

Diagnostic Value of Peripheral Zone PSA Density for Detecting Clinically Significant Prostate Cancer in Men with Peripheral Zone MRI Lesions

Running title: Peripheral Zone PSA Density in Prostate Cancer

Min Hyuk Kim

Seoul National University

Hyo Myoung Lee

Seoul National University

Jang Hee Han

Seoul National University

Seung-hwan Jeong

Seoul National University

Ja Hyeon Ku

Seoul National University

Cheol Kwak

Seoul National University

Chang Wook Jeong

Seoul National University

Hyeong Dong Yuk

`armenia8@snu.ac.kr`

Seoul National University

Research Article

Keywords: Prostate cancer, Prostate-specific antigen density, Peripheral zone, Transition zone, Multiparametric magnetic resonance imaging, PI-RADS, Prostate biopsy

Posted Date: October 23rd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11216664/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

Whole-gland prostate-specific antigen density (PSAD) may underestimate the diagnostic contribution of peripheral zone (PZ) tumors, as it is diluted by transition zone (TZ) volume, which expands with age independent of cancer risk. We investigated whether PZ-specific PSAD (PSAD_PZ) improves the detection of clinically significant prostate cancer (csPCa) in men with PZ-only multiparametric MRI (mpMRI) target lesions, and evaluated the analogous TZ-specific PSAD (PSAD_TZ) in men with TZ-only targets.

Methods

We analyzed 651 men from the prospectively enrolled SUPER-PC registry, supplemented by a retrospectively identified non-cancer cohort, who underwent combined systematic and MRI-targeted fusion biopsy (416 with PZ-only and 235 with TZ-only mpMRI targets). Clinically significant prostate cancer was defined as International Society of Urological Pathology Grade Group 2 or greater. The diagnostic performance of PSA, whole-gland PSAD, and zone-specific PSAD was compared using receiver operating characteristic curve analysis, and optimal cut-off values were determined using the Youden index.

Results

In the PZ-target group, PSAD_PZ achieved a significantly higher area under the curve (AUC) than PSA (0.825 vs. 0.707, $p < 0.001$) and whole-gland PSAD (0.825 vs. 0.702, $p < 0.001$). This advantage persisted among men with Prostate Imaging Reporting and Data System (PI-RADS) category 4 or higher lesions (AUC 0.842) and remained significant after multivariable adjustment. The optimal PSAD_PZ cut-off value was 0.285 ng/mL/cm³, yielding a sensitivity of 70.8% and specificity of 84.3%. PSAD_TZ did not outperform PSA or whole-gland PSAD in the TZ-target group.

Conclusions

PSAD_PZ improves the detection of csPCa in men with PZ-only mpMRI targets and outperforms conventional whole-gland PSAD, supporting a zone-matched normalization strategy that may help reduce unnecessary biopsies and guide treatment decisions. PSAD_TZ conferred no comparable benefit among men with TZ-only targets.

Background

Prostate cancer remains the second most commonly diagnosed malignancy in men worldwide, with more than 1.4 million new cases estimated in 2022[1]. Multiparametric magnetic resonance imaging (mpMRI), interpreted with the Prostate Imaging Reporting and Data System (PI-RADS), has become the standard first step in the diagnostic pathway, allowing MRI-targeted biopsy to increase the detection of clinically significant prostate cancer (csPCa) while reducing overdiagnosis of indolent disease compared with systematic biopsy alone[2–4]. PI-RADS version 2.1 further refined lesion scoring criteria to improve reproducibility across readers[5]. Despite these advances, PI-RADS retains a substantial false positive rate, particularly for PI-RADS 3 and 4 lesions, for which biopsy still fails to detect csPCa in a large proportion of men[6–8]. This limitation has prompted interest in adjunctive clinical biomarkers, most notably PSA density (PSAD), to refine biopsy selection and reduce unnecessary procedures[9]. PSAD, first described by Benson et al. as the ratio of serum PSA to whole-gland prostate volume, was developed to better distinguish benign prostatic hyperplasia (BPH) from prostate cancer[10]. However, whole-gland PSAD has an inherent biological limitation: benign hyperplastic tissue is concentrated almost exclusively in the transition zone (TZ), and TZ volume increases disproportionately with age, independent of cancer risk[11]. Because whole-gland volume is dominated by this non-neoplastic TZ component, conventional PSAD dilutes the contribution of PSA arising from a peripheral zone (PZ) lesion, potentially attenuating its diagnostic signal in the population in which most csPCa actually originates[12].

Prior studies have largely used TZ-adjusted metrics or combined PSAD/MRI decision frameworks without stratifying patients by the mpMRI target zone[13–16]. In particular, no prior study has evaluated PZ-specific PSAD (PSAD_PZ) for diagnosing csPCa in men with PZ-only mpMRI targets. Therefore, we hypothesized that PSAD_PZ would outperform the conventional PSA and whole-gland PSAD in the detection of csPCa in men with PZ-only mpMRI targets.

Methods

Study Design and Patient Population

Between January 2024 and December 2025, 1,017 men underwent prostate biopsy for suspected prostate cancer at Seoul National University Hospital (SNUH) or at an outside institution. Data for men diagnosed with prostate cancer were obtained from the Seoul National University Prospectively Enrolled Registry for Prostate Cancer (SUPER-PC; $n = 936$), and data for men without a diagnosis of prostate cancer were collected retrospectively ($n = 81$). Of these, 161 men were excluded because MRI was performed after prostate biopsy, and four were excluded because no discrete target lesion was identified on mpMRI. The remaining 852 men underwent combined systematic and MRI-targeted fusion biopsy for suspected prostate cancer. Men were eligible for this analysis if all mpMRI target lesions were confined entirely to either the PZ or TZ on radiologist review. Of these 852 men, five were excluded because biopsy did not confirm prostate adenocarcinoma, and 196 were excluded because target lesions were present in both the PZ and TZ. The final study group consisted of 416 men with PZ-only targets and 235

men with TZ-only targets (Fig. 1). This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. H-2607-155-1762).

Image Acquisition and Interpretation

All mpMRI examinations were reviewed by genitourinary radiologists with more than 10 years of experience in prostate MRI interpretation and scored according to the PI-RADS version 2.1. mpMRI was performed using T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences according to PI-RADS v2.1 technical specifications. The PI-RADS category, lesion zone, and total prostate volume were extracted from the radiology reports.

Volumetric Measurements

Total prostate volume was obtained from the radiology report and calculated using the ellipsoid formula ($0.52 \times \text{width} \times \text{height} \times \text{depth}$) applied to the whole gland on T2-weighted imaging. TZ volume was measured manually by a urologist (M. H. K.) using the same formula applied to the transition zone on the corresponding images; PZ volume was derived by subtracting TZ volume from total prostate volume. To assess the reliability of TZ volume measurement, a random sample of 30 scans was selected using a computer-generated random number sequence (R version 4.6.1), and TZ volume was measured independently by two urologists (M. H. K. and H. M. L.) in this subset. Agreement was quantified using the intraclass correlation coefficient (ICC) under a two-way random-effects, absolute-agreement, single-measures model and further evaluated using Bland–Altman analysis to assess the mean difference and limits of agreement between the two measurements (Supplementary Table 1, Supplementary Fig. 1).

Biopsy Technique and Pathological Assessment

All men underwent combined systematic and MRI-targeted fusion biopsies of the identified lesions. Three targeted cores were obtained per lesion, and each systematic biopsy consisted of a template of up to 14 cores. Specimens were reviewed by genitourinary pathologists and graded according to the International Society of Urological Pathology (ISUP) Grade Group (GG) system. The overall GG for each patient was assigned as the highest grade identified across the combined targeted and systematic cores, without distinguishing the core origin. Clinically significant prostate cancer (csPCa) was defined as GG ≥ 2 .

PSA Density Variables

Serum PSA levels were measured before biopsy. Three PSA-based density variables were calculated for each patient: (1) PSA, defined as the unadjusted serum concentration (ng/mL); (2) whole-gland PSAD, defined as PSA divided by total prostate volume (ng/mL/cm³); and (3) zone-specific PSAD, defined as

PSA divided by PZ volume (PSAD_PZ) for men with PZ-only targets or by TZ volume (PSAD_TZ) for men with TZ-only targets (ng/mL/cm³).

Statistical Analysis

Continuous variables were summarized as mean $\pm$ standard deviation. Equality of variances between the PZ-target- and TZ-target groups was assessed using Levene's test, and group means were compared using Student's t-test for equal variances or Welch's t-test for unequal variances. Categorical variables were summarized as frequencies (percentages) and compared using the chi-square test or Fisher's exact test. The diagnostic performance of PSA, PSAD, and zone-specific PSAD for detecting csPCa was assessed separately in the PZ-target and TZ-target groups using ROC curve analysis, with areas under the curve (AUCs) compared using the DeLong test. The optimal cutoff value was determined by maximizing the Youden index with the corresponding sensitivity, specificity, and Youden index. Subgroup analyses were performed within the PZ-target group stratified by PI-RADS category (PI-RADS $\geq$ 4 and PI-RADS 5). As a sensitivity analysis, multivariate logistic regression was performed within the PZ target group to assess whether PSAD_PZ remained independently associated with csPCa after adjusting for age, total prostate volume, and PI-RADS category. All tests were two-sided, with $p < 0.05$ considered statistically significant. Statistical analyses were performed using SPSS software (version 21.0; IBM Corp., Armonk, NY, USA) and R version 4.6.1 (R Foundation for Statistical Computing, Vienna, Austria). Figures were generated using Python script (version 3.12.3).

Results

Baseline Characteristics and Clinico-pathological Findings

A total of 651 men met the inclusion criteria and were analyzed, comprising 416 men with PZ-only targets and 235 with TZ-only targets (Fig. 1). Age, body mass index (BMI), and PSA level before biopsy were comparable between the two groups, as were whole-gland and zone-specific PSAD (Table 1). Total prostate volume and PZ volume were significantly larger in the TZ-target group than in the PZ-target group (both $p < 0.001$), whereas TZ volume did not differ significantly between the groups. The PI-RADS category and GG distribution both differed significantly between the groups (both $p < 0.001$); men in the TZ-target group were considerably more likely to have no cancer on biopsy (26.0% vs. 4.3%), whereas GG 4–5 disease was more common among men with PZ-only targets. The number of positive biopsy cores was higher in the PZ-target group (5.3 ± 3.5 vs 4.0 ± 2.6 , $p < 0.001$), while the total number of biopsy cores obtained did not differ significantly between groups (Table 1).

Table 1
Baseline clinical, laboratory, mpMRI, and biopsy characteristics of patients.

Age (years)	Peripheral zone-target group (n = 416)	Transition zone-target group (n = 235)	<i>p</i> value
	69.2 ± 6.7	68.6 ± 6.8	0.271
BMI (kg/m ²)	25.0 ± 2.6	24.7 ± 2.7	0.320
PSA before biopsy (ng/mL)	9.3 ± 10.5	10.4 ± 10.7	0.185
PSAD (ng/mL/cm ³)	0.23 ± 0.22	0.23 ± 0.24	0.928
Zone-specific PSAD (ng/mL/cm ³)	0.50 ± 0.55	0.50 ± 0.51	0.997
PI-RADS category			< 0.001
3	22 (5.3)	73 (31.1)	
4	235 (56.5)	75 (31.9)	
5	159 (38.2)	87 (37.0)	
Prostate volume (mL)	43.6 ± 17.0	51.5 ± 21.2	< 0.001
Transition zone volume (mL)	23.0 ± 13.1	23.9 ± 12.8	0.404
Peripheral zone volume (mL)	20.6 ± 7.6	27.6 ± 11.7	< 0.001
Grade Group			< 0.001
1	52 (12.5)	41 (17.4)	
2	125 (30.0)	68 (28.9)	
3	118 (28.4)	40 (17.0)	
4	73 (17.5)	23 (9.8)	
5	30 (7.2)	2 (0.9)	
No cancer	18 (4.3)	61 (26.0)	
No. of total biopsy cores	14.5 ± 3.2	14.6 ± 3.0	0.768
No. of positive cores	5.3 ± 3.5	4.0 ± 2.6	< 0.001
Values are presented as mean ± standard deviation or number (%). Zone-specific PSAD refers to PSAD_PZ for men with PZ-only targets and PSAD_TZ for men with TZ-only targets.			
BMI, body mass index; mpMRI, multiparametric magnetic resonance imaging; PSA, prostate-specific antigen; PSAD, prostate-specific antigen density; PI-RADS, Prostate Imaging Reporting and Data System.			

Diagnostic Performance for Detecting Clinically Significant Prostate Cancer

In the PZ-target group (n = 416), PSAD_PZ showed significantly higher diagnostic accuracy for csPCa detection than PSA (AUC, 0.825 vs. 0.707; $p < 0.001$) or whole-gland PSAD (AUC, 0.825 vs. 0.702; $p < 0.001$). This advantage of PSAD_PZ persisted across the PI-RADS subgroups. Among men with PI-RADS ≥ 4 lesions (n = 394), PSAD_PZ outperformed both PSA (AUC, 0.842 vs 0.730; $p < 0.001$) and PSAD (AUC, 0.842 vs 0.707; $p < 0.001$). Among men with PI-RADS 5 lesions (n = 159), PSAD_PZ showed the strongest discriminative performance among the three markers (AUC, 0.820), significantly exceeding both PSA (AUC, 0.733; $p = 0.009$) and PSAD (AUC, 0.695; $p < 0.001$). In the TZ-target group (n = 235), the pattern differed; whole-gland PSAD significantly outperformed PSA (AUC, 0.691 vs. 0.622; $p = 0.003$), whereas PSAD_TZ did not differ significantly from PSA (AUC, 0.658 vs. 0.622; $p = 0.149$) and was significantly inferior to whole-gland PSAD (AUC, 0.658 vs. 0.691; $p < 0.001$) (Table 2, Fig. 2).

Table 2

Comparison of AUC values for PSA, PSAD, and zone-specific PSA density in the detection of clinically significant prostate cancer, stratified by mpMRI target zone and PI-RADS category.

Groups	Variables	AUC	95% CI	p value (vs. PSA)	p value (vs. PSAD)
Peripheral zone-target group (n = 416)	PSA	0.707	0.647–0.768	Reference	—
	PSAD	0.702	0.642–0.762	0.844	Reference
	PSAD_PZ	0.825	0.775–0.875	< 0.001	< 0.001
Peripheral zone-target group with PI-RADS ≥ 4 (n = 394)	PSA	0.730	0.670–0.791	Reference	—
	PSAD	0.707	0.646–0.768	0.397	Reference
	PSAD_PZ	0.842	0.794–0.890	< 0.001	< 0.001
Peripheral zone-target group with PI-RADS 5 (n = 159)	PSA	0.733	0.559–0.907	Reference	—
	PSAD	0.695	0.554–0.836	0.281	Reference
	PSAD_PZ	0.820	0.690–0.949	0.009	< 0.001
Transition zone-target group (n = 235)	PSA	0.622	0.550–0.693	Reference	—
	PSAD	0.691	0.624–0.758	0.003	Reference
	PSAD_TZ	0.658	0.589–0.728	0.149	< 0.001
AUC, area under the curve; PSAD, PSA density; PZ, peripheral zone; TZ, transition zone; CI, confidence interval.					

Optimal Cut-off Values

Using the Youden index, the optimal cut-off value for PSAD_PZ in the PZ-target group was 0.285 ng/mL/cm³, yielding a sensitivity of 70.8% and specificity of 84.3% (Youden index, 0.551). This represented a more balanced sensitivity–specificity trade-off than PSA (cut-off value, 6.070 ng/mL; sensitivity, 61.3%; specificity, 75.7%; Youden index, 0.370) or whole-gland PSAD (cut-off value, 0.185 ng/mL/cm³; sensitivity, 47.4%; specificity, 87.1%; Youden index, 0.345) (Table 3).

Table 3

Optimal cut-off value, sensitivity, specificity, and Youden's index for predicting csPCa in the peripheral zone-target group (n = 416).

Variable	Cut-off value	Sensitivity	Specificity	Youden's index
PSA	6.070	0.613	0.757	0.370
PSAD	0.185	0.474	0.871	0.345
PSAD_PZ	0.285	0.708	0.843	0.551
csPCa, clinically significant prostate cancer; PSAD, PSA density; PZ, peripheral zone; TZ, transition zone.				

Reliability of TZ Volume Measurement

Inter-rater reliability for TZ volume measurement was excellent, with an ICC of 0.987 (95% CI, 0.97–0.99; $p < 0.001$) between the two urologists in the 30-scan reliability subset (Supplementary Table 1). Bland–Altman analysis showed close agreement between the two measurements, with narrow limits of agreement and no systematic bias (Supplementary Fig. 1).

Sensitivity Analysis: Independent Association of PSAD_PZ with csPCa

In a sensitivity analysis restricted to the PZ-target group, multivariable logistic regression confirmed that PSAD_PZ remained a significant independent predictor of csPCa (adjusted OR, 2.57; 95% CI, 1.87–3.52; $p < 0.001$) after adjustment for age (OR, 1.07; $p = 0.006$), total prostate volume (OR, 1.02; $p = 0.101$), and PI-RADS category (PI-RADS 4 vs ≤ 3 , OR, 6.92; PI-RADS 5 vs ≤ 3 , OR, 19.90; both $p \leq 0.001$) (Supplementary Table 2).

Discussion

In this prospectively enrolled cohort, PSAD_PZ showed higher diagnostic performance than PSA and whole-gland PSAD for detecting csPCa in men with PZ-only mpMRI target lesions. This advantage persisted in the PI-RADS ≥ 4 subgroup (Table 2, Fig. 2). The rationale for this zone-specific approach stems directly from the biological limitations of the whole-gland PSAD. As first described by Benson et al, PSAD was designed to normalize PSA to gland size in order to distinguish BPH from cancer[10]. However, BPH is confined almost exclusively to the TZ, and TZ volume increases disproportionately with age, independent of cancer risk[11]. As a result, whole-gland volume increasingly reflects non-neoplastic tissue unrelated to PZ lesions, diluting the PSA signal from PZ tumors[12]. In our study, the lack of a difference in diagnostic performance between PSA and whole-gland PSAD in the PZ-target group (AUC, 0.707 vs 0.702; $p = 0.844$) directly supports this dilution effect (Table 2). In other words, normalizing PSA to whole-gland volume provided little diagnostic benefit in men with PZ lesions. In contrast, normalizing PSA to the volume of the zone where the cancer arose, the PZ, yielded a genuine diagnostic advantage.

No prior study has separated patients into PZ-target and TZ-target groups according to the mpMRI target lesion before applying zone-specific PSAD, as in the present study. However, some studies have compared the diagnostic value of PSAD_TZ and PSAD_PZ. Wang et al. reported that PSAD_PZ outperformed PSA, whole-gland PSAD, and PSAD_TZ for diagnosing prostate cancer[19]. In their cohort, PSAD_PZ raised the biopsy-positive rate from 21.7% to 54.7% among men with equivocal findings on transrectal ultrasonography or mpMRI, and avoided 63.8% of unnecessary biopsies[19]. In contrast, Esengur et al. and Pausch et al. each reported lower csPCa detection performance for PSAD_PZ (AUC 0.70 and 0.63, respectively) than for PSAD_TZ (AUC 0.77 and 0.78, respectively), conflicting with our findings[20, 21]. This discrepancy across prior studies likely arose because none of them stratified patients by the mpMRI target lesion before applying PSAD_PZ and PSAD_TZ; instead, both parameters were calculated across the whole, unselected patient population. TZ-origin prostate cancer is biologically distinct from PZ cancer. Even as the tumor volume increases, TZ-origin prostate cancers contain a smaller proportion of high-grade (Gleason 4/5) disease, less frequently harbor TMPRSS2-ERG gene fusions, and proliferate more slowly[17]. In cohorts that do not separate lesions by zone, this biological heterogeneity between PZ-origin and TZ-origin tumors may cause the diagnostic significance of PSAD_PZ and PSAD_TZ to be distorted inconsistently across studies. Consistent with this biological distinction, Table 1 shows a significantly lower proportion of GG 4–5 disease in the TZ target group (10.7%) than in the PZ target group (24.7%, $p < 0.001$). By stratifying patients into PZ-target and TZ target groups before applying the corresponding zone-specific PSAD to each group, we were able to overcome this limitation of prior work.

The findings from our TZ-target group provide important support for this biological explanation. PSAD_TZ offered no advantage over PSA or whole-gland PSAD in distinguishing csPCa in the TZ-target group (Table 2, Fig. 2). If the superior performance of PSAD_PZ merely reflected a mathematical artifact of dividing PSA by any small volume, the same principle applied to the TZ should have resulted in PSAD_TZ outperforming PSA and whole-gland PSAD in the TZ-target group. This finding supports the interpretation that the diagnostic advantage of PSAD_PZ in the PZ-target group is driven by a biological mechanism specific to PZ lesions rather than a statistical artifact, and suggests that the TZ-target group served as a negative control. This observation supports the validity of our zone-matched design, in which whole-gland PSAD, PSAD_TZ, and PSAD_PZ were applied according to the mpMRI target lesion.

According to the EAU guidelines and prior studies, the conventional whole-gland PSAD cut-off value is 0.15 ng/mL/cm³ for prostate cancer overall[22] and 0.20 ng/mL/cm³ for csPCa[18]. In our cohort, the optimal whole-gland PSAD cut-off value for csPCa was 0.185 ng/mL/cm³, closely matching these prior reports and supporting the validity of our results. The PSAD_PZ cut-off value was higher, at 0.285 ng/mL/cm³, reflecting normalization to the smaller PZ volume. The PSAD_PZ cut-off value achieved a sensitivity of 70.8% and a specificity of 84.3%, with a higher Youden index than PSA or whole-gland PSAD (0.551 vs. 0.370 vs. 0.345, respectively), indicating its superior utility for identifying csPCa (Table 3). Therefore, when PSA and PI-RADS scores are inconclusive in men with a PZ-zone target lesion on mpMRI, clinicians may use PSAD_PZ to determine the need for prostate biopsy.

This study has several strengths. First, to the best of our knowledge, this is the first study to demonstrate the diagnostic value of zone-specific PSAD for csPCa by separating mpMRI target lesions into PZ-target and TZ-target groups within a prospectively established registry cohort (the SUPER-PC registry). Second, by analyzing the PZ-target- and TZ-target groups in parallel and using the TZ-target group as a negative control, we showed that the benefit of PSAD_PZ reflects a biological mechanism specific to PZ lesions rather than a generic statistical advantage of zone-specific normalization.

This study has several limitations. First, the SUPER-PC registry, which formed the basis of our cohort, prospectively enrolled only men with biopsy-confirmed prostate cancer. The 81 men with no cancer on biopsy included in our analysis constituted a control group identified retrospectively but consecutively from men who had an mpMRI target lesion and a negative biopsy during the same period. Variables for the prospectively enrolled cancer cohort were collected in real time under a standardized study protocol, whereas data for the non-cancer control group were retrospectively reconstructed from medical records, which may have introduced some inconsistencies in variable measurements between the two groups. Accordingly, establishing PSAD_PZ as a pre-biopsy triage tool requires a validation study that prospectively enrolls all candidates from the outset, irrespective of the eventual cancer diagnosis. Second, this was a single-center retrospective analysis, and external validation in other populations is required. Third, TZ volume was calculated manually using the ellipsoid formula rather than semi-automated three-dimensional volumetric segmentation; however, inter-rater reliability was validated in a separate subset of 30 scans and was excellent (ICC, 0.987).

Conclusions

In conclusion, PSAD_PZ showed improved detection of csPCa among men with PZ-only mpMRI targets compared with conventional PSA and whole-gland PSAD, particularly among men with higher-suspicion PI-RADS lesions. This zone-specific approach may help reduce unnecessary biopsies and guide treatment decisions in this population, although prospective validation in cohorts including biopsy-negative men is warranted before broader clinical adoption.

Abbreviations

AUC
Area under the curve
BMI
Body mass index
BPH
Benign prostatic hyperplasia
CI
Confidence interval
csPCa
Clinically significant prostate cancer

EAU
European Association of Urology
GG
Grade Group
ICC
Intraclass correlation coefficient
IRB
Institutional Review Board
ISUP
International Society of Urological Pathology
mpMRI
Multiparametric magnetic resonance imaging
OR
Odds ratio
PI-RADS
Prostate Imaging Reporting and Data System
PSA
Prostate-specific antigen
PSAD
Prostate-specific antigen density
PSAD_PZ
Peripheral zone-specific PSA density
PSAD_TZ
Transition zone-specific PSA density
PZ
Peripheral zone
ROC
Receiver operating characteristic
SNUH
Seoul National University Hospital
SUPER-PC
Seoul National University Prospectively Enrolled Registry for Prostate Cancer
TZ
Transition zone.

Declarations

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. H-2607-155-1762), which waived the requirement for individual informed consent given the retrospective and registry-based nature of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

This study received no financial support from any public, commercial, or not-for-profit funding agency.

Author Contribution

MHK: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing – Original Draft, Visualization. HML: Validation, Formal analysis, JHH: Formal analysis, Validation. SHJ: Formal analysis, Validation. JHK: Formal analysis, Validation. CK: Formal analysis, Validation. CWJ: Conceptualization, Resources, Data Curation, Supervision. HDY: Conceptualization, Resources, Data Curation, Supervision. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

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Figures

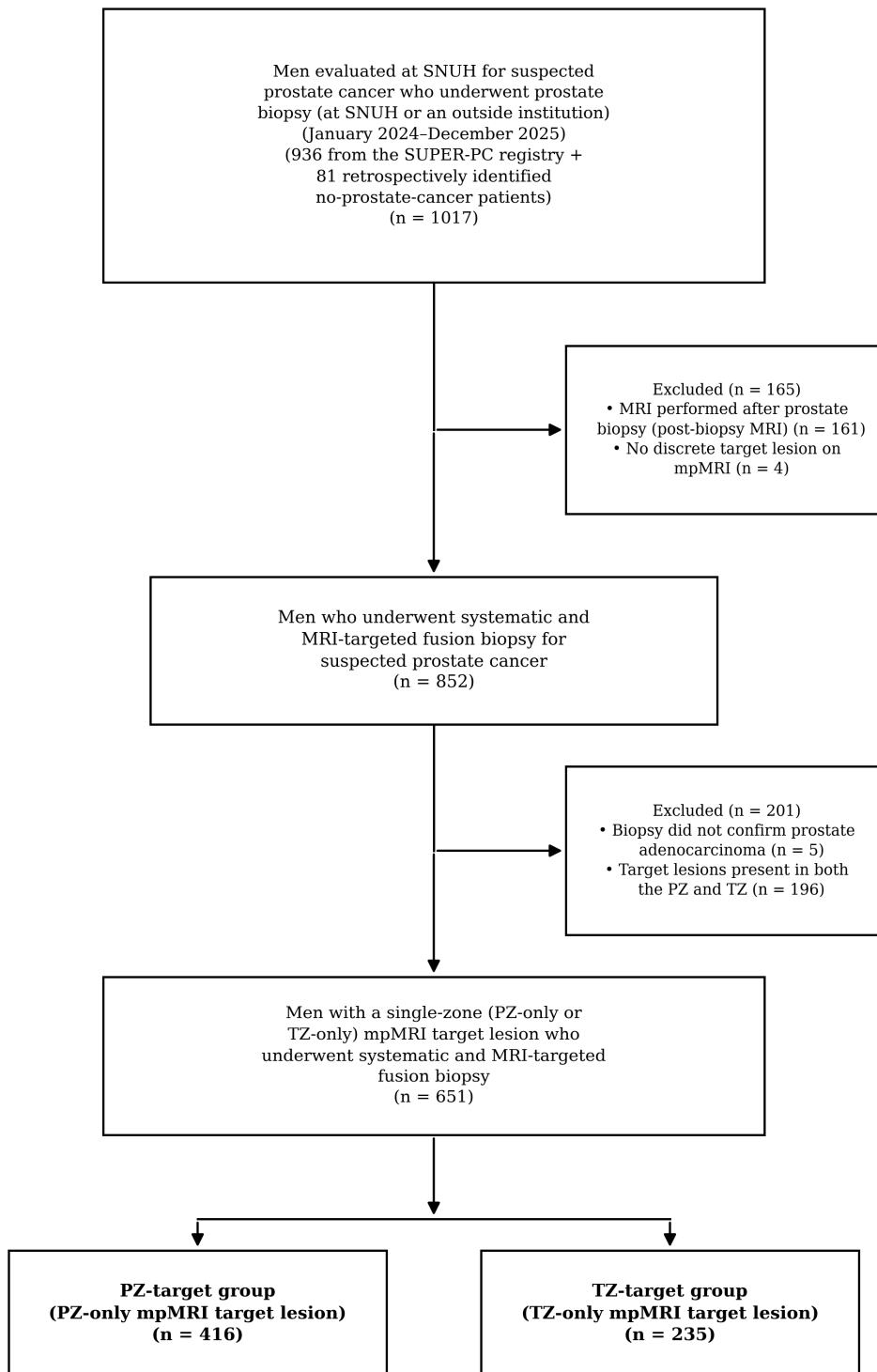


Figure 1

Flow diagram of patient selection. A total of 1,017 men underwent prostate biopsy for suspected prostate cancer at SNUH or an outside institution between January 2024 and December 2025, comprising 936 patients from the prospectively enrolled SUPER-PC registry and 81 retrospectively identified patients without a diagnosis of prostate cancer. After excluding 165 men (161 with post-biopsy mpMRI and 4 without a discrete mpMRI target lesion), 852 men underwent combined systematic and

MRI-targeted fusion biopsy. A further 201 men were excluded (5 without adenocarcinoma on biopsy and 196 with mpMRI target lesions in both the PZ and TZ), yielding a final cohort of 651 men with a single-zone mpMRI target lesion: 416 in the PZ-target group and 235 in the TZ-target group. mpMRI, multiparametric magnetic resonance imaging; PZ, peripheral zone; SNUH, Seoul National University Hospital; TZ, transition zone.

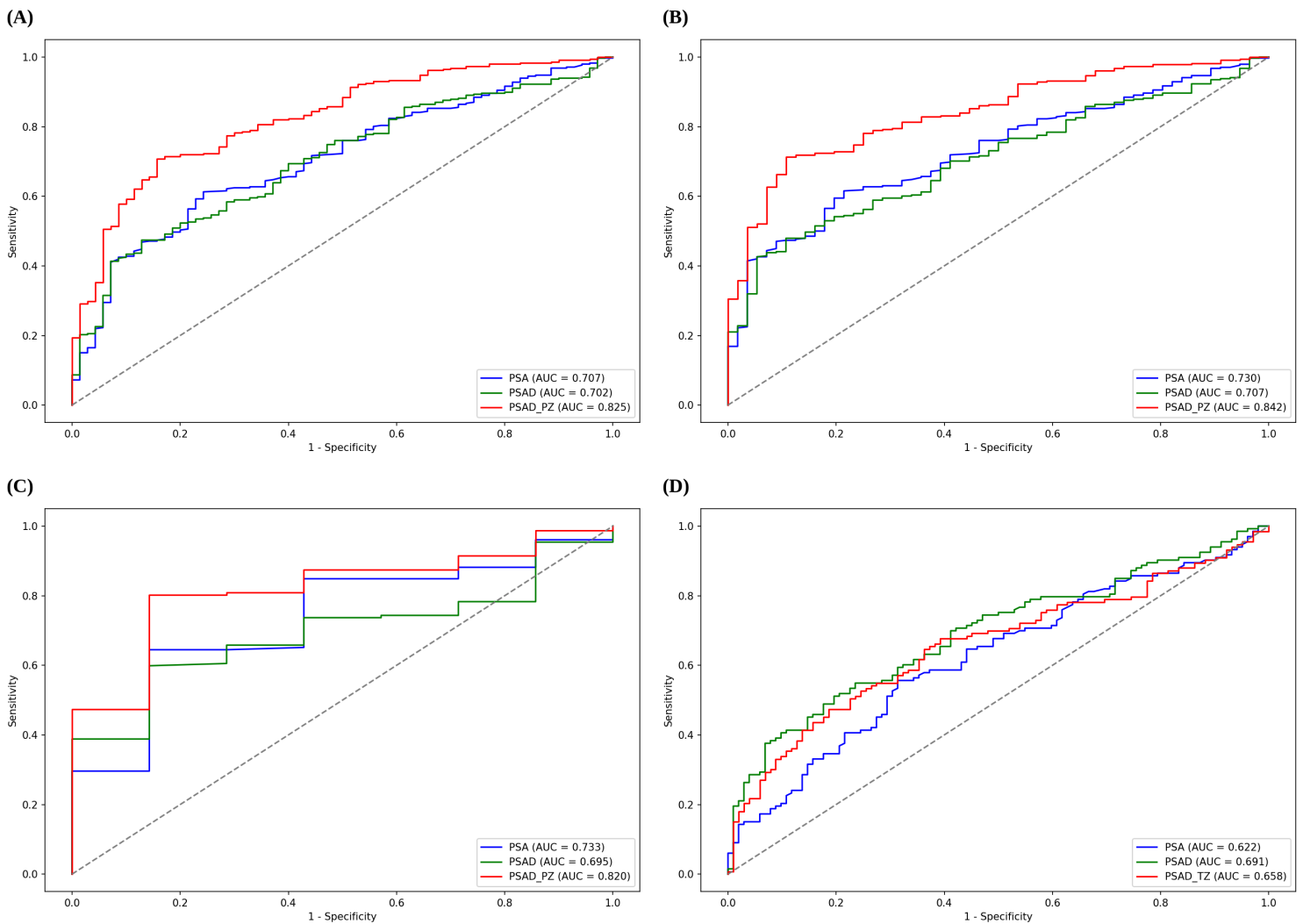


Figure 2

Receiver operating characteristic curves for PSA, whole-gland PSAD, and zone-specific PSAD in detecting clinically significant prostate cancer. (A) PZ-target group (n=416). (B) PI-RADS ≥ 4 subgroup of the PZ-target group (n=394). (C) PI-RADS 5 subgroup of the PZ-target group (n=159). (D) TZ-target group (n=235). The diagonal dashed line represents the line of no discrimination (AUC = 0.5). Curves reflect point estimates from a single ROC analysis in each group; error bars are not displayed, and the corresponding 95% confidence intervals for each AUC are provided in Table 2. PSA, prostate-specific antigen; PSAD, PSA density; PSAD_PZ, peripheral zone-specific PSA density; PSAD_TZ, transition zone-specific PSA density; PI-RADS, Prostate Imaging Reporting and Data System.

Supplementary Files

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