Original Article

Prostate cancer detection rate using MRI/ultrasound fusion-guided prostate biopsy in Siriraj Hospital

Supisara Boonseana[1], Sittiporn Srinualnad[1], Sunai Leewansangtong[2], Ngoentra Tantranont[2], Varat Woranisarakul[1]

[1]Division of Urology, Department of Surgery, [2]Department of Pathology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

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Abstract

Objective: Systematic transrectal ultrasound (TRUS) guided biopsy has been considered a gold standard for prostate cancer diagnosis for many decades. The problem of this conventional method is the low detection rate especially in the case of repeat biopsy. This results from a limitation associated with ultrasound imaging inhibiting the visualization of cancerous lesions during the procedure. More recently, there has been increasing importance attributed to the use of multiparametric MRI for the identification of cancer inside the prostate gland. Targeted prostate biopsy, using multiparametric MRI/ultrasound (mpMRI/US) fusion-guided technology helps improve the detection of prostate cancer and has become a novel standard for tissue diagnosis. This study was conducted to investigate and report on the cancer detection rate of mpMRI/US fusion guided prostate biopsies at Siriraj Hospital.

Materials and Methods: Data pertinent to patients who underwent mpMRI/US fusion guided biopsy at Siriraj Hospital between September 2017 and December 2019 was retrospectively reviewed.

Results: A total of 499 men underwent mpMRI/US fusion guided biopsy, with the transperineal approach being used in the vast majority of cases (91.8%). Targeted biopsy provides a better cancer detection rate than systematic biopsy (55.3% vs 47.1%, $p = 0.009$). Combined targeted and systematic biopsies improved cancer detection rate compared to systematic biopsy alone (60.3% vs 47.1%, $p < 0.001$). A subgroup analysis of men with positive biopsies showed that detection of clinically significant cancer (Gleason grade group ≥ 2) was no different between targeted and random biopsies (87.2% vs 80.8%, $p = 0.11$). The common complications from transperineal approach were urinary retention (5.4%) and hematuria (5.2%) while complications of infection were rare (0.2%).

Conclusion: We found that targeted biopsy with mpMRI/US fusion guided technology provides a more effective option for prostate cancer diagnosis. A combination of targeted and systematic biopsy improve prostate cancer detection rate more effectively than systematic biopsy alone. The transperineal approach is a safe and effective technique with a rare incidence of infectious complications.

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Corresponding author: Varat Woranisarakul

Address: Division of Urology, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand

E-mail: varatmd@gmail.com

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Introduction

Prostate cancer is the most commonly diagnosed malignancy in men. The early stages of prostate cancer rarely cause symptoms, therefore, presence of symptoms suggests locally advanced or metastatic disease. There is significant potential for the improvement in early detection of prostate cancer with a better screening program. Men who presented with elevation of serum prostate specific antigen (PSA) or abnormal digital rectal examination should be recommended for tissue diagnosis. However, the gold standard for cancer diagnosis has still been systematic or random transrectal ultrasound (TRUS) guided biopsy. As a consequence many men without cancer underwent unnecessary biopsies, clinically insignificant cancers have often been detected, but significant cancers have often been missed.[1]

Multiparametric magnetic resonance imaging and ultrasound (mpMRI/US) fusion guided biopsy or targeted biopsy can be used to solve this problem and improve the rate of detection of prostate cancer. Several studies have shown that mpMRI/US fusion guided biopsies can reduce the overdiagnosis of clinically insignificant prostate cancers and improve the detection rate of those that are clinically significant.[1,2] The aim of this study was to evaluate the rate of cancer detection using the mpMRI/US fusion guided prostate biopsy method in Siriraj Hospital.

Materials and Methods

Study design and participants

This retrospective observational study was conducted after obtaining approval from the Siriraj Institutional Review Board (SIRB Protocol Number: 509/2562(EC3)). Medical records of patients who underwent mpMRI/US fusion guided prostate biopsies between September 2017 and December 2019 at the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand were reviewed. The data collected included patient demographics, preoperative serum PSA level, MRI findings, indication for biopsy, perioperative information, and pathological reports. Patients with missing or incomplete follow up data were excluded from this study.

Imaging

All patients underwent a 1.5 or 3 Tesla multiparametric MRI scan without endorectal coil. The protocol included a T2-weighted imaging, diffusion-weighted imaging, and dynamic contrast-enhanced imaging. All results were reported by radiologists using the Prostate Imaging-Reporting and Data System (PI-RADS) score version 2.1.[3] Patients with a lesion with a PI-RADS score ≥ 3 were scheduled for tissue diagnosis.

Biopsy protocol

Before the biopsy procedure, prostate MRI images were retrieved into the KOELIS Trinity® system (Koelis, France) enabling the creation of 3D images of the prostate gland and the index lesion. All patients were given prophylactic antibiotics as per standard guideline recommendations. Every procedure was performed by urologists or trained physicians under general anesthesia. The volume of the prostate gland was acquired using real-time 3D ultrasonography. An organ-based tracking software package was used to superimpose labeled 3D MRI images over 3D ultrasonography as used to superimpose labeled 3D MRI images over real-time 3D ultrasonography with organ-based tracking technology. All patients underwent targeted biopsies first, followed by systematic biopsies with an 18-gauge needle biopsy gun. All needle tracts were registered and recorded in the 3D mpMRI/US fusion images. A transperineal ultrasound probe, linear-grid needle guidance, and a Steady Pro™ probe holder (Koelis, France) were the accessories utilized in the transperineal approach. All specimens were interpreted and recorded by genitourinary pathologists.

Outcomes

The primary outcomes were overall detection rates of cancer using mpMRI/US fusion guided prostate biopsies and systematic prostate biopsies. The secondary outcomes were detection rates of clinically significant prostate cancer in mpMRI/US fusion guided prostate biopsies compared to systematic prostate biopsies and the complication rate. According to the Epstein criteria,[4-6] the definition of clinically insignificant prostate cancer was a patient with Gleason score ≤ 6 (Gleason Grade Group 1), a tumor involving fewer than three cores, tumor volume ≤ 50% of any given core, and a prostate-specific antigen density of < 0.15 ng/ml per cm.[3]

Statistical analysis

Data was analyzed using PASW Statistics for Windows (version 18.0; SPSS Inc., Chicago, Ill., USA). Sample size was calculated based on cancer detection rate, using nQuery Advisor version 5.0 with an allowable error of 5% and a 95% confidence level. Descriptive statistics were used to describe demographics and clinical characteristics. Quantitative data was described as mean and standard deviation (SD) or median and range (min, max), as appropriate. Qualitative data was expressed as number and percentage. Pearson's chi-squared test, Yates' continuity correction, or Fisher's exact test were used to compare qualitative data between groups, as appropriate. The Kappa statistic was used to assess agreement of findings with regard to detection of prostate cancer.

Results

This study included 499 eligible cases with a mean age of 69.2 years. The median PSA was 8.5 ng/ml (IQR 6.2-13.4) and median prostate volume was 42 ml (IQR 28-61). Of these, more than half (53.1%) were biopsy naïve. The most significant indication for a prostate biopsy was a high PSA (53.3%) and previous negative biopsy (42.6%). The vast majority of the patients (91.8%) underwent the transperineal approach for prostate biopsy with a median of a 23 core needle biopsy, as shown in Table 1. Abnormal lesions in mpMRI categorized as PIRADS 3, 4 and 5 were 19.3%, 57.4% and 23.6%, respectively. The cancer detection rates of PIRADS 3, 4 and 5 were 21.6%, 45.8%, and 82.3%, respectively, as shown in Figure 1. Targeted biopsy provided a more effective cancer detection rate than systematic biopsy (55.3% vs 47.1%, OR 1.39, 95%CI 1.08-1.78, p = 0.009). Sixty-six patients (23.9%) had positive targeted biopsies but negative random biopsies, while 25 patients (10.6%) had positive random biopsies but negative targeted biopsies. Combined targeted and systematic biopsies improved cancer detection rate in comparison to systematic biopsy alone (60.3% vs 47.1%, OR 1.71, 95%CI 1.33-2.2, p < 0.001), but there was no statistically

Table 1. Demographic data

Sample size N = 499	
Mean age, years (SD)	69.2 (7.1)
Median preoperative PSA, ng/ml (IQR)	8.5 (6.2-13.4)
Median prostate volume, ml (IQR)	42 (28-61)
Median number of lesion (min, max)	1 (1-5)
Biopsy-naive, n (%)	265 (53.1)
Indication for biopsy, n (%)	
High PSA	266 (53.3)
Previous negative biopsy	212 (42.6)
Abnormal MRI	11 (2.2)
Active surveillance	10 (2.0)
PI-RADS score version 2.1, lesion n (%)	
3	134 (19.3)
4	397 (57.1)
5	164 (23.6)
Approach n (%)	
Transperineal	458 (91.8)
Transrectal	38 (7.6)
Both	3 (0.6)
Median number of total cores biopsy (IQR)	23 (19-28)
Median number of targeted cores biopsy (IQR)	11 (8-16)
Median number of random cores biopsy (IQR)	12 (10-12)
Median operative time minutes (IQR)	25 (20-35)
Median length of stay days (IQR)	3 (0-3)

SD = standard deviation, PSA = prostate specific antigen, IQR = interquartile range, MRI = magnetic resonance imaging

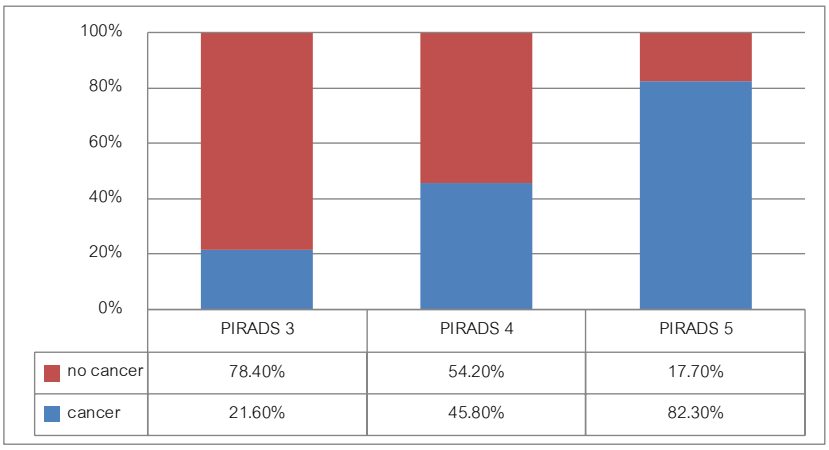

Figure 1. Detection rates of mpMRI/US fusion biopsy, categorized by PI-RADS score version 2.1

Table 2. Prostate cancer detection by targeted or systematic biopsy

Cancer detection	Targeted biopsy n (%)	Systematic biopsy n (%)	P-value
Positive for cancer Negative	276 (55.3) 223 (44.7)	235 (47.1) 264 (52.9)	OR 1.39 (95% CI 1.08-1.78) p = 0.009
Cancer detection	**Combined biopsyn n (%)**	**Systematic biopsyn n (%)**	**P-value**
Positive for cancer Negative	301 (60.3) 198 (39.7)	235 (47.1) 264 (52.9)	OR 1.71 (95% CI 1.33-2.2) p < 0.001
Cancer detection	**Combined biopsyn n (%)**	**Targeted biopsyn n(%)**	**P-value**
Positive for cancer Negative	301 (60.3) 198 (39.7)	276 (55.3) 223 (44.7)	OR 1.23 (95% CI 0.96-1.58) p = 0.11

significant difference when compared to targeted biopsy alone (60.3% vs 55.3%, OR 1.23, 95%CI 0.96-1.58, p = 0.11) as demonstrated in Table 2. A subgroup analysis of all positive biopsies revealed that targeted biopsy detected clinically significant prostate cancer slightly more successfully than random biopsy (87.2% vs 80.8%) and detected fewer insignificant cancers (12.7% vs 19.1%), but there was no statistically significant differences in these data (OR = 1.62, 95% CI 0.89-2.94, p = 0.11) (Table 3).

Of the 499 patients, the most common complications were acute urinary retention (5.4%) and significant gross hematuria (5.2%), all of which were resolved by conservative treatment without morbidity that necessitated surgery. There were a few unusual complications (≤1 %) related to the general anesthesia or medical conditions as shown in Table 4. No complications associated with sepsis or severe infection were found in our study.

Discussion

Transrectal ultrasound-guided biopsy has been considered the standard of care for prostate cancer diagnosis for decades because of its availability and user-friendly platform. However, the limitation of the ultrasound-guided technique was the inability to delineate a suspected lesion within the prostate gland. This conventional method led us to perform only a systematic or random pattern of prostate biopsy. Recent studies have indicated that prostate cancer can be more accurately detected through MRI-targeted biopsy or mpMRI/US fusion-guided biopsy.[7,8] There are however, various perspectives and controversial issues about the integration of this novel technology into an individualized diagnostic pathway.[9-12]

MRI reporting system can represent the cancer detection rate by categorization through

Table 3. Subgroup analysis of positive biopsy

Group	Targeted positive n (%)	Systematic positive n (%)	P-value
Gleason grade group ≥ 2	164 (87.2)	118 (80.8)	OR 1.62
Gleason grade group 1	24 (12.7)	28 (19.1)	(95% CI 0.89-2.94)
			p = 0.11
Group	**Combined positive n (%)**	**Systematic positive n (%)**	**P-value**
Gleason grade group ≥ 2	177 (83.4)	118 (80.8)	OR 1.2
Gleason grade group 1	35 (16.5)	28 (19.1)	(95% CI 0.69-2.08)
			p = 0.51

Table 4. Demographic data

Complication	n (%)
Acute urinary retention	27 (5.4)
Gross hematuria	26 (5.2)
Hypertensive urgency	5 (1.0)
Anesthesia complication (aspiration)	2 (0.4)
Prostatitis with negative culture	1 (0.2)
Cerebrovascular event (TIA)	1 (0.2)
Atrial fibrillation	1 (0.2)

use of PIRADS. We noted that the higher the PIRADS score, the greater likelihood of prostate cancer detection. Our study showed a similar outcome but a slightly lower detection rate in each PIRADS compared to those of Kasivisvanathan et al.[2] This might reflect the progressive learning curve by various means, including the sharing of good practice, since this procedure was first advocated in our institute. Moreover, 47% of the participants underwent repeated biopsies, which could lower the efficacy of the performance of systematic biopsy. Our results emphasized the efficacy of the implementation of mpMRI/US fusion guided prostate biopsy, which could detect prostate cancer more accurately than random biopsy (55.3% vs 46.7%). Our findings also showed that a combination of the two methods improved cancer detection performance when compared to random biopsy alone.

A subgroup analysis of all positive biopsies demonstrated that mpMRI/US fusion guidance was effective for the detection of clinically significant cancer. In a PRECISION trial, the mpMRI/US fusion-guided prostate biopsy method had a higher detection rate of significant prostate cancer, which matched our findings. In the mpMRI/US fusion-guided prostate biopsy group, there was a similar higher detection rate of significant cancer (87.6%) and a lower detection rate of insignificant cancer (12.4%). This was beneficial for reducing overtreatment in patients with insignificant prostate cancer, as well as reducing the morbidity and mortality associated with treatment.

Complications associated with prostate biopsies included bleeding (hematuria, hematospermia), infection, discomfort, and urinary retention. According to a systematic review and meta-analysis, minor hematuria is common following a prostate biopsy, while significant bleeding requiring hospitalization occurred in 1% of all cases and risk of urinary retention in 2%.[13,14] Gross hematuria (5.2%) and acute urinary retention (5.4%) were noted as minor complications in our study. These higher rates of self-limiting events may be due to several causes. First, our preferred technique involved a transperineal approach in which the needle tracts are directly passed from the apex to the base of the prostate gland and involve a greater periurethral area when compared to the conventional method. Second, nearly half of our patients were repeated biopsies, in which there may have been some subclinical inflammation, causing additional reaction after our procedure. On the positive side, our transperineal technique showed a zero percent incidence of re-admission due to sepsis or serious infectious complication, similar findings to previous studies.[15,16]

To the best of our knowledge, this was the largest study in Thailand to demonstrate the impact of the transperineal approach with mpMRI/US fusion prostate biopsy. The outcomes emphasized this was not only a better option but also a safer method in the detection of prostate cancer for Thai people. However, as with all live studies, there are potential limitations in this study. First, its retrospective design lacked a matched control group. Second, as it is a retrospective study of

medical records, there is naturally interobserver variability among radiologists, which could lead to misinterpretation of the PIRADS scores and different annotation of the index lesions. Finally, the fusion software may not represent an identical match between MRI and ultrasound imaging. This discordance could have resulted in the different prostate volume measurements and discrepancies in the settings of both prostate imaging techniques.

Conclusion

Targeted biopsy with mpMRI/US fusion guided technology provides a more effective alternative option for prostate cancer diagnosis. A combination of both targeted and systematic biopsy improves prostate cancer detection rate in comparison to systematic biopsy alone. The transperineal approach is a safe and effective technique with a rare incidence of infectious complications.

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Conflict of Interest

The authors declare no conflict of interest.

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