



Research Article

What is the ideal number of biopsy cores per lesion in targeted prostate biopsy?

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ABSTRACT

Background: The number of cores to be obtained in targeted biopsy (TB) is important. This study aimed to evaluate the TB outcomes in suspicious prostate lesions classified according to the Prostate Imaging Reporting and Data System (PI-RADS) and to determine the ideal number of biopsy cores per lesion.

Methods: This retrospective study included patients who underwent multiparametric magnetic resonance imaging–guided fusion prostate biopsy owing to increased serum prostate-specific antigen (PSA) levels and suspicious digital rectal examination outcomes in our institute. Patients with PI-RADS <3 lesions, PSA levels >10 ng/ml, and a prior diagnosis of prostate cancer (PCa) (active surveillance) were excluded from the study. The number of biopsy cores to be obtained from each lesion was determined by the clinician.

Results: The study included a total of 418 patients and 684 lesions. Among PI-RADS 3 lesions, clinically significant PCa (sPCa) detection rate was similar in the lesions from which 2 and 3 cores were obtained (9.1% and 10.0%, respectively), whereas it was relatively higher in the lesions from which 4 biopsy cores were obtained (18.5%). Among PI-RADS 4 lesions, sPCa detection rate was similar in the lesions from which 3 and 4 cores were obtained (35.6% and 32.3%, respectively), whereas it was relatively lower in the lesions from which 2 biopsy cores were obtained (17.9%). Among PI-RADS 5 lesions, however, sPCa detection rate was similar in the lesions from which 2, 3, or 4 cores were obtained (47.6%, 46.0%, 48.9%, respectively).

Conclusion: The results indicated that the ideal number of cores to be obtained from each suspicious lesion in TB depends on the characteristics of the lesions. Accordingly, while obtaining 2–3 biopsy cores could be adequate in PI-RADS 4 and 5 lesions, which have a serious risk of cancer, a minimum of 4 biopsy cores should be obtained from PI-RADS 3 lesions to ensure accurate histopathological results.

Clinical trial number ([ClinicalTrials.gov](https://clinicaltrials.gov)) NCT03936296.

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1. Introduction

Prostate cancer (PCa) is commonly diagnosed by digital rectal examination (DRE), the serum prostate-specific antigen (PSA) test, and prostate needle biopsy (PNB).¹ Multiparametric magnetic resonance imaging (mpMRI)–guided fusion prostate biopsy (FPB)

is a PNB technique that has been shown as an effective approach in numerous studies.²

FPB is typically performed as targeted biopsy (TB) or in combination with TB or standard prostate biopsy (SPB).³ The literature recommends the use of 2–4 cores per suspicious lesion in TB.^{4,5} However, the ideal number of biopsy cores to be obtained from each lesion with regard to the type and characteristics of the lesion remains controversial, and there is no consensus in the literature regarding this controversy, which is a major concern in clinical practice.^{6–9} As a matter of fact, however, obtaining an insufficient number of biopsy cores from suspicious lesions may lead to false negative results, whereas obtaining an excessive number of biopsy

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cores may result in additional complications, reduced patient comfort, and workforce and time loss.^{10,11}

In the present study, we aimed to evaluate the TB outcomes in suspicious prostate lesions classified according to the Prostate Imaging Reporting and Data System (PI-RADS) and to determine the ideal number of biopsy cores per lesion.

2. Materials and methods

2.1. Patient selection and data collection

The retrospective study included patients who underwent mpMRI-guided FPB owing to increased PSA levels and suspicious DRE outcomes in Erciyes University Department of Urology between December 2016 and November 2019. Patients who had no suspicious lesions on mpMRI before the FPB procedure and patients with PI-RADS <3 lesions, PSA levels >10 ng/ml, and a prior diagnosis of PCa (active surveillance) were excluded from the study. In addition, patients who were previously diagnosed with atypical small acinar proliferation (ASAP) or high-grade prostatic intraepithelial neoplasia (HGPIN) were excluded from the study and were referred for appropriate treatment and follow-up. Demographic characteristics including age, body weight, height, and body mass index and clinical characteristics including serum PSA level, prostate volume, history of prior negative biopsy, and histopathological results were recorded for each patient.

2.2. Multiparametric magnetic resonance imaging

A prostate mpMRI was performed for each patient before biopsy procedure using a Siemens Magnetom 1.5 Tesla MRI device (Siemens Medical Solutions, Malvern, USA). Suspicious lesions identified on contrast-enhanced T1-, T2-, and diffusion-weighted MRI sequences were classified based on PI-RADS version 2 grouping.¹² PI-RADS scores were recorded for each patient. In patients with multiple lesions and varying PI-RADS scores, the highest PI-RADS score was considered as the overall PI-RADS score.

2.3. Prebiopsy and FPB

All the patients underwent sterile urine culture testing before biopsy. Twenty-four hours before the procedure, three oral doses of 750 mg of ciprofloxacin (at a 12-h interval) were administered. No bowel preparation was performed in any patient before the procedure. The entire biopsy procedure was performed in polyclinic conditions under local or general anesthesia. mpMRI images were transferred to the ultrasonography (US) system using rigid fusion software (Logic E9; GE health, USA). After the segmentation of sonographic images with mpMRI images, the lesions detected on mpMRI were marked. Total prostate volume was calculated using the following formula: height (H) × width (W) × length (L) × 0.523. Afterward, periprostatic nerve block was induced by injecting 2% prilocaine hydrochloride (20 mg/mL) into the neurovascular bundle on both sides of the prostate, with 5 mL to the right and 5 mL to the left side. After the induction of periprostatic block, 2–4 core biopsies were obtained from the MRI-targeted PI-RADS ≥3 lesions. All the data transfers and markings were carried out by two urologists experienced and trained in transrectal prostate US and biopsy (A.D., G.S. and S.T.T.). After the completion of TB, 12-core SPB was performed for each patient at the same session.

2.4. Histopathological analysis

Tissue samples obtained from suspicious lesions were separately placed in previously labeled containers and were sent for

histopathological analysis. All the examinations were conducted by the same uropathologist with more than 10 years of experience (F.Ö.). Clinically significant PCa (sPCa) was considered as biopsy Gleason score ≥3 + 4 or maximum cancer core length ≥5 mm.

2.5. Statistical analysis

Normal distribution of data was analyzed using the Shapiro-Wilk test and histogram plots. Continuous variables with normal distribution were presented as mean ± standard deviation, and the variables with non-normal distribution were presented as median (1st–3rd quartile). Categorical variables were presented as percentages (%) and were compared using Pearson's chi-square test and Fisher's exact test. The difference among two or more groups was compared using one-way analysis of variance followed by Tukey's test if data showed normal distribution and Kruskal-Wallis test if data showed non-normal distribution. A *p* value of <0.05 was considered significant.

2.6. Ethical issues

Erciyes University Medical School Ethics Committee approved the study protocol (approval no: 2014/508). A written consent was obtained from each patient (T.D.).

2.7. Funding

The retrospective data of this study were obtained from the other study, which was funded by the Erciyes University Scientific Research Projects Coordination Unit (project number: TSG-2016-5200).

3. Results

3.1. Patient characteristics

The study included 418 patients, with a mean age of 62.39 ± 7.17 years and a median PSA level of 6.88 (range, 5.20–5.80) ng/ml. The maximum PI-RADS score was 3 in 242 (57.9%), 4 in 110 (26.3%), and 5 in 66 (15.8%) patients. Of the 418 patients, 111 (26.6%) patients had a history of one or more prior negative biopsies. The overall sPCa detection rate in TB was 24.4% (Table 1).

3.2. Lesion characteristics and number of cores

A total of 684 lesions were evaluated in the study. Of these, 2 biopsy cores were obtained from 219 (32.0%), 3 biopsy cores were obtained from 217 (31.7%), and 4 biopsy cores were obtained from 248 (36.3%) lesions. Among PI-RADS 3 lesions, sPCa detection rate was similar in the lesions from which 2 and 3 cores were obtained (9.1% and 10.0%, respectively), whereas it was relatively higher in the lesions from which 4 biopsy cores were obtained (18.5%). Among PI-RADS 4 lesions, sPCa detection rate was similar in the lesions from which 3 and 4 cores were obtained (35.6% and 32.3%, respectively), whereas it was relatively lower in the lesions from which 2 biopsy cores were obtained (17.9%). Among PI-RADS 5 lesions, however, sPCa detection rate was similar in the lesions from which 2, 3, or 4 cores were obtained (47.6%, 46.0%, and 48.9%, respectively) (Table 2).

On the other hand, among patients who were biopsy naive or had a history of prior negative biopsies, sPCa detection rate was similar in the lesions from which 3 and 4 cores were obtained, whereas it was relatively lower in the lesions from which 2 biopsy cores were obtained (Table 3).

Table 1
Comparison of demographic and clinical characteristics based on PI-RADS scores.

Characteristics	Higher PI-RADS score			p	Overall (n = 418)
	PI-RADS 3 (n = 242)	PI-RADS 4 (n = 110)	PI-RADS 5 (n = 66)		
Age (years)	62.26 ± 7.15	62.47 ± 7.11	62.74 ± 7.46	0.882	62.39 ± 7.17
BMI (kg/m ²)	27.25 (25.00–30.05)	27.20 (25.50–29.05)	27.55 (25.45–30.10)	0.756	27.30 (25.20–29.60)
PSA (ng/ml)	6.76 (5.11–8.50)	7.14 (5.47–8.38)	6.95 (5.14–8.63)	0.518	6.88 (5.20–8.50)
PV (mm ³)	54.11 (38.48–74.47)	63.44 (46.44–88.41)	60.89 (46.06–95.71)	0.053	57.57 (42.11–81.10)
History of prior negative biopsy, n (%)	59 (24.4%)	36 (32.7%)	16 (24.2%)	0.233	111 (26.6%)
sPCa, n (%)	30 (12.4%) ^a	42 (38.2%) ^b	30 (45.5%) ^b	<0.001	102 (24.4%)

Different superscripts given in the same line indicate a statistically significant difference.

PI-RADS = Prostate Imaging Reporting and Data System; PV = prostate volume; sPCa = clinically significant prostate cancer; BMI = body mass index; PSA = prostate-specific antigen.

Table 2
Comparison of cancer detection rates according to PI-RADS scores and the number of cores per lesion.

	Clinically significant prostate cancer rates			p
	2 cores (n = 219)	3 cores (n = 217)	4 cores (n = 248)	
PI-RADS 3	10/110 (9.1%) ^a	8/80 (10.0%) ^a	20/108 (18.5%) ^b	0.042
PI-RADS 4	12/67 (17.9%) ^a	31/87 (35.6%) ^b	30/93 (32.3%) ^b	0.044
PI-RADS 5	20/42 (47.6%)	23/50 (46.0%)	23/47 (48.9%)	0.959
Overall	42/219 (19.2%) ^a	62/217 (28.6%) ^b	73/248 (29.4%) ^b	0.015

Different superscripts given in the same line indicate a statistically significant difference.

PI-RADS = Prostate Imaging Reporting and Data System.

4. Discussion

The results indicated that the ideal number of biopsy cores to be obtained from suspicious lesions in TB depends on the characteristics of the lesions. Moreover, it was also revealed that obtaining 4 biopsy cores from PI-RADS 3 lesions, 3 biopsy cores from PI-RADS 2 lesions, and 2 cores from PI-RADS 5 lesions could be adequate for ensuring accurate histopathological results. However, obtaining 3 biopsy cores per lesion was found to be an ideal approach for all patients, regardless of their PI-RADS scores.

A recent study evaluated biopsy results of patients who underwent radical prostatectomy owing to PCa and also analyzed the number of biopsy cores obtained from cancer foci and the PCa

detection rates. The authors reported that the PCa detection rates on first TB core in PI-RADS 3, 4, and 5 lesions were 67%, 79%, and 87%, respectively. The authors also noted that obtaining 2 cores per lesion could be adequate for ensuring accurate histopathological results.⁹ In a 2018 study, Dimitroulis et al.⁶ evaluated the PCa detection rates on the first and second biopsy cores obtained from suspicious lesions. The authors reported that the first biopsy core detected 89% of PCAs and also indicated that obtaining more than one biopsy core per lesion had no significant effect on PCa detection rate. Similarly, a 2019 study reported that obtaining 2 cores missed almost one-fourth of sPCas and that obtaining five biopsy cores could provide the most accurate diagnosis.⁷ From these findings, it is clear that there is no consensus in the literature with regard to the ideal number of biopsy cores to be obtained from suspicious lesions. In our study, unlike in other studies, the patients were grouped based on their PI-RADS scores, and the findings indicated that the number of cores to be obtained from suspicious lesions might vary depending on the characteristics of the lesions.

In our study, the sPCa detection rates in patients with PI-RADS 3, 4, and 5 lesions were 12.4%, 38.1%, and 45.6%, respectively, and the overall sPCa detection rate was 24.4%. Literature reviews indicate that the overall sPCa detection rates in TB and the sPCa detection rates according to PI-RADS scores remain controversial and that these rates vary according to patient characteristics (Table 4). A recent study reported that the overall sPCa detection rate in TB was 32% and the sPCa detection rates for PI-RADS 3, 4, and 5 lesions

Table 3
Comparison of cancer detection rates in biopsy-naive patients and patients with a history of prior negative biopsy according to the number of cores per lesion.

	Clinically significant prostate cancer rates			p	Overall
	2 cores (n = 219)	3 cores (n = 217)	4 cores (n = 248)		
Biopsy naive	31/163 (19.0%) ^a	45/153 (29.4%) ^b	45/144 (31.3%) ^b	0.035	26.3%
Prior biopsy history	9/56 (16.1%) ^a	18/64 (28.1%) ^b	29/104 (27.9%) ^b	0.039	25.0%

Different superscripts given in the same line indicate a statistically significant difference.

Table 4
Comparison of clinically significant prostate cancer (sPCa) detection rates and PI-RADS scores reported in previous studies.

Study group	Number of patients	Biopsy naive (BN) or not	PSA (ng/ml)	PI-RADS/sPCa			Overall sPCa
				3	4	5	
John et al ¹³	131	Mixed	12.8 ± 11.3	11%	42.9%	35.6%	32%
Sonn et al ¹⁴	105	Not	7.5 (5.0–11.2) ^{a)}	NR	NR	NR	24%
Boesen et al ¹⁵	206	Not	12.8 (8.9–19.6) ^{a)}	22.2%	62.7%	94.1%	31%
Baco et al ¹⁶	175	BN	6.9 (5.2–9.2) ^{a)}	29%	69% ^{b)}	69% ^{b)}	38%
Fourcade et al ³	191	Mixed	9 (0.7–48) ^{a)}	14%	35%	61%	38.2%
Venderink et al ¹⁷	1,057	Mixed	10.4 (7.1–16.7) ^{a)}	17%	34%	67%	48%

PSA = prostate-specific antigen; PI-RADS = Prostate Imaging Reporting and Data System, NR = not reported,

^{a)} Median (interquartile range).

^{b)} PI-RADS 4 and 5 together.

were 11.0%, 42.9%, and 35.6%, respectively.¹³ In a 2014 study, Sonn et al.¹⁴ reported the overall sPCa detection rate in patients who underwent TB as 24%. Boasen et al.¹⁵ reported that the overall sPCa detection rate in patients who underwent TB was 31% and the sPCa detection rates for PI-RADS 3, 4, and 5 lesions were 22.2%, 62.7%, and 94.1%, respectively. The sPCa detection rate for PI-RADS 5 lesions was remarkably high, and the authors also noted that the median PSA level was 12.8 (range, 8.9–19.6) ng/ml, which was higher than that of our patients.¹⁵ On the other hand, two recent studies reported that the overall sPCa detection rate in their patients who underwent TB was 38%.^{3,16} However, these two studies, unlike our study, included not only patients with PSA levels <10 ng/ml but also patients with higher serum PSA levels, which could be the reason for the difference between the sPCa detection rates in our study and in those two studies.

Another study evaluated a total of 1,042 patients and reported that the overall sPCa detection rate was 30% in biopsy-naïve patients and 19% in patients with a history of prior negative biopsy.¹⁸ On the other hand, Siddiqui et al.⁵ compared biopsy-naïve patients and patients with a history of prior negative biopsy in terms of sPCa detection rate in TB and found no significant difference between the two groups. Similarly, in our study, biopsy-naïve patients and patients with a history of prior negative biopsy were similar with regard to sPCa detection rates despite minor differences.

Our study has several key limitations. First and foremost, the study had a retrospective design and a small patient population. Second, the histopathological results were not evaluated based on a definitive diagnosis method such as radical prostatectomy but were evaluated based on biopsy outcomes, which led to false negative results and thus might have resulted in incomplete conclusions. Fourth, patients with a diagnosis of ASAP and HG PIN were excluded from the study, and no information could be obtained regarding their clinical outcomes owing to their short follow-up period. Finally, as the study had a retrospective nature, the number of biopsy cores to be obtained from each lesion was not determined based on a standard approach but was determined by the clinician performing the biopsy procedure. This limitation is associated with the lack of standardization and could have caused a bias.

In conclusion, our results indicated that the ideal number of cores to be obtained from each suspicious lesion in TB depends on the characteristics of the lesions (i.e., PI-RADS scores). Accordingly, while obtaining 2–3 biopsy cores could be adequate in PI-RADS 4 and 5 lesions that have a serious risk of cancer, a minimum of 4 biopsy cores should be obtained from PI-RADS 3 lesions to ensure accurate histopathological results.

Conflicts of interest

All authors declare that there is no conflict of interest in connection with this article.

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