

# Predicting cancer detection rates from multiparametric prostate MRI

## Beyond the PI-RADS classification system

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### ABSTRACT

**INTRODUCTION:** Although the Prostate Imaging-Reporting and Data System (PI-RADS) categorization represents the standard method for assessing the risk of prostate cancer using prostate magnetic resonance imaging (MRI), there exists wide variation in cancer detection rates (CDRs) in real-world practice. We therefore evaluated the association of clinical and radiographic features with CDRs and developed a predictive model to improve clinical management.

**METHODS:** We identified men aged 18–89 years with elevated prostate-specific antigen (PSA) or on active surveillance for prostate cancer who underwent MRI-ultrasound (US) fusion biopsy or in-bore MRI-targeted biopsy. The associations of features with the per-lesion CDR (Gleason 6–10) and clinically significant (cs) CDR (Gleason 7–10) were examined using logistic regression, and results were operationalized into a predictive model.

**RESULTS:** Targeted biopsy was performed for 347 lesions in 281 patients. Overall, the CDR was 49.0% and the csCDR was 28.0%. On multivariable analysis, increasing PI-RADS category, smaller prostate size, and increasing PSA density were independently associated with higher CDR, while prior prostate biopsy was associated with lower CDR. A solitary PI-RADS 3–5 lesion was independently associated with higher csCDR, while 2+ prior prostate biopsies was associated with a lower csCDR. A predictive model provided a greater net benefit than a strategy of performing biopsy in all PI-RADS 3–5 lesions across a wide range of threshold probabilities.

**CONCLUSIONS:** Several clinical and radiographic features are independently associated with the risk of prostate cancer in men undergoing MRI-targeted biopsy. A predictive model based on these features can improve clinical decisions regarding biopsy compared to the conventional strategy of performing biopsy for all PI-RADS 3–5 lesions.

### INTRODUCTION

Multiparametric magnetic resonance imaging (mpMRI) of the prostate has become the standard of care in the evaluation of men with elevated prostate-specific antigen (PSA), as well as the active surveillance of prostate cancer.<sup>1,2</sup> Several seminal prospective trials have demonstrated that the use of mpMRI reduces rates of prostate biopsy and over-diagnosis compared with traditional PSA-based paradigms.<sup>3,4</sup> Accordingly, use of mpMRI in men with suspected prostate cancer has increased dramatically, with rates as high as 89% in biopsy-naive patients.<sup>5</sup>

The Prostate Imaging-Reporting and Data System (PI-RADS) was developed to standardize the interpretation and reporting of prostate MRI findings.<sup>6</sup> In randomized trials, such as PRECISION and STHLM3-MRI, MRI findings as classified by the PI-RADS categorization demonstrated very high positive predictive value for the detection of clinically significant (cs) disease, with cancer detection rates (CDR) of 80–90% for PI-RADS 5 and 60–75% for PI-RADS 4;<sup>1,2</sup> however, real-world CDRs vary dramatically, ranging from 13–97%, and can be much lower than those reported in seminal prospective trials.<sup>7–9</sup> Moreover, evidence suggests that CDRs may be affected by a variety of factors, such as prior biopsy status.<sup>10</sup>

We hypothesized that prostate cancer detection rates vary according to characteristics beyond those captured by the PI-RADS categorization system, such as patient characteristics and other imaging features.

## KEY MESSAGES

- Several features are independently associated with the risk of prostate cancer detection in mpMRI.
- Not all features are captured by the PI-RADS classification.
- A solitary PI-RADS 3–5 lesion was independently associated with higher csCDR, while 2+ prior prostate biopsies was associated with a lower csCDR.
- A predictive model provided a greater net benefit than biopsying all PI-RADS 3–5 lesions.

We therefore examined the associations of clinical and radiographic features with CDRs, and developed a predictive model to improve clinical management.

## METHODS

## Study cohort

After obtaining an exempt status determination from our institutional review board, we identified men aged 18–89 years with elevated PSA or Gleason 6 prostate cancer on active surveillance and at least one PI-RADS 3–5 lesion on prostate mpMRI (mpMRI) who underwent MRI-targeted biopsy. We included patients who underwent MRI-targeted biopsy from August 2019 to February 2020 to ensure that MRI interpretation was performed using PI-RADS v2.0-2.1. In addition, we included patients who underwent in-gantry MRI-targeted biopsy from March 2015 to November 2017, whose MRI was re-interpreted by a single radiologist (LT) as part of a separate study.<sup>11</sup> The cohort is summarized in Supplementary Figure 1 (available at [cuaj.ca](http://cuaj.ca)).

MRI-targeted biopsy was performed either in the office using MRI-ultrasound (US) fusion by urologists with the bkFusion system (BK Medical, Burlington, MA, U.S.) or in-gantry by interventional radiologists. In the setting of multiple MRI-targeted biopsies for a patient, we considered only the first biopsy for the present study.

## Clinicopathologic features and outcomes

Clinicopathologic features abstracted from the electronic health record included the following: age, pre-

biopsy PSA level, digital rectal exam (DRE), number of prior prostate biopsies, prior diagnosis of Gleason 6 prostate cancer (on active surveillance), prostate volume, PSA density, number of PI-RADS 3–5 lesions, and characteristics for each PI-RADS 3–5 lesion, including size (largest dimension in mm), location (peripheral, anterior/transition zone), number of cores sampled, and biopsy pathology. All biopsies were reviewed by a trained genitourinary pathologist as part of standard clinical care.

The primary endpoints were CDR, defined as a Gleason 6–10 lesion on biopsy, and csCDR, defined as Gleason 7–10 on biopsy. Patients with a prior diagnosis of Gleason 6 prostate cancer on active surveillance were excluded from CDR analyses.

## Statistical analysis

Baseline characteristics for the overall cohort were summarized using medians and interquartile ranges (IQR) for continuous variables, or frequencies and percentages for categorical variables, and compared across MRI-US fusion and in-bore MRI biopsy groups using Wilcoxon rank-sum and Chi-squared tests.

The associations of baseline characteristics with CDR and csCDR were evaluated using univariable and multivariable logistic regression using each patient as the unit of analysis. Results are summarized using odds ratios (OR) and 95% confidence intervals (CI). All available covariates were included in the multivariable model, and each covariate was modeled as described in the respective table. We conducted a complete case analysis.

Finally, we operationalized these results into a predictive model developed using lasso regression to minimize overfitting. Model performance was assessed using the c-statistic, including optimism-adjusted c-statistic with bootstrapping, calibration, and decision curve analysis.<sup>12</sup>

Statistical analyses were performed using R version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria). All tests were two-sided, with p-values <0.05 considered statistically significant.

## RESULTS

Baseline characteristics are listed in Table 1. The study cohort included 281 patients, of whom 68 (24.2%) had a prior diagnosis of Gleason 6 prostate cancer and underwent MRI-targeted biopsy as part of active surveillance, 106 (37.7%) who were biopsy-naïve, and 107 (38.1%) who had prior negative biopsies. Median age at biopsy was 67.1 years (IQR 62.3–71.4), and median pre-biopsy PSA was 7.1 ng/ml (IQR 5.1–10.0). Forty-three patients

(15.3%) had an abnormal DRE. The median prostate volume on MRI was 56 cc (IQR 40–91), and median PSA density was 0.1 ng/ml<sup>2</sup> (IQR 0.1–0.2). Patients who underwent MRI-US fusion biopsy were more likely to be biopsy-naïve compared to those who underwent in-gantry MRI biopsy (47.9% vs. 32.4%, p=0.04).

A total of 347 lesions underwent MRI-targeted biopsy. PI-RADS classification was 5 in 83 (23.9%) lesions, 4 in 216 (62.2%) lesions, and 3 in 48 (13.8%) lesions. Lesions were located in the peripheral zone in 63.3% of cases, and median lesion diameter was 12 mm (IQR 8–16). A median of three targeted cores were sampled from each lesion (IQR 2–3). There were several statistically significant differences in lesional characteristics between the two biopsy techniques, with those undergoing MRI-US biopsy more likely to be PI-RADS 5 (34.1% vs. 17.9%, p=0.01), located in the anterior/transition zone (45.7% vs. 31.3%, p=0.01), and have a larger diameter (14 vs. 10 mm, p<0.01).

The per-patient CDR was 49.0%. The univariable and multivariable associations of baseline characteristics with CDR are summarized in Table 2. On multivariable analysis, higher PI-RADS categorization (OR 6.08, 95% CI 2.19–18.50 for PI-RADS 5; OR 4.08, 95% CI 1.70–11.10 for PI-RADS 4 vs. PI-RADS 3) and higher PSA density (unit OR 1.61, 95% CI 1.03–2.59) were associated with a higher risk of cancer detection, while increasing number of prior prostate biopsies (OR 0.22, 95% CI 0.11–0.45 for 2+; OR 0.36, 95% CI 0.19–0.66 for 1 vs. 0) and larger prostate volume (unit OR 0.99, 95% CI 0.98–1.00) were associated with a lower risk of cancer detection.

The per-patient csCDR was 28.0%. The univariable and multivariable associations of baseline characteristics with csCDR are summarized in Table 3. On multivariable analysis, a solitary PI-RADS 3–5 lesion (OR 2.56, 95% CI 1.36–4.99 vs. 2+ lesions) was associated with an increased risk of clinically significant cancer, while 2+ prior prostate biopsies (OR 0.27, 95% CI 0.10–0.64 vs. 0) and MRI-US biopsy technique (OR 0.55, 95% CI 0.29–1.00) were associated with a lower risk of clinically significant cancer.

To operationalize the associations of baseline characteristics with cancer detection, we developed separate predictive models for CDR and csCDR using lasso regression. The β coefficients for each covariate in the models for CDR and csCDR are summarized in Table 4. The optimism-adjusted c-statistic for the CDR model was 0.77, while the optimism-adjusted c-statistic for csCDR was 0.75. The model demonstrates excellent calibration for CDR (Supplementary Figure

**Table 1. Baseline characteristics**

	Overall (patients, n=281) (lesions, n=347)	MRI-U/S (patients, n=96) (lesions, n=129)	In-bore MRI (patient, n=185) (lesions, n=218)	p
<b>Patient characteristics</b>				
Age, yrs, median (q1–q3)	67.1 (62.3–71.4)	67.3 (62.6–71.7)	66.9 (62.3–71.2)	0.62
Pre-biopsy PSA, ng/mL, median (q1–q3)	7.1 (5.1–10.0)	6.6 (5.1–9.5)	7.4 (5.2–10.6)	0.34
Abnormal DRE, n (%)	43 (15.3)	15 (15.6)	28 (15.1)	0.13
Number of prior prostate biopsies, n (%)				0.04
0	106 (37.7)	46 (47.9)	60 (32.4)	
1	91 (32.4)	28 (29.2)	63 (34.1)	
2	41 (14.6)	8 (8.3)	33 (17.8)	
3+	43 (15.3)	14 (14.6)	29 (15.7)	
Prior diagnosis, yes, n (%)	68 (24.2)	21 (21.9)	47 (25.4)	0.61
<b>Lesion characteristics</b>				
Number of lesions, median (q1–q3)	1 (1–1)	1 (1–2)	1 (1–1)	0.06
PI-RADS, n (%)				0.01
3	48 (13.8)	17 (13.2)	31 (14.2)	
4	216 (62.2)	68 (52.7)	148 (67.9)	
5	83 (23.9)	44 (34.1)	39 (17.9)	
Lesion locations, n (%) (n= 346, n=1 missing)				0.01
Non-peripheral zone (anterior/transition zone)	127 (36.7)	59 (45.7)	68 (31.3)	
Peripheral zone	219 (63.3)	70 (54.3)	149 (68.7)	
Lesion size, largest dimension, mm, median (q1–q3) (n=345, n=2 missing)	12 (8–16)	14 (10–17)	10 (7–15)	<0.01
Number of cores per target, median (q1–q3) (n=344, n=3 missing)	3 (2–3)	3 (3–4)	2 (2–3)	<0.01
Prostate volume on MRI, median (q1–q3)	56 (40–91)	52 (37.0–78.2)	57 (41–93)	0.15
PSA density, median (q1–q3)	0.1 (0.1–0.2)	0.1 (0.1–0.2)	0.1 (0.1–0.2)	0.36

DRE: digital rectal examination; MRI: magnetic resonance imaging; PI-RADS: Prostate Imaging-Reporting and Data System; PSA: prostate-specific antigen; US: ultrasound.

2; available at [cuaj.ca](http://cuaj.ca)) and good calibration for csCDR (Supplementary Figure 3; available at [cuaj.ca](http://cuaj.ca)), with the csCDR model slightly underestimating csCDR rates.

Finally, we performed decision curve analysis as a measure of clinical utility. In these analyses, the CDR model provided a greater net benefit than strategies

**Table 2. Univariable and multivariable logistic regression – CDR**

	CDR outcome unadjusted OR (95% CI)	CDR outcome adjusted OR (95% CI)
<b>Patient characteristics</b>		
Age, yrs	1.00 (0.97, 1.03)	1.02 (0.98, 1.06)
Pre-biopsy PSA, ng/mL	1.04 (1.00, 1.08)	1.03 (0.94, 1.13)
<b>DRE</b>		
Normal/not performed (ref)	–	–
Abnormal	1.30 (0.73, 2.34)	1.36 (0.66, 2.82)
<b>Number of prior prostate biopsies</b>		
0 (ref)	–	–
1	0.48 (0.29, 0.79)	0.36 (0.19, 0.66)
2+	0.39 (0.23, 0.67)	0.22 (0.11, 0.45)
<b>Biopsy type</b>		
In-bore (ref)	–	–
MRI-US fusion	1.15 (0.74, 1.78)	0.86 (0.49, 1.50)
<b>Lesion characteristics</b>		
<b>Number of lesions</b>		
2+ (ref)	–	–
1	1.88 (1.21, 2.94)	1.60 (0.94, 2.74)
<b>PI-RADS</b>		
3 (ref)	–	–
4	4.02 (1.94, 9.23)	4.08 (1.70, 11.10)
5	9.50 (4.17, 23.60)	6.08 (2.19, 18.50)
<b>Lesion locations</b>		
Non-peripheral zone (anterior/transition zone) (ref)	–	–
Peripheral zone	0.55 (0.35, 0.85)	0.67 (0.38, 1.20)
Lesion size, largest dimension, mm	1.05 (1.02, 1.09)	1.03 (0.98, 1.08)
Prostate volume on MRI	0.98 (0.98, 0.99)	0.99 (0.98, 1.00)
PSA density (0.1 unit increase)	1.88 (1.50, 2.44)	1.61 (1.03, 2.59)

CDR: cancer detection rate; DRE: digital rectal examination; MRI: magnetic resonance imaging; OR: odds ratio; PI-RADS: Prostate Imaging-Reporting and Data System; PSA: prostate-specific antigen; US: ultrasound.

of performing biopsy for all PI-RADS 3–5 lesions (treat all) or never performing a biopsy (treat none) across threshold probabilities from approximately 12.5–100% (Supplementary Figure 4; available at *cuaj.ca*). Similarly, the csCDR model provided a greater net benefit compared to strategies of performing biopsy for all PI-RADS 3–5 lesions (treat all) or never performing a

biopsy (treat none) across threshold probabilities from approximately 10–80% (Supplementary Figure 5; available at *cuaj.ca*).

**DISCUSSION**

We identified several clinical and radiographic characteristics that were associated with the risk of cancer detection for men undergoing MRI-targeted prostate biopsy. Specifically, in addition to higher PI-RADS categorization, we observed that higher PSA density, fewer number of prior prostate biopsies (e.g., biopsy-naive status), and smaller prostate volume were each associated with a higher risk of cancer detection. PSA density and prostate volume represent related concepts, suggesting that pre-test (i.e., pre-MRI) probability of cancer is an important factor to reduce false-positive MRI findings. Similarly, the prevalence of cancer may be lower among men with prior negative prostate biopsies, although it is important to consider that MRI can detect some anterior/apical lesions that may be missed with traditional biopsy approaches. Interestingly, we observed that having multiple PI-RADS lesions was associated with a lower risk of cancer detection. We hypothesize that the presence of multiple lesions on MRI may be more likely to reflect the occurrence of a multifocal non-malignant process (e.g., inflammatory etiologies) rather than multifocal radiographic prostate cancer.

Importantly, when operationalized into a predictive model for clinical use, the combination of clinical and radiographic characteristics was associated with very good performance for prediction of cancer detection (adjusted c-statistics 0.75–77 and very good calibration). More practically perhaps, both the CDR and csCDR models demonstrated greater benefit than a strategy of performing biopsy for all PI-RADS 3–5 lesions across a wide range of threshold probabilities.

It should be noted that this study included patients undergoing two biopsy modalities (MRI-US fusion and in-bore MRI), which may have different cancer detection rates in certain circumstances; however, the analyses presented herein adjusted for biopsy type to allow generalizability of results. Overall, the findings in this study support the hypothesis that additional patient and radiographic features are associated with cancer detection rates beyond the PI-RADS categorization, which has implications for personalizing the decision to proceed with biopsy and may explain the wide observed variation in CDRs in real-world settings.

Prior studies have supported the utility of PSA density in providing discrimination for clinically significant prostate cancer among patients with positive mpMRI

findings.<sup>13,14</sup> In one study, Bhat and colleagues reported that a model including MRI-defined PSA density combined with MRI interpretation had a significantly improved performance for clinically significant prostate cancer when compared to other models.<sup>13</sup> Other studies have shown that the addition of PSA density to the PI-RADS category improves the detection of clinically significant prostate cancer in patients with equivocal MRI results.<sup>15</sup> These results are consistent with our findings on cancer detection rates and support the value of PSA density in improving the prediction of cancer detection based on MRI findings.

Several studies have reported that patients with prior negative biopsies have a lower risk of high-grade prostate cancer when compared to biopsy-naive men.<sup>16</sup> Similarly, a prospective study performed by Patel et al demonstrated that prior negative biopsy lowered the risk of cancer detection even after stratification by PI-RADS category. This effect persisted after stratification by PI-RADS category, highlighting the importance of non-imaging predictors of cancer detection.<sup>17</sup> In the present study, we observed a three- to five-fold reduction in the risk of cancer detection among men with one or more prior negative biopsies, similar in magnitude to the PI-RADS categorization, further underscoring the importance of considering this factor in estimating cancer risk.

Prior studies have attempted to improve clinically significant cancer risk prediction using models that combine MRI features and clinical parameters. Triquell et al performed a systematic review of MRI-based prediction models for the detection of clinically significant prostate cancer, including 18 studies that evaluated imaging and clinical predictors similar to those considered in our model.<sup>18</sup> The c-statistics for these models ranged from 0.78–0.92, highlighting the utility of MRI-based prediction models that incorporate features beyond the PI-RADS score.

Although all models improved the prediction of clinically significant cancer, only a few had external validation or available risk calculators. In one study, Kinnaird and colleagues developed a risk calculator that combined MRI and clinical characteristics from 2354 North American men.<sup>19</sup> Clinical characteristics and the per-lesion PI-RADS score were associated with an increased risk of cancer detection, while Asian ethnicity was associated with a lower risk of cancer detection. In another study by Morote and colleagues, the authors developed and externally validated a risk calculator for the prediction of csCDR.<sup>20</sup> In this study, the addition of clinical parameters, such as age, PSA level, DRE findings, family history, prostate volume, and number of prior biopsies,

**Table 3. Univariable and multivariable logistic regression – csCDR**

	csCDR outcome unadjusted OR (95% CI)	csCDR outcome adjusted OR (95% CI)
<b>Patient characteristics</b>		
Age, yrs	1.02 (0.99, 1.06)	1.03 (0.99, 1.08)
Pre-biopsy PSA, ng/mL	1.08 (1.04, 1.13)	1.08 (0.98, 1.19)
<b>DRE</b>		
Normal/not performed (ref)	–	–
Abnormal	1.76 (0.95, 3.19)	1.96 (0.94, 4.05)
<b>Number of prior prostate biopsies</b>		
0 (ref)	–	–
1	0.65 (0.37, 1.13)	0.50 (0.24, 1.02)
2+	0.57 (0.31, 1.02)	0.27 (0.10, 0.64)
<b>Biopsy type</b>		
In-bore (ref)	–	–
MRI-US fusion	0.68 (0.41, 1.12)	0.55 (0.29, 1.00)
<b>Prior diagnosis</b>		
No	–	–
Yes	0.92 (0.53, 1.56)	1.03 (0.49, 2.17)
<b>Lesion characteristics</b>		
<b>Number of lesions</b>		
2+ (ref)	–	–
1	2.80 (1.65, 4.92)	2.56 (1.36, 4.99)
<b>PI-RADS</b>		
3 (ref)	–	–
4	2.05 (0.92, 5.23)	1.94 (0.74, 5.80)
5	4.06 (1.71, 10.90)	2.60 (0.86, 8.67)
<b>Lesion locations</b>		
Non-peripheral zone (anterior/transition zone) (ref)	–	–
Peripheral zone	0.77 (0.47, 1.24)	1.13 (0.61, 2.12)
Lesion size, largest dimension, mm	1.04 (1.01, 1.08)	1.03 (0.98, 1.09)
Prostate volume on MRI	0.99 (0.98, 0.99)	0.99 (0.98, 1.00)
PSA density (0.1 unit increase)	1.68 (1.38, 2.08)	1.38 (0.90, 2.10)

csCDR: clinically significant cancer detection rate; DRE: digital rectal examination; MRI: magnetic resonance imaging; OR: odds ratio; PI-RADS: Prostate Imaging-Reporting and Data System; PSA: prostate-specific antigen; US: ultrasound.

**Table 4. Lasso regression for the outcomes of CDR and csCDR (N=344)**

	CDR outcome* β coefficient	csCDR outcome** β coefficient
Intercept	-0.78	-3.52
<b>Patient characteristics</b>		
Age, yrs	0.01	0.02
Pre-biopsy PSA, ng/mL	–	0.04
<b>DRE</b>		
Normal/not performed (ref)	–	–
Abnormal	–	0.52
<b>Number of prior prostate biopsies</b>		
0 (ref)	–	–
1	-0.53	-0.45
2+	-0.91	-0.93
<b>Biopsy type</b>		
In-bore (ref)	–	–
MRI-US fusion	–	-0.37
Prior diagnosis of Gleason 6 prostate cancer	N/A	–
<b>Lesion characteristics</b>		
<b>Number of lesions</b>		
2+ (ref)	–	–
1	0.29	0.77
<b>PI-RADS</b>		
3 (ref)	–	–
4	0.48	0.10
5	0.93	0.38
<b>Lesion locations</b>		
Non-peripheral zone (anterior/transition zone) (ref)	–	–
Peripheral zone	-0.12	--
Lesion size, largest dimension, mm	0.01	0.02
Prostate volume on MRI	-0.01	-0.01
PSA density (0.1 unit increase)	0.36	0.32

\*Shrinkage parameter (λ) used in the model that minimizes the misclassification error: 0.02. It was estimated by performing k-fold cross-validation using k=10 folds. c-statistic=0.80, optimism adjusted c-statistic=0.77. \*\*Shrinkage parameter (λ) used in the model that minimizes the misclassification error: 0.01. It was estimated by performing k-fold cross-validation using k=10 folds. c-statistic=0.79, optimism adjusted c-statistic=0.75. CDR: cancer detection rate; csCDR: clinically significant cancer detection rate; DRE: digital rectal examination; MRI: magnetic resonance imaging; OR: odds ratio; PI-RADS: Prostate Imaging-Reporting and Data System; PSA: prostate-specific antigen; US: ultrasound.

improved model performance in both development and validation cohorts.

**Limitations**

Our study is not without limitations. First and foremost, this is a retrospective study and subject to the limitations of that design, including selection bias and confounding. Moreover, we were unable to assess certain variables that may be important for prostate cancer risk prediction, such as family history, race, ancillary biomarker testing, or certain imaging characteristics.

Furthermore, although MRIs were reviewed by trained genitourinary radiologists, interobserver variability likely exists and may introduce a source of measurement error. Importantly, prior negative biopsies were systematic ultrasound-guided biopsies. Accordingly, these data may not be applied to contemporary patients with prior negative MRI-guided biopsy.

As with any predictive model, incorporation into clinical care requires consideration of the value placed upon the relative risks of false-negative and false-positive results by the patient and clinician. Although we present decision curve analysis to illustrate clinical utility over a range of threshold probabilities, the ultimate decision to perform a biopsy must be individualized.

Finally, The present study requires external validation, and results must be interpreted accordingly.

**CONCLUSIONS**

Several clinical and radiographic features are independently associated with risk of prostate cancer in men undergoing MRI-targeted biopsy. A predictive model based on these features can provide personalized risk stratification beyond the PI-RADS categorization and improve clinical decisions regarding biopsy compared to the conventional strategy of performing biopsy for all PI-RADS 3–5 lesions on MRI.

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This paper has been peer reviewed.

**REFERENCES**

1. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically localized prostate cancer: AUA/ASTRO guideline, part I: Introduction, risk assessment, staging, and risk-based management. *J Urol* 2008;208:10-8. <https://doi.org/10.1097/JU.00000000000002757>
2. Wei JT, Barocas D, Carlsson S, et al. Early detection of prostate cancer: AUA/SUO guideline part I: Prostate cancer screening. *J Urol* 2023;46-53. <https://doi.org/10.1097/JU.00000000000003491>
3. Kasivisvanathan V, Stabile A, Neves JB, et al. Magnetic resonance imaging-targeted biopsy versus systematic biopsy in the detection of prostate cancer: A systematic review and meta-analysis. *Eur Urol* 2019;76:284-303. <https://doi.org/10.1016/j.eururo.2019.04.043>

4. Eklund M, Jäderling F, Discacciati A, et al. MRI-targeted or standard biopsy in prostate cancer screening. *N Engl J Med* 2021;385:908-20. <https://doi.org/10.1056/NEJMoa2100852>
5. Siddiqui MR, Ansbro B, Shah PV, et al. Real-world use of MRI for risk stratification prior to prostate biopsy. *Prostate Cancer Prostatic Dis* 2023;26:353-9. <https://doi.org/10.1038/s41391-022-00543-4>
6. Turkbey B, Rosenkrantz AB, Haider MA, et al. Prostate imaging reporting and data system version 2.1: 2019 update of prostate imaging reporting and data system version 2. *Eur Urol* 2019;76:340-51. <https://doi.org/10.1016/j.eururo.2019.02.033>
7. Ahmed HU, El-Shater Bosaily A, Brown LC, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): An paired validating confirmatory study. *Lancet* 2017;389:815-22. [https://doi.org/10.1016/S0140-6736\(16\)32401-1](https://doi.org/10.1016/S0140-6736(16)32401-1)
8. Oerther B, Engel H, Bamberg F, et al. Cancer detection rates of the PI-RADSv2.1 assessment categories: Systematic review and meta-analysis on lesion level and patient level. *Prostate Cancer Prostatic Dis* 2022;25:256-63. <https://doi.org/10.1038/s41391-021-00417-1>
9. Westphalen AC, McCulloch CE, Anaokar JM, et al. Variability of the positive predictive value of PI-RADS for prostate MRI across 26 centers: Experience of the society of abdominal radiology prostate cancer disease-focused panel. *Radiology* 2020;296:76-84. <https://doi.org/10.1148/radiol.2020190646>
10. Mazzone E, Stabile A, Pellegrino F, et al. Positive predictive value of prostate imaging reporting and data system version 2 for the detection of clinically significant prostate cancer: A systematic review and meta-analysis. *Eur Urol Oncol* 2021;4:697-713. <https://doi.org/10.1016/j.euo.2020.12.004>
11. Johnson M, Tsai L, McMahon C, et al. Impact of proposed changes to PI-RADSv2 on diagnostic performance of MRI: Pathologic correlation with in-bore MRI-guided prostate biopsies. Scientific paper abstracts presented at the Society of Abdominal Radiology 2019 Annual Scientific Meeting and Educational Course (March 17-22, 2019, Orlando, FL). *Abdom Radiol* 2019;44:3210-34. <https://doi.org/10.1007/s00261-019-02157-2>
12. Vickers AJ, Elkin EB. Decision curve analysis: A novel method for evaluating prediction models. *Med Decis Making* 2006;26:565-74. <https://doi.org/10.1177/0272989X06295361>
13. Bhat NR, Vetter JM, Andriole GL, et al. Magnetic resonance imaging-defined prostate-specific antigen density significantly improves the risk prediction for clinically significant prostate cancer on biopsy. *Urology* 2019;126:152-7. <https://doi.org/10.1016/j.urology.2018.12.010>
14. Yusim I, Krenawi M, Mazor E, et al. The use of prostate specific antigen density to predict clinically significant prostate cancer. *Sci Rep* 2020;10:20015. <https://doi.org/10.1038/s41598-020-76786-9>
15. Stevens E, Truong M, Bullen JA, et al. Clinical utility of PSAD combined with PI-RADS category for the detection of clinically significant prostate cancer. *Urol Oncol* 2020;38:846.e9-16. <https://doi.org/10.1016/j.urolonc.2020.05.024>
16. Grivas N, Lardas M, Espinós EL, et al. Prostate cancer detection percentages of repeat biopsy in patients with positive multiparametric magnetic resonance imaging (prostate imaging reporting and data system/Likert 3-5) and negative initial biopsy: A mini systematic review. *Eur Urol* 2022; 82:452-7. <https://doi.org/10.1016/j.eururo.2022.07.025>
17. Patel HD, Koehne EL, Shea SM, et al. Risk of prostate cancer for men with prior negative biopsies undergoing magnetic resonance imaging compared with biopsy-naive men: A prospective evaluation of the PLUM cohort. *Cancer* 2022;128:75-84. <https://doi.org/10.1002/cncr.33875>
18. Triquell M, Campistol M, Celma A, et al. Magnetic resonance imaging-based predictive models for clinically significant prostate cancer: A systematic review. *Cancers* 2022;14:4747. <https://doi.org/10.3390/cancers14194747>
19. Kinnaird A, Brisbane W, Kwan L, et al. A prostate cancer risk calculator: Use of clinical and magnetic resonance imaging data to predict biopsy outcome in North American men. *Can Urol Assoc J* 2022;16:E161-6. <https://doi.org/10.5489/cuaj.7380>
20. Morote J, Borque-Fernando A, Triquell M, et al. The Barcelona predictive model of clinically significant prostate cancer. *Cancers* 2022;14:1589. <https://doi.org/10.3390/cancers14061589>

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