

Evaluation of the Prostate Imaging Reporting and Data System for Magnetic Resonance Imaging Diagnosis of Prostate Cancer in Patients with Prostate-specific Antigen <20 ng/ml

Xuan Wang¹, Jian-Ye Wang¹, Chun-Mei Li², Ya-Qun Zhang¹, Jian-Long Wang¹, Ben Wan¹, Wei Zhang³, Min Chen², Sa-Ying Li², Gang Wan⁴, Ming Liu¹

¹Department of Urology, Beijing Hospital, Beijing 100730, China

²Department of Radiology, Beijing Hospital, Beijing 100730, China

³Department of Pathology, Beijing Hospital, Beijing 100730, China

⁴Department of Medical Statistics, Beijing Ditan Hospital, Beijing 100015, China

Abstract

Background: The European Society of Urogenital Radiology has built the Prostate Imaging Reporting and Data System (PI-RADS) for standardizing the diagnosis of prostate cancer (PCa). This study evaluated the PI-RADS diagnosis method in patients with prostate-specific antigen (PSA) <20 ng/ml.

Methods: A total of 133 patients with PSA <20 ng/ml were prospectively recruited. T2-weighted (T2WI) and diffusion-weighted (DWI) magnetic resonance images of the prostate were acquired before a 12-core transrectal prostate biopsy. Each patient's peripheral zone was divided into six regions on the images; each region corresponded to two of the 12 biopsy cores. T2WI, DWI, and T2WI + DWI scores were computed according to PI-RADS. The diagnostic accuracy of the PI-RADS score was evaluated using histopathology of prostate biopsies as the reference standard.

Results: PCa was histologically diagnosed in 169 (21.2%) regions. Increased PI-RADS score correlated positively with increased cancer detection rate. The cancer detection rate for scores 1 to 5 was 2.8%, 15.0%, 34.6%, 52.6%, and 88.9%, respectively, using T2WI and 12.0%, 20.2%, 48.0%, 85.7%, and 93.3%, respectively, using DWI. For T2WI + DWI, the cancer detection rate was 1.5% (score 2), 13.5% (scores 3–4), 41.3% (scores 5–6), 75.9% (scores 7–8), and 92.3% (scores 9–10). The area under the curve for cancer detection was 0.700 (T2WI), 0.735 (DWI) and 0.749 (T2WI + DWI). The sensitivity and specificity were 53.8% and 89.2%, respectively, when using scores 5–6 as the cutoff value for T2WI + DWI.

Conclusions: The PI-RADS score correlates with the PCa detection rate in patients with PSA <20 ng/ml. The summed score of T2WI + DWI has the highest accuracy in detection of PCa. However, the sensitivity should be further improved.

Key words: Diagnosis; Magnetic Resonance Imaging; Prostate Cancer; Prostate Imaging Reporting and Data System

INTRODUCTION

Prostate cancer (PCa) is the most common malignancy and the second leading cause of cancer deaths in American adult men.^[1] The disease has become more common in Asian countries with the increasingly aged population and the increasing trend of leading a westernized lifestyle in recent years.^[2] Currently, digital rectal examination (DRE) and serum prostate-specific antigen (PSA) are the most commonly used methods for PCa screening. Transrectal ultrasound-guided (TRUS-guided) biopsy is performed as a

diagnostic tool in patients who are suspected to have PCa.^[2,3] However, the sensitivity and specificity of these methods are unsatisfactory and the assessment of disease prognosis

Address for correspondence: Dr. Ming Liu,
Department of Urology, Beijing Hospital, Beijing 100730, China
E-Mail: liuming19731029@163.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

© 2016 Chinese Medical Journal | Produced by Wolters Kluwer - Medknow

Received: 23-11-2015 **Edited by:** Li-Shao Guo
How to cite this article: Wang X, Wang JY, Li CM, Zhang YQ, Wang JL, Wan B, Zhang W, Chen M, Li SY, Wan G, Liu M. Evaluation of the Prostate Imaging Reporting and Data System for Magnetic Resonance Imaging Diagnosis of Prostate Cancer in Patients with Prostate-specific Antigen <20 ng/ml. Chin Med J 2016;129:1432-8.

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.4103/0366-6999.183419

is not accurate enough, especially in patients with low PSA levels.^[4,5] In this study, we therefore investigated another method that can provide more information before a biopsy, to avoid unnecessary biopsies and to increase the accuracy of necessary biopsies.

Magnetic resonance imaging (MRI) has been accepted as a primary imaging modality for evaluating the stage of PCa. MRI provides excellent soft tissue resolution due to the variation in tissues' T1 and T2 relaxation times. These times are related to the time required for the protons in a tissue to emit their signals. T2-weighted imaging (T2WI) can obtain high-resolution images of internal prostate structures such as the zonal anatomy and capsule. Advances in MRI show promise for improved detection and characterization of PCa, using a multi-parametric approach, including adding diffusion-weighted imaging (DWI) or dynamic contrast-enhanced MRI (DCE-MRI). Currently, the basis of MRI diagnosis is T2WI.

The European Society of Urogenital Radiology (ESUR) has built a Prostate Imaging Reporting and Data System (PI-RADS) to standardize the diagnosis of PCa.^[6] However, this PI-RADS system was established and finalized by two consensus meetings and E-mail discussions, which lacked evidence-based study. The purpose of this study, therefore, was to test the PI-RADS scoring system for T2WI and DWI of the peripheral zone.

METHODS

Patients

This prospective study was approved by the Institutional Review Board of Beijing Hospital, and informed consent was obtained from all patients. From December 2011 to January 2013, patients with suspected PCa were referred from Department of Urology at Beijing Hospital. Our patient selection criteria were as follows: (1) all patients had been referred for routine TRUS-guided prostate biopsies because of abnormal PSA, DRE, or prostate MRI; (2) all patients had a PSA level <20 ng/ml. According to the criteria, 167 patients were selected. From these patients, 34 were excluded for the following reasons: (1) surgery or other therapy that might alter the morphology or metabolism of the prostate occurred before prostate biopsy, including transurethral resection of prostate ($n = 4$) and pelvic radiation therapy ($n = 1$); (2) unwillingness to undergo prostate MRI ($n = 13$); (3) inability to undergo an MRI because of contraindications ($n = 5$); (4) the time interval between the prostate biopsy and the MRI was longer than 2 months ($n = 2$); (5) MRI was performed after prostate biopsy ($n = 2$); and (6) prostate biopsy was not performed according to the unified standards ($n = 7$). The left 133 consecutive patients underwent prostate biopsy with PSA <20 ng/ml who were then enrolled. The median age was 68.0 years (standard deviation: 7.9 years, range: 46–92 years) and median PSA was 6.9 ng/ml (standard deviation: 4.0 ng/ml, range: 0.2–19.8 ng/ml). The PSA level was <10 ng/ml in 101 patients (75.9%). PCa was diagnosed in 60 patients (45.1%), of whom 29 patients (48.3%) had tumors

with a Gleason score of 6 or lower, 22 patients (36.7%) had 7, and nine patients (15.0%) had 8 or higher.

Magnetic resonance imaging technique

All examinations were performed using a 1.5T MRI System (Magnetom Espree; Siemens, Beijing, China) within the 2 months before the TRUS-guided prostate biopsy. A spine receiver coil was used for optimal signal reception while the body coil acted as a transmitter only. Each subject was placed in the supine position with the pelvic region at the center of the coil. A low-residue diet and a mild purgative were implemented 1 day before the examination to reduce bowel peristalsis.

Transverse T1-weighted turbo spin-echo (TSE) MRIs were obtained using the following parameters: repetition time (TR) 450 ms, echo time (TE) 12 ms, section thickness 5 mm, intersection gap 0.5 mm, field of view (FOV) 24 cm, and matrix 256×192 . Transverse thin-section, high-spatial-resolution and coronal T2-weighted TSE MRIs of the prostate were obtained using the following parameters: TR/TE 3500/85 ms, echo train length 19, section thickness 5 mm, intersection gap 0.5 mm, FOV 24 cm, and matrix 320×256 .

Transverse DWIs were obtained by single-shot echoplanar imaging using TR/TE 2900/84 ms, section thickness 3 mm, intersection gap 0.6 mm, FOV $23 \text{ cm} \times 23 \text{ cm}$, matrix 230×256 , and using diffusion gradients with two b values (0 and 1000 s/mm^2) in three orthogonal planes. The apparent diffusion coefficient maps were constructed on a workstation and simultaneously displayed.

Image analysis

All images were reviewed by two radiologists with 11 and 5 years of experience in interpreting prostate MRIs respectively, who were blinded to both pathology results and clinical data. The peripheral zone of the prostate was divided into six regions in the same fashion as a biopsy: right and left at apex, mid, and base level [Figure 1]. Thus, a total of

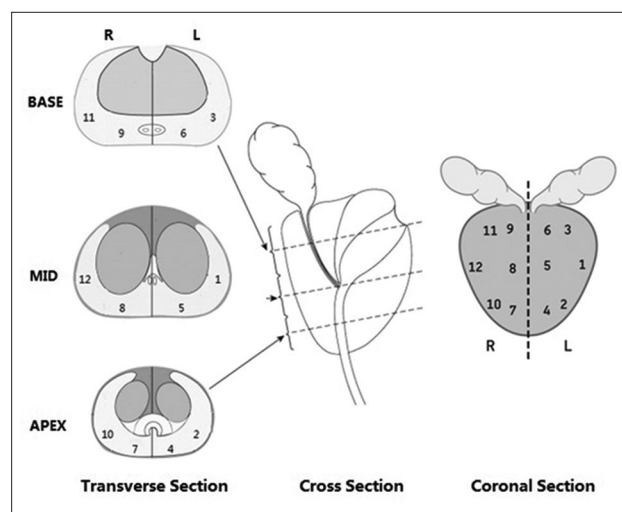


Figure 1: Transrectal ultrasound-guided prostate biopsy sites in the peripheral zone.

798 regions were evaluated. Each observer independently reviewed each patient's T2WI and DWI of the peripheral zone and assigned a score to each sextant according to the scoring system based on the PI-RADS [Figures 2 and 3].^[6] In addition, a summed score of T2WI + DWI was calculated for all lesions. The observers would discuss to reach consensus when their evaluations were discrepant.

Pathology

A TRUS-guided prostate biopsy was performed for histological diagnosis of PCa with two cores in each corresponding sextant in the peripheral zone region. Figure 1 shows 2nd and 4th cores at left apex, 1st and 5th cores at left mid, 3rd and 6th cores at left base, 7th and 10th cores at right apex, 8th and 12th cores at right mid, and 9th and 11th cores at right base. Thus, 12-core biopsy specimens were obtained from each patient.

Biopsy specimens were fixed in 10% formalin for at least 24 h and evaluated by a pathologist with 12 years of experience in prostate pathology, who was blinded to the MRI and TRUS findings. Specimens were defined as cancerous or noncancerous. If there was a positive result, the Gleason score and the exact distributions of positive biopsy cores were evaluated. The results were verified by a pathologist with 25 years of experience in prostate pathology.

Statistical analysis

All data were analyzed using the statistical software package SAS (version 9.2; SAS Institute, Cary, NC, USA). The Cochran-Armitage trend test was used to evaluate the relationship between MRI scores and positive biopsy rates. Receiver operating characteristic (ROC) analysis was used

to evaluate the ability of MRI to detect PCa. The area under each ROC curve (AUC) was calculated and then compared among different sequences using the Z-test. Sensitivity and specificity were calculated and compared using the McNemar test. A $P < 0.05$ was considered statistically significant.

RESULTS

Histopathology confirmed PCa in 60 of the 133 patients (45.1%). There were 169 (21.2%) regions diagnosed with tumors within a total of 798 regions evaluated in the peripheral zone. Among the regions evaluated, the number of regions that scored one to five using T2WI was 72 (9.0%), 507 (63.5%), 153 (19.2%), 57 (7.1%), and nine (1.1%), respectively. The number of regions that scored one to five using DWI was 600 (75.2%), 84 (10.5%), 50 (6.3%), 49 (6.1%), and 15 (1.9%), respectively.

The positive biopsy rates of different scores in T2WI, DWI, or T2WI + DWI are shown in Table 1. As the score increased, the positive biopsy rate increased from 2.8% to 88.9% for T2WI, 12.0% to 93.3% for DWI, and 1.5% to 92.3% for T2WI + DWI. There were statistically significant increases in positive biopsy rate with increasing scores ($Z = -9.910$, $P < 0.001$ for T2WI; $Z = -14.451$, $P < 0.001$ for DWI; and $Z = -13.610$, $P < 0.001$ for T2WI + DWI).

When using a score of 3 as the cutoff value, T2WI had a sensitivity of 53.8% and specificity of 79.7%; DWI had a sensitivity of 47.3% and specificity of 94.6%. The sensitivity and specificity of T2WI + DWI were 53.8% and 89.2%, respectively, using scores 5–6 as the cutoff value. ROC analysis showed that T2WI + DWI led to the

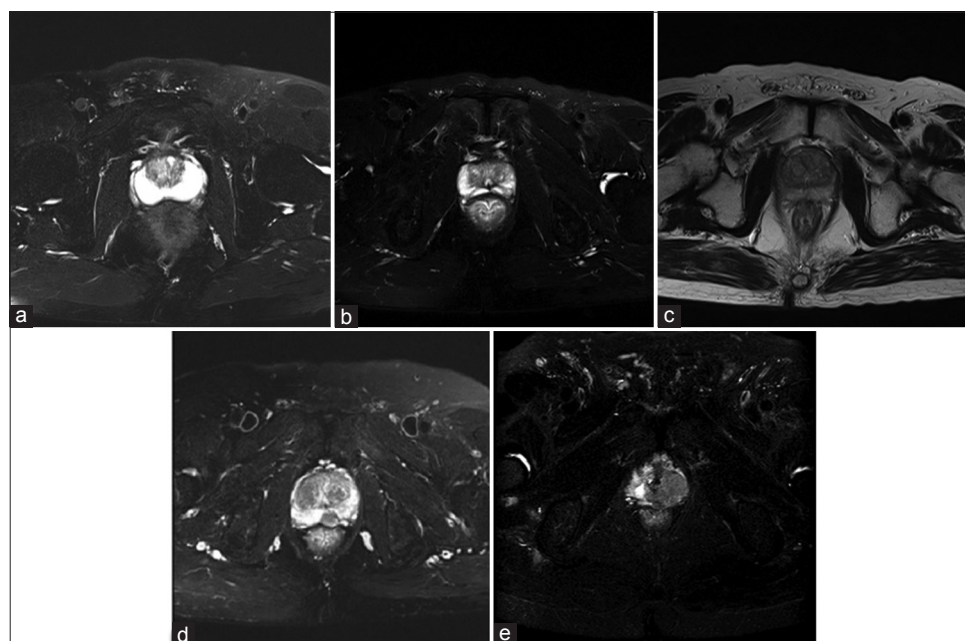


Figure 2: Scoring criteria of T2WI in the patient with PCa. (a) Score 1: uniform high SI; (b) score 2: Linear, wedge-shaped, or geographic areas of lower SI, usually not well demarcated; (c) score 3: intermediate appearances not in categories 1/2 or 4/5; (d) score 4: discrete, homogeneous, low signal focus/mass confined to the prostate; (e) score 5: discrete, homogeneous low SI focus with extracapsular extension/invasive behavior, mass effect on the capsule (bulging), or broad (>1.5 cm) contact with surface. T2WI: T2-weighted imaging; SI: Signal intensity; PCa: Prostate cancer.

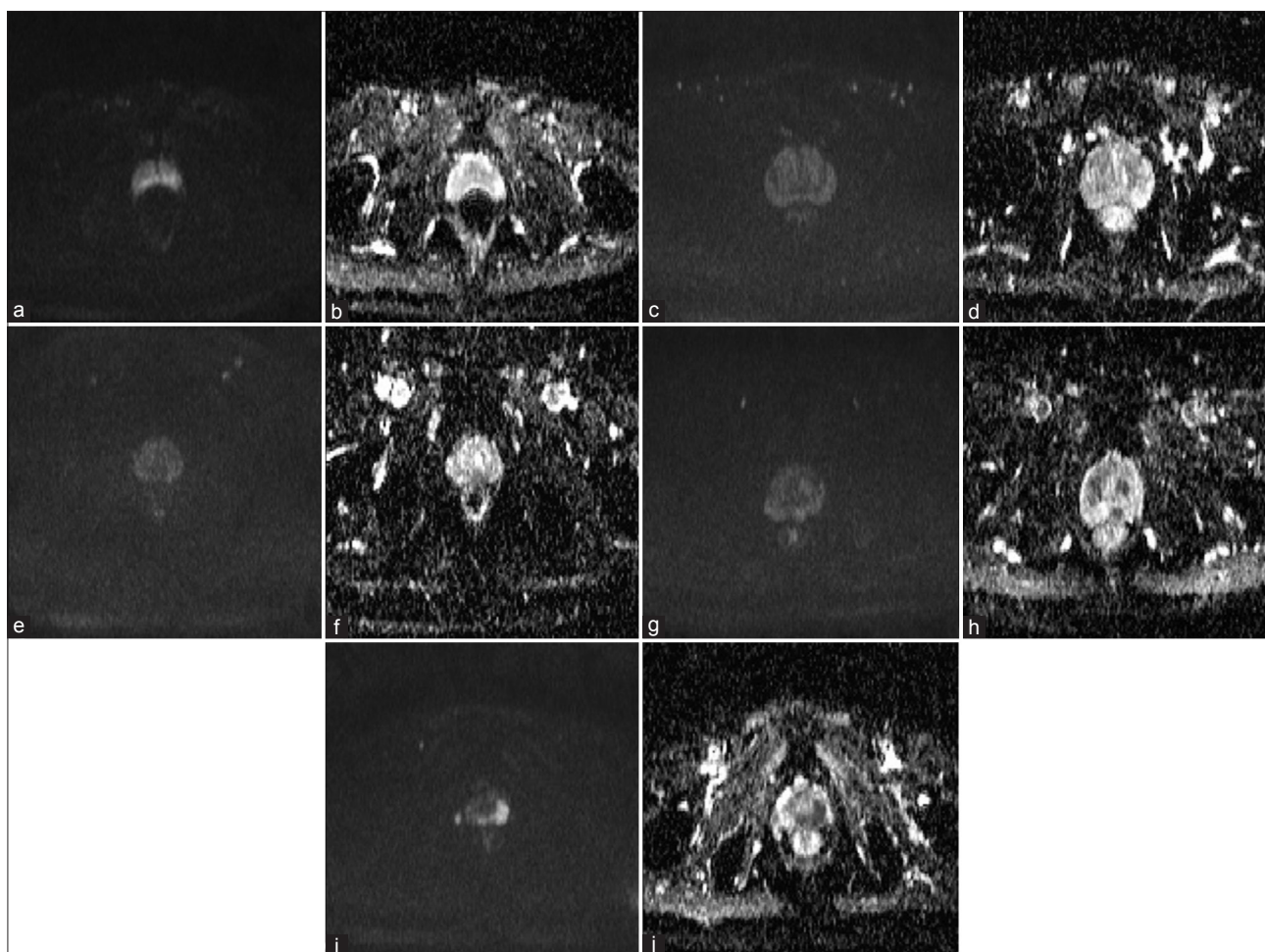


Figure 3: Scoring criteria of DWI. (a and b) Score 1: no reduction in ADC compared with normal glandular tissue. No increase in SI on any high b-value image ($b \geq 800$); (c and d) score 2: Diffuse, hyper SI on $b \geq 800$ image with low ADC; no focal features. However, linear, triangular, or geographical features are allowed; (e and f) score 3: intermediate appearances not in categories 1/2 or 4/5; (g and h) score 4: focal area(s) of reduced ADC, but iso-intense SI on high b-value images ($b \geq 800$); (i and j) score 5: focal area/mass of hyper SI on the high b-value images ($b \geq 800$) with reduced ADC. DWI: Diffusion-weighted imaging; ADC: Apparent diffusion coefficient; SI: Signal intensity.

highest test accuracy for PCa detection and the AUC for this method was 0.749 ± 0.023 . The AUCs of T2WI and DWI were 0.700 ± 0.024 and 0.735 ± 0.024 , respectively [Table 2 and Figure 4]. There was a significant difference between T2WI and T2WI + DWI ($P = 0.004$). If using score 4 as the cutoff value, T2WI had a sensitivity of 22.5% and specificity of 95.5% and DWI had a sensitivity of 33.1% and specificity of 98.7%, respectively.

DISCUSSION

MRI has been commonly used in diagnosis and staging of PCa. However, worldwide consensus has not been reached on the optimal image acquisition and evaluation protocols. Cruz *et al.*^[7] studied which morphological features of low-intensity lesions in the peripheral zone were predictive of PCa at prebiopsy T2WI. They found that a wedge-shaped and diffuse extensions without mass effect were significantly associated with benign lesions. Lesion size was significantly associated with malignancy. Engelhard *et al.*^[8] demonstrated that low signal intensity (SI) cancerous areas appeared

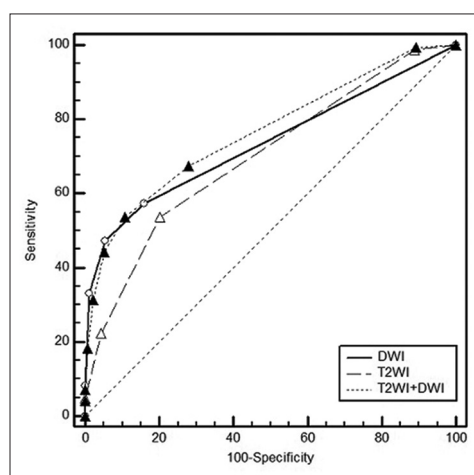


Figure 4: ROC analysis of T2WI, DWI, and T2WI + DWI. ROC: Receiver operating characteristic; DWI: Diffusion-weighted imaging; T2WI: T2-weighted imaging.

more often as round- and triangular-shaped lesions whereas hypointense, benign tissue lesions showed more

wedge-shaped, linear, and striped forms. They also noticed that the benign lesion-to-muscle SI ratios were significantly higher than the tumor-to-muscle SI ratios. The probability of being histologically diagnosed with PCa is higher when a low SI nodule is found in the peripheral zone. Although PCa typically manifests as a low SI anywhere inside the peripheral zone, low SI does not exclusively imply PCa. Some benign lesions, such as prostatitis, hemorrhage, prostate intra-epithelial neoplasia, scars, and posttreatment changes can result in similar low SI areas in T2WI. Conversely, some early-stage cancers or poorly differentiated PCas infiltrating into the surrounding tissues lack the typical low SI manifestation in T2WI.^[9]

A group of prostate MRI experts from the ESUR has developed clinical guidelines for multi-parametric MRI of the prostate.^[6] Using their previous experience, they built a structured PI-RADS system to evaluate the risk of PCa by analysis of MRIs. By describing and using a defined scoring system, MRI data can be interpreted and presented in a more “standardized” way, which links the scales with the risks of PCa. However, this PI-RADS system was established and

finalized by two consensus meetings and E-mail discussions, which lacked evidence-based study.

In the present work, we performed a prospective study to evaluate part of this PI-RADS. We focused on the scoring system of T2WI, DWI, and T2WI + DWI for the peripheral zone of the prostate. We chose the peripheral zone as the target because it is the most common area of PCa occurrence and a biopsy can frequently miss cancer present in the transition zone. The results showed that the cancer detection rate correlated with different PI-RADS scores. A threshold of score 3 resulted in a sensitivity of 53.8% and specificity of 79.7% using T2WI and a sensitivity of 47.3% and specificity of 94.6% using DWI. Even using T2WI + DWI, scores 5–6 as the cutoff led to a sensitivity of 53.8% and specificity of 89.2%, which was not a high sensitivity. Some previous studies, which included only patients without previous biopsies, showed that the PI-RADS system had a sensitivity of 71.0% and specificity of 77.0%.^[10] However, it is difficult to compare among these studies because the methodology varied in the following ways: analysis per patient or per lesion, TRUS-guided biopsy or MRI-guided biopsy, and different cutoff values.

If applying score 4 as the cutoff value, T2WI had a sensitivity of 22.5% and specificity of 95.5% and DWI had a sensitivity of 33.1% and specificity of 98.7%. Although the specificity for both T2WI and DWI was improved, the sensitivity became even lower, especially in patients with relatively low PSA level. In other words, using a score of 4 as the cutoff value caused a higher false-negative rate. The scores 5–6 were chosen as the cutoff value for T2WI + DWI because having at least one of T2WI and DWI to be scored 3 or higher was required.

Junker *et al.*^[11] prospectively evaluated the PI-RADS scoring system for classifying multi-parametric MRI findings of the prostate and analyzed the correlation between the PI-RADS scoring system and tumor aggressiveness using whole-mount step-section slides as the reference standard. They concluded that the PI-RADS scoring system showed good diagnostic accuracy and only PI-RADS four and five showed high-grade PCa. The high-PCa incidences in PI-RADS category four of that study may be explained by selection bias: all included patients were scheduled for radical prostatectomy because of a biopsy-proven PCa. Schimmöller *et al.*^[12] performed a study to test the application of PI-RADS for the diagnosis of PCa using

Table 1: The distribution of positive biopsy rates for each score for T2WI, DWI, or T2WI + DWI

Score	Cancer regions*	Total regions†	Positive rate (%)
T2WI			
1	2	72	2.8
2	76	507	15.0
3	53	153	34.6
4	30	57	52.6
5	8	9	88.9
DWI			
1	72	600	12.0
2	17	84	20.2
3	24	50	48.0
4	42	49	85.7
5	14	15	93.3
T2WI + DWI			
1–2	1	68	1.5
3–4	77	571	13.5
5–6	38	92	41.3
7–8	41	54	75.9
9–10	12	13	92.3
All	169	798	21.2

*The prostate tissue regions where biopsy is positive for prostate cancer;

†Total prostate tissue regions, ignoring biopsy status. T2WI: T2-weighted imaging; DWI: Diffusion-weighted imaging.

Table 2: ROC analysis of T2WI, DWI, and T2WI + DWI

Items	AUC	SD	95% CI for AUC		P	Cutoff value	Sensitivity (%)	Specificity (%)	Youden index
			Lower	Upper					
DWI	0.735	0.024	0.703	0.766	<0.001	3	47.3	94.6	0.419
T2WI	0.700	0.024	0.667	0.732	<0.001	3	53.8	79.7	0.335
T2WI + DWI	0.749	0.023	0.717	0.778	<0.001	5–6	53.8	89.2	0.430

T2WI: T2-weighted imaging; DWI: Diffusion-weighted imaging; ROC: Receiver operating characteristic; AUC: Area under ROC curve; CI: Confidence interval; SD: Standard deviation.

TRUS-guided prostate biopsy rather than MRI-guided biopsy. Although MRI-guided biopsy is more consistent in overlapping the radiologically suspicious site and the biopsy site, it tends to focus on patients with higher PI-RADS levels, because one prerequisite indication for MRI-guided biopsy is the existence of a suspicious area on MRI. In their study, Schimmöller *et al.* used a summed score of T2WI + DWI + DCE to evaluate the combination effect of these three MRI sequences. For all lesions, sensitivity and specificity for detection of PCa were 76.0% and 73.8%, respectively, when applying a cutoff PI-RADS summed score value of 11. We followed this method and obtained a similar result in which T2WI + DWI had higher AUC than T2WI only although the sensitivity in our study was lower. The different levels of summed score reflected the different cancer detection rates. This suggests that the summed score could be an evaluation method. The ESUR guideline does not provide a fixed threshold at which to consider a lesion as suspicious for PCa. Establishment of a threshold requires more study, especially for establishment of a threshold for the summed score of different sequences.

One reason for the low sensitivity in the present study could be the patient population. We chose patients with PSA <20 ng/ml as candidates for the study, which was different from many other previous MRI studies.^[13,14] Among PCa patients with higher PSA levels, the incidence of PCa is high and a biopsy is strongly recommended.^[15] Therefore, MRI diagnosis in these patients is not as important as its application in lower PSA level patients, which was one reason why we chose those with PSA <20 ng/ml as targets. In addition to targeting a group that may be safely spared an unnecessary biopsy, one of our previous retrospective studies demonstrated that the distribution of abnormal T2WI manifestations was significantly different between patients with PSA above and below 20 ng/ml.^[16] The incidence of cancer-specific T2WI features, such as abnormal prostate morphology, invasion to the periprostatic fat, or neurovascular bundle involvement, was much lower in patients with PSA <20 ng/ml compared to patients with higher PSA. In the present study, only 1.1% of regions evaluated scored 5 in T2WI. More than 70% and 80% of the regions evaluated in T2WI and DWI scored 1 or 2.

Several limitations exist in this study. First, this is a prospective study performed only in one hospital. Further multi-center studies with a larger patient population are required to strengthen the conclusion. Second, our reference standard was TRUS-guided biopsy and, as a result, the intrinsic limitations of false-negative biopsies could not be avoided. Although some other studies used whole-mount histopathologic examination to improve the agreement between MRIs and histopathology, studying only those men who underwent radical prostatectomy introduced a nonnegligible selection bias. Such a study excluded those patients who received other treatments. Patients who receive radical surgery are more likely to harbor high-risk tumors.^[17] Moreover, prostate biopsy plays an important role not only in diagnosis but also in determining the disease prognosis,

particularly before radical prostatectomy.^[18] Even so, the findings of our study still possessed significance and merit for early stage PCa detection in clinic practice, compared with tissue biopsy. Third, central gland tumors were not assessed because of their different genetic mutations, biologic behavioral features, and prognoses.^[19,20]

In conclusion, our study suggests that the PI-RADS includes a diagnostic scoring method that has a good correlation with tumor detection rate in patients with PSA <20 ng/ml. PCa detection rate increases when the PI-RADS score increases. The combination of T2WI + DWI scores into a single score is more successful at PCa detection than that of the score of T2WI alone. Such a method can help improve PCa diagnosis and reduce unnecessary prostate biopsies.

Acknowledgments

We would like to thank the urologist, Yong Zhang, from Department of Urology, Beijing Tiantan Hospital. We also thank Professor Yuan-Yuan Zhang from Wake Forest University, Institute for Regenerative Medicine.

Financial support and sponsorship

This work was supported by a grant from Beijing Municipal Science and Technology Commission (No. Z121107001012155).

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013;63:11-30. doi: 10.3322/caac.21166.
2. Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, *et al.* EAU guidelines on prostate cancer. Part 1: Screening, diagnosis, and treatment of clinically localised disease. *Eur Urol* 2011;59:61-71. doi: 10.1016/j.eururo.2010.10.039.
3. Kawachi MH, Bahnson RR, Barry M, Busby JE, Carroll PR, Carter HB, *et al.* NCCN clinical practice guidelines in oncology: Prostate cancer early detection. *J Natl Compr Canc Netw* 2010;8:240-62.
4. Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL, *et al.* Prevalence of prostate cancer among men with a prostate-specific antigen level < or = 4.0 ng per milliliter. *N Engl J Med* 2004;350:2239-46. doi: 10.1056/NEJMoa031918.
5. Al-Ghazo MA, Ghalayini IF, Matalka II. Ultrasound-guided transrectal extended prostate biopsy: A prospective study. *Asian J Androl* 2005;7:165-9. doi: 10.1111/j.1745-7262.2005.00019.x.
6. Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs G, *et al.* ESUR prostate MR guidelines 2012. *Eur Radiol* 2012;22:746-57. doi: 10.1007/s00330-011-2377-y.
7. Cruz M, Tsuda K, Narumi Y, Kuroiwa Y, Nose T, Kojima Y, *et al.* Characterization of low-intensity lesions in the peripheral zone of prostate on pre-biopsy endorectal coil MR imaging. *Eur Radiol* 2002;12:357-65. doi: 10.1007/s003300101044.
8. Engelhard K, Hollenbach HP, Deimling M, Kreckel M, Riedl C. Combination of signal intensity measurements of lesions in the peripheral zone of prostate with MRI and serum PSA level for differentiating benign disease from prostate cancer. *Eur Radiol* 2000;10:1947-53. doi: 10.1007/s003300000524.
9. Ikonen S, Kärkkäinen P, Kivisaari L, Salo JO, Taari K, Vehmas T, *et al.* Endorectal magnetic resonance imaging of prostatic cancer: Comparison between fat-suppressed T2-weighted fast spin echo and three-dimensional dual-echo, steady-state sequences. *Eur Radiol* 2001;11:236-41. doi: 10.1007/s003300000598.
10. Hamoen EH, de Rooij M, Witjes JA, Barentsz JO, Rovers MM. Use

- of the prostate imaging reporting and data system (PI-RADS) for prostate cancer detection with multiparametric magnetic resonance imaging: A diagnostic meta-analysis. *Eur Urol* 2015;67:1112-21. doi: 10.1016/j.eururo.2014.10.033.
11. Junker D, Quentin M, Nagele U, Edlinger M, Richenberg J, Schaefer G, *et al.* Evaluation of the PI-RADS scoring system for mpMRI of the prostate: A whole-mount step-section analysis. *World J Urol* 2015;33:1023-30. doi: 10.1007/s00345-014-1370-x.
 12. Schimmöller L, Quentin M, Arsov C, Hiester A, Kröpil P, Rabenalt R, *et al.* Predictive power of the ESUR scoring system for prostate cancer diagnosis verified with targeted MR-guided in-bore biopsy. *Eur J Radiol* 2014;83:2103-8. doi: 10.1016/j.ejrad.2014.08.006.
 13. Lim HK, Kim JK, Kim KA, Cho KS. Prostate cancer: Apparent diffusion coefficient map with T2-weighted images for detection – A multireader study. *Radiology* 2009;250:145-51. doi: 10.1148/radiol.2501080207.
 14. Baur AD, Maxeiner A, Franiel T, Kilic E, Huppertz A, Schwenke C, *et al.* Evaluation of the prostate imaging reporting and data system for the detection of prostate cancer by the results of targeted biopsy of the prostate. *Invest Radiol* 2014;49:411-20. doi: 10.1097/RLI.0000000000000030.
 15. Andriole GL, Levin DL, Crawford ED, Gelmann EP, Pinsky PF, Chia D, *et al.* Prostate cancer screening in the prostate, lung, colorectal and ovarian (PLCO) cancer screening trial: Findings from the initial screening round of a randomized trial. *J Natl Cancer Inst* 2005;97:433-8. doi: 10.1093/jnci/dji065.
 16. Xuan W, Ming L, Min C, Chun-Mei L, Ben W, Dong W, *et al.* The significance of peripheral zone imaging features on pelvic T2 weighted imaging for the diagnosis of prostate cancer with PSA <20 µg/L (in Chinese). *Chin J Urol* 2013;34:292-7. doi: 10.3760/cma.j.issn.1000-6702.2013.04.017.
 17. Furuno T, Demura T, Kaneta T, Gotoda H, Muraoka S, Sato T, *et al.* Difference of cancer core distribution between first and repeat biopsy: In patients diagnosed by extensive transperineal ultrasound guided template prostate biopsy. *Prostate* 2004;58:76-81. doi: 10.1002/pros.10298.
 18. Salomon G, Köllerman J, Thederan I, Chun FK, Budäus L, Schlomm T, *et al.* Evaluation of prostate cancer detection with ultrasound real-time elastography: A comparison with step section pathological analysis after radical prostatectomy. *Eur Urol* 2008;54:1354-62. doi: 10.1016/j.eururo.2008.02.035.
 19. Guo CC, Zuo G, Cao D, Troncoco P, Czerniak BA. Prostate cancer of transition zone origin lacks TMPRSS2-ERG gene fusion. *Mod Pathol* 2009;22:866-71. doi: 10.1038/modpathol.2009.57.
 20. Augustin H, Hammerer PG, Graefen M, Erbersdobler A, Blonski J, Palisaar J, *et al.* Insignificant prostate cancer in radical prostatectomy specimen: Time trends and preoperative prediction. *Eur Urol* 2003;43:455-60. doi: 10.1016/S0302-2838(03)00139-8.