

Outcomes of Multi-parametric MRI-US Cognitive Fusion Template-guided Transperineal Prostate Biopsy: A Single Centre Experience

Mohd Najib Aziz^{1*} and Vijayan Manogran¹

¹Department of Urology, Kuala Lumpur General Hospital, Jalan Pahang, 50586 Kuala Lumpur, Malaysia.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

Editor(s):

(1) Dr. Punit Bansal, RG Stone And Super Speciality Hospital, Ludhiana, India.

Reviewers:

(1) Ebuka David, Alex Ekwueme Federal University, Nigeria.

(2) Roberto Carlos Mourão Pinho, Unifacol Pernambuco, Brazil.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/76621>

Original Research Article

Received 30 August 2021

Accepted 07 November 2021

Published 09 November 2021

ABSTRACT

Aims: The aim of this study was to report the outcomes of multiparametric Magnetic Resonance Imaging-Ultrasound (mpMRI-US) cognitive fusion template-guided transperineal prostate biopsy (TPB) performed in a single tertiary institution.

Study Design: Retrospective.

Place and Duration of Study: Sample: Department of Urology, Kuala Lumpur General Hospital, between April 2017 and December 2019.

Methodology: Patients with Prostate Imaging-Reporting and Data System (PI-RADS) 3-5 on mpMRI who underwent cognitive mpMRI-US fusion template-guided TPB were recruited retrospectively. Data was analyzed to determine prostate cancer (PCa) detection rate, diagnostic accuracy of mpMRI and post-TPB complication rates. Clinically significant PCa (csPCa) was defined as Gleason $\geq 3+4$.

Results: 122 patients were enrolled and 330 PI-RADS 3-5 lesions were analyzed. The mean age was 66, mean prostate specific antigen was 15.5 ng/mL and mean number of biopsy cores was 56.6. 54.1% were Chinese, 38.5% were Malays, 4.9% were Indian and 2.5% were Others. There were 3 subgroups: repeat biopsy (70.5%), biopsy naïve (21.3%) and re-staging (8.2%). The

*Corresponding author: Email: mnajib.aziz@gmail.com;

detection rate of overall PCa and csPCa was 43.4% and 24.6% respectively. csPCa was detected in 43.8%, 48.6% and 66.7% in PI-RADS 3, 4 and 5 respectively. mpMRI missed 19.4% of PCa, of these 66.7% was Gleason 6. 50% patients on active surveillance had disease upstaged. For csPCa detection, mpMRI had a sensitivity of 87%, specificity of 86.1%, positive predictive value of 13.1% and negative predictive value of 99.6%. On multivariate analysis, age ($P < .001$), Indian race ($P = .007$) and prostate volume ($P < .001$) were statistically significant. The complication rate was low (acute urinary retention 4.9%, hematuria 9%, infection 0.8%) and mortality was zero.

Conclusion: mpMRI plays a major role in diagnosing csPCa. The higher the PI-RADS, the more csPCa was detected. Our experience with cognitive MRI-US fusion template-guided TPB yield a consistent result with other studies in terms of overall PCa detection, rate of low-grade PCa in 'missed' lesions in mpMRI, correlation between PCa detection and larger prostate size and comparable diagnostic accuracy of mpMRI. We also reported a high diagnostic accuracy of mpMRI in PCa detection and low complication rates of TPB.

Keywords: Prostate cancer; multi-parametric magnetic resonance imaging; transperineal biopsy of prostate.

1. INTRODUCTION

Trans-rectal ultrasound-guided biopsy of prostate (TRUS-biopsy) has been the gold standard investigation in prostate cancer (PCa) detection for many decades. However, there were issues of low cancer detection rate, under-sampling, over-diagnosis and over-treatment of clinically insignificant prostate cancer (cisPCa) [1-5]. It was reported that PCa detection rate was 40 – 50% from the initial TRUS-biopsy [6]. The standard 12-cores TRUS-biopsy could still miss PCa in up to one-third of patients [7]. In a repeat TRUS-biopsy setting, the cancer detection rate was even lower [8-10].

Multi-parametric MRI (mpMRI) has played significant role in detection of clinically significant PCa (csPCa). The location of the suspicious lesions (SL) in prostate detected on mpMRI allows targeted biopsy, thereby avoiding under-sampling. It's high sensitivity and negative predictive value in detecting csPCa was reported in PROMIS trial [11]. If mpMRI is used as triage test, a prostate biopsy could be avoided in 27% of patients.

Transperineal prostate biopsy (TPB) approach has gained popularity due to its advantages in improving PCa detection and negligible risk of infection compared to TRUS-biopsy. TPB is performed via cognitive-fusion, software-assisted fusion or in-bore biopsy. The cognitive-fusion method is a relatively simple technique; the location of SL seen on mpMRI images is visually registered on a real-time TRUS image.

In this study, we report the outcomes of cognitive mpMRI-US fusion template-guided TPB

performed in a single tertiary institution. We aim to determine the detection rates of PCa from this technique, to assess diagnostic accuracy of mpMRI, to evaluate predictive factors for PCa detection and to report TPB complications.

2. MATERIAL AND METHODS

2.1 Patients

Between April 2017 and December 2019, 123 patients underwent cognitive mpMRI-US fusion template-guided TPB at Department of Urology, Kuala Lumpur General Hospital, Malaysia. One patient's record was not found and were excluded, resulting in 122 patients for final analysis. Inclusion criteria was clinical suspicious of PCa (raised PSA \pm abnormal digital rectal examination) and positive mpMRI (PI-RADS 3-5). There were three groups of patients: repeat biopsy (who had prior negative TRUS biopsy), biopsy naïve and re-staging (patients on active surveillance for low risk PCa). Patients with history of radical treatment for PCa, use of androgen deprivation therapy and PSA >100 ng/mL were excluded. All data were collected retrospectively from patient records.

2.2 Multi-parametric MRI protocol

The mpMRI was performed using Phillips Ingenia 1.5 Tesla without endo-rectal coil, utilizing T2-weighted, diffusion-weighted and dynamic contrast-enhanced (DCE) imaging. Our institution mpMRI protocol involved T2WI acquisition as the first sequence followed by multi-shot echo-planar diffusion-weighted (DW) sequence and 3 orthogonal diffusion gradients. Then, contrast-enhanced MRI was performed with intravenous

infusion of 10 ml of Gadovist. Post-contrast T1WI and DCE images were acquired. The mpMRI sequences were systematically reviewed by trained and experienced uro-radiologists. SL were reported according to the standardized Prostate Imaging Reporting and Data System (PI-RADS) version 2 score. Location of SL were described by dividing the prostate gland into base, mid and apical regions and were drawn on prostate MRI template map (Fig. 1). Prior to TPB, all cases were discussed in a multi-disciplinary meeting involving urologists and uro-radiologists. In case of mpMRI which was done in other centers, the findings and PI-RADS score were re-confirmed during the meeting.

TPB was performed by either urology consultants or trainees (under direct supervision by consultant) by cognitive-fusion technique. A modified Barzell zones was used as a template mapping biopsies. Both systematic and targeted biopsies were undertaken; 2 cores from each zones and at least 4 cores respectively. A schema representing the correspondence of Barzell zones and SL on mpMRI regions is illustrated in Fig. 1. The biopsy cores were then examined by an experienced uro-pathologist and any cancer detected was graded according to the Gleason scoring system. Patients were discharged the next day.

2.3 Trans-perineal Prostate Biopsy (TPB) Technique

All patients were electively admitted a day before the procedure and pre-operative urine sample was collected to rule out infection. Only a stat dose of intravenous ciprofloxacin 400 mg was given just before the TPB. After informed consent, the procedure was performed under spinal anesthesia and dorsal lithotomy position.

2.4 Statistical Analysis

Data regarding baseline patient characteristics, PSA, previous TRUS-biopsy, characteristics of SL on mpMRI, final TPB histopathology results, total number of biopsy cores taken and post-operative complications were recorded and collected. The SL detected on mpMRI was considered positive for PCa if the histopathology biopsy result of the corresponding Barzell zones was positive for PCa (true positive result).

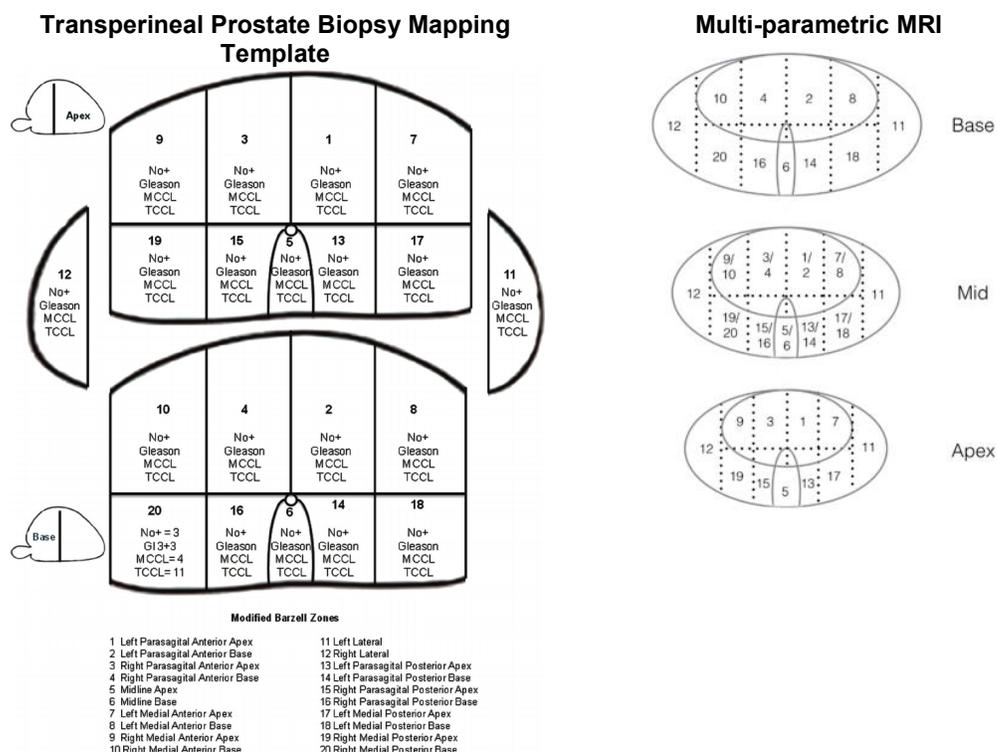


Fig. 1. Schema illustrating the modified Barzell zones (20 zones) from template mapping biopsy (left) to the corresponding regions on mpMRI (right)
 MCCL: maximum cancer core length; mpMRI: multi-parametric MRI.

If there was no PCa on that corresponding Barzell zones, the SL was considered negative (false positive result). Likewise, if there was no SL on other mpMRI regions which was matched to negative histopathology result of that corresponding Barzell zones, it was considered negative (true negative result). All collected data were entered into Statistical Package for the Social Sciences (SPSS®) version 22.0 (SPSS Inc., IBM Corp., Armonk, NY, USA) for statistical analyses. csPCa was defined as Gleason score $\geq 3+4$ and cisPCa was defined as Gleason score 3+3. A sensitivity and specificity analysis were performed with receiver operator statistics, comparing the mpMRI to TPB as reference test. A regression analysis of mpMRI characteristics was used as independent variables comparing the TPB results. P value = .05 was considered significant.

3. RESULTS

3.1 Descriptive Statistics

A total of 122 patients with positive mpMRI findings underwent cognitive mpMRI-US fusion template-guided TPB from April 2017 until December 2019. Table 1 and 2 show the baseline characteristics of patients and

suspicious lesions detected on mpMRI respectively. The mean age was 66.0 years (SD = 6.0), mean PSA was 15.5 ng/mL (SD = 15.8) and mean PSAD was 0.3 (SD = 0.2). Most of the patients enrolled were Chinese (54.1%), followed by Malay (38.5%), Indian (4.9%) and Others (2.5%). Repeat biopsy group comprised 70.5% of study populations, whereas biopsy naïve and re-staging groups were 21.3% and 8.2% respectively. Most patients had prostate volume ≥ 50 cm³ (59%) and mean number of biopsy cores was 56.6 (SD = 20.7). There was a total of 330 suspicious lesions (SL) detected on mpMRI which were reported as PI-RADS 3 (42.1%), 4 (31.8%) and 5 (20.3%). Most of SL was located at transitional zone of prostate (65.7%) and the rest was at peripheral zone (34.3%).

3.2 Cancer Detection

Overall, PCa was diagnosed in 53/122 (43.4%) patients, while 30/122 patients (24.6%) had csPCa (Table 3). PCa detection was higher in repeat biopsy group (30/53, 56.6%) followed by biopsy naïve (17/53, 32.1%) and re-staging (6/53, 11.3%) groups. Similarly, more csPCa was found in repeat biopsy group (16/53, 30.2%) compared to biopsy naïve (9/53, 17.0%) and re-staging groups (5/53, 9.4%). On the other hand,

Table 1. Baseline characteristics of patients

Patient characteristics (n = 122 patients)	Total, n (%)
Mean age, years (SD)	66.0 (6.0)
Race	
Chinese	66 (54.1)
Malay	47 (38.5)
Indian	6 (4.9)
Others	3 (2.5)
Mean PSA, ng/mL (SD)	15.5 (15.8)
Mean PSAD (SD)	0.3 (0.2)
PSA range, ng/mL	
< 4	3 (2.5)
4 – 10	61 (50.0)
11 – 20	36 (29.5)
21 – 30	11 (9.0)
31 – 40	4 (3.3)
> 40	7 (5.7)
Abnormal DRE	26 (21.5)
Mean prostate volume, cm ³ (SD)	68.2 (36.4)
< 50 cm ³	48 (39.3)
≥ 50 cm ³	74 (60.7)
Patient subgroups	
Repeat biopsy (prior negative TRUS biopsy)	86 (70.5)
Biopsy naïve	26 (21.3)
Re-staging (for active surveillance)	10 (8.2)

SD, standard deviation; PSA, prostate specific antigen; DRE, digital rectal examination; TRUS, trans-rectal ultrasound

Table 2. Baseline characteristics of suspicious lesions detected on mpMRI

Suspicious lesion characteristics (n = 330)	
Location	
Peripheral zone	113 (34.2)
Transitional zone	217 (65.8)
PI-RADS category	
3	139 (42.1)
4	105 (31.8)
5	67 (20.3)
None	19 (5.8)

mpMRI, multi-parametric magnetic resonance imaging; PI-RADS, prostate imaging reporting and data system.

Table 3. Prostate cancer detection from transperineal prostate biopsy, per-patient analysis (n = 122 patients)

Result	Total, n (%)
Detection rate	
Overall PCa (any GS)	53 (43.4)
csPCa (GS \geq 3+4)	30 (24.6)
Detection by patient subgroups	
Repeat biopsy	
No cancer	56 (65.1)
GS 6	14 (16.3)
GS 3+4	9 (10.5)
GS 4+3	2 (2.3)
GS 8	4 (4.7)
GS 9	1 (1.2)
Biopsy naïve	
No cancer	9 (34.6)
GS 6	8 (30.8)
GS 3+4	3 (11.5)
GS 4+3	1 (3.8)
GS 8	3 (11.5)
GS 9	2 (7.7)
Re-staging	
No cancer	4 (40.0)
GS 6	1 (10.0)
GS 3+4	4 (40.0)
GS 4+3	1 (10.0)
GS 8	0 (0.0)
GS 9	0 (0.0)

PCa, prostate cancer; csPCa, clinically significant prostate cancer; GS, gleason score

50% of men on active surveillance who underwent re-staging biopsy had disease upstaged (from Gleason 3+3 upstaged to Gleason \geq 3+4).

In order to correlate the PI-RADS with PCa Gleason score, per-lesion analysis was performed. Of 330 SL detected by mpMRI, 93 lesions (28.7%) harboured PCa. Fig. 2 shows the distribution of PCa Gleason score stratified by PI-RADS. As PI-RADS score increased, more csPCa was detected. Of PCa detected in each PI-RADS categories, the detection rate of csPCa for PI-RADS 3, 4 and 5 was 7/16 (43.8%), 17/35 (48.6%) and 16/24 (66.7%) respectively (P <

.001). Among 93 PCa lesions detected by TPB, a total of 18 PCa foci (19.4%) were not picked up by mpMRI. However, a majority of these 'missed' PCa (66.7%) from mpMRI were cisPCa (Gleason 6) and only 2 lesions were high grade PCa (Gleason 8).

In per-lesion analysis, higher grade PCa was found in higher PSA level (Fig. 3). In PSA range of 4-10 ng/mL, most PCa detected was cisPCa (GS 6, 36/50, 72.0%) and the rest was csPCa (14/50, 28.0%). However, the opposite trend of both cisPCa and csPCa was observed in higher PSA groups. The percentage of csPCa was higher as PSA increases (70.4%, 75.0%, 75.0%

and 100% in PSA groups of 11-20, 21-30, 31-40 and >40 ng/mL respectively). In PSA group of >40 ng/mL, there was none cisPCa detected.

volume was divided into 2 groups of <50 cm³ and >50 cm³. There was a significant difference in terms of PCa detection between the two groups, where there were 65% positive biopsy rates in prostate volume of <50 cm³ compared to 29% in prostate volume of >50 cm³ (P < .001).

Analysis of PCa detection by prostate gland volume was performed (Fig. 4). Prostate gland

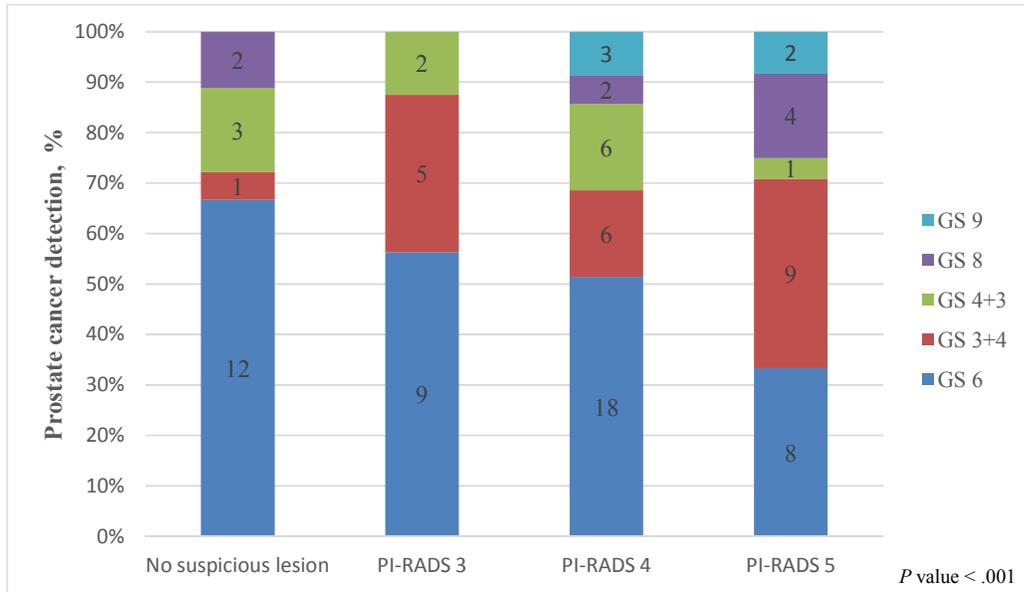


Fig. 2. Distribution of PCa Gleason score by PI-RADS score (n = 93 lesions)

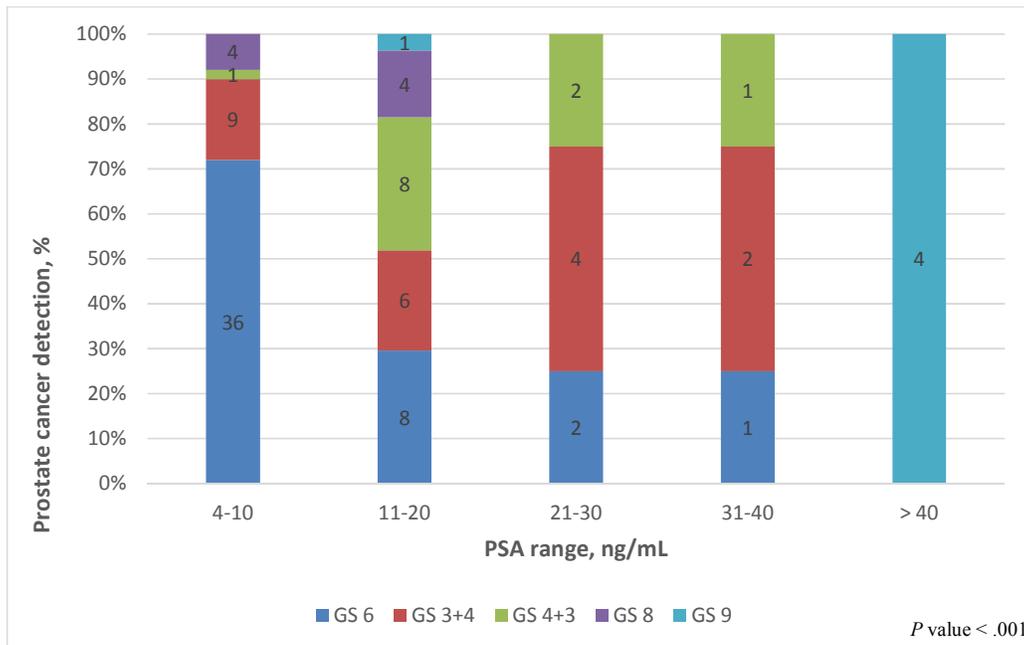


Fig. 3. Distribution of PCa detection by PSA categories, per-lesion analysis (n = 93 lesions)

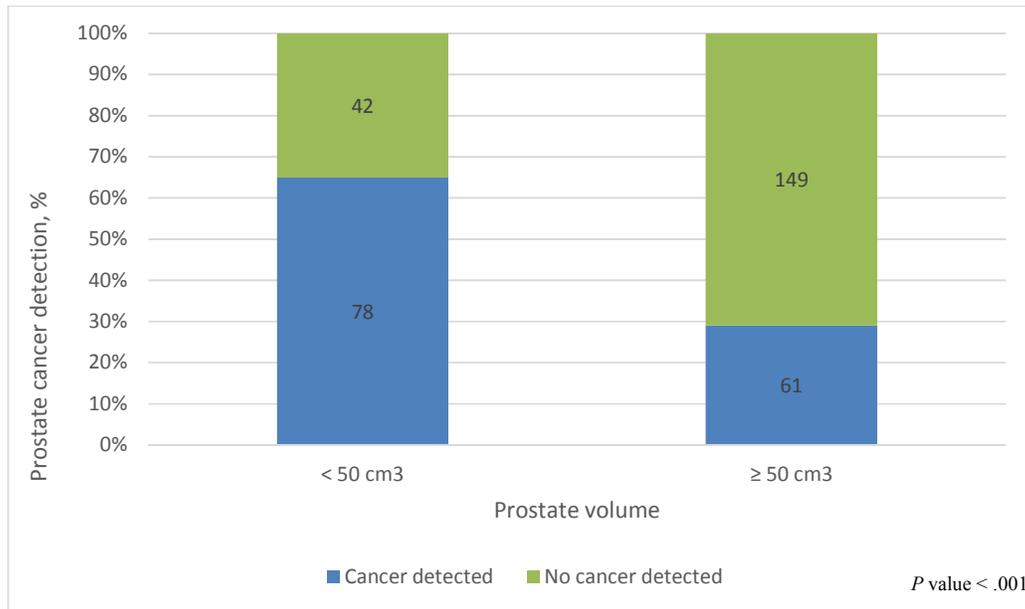


Fig. 4. Distribution of PCa detection by prostate volume, per-lesion analysis (n = 330 lesions)

Table 4. The regression analysis of univariate and multivariate analysis of transperineal prostate biopsy outcome

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	AOR	95% CI	P value
Age	0.92	0.87-0.96	< .001	0.84	0.79-0.89	< .001
Race			.004			.02
Malay	Ref					
Chinese	0.59	0.37-0.97		0.73	0.39-1.36	Indian .007
Indian	5.35	1.18-24.24		12.79	2.00-81.71	
Others	0.24	0.04-1.28		0.87	0.08-10.08	
PSA	0.99	0.98-1.01	.34	-	-	-
DRE						
Normal	Ref		.62			
Abnormal	1.15	0.67-1.97				
Prostate volume	1.04	1.03-1.05	< .001	1.04	1.03-1.06	< .001
PI-RADS			< .001			.07
No cancer	Ref					
3	49.08	6.34-380.27		>1000	-	
4	19.00	2.45-147.40		>1000	-	
5	20.19	2.55-159.67		>1000	-	
Location of SL			.63			
Base	Ref			-	-	-
Mid	1.08	0.60-1.95		-	-	-
Apex	0.94	0.47-1.88		-	-	-
Apex-Mid	0.96	0.36-2.56		-	-	-
Mid-Base	0.42	0.15-1.19		-	-	-
Base-Apex	>1000	-		-	-	-
SL size	0.99	0.90-1.09	.84	-	-	-

PSA, prostate specific antigen; DRE, digital rectal examination; PI-RADS, prostate imaging reporting and data system; SL, suspicious lesion; OR, odds ratio; AOR, adjusted odds ratio; CI, confidence interval

3.3 Diagnostic Accuracy of mpMRI in Prostate Cancer Detection

The mpMRI findings were compared to TPB result for overall PCa (of any Gleason) and csPCa detection. The TPB was considered the reference standard. For overall PCa detection, the sensitivity, positive predictive value (PPV), specificity and negative predictive value (NPV) of mpMRI were 81.7%, 24.8%, 87.7% and 99% respectively. For csPCa detection, the sensitivity, positive predictive value (PPV), specificity and negative predictive value (NPV) of mpMRI were 87%, 13.1%, 86.1% and 99.6% respectively. The area under the curve reported a value of 0.847, indicating usefulness of mpMRI in PCa detection.

3.4 Regression Analysis

Table 4 shows the regression analysis performed for the outcome of positive TPB result compared to negative result. Independent variables measured were age, race, PSA, abnormal DRE, prostate volume, PI-RADS score, location and size of SL. These variables showed a good fit model (Hosmer and Lemeshow 0.83). In univariate analysis, age, race, prostate volume and PI-RADS score were statistically significant ($P \leq .30$). In multivariate analysis, age, race (Indian) and prostate volume were statistically significant and PI-RADS score was a confounder. When age increased by 0.84 (95% CI: 0.79-0.89), it was more likely that SL was a malignant ($P < .001$). Indian race was 12.79 (95% CI: 2.00-81.71) times more likely to have PCa compared to Malays ($P = .02$ for race and $P = .007$ for Indian). If prostate volume increase by 1.04 (95% CI: 1.03-1.06), it was most likely to harbour PCa.

3.5 Complication Post TPB

We reported a low overall complication rate post TPB (Table 5). 11 patients had hematuria post TPB (9.0%); 8 patients resolved with bladder irrigation while the other 3 patients underwent emergency clot evacuation under spinal anesthesia. These patients had larger prostate gland and more biopsy cores taken; the mean prostate volume was 75.6 cm³ and the mean cores of 61.5 in hematuria cases, while it was 103.3 cm³ prostate and mean cores of 74.7 in clot evacuation cases. The 0.8% infection rate referred to a case where a patient was admitted to intensive care unit for urosepsis a month post TPB. No mortality was reported in this study.

Table 5. Complication rate post transperineal prostate biopsy

Complication	n (%)
Nil	104 (85.2)
AUR	6 (4.9)
Infection	1 (0.8)
Hematuria	11 (9.0)
Clavien-Dindo grade	
1	117 (95.9)
2	0
3	4 (3.3)
4	1 (0.8)

AUR, acute urinary retention

4. DISCUSSIONS

The present study is the first to report the outcomes of mpMRI-US cognitive fusion template-guided TPB performed in a tertiary hospital in Malaysia. This study aimed to evaluate the overall PCa and csPCa detection rate, mpMRI performance in diagnosing PCa and complication rate post TPB.

4.1 Prostate Cancer Detection

In the per-patient analysis, we reported an overall PCa (of any Gleason) and csPCa detection rate of 43.4% and 24.6% respectively. This was consistent with some studies on MRI fusion TPB, but other studies notably reported higher detection rate (Table 6). For example, the reported higher detection rate of both overall PCa (83.2%) and csPCa (54.7%) by Gorin et al. [12] could be attributed to higher inclusion number of patients on active surveillance (41.1%, as compared to 8% in our study), whom PCa was already present before study enrolment. In addition, the prostate volume was smaller in their study (36 cm³ compared to 68 cm³ in our study), which had been shown in multiple studies that more PCa was detected in smaller prostate gland. Similarly, Valerio et al. [13] reported higher percentage of patient on active surveillance (32%) and lower prostate volume (38 cm³) which could have resulted in higher PCa detection rate of 64% compared to our study. Furthermore, this study recruited higher Likert scale 4 and 5 (35% and 31% respectively, which correspond to higher grade of PCa detected) compared to only 31.8% PI-RADS 4 and 20.3% PI-RADS 5 in our study. Although Likert scale and PI-RADS performed well in csPCa detection, Likert scale had been shown superior to PI-RADS in terms of higher area under receiver-operating characteristics (ROC) curve [14]. We

applied PI-RADS in the interpretation of mpMRI in our study as it has shorter learning curve.

Despite higher detection rate in those 2 studies, the finding of more csPCa detected from higher PI-RADS score (4 and 5) from present study was consistent with all studies. The higher the PI-RADS score, the lesser the cisPCa and the more the csPCa were diagnosed. 11/13 lesions (84.6%) which harbour Gleason 8 and 9 PCa were reported as PI-RADS 4 and 5, indicating the superior performance of mpMRI in detecting higher grade of csPCa.

In current study, we found that 18/93 lesions (19.4%) harbouring PCa was not detected initially by mpMRI. Of these, majority of 'missed' PCa (12 lesions or 66.7%) were of Gleason 6 which is clinically insignificant. This was concordant with other studies [15-17]. In a study by Tan N et al. [16] which compared MRI of 122 patients with whole-mount histopathology from prostatectomy, about 53.3% cancer foci was

missed but 75.2% of these were low-grade PCa. Similarly, De Visschere PJ et al. [17] reported that 67.7% of 'missed' PCa were low-grade. In Fig. 2, the 3 'missed' lesions with Gleason 4+3 derived from a repeat biopsy (from the same location) of a patient who was on active surveillance for Gleason 3+3 PCa, where the initial mpMRI did not pick up the lesions. The remaining 2 'missed' lesions (which came out as Gleason 8) derived from a patient, whom mpMRI was retrospectively reviewed again and we concluded that these lesions either could not be seen or if were present, the lesions were too small to be characterized. Hence this reflected the spatial resolution limitations of mpMRI. As Tan N et al. [16] reported, the mpMRI sensitivity for subcentimeter lesion was significantly lower than that of larger lesion of >1 cm (18.9% vs 81.1%).

In subgroup analysis, among 10 patients on active surveillance who underwent re-staging biopsy, 5 (50%) had disease upstaged from

Table 6. Comparison with other studies on MRI fusion TPB

Study	Nature of study	Sample size	PCa DR	csPCa DR
Kasivisvanathan et al. [20]	Retrospective. Cognitive MRI fusion TPB.	182		57%
Kuru et al. [31]	Retrospective. TRUS biopsy, saturation TPB or MRI/TRUS fusion TPB	383 with prior negative TRUS biopsy	44.5%	
Dekalo et al. [32]	Retrospective. Cognitive MRI fusion TPB.	114 with prior negative TRUS biopsy and biopsy naïve	45%	35%
Otti et al. [33]	Retrospective. Cognitive MRI fusion TRUS and TPB.	1023 biopsy naïve 792 biopsied (106 were TPB)	53%	37%
Gorin et al. [12]	Retrospective and prospective. Cognitive MRI fusion TPB.	95 124 MRI lesions	83.2%	54.7%
Kasivisvanathan et al. [34]	RCT, non-inferior trial MRI-targeted vs TRUS biopsy	500		MRI-targeted: 38% TRUS biopsy: 26%
Valerio et al. [13]	Prospective. MRI cognitive vs software-based fusion targeted biopsy	50	Cognitive fusion: 64% Software-based fusion: 68%	
Gayet et al. [35]	Systemic review of prospective, non-randomized studies. Various MRI/US fusion biopsy platform.	2626 (11 studies)	33.7-79.5%	35.7-71.8%

PCa: prostate cancer; csPCa: clinically significant prostate cancer; DR: detection rate; MRI: magnetic resonance imaging; TPB: transperineal prostate biopsy; TRUS: trans-rectal ultrasound; RCT: randomized controlled trial

Gleason 6 to Gleason $\geq 3+4$. Others reported rate between 21 – 71% [18-20]. This would suggest that mpMRI should be performed prior confirmatory prostate biopsy to accurately characterize the PCa, further supporting the superior performance accuracy of mpMRI in csPCa detection. Consequently, management of localized PCa can be optimized by precluding more patients from continuing the active surveillance protocol. The number of patients on active surveillance included in present study was rather small as mpMRI was not incorporated yet in our active surveillance protocol at that time. Although this data may not be significant, we believe that with more emerging evidence of usefulness of mpMRI in active surveillance, this is becoming a standard in our protocol.

The inverse relationship between PCa detection and larger prostate size had been documented in many studies [21-27]. The result of current study was concordant with some studies. In a prospective study of TPB involving larger cohort of 409 patients, Symons et al. [26] reported a significantly lower detection rate of PCa in larger prostates $>50 \text{ cm}^3$ compared to $<50 \text{ cm}^3$ (38.3 vs 65.2%). De Gorski et al. [27] found 34% PCa detection rate in $>55 \text{ cm}^3$ prostate as compared to 77% in $<30 \text{ cm}^3$ prostate. It was hypothesized that this inverse relationship relates to histo-anatomical changes to PZ (where PCa generally originates from) as a result of compression by BPH in TZ and hence may explain the low incidence of PCa detection in larger prostate [28]. Although 65.8% of PCa lesions were detected from TZ in current study, we could not identify the reason for this finding.

4.2 Diagnostic Test Analysis of mpMRI

For overall PCa detection, the present study revealed a comparable diagnostic accuracy of mpMRI with other studies. In a recent meta-analysis by Woo S et al. [29] which evaluated the updated PI-RADS version 2, a pooled sensitivity of 89% and specificity of 73% was demonstrated. As for the diagnostic accuracy for csPCa detection, the present study findings were also consistent with other studies [20,30].

4.3 Limitations

First, our study was a retrospective, non-randomized study conducted at a single institution. Patients included were those who were referred from other hospitals and hence potential selection bias. Furthermore, there was no blinding on radiologists and pathologists.

Second, patients with negative mpMRI findings were excluded from this study. This reflects our local practice whereby shared decision making between patient and clinician is made that these patients are followed up rather than offered biopsy immediately. As mpMRI has high NPV in ruling out csPCa, over-diagnosis and over-treatment of cisPCa can be avoided. In addition, these patients would not be exposed to unnecessary risk of general anesthesia when undergoing TPB.

Third, there was potential interpretation and sampling error. This could be attributed to inter-reader variability for MRI interpretation and multiple operators of varied experiences in performing TPB. In order to reduce this problem, multidisciplinary meeting between urologists and uro-radiologists was routinely conducted prior to TPB. Urologists experienced in performing TPB were in theatre to supervise the junior doctors during the procedure. In the future, dedicated radiologist and facilities will likely improve outcome in our local institution.

5. CONCLUSION

mpMRI plays a major role in diagnosing csPCa. The higher the PI-RADS, the more csPCa was detected. Our experience with cognitive MRI-US fusion template-guided TPB yield a consistent result with other studies in terms of overall PCa detection, rate of low-grade PCa in 'missed' lesions in mpMRI, correlation between PCa detection and larger prostate size and comparable diagnostic accuracy of mpMRI. We also reported a high diagnostic accuracy of mpMRI in PCa detection and low complication rates of TPB.

ETHICAL APPROVAL

The study protocol and ethics had been approved by Medical Research and Ethics Committee (National Medical Research Register ID NMRR-18-1092-41548).

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Bangma CH, Roemeling S, Shroder FH. Overdiagnosis and overtreatment of early detected prostate cancer. *World J Urol.* 2007;25: 3-9.
2. Bjurlin MA, Taneja SS. Standards for prostate biopsy. *Curr Opin Urol.* 2014;24(2):155-161. doi:10.1097/MOU.0000000000000031
3. Serefoglu EC, Altinova S, Ugras NS, Akincioglu E, Asil E, Balbay MD. How reliable is 12-core prostate biopsy procedure in the detection of prostate cancer? *Canadian Urological Association journal = Journal de l'Association des urologues du Canada.* 2012:1–6
4. Resnick MJ, Lee DJ, Magerfleisch L, Vanarsdalen KN, Tomaszewski JE, Wein AJ, et al. Repeat prostate biopsy and the incremental risk of clinically insignificant prostate cancer. *Urology.* 2011;77:548–52
5. Bjurlin MA, Carter HB, Schellhammer P, Cookson MS, Gomella LG, Troyer D, et al. Optimization of initial prostate biopsy in clinical practice: sampling, labeling and specimen processing. *J Urol.* 2013;189:2039–46. Literature review and summary of the American Urological Association White paper on the optimal biopsy technique and specimen handling
6. Serag H, Banerjee S, Saeb-Parsy K, Irving S, Wright K, Stearn S et al. Risk profiles of prostate cancers identified from UK primary care using national referral guidelines. *Br J Cancer.* 2012;106:436-439.
7. Scattoni V, Zlotta A, Montironi R, Schulman C, Rigatti P, Montorsi F. Extended and saturation prostatic biopsy in the diagnosis and characterization of prostate cancer: A critical analysis of the literature. *Eur Urol.* 2007;52:1309-1322.
8. Djavan B, Ravery V, Zlotta A, Dobronski P, Dobrovits M, Fakhari M et al. Prospective evaluation of prostate cancer detected on biopsies 1,2,3 and 4: when should we stop? *J Urol.* 2001;166:1679-1683.
9. Yuasa T, Tsuchiya N, Kumazawa T, Inoue T, Narita S, Saito M et al. Characterization of prostate cancer detected at repeat biopsy. *BMC Urol.* 2008;8:14.
10. Aganovic D, Prcic A, Kulovac B, Hadziosmanovic O. Prostate cancer detection rate and the importance of premalignant lesion in rebiopsy. *Med Arh.* 2011;65:109-112.
11. Ahmed HU, Bosaily AE, Brown LC, Gabe R, Kaplan R, Parmar MK et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet.* 2017 Feb 25;389:815-822.
12. Gorin MA, Meyer AR, Zimmerman M, Harb R, Joice GA, Schwen ZR et al. Transperineal prostate biopsy with cognitive magnetic resonance imaging/biplanar ultrasound fusion: description of technique and early results. *World J Urol.* 2020;38:1943-1949.
13. Valerio M, McCartan N, Freeman A, Punwani S, Emberton M, Ahmed HU. Visually directed vs. software-based targeted biopsy compared to transperineal template mapping biopsy in the detection of clinically significant prostate cancer. *Urol Oncol.* 2015;33:e9-16.
14. Khoo CC, Eldred-Evans D, Peters M, Bertonecchi Tanaka M, Noureldin M, Miah S et al. Likert vs PI-RADS v2: A comparison of two radiological scoring systems for detection of clinically significant prostate cancer. *BJU Int.* 2020 Jan;125(1):49-55. Epub 2019 Nov 1. PMID:31599113
15. Rosenkrantz AB, Mendrinos S, Babb JS, Taneja SS. Prostate cancer foci detected on multiparametric magnetic resonance imaging are histologically distinct from those not detected. *J Urol.* 2012;187(6):2032-2038.
16. Tan N, Margolis DJ, Lu DY, King KG, Huang J, Reiter RE et al. Characteristics of detected and missed prostate cancer foci on 3-T Multiparametric MRI Using an *Endorectal coil* Correlated With Whole-Mount Thin-Section Histopathology. *AJR Am J Roentgenol.* 2015;205(1):W87-W92.
17. De Visschere PJ, Naesens L, Libbrecht L, Van Praet C, Lumen N, Fonteyne V et al. What kind of prostate cancers do we miss on multiparametric magnetic resonance imaging? *Eur Radiol.* 2016;26(4):1098-1107.
18. Benelli A, Vaccaro C, Guzzo S, Nedbal C, Varca V, Gregori A. The role of MRI/TRUS fusion biopsy in the diagnosis of clinically significant prostate cancer. *Ther Adv Urol.* 2020;12:1756287220916613.
19. Taira AV, Merrick GS, Bennett A, Andreini H, Taubenslag W, Galbreath RW et al. Transperineal template-guided mapping biopsy as a staging procedure to select patients best suited for active surveillance. *Am J Clin Oncol.* 2013;36:116-120.

20. Kasivisvanathan V, Dufour R, Moore CM, Ahmed HU, Abd-Alazeez M, Charman SC et al. Transperineal magnetic resonance image targeted prostate biopsy versus transperineal template prostate biopsy in the detection of clinically significant prostate cancer. *J Urol.* 2013;189:860–866.
21. Uzzo RG, Wei JT, Waldbaum RS, Perlmutter AP, Byrne JC and Vaughan ED Jr. The influence of prostate size on cancer detection. *Urology.* 1995;46:831–836.
22. Karakiewicz PI, Bazinet M, Aprikian AG, Trudel C, Aronson S, Nachabe M et al. Outcome of sextant biopsy according to gland volume. *Urology.* 1997;49:55–59.
23. Ung JO, San Francisco IF, Regan MM, DeWolf WC, Olumi AF. The relationship of prostate gland volume to extended needle biopsy on prostate cancer detection. *J Urol.* 2003 Jan;169(1):130-5.
24. Ficarra V, Novella G, Novara G, Galfano A, Pea M, Martignoni G et al. The potential impact of prostate volume in the planning of optimal number of cores in the systematic transperineal prostate biopsy. *Eur Urol.* 2005;48(6):932-7.
25. Al-Khalil S, Ibilibor C, Cammack JT, de Riese W. Association of prostate volume with incidence and aggressiveness of prostate cancer. *Res Rep Urol.* 2016;8:201-205.
26. Symons JL, Huo A, Yuen CL, Haynes A-M, Matthews J, Sutherland RL et al. Transperineal biopsy. *BJU Int.* 112:585-593.
27. de Gorski A, Rouprêt M, Peyronnet B, Le Cossec C, Granger B, Comperat E et al. Accuracy of magnetic resonance imaging/ultrasound fusion targeted biopsies to diagnose clinically significant prostate cancer in enlarged compared to smaller prostates. *J Urol.* 2015 Sep;194(3):669-73.
28. Holder K, Galvan B, Sakya J, Frost J, de Riese W. Anatomical changes of the peripheral zone depending on benign prostatic hyperplasia size and their potential clinical implications: a review for clinicians. *Urol Pract.* 2021;8(2):259–263. DOI:10.1097/UPJ.000000000000201
29. Woo S, Suh CH, Kim SY, Cho JY, Kim SH. Diagnostic performance of prostate imaging reporting and data system version 2 for detection of prostate cancer: A systematic review and diagnostic meta-analysis. *Eur Urol.* 2017;72(2):177-188.
30. JJ Fütterer, A Briganti, P De Visschere, Emberton M, Giannarini G, Kirkham A et al. Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. *Eur Urol.* 2015;68:1045-1053.
31. Kuru TH, Saeb-Parsy K, Cantiani A, Frey J, Lombardo R, Serrao E et al. Evolution of repeat prostate biopsy strategies incorporating transperineal and MRI-TRUS fusion techniques. *World J Urol.* 2014; 32(4):945-950.
32. Dekalo S, Matzkin H, Mabjeesh NJ. High cancer detection rate using cognitive fusion - targeted transperineal prostate biopsies. *Int Braz J Urol.* 2017;43(4):600-606.
33. Otti VC, Miller C, Powell RJ, Thomas RM and McGrath JS. The diagnostic accuracy of multiparametric magnetic resonance imaging before biopsy in the detection of prostate cancer. *BJU Int.* 2019;123:82-90.
34. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N Engl J Med.* 2018;378(19):1767-1777.
35. Gayet M, van der Aa A, Beerlage HP, Schrier BP, Mulders PF, Wijkstra H et al. The value of magnetic resonance imaging and ultrasonography (MRI/US)-fusion biopsy platforms in prostate cancer detection: a systematic review. *BJU Int.* 2016 Mar;117(3):392-400.

© 2021 Aziz and Manogran; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<https://www.sdiarticle4.com/review-history/76621>