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ARTICLE

Comparison of micro-ultrasound and multiparametric magnetic resonance imaging in detecting clinically significant prostate cancer: a single-center experience

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Objectives: *Multiparametric magnetic resonance imaging (mpMRI) represents a cornerstone of prostate cancer (PCa) diagnosis; however, it is not without limitations, particularly in terms of specificity and real-world implementation. High-resolution 29-MHz micro-ultrasound (microUS) has recently emerged as a complementary imaging modality, with the potential to enhance lesion detection and refine mpMRI-based diagnostic pathways. This study aims to compare the diagnostic performance of microUS and mpMRI for the detection of clinically significant prostate cancer (csPCa), and to evaluate the clinical value of integrating microUS into mpMRI-based diagnostic pathways.*

Methods: *This single-center retrospective study included 457 men undergoing prostate biopsy for suspected prostate cancer or during active surveillance between May 2023 and November 2025. All patients underwent microUS-guided biopsy using the ExactVu™ system, along with systematic biopsies and mpMRI-targeted biopsies performed when indicated. csPCa was defined as ISUP Grade Group $\geq$ 2. Diagnostic performance metrics were calculated for mpMRI and microUS. Receiver operating characteristic (ROC) analysis was performed using ordinal PI-RADS and PRIMUS scores. Decision curve analysis was used to assess the net clinical benefit of integrated diagnostic strategies. Multivariate logistic regression adjusted for age, initial PSA, and clinical stage was performed.*

Results: *csPCa was detected in 44% of patients. mpMRI showed high sensitivity (92%) but low specificity (28%), whereas microUS showed a more balanced profile (sensitivity 70%, specificity 66%) and higher overall accuracy (68% vs. 57%). ROC analysis based on imaging scores showed comparable performance between mpMRI (AUC = 0.7) and microUS (AUC = 0.72; p = 0.41). Decision curve analysis demonstrated that diagnostic pathways integrating microUS with mpMRI provided greater net clinical benefit across clinically relevant threshold probabilities compared with strategies based on either modality alone. On multivariate analysis, both mpMRI and microUS positivity were independently associated with csPCa detection.*

Conclusions: *MicroUS demonstrated diagnostic performance comparable to mpMRI and provided complementary information when integrated into mpMRI-based diagnostic pathways. These findings support the use of microUS as an adjunct to mpMRI to improve clinical decision-making within the PCa diagnostic workflow.*

Key Words: prostate cancer, imaging techniques, micro-ultrasound, multiparametric magnetic resonance, diagnostic accuracy

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Introduction

Systematic prostate biopsies often detect a high rate of non-clinically significant prostate cancer (PCa), while potentially missing up to 30% of clinically significant (cs)PCa.[1] Current guidelines recommend multiparametric magnetic resonance imaging (mpMRI) before biopsy as the diagnostic standard.[2–4] However, issues such as limited mpMRI availability, waiting times, and increased costs pose challenges to healthcare systems.[5] The need for dedicated uro-radiologists, variability in Prostate Imaging Reporting and Data System (PI-RADS) interpretation, and differences in image quality standards further complicate the mpMRI pathway.[6,7] Furthermore, effective communication and experience transfer between radiologists and urologists are crucial for the mpMRI pathway, as they can lead to inconsistent interpretation and false positives.[8,9]

Micro-ultrasonography (microUS) is an emerging imaging technology that operates at a high frequency of 29 MHz, offering three times the resolution of conventional ultrasound. The microUS procedure closely resembles standard transrectal ultrasound (TRUS), allowing practitioners to visualize the entire prostate and target suspicious areas in real time.[10] Findings suspicious for PCa are scored using the Prostate Risk Identification using microUS (PRIMUS) protocol, analogous to PI-RADS for mpMRI.[11] Growing evidence supports the clinical relevance of microUS in PCa diagnostics. In particular, the OPTIMUM randomized clinical trial, the first large randomized comparison between microUS-guided and mpMRI-guided biopsy strategies, demonstrated non-inferiority of microUS for the detection of csPCa.[12] While these findings suggest that microUS may represent a reliable and accessible imaging modality, its optimal role within contemporary diagnostic pathways, particularly in relation to mpMRI, remains to be fully defined.

The present study aimed to evaluate the diagnostic performance of the ExactVu™ 29-MHz microUS system in a real-world clinical setting and to compare its accuracy with mpMRI, with a specific focus on the potential complementary value of integrating microUS into mpMRI-based diagnostic workflows for the detection of csPCa.

Materials and Methods

Study population and design

From May 2023 to November 2025, patients with suspected prostate cancer (PCa) or under active surveillance (AS) underwent prostate biopsy using the ExactVu™ 29-MHz micro-ultrasound system (Exact Imaging, Markham, Canada) at ASST Papa Giovanni XXIII, a high-volume center in Bergamo, Italy. The study protocol was approved by the Ethics Committee of ASST Papa Giovanni XXIII, Bergamo, Italy. No specific approval number was assigned due to the retrospective nature of the study. As the data were anonymized, the requirement for informed consent was waived.

Suspicion of PCa was based on elevated prostate-specific antigen (PSA) levels ($\geq$3 ng/mL), abnormal digital rectal examination (DRE), or the presence of at least one Prostate Imaging-Reporting and Data System (PI-RADS) $\geq$ 3 lesion on mpMRI. All patients included in the study were scheduled for prostate biopsy due to clinical suspicion and/or positive mpMRI findings; therefore, this study was not designed to evaluate microUS or mpMRI as standalone triage or screening tools to avoid biopsy, and no patient avoided biopsy based on imaging findings alone.

The primary outcome was the detection rate of csPCa, defined as prostate cancer with an International Society of Urological Pathology (ISUP) Grade Group (GG) $\geq$ 2, and the diagnostic accuracy of microUS, assessed by sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Secondary outcomes included the comparative diagnostic performance of microUS and mpMRI and the evaluation of their complementary value within integrated diagnostic pathways.

Multiparametric magnetic resonance imaging

mpMRI was performed on a 1.5T or 3T magnet, employing tri-planar T2-weighted imaging, axial diffusion-weighted imaging, and dynamic contrast-enhanced sequences as per PI-RADS version 2.1 guidelines.[13] Not all mpMRIs were conducted at the referral center; some were performed at smaller facilities with varying radiologist expertise.

ExactVu™ 29 MHz micro-ultrasound imaging and biopsy procedure

MicroUS examinations were performed by two urologists experienced in conventional ultrasound and image-guided prostate biopsies (more than 500 each), who completed a standardized microUS training program. During the initial phase of the study, operators were supported by a dedicated product specialist (first 100 patients).

Suspicious lesions were identified and documented in real time using the PRIMUS scoring system.[11] The urologist performing the microUS examination was initially blinded to mpMRI results, images were uploaded the day before by another urologist.

All patients underwent prostate biopsy during a single session. MicroUS imaging was performed immediately before and during the biopsy. When lesions identified on mpMRI and microUS were concordant, a single targeted biopsy (three cores) was performed. In cases of discordant findings, each suspicious lesion identified by either modality was sampled separately. mpMRI-targeted biopsies were performed using the Fusion-Vu™ Exact Imaging software (version 3.1, Exact Imaging, Markham, ON, Canada). Systematic biopsies were conducted in areas without suspicious lesions. All patients underwent transrectal biopsies.

Statistical analysis

Statistical analyses adhered to validated guidelines.[14] Baseline characteristics of the study population were summarized using median and interquartile range (IQR) for continuous variables and percentages for categorical variables.

Sensitivity, specificity, PPV, and NPV were calculated to assess the diagnostic performance of microUS and mpMRI in detecting csPCa. Receiver operating characteristic (ROC) curves and the corresponding Area Under the Curve (AUC) were generated using ordinal PRIMUS and PI-RADS scores, treating each score as an ordinal predictor of csPCa. Differences between AUCs were compared using the DeLong test. All analyses were performed using histopathological findings from any biopsy core (including systematic biopsy, mpMRI-targeted biopsy, and microUS-targeted biopsy) as the reference standard. In the absence of whole-mount prostatectomy specimens, diagnostic accuracy estimates were interpreted as relative measures of performance.

To assess the learning curve associated with microUS use, procedures were chronologically grouped into deciles. For each decile, the mean PPV and NPV for csPCa between the two urologists were calculated and visualized using LOESS curves.

A discordance analysis was performed by classifying patients into four groups based on the correctness of mpMRI and microUS relative to the reference standard. Predicted probabilities of csPCa were obtained from a multivariable logistic regression model including both modalities, and mean predicted probabilities were calculated for each group. This analysis was exploratory in nature, and no formal hypothesis testing was performed.

A clinically oriented and exploratory decision-tree model, based on predefined clinical criteria rather than data-driven optimization, was constructed to illustrate the potential impact of integrating microUS into an mpMRI-first diagnostic pathway. Decision curve analysis (DCA) was performed to evaluate the net clinical benefit of different diagnostic strategies across a range of threshold probabilities.

Chi-square tests explored correlations between imaging techniques and csPCa presence. Multivariate logistic regression analyzed the impact of imaging positivity and scores on csPCa likelihood, adjusting for age, initial PSA (iPSA), and clinical stage. For all statistical analyses, R software environment for statistical computing and graphics (version 3.4.3) was used. All tests were two-sided, with a level of statistical significance set at $p < 0.05$.

Results

Baseline characteristics

Baseline characteristics of the 457 patients undergoing prostate biopsy using the ExactVu™ 29 MHz micro-ultrasound system are summarized in Table 1. Median age was 68 years (IQR: 62.0–74.0). Median PSA was 5.9 ng/mL (IQR: 4.5–8.2), and median prostate volume was 52.0 mL (IQR: 36.0–75.0). Median PSA density (PSAD) was 0.11 ng/mL^2 (IQR: 0.08–0.17). Clinical assessment revealed 73% of patients as cT1, 19% as cT2a, 2% as cT2b, 2% as cT2c and 4% as cT3. Overall, 64% were biopsy-naïve, while 36% had undergone previous biopsy. Therefore, 86 patients (19%) were on AS for a GG1 PCa. mpMRI was performed prior to biopsy in 388 patients (85%); among these, 315 (69%) had a positive mpMRI (PI-RADS ≥ 3), while 73 (16%) had a negative mpMRI.

Lesion detection and imaging concordance

A total of 637 suspicious lesions were detected across imaging modalities (Table 1). mpMRI identified 375 significant lesions with PI-RADS scores 3 (26%), 4 (54%), and 5 (20%). MicroUS detected 262 significant lesions with PRIMUS scores 3 (50%), 4 (38%), and 5 (12%). Overall concordance between mpMRI and microUS was observed in 238 cases (52%). Discrepancies included 136 (30%) lesions detected by mpMRI and missed by microUS, and 14 (3%) lesions detected by microUS and missed by mpMRI.

Biopsy outcomes

Overall, PCa detection was 59%. Systematic biopsies (SB) were positive in 55% of cases, while microUS-targeted biopsies (microUS-TB) detected PCa in 57% of patients and mpMRI-targeted biopsies (mpMRI-TB) in 50% (Table 2). GG1 was detected in 15%, GG2

TABLE 1. **Baseline characteristics of 457 patients undergoing prostate biopsy using the ExactVu™ (Exact Imaging, Markham, Canada) 29 MHz micro-ultrasound system and descriptive table of lesions detected with multiparametric magnetic resonance imaging (mpMRI) and micro-ultrasound (microUS) system**

Characteristics	Media [IQR] or n (%)
Age (years), media [IQR]	68.0 [62.0, 74.0]
PSA (ng/mL), median [IQR]	5.9 [4.5, 8.2]
Prostate volume (mL), median [IQR]	52.0 [36.0, 75.0]
PSA density (ng/mL^2), median [IQR]	0.11 [0.08, 0.17]
Digital rectal examination, n (%)	
cT1	333 (73)
cT2a	88 (19)
cT2b	10 (2)
cT2c	9 (2)
cT3	17 (4)
Previous biopsy, n (%)	
No	293 (64)
Yes	164 (36)
Active surveillance, n (%)	
No	371 (81)
Yes	86 (19)
mpMRI, n (%)	
Performed	388 (85)
Not performed	69 (15)
mpMRI result, n (%)	
Negative	73 (16)
Positive	315 (69)
Not performed	69 (15)
mpMRI multiple lesions, n (%)	
No	328 (72)
Yes	60 (13)
Not performed	69 (15)
mpMRI nodes involvement, n (%)	
No	376 (82)
Yes	12 (3)
Not performed	69 (15)
microUS result, n (%)	
No	229 (50)
Yes microUS multiple lesions, n (%)	228 (50)
No	423 (93)
Yes	34 (7)
mpMRI n° significant lesions detected, n (%) PI-RADS score, n (%)	375
3	99 (26)
4	201 (54)
5	75 (20)
microUS n° significant lesions detected, n (%) PRIMUS score, n (%)	262
3	131 (50)
4	98 (38)
5	33 (12)

(Continued)

TABLE 1. **(Continued)**

Characteristics	Media [IQR] or n (%)
Concordance of positivity between the two techniques, n (%)	
mpMRI−/microUS−	60 (13)
mpMRI+/microUS−	136 (30)
mpMRI−/microUS+	14 (3)
mpMRI+/microUS+	178 (39)
mpMRI not available/microUS +	35 (8)
mpMRI not available/microUS−	34 (7)

Note. PSA, prostate-specific antigen; PI-RADS, Prostate Imaging-Reporting and Data System; PRIMUS, Prostate Risk Identification using microUS.

TABLE 2. **Prostate biopsy results of 457 patients undergoing prostate biopsy using the ExactVu™ (Exact Imaging, Markham, Canada) 29 MHz micro-ultrasound system and performance metrics comparing multiparametric magnetic resonance imaging (mpMRI) and micro-ultrasound (microUS) in detecting clinically significant prostate cancer (csPCa)**

Biopsy results positive biopsy	Total	Systematic BX	mpMRI target BX	microUS target BX
No	189 (41)	205 (45)	157 (50)	97 (43)
Yes	268 (59)	252 (55)	158 (50)	131 (57)
Not performed ISUP grade group	–	–	142	229
Neg	189 (41)	205 (45)	157 (50)	97 (43)
GG1	67 (15)	78 (17)	30 (10)	24 (11)
GG2	70 (15)	61 (13)	51 (16)	43 (19)
GG3	60 (13)	52 (11)	44 (14)	31 (14)
GG4	57 (13)	49 (11)	25 (8)	24 (11)
GG5	14 (3)	12 (3)	8 (3)	9 (4)
Not performed csPCa	–	–	142	229
No	256 (56)	283 (62)	187 (59)	121 (53)
Yes	201 (44)	174 (38)	128 (41)	107 (47)
Not performed	.	–	142	229

Note. BX, biopsy; csPCa, clinically significant prostate cancer.

in 15%, GG3 in 13%, GG4 in 13%, and GG5 in 3% of the patients. csPCa was detected in 44% of the cohort. SB detected csPCa in 38% of patients, mpMRI-TB in 41%, and microUS-TB in 47%. Among patients who underwent both mpMRI and microUS, reliance on a single biopsy strategy would have resulted in missed csPCa cases. In patients with PRIMUS ≥ 3 (n = 228), SB alone would have missed 7% (n = 16) of csPCa cases, whereas microUS-TB alone would have missed 12% (n = 28). Similarly, in patients with PI-RADS ≥ 3 lesions (n = 384), mpMRI-TB alone would have missed 8% (n = 31) of csPCa cases, while systematic biopsy alone would have missed 7% (n = 25).

At the patient level, patterns of agreement and discordance between mpMRI and microUS in detecting csPCa are illustrated in Figure 1. Both imaging modalities were concordantly correct in 168 patients, while both failed to correctly classify disease status in 73 cases. Notably, microUS alone correctly identified clinically significant disease in 95 patients in whom mpMRI was incorrect, whereas mpMRI alone was correct in 52 patients.

Diagnostic performance and ROC analysis

Sensitivity, specificity, PPV, and NPV to detect csPCa for mpMRI were 92%, 28%, 51%, and 81%, respectively. For microUS, sensitivity was 70%, specificity

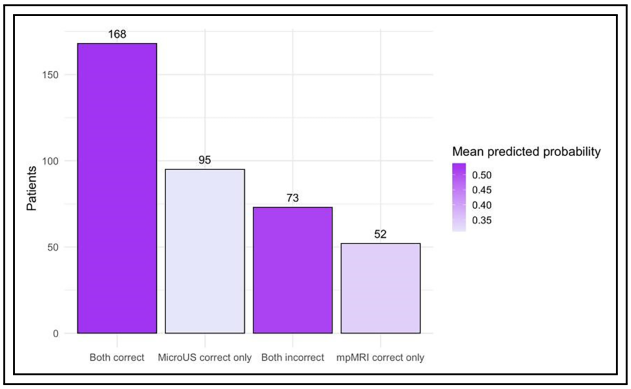

FIGURE 1. Patterns of agreement and discordance between multiparametric magnetic resonance imaging (mpMRI) and micro-ultrasound (microUS) in detecting clinically significant prostate cancer (csPCa)

TABLE 3. **Performance metrics comparing multiparametric magnetic resonance imaging (mpMRI) and micro-ultrasound (microUS) in detecting clinically significant prostate cancer (csPCa)**

Diagnostic performance metrics	mpMRI	microUS
Sensitivity	0.92	0.70
Specificity	0.28	0.66
PPV	0.51	0.63
NPV	0.81	0.73
Prevalence	0.45	0.45
Detection rate	0.42	0.31
Detection prevalence	0.81	0.50
Balanced accuracy	0.60	0.68
Accuracy (95%CI)	57% (52%, 62%)	68% (63%, 72%)

Note. PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

66%, with PPV and NPV both at 63% and 73%, respectively. Overall accuracy was 57% (95%CI: 52%–62%) for mpMRI and 68% (95%CI: 63%–72%) for microUS (Table 3).

ROC analysis based on ordinal imaging scores demonstrated comparable discrimination between mpMRI and microUS. The area under the curve (AUC) was 0.7 for PI-RADS-based mpMRI and 0.72 for PRIMUS-based microUS (Figure 2), with no

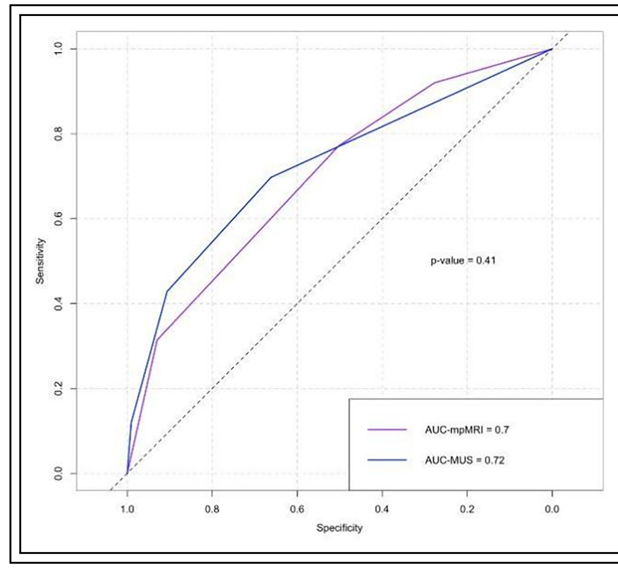

FIGURE 2. Receiver operating characteristic (ROC) curves comparing the diagnostic performance of multiparametric magnetic resonance imaging (mpMRI) and micro-ultrasound (microUS) in detecting clinically significant prostate cancer (csPCa), based on PI-RADS and PRIMUS scores. The gray dashed diagonal line represents the line of no discrimination (AUC = 0.5). Differences between AUCs were assessed using the DeLong test

statistically significant difference between the two approaches (DeLong test, $p = 0.41$). An exploratory ROC analysis treating imaging results as binary variables (positive vs. negative) is reported in Figure A1.

Learning curve analysis

Learning curve analysis of microUS performance is shown in Figure 3. When procedures were stratified into chronological deciles, PPV and NPV for csPCa detection remained relatively stable over time, without evidence of an initial performance peak or decline. This finding may be explained by the structured implementation of microUS in our center, including formal training and on-site support by a dedicated product specialist during the initial phase of the study (first 100 patients), which may have mitigated the impact of early operator inexperience.

Decision-tree model and decision curve analysis

A clinically oriented decision-tree model reflecting an mpMRI-first diagnostic pathway with adjunctive microUS is shown in Figure 4. In this model, the addition of microUS following mpMRI allowed further risk stratification within negative or suspicious

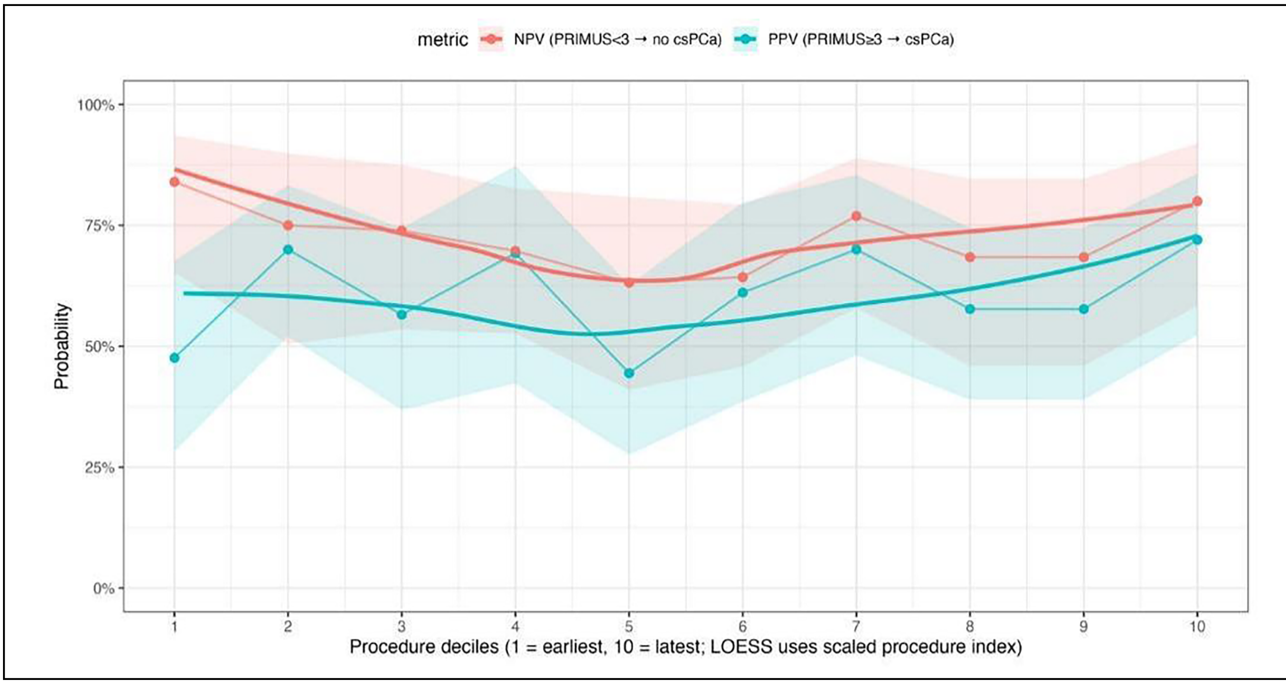

FIGURE 3. Learning curve (microUS): positive predictive value (PPV) and negative predictive value (NPV) across procedure deciles. Note. Positive predictive value (PPV) was calculated among patients with PRIMUS ≥ 3 lesions, while negative predictive value (NPV) was calculated among patients with PRIMUS < 3 findings. Smoothed curves were generated using locally estimated scatterplot smoothing (LOESS). Shaded areas represent 95% confidence intervals of the LOESS fit.

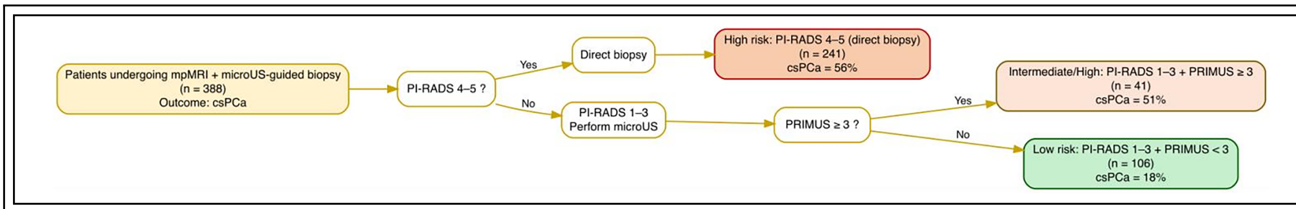

FIGURE 4. Decision-tree model of an mpMRI-first diagnostic workflow incorporating adjunctive microUS to refine risk stratification and biopsy decision-making for clinically significant prostate cancer (csPCa)

mpMRI findings (PIRADS 1–3). In a cohort of 100 patients, implementation of the decision-tree model would spare 10 procedures, at the expense of missing one case of clinically significant prostate cancer.

Decision curve analysis demonstrated that diagnostic strategies integrating microUS with mpMRI provided a higher net clinical benefit across a wide range of clinically relevant threshold probabilities compared with strategies based on either modality alone (Figure 5). In addition, the integrated pathway showed superior net benefit at low-tointermediate threshold probabilities, a range in which the clinical trade-off between avoiding unnecessary biopsies and missing csPCa is most relevant. In this range, the combined mpMRI–microUS strategy consistently outperformed mpMRI-only and microUS-only approaches.

Additional analysis

Chi-square analysis confirmed a significant correlation between imaging techniques, scores, and csPCa (Tables A1–A3). A strong link was confirmed between PI-RADS scores and csPCa ($\chi^2 = 54.648$ $p < 0.001$), notably with PIRADS 5 showing 79% of cases as clinically significant. PRIMUS scores also correlated strongly with csPCa ($\chi^2 = 80.601$, $p < 0.001$), with

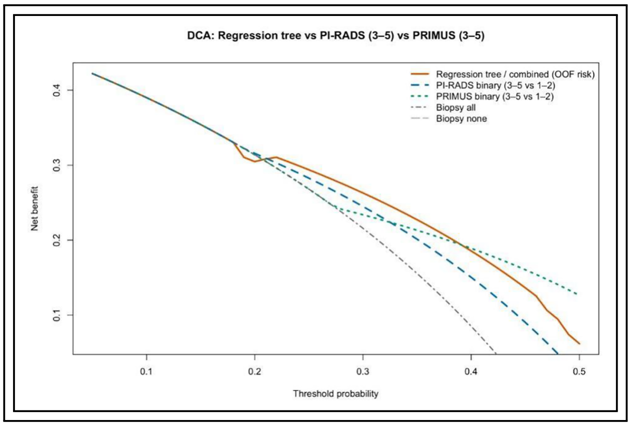

FIGURE 5. Decision curve analysis (DCA) of diagnostic strategies for the detection of clinically significant prostate cancer (csPCa). Note. The horizontal line at net benefit = 0 represents the "Biopsy none" strategy.

PRIMUS 5 showing 90% predictability for significant cases.

Multivariate logistic regression analysis (adjusting for age, iPSA, and clinical stage) demonstrated that imaging positivity was a strong predictor for csPCa, both for mpMRI (OR = 2.63, 95%CI: 1.39–5.26, $p = 0.004$) and microUS (OR = 3.45, 95%CI: 2.20–5.46, $p < 0.001$).

Discussion

mpMRI is well-regarded for its capability to improve PCa diagnostics by allowing targeted biopsies, thereby reducing the detection of insignificant tumors and unnecessary procedures.[1,15,16] However, mpMRI presents limitations such as accessibility, expense, required expertise, and the necessity for good imaging and specialized uro-radiologists. Additionally, there is the complexity associated with the mpMRI-guided biopsy process.[17–20] Furthermore, mpMRI may miss a non-negligible percentage of csPCa[21] and its NPV means that systematic or perilesional biopsies cannot be completely avoided, especially during initial biopsy procedures or for patients under active surveillance.[22] In this context, microUS has emerged as an attractive alternative imaging modality. Its main advantages include real-time lesion visualization, immediate targeting during biopsy, and operational similarities with conventional transrectal ultrasound, allowing a faster learning curve and easier integration into daily practice.[23–27] The present study evaluated the diagnostic performance of ExactVu™ (Exact Imaging, Markham, ON, Canada) 29 MHz micro-ultrasound compared with mpMRI in detecting csPCa and explored their complementary value within biopsy-based diagnostic pathways.

The diagnostic accuracy of microUS has been extensively investigated, and a systematic review by Sountoulides et al., including 18 comparative studies, reported csPCa detection rates comparable to those of mpMRItargeted biopsy.[26] Recently, high-level evidence supporting the role of microUS has been provided by the OPTIMUM randomized clinical trial.[12] In this multicenter study, microUS-guided biopsy demonstrated noninferiority to MRI-guided biopsy for the detection of csPCa. OPTIMUM represents the first randomized comparison between these two imaging-guided strategies and directly challenges the assumption that mpMRI is an indispensable prerequisite for targeted biopsy. The consistency between the results of OPTIMUM and those observed in our realworld cohort strengthens the external validity of our findings.

In our study, microUS demonstrated a diagnostic performance comparable to mpMRI, with a favorable balance between sensitivity and specificity and a slightly higher overall accuracy, although discrimination based on ordinal PRIMUS and PI-RADS scores did not differ significantly between the two modalities. These findings are in line with OPTIMUM[12] and with previous non-randomized studies reporting similar or complementary diagnostic capabilities between the two techniques.[23,24,28–33] Furthermore, higher PRIMUS and PI-RADS scores were independently associated with csPCa detection, confirming the clinical relevance of standardized risk stratification systems for both modalities.

The study cohort represents a highly selected population enriched for csPCa, either due to positive pre-biopsy mpMRI findings or strong clinical suspicion. As a result, an inherent selection bias limits the evaluation of microUS as a triage tool to reduce the use of mpMRI. However, precisely because of this study design, our data are well-suited to explore the complementary role of microUS when added to mpMRI, rather than its use as a stand-alone or replacement diagnostic strategy.

Within this context, a key finding of our study is the partial discordance between mpMRI and microUS. While both techniques frequently identified the same lesions, each modality also detected csPCa missed by the other. MicroUS alone correctly identified csPCa in a substantial number of patients in whom mpMRI was non-informative, whereas mpMRI alone was correct in fewer cases. This observation is consistent with previous reports. Cornud et al. showed that lesions detected exclusively by microUS were more frequently clinically significant than those detected only by MRI.[34] Similarly, Wiemer et al. reported that microUS-targeted biopsy upgraded disease in a relevant proportion of patients compared with mpMRI-targeted biopsy.[35] Avolio et al. demonstrated that microUS could identify csPCa in patients with negative or equivocal mpMRI findings, particularly in PI-RADS 3 lesions and MRI-negative cases with persistent clinical suspicion.[24,36]

Importantly, the complementary nature of mpMRI and microUS was further supported by decision curve analysis. When evaluated within an mpMRI-first diagnostic pathway, the integration of microUS provided a higher net clinical benefit across clinically relevant threshold probabilities compared with strategies based on either modality alone. These findings suggest that the added value of microUS could lie in refining diagnostic decision-making and improving risk stratification in patients already selected for biopsy. Future multicenter, randomized studies specifically designed to address this question are warranted to determine whether microUS may ultimately replace mpMRI or be used as an initial screening tool to select patients for immediate biopsy or for further evaluation with mpMRI.

These data, together with the results of OPTIMUM,[12] suggest that microUS and mpMRI may identify complementary tumor phenotypes rather than being purely interchangeable modalities. From a clinical perspective, their combined use may increase diagnostic confidence, improve risk stratification, and reduce the likelihood of missing csPCa, particularly in real-world settings where access to high-quality mpMRI and expert radiological interpretation may be variable. In such scenarios, microUS represents a valuable adjunct to mpMRI, providing real-time information that can complement prebiopsy imaging and support targeted sampling.

This study has several limitations that warrant discussion. First, the relatively small sample size and its singlecenter design may affect the generalizability of the findings. Second, the lack of randomization presents an inherent limitation in the study design. Since mpMRI is recommended for biopsy-naïve patients, microUS-TB was only evaluated as an addition to the standard of care, with practitioners blinded to mpMRI results. Furthermore, as all patients were scheduled for biopsy based on clinical suspicion and/or mpMRI findings, this study was not designed to assess the role of microUS as an initial screening or triage tool prior to mpMRI. Third, there were varying levels of radiologist expertise in mpMRI across different institutions, which could have influenced diagnostic outcomes. This variability was particularly evident in patients who underwent mpMRI at external facilities, where the expertise and training of radiologists may not have been uniform. Differences in image interpretation and reporting can lead to variability in the detection rates of significant lesions, thereby impacting the study's findings on the effectiveness of mpMRI compared to microUS. However, such a condition reflects the real-life clinical practice, when a single referral center is not able to cope with the diagnostic needs of the entire population. Another important limitation relates to the use of biopsy histopathology as the reference standard instead of whole-mount prostatectomy specimens. Since prostate biopsy itself may miss a proportion of clinically significant prostate cancer (csPCa), the diagnostic performance of both mpMRI and microUS may have been overestimated. Therefore, the reported sensitivity and specificity values should be interpreted as relative measures within a biopsy-based diagnostic framework rather than absolute estimates of tumor detection accuracy. Furthermore, the proposed decision-tree model integrating mpMRI and microUS should be interpreted as exploratory and hypothesis-generating. The model was designed as a clinically oriented framework based on predefined diagnostic criteria, rather than as a statistically optimized prediction model, and was not internally or externally validated. Therefore, the estimated reduction in biopsy procedures requires prospective confirmation in independent cohorts. To address these limitations, future multicenter and prospective studies with larger and more diverse cohorts are warranted to better define the role of microUS within contemporary prostate cancer diagnostic pathways.

Conclusions

MicroUS represents a valuable adjunct to mpMRI for the detection of csPCa. In this study, microUS showed diagnostic performance comparable to mpMRI and provided complementary real-time information that may improve lesion targeting within biopsy-based diagnostic pathways. The integration of microUS with mpMRI was associated with improved clinical decision-making, as supported by decision curve analysis. While microUS may be particularly useful in settings with limited access to high-quality mpMRI, further multicenter, randomized studies are needed to define its optimal role within the prostate cancer diagnostic workflow.

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Author Contributions

The authors confirm contribution to the paper as follows: Study conception and design: Daniele Cignoli, Paolo Barzaghi, Stefano Corti, Daniele Robesti, Michele Catellani, Giovanni La Croce, Marco Roscigno. Acquisition of data: Daniele Cignoli, Paolo Barzaghi, Giuliana Martello, Sara Carminati. Analysis and interpretation of data: Daniele Cignoli. Drafting of the manuscript: Daniele Cignoli. Critical revision of the manuscript for important intellectual content: Luigi Filippo Da Pozzo, Marco Roscigno. Statistical analysis: Daniele Cignoli.
Obtaining funding: None. Supervision: Luigi Filippo Da Pozzo, Marco Roscigno. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

The data that support the findings of this study are available from the Corresponding Author, Daniele Cignoli, upon reasonable request.

Ethics Approval

This retrospective study involving human participants was conducted in accordance with the Declaration of Helsinki and local regulatory requirements. The study protocol was approved by the Ethics Committee of ASST Papa Giovanni XXIII, Bergamo, Italy. No specific approval number was assigned due to the retrospective nature of the study. No specific approval number was assigned due to the retrospective nature of the study. Due to the retrospective design and anonymized data collection, the requirement for informed consent was waived.

Conflicts of Interest

The authors declare no conflicts of interest.

Appendix A

TABLE A1. **Pearson chi-square analysis of correlation between PI-RADS score and detection of clinically significant prostate cancer (csPCa)**

PI-RADS score	Negative	csPCa	Row total
PI-RADS negative	59	14	73
Chi-square contribution	8.94	10.88	
N/Row total	0.81	0.19	0.19
N/column total	0.28	0.08	
N/table total	0.15	0.04	
PI-RADS 3	48	26	74
Chi-square contribution	1.34	1.63	
N/row total	0.65	0.35	0.19
N/column total	0.23	0.15	
N/table total	0.12	0.07	
PI-RADS 4	91	80	171
Chi-square contribution	0.09	0.11	
N/row total	0.53	0.47	0.44
N/column total	0.43	0.46	
N/table total	0.24	0.21	
PI-RADS 5	15	55	70
Chi-square contribution	14.28	17.38	
N/row total	0.21	0.79	0.18
N/column total	0.07	0.31	
N/table total	0.04	0.14	

(Continued)

TABLE A1. **(Continued)**

PI-RADS score	Negative	csPCa	Row total
Column total	213	175	388
Proportion	0.55	0.45	

Note. $\chi^2 = 54.648$, df = 3, $p < 0.001$.

TABLE A2. **Pearson chi-square analysis of correlation between PRIMUS score and detection of clinically significant prostate cancer (csPCa)**

PRIMUS score	Negative	csPCa	Row total
PRIMUS negative	166	63	229
Chi-square contribution	11.09	14.13	
N/row total	0.73	0.28	0.5
N/column total	0.65	0.31	
N/table total	0.36	0.14	
PRIMUS 3	65	50	115
Chi-square contribution	0.01	0.01	
N/row total	0.57	0.44	0.25
N/column total	0.25	0.25	
N/table total	0.14	0.11	
PRIMUS 4	22	60	82
Chi-square contribution	12.47	15.88	
N/row total	0.27	0.73	0.18
N/column total	0.09	0.3	
N/table total	0.05	0.13	
PRIMUS 5	3	28	31
Chi-square contribution	11.88	15.14	
N/row total	0.1	0.9	0.07
N/column total	0.01	0.14	
N/table total	0.01	0.06	
Column total	256	201	457
Proportion	0.56	0.44	

Note. $\chi^2 = 80.601$, df = 3, $p < 0.001$.

TABLE A3. **Pearson chi-square analysis of correlation between imaging positivity and detection of clinically significant prostate cancer (csPCa)**

Concordance mpMRI/microUS	Negative	csPCa	Row total
mpMRI−, microUS−	51	9	60
Chi-square contribution	9.90	12.06	
N/row total	0.85	0.15	0.16
N/column total	0.24	0.05	
N/table total	0.13	0.02	
mpMRI+, microUS−	90	46	136
Chi-square contribution	3.15	3.84	
N/row total	0.66	0.34	0.35
N/column total	0.42	0.26	
N/table total	0.23	0.12	
mpMRI−, microUS+	8	6	14
Chi-square contribution	0.01	0.02	
N/row total	0.57	0.43	0.04
N/column total	0.04	0.03	
N/table total	0.02	0.02	

(Continued)

TABLE A3. **(Continued)**

Concordance mpMRI/microUS	Negative	csPCa	Row total
mpMRI−, microUS+	8	6	14
Chi-square contribution	0.01	0.02	
N/row total	0.57	0.43	0.04
N/column total	0.04	0.03	
N/table total	0.02	0.02	
mpMRI+, microUS+	64	114	178
Chi-square contribution	11.63	14.16	
N/row total	0.36	0.64	0.46
N/column total	0.30	0.65	
N/table total	0.17	0.29	
Column total	213	43	388
Proportion	0.549	0.43	

Note. $\chi^2 = 54.77$, df = 3, $p < 0.001$.

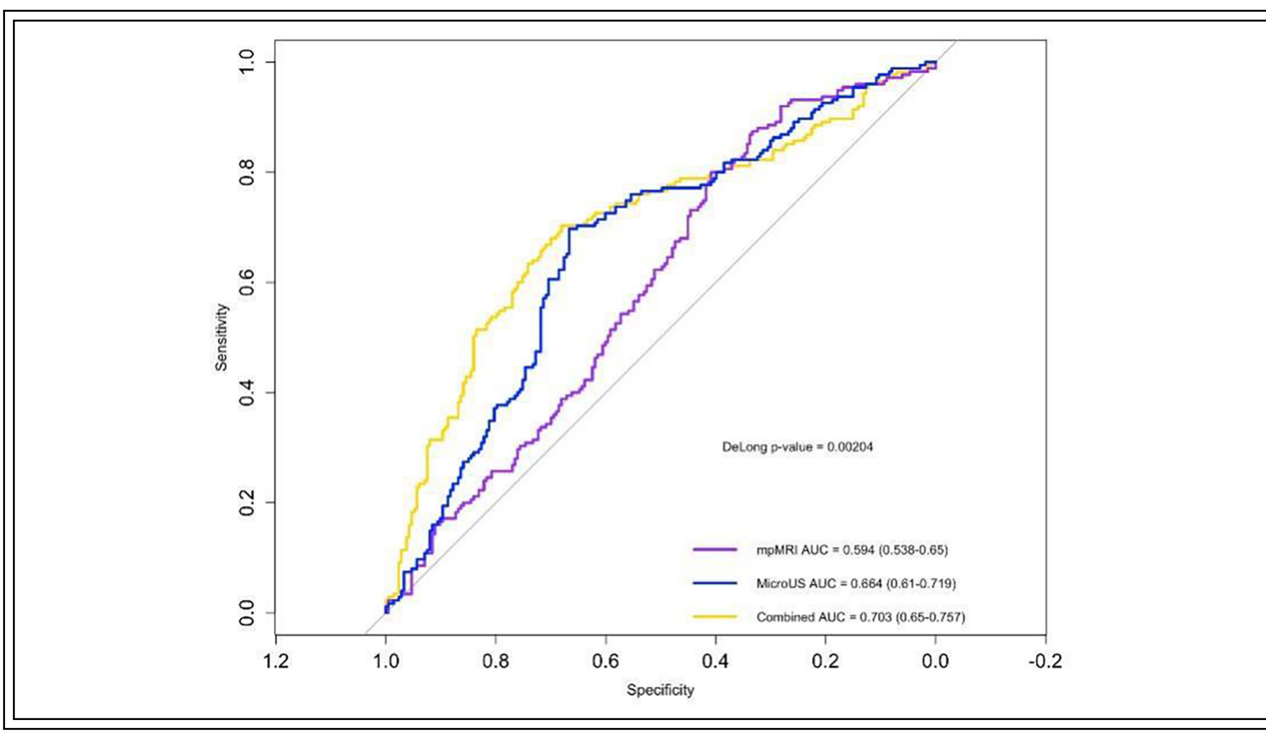

FIGURE A1. Receiver operating characteristic (ROC) curves comparing multiparametric magnetic resonance imaging (mpMRI), micro-ultrasound (microUS), and their combined positivity for clinically significant prostate cancer (csPCa) detection. Note. AUC, area under the curve. ROC analysis treating imaging results as binary variables, microUS alone demonstrated a higher discriminative ability than mpMRI alone, while the combined model (concurrent positivity on mpMRI and microUS) achieved the highest diagnostic performance. Specifically, the AUC was 0.594 (95% CI: 0.538–0.650) for mpMRI, 0.664 (95% CI: 0.610–0.719) for microUS, and 0.703 (95% CI: 0.650–0.757) for the combined model. Comparison of these ROC curves using DeLong's test showed a statistically significant difference among the three approaches ($p = 0.002$).

References

1. Rouvière O, Puech P, Renard-Penna R et al. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. *Lancet Oncol* 2019;20(1):100–109. doi:10.1016/j.eururo.2019.04.022.
2. Schaeffer EM, Srinivas S, Adra N et al. Prostate cancer, version 4. 2023, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2023;21(10):1067–1096. doi:10.6004/jnccn.2023.0050.
3. 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* 2022;208(1):10–18. doi:10.1097/ju.0000000000002757.
4. Cornford P, van den Bergh RCN, Briers E et al. EAU-EANM-ESTROESUR-ISUP-SIOG guidelines on prostate cancer—2024 update. part I: screening, diagnosis, and local treatment with curative intent. *Eur Urol* 2024;86(2):148–163.
5. Walz J. The “PROMIS” of magnetic resonance imaging cost effectiveness in prostate cancer diagnosis? *Eur Urol* 2018;73(1):31–32. doi:10.1016/j.eururo.2017.09.015.
6. Sonn GA, Fan RE, Ghanouni P et al. Prostate magnetic resonance imaging interpretation varies substantially across radiologists. *Eur Urol Focus* 2019;5(4):592–599.
7. Caglic I, Barrett T. Optimising prostate mpMRI: prepare for success. *Clin Radiol* 2019;74(11):831–840. doi:10.1016/j.crad.2018.12.003.
8. Stabile A, Dell’Oglio P, Gandaglia G et al. Not all multiparametric magnetic resonance imaging-targeted biopsies are equal: the impact of the type of approach and operator expertise on the detection of clinically significant prostate cancer. *Eur Urol Oncol* 2018;1(2):120–128.
9. Garcia-Reyes K, Passoni NM, Palmeri ML et al. Detection of prostate cancer with multiparametric MRI (mpMRI): effect of dedicated reader education on accuracy and confidence of index and anterior cancer diagnosis. *Abdom Imaging* 2015;40(1):134–142. doi:10.1007/s00261-014-0197-7.
10. Ghai S, Eure G, Fradet V et al. Assessing cancer risk on novel 29 MHz micro-ultrasound images of the prostate: creation of the micro-ultrasound protocol for prostate risk identification. *J Urol* 2016;196(2):562–569. doi:10.1016/j.juro.2015.12.093.
11. Luger F. Does 29Mhz micro-ultrasound provide uniform diagnostic accuracy within and beyond the peripheral zone? *Ann Urol Nephrol* 2019;1(4). doi:10.33552/aun.2019.01.000519.
12. Kinnaird A, Luger F, Cash H et al. Microultrasonography-guided vs. MRI-guided biopsy for prostate cancer diagnosis. *JAMA* 2025;333(19):1679. doi:10.1001/jama.2025.7944.
13. 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(3):340–351.
14. Vickers AJ, Sjoberg DD. Guidelines for reporting of statistics in European Urology. *Eur Urol* 2015;67(2):181–187. doi:10.1016/j.eururo.2014.06.024.
15. Ahmed HU, El-Shater Bosaily A, Brown LC et al. Diagnostic accuracy of multiparametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet* 2017;389(10071):815–822. doi:10.1016/s0140-6736(16)32401-1.
16. Stabile A, Giganti F, Rosenkrantz AB et al. Multiparametric MRI for prostate cancer diagnosis: current status and future directions. *Nat Rev Urol* 2020;17(1):41–61. doi:10.1038/s41585-019-0212-4.
17. Layne KA, Dargan PI, Archer JRH, Wood DM. Gadolinium deposition and the potential for toxicological sequelae—a literature review of issues surrounding gadolinium-based contrast agents. *Br J Clin Pharmacol* 2018;84(11):2522–2534. doi:10.1111/bcp.13718.
18. Stabile A, Giganti F, Emberton M, Moore CM. MRI in prostate cancer diagnosis: do we need to add standard sampling? A review of the last 5 years. *Prostate Cancer Prostatic Dis* 2018;21(4):473–487.
19. Padhani AR, Haider MA, Villers A, Barentsz JO. Multiparametric magnetic resonance imaging for prostate cancer detection: what we see and what we miss. *Eur Urol* 2019;75(5):721–722. doi:10.1016/j.eururo.2018.12.004.
20. Marra G, Ploussard G, Futterer J, Valerio M. Controversies in MR targeted biopsy: alone or combined, cognitive versus software-based fusion, transrectal versus transperineal approach? *World J Urol* 2019;37(2):277–287. doi:10.1007/s00345-018-02622-5.
21. 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(5):697–713. doi:10.1016/j.euo.2020.12.004.
22. Sathianathen NJ, Omer A, Harriss E et al. Negative predictive value of multiparametric magnetic resonance imaging in the detection of clinically significant prostate cancer in the prostate imaging reporting and data system era: a systematic review and meta-analysis. *Eur Urol* 2020;78(3):402–414. doi:10.1016/j.eururo.2020.03.048.
23. Lughezzani G, Saita A, Lazzeri M et al. Comparison of the diagnostic accuracy of micro-ultrasound and magnetic resonance imaging/ultrasound fusion targeted biopsies for the diagnosis of clinically significant prostate cancer. *Eur Urol Oncol* 2019;2(3):329–332.
24. Avolio PP, Lughezzani G, Paciotti M et al. The use of 29 MHz transrectal microultrasound to stratify the prostate cancer risk in patients with PI-RADS III lesions at multiparametric MRI: a single institutional analysis. *Urol Oncol Semin Orig Investig* 2021;39(12):832.e1–832.e7. doi:10.1016/j.urolonc.2021.05.030.
25. Lughezzani G, Maffei D, Saita A et al. Diagnostic accuracy of microultrasound in patients with a suspicion of prostate cancer at magnetic resonance imaging: a single-institutional prospective study. *Eur Urol Focus* 2021;7(5):1019–1026.
26. Sountoulides P, Pyrgidis N, Polyzos SA et al. Micro-ultrasound-guided vs. multiparametric magnetic resonance imaging-targeted biopsy in the detection of prostate cancer: a systematic review and meta-analysis. *J Urol* 2021;205(5):1254–1262. doi:10.1097/ju.0000000000001639.
27. Dariane C, Ploussard G, Barret E et al. Micro-ultrasound-guided biopsies versus systematic biopsies in the detection of prostate cancer: a systematic review and meta-analysis. *World J Urol* 2022;41(3):641–651. doi:10.1007/s00345-022-04087-z.
28. Lorusso V, Kabre B, Pignot G et al. Comparison between microultrasound and multiparametric MRI regarding the correct identification of prostate cancer lesions. *Clin Genitourin Cancer* 2022;20(4):e339–e345. doi:10.1016/j.clgc.2022.01.013.
29. Klotz L, Lughezzani G, Maffei D et al. Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: a multicenter, prospective analysis. *Can Urol Assoc J* 2020;15(1):E11–E16. doi:10.5489/cuaj.6712.
30. Wang B, Broomfield S, Medina Martín A, Albers P, Fung C, Kinnaird A. Detection of clinically significant prostate

cancer by micro-ultrasound-informed systematic biopsy during MRI/micro-ultrasound fusion biopsy. *Can Urol Assoc J* 2022;17(4):117–120. doi:10.5489/cuaj.8094.

31. Hofbauer SL, Luger F, Harland N et al. A non-inferiority comparative analysis of micro-ultrasonography and MRI-targeted biopsy in men at risk of prostate cancer. *BJU Int* 2022;129(5):648–654. doi:10.1111/bju.15635.
32. Chessa F, Schiavina R, Ercolino A et al. Diagnostic accuracy of the novel 29 MHz micro-ultrasound "ExactVuTM" for the detection of clinically significant prostate cancer: a prospective single institutional study. A step forward in the diagnosis of prostate cancer. *Arch Ital Urol Androl* 2021;93(2):132–138. doi:10.4081/aiua.2021.2.132.
33. Rodríguez Socarrás ME, Gomez Rivas J, Cuadros Rivera V et al. Prostate mapping for cancer diagnosis: the madrid protocol. Transperineal prostate biopsies using multiparametric magnetic resonance imaging fusion and micro-ultrasound guided biopsies. *J Urol* October 2020;204(4):726–733. doi:10.1097/JU.0000000000001083.
34. Cornud F, Lefevre A, Flam T et al. MRI-directed high-frequency (29MhZ) TRUSguided biopsies: initial results of a single-center study. *Eur Radiol* 2020;30(9):4838–4846.
35. Wiemer L, Hollenbach M, Heckmann R et al. Evolution of targeted prostate biopsy by adding micro-ultrasound to the magnetic resonance imaging pathway. *Eur Urol Focus* 2021;7(6):1292–1299.
36. Avolio PP, Lughezzani G, Fasulo V et al. Assessing the role of highresolution microultrasound among naïve patients with negative multiparametric magnetic resonance imaging and a persistently high suspicion of prostate cancer. *Eur Urol Open Sci* 2023;47:73–79. doi:10.1016/j.euros.2022.11.015.

