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ORIGINAL RESEARCH

Does Size Matter? A Retrospective Study Analysing the Size of PI-RADS 4 Lesions and Its Associated Prostate Cancer Positivity with Transperineal Prostate Biopsy

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Introduction: Magnetic resonance imaging (MRI) is an essential tool in Prostate Cancer (PCa) diagnosis. PI-RADS v2.1 score correlates with clinically significant prostate cancer (CSPCa) and according to the most recent guidelines, prevalence of CSPCa with PI-RADS 4 is 33–41%, while PI-RADS 5 is 62–79%. These groups are separated only by a size of 15 mm yet the difference in risk is significant. This study aims to find a size threshold associated with CSPCa within the PI-RADS 4 group, which may be used in combination with other prostatic parameters, such as PSA density in order to help with risk stratification and patient counselling in the pre-biopsy setting. This may also aid with surveillance of smaller PI-RADS 4 lesions in the setting of a negative biopsy and avoid unnecessary repeat biopsies unless triggered by a size threshold.

Methods: A retrospective study was performed with data from 407 patients undergoing transperineal prostate biopsy (TPPB) between April 2022 and November 2023. A subgroup of patients with PI-RADS 4 was included for analysis. A ROC-AUC was obtained.

Results: Median age was 67 (interquartile range: 61–71) and PSA density 0.20 (interquartile range 0.13–0.28). PI-RADS score correlated with CSPCa: for PI-RADS 1 and 2, the frequency of CSPCa was 10%; for PI-RADS 3, it was 20%; for PI-RADS 4, it was 60%; and for PI-RADS 5, it was 80%, Pearson correlation = 0.51, $p < 0.001$. The Receiver Operating Characteristic Area Under the Curve (ROC-AUC) was determined to be 0.664 [0.579–0.7499]. The optimal cut-off point was 8.5 mm. Patients with lesions larger than 8.5 mm had 2.31 times higher risk CSPCa.

Conclusion: PI-RADS 4 size does matter and is a useful predictor of CSPCa. In our study, a cut-off of 8.5 mm was identified. The combination of PI-RADS 4 with PSA density provides a specificity higher than 80% for CSPCa detection.

Keywords: PI-RADS 4, mpMRI, transperineal prostate biopsy, prostate cancer, size

Introduction

Transperineal prostate biopsy (TPPB) has become the preferred method to sample prostatic tissue in order to confirm or exclude prostate cancer. Both the American Urological Association (AUA)[1] and European (EAU)[2] guidelines recommend this method as it allows better sampling from anterior and apical areas of the prostate and leads to greater detection of CSPCa, particularly in men undergoing re-biopsy as part of active surveillance.[1,3] TPPB has a much lower risk of post-biopsy infection, as evidenced by Pepe and Pennisi, who performed a retrospective review of 8500 men over 22 years and found the incidence of post-TPPB infection to be less than 0.2% and even more reassuringly, none of their

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patients developed sepsis.[3] TPPB is also impactful in that it facilitates improved antibiotic stewardship, with a recent non-inferiority trial showing that TPPB can be safely performed without antibiotic prophylaxis.[4]

Multiparametric Magnetic Resonance Imaging of the Prostate (mpMRI) has shifted the prostate biopsy paradigm. Initially indicated as a tool in a re-biopsy setting, its use even before the first biopsy has gained momentum and the EAU guidelines now recommend it for biopsy naive patients (strong strength ratio). The PRECISION trial[5] was an important study that suggested that mpMRI before the first biopsy leads to higher detection of clinically significant prostate cancer (CSPCa) and can avoid unnecessary biopsies and subsequent detection of low-risk prostate cancer (Gleason 6/ISUP1).

The diagnostic reliability of mpMRI in the re-biopsy setting for patients that have previously had a negative biopsy was confirmed in a study by Barone et al in 2023.[6] This was a retrospective observational study out of the University of Naples, Italy, which separated 389 biopsy patients into biopsy naïve and re-biopsy groups. The findings of the study were of comparable detection rates of CSPCa in both groups. Barone et al suggest that obtaining an mpMRI prior to a repeat biopsy harbors several advantages including an increased detection rate of any PCa and csPCa compared to systematic biopsy alone. This leads to a reduction in the number of biopsies needed and can contribute to significant cost savings compared to biopsy alone. Furthermore, the ability of mpMRI to highlight suspicious target lesions aids the operator to perform either systematic or targeted biopsies and obtain cores from the prostate zone that was most suspicious on mpMRI.

Massanova et al have suggested the combination of mpMRI and PSA density to predict the risk of CSPCa whereby their retrospective study of 630 men demonstrated that men with a PI-RADS score of 3 or less with a PSA density of <0.3 were at low risk of prostate cancer and could potentially avoid a biopsy. This demonstrates the utility of mpMRI to aid with avoiding biopsy in certain patients, which in itself leads to preservation of cost, resources and procedural risk reduction.[7]

The Prostate Imaging Reporting and Data System (PI-RADS) system has been in place since 2011 and since 2019 radiologists should be using the most up-to-date version, PI-RADS v2.1,[8] while reporting mpMRI. The previously mentioned AUA paper[2] states that the prevalence of CSPCa detection for PI-RADS 4 and 5 are, respectively, 37% and 70% (CI95%). These groups are separated only by a size threshold of 15 mm yet the difference in risk of CSPCa is significant. Therefore, this study aims to find a size threshold associated with CSPCa within the PI-RADS 4 group, which may be used in combination with other prostatic parameters, such as PSA density in order to help with risk stratification and patient counselling in the pre-biopsy setting. This may also aid with surveillance of smaller PI-RADS 4 lesions in the setting of a negative biopsy and avoid unnecessary repeat biopsies unless triggered by a size threshold.

Patients and Methods

A retrospective study was performed collecting data from a total of 407 patients undergoing prostate biopsy between April 2022 and November 2023 at Tauranga Hospital. All patients underwent cognitive-fusion TPPB whereby the urologist performing the procedure would revise the patient's mpMRI prior to the procedure, display the mpMRI images on a high-resolution monitor and then perform the biopsy using a freehand technique, referring back to the mpMRI and utilising the real time transrectal ultrasound image at each step of the procedure. A large majority of patients with a targetable lesion underwent standard template and targeted biopsy. Patients with no targetable lesion underwent standard template biopsy only. Only a small group of patients with either anticoagulation or advanced age and very large lesions had target biopsy alone. The majority of biopsies were done under local anaesthetic (LA) in the outpatient clinic department, and a small number were performed in the operating theatre; however, with the same LA technique. A 10 millilitre (mL) syringe containing 10 mL of Lignocaine 1% +1 mL of sodium bicarbonate 8.4% is used via an 11-gauge needle for the perineal skin and subcutaneous tissue as a superficial block. Following this, a 20 mL syringe containing 15 mL of lignocaine 1% +1.5 mL of sodium bicarbonate 8.4% is used via a 20-gauge spinal needle for the pelvic wall muscles, periapical triangle, and Allaway's space using 8 mL in each side as a deep block as described by Ordones et al.[9] Informed consent was obtained from the patients, and ethical approval was provided by the National Ethics Committee of New Zealand (Reference Number 2022–206). The Māori committee approval was also granted. All research was performed in accordance with relevant guidelines/regulations (Declaration of Helsinki).

Predictor Variables

We collected the variables: age, body mass index (BMI), ethnicity, PSA, prostate volume, PSA density, PI-RADS scores measured using a 5-point scale, previous biopsy, and corresponding histology results. PSA density was calculated by dividing PSA by prostate volume (obtained from the MRI). We defined clinically significant prostate cancer as a Gleason score of 7 or more (ISUP2).

MRI Evaluation

All MRI scans were acquired on 3-Tesla scanners with a standard surface phased-array coil, with T2-weighted, diffusion-weighted and dynamic contrast-enhanced sequences. In total, five specialist MRI radiologists reported the mpMRI's. Each mpMRI was reported individually and then double read by a second radiologist from the same group. The mpMRI findings were reported in accordance with PI-RADS v2.1 utilizing a 5-point likelihood scale for CSPCa and providing a measurement of the index lesion in millimetres. The index lesion was defined as the largest lesion and its maximum diameter was recorded alongside the histological result obtained from TPPB as seen in figure 1. A subgroup of all patients with PI-RADS 4 on MRI was evaluated in this study.

Statistics

Continuous variables were presented as medians and percentiles (25th and 75th), while categorical variables were depicted as numbers and percentages. Group comparisons for continuous variables were performed using the Wilcoxon rank-sum test. For categorical variables, the chi-square test was employed. Correlations were assessed using the Pearson correlation test.

We determined the accuracy of tests in detecting CSPCa through the calculation of Receiver Operating Characteristic Area Under the Curve (ROC-AUC) values. To establish the precision of these values, we computed the 95% confidence interval for ROC-AUC using 2000 stratified bootstrap replicates. The optimal cut-point, balancing sensitivity and specificity, was identified on the ROC-AUC plot using the "best threshold" function from the pROC package. This is the value to the highest left point of the graph, which is selected to represent the value that enjoys the highest sensitivity and specificity simultaneously. The statistical analysis was performed using univariate analysis with R software version 4.1.2.

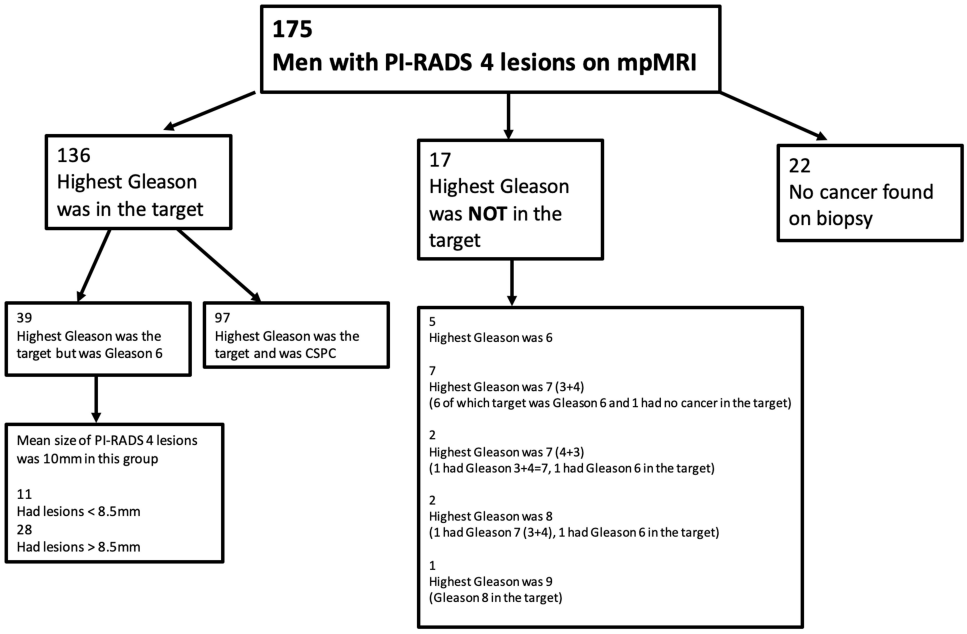

Figure 1 Flowchart depicting analysis of PI-RADS 4 lesions with their positivity and comparison to template biopsy.

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Results

Cohort Demographics, mpMRI Lesion Distribution, CSPCa Positivity and ROC-AUC Analysis

Four hundred and seven patients underwent TPPB between April 2022 and November 2023. The median age of the participants was 67 years (interquartile range: 61–71). Most of the patients were of New Zealand European descent, constituting 79% of the cohort. The median PSA density was 0.20 (interquartile range: 0.13–0.28).

Regarding PI-RADS scores, 42% of our patients had PI-RADS 4, and 33% had PI-RADS 5. Notably, 56% of the total cases were found to have CSPCa.

Nine patients (2.2%) had target biopsies only, 76 patients (19%) had template biopsies only as they did not have a target lesion and 321 (79%) had both target and template biopsies.

Fifty-four patients (14%) were having repeat biopsies as part of their active surveillance pathway.

Eighty-four patients (22%) had anterior lesions that were targeted at biopsy.

The median number of cores was 17 (Table 1).

The PI-RADS values correlated with the CSPCa as follows; for PI-RADS 1 and 2, the frequency of CSPCa was 10%; for PI-RADS 3, it was 20%; for PI-RADS 4, it was 65%; and for PI-RADS 5, it was 80%, Pearson correlation = 0.51, $p < 0.001$ (Figure 2).

Table 1 Baseline Characteristics

Characteristic	N = 407
Age, Median (IQR)	67 (61–71)
Ethnicity, n (%)	
European	320 (79)
Maori	74 (18)
Pasifika	4 (1.0)
Asian	6 (1.5)
Other	3 (0.7)
BMI, Median (IQR)	27.8 (25.8–31.0)
PSA, Median (IQR)	9 (6–13)
Prostate Volume, Median (IQR)	44 (34–60)
PSA Density, Median (IQR)	0.20 (0.13–0.28)
PiRads Score, n (%)	
1+2	66 (16)
3	37 (9.0)
4	175 (43)
5	129 (32)
Index Lesion Location, n (%)	
No Lesion MRI	57 (15)
Anterior	84 (22)
Central	10 (2.6)
Peripheral	231 (60)
Previous active surveillance, n (%)	54 (14)
Procedure time, Median (IQR)	11.0 (10.0–12.0)
Failure, n (%)	7 (1.7)
Number of cores, Median (IQR)	17.0 (15.0–21.0)
Target vs template, n (%)	
Target	9 (2.2)
Template	76 (19)
Both	321 (79)
Clinically Significant Prostate Cancer (CSPCa), n (%)	227 (56)

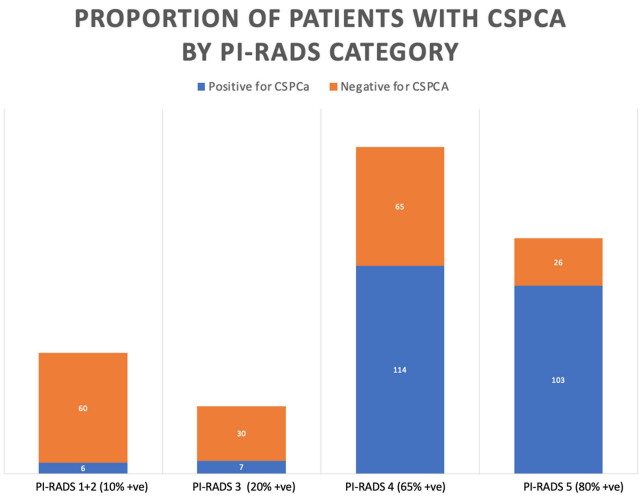

Figure 2 Percentage positivity of CSPCa by PI-RADS score.

The Receiver Operating Characteristic Area Under the Curve (ROC-AUC) values for PSA, PSA density, and PI-RADS value in detecting CSPCa were as follows: 0.671 [0.620–0.724] for PSA, 0.744 [0.697–0.792] for PSA density, and 0.786 [0.744–0.828] for PI-RADS value (Figure 3).

PI-RADS 4 Subgroup Analysis

We evaluated a subgroup of PI-RADS 4, consisting of 175 patients, to determine the value of the size of the PI-RADS 4 lesion in the accuracy of detecting CSPCa.

Mean Size and Size Thresholds

In the univariate analysis, patients without CSPCa had a median size of 10 mm [7–12], whereas those with CSPCa had a median size of 11 mm [9–13], with a p-value of less than 0.001 (Figure 4). The Receiver Operating Characteristic Area Under the Curve (ROC-AUC) was determined to be 0.664 [0.579–0.7499]. The optimal cut-off point was identified as

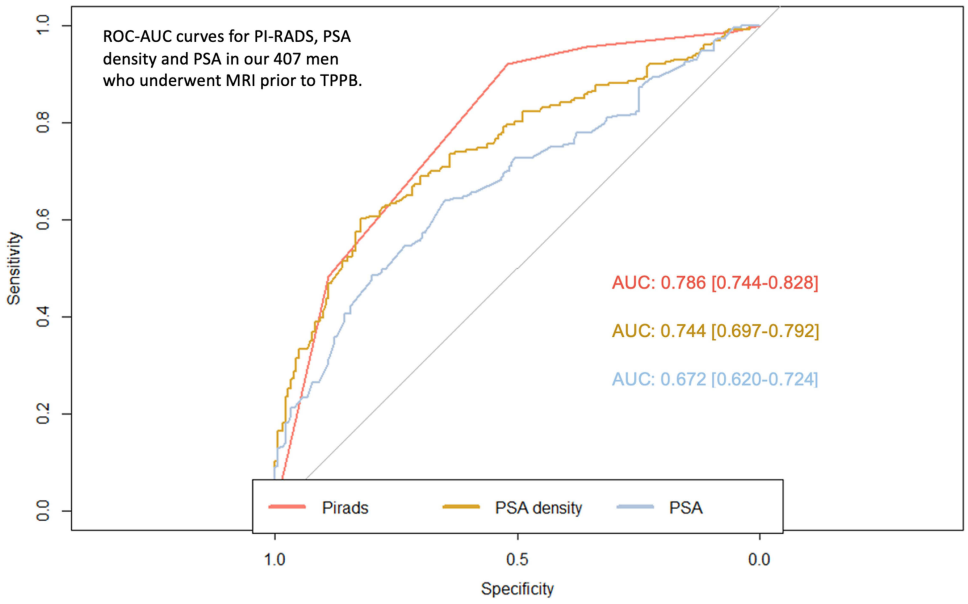

Figure 3 The Receiver Operating Characteristic Area Under the Curve (ROC-AUC) values for PSA, PSA density, and PI-RADS detecting CSPCa.

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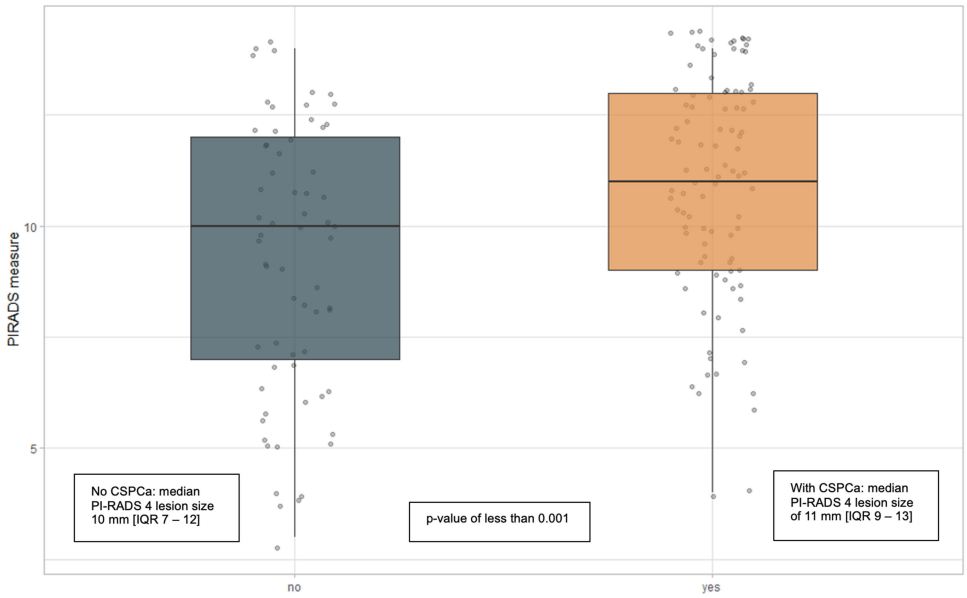

Figure 4 Median size after univariate analysis of mpMRI index lesion size for patients without (10 mm) and with CSPCa (11 mm).

8.5 mm with a sensitivity of 84% and a specificity of 41% (Figure 5). Using 8.5 mm as the cut-off point, patients with lesions larger than 8.5 mm had a 2.31 [1.31–4.07] times higher risk of CSPCa.

Correlation Between Size and PSA Density

The association between PI-RADS 4 index lesion size >8.5 mm with a PSA density results in the following; for PSA density below 0.15 = 0.5706 (95% CI: 0.4237–0.7176) ROC. Meanwhile, for PSA density above 0.15 = 0.7061 (95% CI: 0.5937–0.8185) ROC.

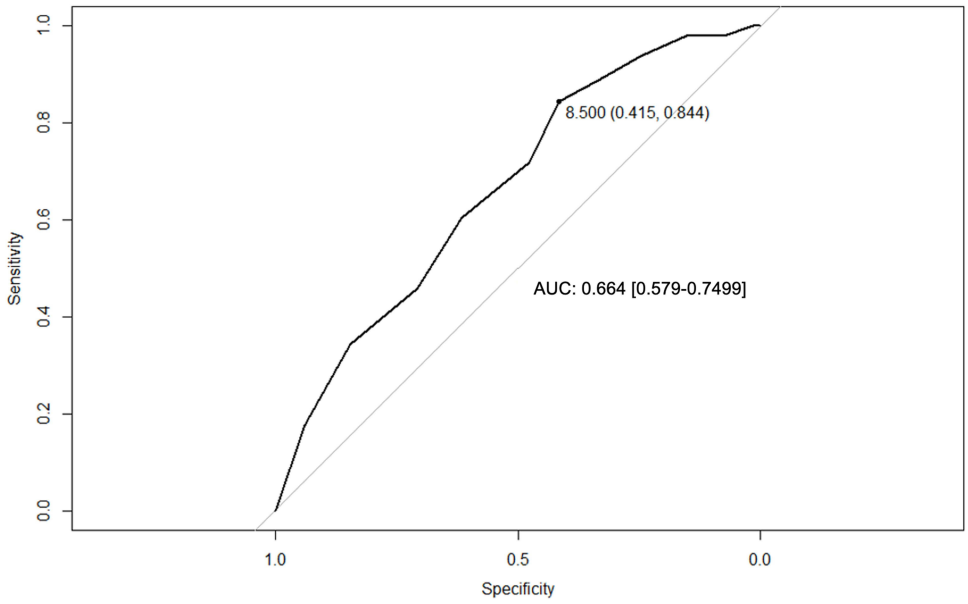

Figure 5 ROC Curve with optimal cut-off identified at 8.5 mm.

Clinical Significance of the Index Lesion

Furthermore, we reviewed the full histological reports for biopsies undertaken on these 175 patients with PI-RADS 4 lesions to determine if the highest Gleason score was found in the index target lesion or elsewhere within the prostate.

172/175 patients had target and template TPPB done with only 3 patients having target TPPB alone.

Of the 175 patients, 22 had no evidence of cancer, with 153 patients receiving a cancer diagnosis. The highest Gleason score was found in the target lesion in 136 of the 153 patients (89%), while it was found elsewhere in the prostate in 17 of the 153 patients (11%).

In the 17 patients who had a higher Gleason outside of the target lesion, the template biopsy led to a change in management in 9 due to the identification of CSPCa elsewhere in the prostate with a rate of 5% overall (9/153) (Figure 1).

Discussion

The current Prostate Imaging Reporting and Data System states that the difference between PI-RADS 4 and 5 relies solely on size, with PI-RADS 5 being 15 mm or larger. That makes PI-RADS 4 a heterogeneous group of lesions that could range from anything between 1 and 14 mm, as long as they are markedly hypointense on ADC (apparent diffusion coefficient) and markedly hyperintense on DWI (diffusion-weighted imaging).

In our study, we identified an optimal cut-off point of 8.5 mm, which carried a sensitivity of 84% and specificity of 41% (Figure 5). Patients with lesions larger than 8.5 mm had a 2.31 [1.31–4.07] times higher risk of CSPCa. While these results are statistically significant and our findings boast a moderately high sensitivity of 84%, the specificity is lacking at just 41%. In the clinical setting, it would be ill-advised to make decisions about proceeding to biopsy based on the size of the PI-RADS 4 lesion alone. Our results demonstrate that by combining a PI-RADS 4 lesion larger than 8.5 mm with a PSA density greater than 0.15 the ROC-AUC increases from 0.664 to 0.7061.

As clinicians, we must be able to collect information from a variety of different investigative modalities and then use a variety of parameters to consciously risk stratify our patients. By combining demographic factors, family history, PSA density, mpMRI lesion type and size, as well as patient wishes, we can perform shared decision-making to identify which patients have indications for an initial biopsy as well as which patients should be offered ongoing surveillance following a negative biopsy, ie surveillance mpMRI in the patient with a negative biopsy of a small PI-RADS 4 lesion.

As far as we know, this is the first study to analyze the PI-RADS 4 size threshold associated with CSPCa in patients who undergo TPPB under local anaesthetic. Some other papers were recently published (2023) but both utilized a transrectal prostate (TRUS) biopsy approach.

The first one, a retrospective study published by Kilic et al[10] utilized the transrectal approach and in-bore MRI-guided type of biopsies for targeted biopsies only. Thus, the biopsy route and fusion technique differ. Univariate and multivariate regression analyses were performed to evaluate the factors which contribute to making a diagnosis of PCa and CSPCa. The cohort was similar to ours in that it had 159 patients compared to our 175. About 86% of patients were biopsy naïve which is the same proportion as our study. About 71% of their cohort at PCa, compared to 87% of ours. About 54.1% had CSPCa compared to 61% of ours. This study did not aim to identify an optimal cut-off point but rather, the authors subdivided the PI-RADS 4 groups into index lesions smaller than 5 mm, between 5 and 10 mm and bigger than 10 mm and the detection rates of CSPCa were 42%, 51% and 64%, respectively. Also, the presence of one or more lesions was not associated with CSPCa.

The later study, written by de Souza et al[11] was different in that the study aimed to establish a size threshold associated with benign results. Furthermore, they used 1.5 and 3.0 Tesla MRI to map the prostate. Their biopsy technique was TRUS compared to our TPPB; however, like our study, they did utilise cognitive fusion during their biopsies. Multivariate analysis determined that a previous negative biopsy and a PI-RADS 4 lesion smaller than 6 mm were both independent variables associated with a negative biopsy result.

In 2020, Park et al[12] wrote about the need to divide the PI-RADS 4 groups into two groups of lesions smaller or larger than 10 mm and also suggested that PI-RADS 4 larger than 10 mm should be reclassified as PI-RADS 5. The decision

and process to re-classify PI-RADS reporting is significant and should not be taken lightly; however, this study highlights the need to consider lesion size in clinical decision-making.

There is an emergent role for PSMA PET/CT to improve the detection rate of CSPCa, and this has been well reported by Pepe et al[13] in a prospective study comparing the accuracy of 68Ga-PSMA PET/CT versus mpMRI transperineal targeted biopsy in the diagnosis of CSPCa in men who are at high risk for PCa. The findings of this study demonstrated diagnostic accuracies of 92% and 86% in PSMA PET/CT and mpMRI PI-RADS ≥3, respectively, with regard to CSPCa. The authors conclude that 68GaPSMA PET/CT demonstrated good diagnostic accuracy as a single procedure for the diagnosis and staging of high-risk PCa.

Prostate cancer is known to be multifocal, and surely a point of weakness of our study is that the highest Gleason/ISUP was taken into consideration, rather than the index lesion biopsy result, remembering that 98% (172/175) of our cohort had combined target and template biopsies. Inclusion of the 11% of patients who had a higher Gleason outside of the index lesion may impact our results as these lesions have contributed to the positivity rate for CSPCa.

A prospective study out of Italy in 2023 by Novara et al[14] sought to compare the rates of CSPCa detected in mpMRI/TRUS fusion transperineal targeted biopsy, perilesional biopsy and random biopsies. One hundred and sixty-eight biopsy naïve patients were included, and the diagnostic yields of the different biopsy schemes were compared. The overall detection rate of CSPCa increased to 35%, 45% and 49% by adding 4 perilesional cores, 12 random cores and 24 cores respectively. Interestingly, targeted biopsy alone identified only 62% of CSPCa which was increased to 72% by adding 4 perilesional cores and to 91% by adding 14 random cores.

As mentioned, our biopsies are performed using cognitive fusion, and this is very much operator dependent. Identification of what is deemed to be the index target lesion may differ between the operators and may not be entirely consistent with what is seen on the mpMRI. We do, however, believe that having a small number of just two consultant urologists performing this procedure, the chance of this operator variability is reduced and hence the risk of sampling error is reduced.

A further limitation in identifying the index lesion may arise via disagreement between the urologist performing the biopsy and the radiologist who has reported the mpMRI, as well as the obvious differing nature between ultrasound and MRI.

It must also be noted that similar to the findings from Kilic et al as mentioned above, an earlier study done by Johnson et al[15] demonstrated that multifocality was negatively associated with tumor detection when controlling for other factors. In the same paper, mpMRI detected less than two-thirds of all CSPCa.

Other limitations worth noting are with regard to potential bias. Misclassification bias may arise during radiology reporting, for example, when a lesion is reported into the incorrect PI-RADS category. We do believe this is reduced by the double-read process employed by our radiology department as well as the cognitive fusion by our proceduralists. Also worth noting is the potential for selection bias; however, we believe this is greatly reduced by the government funded access to PSA screening and mpMRI upon general practitioner referral to a public urology service. This, however, does not account for the poorest of the socioeconomic scale who may not have access to a general practitioner. No lost to follow-up bias is evident in our study as all patients who were reported to have a PI-RADS 4 lesion on MRI proceeded to biopsy.

Conclusion

We have identified a statistically significant size threshold of 8.5 mm for PI-RADS 4 lesions which, when reached, carries a 2.31 [1.31–4.07] times higher risk of CSPCa compared to lesions below this size threshold. As such, the size of a PI-RADS 4 lesion does matter and is, in fact, a useful predictor of the probability of a positive biopsy for CSPCa. Our study has highlighted the importance of thinking about PI-RADS 4 lesions in size-specific groups. When combined with PSA density, this is a useful tool in order to improve accuracy in patient counselling and optimisation of follow-up or surveillance strategies.

Ethics Statement

Informed consent was obtained from the patients, and ethical approval was provided by the National Ethics Committee of New Zealand (Reference Number 2022-206). The Māori committee approval was also granted. All research was performed in accordance with relevant guidelines/regulations (Declaration of Helsinki).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wei JT, Barocas D, Carlsson S, et al. Early detection of prostate cancer: AUA/SUO guideline part I: prostate cancer screening. *J Urol*. 2023;210(1):46–53. doi:10.1097/JU.0000000000003491
2. EAU Guidelines. Edn. presented at the EAU Annual Congress Milan 2023. ISBN 978-94-92671-19-6.
3. Pepe P, Pennisi M. Morbidity following transperineal prostate biopsy: our experience in 8.500 men. *Archivio Italiano di Urologia e Andrologia*. 2022;94(2):155–159. doi:10.4081/aiua.2022.2.155
4. Jacewicz M, Günzel K, Rud E, et al. Antibiotic prophylaxis versus no antibiotic prophylaxis in transperineal prostate biopsies (NORAPP): a randomised, open-label, non-inferiority trial. *Lancet Infect Dis*. 2022;22(10):1465–1471. doi:10.1016/S1473-3099(22)00373-5
5. Kasivisvanathan V, Rannikko AS, Borghi M, et al.; PRECISION Study Group Collaborators. MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N Engl J Med*. 2018;378(19):1767–1777.
6. Barone B, Napolitano L, Calace FP, et al. Reliability of multiparametric magnetic resonance imaging in patients with a previous negative biopsy: comparison with biopsy-naïve patients in the detection of clinically significant prostate cancer. *Diagnostics*. 2023;13(11):1939. doi:10.3390/diagnostics13111939
7. Massanova M, Vere R, Robertson S, et al. Clinical and prostate multiparametric magnetic resonance imaging findings as predictors of general and clinically significant prostate cancer risk: a retrospective single-center study. *Current Urol*. 2023;17(3):147–152. doi:10.1097/CU9.0000000000000173
8. 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. *Europ urol*. 2019;76(3):340–351. doi:10.1016/j.eururo.2019.02.033
9. Ordones FV, Vermeulen L, Bressington M, et al. How I do it: transperineal prostate biopsy using local anesthetic in an outpatient setting. *Can J Urol*. 2023;30(1):11453–11456.
10. Kilic M, Madendere S, Vural M, Koseoglu E, Balbay MD, Esen T. The role of the size and number of index lesion in the diagnosis of clinically significant prostate cancer in patients with PI-RADS 4 lesions who underwent in-bore MRI-guided prostate biopsy. *World J Urol*. 2023;41(2):449–454. doi:10.1007/s00345-022-04274-y
11. de Souza BCA, Novaes MAS, de Souza MAS, et al. Analysis of false positive PI-RADS 4 lesions: experience from a single nonacademic center using cognitive fusion. *Int Urol Nephrol*. 2023;55(5):1081–1085. doi:10.1007/s11255-023-03508-1
12. Park SY, Park BK. Necessity of differentiating small (< 10 mm) and large (≥ 10 mm) PI-RADS 4. *World J Urol*. 2020;38(6):1473–1479. doi:10.1007/s00345-019-02924-2
13. Pepe P, Pennisi M. Targeted biopsy in men high risk for prostate cancer: 68Ga-PSMA PET/CT versus mpMRI. *Clin Genitourinary Cancer*. 2023;21(6):639–642. doi:10.1016/j.clgc.2023.06.007
14. Novara G, Zattoni F, Zecchini G, et al. Role of targeted biopsy, perilesional biopsy, and random biopsy in prostate cancer diagnosis by mpMRI/transrectal ultrasonography fusion biopsy. *World J Urol*. 2023;41(11):3239–3247. doi:10.1007/s00345-023-04382-3
15. Johnson DC, Raman SS, Mirak SA, et al. Detection of individual prostate cancer foci via multiparametric magnetic resonance imaging. *Eur Urol*. 2019;75(5):712–720. doi:10.1016/j.eururo.2018.11.031