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RESEARCH ARTICLE

Additive Diagnostic Value of Biparametric 3T MRI for Prostate Cancer Detection in PSA Gray-Zone Patients

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Abstract

Introduction: Prostate-specific antigen (PSA) levels between 4.0 and 9.9 ng/mL (the "gray zone") present a diagnostic challenge, often leading to unnecessary prostate biopsies. We evaluated the additive diagnostic value of biparametric 3T MRI—particularly diffusion-weighted imaging (DWI) with a b-value of 2000—for detecting prostate cancer in these patients.

Methods: Consecutive patients with gray-zone PSA levels (n=446) were prospectively enrolled between July 2014 and August 2022. Transrectal ultrasound-guided prostate biopsy was performed in patients with positive MRI findings or in those whose PSA levels rose on three consecutive tests or exceeded 10 ng/mL during follow-up. All patients were monitored for at least 2 years. Two predictive models—incorporating MRI findings or not—were compared using receiver operating characteristic (ROC) analysis, category-free net reclassification improvement, and integrated discrimination improvement (IDI).

Results: The addition of MRI findings improved the ROC area from 0.764 to 0.933 ($p < 0.001$), and helped reclassify 84.5% of non-events (95% CI: 78.2–90.7) to a lower-risk category and 72.8% of events (95% CI: 61.7–83.9) to a higher-risk category. The IDI increased by 0.453 (95% CI: 0.402–0.505).

Conclusions: Biparametric MRI offers diagnostic value in patients with PSA levels in the gray zone, beyond conventional clinical predictors.

Keywords: PSA. Prostate Cancer, MRI, b-value, Diagnosis.

1. Introduction

Prostate-specific antigen (PSA) is a protein produced by the prostate gland and measured through a routine blood test. Although PSA is not specific to cancer, elevated (or a sudden change) levels may indicate the presence of prostate cancer and thus is widely used to guide decisions about whether to perform a prostate biopsy. Biopsy remains the gold standard for diagnosis; however, among men with PSA levels in the gray zone (4.0–10.0 ng/mL), the positive predictive value is at most 30%,[1] meaning that approximately 70% of these patients undergo biopsy unnecessarily. Biopsy-related complications—including bleeding, infection, and discomfort—are not negligible,[2–4] making it important to reduce the number of avoidable procedures.

To reduce unnecessary biopsies, improved triage strategies are needed to identify patients who are more likely to have clinically significant prostate cancer. Magnetic resonance imaging (MRI), particularly diffusion-weighted imaging (DWI), has gained attention as a non-invasive diagnostic tool with the potential to improve, stratification in this setting.[5] Biparametric MRI, which excludes contrast

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enhancement, offers a shorter scan time and avoids contrast-related risks while maintaining diagnostic performance compared to multiparametric MRI.[6]

In this study, we evaluated the additive diagnostic value of biparametric 3T MRI—specifically DWI with a b-value of 2000—in patients with gray-zone PSA levels. Our aim was to determine whether MRI could improve diagnostic accuracy and support better decision-making regarding the need for biopsy.

2. Materials and Methods

2.1 Study Design and Participants

A total of 446 consecutive patients with PSA levels in the gray zone were prospectively enrolled between July 2014 and August 2022 in our center. PSA follow-up was continued until October 2024. Gray-zone PSA was defined as values between 4.0 and 9.9 ng/mL. Patient characteristics are presented in Table 1.

All patients underwent biparametric 3T MRI, which included DWI with a b-value of 2000 and apparent diffusion coefficient mapping. Imaging was performed using a GE Healthcare Discovery MR750w 3.0T MRI scanner (Version DV26.0). MRI scans were interpreted by a board-certified radiologist with over 30 years of experience in prostate cancer imaging, who was blinded to all clinical and laboratory data.

2.2 Inclusion and Exclusion Criteria

Patients were eligible for inclusion if they: (1) presented with gray-zone PSA levels at their initial visit, (2) underwent PSA monitoring every four months for at least 2 years, and (3) were able to undergo MRI.

Patients were excluded if they: (1) had been prescribed 5α-reductase inhibitors, (2) had a history of prostate cancer treatment, (3) had previously undergone surgical intervention for benign prostatic hyperplasia (e.g., HoLEP), or (4) exhibited signs or symptoms of urinary tract infection at the initial visit. The follow-up algorithm is shown in Figure 1.

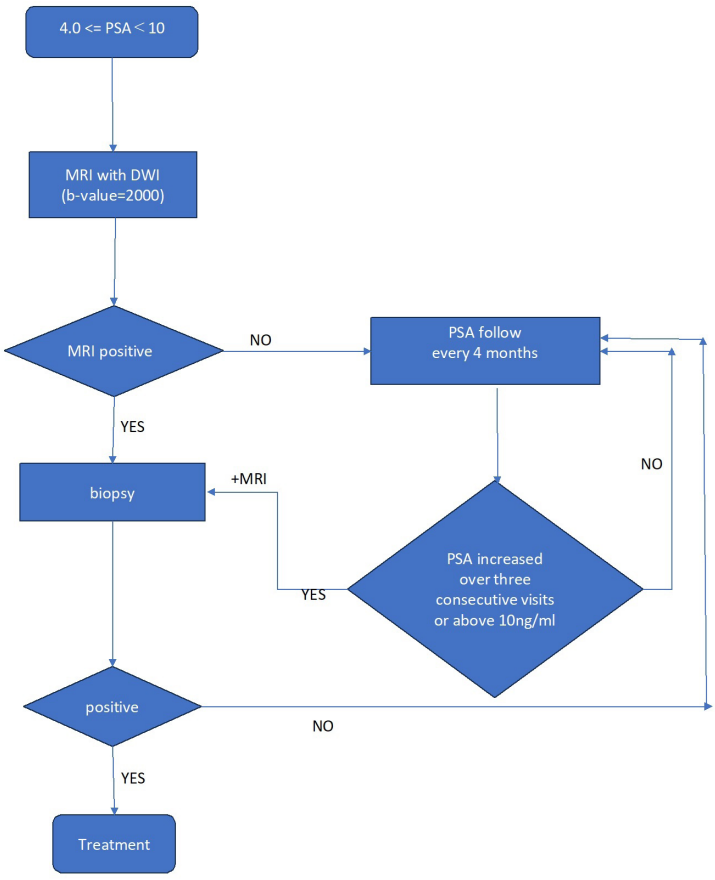

Figure 1. *Follow-up algorithm. When PSA elevation was observed, repeat MRI was performed.*

2.3 Biopsy Procedure and Diagnostic Classification

Transrectal ultrasound-guided prostate biopsy was performed in patients with MRI-positive findings (DWI-positive) or those with rising PSA values—defined as three consecutive increases or a level exceeding 10 ng/mL—during the follow-up period. Eight-core systematic biopsy specimens were obtained transrectally, and additional targeted biopsy specimens were collected when suspicious lesions were identified on DWI. A cognitive MRI-ultrasound fusion technique was employed to guide targeted biopsies.[7]

Patients who were negative on both MRI and PSA trajectory and completed at least 2 years of follow-up without biopsy were classified as cancer-negative. These patients were not histologically confirmed as cancer-free.

2.4 Model Development

Two predictive models were constructed. Model 1 included age at data analysis, initial PSA, prostate volume, and PSA elevation. Model 2 incorporated all variables in Model 1, with the addition of MRI findings. Model performance was assessed using receiver operating characteristic (ROC) curve analysis to compare the area under the curve (AUC). To further evaluate the incremental value of MRI, multivariable logistic regression was performed, and reclassification metrics were calculated: the category-free net reclassification improvement (cfNRI) and the integrated discrimination improvement (IDI). Internal validation was conducted using bootstrap resampling to obtain optimism-corrected estimates of model performance.

2.5 Statistical Analysis

All statistical analyses were conducted using R version 4.3.1 (The R Foundation for Statistical Computing, Vienna, Austria) and EZR version 1.6.8 (Saitama Medical Center, Jichi Medical University), a modified version of R Commander that includes statistical functions commonly used in biostatistics.[8]

3. Results

3.1 Baseline Characteristics

We first compared baseline clinical variables between MRI-positive and MRI-negative groups. We observed no significant differences in initial PSA levels or PSA elevation patterns. Patients in the MRI-positive group, however, were significantly older and had smaller prostate volumes compared with those in the MRI-negative group ($p < 0.001$ for both comparisons; Table 1). The median follow-up duration was 44.1 months (IQR: 67.2–87.3) for MRI-negative patients and 34.7 months (IQR: 58.9–84.7) for MRI-positive patients.

Table 1. *Patient characteristics. Abbreviations: SMD, standardized mean difference; i-PSA, initial PSA; GG, Grade Group; GS, Gleason Score; PV, Prostate Volume; RT, radiation therapy; HT, hormone therapy; AS, active surveillance. Ages are reported as of the time of data analysis.*

Factor	Group	MRI negative	MRI positive	p.value	SMD
n		287	159		
cstage (%)	cT1c	4 (21.1)	0 (0.0)	0.001	0.843
	cT2a	14 (73.7)	111 (81.0)		
	cT2b	0 (0.0)	4 (2.9)		
	cT2c	1 (5.3)	20 (14.6)		
	cT3a	0 (0.0)	1 (0.7)		
	cT4	0 (0.0)	1 (0.7)		
PSA elevation (%)	no	248 (86.4)	137 (86.2)	1	0.007
	yes	39 (13.6)	22 (13.8)		
re-biopsy (%)	no	266 (92.7)	138 (86.8)	0.061	0.195
	yes	21 (7.3)	21 (13.2)		
treatment (%)	none	262 (91.3)	23 (14.5)	<0.001	2.43
	surgery	22 (7.7)	114 (71.7)		
	RT	1 (0.3)	15 (9.4)		
	HT	0 (0.0)	5 (3.1)		
	AS	2 (0.7)	2 (1.3)		
alive (%)		267 (98.9)	151 (99.3)	1	0.048
	non-cancer death	3 (1.1)	1 (0.7)		
pathology (%)	negative	262 (91.3)	23 (14.5)	<0.001	2.41
	positive	25 (8.7)	136 (85.5)		
age (mean+/-SD)		75.00 (7.76)	77.69 (6.97)	<0.001	0.365
GG (median [IQR])		1.00 [1.00, 2.00]	2.00 [1.00, 3.00]	0.007	0.608
GS (median [IQR])		6.00 [6.00, 7.00]	7.00 [6.00, 7.00]	0.009	0.463
i.PSA (median [IQR])		5.20 [4.53, 6.85]	5.50 [4.71, 6.97]	0.132	0.122
PV (median [IQR])		47.30 [35.08, 62.08]	35.00 [27.70, 43.20]	<0.001	0.713
follow-up period (month)		44.1[67.2, 87.3]	34.7 [58.9, 84.7]	0.036	0.194

3.2 Diagnostic Accuracy of MRI

Among MRI-positive patients, the positive predictive value for prostate cancer was 85.5% ($p < 0.001$), indicating that MRI positivity was strongly associated with biopsy-confirmed disease. The false-negative rate (i.e., the proportion of MRI-negative patients who were later diagnosed with prostate cancer) was 8.7%, supporting the safety of using MRI as a triage tool (Table 1).

3.3 Model Performance with and without MRI

We next compared two predictive models: Model 1, which included only clinical variables, and Model 2, which incorporated MRI findings. Adding MRI significantly improved the area under the ROC curve from 0.764 to 0.933 ($p < 0.001$; Figure 2). Risk reclassification analysis showed that the MRI-inclusive model correctly reclassified 84.5% of patients without cancer to a lower-risk category (non-event NRI; 95% CI: 78.2–90.7) and 72.8% of patients with cancer to a higher-risk category (event NRI; 95% CI: 61.7–83.9). The IDI also improved by 0.453 (95% CI: 0.402–0.505), reflecting enhanced overall discrimination. Bootstrap internal validation yielded an optimism-corrected AUC of 0.757. The calibration slope was 0.9591, indicating good model fit (Figure3).

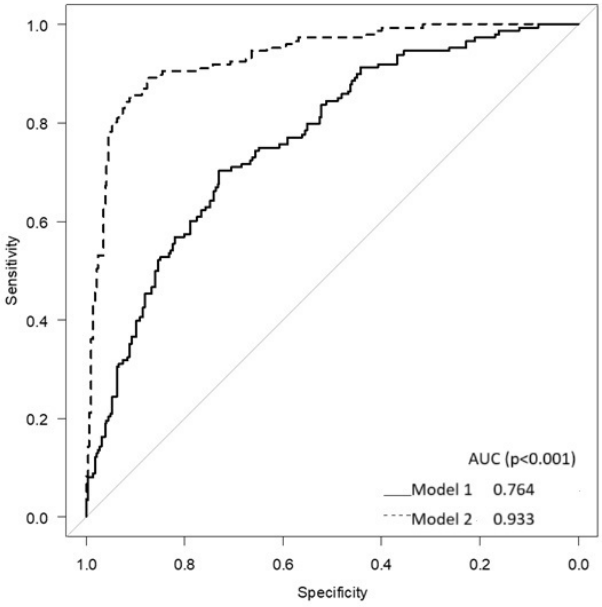

Figure 2. *Comparison of predictive models. Model 1 included age, initial PSA (i-PSA), prostate volume (PV), and PSA elevation. Model 2 included all Model 1 variables plus MRI findings. The area under the ROC curve increased from 0.764 to 0.933 ($p < 0.001$) with the addition of MRI.*

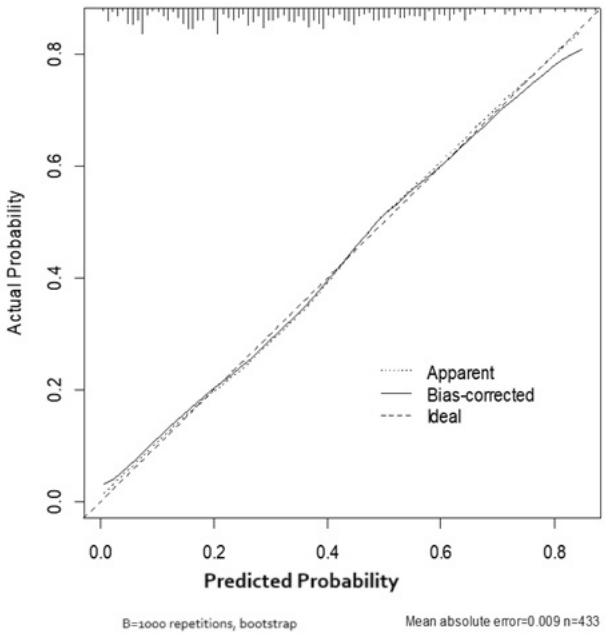

Figure 3. *Internal validation of the MRI-inclusive model. The bootstrap optimism-corrected AUC was 0.757, and the calibration slope was 0.9591.*

4. Discussion

Patients with PSA levels in the gray zone (4.0–10.0 ng/mL) frequently undergo unnecessary prostate biopsies to make a cancer diagnosis, despite the low predictive value of PSA alone. We therefore established a prospective diagnostic study to evaluate whether biparametric MRI, particularly DWI at a b-value of 2000,[5] could improve risk stratification and reduce unnecessary biopsies when used alongside established clinical predictors. We hypothesized that DWI would contribute incremental diagnostic information when combined with known clinical risk factors. Our findings support this hypothesis, demonstrating that MRI offers both independent and complementary value in improving the detection of prostate cancer in this population.

Recent reports, including those by Park et al., suggest that monoparametric MRI (monoMRI) using only DWI may yield comparable diagnostic performance to biparametric or multiparametric MRI for detecting clinically significant prostate cancer (csPCa). In combination with PSA, monoMRI has also shown potential for effective patient triage.[9] Multiparametric MRI is widely used in clinical practice and often assessed using the Prostate Imaging Reporting and Data System (PI-RADS).[6,10–11] According to PI-RADS version 2.1, DWI is central to the evaluation of peripheral zone lesions, while T2-weighted imaging (T2WI) is emphasized for transitional zone (TZ) lesions. Distinguishing TZ cancers from benign prostatic hyperplasia using T2WI, however, can be challenging due to overlapping imaging features.[12] Biparametric MRI offers several advantages over multiparametric protocols, including shorter acquisition times, lower cost, and the avoidance of contrast agents. Given these benefits, we focused on DWI-based biparametric MRI as a simplified yet effective approach for prostate cancer diagnosis.

To evaluate the added value of MRI, we compared two models: one using clinical parameters alone (Model 1), and one that incorporated MRI findings (Model 2). Although the area under the ROC curve, or c-index, has traditionally been used to quantify model performance, its limitations—such as insensitivity to clinically meaningful improvements—are well recognized.[13] We thus also applied the cfNRI and the IDI, which provide more clinically interpretable measures of model improvement.[14–16] Our analyses showed that including MRI data significantly improved discrimination by 0.453 (95% CI: 0.402–505). The total cfNRI was largely driven by accurate reclassification of non-events into lower-risk categories, and the IDI for non-events was statistically significant. MRI also improved risk classification among events, with significant cfNRI and IDI values. Additionally, bootstrap optimism-corrected AUC confirmed the high discriminative performance of the MRI-inclusive model. We thus conclude that MRI substantially enhances the accuracy of prostate cancer prediction in patients with gray-zone PSA levels.

The strengths of this study include the prospective design, appropriate cohort size, models, and validation approaches, with sufficient follow-up duration. The same kind of study has not been reported so far. Several limitations of this study should be acknowledged when interpreting these results. As with all diagnostic studies, it is not possible to definitively identify true-negative cases. In our study, patients with negative MRI findings and no PSA elevation over at least 2 years of follow-up were classified as cancer-negative. Although false negatives in cancer diagnosis are a serious concern, we believe that long-term PSA monitoring mitigates the associated risk. In our protocol, biopsy is promptly performed when PSA rises on three consecutive occasions or exceeds 10 ng/mL.

In summary, biparametric MRI provided significant independent and additive diagnostic value in the PSA gray-zone patients in our cohort when used alongside established clinical predictors. MRI improved model performance and risk stratification, offering a practical approach to reduce unnecessary biopsies while maintaining diagnostic safety. Based on our data, we propose that incorporating biparametric MRI into routine evaluation of PSA gray-zone patients could improve diagnostic precision and reduce unnecessary biopsies. Further studies are warranted to validate these findings in larger, multi-center cohorts and assesses the feasibility, cost-effectiveness, and clinical utility of implementing this approach in practice.

5. References

1. Hass GP, Montie JE, Pontes JE. The state of prostate cancer screening in the United State. Eur Urol 1993; 23: 337-347

2. Chapman L, Keihani S, Sanchez A. Intraperitoneal Bleeding After Ultrasound-Guided Transperineal Prostate Biopsy. Case reports in urology. 2024;8819291. pii: 8819291.

3. Borghesi M, Ahmed H, Nam R et al. Complications after systematic, random, and image-guided prostate biopsy. Eur Urol. 2017; 71:353–365.

4. Ando T, Watanabe K, Mizusawa T et al. Late onset rectal bleeding with hemorrhagic shock after transrectal prostate biopsy. Urology 2018; 21: 41-43

5. Yamaya N, Kimura K, Ichikawa R et al. Prospective evaluation of PI-RADSv2.1 using multiparametric and biparametric MRI for detecting clinically significant prostate cancer based on MRI/US fusion-guided biopsy. Japanese journal of radiology. 2024; 16; doi: 10.1007/s11604-024-01675-4.

6. Kanda Y. Investigation of freely available easy-to-use software 'EZR' for medical statistics. Bone marrow transplant 2013; 48: 452-458

7. Godley KH, Syer TJ, Toms AP et al. Accuracy of high b-value diffusion-weighted MRI for prostate cancer detection: a meta-analysis. Acta radiologica (Stockholm, Sweden: 1987). 2018 Jan;59(1);105-113. doi: 10.1177/0284185117702181.

8. Park SH, Choi MH, Lee YJ et al. Rationale for adopting a combination of monoparametric MRI with the prostate-specific antigen in detecting clinically significant prostate cancer: comparison with standard biparametric and multiparametric MRI. The British journal of radiology. 2024; 97(1163): 1775-1781. doi: 10.1093/bjr/tqae134.

9. Li EV, Kumar SK, Aguiar JA et al. Utility of dynamic contrast enhancement for clinically significant prostate cancer detection. BJUI compass. 2024; 5(9): 865-873. doi: 10.1002/bco2.415.

10. Twilt JJ, Saha A, Bosma JS et al. Evaluating Biparametric Versus Multiparametric Magnetic Resonance Imaging for Diagnosing Clinically Significant Prostate Cancer: An International, Paired, Noninferiority, Confirmatory Observer Study. Eur Urol. 2024; 21; pii: S0302-2838(24)02640-X

11. Dhiman A, Kumar V, Das CJ. Quantitative magnetic resonance imaging in prostate cancer: A review of current technology. World journal of radiology. 2024; 16(10): 497-511. doi: 10.4329/wjr. v16.i10.497.

12. Xiaohang S, Bingni Z, Liangping Z et al. Differentiation of prostate cancer and stromal hyperplasia in the transition zone with histogram analysis of the apparent diffusion coefficient. Acta radiologica (Stockholm, Sweden: 1987). 2017 Jan 01;284185117698861. doi: 10.1177/0284185117698861.

13. Cook NR: Use and misuse of the receiver operating characteristic curve in risk prediction. Circulation. 2007; 115(7): 928-935.

14. Leening MJG, Vedder MM, Witteman JCM et al. Net reclassification improvement: computation, interpretation, and controversies: a literature review and clinician's guide. Ann Intern Med. 2014; 160(2):122-131.

15. Pencina MJ, D'Agostino Sr RB and Steyerberg, EW. Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. Statistics in medicine. 2011; 30(1): 11-21.

16. Pencina MJ, Demler OV. Novel metrics for evaluating improvement in discrimination: net reclassification and integrated discrimination improvement for normal variables and nested models. Stat Med. 2011; 31(2):101–113.