

Original paper

Clinically significant prostate cancer in PI-RADS 3 lesions: real-world outcomes of robotic in-bore MRI-guided biopsy

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Abstract

Purpose: Prostate Imaging Reporting and Data System (PI-RADS) 3 lesions on multiparametric magnetic resonance imaging (mpMRI) represent an equivocal category with an uncertain risk of clinically significant prostate cancer (csPCa), resulting in persistent controversy regarding biopsy indications. Our objective was to evaluate the detection rate of csPCa in patients with PI-RADS 3 only lesions undergoing robot-assisted in-bore magnetic resonance imaging (MRI)-guided prostate biopsy (RA-MRGB) and to identify clinical factors associated with cancer detection.

Material and methods: This retrospective, single-centre study represents a predefined subgroup analysis of a previously reported institutional cohort. Men undergoing RA-MRGB between January 2021 and March 2025 were screened, and patients with a PI-RADS score of 3 on pre-biopsy mpMRI and no coexisting PI-RADS 4-5 lesions were included. Biopsy decisions were based on multidisciplinary review and shared decision-making. csPCa was defined as International Society of Urological Pathology grade group ≥ 2 .

Results: Seventeen of 84 patients with PI-RADS 3 only lesions were identified. Prostate cancer of any grade was detected in 3 patients (17.6%). csPCa was found in 2 patients (11.8%), while 14 patients (82.4%) had benign histopathology. csPCa cases demonstrated heterogeneous clinical profiles, including elevated prostate-specific antigen density or larger lesion size and prior negative biopsy. No single clinical parameter reliably excluded csPCa.

Conclusions: When evaluated using robotic in-bore MRI-guided biopsy, PI-RADS 3 only lesions demonstrate a low but clinically relevant risk of csPCa. Biopsy decision-making in this group should rely on a multifactorial assessment rather than MRI score alone, and highly precise targeting techniques may enhance confidence in negative results.

Key words: multiparametric magnetic resonance imaging, prostatic neoplasms, image-guided biopsy, robotic surgical procedures, PI-RADS 3.

Introduction

Multiparametric magnetic resonance imaging (mpMRI) has become integral to prostate cancer diagnostics, improving lesion localisation and risk stratification compared with systematic ultrasound-guided biopsy alone [1]. The Pros-

tate Imaging Reporting and Data System (PI-RADS) provides a standardised framework for mpMRI interpretation, categorising lesions according to the likelihood of clinically significant prostate cancer (csPCa), commonly defined as International Society of Urological Pathology (ISUP) grade group ≥ 2 [2].

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A Study design · B Data collection · C Statistical analysis · D Data interpretation · E Manuscript preparation · F Literature search · G Funds collection

Despite advances in magnetic resonance imaging (MRI)-based diagnostics, PI-RADS 3 lesions remain a major clinical challenge. These lesions are defined as equivocal findings that do not allow reliable prediction of csPCa [3]. PI-RADS 3 lesions account for approximately 17–30% of prostate MRI examinations, yet only a minority are associated with clinically significant disease [3,4]. Meta-analyses and large retrospective cohorts report csPCa detection rates of roughly 10–20% for PI-RADS 3 lesions, substantially lower than those observed for PI-RADS 4 and 5 categories [4–6].

This uncertainty contributes to heterogeneity in clinical management. Approaches to PI-RADS 3 lesions range from immediate biopsy to MRI surveillance or risk-adapted strategies incorporating additional clinical parameters [7]. Prostate-specific antigen density (PSAD) has consistently emerged as an important modifier of csPCa risk in equivocal MRI findings, with lower PSAD values associated with reduced cancer detection and potential biopsy deferral in selected patients [8–10]. Nevertheless, no single variable has proven sufficient to guide biopsy decisions in isolation, and PI-RADS 3 lesions continue to represent a diagnostic grey zone.

In this setting, biopsy techniques that minimise targeting error may provide added value by increasing confidence in histological outcomes. In-bore MRI-guided biopsy enables direct MRI visualisation of needle position and avoids image-registration inaccuracies inherent to fusion-based approaches [11]. Comparative studies have demonstrated similar cancer detection between manual and robot-assisted in-bore biopsy, while robotic assistance may improve standardisation and procedural reproducibility [12]. However, data specifically addressing PI-RADS 3 only lesions assessed with robotic in-bore biopsy remain scarce. The aim of this study was therefore to evaluate csPCa detection in patients with PI-RADS 3 only lesions undergoing MRI-guided prostate biopsy (RA-MRGB) and to explore clinical factors associated with biopsy outcomes.

Material and methods

Study design and patient selection

This retrospective, single-centre study represents a predefined subgroup analysis of a previously reported institutional cohort. Consecutive men undergoing robot-assisted in-bore RA-MRGB between January 2021 and March 2025 were screened. All patients had pre-biopsy mpMRI interpreted according to PI-RADS version 2.1 criteria [2].

For the present analysis, we included patients with PI-RADS 3 only lesions, defined as a maximum PI-RADS score of 3 on pre-biopsy mpMRI, with no coexisting PI-RADS 4 or 5 lesions. Patients with contraindications to MRI or prior definitive treatment for prostate cancer

were excluded. Only the first biopsy session per patient was analysed.

Collected clinical variables included age, serum prostate-specific antigen (PSA), prostate volume measured on MRI, PSA density, number of MRI-visible lesions, maximal lesion diameter, lesion location, and prior biopsy history.

Biopsy indication and clinical decision-making

Biopsy decisions were not based on MRI findings alone. Each case underwent a multidisciplinary review involving urologists and radiologists experienced in prostate MRI interpretation. Indications for biopsy included persistent clinical suspicion despite equivocal MRI findings, elevated or rising PSA or PSA density, prior negative biopsy with ongoing concern, and informed patient preference following counselling regarding biopsy versus surveillance. This approach reflects real-world practice and acknowledged variability in PI-RADS 3 management [1,7].

MRI acquisition and lesion assessment

Diagnostic mpMRI was performed using a standardised prostate MRI protocol on a 1.5-Tesla scanner (Signa Voyager; GE HealthCare, Chicago, IL, USA) equipped with a pelvic phased-array surface coil. Sequences included high-resolution T2-weighted imaging, diffusion-weighted imaging with apparent diffusion coefficient maps, and dynamic contrast-enhanced imaging when indicated. Lesions were scored according to PI-RADS v2.1 criteria by a radiologist with dedicated experience in prostate mpMRI interpretation. The index lesion was defined as the lesion with the highest PI-RADS score or, when equal, the largest lesion by maximal diameter. For the present analysis, a dedicated retrospective re-review of the mpMRI examinations of the two patients with csPCa detected within the PI-RADS 3 only subgroup was performed by the same radiologist. In both cases the PI-RADS 3 assessment was upheld, and no additional radiological features were identified that would have warranted reclassification to PI-RADS 4.

Robotic in-bore MRI-guided biopsy technique

RA-MRGB was performed using an magnetic resonance-compatible Soteria Robotic Positioning Device (RPD; Soteria Medical B.V., Arnhem, Netherlands) designed to assist transrectal in-bore prostate biopsy. Robotic assistance was used to standardise trajectory planning and intraprocedural targeting under direct MRI visualisation, thereby reducing operator-dependent variability and eliminating MRI–ultrasound registration error [11,12]. Two or more targeted cores were obtained from the index lesion if needed. All procedures were performed under

local intrarectal anaesthesia with lidocaine-chlorhexidine gel (Instillagel; Farco-Pharma GmbH, Cologne, Germany) instilled into the rectum prior to probe insertion.

Periprocedural management and follow-up

Antibiotic prophylaxis consisted of oral cefixime 400 mg (Cetix; Aflofarm Farmacja Polska, Pabianice, Poland) administered on the day before the biopsy. Following the procedure, patients were observed in the radiology outpatient area for approximately three hours. Vital signs, post-procedural rectal bleeding, severity of haematuria, and pain were monitored, and oral fluid intake was encouraged. Discharge criteria comprised stable vital signs with no fever or chills, spontaneous voiding without significant macroscopic haematuria, absence of clinically significant rectal bleeding, and adequate general condition. At discharge, patients received written instructions and a contact number to the department in case of post-procedural complications. A telephone follow-up was performed on the following day to assess for fever, dysuria, persistent haematuria, urinary retention, and tolerance of antibiotic prophylaxis. Patients with a negative biopsy result for a PI-RADS 3 lesion were scheduled for follow-up mpMRI at 12 months, together with continued clinical and PSA monitoring. All patients were scheduled for a clinical review with histopathological results approximately four weeks after the procedure.

Histopathological assessment

Biopsy specimens were processed using standard protocols and evaluated by dedicated genitourinary pathologists. Histopathological assessment followed the ISUP 2019 consensus recommendations [13]. Tumours were graded using the ISUP grade group system, and csPCa was defined as ISUP grade group ≥ 2 .

Outcomes and statistical analysis

The primary outcome was detection of csPCa in the PI-RADS 3 only cohort. Secondary outcomes included detection of prostate cancer of any grade and exploratory assessment of clinical risk modifiers. Analyses were descriptive. Multivariable modelling was not performed due to the limited number of csPCa events.

Baseline clinical and imaging characteristics are summarised in Table 1.

Results

Among 84 men undergoing RA-MRGB during the study period, 17 (20.2%) met inclusion criteria for PI-RADS 3 only lesions. Most patients had a single MRI-visible lesion, and a minority had a history of prior negative biopsy.

Table 1. Baseline clinical and imaging characteristics of patients with Prostate Imaging Reporting and Data System (PI-RADS) 3 only lesions

Variable	PI-RADS 3 only (n = 17)
Age (years)	65.8 $\pm$ 7.6
PSA (ng/ml)	7.17 $\pm$ 3.60
Prostate volume (ml)	62.9 $\pm$ 29.7
PSA density (ng/ml/cm ³)	0.128 $\pm$ 0.066
Number of MRI-visible lesions	1 (range 1-3)
Maximum lesion diameter (mm)*	11.5 $\pm$ 3.8
Lesion location – right lobe, n (%)	8 (47.1)
Lesion location – left lobe, n (%)	11 (64.7)
Prior negative biopsy, n (%)	5 (29.4)

Data are presented as mean $\pm$ standard deviation, median (range), or n (%) as appropriate.

*Maximum diameter of the index lesion on pre-biopsy multiparametric MRI. Lesion location percentages sum to $> 100\%$ because some patients had bilateral PI-RADS 3 lesions.

MRI – magnetic resonance imaging, PSA – prostate-specific antigen

Table 2. Histopathological outcomes in patients with Prostate Imaging Reporting and Data System (PI-RADS) 3 only lesions

Histopathological outcome	n (%)
Benign findings (overall)	14 (82.4)
No malignancy (benign tissue)	13 (76.5)
Granulomatous inflammation after BCG	1 (5.9)
Prostate cancer (any grade)	3 (17.6)
ISUP grade group 1 (Gleason 3 + 3)	1 (5.9)
Clinically significant PCa (ISUP ≥ 2)	2 (11.8)
ISUP grade group 2 (Gleason 3 + 4)	1 (5.9)
ISUP grade group 3 (Gleason 4 + 3)	1 (5.9)

BCG – bacillus Calmette-Guérin, ISUP – International Society of Urological Pathology,

PCa – prostate cancer

Prostate cancer of any grade was detected in 3 of 17 patients (17.6%). CsPCa (ISUP ≥ 2) was identified in 2 patients (11.8%), while ISUP grade group 1 cancer was detected in 1 patient (5.9%). The remaining 14 patients (82.4%) had benign histopathological findings (Table 2).

Across the overall cohort, csPCa detection increased with higher PI-RADS categories, with PI-RADS 3 demonstrating the lowest detection rate and PI-RADS 5 the highest (Figure 1).

The detection rate of csPCa (ISUP grade group ≥ 2) increased with higher PI-RADS category, with the lowest rate observed in PI-RADS 3 lesions and the highest in PI-RADS 5 lesions.

Histopathological outcomes of patients with PI-RADS 3 only lesions are detailed in Table 2 and illustrated in Figure 2.

The majority of PI-RADS 3 only lesions were benign. csPCa (ISUP grade group ≥ 2) was detected in 2 of 17 patients (11.8%), while ISUP grade group 1 cancer was identified in 1 of 17 patients (5.9%).

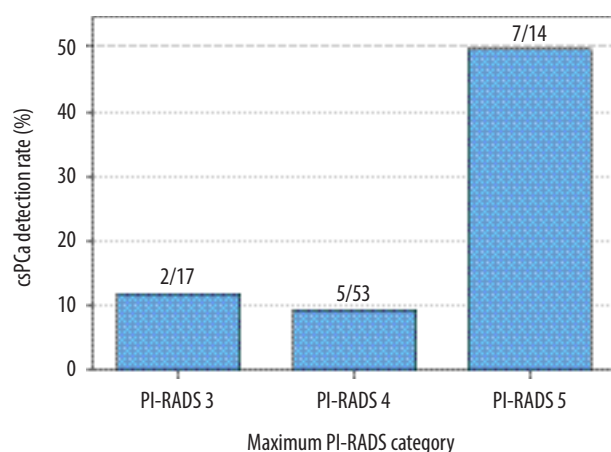


Figure 1. Clinically significant prostate cancer (csPca) detection according to maximum Prostate Imaging Reporting and Data System (PI-RADS) category

The two csPca cases in the PI-RADS 3 subgroup showed heterogeneous clinical profiles. One was associated with markedly elevated PSA density, while the other involved a larger MRI-visible lesion and a history of prior negative biopsy. No single clinical parameter reliably excluded csPca.

No periprocedural or post-procedural complications were recorded in the PI-RADS 3 only cohort. Specifically, no cases of febrile urinary tract infection, sepsis, clinically significant rectal bleeding, acute urinary retention, or hospital readmission related to the biopsy procedure occurred. Self-limiting mild haematuria and haematospermia, which are expected after transrectal biopsy, were not considered complications.

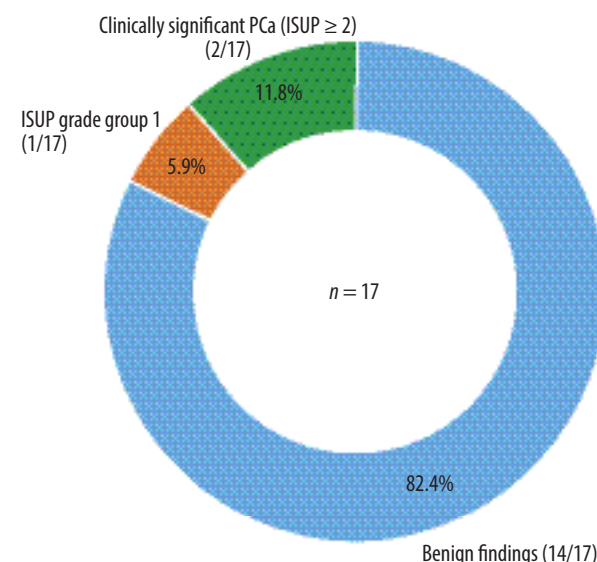
Discussion

PI-RADS 3 lesions remain a diagnostic grey zone in prostate MRI-based pathways. In this predefined subgroup analysis, PI-RADS 3 only lesions were evaluated using robotic in-bore MRI-guided biopsy, a technique designed to minimise targeting error.

The observed csPca detection rate of 11.8% is consistent with the lower range reported for PI-RADS 3 lesions in prior studies [3-6]. The use of in-bore robotic targeting suggests that negative biopsy results in this setting may provide high diagnostic confidence.

PSA density has been widely reported as an important modifier of csPca risk in PI-RADS 3 lesions [8-10]. Our findings support its relevance but also highlight its limitations, as csPca occurred across different PSA density and lesion size profiles, underscoring the need for multifactorial risk assessment.

Notably, the proportion of csPca observed in the PI-RADS 3 subgroup was numerically higher than that in the PI-RADS 4 group. This finding should not be interpreted as indicating a higher intrinsic risk of PI-RADS 3 lesions. Rather, it probably reflects selection bias and small



ISUP – International Society of Urological Pathology, Pca – prostate cancer

Figure 2. Histopathological outcomes in patients with Prostate Imaging Reporting and Data System (PI-RADS) 3 only lesions

sample size, as PI-RADS 3 lesions are typically biopsied only in the presence of additional clinical risk factors, resulting in a risk-enriched cohort, whereas PI-RADS 4 lesions are more uniformly sampled.

Consistent with broader trends in contemporary prostate cancer pathways, biopsies of equivocal PI-RADS 3 lesions are performed less frequently than in the past, reflecting improved radiologist experience, optimised mpMRI protocols, and increasing use of clinical risk stratification prior to biopsy. This evolution has been highlighted in earlier reports from Polish reference centres performing in-bore MRI-guided biopsy [14] and has been further synthesised in a recent review on current evidence and clinical applications of in-bore MRI-guided prostate biopsy [15]. The findings of the present subgroup analysis are aligned with this trend: PI-RADS 3 only lesions represented a minority of all biopsied patients and demonstrated a relatively low csPca detection rate, supporting risk-adapted strategies that reserve biopsy for PI-RADS 3 cases with additional clinical risk modifiers, while highly precise targeting techniques may provide added value when biopsy is undertaken.

This study is limited by its retrospective design, single-centre setting, and small sample size. Nevertheless, the use of a uniform biopsy technique and a clearly defined PI-RADS 3 only cohort strengthens the validity of the findings.

Conclusions

PI-RADS 3 only lesions evaluated with robot-assisted in-bore MRI-guided biopsy demonstrate a low but clinically relevant risk of csPca. Management should not rely on MRI score alone but incorporate clinical risk modi-

fiers and patient-specific factors. Highly precise targeting techniques may enhance confidence in negative biopsy results and contribute to risk-stratified decision-making in this diagnostically challenging group.

Disclosures

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