N, Kaplan M, Altaner S, et al. Value of dynamic contrast-enhanced MRI and correlation with tumor angiogenesis in bladder cancer. *AJR Am J Roentgenol* 2009;192(4):949–955.

[12] Afifi AH, Maksoud TASA, El-noueam KI, Ataa MA, Abdallah DM. Multiparametric-MRI as a comprehensive study in evaluation, characterization & local staging of urinary bladder carcinomas. *Egypt J Radiol Nucl Med* 2017;48(2):493–507.

[13] Panebianco V, Narumi Y, Altun E, et al. Multiparametric magnetic resonance imaging for bladder cancer: Development of VI-RADS (Vesical Imaging-Reporting and Data System). *Eur Urol* 2018;74(3):294–306.

[14] Takeuchi M, Sasaki S, Ito M, et al. Urinary bladder cancer: Diffusion-weighted MR imaging - Accuracy for diagnosing T stage and estimating histologic grade. *Radiology* 2009;251(1):112–121.

[15] Cheng L, Li X. Breast magnetic resonance imaging: Kinetic curve assessment. *Gland Surg* 2013;2(1):50–53.
[16] Abou-El-Ghar ME, El-Assmy A, Refaie HF, El-Diasty T. Bladder cancer: Diagnosis with diffusion-weighted MR imaging in patients with gross hematuria. *Radiology* 2009;251(2):415–421.
[17] Wang HJ, Pui MH, Guan J, et al. Comparison of early submucosal enhancement and tumor stalk in staging bladder urothelial carcinoma. *AJR Am J Roentgenol* 2016;207(4):797–803.
[18] Rajesh A, Sokhi HK, Fung R, Mulcahy KA, Bankart MJ. Bladder cancer: Evaluation of staging accuracy using dynamic MRI. *Clin Radiol* 2011;66(12): 1140–1145.
[19] Gupta N, Sureka B, Kumar MM, Malik A, Bhushan TB, Mohanty NK. Comparison of dynamic contrast-enhanced and diffusion weighted magnetic resonance image in staging and grading of carcinoma bladder with histopathological correlation. *Urol Ann* 2015;7(2):199–204.
[20] Takeuchi M, Sasaki S, Naiki T, et al. MR imaging of urinary bladder cancer for T-staging: A review and a pictorial essay of diffusion-weighted imaging. *J Magn Reson Imaging* 2013;38(6):1299–1309.
[21] Wu LM, Chen XX, Xu JR, et al. Clinical value of T2-weighted imaging combined with diffusion-weighted imaging in preoperative T staging of urinary bladder cancer: A large-scale, multiobserver prospective study on 3.0-T MRI. *Acad Radiol* 2013;20(8):939–946.
[22] Kobayashi S, Koga F, Yoshida S, et al. Diagnostic performance of diffusion-weighted magnetic resonance imaging in bladder cancer: Potential utility of apparent diffusion coefficient values as a biomarker to predict clinical aggressiveness. *Eur Radiol* 2011;21(10):2178–2186.
[23] Kobayashi S, Koga F, Kajino K, et al. Apparent diffusion coefficient value reflects invasive and proliferative potential of bladder cancer. *J Magn Reson Imaging* 2014;39(1):172–178.
[24] van der Pol CB, Shinagare AB, Tirumani SH, Preston MA, Vangel MG, Silverman SG. Bladder cancer local staging: Multiparametric MRI performance following transurethral resection. *Abdom Radiol (NY)* 2018;43(9):2412–2423.
[25] Wang HJ, Pui MH, Guo Y, et al. Multiparametric 3-T MRI for differentiating low- versus high-grade and category T1 versus T2 bladder urothelial carcinoma. *AJR Am J Roentgenol* 2015;204(2):330–334.
[26] Wang H, Luo C, Zhang F, et al. Multiparametric MRI for bladder cancer: Validation of VI-RADS for the detection of detrusor muscle invasion. *Radiology* 2019;291(3):668–674.

How to cite this article: Shalaby EA, Mohamed AR, Elkammash TH, Abouelkheir RT, Housseini AM. Role of multiparametric magnetic resonance imaging in the diagnosis and staging of urinary bladder cancer. *Curr Urol* 2022;16(3):127–135. doi: 10.1097/CU9.0000000000000128