Original Article

Multiparametric MRI for Prostate Cancer Detection Using PI-RADS v2 Compared with MRI/Ultrasound Fusion-Guided Biopsy

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Objective: To determine the diagnostic performance of multiparametric magnetic resonance imaging (mp-MRI) for prostate cancer (PCa) detection compared with MRI/ultrasound fusion-guided prostate biopsy.

Materials and Methods: Pre-biopsy prostate mp-MRI of 100 consecutive men were retrospectively compared with prostate biopsy obtained by MRI/ultrasound fusion guidance between June 2017 and July 2018. Two experienced radiologists assigned PI-RADS score and localization the suspicious lesions by consensus. Tumor detection rates were calculated for each PI-RADS scores, Gleason scores, and tumor location.

Results: Of the 151 target lesions on mp-MRI from 100 patients, 21% (31/151) were pathologically determined as clinically significant PCa. The detection rates on targeted biopsy for PI-RADS scores of 3, 4, and 5 were 10%, 29%, and 54%, respectively. No cancer was detected in PI-RADS score of 2 lesions. Higher level of suspicion PI-RADS scores indicated higher percentages of high Gleason scores. The percentages of PCa for Gleason scores of 7, 8, and 9 were 17%, 11%, and 0% for PI-RADS 3, 50%, 44%, and 25%, for PI-RADS 4, and 33%, 44%, and 75% for PI-RADS 5. High rates at 82% (23/28) of false-positive mp-MRI findings were found for small of less than 0.5 mL peripheral zone targets and 91%(10/11) of targets in the anterior location of the transition zone.

Conclusion: PI-RADS v2 showed satisfactory performance for diagnosing clinically significant PCa and provided predictive information on tumor grade. High negative predictive values for PI-RADS v2 could be used in clinical management workflow to confidently avoid prostate biopsies.

Keywords: Multiparametric MRI; MRI/ultrasound fusion-guided prostate biopsy; Prostate cancer detection; PI-RADS v2

Received 10 August 2021 | Revised 23 February 2022 | Accepted 28 February 2022

J Med Assoc Thai 2022;105(3):254-62

Website: http://www.jmatonline.com

Prostate cancer (PCa) is the second most frequent cancer diagnosis made in men and the fifth leading cause of cancer-related deaths worldwide[1]. Classically, PCa was diagnosed with age-appropriate screening and based on digital rectal examination (DRE) and serum prostate-specific antigen (PSA) determination. Transrectal ultrasound (TRUS)-guided biopsy or transperineal (TP) sextant biopsy were the two main anatomic approaches to obtain prostate tissue for diagnosis of PCa and presently remains the gold standard. However, it may cause cancer up/down staging with the final pathology and still had high false negative rates using the 10 to 12-core extended-sampling protocols. In response to limitation of the standard sextant biopsy, multiparametric magnetic resonance imaging (mp-MRI) and MRI/ultrasound fusion-guided prostate biopsy have been introduced to the clinical practice. According to increased tumor cellularity, structural change, and disorganized texture properties of high grade PCa resulting in restricted diffusion of water molecules, diffusion-weighted images (DWI) have the most potential role of diagnosis and provide tumor aggressiveness information[2]. Mp-MRI demonstrated high performance in diagnosing clinically significant

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How to cite this article:

Wibulpolprasert P, Hawanit J, Phongkitkarun S, Kijvikai K, Worawichawong S. Multiparametric MRI for Prostate Cancer Detection Using PI-RADS v2 Compared with MRI/ultrasound Fusion-Guided Biopsy. J Med Assoc Thai 2022;105:254-62.

DOI: 10.35755/jmedassocthai.2022.03.13284

Table 1. MRI acquisition parameters

	T2W FSE	Transverse axial T1W FSE	DWI	DCE-MRI
Fat suppression				3D-LAVA or THRIVE
TR	3,000-6,000 ms	400-600 ms	3,000-6,000 ms	4.1 ms
TE	104 ms	10-15 ms	60-120 ms	1.9 ms
ETL	18			
FOV	18×20 cm^2		18-20 cm^2	20×22 cm^2
Slice thickness	3 mm		3 mm	3 mm
Interslice gap	0		0	
Acquisition time (minutes)	8	5	10	7
Matrix	360×360		128×128	140×140
NEX	4	340x250	1	

MRI=magnetic resonance imaging; T2W=T2-weighted; T1W=T1-weighted; DWI=diffusion weighted imaging; DCE=dynamic-contrast enhancement; LAVA=liver acquisition with volume acceleration; THRIVE=T1-weighted high resolution isotropic volume examination; TR=repetition time; TE=time to echo; ETL=echo train length; FOV=field of view; NEX=number of excitation

PCa, and even small high-grade cancer foci that determined poor pathologic outcomes and prognosis.

The Prostate Imaging-Reporting and Data System (PI-RADS) scoring system[3] is gradually being adopted in different centers for the reporting of MRI findings in patients with suspected PCa. A previous large-scale study[4] showed that mp-MRI and PI-RADS v2 have high sensitivity for PCa detection, particularly in large and significant cancer. However, the diagnostic performance of PI-RADS v2 comparing to MRI/ultrasound fusion-guided biopsy were disparately reported. In addition, the causes of false positive and false negative are still not known[5-7]. The objective of the present study was to determine the performance of mp-MRI for PCa detection using the PI-RADS v2 scoring system, and to investigate its correlations with histopathology specimens obtained by MRI/ultrasound fusion guidance.

Materials and Methods

The present retrospective study was approved from the Ethics Committee on Human Rights Related to Research Involving Human Subjects at Ramathibodi Hospital (COA No. MURA 2018/583) and the informed consent was waived due to the retrospective analyses (patients agreed to treatment by written consent).

Study populations and clinical data

The authors conducted a retrospective analysis of all men who underwent pre-biopsy mp-MRI followed by MRI/ultrasound fusion-guided prostate biopsy between June 2017 and July 2018. The reason for the dual test is due to presence of suspicious lesions with a PI-RADS score of 3 or more from the initial MRI interpretation reports. Demographic data were collected from the patients' medical records, including age at diagnosis, PSA level, and time duration between pre-biopsy mp-MRI and MRI/ultrasound fusion-guided prostate biopsy.

Pre-biopsy mp-MRI technique

All pre-biopsy mp-MR imaging were performed in the supine position with a 1.5-T MR system (Ingenia, Phillips Healthcare, USA) or a 3.0-T MR system (Ingenia, Philips Healthcare, USA), both using a dStream Torso body coil. All patients received an injection of 20 mg hyoscine-butylbromide intravenously before the scan. After the acquisition of localizing images thin-slice T2W fast spin-echo (FSE) images through the prostate gland and seminal vesicles and transverse axial T1-weighted FSE were acquired (Table 1). Axial free-breathing diffusion MRI was performed using a single-shot echo-planar imaging technique along the three orthogonal directions with b values of 0, 200, and 1,500 s/mm^2 before injection of a 0.1-mmol/kg bolus of gadobutrol (Gadovist, Bayer) at a rate of 3 mL/second, followed by a 30 mL saline flush at the same rate as contrast medium injected, using an MR-compatible automated injector (MedRad, USA) to perform dynamic contrast enhanced (DCE) MRI. Total DCE-MRI scan time was five minutes. All the MR images were achieved into picture archiving and communication system (PACS).

mp-MRI interpretation

Images were retrieved from the Picture Archiving and Communication System and reviewed by two genitourinary radiologists (SP and PW with 15

years and 8 years-experience, respectively). They interpreted prostate mp-MRI and formed consensus assessment of all mp-MRI according to PI-RADS v2, while blinded to the pathologic results. Other mp-MRI findings, including size such as volume of targeted lesion, zonal location of tumor such as transition and peripheral zone, and anteroposterior axis such as anterior or posterior, based on the PI-RADS v2 39-sector map were also recorded.

MRI/ultrasound fusion-guided prostate biopsy

MRI/ultrasound fusion-guided biopsy was performed with the BioJet™ fusion system and software (D&K Technologies, Barum, Germany). Targeted localized lesions including all PI-RADS scores of 3 and above based on mp-MRI features such as T2W, DWI with ADC maps, and DCE, accordingly to the initial official MRI report were recorded. One experienced radiologist (SP) contoured the target lesions and prostate margins on the transverse T2 TSE-images and re-assessment of all mp-MRI according to PI-RADS v2. Fusion of real-time TRUS with organ contours using BK Flex Focus ultrasound system (BK Medical, Mileparken, Denmark) was made by the urologist during the biopsy session. The biopsy tissue with MRI-TRUS fusion image navigation was obtained by using an 18-G automatic biopsy gun (Bard Magnum; Bard Medical, Covington, GA, USA) with a specimen length of 25 mm and started at the center of the target lesion followed by a systematic biopsy (Figure 1).

Histopathological study

Histopathological diagnoses of tumors in prostate tissue biopsy after hematoxylin and eosin (H&E) staining were performed by the attending pathologists according to the International Society of Urological Pathology (ISUP) 2005 recommendations. Two Gleason grades were assigned for each patient. The primary grade was described for PCa aggressiveness that make of the largest area of tumor and a secondary grade was described for the next largest area. A Gleason score (GS) of 7 or more was considered as clinically significant cancer.

Statistical analysis

Descriptive statistics were used to analyze the patient characteristic such as age, PSA, PSA density, and prostate volume. Chi-square analysis was performed for categorical variable. Diagnostic performance of mp-MRI was calculated by sensitivities, specificities, positive and negative predictive values, and area under receiver operating characteristic curve (ROC). All statistical analyses were performed using Stata, version 13.0 (StataCorp LP, College Station, TX, USA). Statistical significance was defined as p-value of less than 0.05.

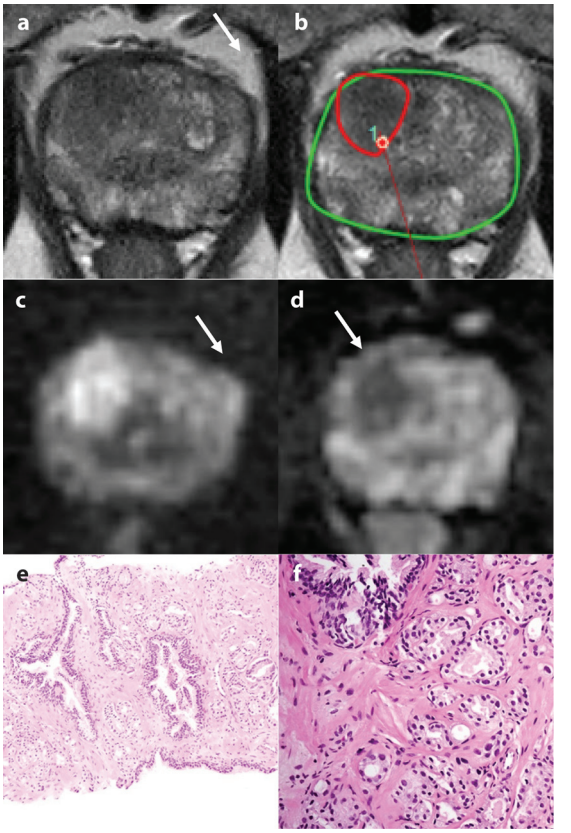

Figure 1. A 61-year-old man with PCa who presented with a high serum PSA level (7.01 ng/mL) and high PSA density (0.18 ng/mL). Axial T2-weighted image of the mid gland show a hypointense lesion (arrow) in the right anterior transition zone (a, b), the image was used for contouring of the prostate margins (green) and targeted lesions (red) (b). Axial DWI with a b-value of 1,500 s/mm^2 (c) with ADC map (d) at the same level as (a), the lesion (white arrow) shows a low ADC value due to diffusion restriction. Hematoxylin and eosin (H&E) stain, original magnification x10 (e) and x40 (f), histopathology of prostate tissue from MRI-ultrasound fusion guided biopsy of the target lesion in (b) revealed GS 7 (3+4) cancer.

Results

Patient-based analysis

The present study cohort included 100 consecutive patients with overall 151 targeted lesions that underwent MRI/ultrasound fusion-guided prostate biopsy between June 2017 and July 2018. The patient demographics and biopsy characteristics are shown in Table 2. The mean patient age was 68 years (SD 6.66 years). The median serum PSA and

Table 2. Patient demographics (total number=100) and biopsy characteristics (total target lesions=150)

Variables	Values
Age (years); mean (SD)	68.00 (6.66)
PSA (ng/mL); median (P_{25}, P_{75})	8.72 (5.8, 13.01)
PSA density (ng/mL/cm^3); median (P_{25}, P_{75})	0.17 (0.10, 0.30)
Prostate volume (mL), mean (SD)	55.89 (42.74)
No. of targeted lesions per patient; median	1
1 lesion; n (%)	64 (64)
2 lesions, n (%)	26 (26)
3 lesions, n (%)	6 (6)
4 lesions, n (%)	3 (3)
5 lesions, n (%)	1 (1)
Overall PI-RADS; n (%)	
PI-RADS 2	21 (21)
PI-RADS 3	21 (21)
PI-RADS 4	36 (36)
PI-RADS 5	22 (22)
No. of cores per patient; median (P_{25}, P_{75})	
MRI-targeted biopsy	6 (4, 10)
Standard systematic biopsy	6 (4, 10)
Maximum cancer core length (mm/patient); mean (SD)	
MRI-targeted biopsy	14.20 (5.23)
Standard systematic biopsy	16.54 (5.32)
Maximum cancer core length (mm/lesion); mean (SD)	
MRI-targeted biopsy	13.07 (5.31)
Standard systematic biopsy	15.06 (5.47)
Volume of targeted lesions (mL); median (P_{25}, P_{75})	0.22 (0.10, 0.72)
No. of prior biopsies; n (%)	
Primary biopsy	27 (27)
1	49 (49)
≥2	24 (24)
PCa; n (%)	39 (39)
Clinically significant cancers*	27 (27)
Clinically insignificant cancers	12 (12)
GS; n (%)	
6	12 (12)
7	16 (16)
8	8 (8)
9	3 (3)

SD=standard deviation; PSA=prostate specific antigen; P_{25}=25th percentile; P_{75}=75th percentile; MRI=magnetic resonance imaging; PCa=prostate cancer; GS=Gleason score.

* Clinically significant cancer was defined as Gleason ≥3+4 according to the updated Epstein criteria

PSA density with 25th (P_{25}) and 75th (P_{75}) percentiles of the present study cohort were 8.72 (5.8, 13.1) ng/mL and 0.17 (0.10, 0.30) ng/mL/cm^3, respective. The median time (P_{25}, P_{75}) between pre-biopsy mp-MRI and MRI/ultrasound fusion-guided prostate biopsy was 53 (23, 175) days.

Of the 100 patients, 64 patients had solitary target lesion and the remainder had between two and five multifocal target lesions. The overall assessment PI-RADS scores were 2 in 21 (21%) men, 3 in 21 (21%) men, 4 in 36 (36%) men, and 5 in 22 (22%) men. Seventy-three men (73%) had previously undergone a conventional TRUS biopsy, and of these 73 men, 57 had been diagnosed with benign findings and 16 men had previously been diagnosed with atypical small acinar proliferation or high-grade prostatic intraepithelial neoplasia. The median cumulative number (P_{25}, P_{75}) of cores taken by MRI-targeted biopsy and standard systematic biopsy approaches was 6 (4, 10) cores. The mean maximal core lengths for MRI-targeted biopsy and standard systemic biopsy were 14.20 (SD 5.23) mm and 16.54 (SD 5.32) mm, respectively. Forty-nine percent of the study cohort received negative results from the previous biopsy and persistent suspicion of harboring disease.

Overall, of the 100 patients, a diagnosis of PCa was established in 39% (39/100) of men and 27% (27/100) had clinically significant cancer with GS of 7 or more. There were 12% (12/100) of significant cancer diagnosed by targeted biopsy approach, 2% (2/100) by simultaneous standard systematic biopsy approach, and 13% (13/100) by both targeted and standard systematic biopsies.

Lesion-based analysis

Of the 151 targeted lesions detected on mp-MRI, the histological results for GS 6, 7, 8, and 9 were 7% (11/151), 12% (18/151), 6% (9/151), and 3% (4/151), respectively. The histological results characterized by PI-RADS score are shown in Table 3. Thirty-one lesions (21%) were pathologically confirmed as clinically significant PCa.

The sensitivity, based on all values that were calculated for detection of clinically significant PCa, of PI-RADS of 4 or more was 87%, the specificity of 62%, the positive predictive value (PPV) of 37%, and the negative predictive value (NPV) of 95% with an area ROC of 0.744. The sensitivity of significant PCa detection by PI-RADS of 3 or more was 100%, the specificity of 32.5%, the PPV of 27.7% and NPV of 100% with a ROC of 0.67.

The highest percentage of clinically significant cancer was found among men with a PI-RADS score of 5, in 13 of 24 lesions (54%), followed by PI-RADS of 4 in 14 of 49 lesions (29%), and PI-RADS of 3 in 4 of 39 lesions (10%). No clinically significant cancer was found in PI-RADS of 2 lesions. There were significantly higher performances of significant

Table 3. Characteristics of overall 151 targeted prostate lesions from MRI/ultrasound fusion-guided biopsy stratified by PI-RADS v2 score and pathological findings

Overall PI-RADS score	mp-MRI (n=151); n (%)	Pathological findings; n (%)					
		Non-cancer (n=109)		Clinically insignificant cancer (n=11)		Clinically significant cancer (n=31)	
		BPH (n=85)	Others* (n=24)	GS 6 (n=11)	GS 7 (n=18)	GS 8 (n=9)	GS 9 (n=4)
2	39 (25.8)	31 (79)	8 (21)	-	-	-	-
3	39 (25.8)	23 (59)	8 (21)	4 (10)	3 (8)	1 (3)	-
4	49 (32.5)	25 (51)	4 (8)	6 (12)	9 (18)	4 (8)	1 (2)
5	24 (15.9)	6 (25)	4 (17)	1 (4)	6 (25)	4 (17)	3 (13)

MRI=magnetic resonance imaging; BPH=benign prostatic hyperplasia; GS=Gleason score

* Other non-cancer included benign fibrous, muscular, adipose tissue, colonic mucosa, or high-grade prostatic intraepithelial neoplasia

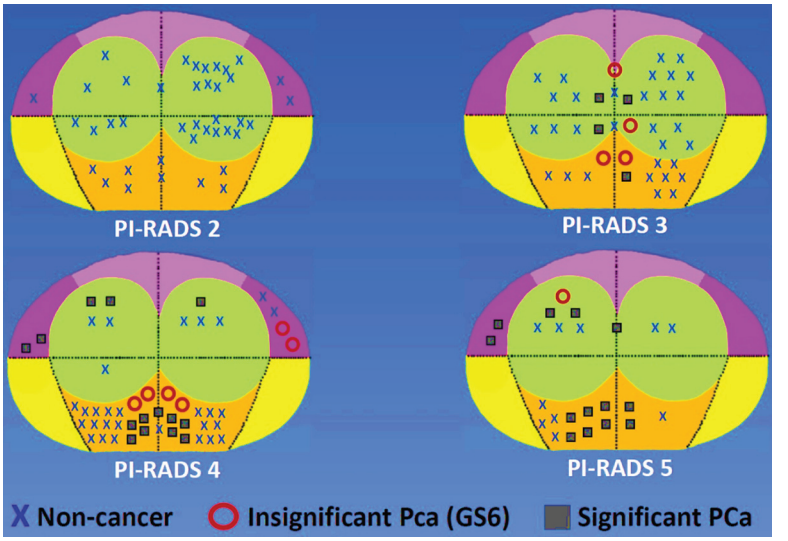

Figure 2. Two-dimensional (2D) prostate model illustrates the location of non-cancer (X), clinically insignificant PCa (◯), and clinically significant PCa (■) target lesions from MRI/ultrasound fusion-guided biopsy stratified by PI-RADS v2 score.

PCa detection of PI-RADS score of 5 than score 4 (odds ratio [OR] 2.95 with 95% confidence interval (CI) 1.07 to 8.15; p=0.04) and score 3 (OR 10.3 with 95% CI 2.79 to 38.30; p<0.01) as well as score 4 higher than score 3 (OR 3.5 with 95% CI 1.05 to 11.69; p=0.04).

The detection rate for clinically significant cancer on targeted biopsy alone was significant higher in PI-RADS 4 and 5 lesions [37% (27/73)] than lower suspicion PCa lesion [PI-RADS 2 and 3, 5% (4/78)] with a p-value of less than 0.001.

There was higher rate of clinically significant PCa detection on targeted biopsy in peripheral zone lesion (n=22) than those located in the transition zone (n=9) at 28% (22/80) versus 13% (9/71), (p=0.025) (Figure 2).

Radiologic-pathologic discordance

Discordant results between the mp-MRI diagnosis and MRI/ultrasound fusion-guided prostate biopsy were found in 33% (47/151) of targeted lesions. These discordant lesions included all benign pathological findings and no malignancy, in highly suspicious MRI lesions of PI-RADS 4 and 5, false positive MRI lesions, and PCa in less suspicious lesions of PI-RADS 2 and 3, false negative MRI lesions. Twenty six percent (39/151) of highly suspicious MRI lesions or 29 of PI-RADS 4 lesions (19%) and 10 PI-RADS 5 lesions (7%) in 35 patients had no PCa or false positive mp-MRI. In addition, false positive mp-MRI lesions were more frequently found in the peripheral zone (35%, 28/80) than in the transition zone (15%, 11/71), with the difference being statistically significant (p=0.006). In the peripheral zone, the false positive mp-MRI lesions were PI-RADS 4 in 29% (23/80) of cases and PI-RADS 5 in 6% (5/80; p=0.114). Eighty two percent (23/28) of the false positive MRI lesions in the peripheral

zone were small size below 0.5 mL, with a mean of 0.33 mL and a range of 0.02 to 1.95 mL. In the transition zone, the false positive mp-MRI lesions (5/6 of PIRADS 4 and 5/5 of PI-RADS 5) were located in the anterior aspect (p=0.025) but were not small size (Figure 2). A negative targeted MRI/ultrasound fusion-guided prostate biopsy but positive standard systematic biopsy was observed in four patients. Nine of 35 patients underwent re-biopsy in the next 4 to 23 months (mean 12.3 months) due to persistent rising of serum PSA level with highly suspicious mp-MRI findings in the follow up scan. One patient had re-analysis of the prostate tissue specimen at next two months and a change from atypical cell to GS 6. Three patients (3/35, 9%) have been diagnosed with PCa GS 9 (4+5) at next 15 months follow up, GS 8 (4+4) and GS 6 (3+3) at next 20 months follow up. Four patients (4/35, 11.4%) have been diagnosed with atypical cell change at next 4 to 23 months follow up duration.

Associations between the PI-RADS score, prostate biopsy, and radical prostatectomy specimen

Twenty-six men with pathologically confirmed PCa from biopsy underwent further treatment with radical prostatectomy. PCa was found in 46% (12/26) with a score of 5, 38% with a score of 4 (10/26), 12% with a score of 3 (3/26) and 4% (1/26) with a PI-RADS score of 2. There were 62% (16/26) concordance overall GS between prostate needle biopsy specimens and the radical prostatectomy. There were Gleason upgrading and downgrading in 27% (7/26) and 12% (3/26), respectively. The majority of Gleason upgrading (5/7, 71%) was accounted by a change from 3+3 to 3+4. Overall Gleason upgrading (GS 3+3 to 3+4) was found less on whom positive targeted biopsy alone (1/7, 14%) than on positive standard systemic biopsy alone (2/4, 50%) and less on targeted biopsy alone than on combined biopsy in one of seven (14%) versus in seven of 26 (27%). Twelve percent (3/26) of radical prostatectomies were downgraded by one grade from combine biopsies techniques and from GS 3+4 to 3+3 (1/26, 4%) and GS 3+5 and 4+4 to 3+4 (2/26, 8%). None were upgraded by two or more grades.

Discussion

The present study showed that the significant cancer detection rate for lesions with a PI-RADS score of 2, 3, 4, and 5 were 0%, 10%, 29%, and 54%, respectively. The rates of significant cancer were higher in PI-RADS score 4 and 5 than in score 2 and 3 at 37% versus 5% (p<0.01). Such findings corresponding with result of Cash et al[8] study with 408 patients underwent MRI-US fusion guided biopsy that showed the rates of clinically significant PCa in relation to PI-RADS in scores of 2 to 5 were 0%, 3%, 24%, and 60%, respectively. While, Hofbauer et al[9] reported clinically significant cancer detection rate by PIRADS v2 score of 3 to 5 were 23%, 49%, and 77%, respectively. The difference of rate of cancer detection was due to relative high proportion of PI-RADS score of 2 in the present study. However, these results harmoniously supported the clinical decision in patient selection for further tissue diagnosis especially in PI-RADS score 4 and 5 lesions by mp-MRI of the prostate.

In the lesion-based analysis, the authors found sensitivity and NPV of 87% and 95%, respectively, which were similar values to those of the original PI-RADS-based meta-analysis of 14 studies by Hamoen et al[10], who found pooled sensitivity of 78%, with NPV ranging from 58% to 95%. The high NPV in the present study (95%) may suggest the utility of the PI-RADS v2 scoring system for identifying patients who were likely to have negative biopsies and could be use in triage decision for prostate biopsy and reassurance for patients.

The present study provides insight into the question of how to manage men with a highly suspicious lesion on mp-MRI, but with a benign pathologic result on MRI/ultrasound fusion-guided prostate biopsy (false positive MRI). In the present study, false positive rate was 26% (19% for PI-RADS 4 and 7% for PI-RADS 5) in which they were small lesions in the peripheral zone and lesions anteriorly located in the transition zone. The false positive rate in the present study conformed to the validated studies earlier ranging from 14% to 40% and more commonly occurred in transition zone lesion[6,7,11]. The biopsy results of these false positive MRI were benign prostatic hyperplasia (79%), and the others (21%) were extraprostatic tissue such as fibromuscular, adipose tissue and colonic mucosa. It should be noted that 20% (7/35) of patients with initial benign biopsy result in PI-RADS score of 4 and 5 were confirmed as atypical cell change and malignancy after re-biopsy at next 4 to 23 months (mean 12.3 months). Factors that may cause these false-positive mp-MRI results are mp-MRI interpretation pitfalls, image misregistration, and tissue sampling errors. The possibility of mp-MRI interpretation pitfalls due to inaccurate PI-RADS assessments, poor image quality, co-existing prostate tissue inflammation[12], and nature of relative dense glandular tissue that can mimic PCa in transition

zone as reported by Chatterjee et al[13] and Langer et al[14]. Image misregistration may be due to bladder filling difference, patient's position change, rectal mis-registration related to the use of TRUS transducer during biopsy, intraprocedural tissue deformation, and bleeding[15,16]. The cause of tissue sampling pitfalls in the present study may be due to missed guided-biopsy according to small size of target lesions or anterior location of target lesions as reported in previous studies[7,17]. Furthermore, anteriorly location of the transition zone lesions is apart from end-firing biopsy probe and limited perspective function due to the distance from end-firing endoluminal probes[18]. Although the negative predictive value for PCa detection by mp-MRI with PI-RADS v2 is high, the occurrence of false positive MRI may be from other reasons that also simultaneously occurred. Mp-MRI with PI-RADS v2 interpretation should be carefully review with a multidisciplinary team approach that include a radiologist, a pathologist, and an urologist. Interval clinical follow-up with serum PSA monitoring or re-biopsy should be taken into consideration especially in men with high clinical suspicion of PCa.

The GS has been validated as the important prognostic factor for patient risk stratification and clinical decision-making[19,20]. The present study confirmed the relationships between the PI-RADS scores and the Gleason pattern distribution. However, the sampling error[21,22] and variability among pathologists[23] are contributed to tumor upgrading at the radical prostatectomy specimen, which has been associated with higher rates of biochemical recurrence[24]. The present study found discordant GS pattern at the radical prostatectomy in 38% of combined biopsies cases, comparing to 20% and 28% discordant rates reported in two studies[25,26]. Among discordant Gleason pattern in the present study, the Gleason downgrading in prostatectomy specimens were shifted to insignificant cancer in only one case. The other two cases were changed from GS 8 to 7. The majority of Gleason upgrading was found in combined biopsy techniques and changed from insignificant to significant PCa (5/7). Furthermore, the present study result showed additional overall and significant cancer detection by standard systemic biopsy alone in 15% and 12%, respectively. These findings were corresponding with An et al[27] study that reported 6% higher cancer detection from target biopsy when combined with systematic biopsy and detected 3 in 27 significant cancers missed by target biopsy. The study of Parsons et al[28] showed that more clinically significant cancers (9%) were detected in men whom fusion biopsy was negative. These findings represent better diagnostic yield of combined biopsy than target biopsy alone[26,28,29].

There were limitations in the present study. First, the study was a single site, retrospective evaluation that may generate selection bias. Second, the present study used biopsy results as the reference, instead of the radical prostatectomy results. It is possible that clinically significant cancers may have been missed or under-estimated by both targeted and systematic biopsies[30-33]. Whole-mount data would enable a more definitive analyses of the nature of the lesions, tumor staging, true tumor volume, and exact tumor locations identified on mp-MRI and MRI/ultrasound fusion-guided prostate biopsy. In addition, there were concerns about patient with low suspicious malignant lesion on mp-MRI who did not undergo biopsy.

Conclusion

In conclusion, the PI-RADS v2 scoring system showed good diagnostic performance for clinically significant PCa and provided predictive information on tumor grade. The high negative predictive values for PI-RADS v2 could be used in clinical management workflow to confidently avoid prostate biopsies.

What is already known on this topic?

Mp-MRI and PI-RADS demonstrate high performance in diagnosing clinically significant PCa. However, the diagnostic performance of PI-RADS comparing to MRI/ultrasound fusion-guided biopsy were dissimilarly reported. In addition, the factors related with false positive and false negative lesions from fusion biopsy have not been addressed.

What this study adds?

This study shows good diagnostic performance of mp-MRI and PI-RADS for clinically significant PCa and provided predictive information on tumor grade. Higher PI-RADS scores from prostate mp-MRI indicated higher percentages of high GSs. Furthermore, the high negative predictive values for PI-RADS v2 could be used in clinical management workflow to confidently avoid prostate biopsies. Factors that may cause false-positive mp-MRI results include small peripheral zone target lesions and anterior position of the transition zone target lesions. Interval clinical follow-up with serum PSA monitoring or re-biopsy should be taken into consideration especially in men with high clinical suspicion of PCa.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Rawla P. Epidemiology of prostate cancer. World J Oncol 2019;10:63-89.
2. Wibulpolprasert P, Phongkitkarun S, Chalermsanyakorn P. Clinical applications of diffusion-weighted-MRI in prostate cancer. J Med Assoc Thai 2013;96:967-75.
3. Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS prostate imaging - reporting and data system: 2015, version 2. Eur Urol 2016;69:16-40.
4. Wibulpolprasert P, Raman SS, Hsu W, Margolis DJA, Asvadi NH, Khoshnoodi P, et al. Detection and localization of prostate cancer at 3-T multiparametric MRI using PI-RADS segmentation. AJR Am J Roentgenol 2019:W1-10. doi: 10.2214/AJR.18.20113.
5. Cash H, Günzel K, Maxeiner A, Stephan C, Fischer T, Durmus T, et al. Prostate cancer detection on transrectal ultrasonography-guided random biopsy despite negative real-time magnetic resonance imaging/ultrasonography fusion-guided targeted biopsy: reasons for targeted biopsy failure. BJU Int 2016;118:35-43.
6. Stolk TT, de Jong IJ, Kwee TC, Luiting HB, Mahesh SVK, Doornweerd BHJ, et al. False positives in PIRADS (V2) 3, 4, and 5 lesions: relationship with reader experience and zonal location. Abdom Radiol (NY) 2019;44:1044-51.
7. Sheridan AD, Nath SK, Aneja S, Syed JS, Pahade J, Mathur M, et al. MRI-ultrasound fusion targeted biopsy of prostate imaging reporting and data system version 2 category 5 lesions found false-positive at multiparametric prostate MRI. AJR Am J Roentgenol 2018;210:W218-25.
8. Cash H, Maxeiner A, Stephan C, Fischer T, Durmus T, Holzmann J, et al. The detection of significant prostate cancer is correlated with the Prostate Imaging Reporting and Data System (PI-RADS) in MRI/transrectal ultrasound fusion biopsy. World J Urol 2016;34:525-32.
9. Hofbauer SL, Maxeiner A, Kittner B, Heckmann R, Reimann M, Wiemer L, et al. Validation of prostate imaging reporting and data system version 2 for the detection of prostate cancer. J Urol 2018;200:767-73.
10. Hamoen EHJ, 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.
11. Viana PCC, Horvat N, do Santos VRJ, Lima TC, Romão DDS, Cerri LMO, et al. Is possible to rule out clinically significant prostate cancer using PI-RADS v2 for the assessment of prostate MRI? Int Braz J Urol 2019;45:724-31.
12. Zhu G, Wang Q. Comparisons between magnetic resonance/ultrasound fusion-guided biopsy and standard biopsy in the diagnosis of prostate cancer: A prospective cohort study. Medicine (Baltimore) 2018;97:e11962.
13. Chatterjee A, Watson G, Myint E, Sved P, McEntee M, Bourne R. Changes in epithelium, stroma, and lumen space correlate more strongly with Gleason pattern and are stronger predictors of prostate ADC changes than cellularity metrics. Radiology 2015;277:751-62.
14. Langer DL, van der Kwast TH, Evans AJ, Plotkin A, Trachtenberg J, Wilson BC, et al. Prostate tissue composition and MR measurements: investigating the relationships between ADC, T2, K(trans), v(e), and corresponding histologic features. Radiology 2010;255:485-94.
15. Rothwax JT, George AK, Wood BJ, Pinto PA. Multiparametric MRI in biopsy guidance for prostate cancer: fusion-guided. Biomed Res Int 2014;2014:439171.
16. Costa DN, Pedrosa I, Donato F Jr, Roehrborn CG, Rofsky NM. MR imaging-transrectal US fusion for targeted prostate biopsies: implications for diagnosis and clinical management. Radiographics 2015;35:696-708.
17. Rourke E, Sunnapwar A, Mais D, Kukkar V, DiGiovanni J, Kaushik D, et al. Inflammation appears as high Prostate Imaging-Reporting and Data System scores on prostate magnetic resonance imaging (MRI) leading to false positive MRI fusion biopsy. Investig Clin Urol 2019;60:388-95.
18. Moosavi B, Flood TA, Al-Dandan O, Breau RH, Cagiannos I, Morash C, et al. Multiparametric MRI of the anterior prostate gland: clinical-radiological-histopathological correlation. Clin Radiol 2016;71:405-17.
19. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA 1998;280:969-74.
20. Kattan MW, Wheeler TM, Scardino PT. Postoperative nomogram for disease recurrence after radical prostatectomy for prostate cancer. J Clin Oncol 1999;17:1499-507.
21. King CR, Long JP. Prostate biopsy grading errors: a sampling problem? Int J Cancer 2000;90:326-30.
22. Daneshgari F, Taylor GD, Miller GJ, Crawford ED. Computer simulation of the probability of detecting low volume carcinoma of the prostate with six random systematic core biopsies. Urology 1995;45:604-9.
23. Burchardt M, Engers R, Müller M, Burchardt T, Willers R, Epstein JI, et al. Interobserver reproducibility of Gleason grading: evaluation using prostate cancer tissue microarrays. J Cancer Res Clin Oncol 2008;134:1071-8.
24. Sved PD, Gomez P, Manoharan M, Kim SS, Soloway MS. Limitations of biopsy Gleason grade: implications for counseling patients with biopsy Gleason score 6

prostate cancer. J Urol 2004;172:98-102.
25. Essid MA, Chakroun M, Nouhaud FX, Lair M, Gobet F, Pfister C. Evolution of prostate cancer diagnosis: retrospective analysis of magnetic resonance imaging/ ultrasound fusion guided biopsies protocol in routine practice and patients management. Transl Androl Urol 2020;9:629-36.
26. Le JD, Stephenson S, Brugger M, Lu DY, Lieu P, Sonn GA, et al. Magnetic resonance imaging-ultrasound fusion biopsy for prediction of final prostate pathology. J Urol 2014;192:1367-73.
27. An T, Park BK. Value of systematic biopsy added to target biopsy for detecting significant cancer in men with Prostate Imaging and Reporting and Data System 5. Precis Future Med 2020;4:107-13.
28. Parsons M, Foy B, Chan E, Crawford B, Sommers D, Bishoff J, et al. Concordance of MRI-guided and systematic prostate biopsy for the detection of prostate cancer (PCa). J Clin Oncol 2020;38(29 Suppl):277.
29. Diamand R, Oderda M, Al Hajj Obeid W, Albisinni S, Van Velthoven R, Fasolis G, et al. A multicentric study on accurate grading of prostate cancer with systematic and MRI/US fusion targeted biopsies: comparison with final histopathology after radical prostatectomy. World J Urol 2019;37:2109-17.
30. Wysock JS, Rosenkrantz AB, Huang WC, Stifelman MD, Lepor H, Deng FM, et al. A prospective, blinded comparison of magnetic resonance (MR) imaging-ultrasound fusion and visual estimation in the performance of MR-targeted prostate biopsy: the PROFUS trial. Eur Urol 2014;66:343-51.
31. Siddiqui MM, Rais-Bahrami S, Turkbey B, George AK, Rothwax J, Shakir N, et al. Comparison of MR/ ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. JAMA 2015;313:390-7.
32. Baco E, Rud E, Eri LM, Moen G, Vlatkovic L, Svindland A, et al. A randomized controlled trial to assess and compare the outcomes of two-core prostate biopsy guided by fused magnetic resonance and transrectal ultrasound images and traditional 12-core systematic biopsy. Eur Urol 2016;69:149-56.
33. Panebianco V, Barchetti F, Sciarra A, Ciardi A, Indino EL, Papalia R, et al. Multiparametric magnetic resonance imaging vs. standard care in men being evaluated for prostate cancer: a randomized study. Urol Oncol 2015;33:17.e1-7.