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Research Article

A new parameter to increase the predictive value of multiparametric prostate magnetic resonance imaging for clinically significant prostate cancer in targeted biopsies: lesion density

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ABSTRACT

Aim: To investigate the predictive value of lesion length in multiparametric prostate magnetic resonance imaging with respect to prostate volume for clinically significant prostate cancer diagnosis in targeted biopsies.

Materials and methods: The data of biopsy-naïve patients in the Turkish Urooncology Association Prostate Cancer Database who underwent targeted prostate biopsies were included in this study. Lesion density is calculated as the ratio of lesion length (mm) in MR to prostate volume (cc). The biopsy results were divided into either clinically significant or insignificant cancer and benign groups. The difference in parameters between groups is evaluated by multivariable analysis to determine independent risk factors for clinically significant prostate cancer diagnosis.

Results: A total of 590 lesion biopsies were included in the study. In univariable analysis, prostate-specific antigen (PSA), PSA density, number of cores taken, lesion length, lesion density, patient age, and digital rectal examination findings were found to be different at a statistically significant level between groups (*P* values, respectively: 0.001, <0.001, <0.001, <0.001, <0.001, 0.012, 0.001). Subgroup analysis demonstrated that the lesion density was still significantly different between groups for all Prostate Imaging - Reporting and Data System (PI-RADS) 3, 4, and 5 subgroups (*P* values, respectively: 0.001, <0.001, <0.001). The multivariable analysis demonstrated that lesion density, along with the number of cores taken and the PI-RADS score of the lesion is an independent risk factor for predicting clinically significant prostate cancer, with the highest odds ratio among all parameters (OR: 27.31 [CI: 7.9–94.0]).

Conclusion: This study demonstrated that lesion size with respect to prostate volume is an important independent risk factor for the prediction of clinically significant prostate cancer in the lesion-targeted biopsy. Combined with the PI-RADS score and parameters like digital rectal examination (DRE) findings and PSA density may further increase predictive power and help clinicians decide whether to perform a biopsy in low-risk patients or perform a re-biopsy for high-risk patients subsequent to an initial negative biopsy.

1. Introduction

Identifying clinically significant prostate cancer (cs-PCa) while not overdiagnosing clinically insignificant ones is one of the top priorities in the diagnostic process of the disease. The use of multiparametric magnetic resonance imaging (mpMRI) has made it possible to detect cs-PCa with more sensitivity.[1] With the availability of the Prostate Imaging - Reporting and Data System (PI-RADS) scoring system and fusion biopsies, it is now possible to identify and diagnose cs-PCa more accurately.[2–4]

Despite all the technological improvements and developments in the mpMRI evaluation experience, cs-PCa diagnosis continues to

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be an important challenge for clinicians today. Since mpMRI evaluation prior to the initial biopsy is now standard practice with the recommendation of the European Association of Urology guidelines,[5] improving the diagnostic accuracy of mpMRI studies has become more important.

Parameters that can provide additional information to the PI-RADS score to increase the quality of the information obtained from mpMRI imaging are frequently the subject of research in the literature. There are studies aiming to increase the diagnostic accuracy of mpMRI using radiomic parameters,[6] prostate-specific antigen (PSA) density,[7] and prostate cancer antigen 3 (PCA3).[8] In this study, we aimed to investigate the relationship between the ratio of lesion diameter to prostate volume, which we define as lesion density, and the diagnosis of cs-PCa.

2. Materials and methods

This study was conducted through a retrospective analysis of the prostate cancer and benign prostate biopsy databases of the Turkish Urooncology Association. There were 8372 and 5285 patients, respectively, in these two nationwide databases, where patient data were kept anonymized at the time of recording. REDCap[9,10] software was used to record and process patient data in these databases.

The data of biopsy-naïve patients who underwent MR-targeted prostate biopsies were searched in both databases. All MR-targeted biopsies included in the study were performed with software-enhanced fusion biopsy systems. Ultrasound-guided cognitive fusion biopsies from the study were excluded because most of the MR data on these patients were incomplete in our database. There were no in-bore fusion biopsies in our database with complete data. Patients diagnosed with systemic biopsies were not also included in the study. The patients' lesion-based biopsy results, prebiopsy digital rectal examination (DRE) findings, prebiopsy PSA values, PI-RADS scores reported in mpMRI evaluation, lesion diameters, and prostate volumes were investigated. Patient data without any missing parameters are included in the study. Patients were divided into clinically significant- or not-significant cancer and non-cancer groups, and the predictors of cs-PCa were further evaluated with multivariable analysis. Clinically significant prostate cancer was regarded as Gleason grade group 2 or more in biopsy pathology. Since most mpMRI reports in our database included the longest lesion diameter instead of 3-dimensioned diameters, it was decided to include lesion diameter to conduct statistical analysis. Lesion density was defined as the ratio of the longest lesion diameter in millimeters, to prostate volume (cc).

2.1. Statistical analysis

Statistical analysis was performed with the Python programming language (Open source v3.12). Pandas,[11] matplotlib,[12] NumPy,[13] SciPy,[14] scikit-learn,[15] and statsmodels[16] libraries were used for the management of the data and statistical analysis. JupyterLab (Open source v1.2.6) was used as the coding interface.

Histograms, probability plots, and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk's tests) were used to decide whether a scaler variable is normally distributed or not. Normally distributed descriptive variables were given as mean and standard deviation, while median and interquartile range values were given for variables that did not comply with the normal distribution. Two-group comparisons were made with the Mann–Whitney U test.

The chi-square test was used to compare categorical variables between groups. In cases where the assumptions of the chi-square were not valid, the comparison was made with Fisher's exact test. Binary logistic regression with the enter method was performed for multivariable analysis. Parameters that were found to be statistically significant in the univariable analysis were included in the multivariable analysis. Variables that were closely correlated with each other were ruled out for the multivariable analysis. The strong correlation between two variables is defined as a correlation coefficient of 0.6 or more. Statistical significance was defined as a *P*-value below the threshold of 0.05 for all statistical hypothesis tests. Significant figures for variables are given to one decimal place, and *P*-values are displayed to three decimal places.

3. Results

After initial analysis, 590 lesion-targeted biopsies were included in the study. The mean age of the patients was 64.3 ± 7.6. The cancer ratio (including Gleason grade group 1) in these 590 biopsies was 47% ($n = 278$). There were 205 cs-PCa diagnoses. The median PSA, PSA density, number of cores taken per lesion, lesion diameter, and lesion density values were higher in the cs-PCa group. In the digital rectal examination, more patients were reported to have benign findings in the noncancer group (Table 1). The cancer detection rates for PI-RADS 3, 4, and 5 lesions were 9.6%, 33.2%, and 60.1%, respectively.

In the subgroup analysis, lesion density was found to be higher at a statistically significant level in the cs-PCa group for each PI-RADS score compared to benign biopsies. PSA density and number of cores per lesion were also statistically higher in PI-RADS 4 and 5 subgroups with cs-PCa (Table 2). In addition to the lesion

Table 1
Comparison of general risk factors between groups.

		cs-PCa (−) ($n = 385$)	cs-PCa (+) ($n = 205$)	*P*
PSA	Median (IQR)	6.8 (4.7–10.9)	8.4 (5.3–13.2)	0.001[a)]
PSA density	Median (IQR)	0.1 (0.1–0.2)	0.2 (0.1–0.4)	<0.001[a)]
Core number per lesion	Median (IQR)	4.0 (4.0–7.0)	6.0 (4.0–10.0)	<0.001[a)]
Lesion length	Median (IQR)	12.0 (8.5–15.0)	15.0 (10.0–20.0)	<0.001[a)]
Lesion density	Median (IQR)	0.2 (0.1–0.3)	0.39 (0.2–0.6)	<0.001[a)]
Patient age	Median (IQR)	64.0 (59.0–69.0)	66.0 (60.0–71.0)	0.012[a)]
DRE, *n* (%)	Benign	324 (84.7)	150 (73.2)	0.001[b)]
	Malign	61 (15.8)	55 (26.8)	
PI-RADS score, *n* (%)	3	142 (36.9)	15 (7.3)	<0.001[b)]
	4	175 (45.5)	87 (42.4)	
	5	68 (17.7)	103 (50.2)	

cs-PCa, Clinically Significant Prostate Cancer; DRE, Digital rectal Examination; IQR, Interquartile Range; PI-RADS, The Prostate Imaging - Reporting and Data System; PSA, prostate-specific antigen.
[a)] Mann-Whitney U.
[b)] χ^2 Test.

Table 2
Subgroup analysis of general risk factors for PI-RADS scores.

PI-RADS 3 ($n = 157$)				
		cs-PCa (−) ($n = 142$)	cs-PCa (+) ($n = 15$)	***P***
PSA	Median (IQR)	6.0 (4.3–9.9)	5.3 (4.2–7.5)	0.441[a)]
PSA density	Median (IQR)	0.1 (0.1–0.2)	0.1 (0.1–0.2)	0.073[a)]
Core number per lesion	Median (IQR)	4.0 (4.0–5.5)	6.0 (4.0–9.8)	0.045[a)]
Lesion length	Median (IQR)	11.5 (8.0–14.0)	13.0 (10.0–16.5)	0.155[a)]
Lesion density	Median (IQR)	0.2 (0.1–0.3)	0.3 (0.2–0.5)	0.001[a)]
Patient age	Median (IQR)	63.0 (58.3–67.0)	59.0 (50.0–64.5)	0.080[a)]
DRE, *n* (%)	Benign	123 (86.6)	12 (80.0)	0.444[b)]
	Malign	19 (13.4)	3 (20.0)	
PI-RADS 4 ($n = 262$)				
		cs-PCa (−) ($n = 175$)	**cs-PCa (+) ($n = 87$)**	***P***
PSA	Median (IQR)	7.0 (4.9–11.0)	7.0 (5.1–12.1)	0.550[a)]
PSA density	Median (IQR)	0.1 (0.1–0.2)	0.1 (0.11–0.3)	0.003[a)]
Core number per lesion	Median (IQR)	4.0 (4.0–8.8)	5.5 (4.0–10.0)	0.027[a)]
Lesion length	Median (IQR)	10.0 (8.0–13.0)	11.0 (8.0–13.0)	0.410[a)]
Lesion density	Median (IQR)	0.2 (0.1–0.3)	0.3 (0.2–0.4)	<0.001[a)]
Patient age	Median (IQR)	65.0 (59.0–69.0)	66.0 (60.0–71.0)	0.143[a)]
DRE, *n* (%)	Benign	146 (83.4)	66 (75.7)	0.142[c)]
	Malign	29 (16.8)	21 (24.1)	
PI-RADS 5 ($n = 171$)				
		cs-PCa (−) ($n = 68$)	**cs-PCa (+) ($n = 103$)**	***P***
PSA	Median (IQR)	8.6 (4.5–14.4)	10.0 (5.9–17.2)	0.071[a)]
PSA density	Median (IQR)	0.2 (0.1–0.3)	0.4 (0.2–0.5)	<0.001[a)]
Core number per lesion	Median (IQR)	4.0 (3.0–8.0)	6.0 (4.0–9.3)	0.004[a)]
Lesion length	Median (IQR)	20.0 (16.0–24.3)	20.0 (16.0–25.0)	0.316[a)]
Lesion density	Median (IQR)	0.4 (0.3–0.5)	0.6 (0.4–0.8)	<0.001[a)]
Patient age	Median (IQR)	65.0 (59.8–71.0)	68.0 (61.0–71.8)	0.406[a)]
DRE, *n* (%)	Benign	55 (80.9)	72 (69.9)	0.108[c)]
	Malign	13 (19.1)	31 (30.1)	

cs-PCa, Clinically Significant Prostate Cancer; DRE, Digital rectal Examination; IQR. Interquartile Range; PSA, prostate-specific antigen; PI-RADS, The Prostate Imaging - Reporting and Data System.
[a)] Mann-Whitney U.
[b)] Fisher Exact Test.
[c)] χ^2 Test.

density, the only parameter that was found to be different at a statistically significant level between the two groups in PI-RADS 3 lesions was the number of cores per lesion (Table 2).

Multivariable analysis demonstrated that lesion density, number of cores per lesion, and PI-RADS score were independent predictive factors for cs-PCa, with lesion density having the highest odds ratio (Table 3). Since PSA and PSA density levels are closely correlated with each other, multivariable analysis was performed with both variables separately, and while independent predictors did not change, both PSA and PSA density were not independent predictors for cs-PCa. In receiver-operating characteristic (ROC) curve analysis, lesion density had 75.1% sensitivity and 59.7% specificity at the level of 0.240 mm/cc with an area under the curve (AUC) value of 0.743. The positive predictive value at this level was 49.7%, and the negative predictive value was 81.8% (Fig. 1).

Table 3
Multivariable analysis for cs-PCa diagnosis prediction.

Variable	OR (95% CI)	*P*
Patient age	1.0 (1.0–1.05)	0.053
DRE (Benign vs. Malign)	1.5 (0.9–2.5)	0.087
Core number per lesion	1.0 (1.0–1.1)	0.006
PSA density	1.7 (0.6–4.4)	0.249
Lesion density	27.3 (7.9–94.0)	<0.001
PI-RADS 3	Reference	
PI-RADS 4	3.8 (2.0–7.2)	<0.001
PI-RADS 5	4.8 (2.3–9.8)	<0.001

CI, Confidence Interval; cs-PCa, clinically significant prostate cancer; DRE, Digital rectal Examination; PSA, prostate-specific antigen; PI-RADS, The Prostate Imaging - Reporting and Data System; OR, Odds Ratio.

4. Discussion

The introduction of PSA is considered to have a revolutionary impact on PCa diagnosis and follow-up.[17] Although PSA is known to be organ-specific rather than cancer-specific, some studies state PSA as a better independent predictor of PCa compared to DRE or transrectal ultrasound.[18] In our study, PSA levels were significantly higher in the cs-PCa group in univariable analysis, but in multivariable analysis, PSA was not an independent risk factor. Considering that the population of our study consisted of men who underwent biopsy and elevated PSA is still one of the primary factors in deciding on a prostate biopsy, and it is expected result that PSA values are high in all patient groups. Our results support the knowledge that even though elevated PSA may be associated with increased PCa risk, PSA elevation alone is not a reliable indicator for the diagnosis of cs-PCa in targeted biopsies.

Since PSA alone is known to be inadequate, various methods have been developed to increase the power of PSA in predicting prostate cancer. Among these, PSA density has often been the subject of research in the literature because it can be easily calculated and does not require an additional measurement. It is reported that with a cut-off value of 0.15 ng/mL/cc, PSA density may be valuable to predict cs-

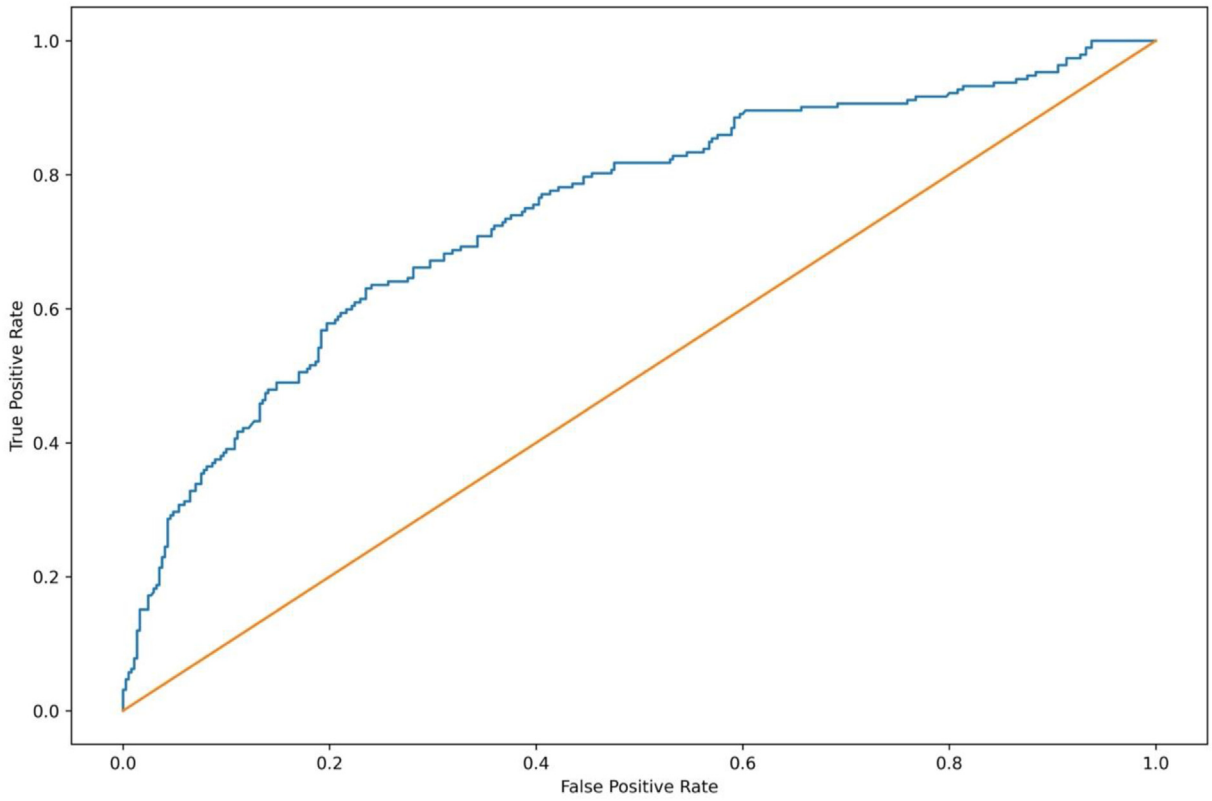

Figure 1. ROC curve for lesion density alone.
ROC, receiver-operating characteristic.

PCa.[19] Also, it has been reported that PSA density at the level of 0.20 ng/mL/cc could be a valuable predictor for PI-RADS 3 lesions.[20] Our results did not show PSA density as an independent predictor for cs-PCa in multivariable analysis, although PSA density was significantly higher in the cs-PCa group in univariable analysis. Since our data only has lesion-targeted biopsies and not all cs-PCa are diagnosed by lesion-targeted biopsies, our results do not mean that elevated PSA density is not a risk factor for cs-PCa. But our data demonstrated that it is not possible to predict the outcome of a lesion-targeted biopsy solely with PSA density.

It is reported that the odds ratio of the prevalence of PCa increases per decade of life.[21] Consistently, the current study showed that the median age of diagnosis in PCa patients was higher compared to patients with benign biopsies in univariable analysis. Our study also showed that age should not be regarded as an independent predictor for lesion-targeted biopsy pathology, since it has not shown statistical significance in multivariable analysis.

In current clinical practice, it is recommended to perform a systemic prostate biopsy with at least 10–12 cores.[5] However, there is no clear recommendation for the number of cores to be taken from lesions in targeted biopsies. A recent study investigating the impact of the number of cores on biopsy results concluded that the first two cores detected the majority of cs-PCa, but there were still several men who would benefit from additional cores.[22] In this study, we demonstrated that biopsies resulting in cs-PCa have a significantly higher number of cores taken per lesion. This was the case for all PI-RADS subgroups, and even in multivariable analysis, the core number was an independent risk factor. Our results do not necessarily mean that a reduced number of cores taken would diminish the diagnostic accuracy of targeted biopsies, but the number of cores to be taken is an issue that clinicians should pay attention to and decide with patient-based risk-adapted strategies. Since the main objective of our study was to assess the predictive value of lesion length with respect to prostate volume, biopsy results were evaluated in a lesion-based manner, and systemic biopsy results were not included in the primary analysis. Our results still do not change the current necessity of systemic biopsies.

The evaluation of the prostate with mpMRI may be defined as the 'next big thing' after the introduction of PSA in the diagnosis process of PCa. It is clearly shown that mpMRI of the prostate has a high sensitivity for cs-PCa, especially tumors larger than 10 mm.[23] A recent study has demonstrated that mpMRI can detect cs-PCa patients in a high AUC in the ROC curve, and it is superior to F-18-fluorocholine positron emission tomography/computerized tomography in terms of AUC.[24] It is demonstrated that the positive predictive value of the PI-RADS score system is high and even increases with scores, reaching up to 94% for PI-RADS 5 lesions in some studies.[25] With recent advancements in MR technology and the update of the PI-RADS scoring system to version 2.1[26] mpMRI had become an even more powerful tool for the diagnosis of prostate cancer. Despite all these developments, the cancer detection rates of PI-RADS 3, 4, and 5 lesions were 16%, 59%, and 85%, respectively, in a recent meta-analysis.[26] In our study, cancer detection for PI-RADS 3, 4, and 5 lesions were 9.6%, 33.2%, and 60.1%, respectively, which were lower than the rates reported in the meta-analysis. This may be the result of the heterogeneity of our data in terms of the used PI-RADS version in mpMRI evaluation. It is also known that interobserver variability in the interpretation of mpMRI is an important issue.[27] Since this study includes data from multiple centers and regions, it may also be difficult to maintain the same standard of mpMRI qualities.

Since there is a considerable error margin, even for high PI-RADS scores, predicting possible cancer cases for low PI-RADS score patients, and deciding to perform re-biopsies after initially negative biopsies for high PI-RADS score patients had been an

important challenge for clinicians. There are not many studies investigating the predictive value of lesion diameter (or length) on the cs-PCa diagnosis. Costa et.al reported that longer lesion sizes were seen in patients with extra-prostatic extension in univariable analysis.[28] Lesion length is also used as one of the independent variables of a nomogram for the prediction of lymph node invasion in PCa patients.[29] These studies show that lesion size may be an important factor for PCa.

In a cognitive fusion biopsy study that was conducted on 219 patients with peripheral lesions, the cancer detection rate was reported to be increasing with the increased lesion size as well as decreased prostate size.[30] The authors had used predefined grouping levels for both lesion length and prostate volume in that study, and instead of investigating the predictive value of the lesion diameter to prostate volume ratio, they had chosen to report both parameters individually. Our study also demonstrated that lesion size was significantly higher in the cs-PCa group for all PI-RADS scores. Furthermore, the multivariable analysis also demonstrated lesion density as an independent risk factor. When we performed the multivariable analysis with lesion diameter instead of lesion density, lesion diameter alone was not seen as a statistically significant independent risk factor for cs-PCa ($P = 0.088$). Also, the subgroup analysis for each PI-RADS score showed that lesion size alone is not different between groups, in contrast to lesion density. Although we performed multivariable analysis for each PI-RADS score subgroup and found lesion density as an independent predictor for each, as a result of the diminished case and event size, the strength of those models for individual PI-RADS score subgroups was not high. To be statistically accurate, we did not report the multivariable analysis results of each PI-RADS score subgroup.

This study is a multicentric retrospective study; thus, all mpMRIs were reported by different radiologists. Since the inter-observer variability of mpMRI is known;[27] this is regarded as one of the main limitations of our study. Likewise, biopsy procedures were conducted by different operators, and different biopsy techniques were used (transperineal vs. transrectal). Also, the used version of the PI-RADS score evaluation was heterogeneous in our data, but since we had a large number of patients the impact of this would not affect the primary endpoint of this study.

In our research, lesion density was found to be a strong predictor of cs-PCa in targeted biopsies. This finding highlights the relationship between the size of a lesion and the volume of the prostate in improving the effectiveness of targeted biopsies for diagnosis. Lesion density is a measure of how noticeable a lesion is within the prostate gland. A larger lesion in a smaller prostate can be easier to target correctly, which increases the chances of a successful biopsy.

Furthermore, an increased lesion density may signify a larger amount of disease inside a smaller region of the gland, which could imply a higher likelihood of cs-PCa. On the other hand, detecting and accurately targeting smaller lesions in larger prostates may be more difficult since the lesions are relatively few and a larger amount of tissue needs to be navigated. Therefore, the density of lesions plays a vital role in helping clinicians make decisions about planning biopsies.

5. Conclusion

In conclusion, we demonstrated that lesion size with respect to prostate volume is an important independent risk factor for the prediction of cs-PCa in the lesion-targeted biopsy. Lesion density alone has the power to predict cs-PCa with 75.1% sensitivity and 59.7% specificity when 0.240 mm/cc is used as the cut-off value. Lesion density was higher in the cs-PCa group in each PI-RADS score subgroup, suggesting that it can be used for both high-risk and low-risk patients to predict cs-PCa diagnosis. Combined with the PI-RADS score and parameters like DRE findings and PSA density predictive power will increase and help clinicians decide whether to perform a biopsy in low-risk patients or perform a re-biopsy for high-risk patients after an initial negative result.

Conflicts of interest

Authors have no conflict of interest to declare.

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References

1. Bratan F, Niaf E, Melodelima C, Chesnais AL, Souchon R, Mège-Lechevallier F, et al. Influence of imaging and histological factors on prostate cancer detection and localisation on multiparametric MRI: a prospective study. Eur Radiol 2013;23:2019–29.
2. Dickinson L, Ahmed HU, Allen C, Barentsz JO, Carey B, Futterer JJ, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European consensus meeting. Eur Urol 2011;59:477–94.
3. Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS prostate imaging–reporting and data system: 2015, version 2. Eur Urol 2016;69:16–40.
4. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378:1767–77.
5. Mottet N, Cornford P, van den Bergh RCN, Briers E, Patient Advocate Expert, De Santis M, et al. *EAU - EANM - ESTRO - ESUR - ISUP - SIOG guidelines on prostate cancer*. Arnhem, the Netherlands: EAU Guidelines Office; 2022 http://uroweb.org/guidelines/compilations-of-all-guidelines.
6. Zhang KS, Schelb P, Kohl S, Radtke JP, Wiesenfarth M, Schimmöller L, et al. Improvement of PI-RADS-dependent prostate cancer classification by quantitative image assessment using radiomics or mean ADC. Magn Reson Imag 2021;82:9–17.
7. Deniffel D, Healy GM, Dong X, Ghai S, Salinas-Miranda E, Fleshner N, et al. Avoiding unnecessary biopsy: MRI-based risk models versus a PI-RADS and PSA density strategy for clinically significant prostate cancer. Radiology 2021;300:369–79.
8. Ploussard G, de la Taille A. The role of prostate cancer antigen 3 (PCA3) in prostate cancer detection. Expet Rev Anticancer Ther 2018;18:1013–20.
9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inf 2009;42:377–81.
10. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inf 2019;95103208.
11. Pandas Development Team T. pandas-dev/pandas: Pandas. Zenodo 2020;21:1–9.
12. Hunter JD. Matplotlib: a 2D graphics environment. Comput Sci Eng 2007;9:90–5.
13. Harris CR, Millman KJ, Van Der Walt SJ, Gommers R, Virtanen P, Cournapeau D, et al. Array programming with NumPy. Nature 2020;585:357–62.
14. Virtanen P, Gommers R, Oliphant TE, Haberland M, Reddy T, Cournapeau D, et al. SciPy 1.0: fundamental algorithms for scientific computing in Python. Nat Methods 2020;17:261–72.
15. Pedregosa F, Varoquaux G, Gramfort A, Michel V, Thirion B, Grisel O, et al. Scikit-learn: machine learning in Python. J Mach Learn Res 2011;12:2825–30.
16. Seabold S, Perktold J. Statsmodels: econometric and statistical modeling with python. In: Proceedings of the 9th Python in Science Conference. Vol 57: Austin, TX 2010:10–25080.
17. Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E. Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. N Engl J Med 1987;317:909–16.
18. Catalona WJ, Richie JP, Ahmann FR, M'Liss AH, Scardino PT, Flanigan RC, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. J Urol 1994;151:1283–90.
19. Omri N, Kamil M, Alexander K, Edmond S, Ariel Z, David K, et al. Association between PSA density and pathologically significant prostate cancer: the impact of prostate volume. Prostate 2020;80:1444–9.
20. Koparal MY, Sözen TS, Karşiyakali N, Akdoğan B, Özen H, Aslan G, et al. Should targeted biopsy be performed in patients who have only pi-rads 3 lesions? Arch Esp Urol 2022;75:410–5.

21. Bell KJ, Del Mar C, Wright G, Dickinson J, Glasziou P. Prevalence of incidental prostate cancer: a systematic review of autopsy studies. Int J Cancer 2015;137:1749–57.
22. Kenigsberg AP, Renson A, Rosenkrantz AB, Huang R, Wysock JS, Taneja SS, et al. Optimizing the number of cores targeted during prostate magnetic resonance imaging fusion target biopsy. Eur Urol Oncol 2018;1:418–25.
23. Johnson DC, Raman SS, Mirak SA, Kwan L, Bajgiran AM, Hsu W, et al. Detection of individual prostate cancer foci via multiparametric magnetic resonance imaging. Eur Urol 2019;75:712–20.
24. Kim JK, Song YS, Lee WW, Lee HJ, Hwang SI, Hong SK. Diagnostic accuracy of F-18-Fluorocholine PET/CT and multiparametric MRI for prostate cancer. Prostate Int 2022;10:152–7.
25. Barkovich EJ, Shankar PR, Westphalen AC. A systematic review of the existing prostate imaging reporting and data system version 2 (PI-RADSv2) literature and subset meta-analysis of PI-RADSv2 categories stratified by Gleason scores. Am J Roentgenol 2019;212:847–54.
26. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, 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.
27. Stabile A, Giganti F, Kasivisvanathan V, Giannarini G, Moore CM, Padhani AR, et al. Factors influencing variability in the performance of multiparametric magnetic resonance imaging in detecting clinically significant prostate cancer: a systematic literature review. Eur Urol Oncol 2020;3:145–67.
28. Costa DN, Passoni NM, Leyendecker JR, De Leon AD, Lotan Y, Roehrborn CG, et al. Diagnostic utility of a Likert scale versus qualitative descriptors and length of capsular contact for determining extraprostatic tumor extension at multiparametric prostate MRI. Am J Roentgenol 2018;210:1066–72.
29. Gandaglia G, Ploussard G, Valerio M, Mattei A, Fiori C, Fossati N, et al. A novel nomogram to identify candidates for extended pelvic lymph node dissection among patients with clinically localized prostate cancer diagnosed with magnetic resonance imaging-targeted and systematic biopsies. Eur Urol 2019;75:506–14.
30. Özden E, Akpınar Ç, İbiş A, Kubilay E, Erden A, Yaman Ö. Effect of lesion diameter and prostate volume on prostate cancer detection rate of magnetic resonance imaging: transrectal-ultrasonography-guided fusion biopsies using cognitive targeting. Turk J Urol 2021;47:22.