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Comparison of Cognitive Registration Transrectal Ultrasound-Guided Targeted Biopsy of Prostate to Systematic 12-Core Biopsy: A Retrospective, Multicentre Study

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Abstract

Introduction: Prostate cancer (PCa) is the third most prevalent cancer among Malaysian males, often diagnosed at advanced stages, leading to suboptimal outcomes. While transrectal ultrasound-guided systematic biopsy (TRUS-SB) is the primary diagnostic method, prebiopsy multiparametric magnetic resonance imaging (mpMRI) is gaining popularity in identifying suspicious lesions. This study addresses the lack of comprehensive investigations into the efficacy of cognitive registration TRUS targeted biopsy (COG-TB) compared to conventional TRUS-SB, considering the resource limitations of the Malaysian healthcare system. **Materials and Methods:** A retrospective cohort study was conducted in two Malaysian healthcare facilities. 116 adult patients with a prostate-specific antigen (PSA) level of more than 4 ng/mL who underwent both COG-TB and TRUS-SB between October 2020 and March 2022 were included. Primary outcomes were cancer detection rate and histopathological outcomes, including Gleason score. **Results:** COG-TB showed a higher overall cancer detection rate (50%) compared to TRUS-SB (44%). Clinically significant cancer detection rates were similar between COG-TB and TRUS-SB (37.1%). Further analysis revealed that both COG-TB and TRUS-SB detected clinically significant cancer in 30.2% of patients, did not detect it in 56.0%, and had conflicting findings in 16 patients ($p < 0.001$). COG-TB detected more Gleason score 6 (15 versus 8) and Gleason score 8 (5 versus 3) cases than TRUS-SB. However, COG-TB also detected more insignificant prostate cancers (12.9%) compared to TRUS-SB (6.9%). **Conclusion:** COG-TB and TRUS-SB have comparable detection rates for clinically significant prostate cancer, with COG-TB showing a higher tendency to detect insignificant prostate cancer. Further studies comparing these methods are warranted.

Keywords

Prostate Cancer, Multiparametric MRI, Targeted Biopsy, Cognitive Fusion, Transrectal Ultrasound-Guided Biopsy

1. Introduction

Prostate cancer is a significant health concern in Malaysia, ranking as the third most prevalent cancer among males, with an incidence of 4189 cases in 2012-2016 [1]. Timely diagnosis and intervention are crucial for improving patient outcomes, as a substantial proportion of prostate cancer cases in Malaysia (approximately three-quarters) are identified at an advanced stage [2].

The current standard diagnostic approach for prostate cancer in Malaysia is the conventional transrectal ultrasound-guided 12-core systematic biopsy (TRUS-SB). However, this method has difficulty in conceptualising the region of interest during the biopsy, leading to the potential for sampling error [3]. Therefore, there is a growing interest in utilizing prebiopsy multiparametric magnetic resonance imaging (mpMRI) of the prostate to identify suspicious lesions before biopsy procedures [4]. Studies conducted in Europe and Asia have shown that targeted biopsy of these suspicious lesions leads to higher detection rates of clinically significant prostate cancer compared to the standard TRUS-SB [5]-[9]. Targeted biopsy also helps mitigate the over-diagnosis of clinically insignificant prostate cancer [5]-[9].

Targeted biopsy techniques include cognitive fusion, software fusion, or in-bore MRI targeted biopsy. Despite the potential benefits of mpMRI-guided targeted biopsy, including improved cancer detection rates and reduced over-diagnosis, its adoption in Malaysia has been limited. Cognitive registration transrectal ultrasound-guided targeted biopsy (COG-TB) is a cost-effective method where the TRUS operator mentally registers the lesion locations based on mpMRI images, requiring no additional equipment. To date, only one study, conducted at a single university hospital in Malaysia has assessed the efficacy of COG-TB versus the standard TRUS-SB [10].

Given the constraints in healthcare resources within the Malaysian context, there is a need for a more comprehensive investigation of the efficacy of prostate cancer detection using COG-TB compared to conventional TRUS-SB. Such investigations can provide valuable insights into the potential benefits and cost-effectiveness of adopting COG-TB as a standard practice for prostate cancer detection. The aim of this study is to evaluate the cancer detection rate between COG-TB and TRUS-SB methods, including clinically significant and insignificant prostate cancer.

2. Materials and Methods

2.1. Design, Setting, and Population

This retrospective cohort study was conducted in two healthcare facilities in Malaysia: Penang General Hospital, a government-funded hospital, and Georgetown Specialist Centre, a private hospital. The inclusion criteria included adult patients with a prostate-specific antigen, PSA level of more than 4 ng/mL, who underwent COG-TB and TRUS-SB prostate biopsy between 1st October 2020 and 31st March 2022 at these facilities. Patients already diagnosed with prostate cancer and/or on active surveillance protocol were excluded from the study.

2.2. Multiparametric MRI Protocol and Imaging Analysis

All patients enrolled in the study underwent multiparametric magnetic resonance imaging (mpMRI) using a 1.5T MRI scanner (Magnetom Aera, Siemens Healthineers, Erlangen, Germany). The imaging protocol adhered strictly to the standards outlined in the Prostate Imaging Reporting and Data System version 2.1 (PI-RADS v2.1) [11]. This protocol included T2-weighted imaging in three orthogonal planes, diffusion-weighted imaging with the subsequent computation of apparent diffusion coefficient (ADC) maps, acquisition of high b-value images (b > 1400 s/mm^2), and dynamic contrast-enhanced imaging [11]. The mpMRI images were interpreted by trained radiologists, who used the PI-RADS v2.1 scoring system to assess all detected lesions. Lesions were categorized as suspicious if they were assigned a PI-RADS score of 3 to 5. Additionally, all suspicious lesions detected on mpMRI were mapped onto a schematic interpretation report, which included a segmental model of the prostate with 38 sectors conforming to the PI-RADS v2.1 sector map.

In addition to the imaging findings, prostate-specific antigen density (PSAD) was calculated for each patient. PSAD was computed by dividing the serum prostate-specific antigen (PSA) level by the corresponding MRI-derived prostate volume. The MRI-derived prostate volume was measured by outlining the prostate gland on the imaging software and calculating its volume based on the provided dimensions. This calculation allows for a more accurate assessment of the PSA level relative to the size of the prostate gland, as it accounts for variations in prostate size among individuals [12].

2.3. Biopsy Procedure and Histopathology

Patients with suspicious findings on mpMRI underwent a two-step biopsy procedure. First, they received a mpMRI-targeted TRUS-guided prostate biopsy using 18-gauge needles with a sampling length of 22 mm, assisted by visual cognitive registration (COG-TB). Subsequently, they underwent a standard TRUS-SB prostate biopsy, also using 18-gauge needles with a sampling length of 22 mm. After undergoing the two-step biopsy procedure, biopsy samples were histopathologically analysed by pathologists. The samples were evaluated for the presence of prostate cancer and assigned a Gleason score based on the Gleason grading system.

2.4. Study Outcomes Assessed

The study's primary outcomes include the cancer detection rate (overall and clinically significant prostate cancer) between COG-TB and TRUS-SB methods. Histopathological outcomes, specifically the highest Gleason score obtained for the lesions biopsied, were also compared, where the clinically significant cancer is defined as a Gleason score equal to or more than seven. Secondary outcomes include the length of the cancer core biopsied and the PI-RADS scores.

2.5. Statistical Analyses

Data analyses were conducted using IBM® SPSS® Statistics Version 23. Patients' age, PSA levels, prostate volume in mpMRI, PSAD, and cancer core length were presented as median and interquartile ranges as it had skewed distribution based on Kolmogorov-Smirnov normality analysis. Meanwhile, the categorical data were reported in frequency and percentage (%). Median cancer core length and core percentage between the groups were compared using the Wilcoxon test (between COG-TB and TRUS-SB) and the Kruskal-Wallis test (between PI-RADS) as it was skewed, while the cancer detection rates were compared using the Chi-square test. Statistical significance was set at $p < 0.05$.

2.6. Ethical Approval

The study was conducted in accordance with the ethical standards of the Medical Research and Ethics Committee (NMRR-22-01406-NNL), Ministry of Health Malaysia, and the Declaration of Helsinki.

3. Results

3.1. Patient Characteristics

During the study period, 160 patients underwent prostate cancer screening, of whom 116 had both COG-TB and TRUS-SB and were included in data analysis. Patient characteristics and assessments were summarised in **Table 1**. Most patients were elderly with a median (IQR) age of 69.0 (11.0), where the majority (70.7%) had PSA ≥ 10 ng/mL. Imaging via mpMRI showed half had PI-RADS 3 category lesions (53.8%), while the remaining 29.9% and 15.4% had PI-RADS 4 and PI-RADS 5 lesions respectively. Half of them were found to have prostate cancer either via COG-TB or TRUS-SB method (53.4%).

Table 1. Characteristics of patients, PI-RADS assessment categories, and final pathology (N = 116).

Characteristics	n (%) or median (IQR)
Age (years old)	
Median (IQR)	69.0 (11.0)
Race	
Malay	5 (4.3)

Continued

Chinese	103 (88.8)
Indian	7 (6.0)
Others	1 (0.9)
PSA level (ng/mL)	
Median (IQR)	13.7 (11.7)
<10	34 (29.3)
≥10	82 (70.7)
Prostate volume in mpMRI	
Median (IQR)	54.5 (41.8)
PSAD	
Median (IQR)	0.24 (0.25)
Number of lesions on mpMRI	
1	29 (25.0)
2	40 (34.5)
3	38 (32.8)
4	9 (7.8)
PI-RADs assessment categories	
PI-RDAS 3	63 (53.8)
PI-RADS 4	35 (29.9)
PI-RADS 5	18 (15.4)
Cancer detection (overall)	
Yes	62 (53.4)
No	54 (46.6)
Cancer detection via COG-TB	
Yes	58 (50.0)
No	58 (50.0)
Cancer detection via TRUS-SB	
Yes	51 (44.0)
No	65 (56.0)

Categorical variables were presented as frequencies and percentages. Continuous variables were presented as median and interquartile range as they have a skewed distribution based on Kolmogorov-Smirnov normality analysis.

3.2. Primary Outcomes

The overall cancer detection rate of COG-TB was 50%, slightly higher than TRUS-SB (44%), while the detection rate of clinically significant cancer by both methods was similar (37.1%). In contrast, further analysis revealed significant differences in the cancer detection rate between the methods, as shown in Table 2. Forty-six (39.7%) patients were detected to have cancer, while 53 (45.7%) were found not to have cancer via both methods. The remaining 17 patients had contradicting findings between the methods, where only either method detected cancer ($p < 0.001$). Similarly, 35 (30.2%) patients were detected to have clinically significant cancer, while 65 (56.0%) were found not to have clinically significant cancer via both COG-TB and TRUS-SB methods. The remaining 16 patients had contradicting findings between the methods ($p < 0.001$). The histopathological findings defined by the Gleason scores are shown in Table 3. COG-TB detected more cases of Gleason score six (15 versus 8) and Gleason score 8 (5 versus 3) compared to the TRUS-SB method. Crucially, COG-TB was unable to detect two additional cases of Gleason score 10.

Table 2. Cancer detection rate between COG-TB and TRUS-SB biopsy methods (N = 116).

Cancer detection	**COG-TB, n (%)**		**p value**[a]
	Yes	**No**	
Overall cancer			
TRUS-SB, n (%)			
Yes	46 (39.7)	5 (4.3)	<0.001*
No	12 (10.3)	53 (45.7)	
Clinically significant cancer			
TRUS-SB, n (%)			
Yes	35 (30.2)	8 (6.9)	<0.001*
No	8 (6.9)	65 (56.0)	

[a]Chi-square test was conducted. Less than 20% of cells have an expected count of less than 5. Clinically significant cancer is defined as Gleason score ≥ 7. *$p < 0.05$ denotes statistical significance.

Table 3. Gleason scores from COG-TB and TRUS-SB biopsy methods (N = 116).

Highest Gleason Score	COG-TB	TRUS-SB
	n (%)	n (%)
No cancer/benign	57 (49.1)	65 (56.0)
PIN	1 (0.9)	0 (0.0)
3 + 3	15 (12.89)	8 (6.9)
3 + 4	19 (16.4)	20 (17.2)
4 + 3	15 (12.9)	14 (12.1)
4 + 4	5 (4.3)	3 (2.6)
4 + 5	0 (0.0)	0 (0.0)
5 + 5	4 (3.4)	6 (5.2)

3.3. Secondary Outcomes

The cancer core length biopsied via the COG-TB method was significantly shorter than that of the TRUS-SB method; median (IQR) 3.6 (5.5) versus 12.5 (5.), p value < 0.001. However, the cancer core percentages were comparable (35.0% versus 40.0%, p = 0.332). Sub-group analysis based on PI-RADS assessment categories is shown in **Table 4** for the total of 259 lesions biopsied from the 116 patients. The cancer detection rates were 17.5%, 60.7%, and 85.7% for PI-RADS 3, 4, and 5 lesions, respectively. Meanwhile, the median cancer core percentage were 40.0% (35.0), 40.0% (35.0), and 60.0% (35.0) for PI-RADS 3, 4, and 5 lesions, respectively, where PI-RADS 5 lesions have significantly higher percentages of cancer core compared to PI-RADS 3 and 4 (p < 0.001).

Table 4. Cancer detection rates and cancer core length based on the PI-RADS assessment categories for each lesion biopsied (N = 259).

Cancer detection rate	PI-RADS 3	PI-RADS 4	PI-RADS 5	Total	p value
	n (%)	n (%)	n (%)	n (%)	
Number of lesions	177 (68.3)	61 (23.6)	21 (8.1)	259 (100)	-
Overall cancer					
Yes	73 (41.2)	47 (77.0)	19 (90.5)	139 (53.7)	<0.001[a]*
No	104 (58.8)	14 (23.0)	2 (9.5)	120 (46.3)	
Clinically significant cancer					
Yes	31 (17.5)	37 (60.7)	18 (85.7)	86 (33.2)	<0.001[a]*
No	146 (82.5)	24 (39.3)	3 (14.3)	173 (66.8)	
Cancer core length (mm)					
Median (IQR)	3.5 (4.7)	4.0 (4.7)	5.4 (6.0)	3.7 (4.8)	<0.001[b]*
Cancer core percentage					
Median (IQR)	40.0 (35.0)	40.0 (40.0)	60.0 (35.0)	40.0 (40.0)	<0.001[b]*

[a]Chi-square test was conducted. Less than 20% cells have expected count less than 5. [b]Kruskal-Wallis test was conducted. Data was continuous with skewed distribution. Clinically significant cancer defined as Gleason score ≥ 7. *p < 0.05 denotes statistical significance.

4. Discussion

Despite mounting evidence recommending TB for those with positive mpMRI and PI-RADS score ≥ 3, TRUS-SB remains the standard for diagnosing PCa in Malaysia [13]. TB techniques may be in the form of cognitive fusion, software fusion or in-bore MRI targeted biopsy. The limited adoption of using the latter two targeted biopsy techniques is due to large costs involved and resource constraints in the Malaysian healthcare setting.

COG-TB involves the TRUS operator reviewing the mpMRI images and mentally registering the location of the lesions during the biopsy. As such, cognitive fusion biopsy of the prostate requires no additional equipment, making it a cost-effective and accessible option for targeted prostate biopsy. Current literature supports the efficacy of COG-TB, showing comparable results to more technologically advanced methods (software fusion or in-bore MRI targeted biopsy) [7] [9] [14].

This study is the first multicenter analysis comparing COG-TB and TRUS-SB in the northern region of Malaysia. Our study demonstrated that both TRUS-SB and COG-TB had a comparable detection rate for csPCa. This is consistent with the findings of other studies [7] [15] [16].

It is interesting to note that even though both TRUS-SB and COG-TB had a similar detection rate for csPCa, COG-TB detected a higher number of insignPCa. This finding contrasts with current literature in that COG-TB has been demonstrated to have a similar detection rate for csPCa with significantly fewer insignPCa [7] [9] [10] [13]. This discrepancy may be attributed to the heterogeneity of biopsy operators in our study, who ranged from urology trainees to specialists and consultants, each with varying levels of experience. Additionally, the radiologist in the study was common to both centers. If this radiologist overreported lower-level lesions as higher-level, it could account for the increased detection rate of clinically non-significant prostate cancer observed in the study. Nevertheless, the finding in our study did not reach statistical significance.

Although the highest yield of overall prostate cancer per percentage core was attained using COG-TB, these results were not statistically significant when compared to TRUS-SB. We would also like to report that our detection rate for csPCA according to PI-RADSv2.1 score is consistent with those reported by Oether and colleagues [17]. Also, higher PI-RADS categories were significantly associated with higher cancer detection rates ($p < 0.001$).

There are a few limitations in our study, of which the most important is the lack of radical prostatectomy specimens for accurate cancer characterization and analysis. Secondly, the retrospective nature of the study may have affected the accuracy of our analysis. The lack of standardization of cognitive fusion biopsy protocols could potentially affect subsequent cancer detection rates. Thirdly, the study cohort was small when compared to other relevant studies conducted overseas. Nevertheless, the study cohort of this study remains the largest of its kind in Malaysia. Finally, both biopsy techniques were performed in the same setting. The visible cognitive fusion biopsy track could have potentially influenced the urologist in systematic biopsy needle placements.

5. Conclusion

COG-TB and TRUS-SB have demonstrated comparable detection rates for clinically significant prostate cancer. However, COG-TB shows a higher tendency to detect insignificant prostate cancer compared to TRUS-SB. Despite this, notable discrepancies in cancer detection between the two methods indicate a need for further studies.

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Conflicts of Interest

The authors declare no competing interests.

References

[1] National Cancer Institute MoHM (2019) Malaysia National Cancer Registry Report (MNCR) 2012-2016. Ministry of Health Malaysia.

[2] Lim, J., Malek, R., Jr, S., Toh, C.C., Sundram, M., Woo, S.Y.Y., *et al.* (2021) Prostate Cancer in Multi-Ethnic Asian Men: Real-World Experience in the Malaysia Prostate Cancer (M-CaP) Study. *Cancer Medicine*, **10**, 8020-8028. https://doi.org/10.1002/cam4.4319

[3] Tyson, M.D., Arora, S.S., Scarpato, K.R. and Barocas, D. (2016) Magnetic Resonance-Ultrasound Fusion Prostate Biopsy in the Diagnosis of Prostate Cancer. *Urologic Oncology*: *Seminars and Original Investigations*, **34**, 326-332. https://doi.org/10.1016/j.urolonc.2016.03.005

[4] Lai, W., Wang, H., Liu, H., Park, B.K., Shen, S., Lin, T., *et al.* (2016) Cognitive MRI-TRUS Fusion-Targeted Prostate Biopsy According to PI-RADS Classification in Patients with Prior Negative Systematic Biopsy Results. *Journal of the Chinese Medical Association*, **79**, 618-624. https://doi.org/10.1016/j.jcma.2016.05.004

[5] Puech, P., Ouzzane, A., Gaillard, V., Betrouni, N., Renard, B., Villers, A., *et al.* (2014) Multiparametric MRI-Targeted TRUS Prostate Biopsies Using Visual Registration. *BioMed Research International*, **2014**, Article ID: 819360. https://doi.org/10.1155/2014/819360

[6] Puech, P., Rouvière, O., Renard-Penna, R., Villers, A., Devos, P., Colombel, M., *et al.* (2013) Prostate Cancer Diagnosis: Multiparametric MR-Targeted Biopsy with Cognitive and Transrectal US-MR Fusion Guidance versus Systematic Biopsy—Prospective Multicenter Study. *Radiology*, **268**, 461-469. https://doi.org/10.1148/radiol.13121501

[7] van der Leest, M., Cornel, E., Israël, B., Hendriks, R., Padhani, A.R., Hoogenboom, M., *et al.* (2019) Head-to-Head Comparison of Transrectal Ultrasound-Guided Prostate Biopsy versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-Guided Biopsy in Biopsy-Naïve Men with Elevated Prostate-Specific Antigen: A Large Prospective Multicenter Clinical Study. *European Urology*, **75**, 570-578. https://doi.org/10.1016/j.eururo.2018.11.023

[8] Siddiqui, M.M., Rais-Bahrami, S., Truong, H., Stamatakis, L., Vourganti, S., Nix, J., *et al.* (2013) Magnetic Resonance Imaging/Ultrasound-Fusion Biopsy Significantly

Upgrades Prostate Cancer versus Systematic 12-Core Transrectal Ultrasound Biopsy. *European Urology*, **64**, 713-719. https://doi.org/10.1016/j.eururo.2013.05.059

[9] Drost, F.H., Osses, D.F., Nieboer, D., Steyerberg, E.W., Bangma, C.H., Roobol, M.J., *et al.* (2019) Prostate MRI, with or without MRI-Targeted Biopsy, and Systematic Biopsy for Detecting Prostate Cancer. *Cochrane Database of Systematic Reviews*, **2019**, CD012663. https://doi.org/10.1002/14651858.cd012663.pub2

[10] Lim, L., Tan, G., Zainuddin, Z., Fam, X., Goh, E., Syaris, O., *et al.* (2020) Prospective Evaluation of Using Multiparametric Magnetic Resonance Imaging in Cognitive Fusion Prostate Biopsy Compared to the Standard Systematic 12-Core Biopsy in the Detection of Prostate Cancer. *Urology Annals*, **12**, 276-282. https://doi.org/10.4103/ua.ua_98_19

[11] Radiology ACo (2019) Prostate Imaging—Reporting and Data System.

[12] Aphinives, C., Nawapun, S. and Tungnithiboon, C. (2023) Diagnostic Accuracy of MRI-Based PSA Density for Detection of Prostate Cancer among the Thai Population. *African Journal of Urology*, **29**, Article No. 4. https://doi.org/10.1186/s12301-023-00335-9

[13] Cornford, P., Vice-chair, D.T., Bergh, R.C.N.V.D., Oort, I.M.V., Ploussard, G., Roberts, M., *et al.* (2024) EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2024_2024-04-09-132035_ypmy_2024-04-16-122605_lqpk.pdf

[14] Wegelin, O., Exterkate, L., Van der Leest, M., Kummer, J.A., Vreuls, W., De Bruin, P.C., *et al.* (2019) The FUTURE Trial: A Multicenter Randomised Controlled Trial on Target Biopsy Techniques Based on Magnetic Resonance Imaging in the Diagnosis of Prostate Cancer in Patients with Prior Negative Biopsies. *European Urology*, **75**, 582-590. https://doi.org/10.1016/j.eururo.2018.11.040

[15] Moore, C.M., Robertson, N.L., Arsanious, N., Middleton, T., Villers, A., Klotz, L., *et al.* (2013) Image-Guided Prostate Biopsy Using Magnetic Resonance Imaging-Derived Targets: A Systematic Review. *European Urology*, **63**, 125-140. https://doi.org/10.1016/j.eururo.2012.06.004

[16] Rouvière, O., Puech, P., Renard-Penna, R., Claudon, M., Roy, C., Mège-Lechevallier, F., *et al.* (2019) Use of Prostate Systematic and Targeted Biopsy on the Basis of Multiparametric MRI in Biopsy-Naive Patients (MRI-FIRST): A Prospective, Multicentre, Paired Diagnostic Study. *The Lancet Oncology*, **20**, 100-109. https://doi.org/10.1016/s1470-2045(18)30569-2

[17] Oerther, B., Engel, H., Bamberg, F., Sigle, A., Gratzke, C. and Benndorf, M. (2021) Cancer Detection Rates of the Pi-Radsv2.1 Assessment Categories: Systematic Review and Meta-Analysis on Lesion Level and Patient Level. *Prostate Cancer and Prostatic Diseases*, **25**, 256-263. https://doi.org/10.1038/s41391-021-00417-1