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Research Article

Diagnostic Comparison of MRI/Ultrasound Fusion Biopsy and Systematic Biopsy in PI-RADS 4-5 Prostate Lesions

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ABSTRACT

Objective: Multiparametric magnetic resonance imaging (mpMRI) has transformed prostate cancer (PCa) diagnosis by enabling lesion-targeted biopsies. The optimal biopsy approach—systematic biopsy (SB), MRI-ultrasound fusion targeted biopsy (TB), or their combination (CB)—remains debated, especially in patients with high-risk Prostate Imaging-Reporting and Data System (PI-RADS) 4-5 lesions. This study compared these strategies for detecting overall and csPCa.

Methods: This retrospective study included 330 patients who underwent MRI-ultrasound fusion TB with 12-core SB between July 2022 and May 2025. Only lesions classified as PI-RADS v2.1 category 4 or 5 were analyzed. Detection rates of overall PCa and csPCa (Gleason score ≥ 7) were compared among SB, TB, and CB. Subgroup analyses were performed by PI-RADS category and lesion location (anterior, middle, posterior). Logistic regression identified independent predictors of csPCa.

Results: A total of 429 lesions were evaluated. Overall, PCa detection rates were 62% for SB, 70% for TB, and 77% for CB ($P < 0.001$); the corresponding csPCa rates were 47%, 56%, and 63% ($P < 0.001$). TB detected csPCa more effectively than SB (56% vs. 47%, $P < 0.01$). PI-RADS 5 lesions had higher detection rates than PI-RADS 4 lesions across all methods. CB achieved the highest rates in all locations, especially in anterior and middle lesions. Age, positive digital rectal examination, prostate-specific antigen density, prior biopsy, and PI-RADS category 5 were independent predictors of csPCa.

Conclusion: In PI-RADS 4–5 lesions, combined SB and TB provide the highest detection rate for csPCa. While TB improves selective detection, SB remains essential to avoid missing significant disease.

Keywords: Prostate cancer, multiparametric MRI, PI-RADS, MRI-ultrasound fusion biopsy, targeted biopsy, systematic biopsy, clinically significant prostate cancer

INTRODUCTION

Prostate cancer (PCa) is one of the most commonly diagnosed solid malignancies in men and ranks among the leading cancers worldwide in terms of incidence.[1,2] Its frequency increases markedly with age; most cases are diagnosed in men over 65 years.[3,4] With the widespread use of prostate-specific antigen (PSA) screening, an increase in diagnoses has also been observed in younger age groups, particularly for tumors with limited clinical significance.[5,6] PCa exhibits highly heterogeneous biological behavior, ranging from indolent lesions to aggressive, life-threatening forms.[7,8]

For many years, the diagnostic evaluation of patients with suspected PCa has relied on standard extended sextant biopsy performed under transrectal ultrasound (TRUS) guidance.[1] While image-guided biopsies have become an essential component of diagnosis in most other solid-organ tumors, PCa has traditionally been diagnosed by systematic and random sampling of the gland. However, this approach has increasingly been questioned, as it may fail to accurately localize clinically significant tumors and lead to the overdiagnosis of low-risk disease.[2,3]

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In recent years, mpMRI has entered clinical practice and led to a significant paradigm shift in the diagnostic algorithm for PCa.[4,5] mpMRI provides high diagnostic accuracy, particularly for detecting high-grade and clinically significant prostate cancers (csPCa), and enables imaging-based localization of tumors.[6,7] This development has paved the way for more targeted diagnostic biopsy strategies.[8]

Advances in imaging technologies have led to the development of MRI-ultrasound fusion biopsy systems, which allow electronic co-registration of lesions identified as suspicious on mpMRI with real-time TRUS images.[9] Using these platforms, direct sampling can be performed from areas identified on prostate mpMRI as at risk for clinically significant cancer, thereby improving diagnostic yield.[10,11]

Targeted biopsy performed after mpMRI provides additional diagnostic value in PCa detection beyond that achieved by systematic biopsy alone. The literature demonstrates that this approach detects csPCas with greater accuracy while reducing diagnoses of low-grade tumors.[4,6,10] This selective diagnostic advantage decreases the risk of overdiagnosis and overtreatment, and may also reduce the number of biopsy cores taken and the related complications.[4,10] Studies by Barış Türkbey et al.[11,12] have further shown that mpMRI-guided targeted biopsy offers high diagnostic accuracy, particularly in Prostate Imaging-Reporting and Data System (PI-RADS) 4-5 lesions.

MAIN POINTS

- Superiority of Combined Biopsy: In high-risk Prostate Imaging-Reporting and Data System (PI-RADS) 4-5 lesions, the concurrent use of systematic and multiparametric magnetic resonance imaging-targeted biopsies significantly outperforms either approach alone in detecting both overall and clinically significant prostate cancer (csPCa).
- Selective Accuracy of Targeted Biopsy: Targeted biopsy enables precise detection of clinically significant cancers, especially in high-risk and anterior or mid-gland lesions; however, relying solely on this method may miss a subset of cancers.
- Impact of Lesion Location: Anatomical location critically influences diagnostic performance. In anterior PI-RADS 5 lesions, combined biopsy is essential, whereas in posterior lesions, targeted biopsy alone suffices in most cases, with minimal added value from systematic sampling.
- PI-RADS as a Key Predictor: The PI-RADS category stands out as the strongest independent predictor of csPCa, with PI-RADS 5 lesions conferring a markedly elevated risk regardless of other clinical or biochemical factors.
- Need for Individualized Biopsy Strategies: These findings highlight that prostate biopsy should not follow a one-size-fits-all model; tailoring approaches based on PI-RADS score and lesion location maximizes diagnostic accuracy and clinical impact.

Nevertheless, it has been reported that a strategy based solely on targeted biopsy may miss a proportion of clinically significant tumors that are not visible or cannot be adequately targeted on mpMRI.[5,9,13] For this reason, current European guidelines recommend the combined use of systematic and targeted biopsies to enhance diagnostic safety, while a targeted-only approach is generally reserved for patients with persistently elevated clinical suspicion despite prior negative biopsies.[7]

A substantial proportion of previous studies have been conducted in heterogeneous patient populations including PI-RADS 3 lesions, making it difficult to delineate the diagnostic contribution of different biopsy strategies in high-risk lesion groups. Although PI-RADS 4 and 5 lesions are considered high risk for clinically significant PCa, the superiority of MRI-ultrasound fusion-guided targeted biopsy over systematic biopsy and the additional diagnostic value of a combined approach in this subgroup remain subjects of ongoing debate.[11,12,14]

In a study published in 2024, Thomas in de Braekt and colleagues compared the diagnostic accuracy of MRI-ultrasound fusion-guided targeted biopsy with systematic biopsy. They reported that targeted biopsy provided higher specificity for detecting clinically significant PCa; however, systematic biopsy continued to contribute diagnostically in certain patient subgroups.[15]

The aim of the present study is to evaluate, in patients with PI-RADS 4 and 5 lesions, the performance of MRI-ultrasound fusion-guided targeted biopsy in detecting clinically significant PCa compared with that of standard systematic biopsy and to determine whether the combined application of the two methods provides additional diagnostic accuracy.

MATERIAL AND METHODS

Study Design and Patient Selection

Approval for this retrospective study was obtained from the Institutional Review Board. Due to the retrospective design of the study, the requirement for informed consent was waived by the Erzincan Binali Yıldırım University Ethics Committee (approval number: 2026-01-01; date: 08.01.2026). This retrospective study included patients who underwent MRI-guided targeted prostate biopsy and simultaneous 12-core systematic prostate biopsy at our institution between July 1, 2022, and May 1, 2025. A total of 330 patients were evaluated. Patient data were retrospectively obtained from the institution's electronic medical record system. The planning, conduct, and reporting of the study followed the Standards of Reporting for MRI-targeted Prostate Biopsy Studies.

The study population consisted of men who were either undergoing their first prostate biopsy or had previously undergone a biopsy with benign results. Patients under active surveillance, with a known diagnosis of PCa, with insufficient imaging quality, or with a history of non-prostate malignancy were excluded. The research protocol was approved by the local ethics committee; because of the study's retrospective design, the requirement for informed consent was waived.

Imaging Protocol

All patients underwent mpMRI using a 1.5 Tesla MRI system (Siemens Healthineers, Erlangen, Germany) with a surface body coil. The imaging protocol included high spatial resolution T2-weighted turbo spin-echo sequences acquired in the axial, coronal, and sagittal planes, and axial diffusion-weighted imaging. Diffusion data were acquired using b-values of 0, 50, 800, and 1500 s/mm^2, from which apparent diffusion coefficient maps were generated for quantitative analysis.

Dynamic contrast-enhanced MRI was performed selectively when deemed necessary to support the diagnostic interpretation of the dominant sequence, in accordance with the PI-RADS version 2.1 guidelines. All mpMRI examinations were conducted in accordance with the technical adequacy and image-quality criteria defined by PI-RADS.

Image Evaluation Criteria

Multiparametric prostate MRI examinations were analyzed by radiologists with extensive experience in urogenital imaging, who took into account patients' clinical data and followed the PI-RADS version 2.1 guidelines. Lesions were assessed and classified based on their anatomical location and on morphological and functional features observed in the dominant imaging sequences. Foci classified as PI-RADS 4 or 5 were considered highly suspicious for clinically significant PCa and were designated as targets for biopsy.

Biopsy Protocol

In this retrospective study, experienced urologists performed prostate biopsies with patients positioned in the left lateral decubitus position. The interpreting radiologist uploaded mpMRI images to a software-based MRI-US fusion biopsy system (Hitachi Hi Vision Preirus, Hitachi, Japan). After defining the prostate's anatomical reference structures, the MRI data were co-registered with real-time TRUS images using the software; cognitive fusion techniques were not used.

Following the completion of image fusion, TRUS-guided targeted biopsies were obtained, using a transrectal firing biopsy probe, from lesions identified as suspicious according to PI-RADS version 2.1 criteria. Targeted biopsy specimens were placed in separate containers, preserving lesion localization information, and sent for pathological evaluation without staining.

After targeted biopsies, systematic TRUS-guided biopsies were performed in both lobes, covering the apex, mid-zone, and base of the prostate. Regardless of prostate volume, all patients underwent a standard 12-core systematic biopsy protocol.

Histopathological

Assessment: All biopsy samples were fixed in formalin and embedded in paraffin, following the institution's routine pathology procedures. From each tissue block, at least three sections were prepared and stained with hematoxylin and eosin. Additionally, at least one section per block underwent immunohistochemical staining to evaluate the basal cell layer.

Evaluation of the specimens was conducted by specialized uropathologists, and the detected malignancies were classified according to the Gleason scoring system.

Statistical Analysis

Descriptive statistics were used to summarize patient demographics, imaging findings, and biopsy data. To assess differences between biopsy methods, Cochran's Q test was applied to the entire cohort and within each PI-RADS category. Post hoc comparisons of cancer detection rates between biopsy techniques, including overall and clinically significant PCa, were performed using the McNemar test.

The relationships between clinical and pathological variables and the likelihood of detecting clinically significant cancer were evaluated using logistic regression analysis. All tests were two-sided, and a P value < 0.05 was considered statistically significant. The Holm-Bonferroni method was applied for multiple testing correction. All analyses were conducted using SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA).

Patient Characteristics

A total of 330 patients were included in this study. The median age of the cohort was 66 years, and the median interval between multiparametric prostate MRI and biopsy was approximately 1.5 months. The median serum PSA level was around 8.5 ng/mL, while the mean prostate volume was approximately 55 cm^2. The median PSA density was 0.15 ng/mL/cm^2. The mean number of suspicious MRI lesions per patient was 1.3, indicating a limited but clinically significant lesion burden.

Only PI-RADS 4 and PI-RADS 5 lesions detected on mpMRI were included in the study. A total of 429 suspicious lesions were identified, of which 279 were PI-RADS 4 and 150 were PI-RADS 5. This distribution indicates a predominance of intermediate- and high-risk prostate lesions in the study population.

Histopathological analysis revealed clinically significant PCa in 198 of the 330 patients. Among patients diagnosed with cancer, the most common pathological subgroup was Gleason score 3+3=6, represented by 78 patients, followed by Gleason score 3+4=7 (52 patients) and Gleason score 4+3=7 (28 patients). High-grade disease (Gleason ≥ 8) was detected in 40 patients. Overall, Gleason ≥ 7 tumors were present in 120 patients, reflecting a cohort with a notable risk profile for clinically significant and intermediate-to-high-risk PCa.

This cohort of 330 patients, with a median age of 66 years and a median MRI-to-biopsy interval of approximately 1.5 months, predominantly consisted of patients with PI-RADS 4-5 lesions. Histopathological findings indicate a substantial representation of intermediate- and high-grade PCa. The mean number of targeted biopsies per patient was 2.5 ± 0 (Table 1).

Representative cases are shown in Figures 1 and 2. A 64-year-old male with a PSA of 7.9 ng/mL and PSA density of 0.14 ng/mL/cm^2 was found to have a PI-RADS 4 lesion, which was confirmed as Gleason 3 + 4 (Grade Group 2) prostate adenocarcinoma on targeted biopsy. Another example is a 69-year-old male with a PSA of 12.4 ng/mL and PSA density of 0.22 ng/mL/cm^2 who

Table 1. Patient Characteristics

Characteristic	First-time biopsy patients	Previously negative biopsy patients	All patients
Age (years), median (IQR)	65 (61-71)	68 (64-73)	66 (62-72)
Digital rectal examination, n (%)			
· Positive	78 (31.2)	32 (40.0)	110 (33.3)
· Negative	172 (68.8)	48 (60.0)	220 (66.7)
PSA level (ng/mL), median (IQR)	8.1 (6.2-11.4)	9.6 (7.4-13.2)	8.5 (6.6-12.1)
Prostate volume (cm^2), median (IQR)	53 (45-62)	58 (48-68)	55 (46-64)
PSA density ($ng/mL/cm^2$), median (IQR)	0.14 (0.10-0.19)	0.17 (0.12-0.22)	0.15 (0.11-0.20)
Interval between MRI and biopsy (days), median (IQR)	42 (30-58)	47 (35-62)	45 (32-60)
Number of MRI lesions (mean ± SD)	1.3 ± 0.5	1.4 ± 0.6	1.3 ± 0.5
Number of targeted biopsies (mean ± SD)	2.5 ± 0.6	2.6 ± 0.7	2.5 ± 0.6
PI-RADS category, n (%)			
· PI-RADS 4	210 (84.0)	69 (86.3)	279 (84.5)
· PI-RADS 5	40 (16.0)	11 (13.7)	51 (15.5)
Gleason score, n (%)			
· 3+3=6	62 (24.8)	16 (20.0)	78 (23.6)
· 3+4=7	40 (16.0)	12 (15.0)	52 (15.8)
· 4+3=7	22 (8.8)	6 (7.5)	28 (8.5)
· ≥ 8	28 (11.2)	12 (15.0)	40 (12.1)
Clinically significant PCa (Gleason ≥ 7), n (%)	90 (36.0)	30 (37.5)	120 (36.4)

PSA, prostate-specific antigen; SD, standard deviation; PCa, prostate cancer; MRI: magnetic resonance ımaging; PI-RADS, prostate ımaging-reporting and data system; IQR, interquartile range.

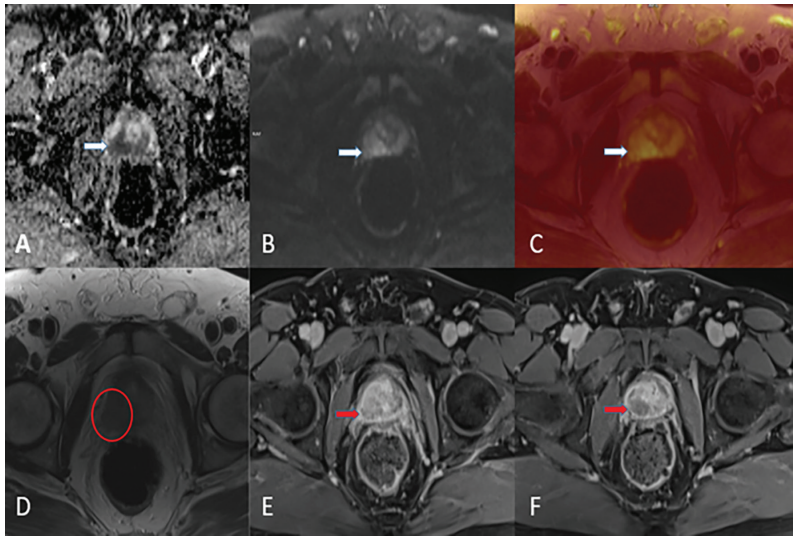


Figure 1. Shows mpMRI of the prostate in a 64-year-old male with elevated PSA, demonstrating a PI-RADS 4 lesion. On axial imaging, a focal lesion is seen in the right peripheral zone at the mid-gland level. The T2-weighted image **A)** demonstrates a moderately hypointense lesion without definite extracapsular extension, whereas the diffusion-weighted image **B)** shows marked hyperintensity of the lesion. The corresponding apparent diffusion coefficient map **C)** confirms restricted diffusion. A T2-weighted image with a red circle **D)** highlights the lesion's exact location. Dynamic contrast-enhanced imaging **E)** reveals early focal enhancement of the lesion compared with the surrounding parenchyma, and the color-coded perfusion map **F)** emphasizes the hypervascularity. The lesion was assigned a PI-RADS 4 score, and targeted MRI-ultrasound fusion biopsy confirmed clinically significant prostate adenocarcinoma (Gleason score 3+4, Grade Group 2).

DCE, dynamic contrast-enhanced; MRI, magnetic resonance imaging; PSA, prostate-specific antigen; PI-RADS, prostate ımaging-reporting and data system.

demonstrated a PI-RADS 5 lesion that was confirmed as high-grade Gleason 4+4 (Grade Group 4) adenocarcinoma. Detailed multiparametric MRI findings for these cases are illustrated in the respective figure legends.

Overall Detection Rate

The detection rates of PCa and clinically significant PCa for all biopsy methods, based on PI-RADS v2.1 classification and considering only PI-RADS 4-5 lesions, are presented in Table 2. The overall PCa detection rate was 62% (267/429) for systematic biopsy alone, 70% (301/429) for targeted biopsy alone, and 77% (331/429) for combined biopsy. Clinically significant PCa detection rates were 47% (203/429), 56% (240/429), and 63% (270/429), respectively. The combined biopsy approach demonstrated significantly higher detection rates for both overall and clinically significant PCa compared with either systematic or targeted biopsy alone ($P < 0.001$ for all comparisons).

When comparing the performance of systematic versus targeted biopsies alone in detecting overall PCa, the targeted biopsy showed a significant advantage (70% vs. 62%, $P < 0.01$). For clinically significant PCa, targeted biopsy achieved a significantly higher detection rate than systematic biopsy (56% vs. 47%, $P < 0.01$).

In the PI-RADS v2.1 subgroup analysis, PI-RADS 5 lesions demonstrated substantially higher detection rates for both overall PCa and clinically significant PCa across all biopsy methods, compared with PI-RADS 4 lesions. This superiority remained significant after correction for multiple testing, with the combined biopsy method showing the highest diagnostic performance in detecting clinically significant PCa in PI-RADS 5 lesions.

Detection Rates According to Lesion Location

For patients with a single suspicious lesion, the detection rates of PCa and csPCa for anterior, middle (mid-gland), and posterior PI-RADS 4/5 lesions are summarized in Table 3. Combined biopsy demonstrated significantly higher detection rates for both overall PCa and csPCa across all anatomical regions than either systematic or targeted biopsy alone (all comparisons, $P < 0.001$).

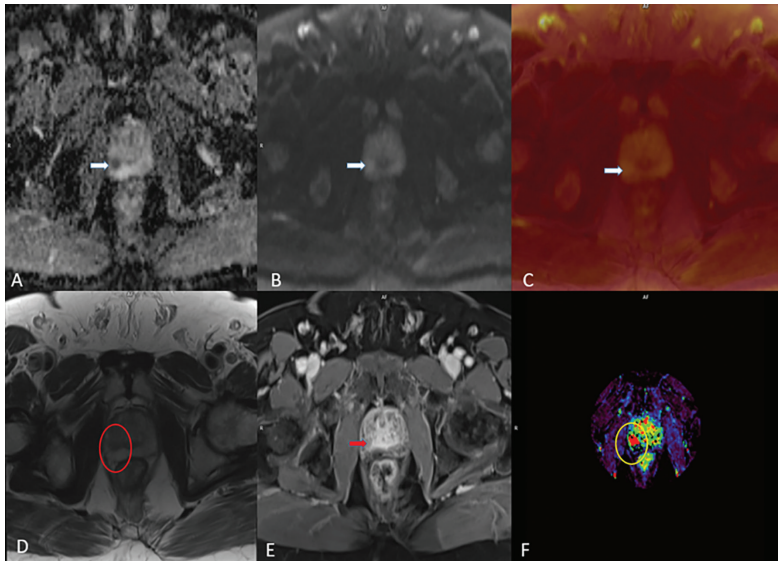


Figure 2. mpMRI of a PI-RADS 5 lesion in a 69-year-old male patient. A) Axial ADC map showing a focal lesion with markedly low signal intensity (white arrow). **B)** High b-value DWI demonstrating pronounced diffusion restriction (white arrow). **C)** Fusion PET/MRI image highlighting hypermetabolic activity corresponding to the lesion (white arrow). **D)** Axial T2-weighted image showing a hypointense lesion in the left peripheral zone (red circle). **E-F)** Axial post-contrast T1-weighted images demonstrate **e**arly enhancement with capsular bulging (red arrows); F additionally shows rapid washout, suggestive of aggressive behavior. Targeted biopsy confirmed clinically significant prostate adenocarcinoma, Gleason 4+4 (Grade Group 4).

DWI,diffusion-weighted imaging; ADC, apparent diffusion coefficien; PI-RADS, prostate ımaging-reporting and data system; MRI, magnetic resonance imaging.

Table 2. (2a and 2b) Detection Rates of Prostate Cancer and Clinically Significant Prostate Cancer According to PI-RADS classification for Systematic Biopsy, Targeted Biopsy, and Combined Biopsy Methods (2a: Total Prostate Cancer, 2b: Clinically Significant Prostate Cancer) -**Table 2a**-

PI-RADS	Total	SB n(%)	FB n(%)	KB n(%)	*P* value
PI-RADS-4	279	155 (%56)	178(%64)	196(%70)	**< 0.001**
PI-RADS 5	150	112 (%75)	123(%82)	135 (%90)	**< 0.001**
Overall total	429	267 (62)	301 (70)	331 (77)	**< 0.001**

SB, systematic biopsy; FB, targeted fusion biopsy; CB, combined biopsy; PI-RADS, prostate imaging-reporting and data system

For anterior lesions, targeted biopsy showed higher detection rates than systematic biopsy for both overall PCa and csPCa. This difference was particularly pronounced in anterior PI-RADS 5 lesions, where systematic biopsy lagged behind targeted biopsy in detecting overall PCa. However, no statistically significant difference was observed between the two methods for detecting csPCa in this subgroup. Additionally, for anterior PI-RADS 5 lesions, no significant advantage in overall PCa detection was observed between targeted and combined biopsies.

For middle (mid-gland) lesions, targeted biopsy yielded higher detection rates than systematic biopsy for both overall PCa and csPCa. Nevertheless, combined biopsy provided the highest detection rates compared to either method alone, highlighting its diagnostic advantage in this region. The superiority of combined biopsy was maintained in PI-RADS 5 middle-segment lesions for both overall and clinically significant cancers.

For posterior lesions, systematic biopsy demonstrated higher overall PCa detection rates than targeted biopsy. However, no significant differences were observed between biopsy methods for csPCa detection. Specifically, in posterior PI-RADS 5 lesions, no statistically significant differences were noted between biopsy techniques in detecting either overall PCa or csPCa.

Associations with and Presence of csPCa

Variables associated with csPCa are summarized in Table 4. In univariable analysis, advanced age, prior biopsy, a positive digital rectal examination (DRE), and elevated PSA density were significantly associated with the detection of csPCa. Among imaging parameters, PI-RADS category emerged as the strongest predictor, with PI-RADS 5 lesions showing a markedly higher likelihood of clinically significant cancer compared to PI-

-**Table 2b**-

PI-RADS	Total	SB n (%)	FB n (%)	KB n (%)	*P value*
PI-RADS-4	279	98 (35)	124 (44)	142 (51)	**< 0.001**
PI-RADS 5	150	105 (70)	116 (77)	128 (85)	**< 0.001**
Overall Total	429	203 (47)	240 (56)	270 (63)	**< 0.001**

SB, systematic biopsy; FB, targeted fusion biopsy; CB, combined biopsy; PI-RADS, prostate ımaging-reporting and data system KB,

Table 3a/3b: Detection Rates of Clinically Significant Prostate Cancer (csPCa) and Overall Prostate Cancer (PCa) Diagnosed by Biopsy Alone, Stratified by Anatomical Location (Anterior, Mid-Gland, and Posterior) of PI-RADS 4-5 Lesions, Using Systematic, Fusion-Targeted, and Combined Biopsy Methods

Anatomic location	PI-RADS	Total (n)	SB kPca (n) (%)	FB kPCa (n) (%)	KB kPCa (n) (%)	*P* value
Anterior	4	92	50 (54)	61(66)	68 (74)	< 0.001
	5	58	43 (74)	48 (83)	52 (90)	< 0.001
	Total	150	93 (62)	109 (73)	120 (80)	**< 0.001**
Orta (middle)	4	84	46 (55)	54 (64)	61 (73)	< 0.001
	5	45	33 (73)	37 (82)	41 (91)	< 0.001
	Total	129	79 (61)	91 (71)	102 (79)	**< 0.001**
Posterior	4	103	59 (57)	63 (61)	67 (65)	0.008
	5	47	36 (77)	38 (81)	42 (89)	< 0.001
	Total	150	95 (63)	101 (67)	109 (73)	**< 0.001**
Anatomic location	**PI-RADS**	**Total (n)**	**SB Pca (n) (%)**	**FB PCa (n) (%)**	**KB PCa (n) (%)**	***P* value**
Anterior	4	92	32 (35)	41 (45)	48 (52)	<0.001
	5	58	40 (69)	45 (78)	49 (84)	<0.001
	Total	150	72 (48)	86 (57)	97 (65)	**<0.001**
Middle	4	84	29 (35)	37 (44)	43 (51)	<0.001
	5	45	31 (69)	35 (78)	39 (87)	<0.001
	Total	129	60 (47)	72 (56)	82 (64)	**<0.001**
Posterior	4	103	37 (36)	46 (45)	51 (50)	<0.001
	5	47	34 (72)	36 (77)	40 (85)	<0.001
	Total	150	71 (47)	82 (55)	91 (61)	**<0.001**

SB, systematic biopsy; FB, targeted fusion biopsy; CB, combined biopsy; PCa, prostate cancer; kPCa, clinically significant prostate cancer; PI-RADS, prostate ımaging-reporting and data system

Note: Data are presented as n(%). P values indicate comparisons between biopsy methods (SB vs. FB, SB vs. CB, and FB vs. CB). For multiple comparisons, Bonferroni correction was applied, and statistical significance was set at $P < 0.0167$. Clinically significant prostate cancer was defined as Gleason score ≥ 7. Only PI-RADS v2.1 lesions scored 4 and 5 were included in the analysis.

Table 4. Single-Variable and Multiple-Variable Regression Analyses for Predicting Significant Prostate Cancer

Variable regressin analysis		Single		Multiple	
Parameter	**Comparison**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
Age (median 66)	≤ 66 vs. > 66	1.48 (1.10-1.98)	**0.009**	1.36 (1.02-1.82)	0.037
DRE	Pos vs. Neg	2.21 (1.45-3.36)	**< 0.001**	1.88 (1.21-2.93)	**0.005**
PSA (Median 8.5 ng/mL	≤ 8.5 vs. > 8.5	1.31 (0.96-1.78)	.086	-	-
Prostate volüme (median 55 cm^2)	≤ 55 vs. > 55	0.71 (0.52-0.98)	.038	-	-
PSA density (median 0.15 bg7mL/cm^2)	≤ 0.15 vs. > 0.15	2.54 (1.88-3.43)	**< 0.001**	2.19 (1.61-2.98)	**< 0.001**
First biopsy	Yes vs. No	0.59 (0.42-0.83)	**0.002**	0.61 (0.43-0.87)	0.006
PI-RADS 4	-	-	-	-	-
PI-RADS 5	According to 4	6.12 (4.02-9.31)	**< 0.001**	5.48 (3.61-8.32)	**< 0.001**

OR, odds ratio; CI, confidence interval; DRE, digital rectal examination; PSA, prostate-specific antigen; MRI, magnetic resonance imaging; PI-RADS, prostate ımaging-reporting and data system

Notes: Clinically significant prostate cancer was defined as Gleason score ≥ 7. Only PI-RADS v2.1 - PI-RADS 4 and 5 lesions were included in the analysis. Variables with $P < 0.10$ in the univariable analysis that were considered clinically relevant were included in the multivariable model. PSA and prostate volume were not included in the multivariable model due to collinearity with PSA densi.

RADS 4 lesions. In contrast, total PSA level and prostate volume were not significantly associated with the presence of csPCa.

In multivariable logistic regression analysis, age, prior biopsy history, positive DRE, PSA density, and higher PI-RADS category remained independent predictors of csPCa. Notably, PI-RADS 5 lesions significantly increased the probability of detecting csPCa, independent of other clinical and biochemical variables.

DISCUSSION

In this retrospective study, the diagnostic contribution of mpMRI-based biopsy strategies for detecting PCa, including clinically significant cases was analyzed in a homogeneous cohort comprising only PI-RADS 4 and 5 lesions. Excluding PI-RADS 3 lesions and earlier PI-RADS versions enhanced the methodological consistency of the study and allowed a clearer assessment of the diagnostic performance specific to high-risk lesions.

The results presented in Table 2 indicate that systematic and targeted biopsies demonstrate comparable overall diagnostic performance when used alone. However, combining these two approaches provides a significant incremental benefit for detecting both overall and csPCa. This finding suggests that in higher PI-RADS categories, intralesional heterogeneity and multifocal tumor architecture may not be fully captured by a single biopsy approach. The superiority of combined biopsy likely reflects not only the increased sampling of lesions but also the capture of tumor foci with distinct biological behaviors.

Targeted biopsy appears to offer an advantage over systematic biopsy in detecting clinically significant cancer. This observation aligns with the ability of mpMRI to localize higher-grade tumors and supports its potential to reduce overdiagnosis of clinically insignificant disease. However, given the additional diagnostic benefit provided by combined biopsy, relying on a single biopsy method may be insufficient, particularly for high-risk patient groups.

Analyses based on lesion location (Table 3) revealed that the diagnostic performance of biopsy strategies anatomical localization significantly influences. In anteriorly located lesions, especially within higher PI-RADS categories, the combined biopsy approach provided the greatest diagnostic yield for clinically significant cancer. This finding reflects the risk that anterior zone lesions are missed due to the posterior sampling bias inherent in systematic biopsy. Nevertheless, targeted biopsy alone was not fully sufficient for anterior lesions, as some clinically significant cancers were detected only through systematic sampling.

For PI-RADS 5 lesions located posteriorly, differences in diagnostic performance among biopsy methods were markedly reduced. This can be explained by the posterior zone being more accessible to both systematic and targeted biopsies. In particular, adding a systematic biopsy when the targeted biopsy is negative may serve as a balanced approach that enhances diagnostic safety. These results strongly support the notion that biopsy strategies should be individualized based on lesion risk and anatomical location rather than adopting a "one-size-fits-all" approach.

The regression analyses presented in Table 4 highlight the central role of imaging-based parameters in the clinical decision-making process. The PI-RADS category emerged as the strongest independent predictor of the presence of csPCa. Notably, PI-RADS 5 lesions significantly increased the risk of clinically significant cancer, independent of other clinical and biochemical variables, thereby reinforcing the indispensable role of mpMRI in risk stratification.

Following PI-RADS, PSA density was identified as the second most powerful predictor. The lack of a significant association with total PSA level or prostate volume further underscores the limited standalone value of these parameters in clinical decision-making. In contrast, PSA density, as a biochemical marker more reflective of tumor burden, serves a complementary role to imaging findings. Additionally, advanced age, prior biopsy history, and positive DRE were independently associated with clinically significant cancer, emphasizing the importance of a multidisciplinary risk assessment approach.

A recent study by Thomas, de Braekt, and colleagues compared the diagnostic accuracy of MRI-ultrasound fusion-guided

targeted biopsy with systematic biopsy, demonstrating the superiority of a combined biopsy approach for detecting both overall and csPCa.[15] These findings align closely with the results of our study, particularly supporting the selective diagnostic advantage of targeted biopsy in high-risk lesions. Both studies emphasize that in posteriorly located PI-RADS 5 lesions, targeted biopsy rarely misses clinically significant cancer, whereas the contribution of systematic biopsy in this subgroup is limited.

The distinguishing feature of our study lies in its exclusive focus on PI-RADS 4 and 5 lesions as defined by PI-RADS v2.1, thereby reducing methodological heterogeneity and systematically analyzing lesion location (anterior-middle-posterior) to provide a more detailed assessment of biopsy strategy performance in an anatomical context. In contrast, the study by in de In de Braekt et al.[15] encompassed a broader PI-RADS spectrum, offering generalizability to routine clinical practice. However, the inclusion of PI-RADS 3 lesions introduces potential issues related to overdiagnosis of clinically insignificant cancer and unnecessary biopsies. In this regard, our study provides a clearer clinical signal specific to high-risk lesions, whereas the comparative study presents a more comprehensive perspective across a wider patient population.

The strengths of this study include its exclusive focus on high-risk PI-RADS categories, adherence to the current PI-RADS v2.1 classification, and detailed subgroup analyses based on lesion location. This approach ensures that the results are both methodologically robust and directly applicable to clinical practice. Additionally, the large patient cohort and the use of real-world data enhance the relevance and generalizability of the findings for routine practice in tertiary care centers.

Study Limitations

However, certain limitations should be acknowledged. The retrospective design cannot completely eliminate the risk of bias related to patient selection and biopsy performance. Furthermore, all biopsies were performed by a single operator familiar with the lesion information, which may have partially enhanced the performance of systematic biopsy. Finally, the use of histopathological thresholds to define clinically significant cancer may not capture the full spectrum of the biological behavior of tumors.

CONCLUSION

This study provides a comprehensive evaluation of mpMRI-based biopsy strategies in a well-defined cohort focused on high-risk lesions. The findings underscore the indispensable role of combined biopsy, particularly in selected patient subgroups, and highlight that tailoring biopsy approaches according to PI-RADS category and lesion location can further optimize diagnostic yield. These insights provide a robust scientific foundation for developing individualized prostate biopsy algorithms.

For the detection of csPCa, the concurrent use of systematic and targeted biopsies emerges as the most reliable strategy. While targeted biopsy allows for more selective sampling of high-risk lesions, relying on it alone may result in missed diagnoses in certain cases. Notably, in posterior PI-RADS 5 lesions, targeted biopsy demonstrates high diagnostic sufficiency, with limited incremental value from systematic biopsy; however, incorporating systematic biopsy when targeted biopsy is negative can enhance overall diagnostic safety.

This evidence emphasizes that an adaptive, lesion-specific approach—rather than a one-size-fits-all method—maximizes both precision and clinical utility in PCa detection.

Ethics

Ethics Committee Approval: Approval for the study was obtained by the Erzincan Binali Yıldırım University Ethics Committee (approval number: 2026-01-01; date: 08.01.2026).

Informed Consent: All imaging data were anonymized, with patients' names and other identifying information removed. Due to the retrospective nature of the study, informed consent was waived.

Footnotes

Author Contributions

Concept – O.D.; Design – O.D., A.L; Supervision – A.L.; Resources – O.D.; Materials – O.D., A.L.; Data Collection and/or Processing – A.L.; Analysis and/or Interpretation – A.L.; Literature Search – O.D., A.L.; Writing Manuscript – O.D.; Critical Review – O.D., A.L.; Other – A.L.

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