

# The Clinical Value of DWI and T2WI MRI in the Detection of Transitional Zone Prostatic Cancer

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## ABSTRACT

**Background:** The prostate cancer is one of the commonest non-cutaneous cancers detected among elderly men. The difficulty in interpretation of the transitional zone prostate MRI arises mainly from the presence of benign prostatic hyperplasia (BPH) nodules in the transitional zone.

**Objective:** The objective of this study is to evaluate the clinical efficacy of DWI in combination with T2WI for the detection of transitional zone prostate cancer, compared with T2WI alone.

**Patients and methods:** A total of 58 patients with clinical suspicion of prostatic cancer were evaluated by 1.5 T MRI. Two diagnostic protocols were designed, protocol A consists of only data obtained from T2WI, protocol B consists of T2WI and DWI. The likelihood of the presence of prostate cancer in transitional and central zone was assigned using a 5 point scale after evaluating the entire prostate in each reading session, scales of 5, 4, and 3 were considered positive results and scales 1 and 2 were considered negative results.

**Results:** Transitional zone prostate cancer was identified histopathologically in 23/58 patients. MRI diagnostic performance: In protocol A, the sensitivity is 56.5%, specificity is 62.9% and accuracy is 60.3%. Positive predictive value PPV is 50% while negative predictive value NPV is 68.8%. In protocol B, the sensitivity is 91.3%, specificity is 80% and accuracy is 84.5%. Positive predictive value is 75% while negative predictive value is 93.3%. Diagnostic protocol B has a significantly better sensitivity and specificity than protocol A ( $p < 0.05$ ). According to ROC curve analysis, the cut point of protocol A scale is 2, so protocol A scale ( $\geq 2$ ) is predictive for the diagnosis of malignant lesions (AUC=67.5%). The cut point of protocol B scale is 4, so protocol B scale ( $\geq 4$ ) is predictive for the diagnosis of malignant lesions (AUC=87.3%). The cut off ADC value is  $0.99 \times 10^{-3} \text{ mm}^2/\text{sec}$ , so ADC value ( $< 0.99 \times 10^{-3} \text{ mm}^2/\text{sec}$ ) is predictive for the diagnosis of malignant lesions with 91.3% sensitivity, 76% specificity, and 83.3% accuracy.

**Conclusion:** Combination of DWI (ultra-high b value) with T2WI significantly increases the diagnostic accuracy of transitional zone prostatic cancer and scale  $\geq 4$  is associated with high proportion of malignancy.

**Keywords:** DWI; T2WI; Transitional zone prostatic cancer

## INTRODUCTION

The prostate cancer is one of the commonest non-cutaneous cancers detected among elderly men. The incidence continues to increase with advancing age. Currently, the majority of prostate cancers are recognized in asymptomatic patients based on the

abnormalities in prostate-specific antigen (PSA) level or the findings on digital rectal exam (DRE) [1].

Multi-parametric MRI is the current reference standard. Multi-parametric MRI offers the single most accurate imaging assessment of the local prostate cancer and regional metastatic spread and aids in many aspects of prostate cancer management,

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including initial detection, biopsy guidance, treatment planning, and follow-up and has further potential emerging roles to replace trans-rectal ultrasound (TRUS) guided biopsy for patients undergoing active surveillance and to initially evaluate patients with suspected prostate cancer before TRUS biopsy [2].

The transitional zone cancers are more likely to be missed by the traditional detection methods, namely DRE and TRUS-guided biopsy, as the transitional zone is further away from the rectum [3]. The difficulty in interpretation of the transitional zone prostate MRI arises mainly from the presence of benign prostatic hyperplasia (BPH) in the transitional zone. BPH comprises nodular masses. These masses cause abnormal signal and enhancement on the various MRI sequences and make detection of prostate cancer in this heterogeneous background more difficult compared with detection of cancer in the peripheral zone [4-6].

DWI is the sequence that currently has gained the widest acceptance, owing to its high accuracy in localization of tumor foci in the prostate. Specifically, the loss of luminal and ductal spaces as well as the increased cellular density that occur in prostate cancer [7]. Furthermore, DWI has a potential role as a non-invasive biomarker for tumor aggressiveness [8]. Diffusion-weighted Images with a high b value ( $b \geq 800 \text{ s/mm}^2$ ) are routinely acquired in order to increase the conspicuity of tumor foci within the prostate [9]. A more powerful approach to increase the conspicuity of tumor foci is to select an ultrahigh b value ( $b \geq 1400 \text{ s/mm}^2$ ), which increases diffusion weighting even further, providing greater suppression of the benign prostate and thus improving the sensitivity of source DW images for prostate cancer detection compared with standard high b values [10].

To the best of our knowledge, there is no published study (in our country) that evaluates the MRI findings of the transitional zone prostatic cancer with the current facilities.

### Aim of the study

The aim of this study is to evaluate the clinical efficacy of DWI in combination with T2WI for detection of transitional zone prostate cancer, compared with T2WI alone.

**Table 1:** MRI Parameters for High Resolution Images of the Prostate.

Sequences	T2WI	DWI Axial	T1WI
Pixel (mm)	0.4 × 0.4	3.1 × 3.1	1.3 × 1.8
TR (ms)	7500	5300	3.92
TE (ms)	108	79	1.24
Gap (mm)	0	0	1.5
Slice (mm)	3	3	3
FOV (mm)	200	200	320

## PATIENTS AND METHODS

This cross-sectional analytic study has been conducted in Al Imamein Al Kadhimain Medical City, Baghdad, Iraq, between January 2018 and January 2019 on 58 patients with clinical suspicion of Prostatic Cancer, age range from 49 to 88 year.

### Inclusion criteria

We have included patients with lower urinary tract symptoms and elevated PSA (above 4 ng/ml).

### Exclusion criteria

We have excluded patients with history of recent prostate biopsy (less than 1 month), patients treated for prostatic cancer, patients with isolated peripheral zone lesions with no obvious involvement of the transitional zone (TZ) or central zones (CZ), and patients with general contraindications for MRI examination.

Written informed consents were taken from all patients included in the study. All the patients underwent trans-perineal targeted biopsy within 10-45 days after MRI examination. The results of histopathology determine the true positive and true negative cases according to the presence or absence of cancerous tissue in the examined specimens.

### MRI protocols

The bi-parametric MRI study was performed, using a 1.5 Tesla MRI scanner (Siemens, Magnetom Area, A Tim and Dot system, Siemens medical system, Germany) Utilizing 8 channel pelvis-phased array surface coil. Large FOV T1W images of the pelvis were included in the MRI protocol, in addition to high resolution images of the prostate, small FOV, tri-planar T2WI, and DWI (Low, Intermediate and Ultrahigh b Value) with ADC maps. Table 1 shows the parameters of MRI sequences performed.

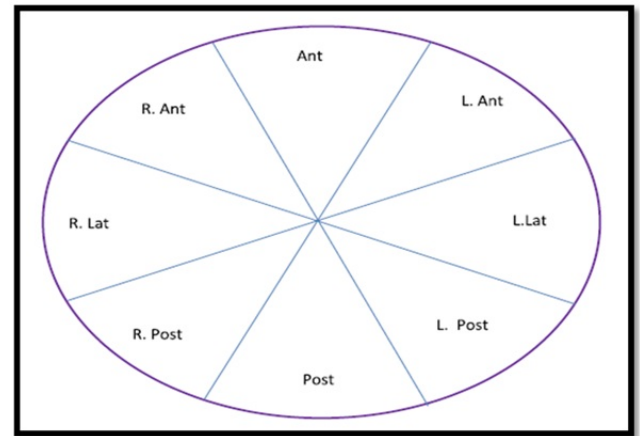
Flip angle	90	90	90
b value s/mm <sup>2</sup>	0	100/500/2000	0
Acquisition time (min)	4.5	6	2.5

### Diagnostic criteria

A suspicious MRI lesion was clarified as having marked hypo intense T2 signal within the TZ/CZ, without corresponding T1 hyper signal intensity, to exclude blood products. The tri-planar small FOV T2WI and axial diffusion-weighted MRI characteristics of each TZ/CZ lesion were described: Regular *vs.* irregular margins, presence or absence of peripheral T2WI Hypo Intense Rim, homogenous or heterogeneous low signal, and subjective presence or absence of restricted diffusion on ADC maps. Quantitative ADC values were also calculated by placing ROI circle in the lesion. On T2-weighted images, features of extra-prostatic extension (EPE) are: Asymmetry, marked thickening and/or irregularity of the neuro-vascular bundles (NVB), bulging of the prostatic capsule, irregular, spiculated borders, tumor-capsule interface more than 1 cm, and capsular breach with bladder wall invasion. However, the involvement of seminal vesicles on T2-weighted images is manifested by focal or diffuse T2 hypo signal intensity within the seminal vesicle, loss of angle in between the base of the prostate and the seminal vesicle, or direct tumor extension from the base of the prostate into the seminal vesicle.

### Interpretation of MRI images

We have designed two image-interpretation protocols. Protocol A consists of only data obtained from T2WI. Protocol B consists of T2WI and DWI. Data obtained from dynamic contrast-enhanced (DCE) were not incorporated into our study analysis as they carry no significant role in differentiation of CZ and TZ cancers from BPH nodules according to PI-RADS v2. Datasets were individually interpreted by two experienced independent radiologists, and any different perceptions between the two readers were resolved by consensus. For each case, there were two separated reading sessions within average 2 week-period between them; the first was for evaluating T2WI of the prostate (Protocol A), in the second session, T2WI, DWI and ADC images have been reviewed simultaneously (Protocol B) in a synchronous scrolling mode. There are 24 possible geographic regions for lesion localization (Figure 1). They were also asked to assign the likelihood of the presence of prostate cancer in TZ/CZ using a 5 point scale after evaluating the entire prostate in each reading session: (Scale 5: Certainly positive (PI-RADS V), Scale 4: Probably positive (PI-RADS IV), Scale 3: Possibly positive (PI-RADS III), Scale 2: Probably BPH (PI-RADS II), and Scale 1: Certainly negative (PI-RADS I). To estimate the Sensitivity, Specificity, and Accuracy of each protocol, scales of 5, 4, and 3 were considered positive results, and Scales 1 and 2 were considered negative results.



**Figure 1:** Trans-axial Representation of CZ/TZ Prostate gland subdivided into 8 Regions per slice. Additionally, the gland is divided into thirds in the Cranio-caudal direction (base, mid, and apex) for a total of 24 Regions.

Trans-perineal targeted biopsy technique was carried out as a day-care procedure using 18G biopsy gun (Tru Path, Boston Scientific, Natick, MA, USA) with an 18 mm sample notch. Two Subsets were considered during tissue biopsy:

Those that showed suspicious lesion in MRI examination: Every effort was made to target the dominant suspicious lesion according to the geographic location previously described.

Those that showed negative MRI findings (in each designed protocol) for the likelihood of existent cancer; eight biopsies were taken from right anterior apical, right anterior basal, left anterior apical, left anterior basal, right lateral, left lateral, right posterior and left posterior.

### Statistical analysis

The data analyzed by using Statistical Package for Social Sciences (SPSS) version 25. The data presented as a 7 mean, standard deviation and ranges. Categorical data are presented by frequencies and percentages. Independent t-test (two tailed) was used to compare the continuous variables among study groups accordingly. Paired t-test was used to assess the change of scale from protocol A to protocol B. Pearson's Chi-square test was used to assess statistical association between Gleason Score System and scale of both protocols. ROC curve analysis was done to find the cut off value of each protocol scale to predict the diagnosis of malignant lesions. Calculations of sensitivity, specificity, positive and negative predictive value, and accuracy for each diagnostic protocol were obtained. The sensitivity and specificity of the two protocols were compared by using the McNemar test. A level of P-value less than 0.05 is considered significant.

**RESULTS**

The age of the patients under study is ranging from 49–88 years with a mean of 64.29 ± 9.39 years. The highest proportion of the study patients was aged ≥ 60 years (65.5%). We noticed that 35/58 patients (60.3%) had benign transitional zone prostatic lesions and 23/58 patients (39.7%) had malignant transitional zone prostatic lesions (correlated with Gleason grade 6 or more).

Scale 2 is more prevalent in both protocols (37.9% in protocol A and 34.5% in protocol B) as shown in Table 2. There was no significant association between Gleason Grading System and scale of both protocols (p value 0.417 and 0.64 respectively) as shown in Table 3.

**Table 2:** Scales in each protocol.

Scale	Protocol A (%), n=58	Protocol B (%), n=58
1	10 (17.2)	10 (17.2)
2	22 (37.9)	20 (34.5)
3	9 (15.5)	0 (0)
4	9 (15.5)	19 (32.8)
5	8 (13.8)	9 (15.5)

**Table 3:** Association between scales of each protocol and Gleason Score System in malignant lesions.

Variable	Gleason Score System		Total (%) (n=23)	p-value
	<7 (n=9)	≥ 7 (n=14)		
<b>Scale of Protocol A</b>				
<3	5 (50.0)	5 (50.0)	10 (43.5)	0.417
≥ 3	4 (30.8)	9 (69.2)	13 (56.5)	
<b>Scale of Protocol B</b>				

<3	1 (50.0)	1 (50.0)	2 (8.7)	0.64
≥ 3	8 (38.1)	13 (61.9)	21 (91.3)	

In malignant lesions, the scale of protocol B was significantly increased in comparison to scale of protocol A (p=0.001), while in benign lesions, no significant change was observed (p=0.118) as shown in Table 4.

**Table 4:** Change in protocol B scale in comparison to protocol A scale according to histopathological finding.

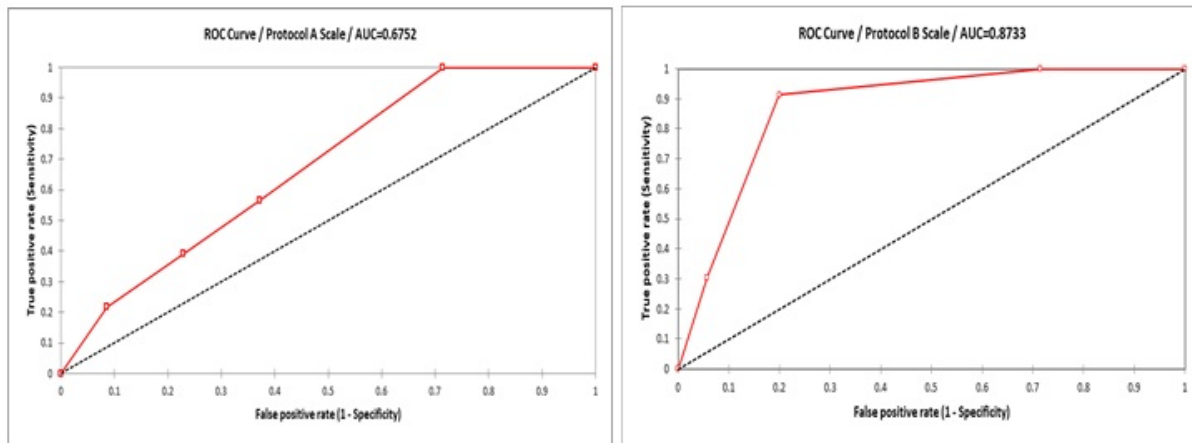
Histopathological Finding	Protocol A Scale	Protocol B Scale	p-value
	Mean ± SD	Mean ± SD	
Malignant Lesion	3.17 ± 1.23	4.13 ± 0.81	0.001
Benign Lesion	2.4 ± 1.28	2.17 ± 1.17	0.118

Receiver operating characteristic (ROC) curve analysis was constructed for protocol A and B scales as diagnostic for malignant lesions. As shown in Figure 2 and Table 5, the cut point of protocol A scale is 2 with 100% sensitivity, 28.6% specificity, and 56.9% accuracy as a marker for diagnosis of malignant lesion (Figure 3).

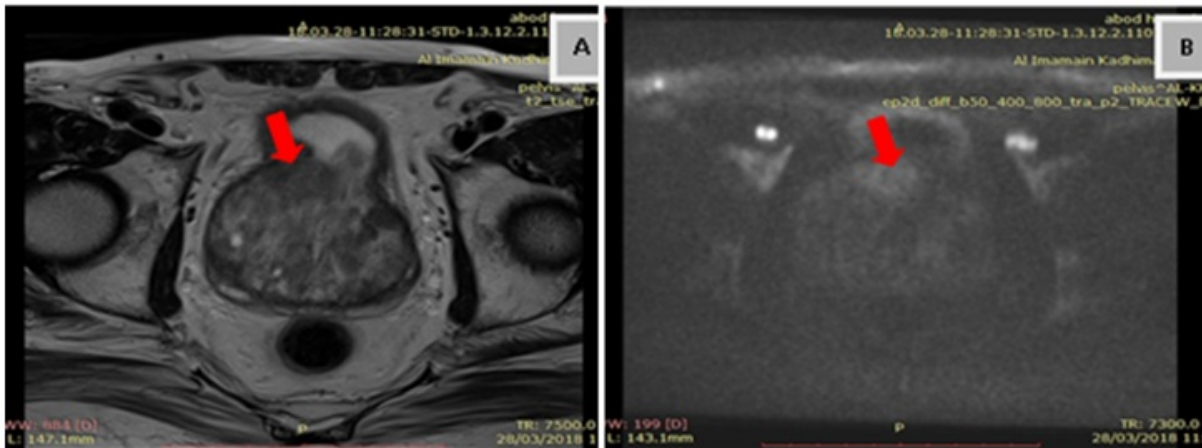
The cut point of protocol B scale is 4 with 91.3% sensitivity, 80% specificity, and 84.5% accuracy as a marker for diagnosis of malignant lesions.

**Table 5:** Diagnostic accuracy for marker of malignant lesion.

Scale	Cut-off value	Sensitivity	Specificity	PPV	NPV	Accuracy
Protocol A	2	100%	28.60%	47.90%	100%	56.90%
Protocol B	4	91.30%	80%	75%	93.30%	84.50%



**Figure 2:** ROC curve for protocol A scale and protocol B scale respectively as a marker of malignant lesion.



**Figure 3:** A 78 Year old patient, presented with urine outlet obstruction symptoms and high PSA level (49 ng/ml), MP-MRI revealed prostate enlargement with protruded median lobe to the Bladder. There is irregular shaped hypointense lesion with speculated margin in the anterior aspect of the RT Lobe depicted by T2WI (A), corresponding hyper-intense signal (arrow) in DWI Ultrahigh b value (B). The lesion reported as highly suspicious (PI-RADS V). Transperineal targeted biopsy was done and histopathology proved prostatic cancer Gleason Grade (3+3).

ADC value according to certain characteristics is shown in Table 6. In this study, the mean of ADC value was higher in benign

lesions than that in malignant lesions (1.15 versus 0.8) and this difference in means was statistically significant (p=0.001).

**Table 6:** ADC value according to histopathological finding.

Histopathological finding	ADC value (*10 <sup>-3</sup> mm <sup>2</sup> /sec)	
	Mean ± Std. Dev.	P-Value
Malignant lesions	0.8 ± 0.18	0.001
Benign lesions	1.15 ± 0.19	0.118

Receiver operating characteristic (ROC) curve analysis was constructed for ADC value as diagnostic for malignant lesions. As shown in Table 7, the cut point of ADC value was 0.99 × 10<sup>-3</sup> mm<sup>2</sup>/sec, so ADC value < 0.99 × 10<sup>-3</sup> mm<sup>2</sup>/sec is predictive for

diagnosis of malignant lesions. ADC value is 91.3% sensitive, 76% specific, and 83.3% accurate as a predictor for diagnosis of malignant lesion.

**Table 7:** Diagnostic accuracy for predictor of malignant lesion.

ADC value	Cut-off value	Sensitivity	Specificity	PPV	NPV	Accuracy
(*10 <sup>-3</sup> mm <sup>2</sup> /sec)	0.99	91.30%	76%	77.80%	90.50%	83.30%

The overall MRI diagnostic performance: In protocol A: Sensitivity is 56.5%, specificity is 62.9% and accuracy is 60.3%. Positive predictive value is 50% while negative predictive value is 68.8%. In protocol B: sensitivity is 91.3%, specificity is 80% and accuracy is 84.5%, Positive predictive value is 75% while negative predictive value is 93.3%.

## DISCUSSION

This study suggests an overall high diagnostic accuracy of combined DWI with T2WI (sensitivity, specificity and accuracy=91.3%, 80% and 84% respectively), and there has been a significant difference between the two protocols (p values < 0.05). When DWI combined with T2WI, the negative predictive value rose to (93.3%), this adds a considerable

potential to MRI for confident reassurance of patients and safe avoidance of unnecessary biopsy. We have made a comparison between benign and malignant lesions, using the scales yielded by each protocol. It has been proved that the mean of scale in protocol A and protocol B is significantly higher in malignant lesions than that in benign lesions. These results suggest that the higher scales in both protocols were significantly associated with a high proportion of malignancy. Furthermore, we have assessed the scales of each protocol with regard to final diagnosis. In benign lesions, the mean of scales in protocol A was 2.4, this mean was insignificantly changed to 2.1 in protocol B, (p=0.118). While in malignant lesions, the change in mean of scales was significant between protocol A and protocol B (3.1, 4.1) respectively, (p=0.001); these results confirm the efficiency of

combined DWI and T2WI in discrimination between benign and malignant lesions.

Thai et al. [11] reported an overall sensitivity in the detection of transitional zone PCa was (68.5%) and specificity was (77.8%) and for clinically important PCa, MR imaging visible lesion sensitivity was 78.9% and specificity was (75.3%), they included 634 TZ lesions in their study. In a study with cognitively MR guided biopsy as a reference standard, Feng et al. [12] reported the sensitivity and specificity of PCa. In the TZ to be (96% and 90%) respectively, with a cut off score 4. In a preliminary study, that included 14 patients with 29 TZ lesions using a three dimensional transperineal mapping biopsy as a standard reference, Pokharel et al. [4] evaluated various T2WI characteristics, they stated that some cancers in the TZ do indeed have a T2 dark rim, Conversely, cancers tend to be ill-defined but so do BPH nodules; our results agree with these interpretations as our ROC curve has shown very low specificity in T2WI alone for detection of TZ prostate cancer. Muller et al. [13] reported PIRADS version 2 had higher sensitivity and lower specificity (85% and 55%) respectively in the detection of PCa in the TZ, with a threshold score of PI-RADS category 3, in a study with fusion US and MR imaging-guided biopsy as a reference standard for 20 TZ PCa lesions.

In a study at 1.5 T using an endo-rectal coil and a maximum b value of 1000 s/mm<sup>2</sup>, Oto et al. [5] reported significantly lower ADC values in TZ tumors ( $1.05 \times 10^{-3}$  mm<sup>2</sup>/s) than in stromal BPH ( $1.27 \times 10^{-3}$  mm<sup>2</sup>/s). Our study has also revealed significantly lower ADC values in malignant than benign transitional zone lesions (0.8 versus 1.15 mm<sup>2</sup>/s respectively). However, this study suggests a cut off ADC value  $0.99 \times 10^{-3}$  mm<sup>2</sup>/s as a predictor for malignant TZ prostatic lesion with a diagnostic accuracy (83%).

There are several limitations in this study. This study has a relative small patient population and small number of malignant lesions due to low prevalence of the disease in the TZ of the prostate. In addition, we compared our results with transperineal targeted biopsy because of unavailability of whole mount prostate histopathology.

## CONCLUSION

Combination of DWI (ultra-high b value) with T2WI significantly increases the diagnostic accuracy of transitional zone prostatic cancer and scale  $\geq 4$  is associated with high proportion of malignancy.

## REFERENCES

1. McAninch J, Smith LT. Blacklick (18th edn), McGraw-Hill Publishing, USA. 2012; 23:350.
2. Murphy G, Haider M, Ghai S, Sreeharsha B. The expanding role of MRI in prostate cancer. *Am J Roentgenol.* 2013;201:1229-38.
3. Kanao K, Eastham JA, Scardino PT, Reuter VE, Fine SW. Can transrectal needle biopsy be optimised to detect nearly all prostate cancer with a volume of  $\geq 0.5$  ml. A three-dimensional analysis. *BJU Int* 2013;112:898-904.
4. Pokharel SS, Patel NU, Garg K, La Rosa FG, Arangua P, Jones C, et al. Multi-parametric MRI findings of transitional zone prostate cancers: Correlation with 3-dimensional transperineal mapping biopsy. *Abdom Imaging.* 2015;40:143-150.
5. Oto A, Kayhan A, Jiang Y, Tretiakova M, Yang C, Antic T, et al. Prostate cancer: Differentiation of central gland cancer from benign prostatic hyperplasia by using diffusion weighted and dynamic contrast-enhanced MR imaging. *Radiology.* 2010; 257:715-23.
6. Hoeks CM, Hambroek T, Yakar D, Hulsbergen-van de Kaa CA, Feuth T, Witjes JA, et al. Transition zone prostate cancer: Detection and localization with 3-T multiparametric MR imaging. *Radiology.* 2013; 266:207-217.
7. Koh DM, Collins DJ. Diffusion-weighted MRI in the body: Applications and challenges in oncology. *Am J Roentgenol.* 2007;188:1622-1635.
8. Padhani AR, Liu G, Koh DM, Chenevert TL, Thoeny HC, Takahara T, et al. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: Consensus and recommendations. *Neoplasia.* 2009;11:102-125.
9. Rosenkrantz AB, Kong X, Niver BE, Berkman DS, Melamed J, Babb JS, et al. Prostate cancer: Comparison of tumor visibility on trace diffusion-weighted images and the apparent diffusion coefficient map. *Am J Roentgenol.* 2011;196:123-129.
10. Metens T, Miranda D, Absil J, Matos C. What is the optimal b value in diffusion-weighted MR imaging to depict prostate cancer at 3T. *Eur Radiol.* 2012;22:703-709.
11. Thai JN, Narayanan HA, George AK, Siddiqui MM, Shah P, Mertan FV, et al. Validation of pi-rads version 2 in transition zone lesions for the detection of prostate cancer. *Radiology.* 2018;288:485-491.
12. Feng ZY, Wang L, Min XD, Shao-Gang W, Guo-Ping W, Cai J. Prostate cancer detection with multi parametric magnetic resonance imaging: prostate imaging reporting and data system version 1 versus version 2. *Chin Med J.* 2016;129:2451-2459.
13. Muller BG, Shih JH, Sankineni S, Marko J, Rais-Bahrami S, George AK, et al. Prostate cancer: Inter-observer agreement and accuracy with the revised prostate imaging reporting and data system at multi-parametric MR imaging. *Radiology.* 2015;277:741-750.