

# Value of MRI in Local Staging of Bladder Cancer

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**Purpose:** To evaluate the accuracy of magnetic resonance imaging (MRI) in bladder cancer staging as well as differentiating superficial from invasive tumors and organ-confined from non-organ-confined tumors.

**Materials and Methods:** A total number of 108 bladder tumors in 86 patients (86% men and 14% women) were evaluated by 1.5 Tesla MRI machine. The tumor stages that were determined by MRI study were compared with pathology results after resection of the tumor.

**Results:** The most common stage determined by both MRI and pathology was T2a. Considering stages in details, the kappa agreement coefficient between MRI and pathology was 0.8 ( $P < .0001$ ). Combining groups a and b in each stage, the kappa agreement coefficient between MRI and pathology was 0.87 ( $P < .0001$ ). Considering stages in details, we had 22 (20.3%) mismatches in staging between MRI and pathology; 10 (45.5%) were underestimation and 12 (54.5%) were overestimation. Combining groups a and b in each stage, we had 14 (13%) mismatch cases; 6 (46.2%) were underestimation and 8 (53.8%) were overestimation. The detection rate of MRI was 0% in stage Ta, 80% in stage T1, 88.1% in stage T2, 81.2% in stage T3, and 100% in stage T4. The sensitivity and specificity of MRI in differentiating superficial from deep tumors were 0.98 and 0.82, respectively. The sensitivity and specificity of MRI in differentiating organ-confined from non-organ-confined tumors were 0.93 and 0.94, respectively.

**Conclusion:** Magnetic resonance imaging is a reliable modality for determining the stage of bladder tumors with high accuracy, and could show the depth of invasion and extension of tumor that is useful for treatment planning.

**Keywords:** urinary bladder neoplasms, magnetic resonance imaging, neoplasm staging

## INTRODUCTION

**B**ladder cancer is one of the most common malignancies of the urinary tract that accounts for almost 4% of all malignancies.<sup>(1)</sup> Bladder tumors considering the depth of invasion are categorized into different stages. TNM staging system is the accepted method for worldwide staging of bladder cancer.<sup>(2)</sup> Histopathologic evaluation of the tumor after surgical resection or transurethral resection (TUR) is the gold standard method for defining the T component of tumor stage.

Since tumor staging is crucial for choosing the treatment method, a reliable modality for pretreatment staging is necessary. Magnetic resonance imaging (MRI) has been recognized as the best imaging modality for bladder cancer staging.<sup>(3,4)</sup> Since there has been no published study about the accuracy of MRI in bladder cancer staging in Iran, we conducted this study to evaluate the accuracy of MRI in determining the tumor stage as well as differentiating superficial tumors from invasive one.

## MATERIALS AND METHODS

Magnetic resonance imaging of the bladder was performed for all the patients who were diagnosed as having bladder masses by means of ultrasonography, computed tomography scan, or MRI, and were referred to the department of radiology in Hazrat Rasoul Akram University Hospital from December 2009 to April 2011.

A total number of 108 tumors in 86 patients confirmed to have bladder cancer by histopathologic study were enrolled in this study. Patients without documented bladder cancer, those who could not perform MRI study because of cardiac pacemakers or metallic objects in their bodies, and patients that refused to undergo MRI because of claustrophobia or any other reasons were excluded from the study.

Magnetic resonance imaging of the bladder was performed in all the patients by a 1.5 Tesla MRI machine (Aventio; Siemens, Erlangen, Germany) using pelvic-phased array coil. Our MRI protocol was as follows: Axial, coronal, and sagittal T2-weighted fast spin-echo, axial T1-weighted fast spin-echo, axial fat suppressed T1-weighted fast spin-echo, and axial and coronal 3D volumetric interpolated breath-hold sequence (VIBE) before and after administration of intravenous contrast medium.

All the images were reviewed by an expert urologist in the workstation. Staging of bladder tumors was performed considering findings in all pulse sequences. Thereafter, the stages that were determined by MRI were compared with

pathologic staging after resection of tumors. In 10 patients with 11 tumors, TUR of the tumor and in 76 patients with 97 tumors, radical cystectomy was performed. In six patients, the procedure was repeated between 3 to 5 weeks after the first TUR.

The following guidelines were used for staging by MRI:

An intact hyposignal line (muscle layer) at the base of the tumor was classified as stage T1 (Figure 1); an irregular inner margin of the hyposignal line, stage T2a; a disrupted hyposignal line without perivesical fat infiltration, stage T2b; a lesion with an irregular, shaggy outer border and streaky areas of the same signal intensity of the tumor in perivesical fat, stage T3b (Figure 2); and a lesion extending into an adjacent organ or abdominal and pelvic side walls with the same signal intensity of the primary tumor, stage T4a or T4b.<sup>(3)</sup> Since the most important factor in the selection of the curative modality is the depth of tumor invasion, we only considered the T stage of the tumor from the TNM system.

Since differentiating superficial tumors from invasive tumors is important and influences treatment planning, other than evaluation of MRI accuracy in each stage, we evaluated the accuracy of MRI in differentiating superficial from invasive tumors. For this purpose, we classified tumors into two groups:<sup>(4)</sup>

- Superficial tumors: if the tumor stage was less than or equal to T1

- Invasive tumors: if the tumor stage was more than or equal to T2a

Extension of the tumor beyond the bladder and involvement of adjacent organs are important and influence the rate of tumor recurrence and patients' survival. The accuracy of MRI in differentiating organ-confined from non-organ-confined tumors was evaluated as well. For this purpose, we classified tumors into two groups:<sup>(4)</sup>

- Organ-confined: if the tumor stage was less than or equal to T2b

- Non-organ-confined: if the tumor stage was more than or equal to T3b

The Ethics Committee of Tehran University of Medical Sciences approved the protocol for the research project. This study conforms to the provisions of the Declaration of Helsinki (as revised in Edinburgh 2000). The objectives and methods of the study were explained to all the subjects and a written informed consent was obtained.

### Statistical Analysis

We calculated the kappa agreement coefficient of the MRI

**Table 1.** Details of tumor stages based on MRI and histopathology.

	Ta	T1	T2	T3	T4		
MRI, n (%)	0	11 (10.2)	43 (39.8)	28 (25.9)	26 (24.1)		
			a	b	a	b	
	0	11 (10.2)	30 (27.8)	13 (12)	----- (25.9)	18 (16.7)	8 (7.4)
Histopathology, n (%)	1	10 (0.9)	42 (38.9)	32 (29.6)	23 (21.3)		
			a	b	a	b	
	1	10 (0.9)	25 (23.1)	17 (15.7)	7 (6.5)	25 (23.1)	15 (13.9)

MRI indicates magnetic resonance imaging.

and pathology. Furthermore, we assessed the diagnostic indices, including sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio of the MRI versus pathology as gold standard results. Data were analyzed by SPSS software (the Statistical Package for the Social Sciences, Version 16.0, SPSS Inc, Chicago, Illinois, USA) and  $P < .05$  was assumed as significant.

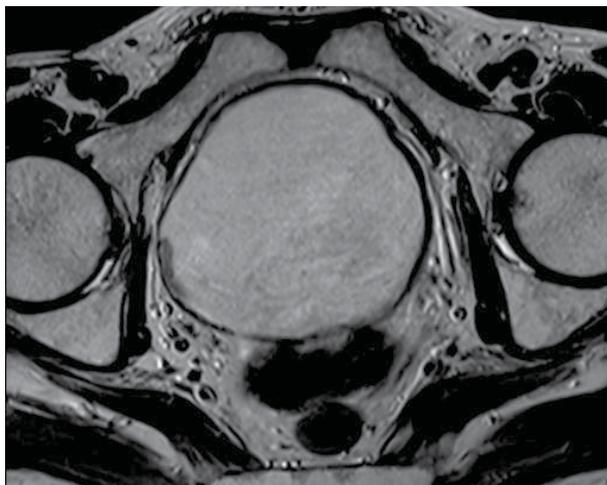
## RESULTS

Overall 108 tumoral lesions were diagnosed histopathologically as transitional cell carcinoma. Seventy-four of the patients were men (86%) and 12 were women (14%). The mean  $\pm$  standard deviation age of the patients was  $59.7 \pm 12$  years (range, 32 to 86 years). The mean age of the men and women

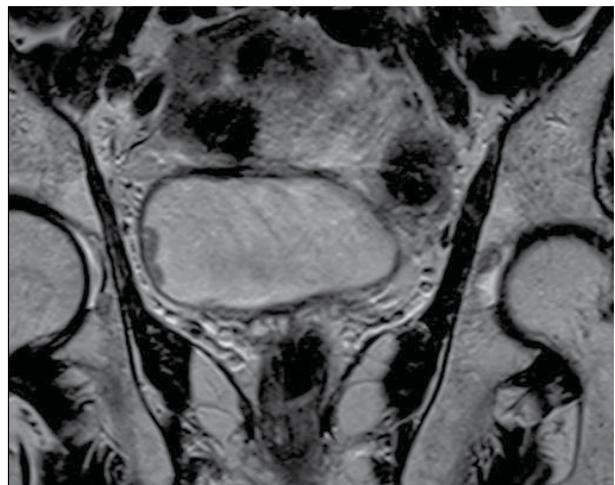
was  $61.9 \pm 15.6$  years and  $59.4 \pm 12.7$  years, respectively ( $P = .53$ ).

Based on MRI, the most common stage was T2 [43 (39.8%) tumors; 30 in the T2a and 13 in the T2b stage; Table 1]. Regarding histopathology results, again stage T2 was the most common stage that was diagnosed in the patients (42 tumors; 25 in the T2a and 17 in the T2b stage; Table 1). Regarding tumor location, the most common tumor site was the posterior wall of the bladder [38 (35.2%)], followed by the lateral wall [35 (32.4%)], anterior wall [13 (12.0%)], base [13 (12.0%)], and the bladder dome [9 (8.3%)].

Considering stages in details, kappa agreement coefficient between MRI and histopathology was 0.8 ( $P < .0001$ ; Table 2). Combining groups a and b in each stage for MRI and pathology, a 0.87 kappa agreement coefficient was yielded



**Figure 1a.** Axial T2-weighted image.



**Figure 1b.** Coronal T2-weighted image.

**Table 2.** Agreement of MRI and histopathology considering staging.

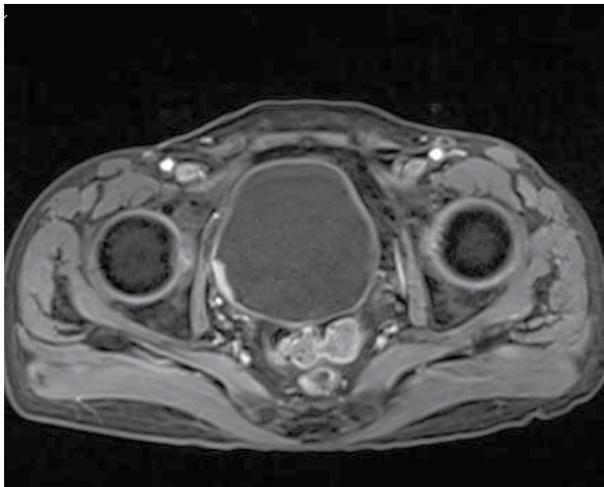
		MRI Staging								Total		
		Ta	T1	T2		T3		T4				
				a	b	a	b	a	b			
Pathology Staging	Ta	Ta	0	1	0	0	0	0	0	0	1	
	T1	T1	0	8	2	0	0	0	0	0	10	
	T2	a	0	2	22	1	0	0	0	0	25	
		b	0	0	4	10	0	2	1	0	17	
	T3	a	0	0	2	2	0	3	0	0	7	
		b	0	0	0	0	0	23	2	0	25	
	T4	a	0	0	0	0	0	0	15	0	15	
		b	0	0	0	0	0	0	0	8	8	
	Total			0	11	30	13	0	28	18	8	108

MRI indicates magnetic resonance imaging.

between MRI and pathology ( $P < .0001$ ; Table 3).

Considering detailed stages, we had totally 22 mismatch cases. As it is shown in Table 2, 10 (45.5%) of these mismatches were underestimation and 12 (54.5%) were overestimation. Eight cases happened in the same stage, but different subdivisions (eg, stage T2a was reported as T2b). Therefore, we had totally 14 (13%) mismatch cases in staging between MRI and pathology. As Table 3 shows, there were totally 8 (53.8%) cases of stage overestimation and 6 (46.2%) cases of stage underestimation.

The detection rates of MRI in each stage were as follows:



**Figure 1c.** Axial fat-suppressed T1-weighted image with contrast. A tumoral mass is evident in the right lateral wall of the bladder that shows enhancement after contrast medium injection. The hyposignal muscular layer under the tumor is intact with no evidence of tumor invasion, a finding that is consistent with stage T1 tumor.

Stage Ta, 0%; stage T1, 80%; stage T2, 88.1%; stage T3, 81.2%; and stage T4, 100%. Considering stages Ta and T1 as superficial tumors and T2, T3, and T4 as deep tumors, we calculated the kappa agreement and diagnostic indices of MRI versus pathology as the gold standard. The sensitivity and specificity of MRI were 0.98 and 0.82, respectively (Table 4). Considering stages Ta, T1, and T2 as organ-confined tumors and T3 and T4 as non-organ-confined tumors, we calculated the kappa agreement and diagnostic indices of MRI versus pathology as the gold standard. The sensitivity and specificity of MRI were 0.93 and 0.94, respectively (Table 5).

## DISCUSSION

T2a was the most common stage that was diagnosed by both MRI and histopathology in our study that is in contrast with western countries, in which T1 is the most common diagnosed bladder cancer.<sup>(5-7)</sup> This could be due to later admission of patients to physicians in Iran.

If we consider all stages in details, including a and b subgroups in each of the T stages, and compare it with pathology results, we had totally 22 (12.2%) cases of mismatch between MRI staging and pathology reports. Of those, 10 (45.5%) were underestimation and 12 (54.5%) were overestimation. Since 8 mismatch cases were seen in the same T stages, then considering the T component of staging alone, regardless of a or b subgroup, the number of over- or under-staging decreases to totally 14 (13%) mismatch cases; of which 6 (46.2%) were underestimation and 8 (53.8%) were overestimation resulting in more accuracy of MRI in staging.

In a study by Tekes and colleagues, most patients (32%) were over-staged ( $P < .0001$ ),<sup>(4)</sup> which is similar to our study. Buy

**Table 3.** Crosstabulation of MRI and pathology results in terms of staging.

		Pathology					Total
		Ta	T1	T2	T3	T4	
MRI	Ta	0	0	0	0	0	0
	T1	1	8	2	0	0	11
	T2	0	2	37	4	0	43
	T3	0	0	2	26	0	28
	T4	0	0	1	2	23	26
Total	1	10	42	32	23	108	

MRI indicates magnetic resonance imaging.

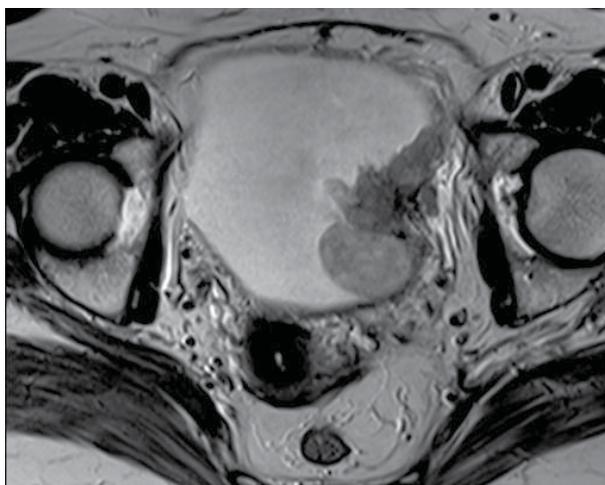
and associates reported 33% underestimation in their study ( $P < .0001$ ). They assessed their patients with a 0.5T MRI scanner without contrast agent injection. Furthermore, their study had a much smaller sample size compared to ours.<sup>(8)</sup> Considering all stages in details, including a and b subdivisions, the detection rate of MRI was equal to 80% that points to a good correlation between MRI and pathology (Table 2). If we consider T stages alone, regardless of a and b subdivisions, the detection rate of MRI becomes even much better and equal to 87% because many over- or under-stagings happened in the same T stage (stage a was diagnosed as stage b or vice versa) (Table 3).

Over-staging was more common than under-staging in our study. Abnormal signals that are detected in perivesical fat at the site of the tumor and are misdiagnosed as tumor invasion are one of the reasons for over-staging of bladder cancer. The source of these abnormal signals could be hyperemia and engorged vessels in the vicinity of the tumors due to their high blood supply. The other reason could be the inflammatory process that happens in perivesical tissues following TUR or

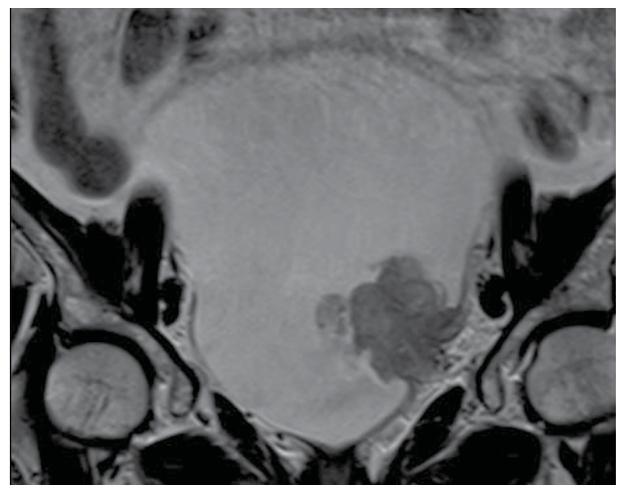
biopsy of bladder tumors,<sup>(1)</sup> especially in T2-weighted and gadolinium-enhanced images.<sup>(3,9-11)</sup> The most common under-staging happened between stages T2a and T2b and was due to underestimation of the depth of tumor invasion into the hyposignal muscular layer of the bladder.

Among all mismatch cases between MRI and pathology, in more than 90% of misstaged tumors, the over- or under-stagings were diagnosed by MRI only as one stage higher or lower than the histopathology diagnosis. Only in one case, a T2b stage tumor was diagnosed in MRI as T4a tumor, which was a posteriorly located tumor with obliterated fat plan between the tumor and the adjacent seminal vesicle presumably due to the inflammatory process, wrongly diagnosed as the seminal vesicle involvement. The overall reported accuracy of MRI in local staging of bladder cancer is between 52% and 93%.<sup>(3,4,12,13)</sup> The use of gadolinium can increase this accuracy to 73% to 100%.<sup>(4)</sup>

To determine the treatment plan and the patient's prognosis, the differentiation between deep and superficial bladder cancer is very important. The treatment is dramatically changed



**Figure 2a.** Axial T2-weighted image.



**Figure 2b.** Coronal T2-weighted image.

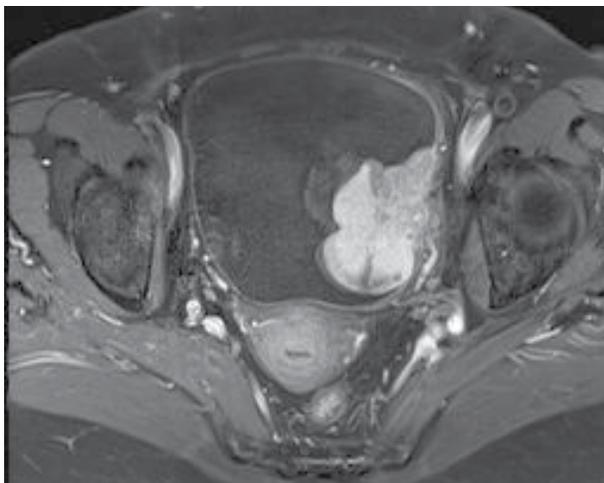
**Table 4.** Diagnostic indices of MRI versus pathology in differentiation of superficial and deep tumors.

Diagnostic Index	
Sensitivity (95% CI)	0.98 (0.93 to 0.99)
Specificity (95% CI)	0.82 (0.48 to 0.98)
Positive predictive value (95% CI)	0.98 (0.93 to 0.99)
Negative predictive value (95% CI)	0.82 (0.48 to 0.98)
Positive likelihood ratio (95% CI)	5.4 (1.5 to 18.9)
Negative likelihood ratio (95% CI)	39.7 (99.8 to 160.8)
Kappa agreement (95% CI)	0.8 (0.61 to 0.99)

MRI indicates magnetic resonance imaging; and CI, confidence interval.

when the tumor involves deep tissues. Superficial tumors are treated with TUR with or without adjuvant intravesical chemotherapeutic agents while deep tumors are treated by more aggressive approaches, including cystectomy and palliative chemotherapy, radiotherapy, or both.<sup>(14)</sup>

In differentiating between superficial and deep bladder tumors, the reported accuracy is 75% to 92%.<sup>(4,15,16)</sup> According to our study, the kappa agreement between MRI and histopathology in differentiating superficial from deep tumors was 0.8. The calculated sensitivity and specificity were 0.98 and 0.82, respectively. Using 1.5 Tesla MRI machine with T1-weighted and T2-weighted images, Tekes and colleagues reported a sensitivity of 97% and a specificity of 67% by reviewer 1 and a sensitivity of 95% and a specificity of 55% by reviewer 2.<sup>(4)</sup> Takeuchi and coworkers used T2-weighted images alone, T2-weighted with diffusion weighted (DW) images, T2-weighted plus contrast agent images, and all three together with a 1.5 Tesla MRI machine. They reported that the sensitivity and specificity of T2-weighted contrast-enhanced images were 94% and 86%, respectively, and of

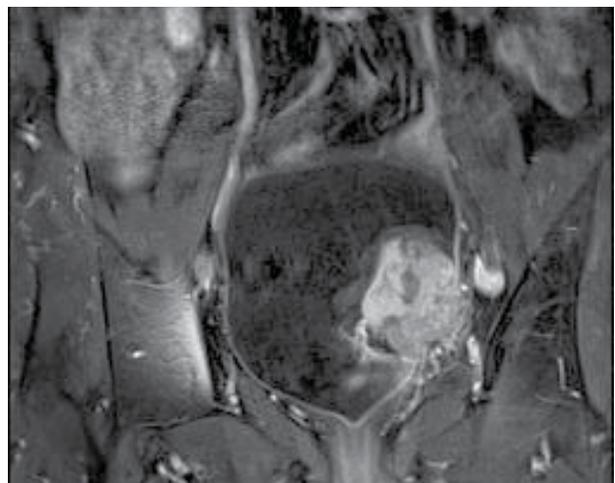
**Figure 2c.** Axial fat-suppressed T1-weighted image with contrast.**Table 5.** Diagnostic indices of MRI versus pathology in differentiation of organ-confined and non-organ-confined tumors.

Diagnostic Index	
Sensitivity (95% CI)	0.93 (0.82 to 0.98)
Specificity (95% CI)	0.94 (0.84 to 0.99)
Positive predictive value (95% CI)	0.94 (0.85 to 0.99)
Negative predictive value (95% CI)	0.93 (0.82 to 0.98)
Positive likelihood ratio (95% CI)	16.4 (5.4 to 49.3)
Negative likelihood ratio (95% CI)	12.9 (5 to 33.4)
Kappa agreement (95% CI)	0.87 (0.78 to 0.96)

MRI indicates magnetic resonance imaging; and CI, confidence interval.

T2-weighted plus DW images were 88% and 100%, respectively.<sup>(7)</sup>

Magnetic resonance imaging has been shown highly accurate in diagnosing perivesical fat involvement considering previous studies.<sup>(17)</sup> Our study showed that the sensitivity and specificity of MRI in differentiating organ-confined from non-organ-confined tumors were 0.93 and 0.94, respectively, which is a satisfying result. Abou-El-Ghar and colleagues evaluated the accuracy of MRI in staging of bladder carcinomas and compared two MRI techniques with a 1.5 Tesla MRI machine. Over-staging of organ-confined tumors was 28.7% in DW images and 75.7% in T2-weighted images. The accuracy of DW-MRI in organ-confined disease staging in comparison with T2-weighted images was significantly higher (69.7% versus 15.1%;  $P < .001$ ).<sup>(18)</sup> Takeuchi and associates found that in T2-weighted contrast enhanced images, MRI

**Figure 2d.** Coronal fat-suppressed T1-weighted image with contrast. A tumoral mass is evident in the left lateral wall of the bladder that shows enhancement after contrast medium injection. The full thickness of the bladder wall is involved by the tumor and invasion of the tumor to perivesical fat is noted, a finding that is consistent with stage T3b tumor.

was 80% sensitive and 92% specific in differentiating stage T2 and lower tumors with stage T3 and higher tumors. They also concluded that despite the belief that tumor contours could be evaluated more accurately by DW images, this technique did not improve MRI accuracy in detecting extravascular involvement in their study.<sup>(7)</sup> Tekes and coworkers reported an accuracy of 82% in differentiating organ-confined from non-organ-confined tumors.<sup>(4)</sup>

## CONCLUSION

Despite some differences between MRI and histopathology results, MRI could be an acceptable modality for bladder cancer staging. Improvement of MRI techniques and utilization of higher magnetic fields might help in better diagnostic accuracy.<sup>(4)</sup>

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## CONFLICT OF INTEREST

None declared.

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