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Original Research

Saturation target biopsy can overcome the learning curve of magnetic resonance imaging/ultrasound fusion biopsy of the prostate

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Abstract

Background: Magnetic resonance imaging (MRI) has emerged as a promising tool for diagnosing prostate cancer. Magnetic resonance imaging/ultrasound (MRI/US) fusion target biopsy (TB) can increase the detection rate of clinically significant prostate cancer (csPC) and decrease the detection rate of clinically insignificant PC (ciPC) compared with systematic biopsy (SB). However, the MRI/US fusion biopsy had a steep learning curve. A new biopsy template, saturation TB (sTB), was reported to provide a cancer detection rate comparable to that of the combination of TB and SB. This study reports our experience with MRI/US fusion prostate biopsy and investigates the role of sTB in MRI/US fusion biopsy. **Methods**: We prospectively enrolled males with elevated prostate-specific antigen or abnormal digital rectal examination (DRE) and Prostate Imaging Reporting & Data System (PI-RADS) score $\geq$3 who underwent MRI/US fusion prostate biopsy in a tertiary referral center. We compared cancer detection rates among different biopsy templates, including TB, SB, sTB, and the combination of TB and SB. The biopsy results and complications were recorded. **Results**: The detection rate of csPC by sTB was significantly higher than that of TB (53% vs. 44%; $p = 0.008$) or SB (53% vs. 43%; $p = 0.002$). The median biopsy cores were 6, 15, and 26 for TB, sTB, and the combination of TB and SB, respectively. In other words, sTB could decrease 11 biopsy cores without compromising the cancer detection rate compared with the combination of TB and SB. There were no Clavien-Dindo score of $\geq$3 complications in any of the patients. **Conclusion**: The sTB template can overcome targeting errors during MRI/US fusion biopsy, offering a cancer detection rate equal to the combination of TB and SB with reduced biopsy cores.

Keywords: Learning curve; Magnetic resonance imaging (MRI); MRI-ultrasound fusion; Prostate cancer; Target biopsy

1. Introduction

Prostate cancer (PC) is the second most common cancer worldwide and the fifth most common cause of cancer-related deaths among males [1]. Traditionally, PC was detected by transrectal ultrasound (US)-guided 12-core systematic biopsy (SB), and up to 50% of cancers could be missed [2,3]. With technical advancement and standardization of acquisition and interpretation, multiparametric magnetic resonance imaging (mpMRI) has emerged as a promising tool for diagnosing PC [4,5]. MRI/US fusion target biopsy (TB) can increase the detection rate of clinically significant prostate cancer (csPC) and decrease the detection rate of clinically insignificant PC (ciPC) compared with SB [6,7]. Currently, the American Urological Association and the European Association of Urology recommend mpMRI before biopsy in males who are biopsy-naïve or previously had a negative biopsy [8,9]. However, urologists beginning to perform TB may encounter some errors in MRI and US coregistration or inaccuracy of TB trajectories. A steep learning curve must be overcome to ensure high-quality TB [10–12].

MRI/US fusion TB can be performed in a transperineal or transrectal route, and a significant advantage of transperineal biopsy is its extremely low infection rate [13]. TB is often combined with SB to maximize the cancer detection rate, especially during the learning curve [14–16]. Transperineal SB using the Ginsburg protocol was reported to have a cancer detection rate similar to that of template mapping biopsy [3,17]. Recently, Hansen *et al.* [18] proposed a biopsy template, saturation target biopsy (sTB), which included biopsy core sampling from the target, target sector, and sectors around the target. They found that sTB yielded a cancer detection rate comparable to the combination of TB and SB, and the number of biopsy cores was reduced from 20–26 cores to 10–20 cores.

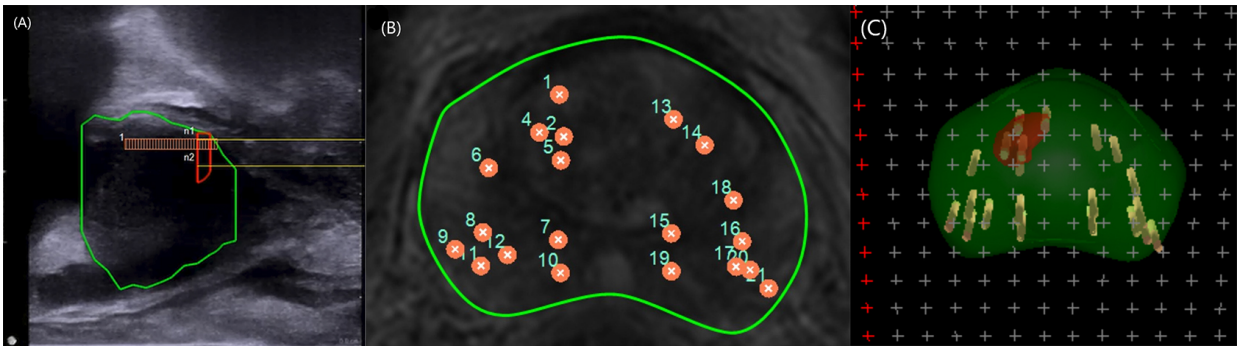

Fig. 1. Record of biopsy trajectory. A sagittal view of ultrasound revealed a biopsy trajectory through the target lesion (A). All targeted and systematic biopsy trajectories were recorded on a 2-D or 3-D model (B,C).

In this study, we report our experience with MRI/US fusion transperineal prostate biopsy and evaluate the role of sTB during the learning curve.

2. Materials and methods

2.1 Study population

We prospectively collected data of MRI/US fusion prostate biopsy from April 2020 to November 2021 in a tertiary referral center. The inclusion criteria were males with a serum prostate-specific antigen (PSA) level $\geq$4 ng/mL or abnormal digital rectal examination. Prebiopsy mpMRI with a PI-RADS score of $\geq$3 was required. Patients with a history of PC or bacterial prostatitis within 3 months were excluded from the study. The patients' clinical characteristics and biopsy results were collected.

2.2 MRI protocol

mpMRI was performed using a 3-T scanner (Signa HDxt, GE Healthcare, Milwaukee, WI, USA). The scanning protocol was performed as described previously [19]. All mpMRIs were interpreted by a uroradiologist (W.C.L.) who had 12 years of experience. Each suspicious lesion was scored according to the Prostate Imaging-Reporting and Data System v2.1 [4]. One urologist (P.F.H.) reviewed the mpMRI and identified suspicious lesions with PI-RADS $\geq$3 as target lesions (maximum three target lesions per patient). If there were two or more target lesions with the same PI-RADS score, the index lesion was defined as the largest lesion. After reviewing mpMRI, T2WI was imported into the Biojet platform (D&K Technologies GmbH, Barum, Germany). The segmentation of the T2WI was then performed to create a 3-D model of the prostate.

2.3 Biopsy protocol

The patients were placed in the lithotomy position under general anesthesia and prophylactic antibiotics. US scanning of the prostate was performed using a transrectal probe (BK 8848, BK Medical, Peabody, MA, USA). The US and mpMRI images were then fused with the Biojet platform. MRI/US fusion biopsy was started with TB and then followed by SB. SB was performed following the Ginsburg protocol, in which biopsy cores were taken from 12 sectors [20]. The biopsy trajectories were recorded using a Biojet system (Fig. 1). Biopsy samples were obtained using an 18 G biopsy gun with a specimen size of 22 mm (Bard Magnum; Bard Medical, Covington, KY, USA). All biopsy was performed transperineally and by a single urologist (P.F.H.).

2.4 Histopathological analysis

One experienced uropathologist (H.C.) interpreted all biopsy specimens. PC was graded according to the 2014 International Society of Urological Pathology Consensus Conference guidelines [21]. We defined csPC as a Gleason grade group (GG) $\geq$2.

2.5 Outcome measures and statistical analysis

We followed the Standards of Reporting for MRI-Target Biopsy Studies (START) guidelines to report the results [22]. Continuous variables were reported as medians (interquartile range, IQR), and categorical variables were reported as proportions. The sTB template was defined as TB plus SB cores taken in the target and adjacent sectors (Fig. 2) [18]. We compared cancer detection rates between different biopsy templates in males with target lesions using McNemar's test. We compared the number of biopsy cores among the biopsy templates. All statistical analyses were performed using SPSS version 22 (IBM Corp, Armonk, NY, USA), assuming a two-sided test with an alpha of 5% for statistical significance.

3. Results

A total of 100 males were enrolled in the study. Detailed characteristics of the patients are shown in Table 1. The overall PC detection rate was 62%, and the csPC detection rate was 53%. The detection rates for overall PC were 54%, 49%, 62%, and 62% for TB, SB, sTB, and TB combined with SB, respectively. The detection rates for csPC were 44%, 43%, 53%, and 53% for TB, SB, sTB, and TB combined with SB, respectively (Fig. 3). The detection rate

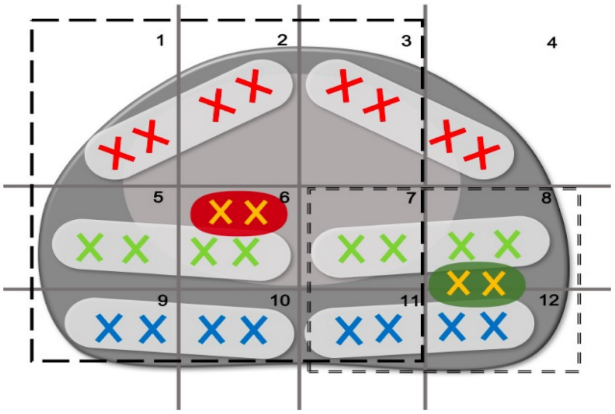

Fig. 2. Schema of sTB. For the red target lesion, the sTB template included TB for 2 cores and SB for 18 cores (sectors 1–3, 5–7, and 9–11 in the dashed frame). For the green target lesion, the sTB template included TB for 2 cores and SB for 8 cores (sectors 7, 8, 11, and 12 in the double dashed frame). SB, systematic biopsy; sTB, saturation target biopsy; TB, target biopsy.

of csPC by sTB was significantly higher than that of TB (53% vs. 44%; $p = 0.008$) or SB (53% vs. 43%; $p = 0.002$). The median (IQR) biopsy cores were 6 (4–7), 15 (12.8–18), and 26 (23–28) for TB, sTB, and the combination of TB and SB. In other words, sTB could decrease a total of 11 biopsy cores without compromising the cancer detection rate compared with the combination of TB and SB.

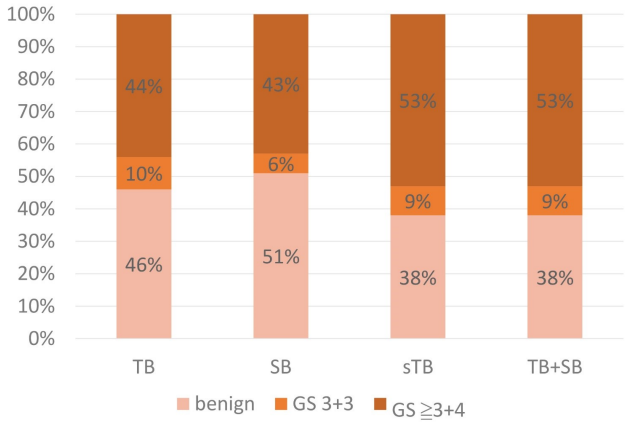

Fig. 3. The cancer detection rate of different biopsy templates.

Fig. 4 shows the cancer detection rates stratified by the different PI-RADS scores. The detection rates for csPC were 27.8%, 44.7%, and 77.1% for PI-RADS 3, 4, and 5 lesions, respectively.

In univariate logistic regression analysis, age, PSA density, maximum size of the target lesion, PI-RADS score >3, and location of the lesion in the transitional zone were significant predictors of the presence of csPC. However, in the multivariate regression analysis, only age remained a significant predictor of csPC (Table 2).

Table 1. Patient characteristics.

Number of patients	100
Age, median (IQR)	66 (61.0–71.25)
Prebiopsy PSA level, ng/dL	7.325 (5.35–12.69)
Prostate volume, cm^3	42.27 (29.69–57.43)
PSA density	0.178 (0.105–0.317)
Median max size of the target lesion, mm	12 (8–17.25)
Biopsy cores per target, n	5.5 (4–7)
Total biopsy core per patient, n	26 (23–28)
PI-RADS score, n	
3	18
4	47
5	35
Negative biopsy within 5 years, n	32
Location of the index lesion	
Anterior/posterior	41/59
PZ/TZ	61/39

All values are given as a number or median (IQR).
IQR, interquartile range; PSA, prostate-specific antigen; PI-RADS, Prostate Imaging-Reporting and Data System; PZ, peripheral zone; TZ, transitional zone.

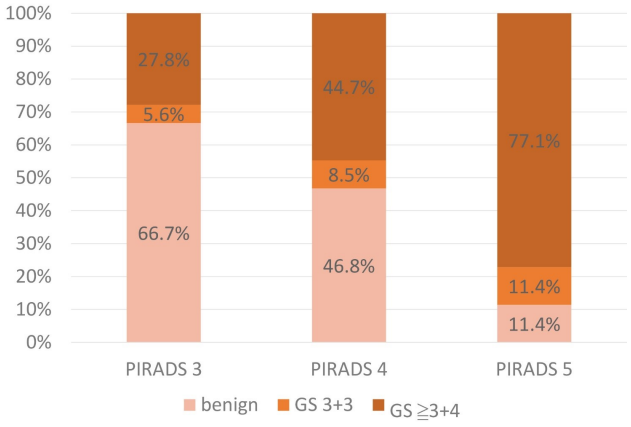

Fig. 4. Cancer detection rate stratified by PI-RADS score.

There were no Clavien-Dindo score of ≥3 complications in any of the patients. Seventeen males developed acute urinary retention (AUR, 17%) the day after surgery. After intermittent catheterization or Foley catheterization for 1 night, as well as oral alpha-blockers, they could all void well.

4. Discussion

According to our results, the detection rate of csPC by sTB was significantly higher than that of TB or SB. Furthermore, cancer detection rates were the same between sTB and the combination of TB and SB, while sTB could reduce the number of biopsy cores.

A steep learning curve is inevitable before mastering MRI/US fusion prostate biopsy. Gaziev *et al.* [10] reported the first study to evaluate the learning curve of transper-

Table 2. Logistic regression of the predictors of csPC.

	Univariate			Multivariate		
Predictor	OR	(95% CI)	*p*-value	OR	(95% CI)	*p*-value
Age	1.095	1.036–1.158	<0.01	1.077	1.015–1.143	0.01
Prior negative biopsy	0.838	0.361–1.943	0.68			
DRE						
Normal	Reference					
Abnormal	1.829	0.760–4.401	0.18			
PSA	1.045	0.989–1.104	0.12			
PSA density	25.219	2.230–285.246	0.01	7.715	0.766–77.661	0.08
Max size of the lesion	1.087	1.025–1.154	0.01	1.063	0.996–1.135	0.07
PI–RADS						
3	Reference					
>3	3.671	1.196–11.262	0.02	2.356	0.671–8.268	0.18
Number of cores	1.056	0.965–1.156	0.23			
Lesion location						
PZ	Reference					
TZ	2.519	1.092–5.809	0.03			
Anterior	Reference					
Posterior	0.487	0.215–1.101	0.08			

DRE, digital rectal exam; OR, odds ratio; PSA, prostate-specific antigen; PZ, peripheral zone; PI-RADS, Prostate Imaging-Reporting and Data System; TZ, transitional zone.

ineal MRI/US fusion biopsy. After 340 cases, the cancer detection rate increased from 42% to 81% [10]. In another study, Halstuch *et al*. [11] suggested that 125 cases are needed to achieve proficiency in transperineal MRI/US fusion biopsy. Minimizing targeting errors during the initial stage of MRI/US fusion biopsy is an important issue. Some tips for biopsy techniques have been suggested [17]. For example, TB should be performed before SB to prevent movement errors or blurring of the image due to bleeding. Prostate tissue should be sampled from anterior to posterior to reduce image blurring due to bleeding or tissue edema. However, the impact of biopsy templates on the learning curve has not yet been studied.

A literature review showed that the pure TB strategy missed 15% of csPC due to limitations in the reading and precision of mpMRI during lesion targeting [15]. Combining TB and SB is generally recommended to achieve a maximal cancer detection rate [14–16]. Furthermore, mpMRI often underestimates the tumor boundary; therefore, it is reasonable to take additional samples around the target [23]. However, the benefits of an increased detection rate by more biopsy cores must be weighed against the risks of increased complications such as urinary retention and perineal discomfort [24]. In our study, sTB and the combination of TB and SB both yielded a detection rate of 62% for overall PC and 53% for csPC. The detection rate for csPC by sTB was also significantly higher than that of TB (53% vs. 44%, $p = 0.008$). Furthermore, we could decrease the median biopsy cores from 26 to 15 by adopting the sTB template.

In our study, the PI-RADS score >3 was a significant predictor for csPC in univariate logistic regression analysis. The PI-RADS score is a well-known imaging biomarker of csPC. A meta-analysis revealed that the positive predictive values for csPC were 13%, 40%, and 69% for PI-RADS 3, 4, and 5 lesions, respectively [25]. In line with previous literature, our study showed that the detection rates for csPC of PI-RADS 4 or 5 lesions were higher than those of PI-RADS 3 lesions (27.8%, 44.7%, and 77.1% for PI-RADS 3, 4, and 5 lesions, respectively). In other words, prostate biopsy should be strongly recommended for males with PI-RADS >3 lesions.

In addition, PSA density is another potential biomarker that may improve sensitivity and specificity compared with total PSA [26]. Recently, PSA density has been proposed as an adjuvant to MRI in the decision-making of prostate biopsy [27,28]. In our study, PSA density was a predictor of csPC in univariate regression analysis. Further large-scale studies are needed to evaluate the role of PSA density in the era of MRI/US fusion TB.

In summary, there are several benefits of sTB: First, by alleviating targeting errors, it provided a significantly better cancer detection rate than TB alone. Second, it provided a cancer detection rate similar to the traditional combination of TB and SB. Third, it reduced the biopsy cores, which, in turn, may reduce the morbidity associated with transperineal biopsy. Fourth, it can be easily performed by beginners who are still in the learning curve of MR/US fusion transperineal biopsy.

Our study had several limitations. First, this was a single-arm study with a limited number of cases. However, all patients were prospectively collected, thus minimizing selection bias. Second, we did not enroll males with PI-RADS 1 or 2 lesions on MRI, precluding us from comparing

positive and negative imaging results. Third, we used the combination of TB and SB as a reference standard for tumor grading instead of the whole amount of prostate. Fourth, the number of TB cores was not standardized. Whether more intensive sampling of the target could result in a detection rate similar to that of sTB remains to be determined.

5. Conclusions

The sTB template can overcome targeting errors during the initial learning curve of MRI/US fusion prostate biopsy by offering a cancer detection rate equal to the combination of TB and SB and reducing the number of biopsy cores.

Abbreviations

csPC, clinically significant prostate cancer; ciPC, clinically insignificant prostate cancer; DRE, digital rectal examination; T2WI, T2-weighted image; TB, target biopsy; sTB, saturation target biopsy; SB, systemic biopsy; MRI, magnetic resonance imaging; PC, prostate cancer; MRI/US, magnetic resonance imaging/ultrasound; GG, Gleason grade group; PI-RADS, Prostate Imaging-Reporting and Data System; PSA, prostate-specific antigen; IQR, interquartile range.

Author contributions

PH, TC—designed the study, collected the data, analyzed and interpreted the result. WL—interpreted all MRI image and determined the PI-RADS score. HC—interpret all the specimen and determine the Gleason score/grade group. CC, CH, CY, WC, YC, YW, HW—help collect the data. WH—help the statistics of the study. TC, PH—analyzed the data. PH, TC—draft the manuscript. HW—review the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of China Medical University Hospital, Taichung, Taiwan (protocol numbers: CMUH109-REC1-045). All methods were carried out in accordance with EAU guidelines. Informed consent was obtained from all subjects.

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Conflict of interest

The authors declare no conflict of interest.

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