EDITORIAL

Prostate biopsy: evolving strategies and perspectives

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"A needle may not see, but it can reveal what the eye cannot," transperineal biopsy pioneer Wilhelm H. Boeminghaus once said, underscoring how prostate biopsy has been—and remains—the critical gateway for diagnosing prostate cancer (PCa).

Today, its role is undergoing profound redefinition. Over the past two decades, the traditional model of systematic transrectal ultrasound (TRUS)-guided biopsy has been challenged by three converging forces: the integration of multiparametric magnetic resonance imaging (mpMRI), the refinement of fusion-guided technologies, and the gradual transition toward transperineal approaches. Each of these shifts aims to improve diagnostic precision, minimizes harm, and aligns the procedure with modern expectations of patient safety and quality of life.

This special collection of *Prostate Cancer and Prostatic Diseases* offers a timely snapshot of this evolving landscape.

One recurring theme is the ongoing debate about the necessity of systematic biopsy (SB) in the MRI era. Li et al. [1] explored the role of potentially omitting biopsy for patients in a screening pathway including advanced serum biomarkers or those with a PIRADS 3 lesion, providing important data on the detection of clinically significant PCa (csPCa) when biopsy is initially omitted. Interestingly, their findings demonstrated that patients with initial PIRADS 1–3 lesion selected to not undergo biopsy are safe to be observed with serial PSA or prostate health index (PHI) and for-cause mpMRI longitudinally. Although a longer follow-up is required to determine whether any of these patients will develop csPCa, according to their results, it seems safe to continue observation if subsequent mpMRI shows PIRADS 1–3.

On the other hand, Zambon et al. [2] addressed whether systematic sampling should still accompany targeted biopsies in patients with MRI-visible (PIRADS ≥ 3) lesions. By dividing the prostate into regions—*same sextant, adjacent sextant, ipsilateral side*, and *contralateral side*—the authors demonstrated an overall 10% added value of SB in diagnosing csPCa. Notably, the added value of performing SB in the contralateral lobe relative to the MRI lesion was very low, suggesting that this practice might safely be omitted.

Overall, these findings contribute to the broader controversy: should systematic cores remain a safeguard, or are we ready to abandon them in favor of purely targeted strategies? According to the EAU Guidelines, current evidence seems to support a shift toward perilesional or regional sampling rather than standard SB [3]. Indeed, peri-lesional (PB) or regional systematic biopsies may reduce the number of cores required and enhance csPCa detection by avoiding sampling of MRI-negative areas and compensating for targeting imprecision [4].

Speaking of reducing unnecessary biopsies, Guo et al. [5] proposed combining the PRIMARY score with PSA density (PSAD) to refine biopsy decision-making. Derived from PSMA PET/CT, the PRIMARY score incorporates lesion location, PSMA activity pattern, and uptake intensity (SUVmax >12) to improve diagnostic accuracy.

In their study, different biopsy strategies integrating the PRIMARY score or PIRADS with PSAD were compared to optimize the diagnostic pathway. PSAD significantly enhanced the performance of the PRIMARY score in detecting csPCa, which showed a higher net benefit and better diagnostic accuracy than PIRADS when combined with PSAD. This integrative approach represents a step toward precision diagnostics, where the biopsy is no longer a "one-size-fits-all" procedure but a personalized intervention guided by imaging, biomarkers, and clinical context [5].

In the era of pre-biopsy mpMRI, SB can detect csPCa missed by MRI-targeted biopsy (TB) in up to 22% of patients [6]. However, the concept of SB is somewhat misleading, as substantial discrepancies exist between planned and actual biopsy locations. Urologists often oversample certain areas while undersampling anterior and apical regions, and the conventional 12-core scheme applies uniformly to all patients [7]. Recent refinements in SB aim to improve csPCa detection, including increasing and laterally displacing cores, using grid-based sampling to reduce operator error, and tailoring sampling to gland anatomy and potential regions of interest [8]. In this context, Rezaee et al. [9] have also developed a novel, systematic biopsy optimization methodology that considers the anatomy of the prostate gland, urethra, potential regions of interest on mpMRI, and best approach angle of the biopsy needle to optimize cancer detection probability, defining a personalized biopsy plan for each patient. In doing so, the authors found out that the diagnostic yield of SB for csPCa decreases with increasing prostate volume. A standard 12-core SB is adequate for small glands but insufficient for glands ≥60 cm^3, leading to undersampling. Finally, adjusting the number of cores to gland size may improve detection, particularly in mpMRI-negative cases [9].

Another important dimension highlighted in this collection is the patient experience. While diagnostic yield remains paramount, clinicians must also consider the anxiety, discomfort, and risks associated with prostate biopsy. The prospective trial by Deivasigamani et al. [10] comparing conventional transrectal ultrasound (TRUS)-guided biopsy with MRI–US fusion-guided approaches illustrates how procedural anxiety and pain differ between techniques. Their results showed that patients undergoing standard TRUS-guided biopsy (STB) reported lower post-procedural anxiety than those undergoing combined MRI/US fusion biopsy (STB + FB), with a mean difference of −7 ($p = 0.001$, $d = 0.92$). Severe post-procedural anxiety occurred in 89% of the STB + FB group compared with 59% in the STB group ($p = 0.002$), while post-procedural pain did not differ significantly ($p = 0.7$). [10] These findings are crucial in an era where shared decision-making and patient-reported outcomes are increasingly central to clinical care.

The role of mpMRI in active surveillance (AS) protocols for low-risk prostate cancer remains less clearly defined. The study by Novara et al. [11] provides valuable insight into the role of targeted, perilesional, and random biopsies (RB) during

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confirmatory assessments. The authors evaluated the diagnostic performance of different biopsy strategies and their combinations for detecting ISUP grade ≥2 cancers in men with very low- and low-risk prostate cancer undergoing transrectal MRI/TRUS fusion confirmatory biopsy. Their findings showed that adding PL biopsy increased the detection of ISUP ≥ 2 cancers compared with TB alone. Specifically, detection rates rose to 30%, 39%, and 49% when 4 PL cores, 14 RB cores, and 24 RB cores, respectively, were added to TB. However, the combination of TB and PL biopsy alone would have missed up to 20% of clinically significant cancers, which were instead identified through the inclusion of extensive RB schemes [11]. Overall, these results highlight the delicate balance between oncologic safety—avoiding disease misclassification—and the need to minimize invasiveness and repeated interventions in men with low-risk disease.

Finally, the long-standing debate between transrectal and transperineal prostate biopsy was explored by four studies in this collection. Miano et al. [12] made a provocative case for a "TRexit," urging the field to abandon the transrectal route altogether. Indeed, many experts now advocate for replacing the transrectal biopsy (TR-B) with the "cleaner" transperineal approach (TP-B), aiming to reduce infectious complications and antimicrobial resistance without compromising diagnostic accuracy.

Histopathological accuracy, hence, remains a pivotal issue. In a large retrospective study, Hagens et al. [13] compared biopsy and radical prostatectomy specimens between transrectal and transperineal approaches in 1058 men (49.3% TR-B and 50.7% TP-B). Histopathological discordance was observed in 37.8% of cases, and American Urological Association (AUA) risk group migration occurred in 30.2%. Importantly, the transperineal approach was independently associated with higher histopathological concordance (OR 1.33, 95% CI 1.01–1.75; $p = 0.04$). These findings underscore that biopsy technique is not merely a matter of safety or patient comfort, but also of diagnostic fidelity—with downstream implications for staging, treatment planning, and patient counseling [13].

Hogenhout et al. [14] provided valuable data on complication rates following the adoption of transperineal biopsy without antibiotic prophylaxis (AP). This study offers reassuring evidence that TP-B without AP is both safe and effective—a milestone in reducing infection risk and antibiotic resistance. Specifically, TP-B without AP showed a significantly lower rate of infectious complications with fever compared to TR-B with AP (1.1% vs. 5.1%; risk difference, 4.0). Hospitalization occurred in 2 (67%) TP-B patients vs. 9 (82%) TR-B patients. Hematuria lasting more than 3 days was less frequent after TP-B (17% vs. 25%; risk difference, −7.7), and none of these TP-B cases required hospitalization, while one TR-B patient was hospitalized for severe hematuria [14].

Beyond its clinical implications, this represents an important advance in antimicrobial stewardship, reducing both infection risk and antibiotic resistance, long associated with transrectal sampling.

On the other hand, Diamand et al. [15] defended the transrectal approach as simple, effective, and safe, reminding us that clinical practice is often guided as much by pragmatism and accessibility as by innovation. Although the EAU guidelines increasingly favor the transperineal route for its cleaner and potentially safer profile, real-world evidence remains nuanced [16, 17]. Two recent randomized controlled trials comparing infectious complications after transperineal and transrectal biopsy found no significant differences in infection rates. In the PREVENT trial, infection occurred in 0% of patients undergoing TP biopsy without antibiotic prophylaxis, vs. 1.4% in those receiving TR biopsy with targeted prophylaxis ($p = 0.059$) [18]. Similarly, the ProBE-PC trial reported nearly identical infection rates—2.7% for TP and 2.6% for TR—despite differing antibiotic strategies [19].

Taken together, the articles in this collection demonstrate that prostate biopsy is no longer a static procedure but a rapidly evolving field at the intersection of technology, biology, and patient-centered care. Key questions emerge:

- Will mpMRI eventually eliminate the need for systematic sampling, or will hybrid protocols remain the norm?
- Can biomarker integration and risk scores sufficiently reduce unnecessary biopsies without compromising cancer detection?
- Is the transrectal approach destined for obsolescence, or will it coexist alongside transperineal techniques in a stratified manner?

The answers to these questions will shape the standard of care for years to come. What is clear, however, is that the field is moving toward a more nuanced, individualized approach to prostate biopsy—one that integrates advanced imaging, risk stratification, and patient preference, while continually striving for safety and accuracy.

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REFERENCES

1. Li EV, Busza AM, Siddiqui MR, Aguiar JA, Keeter M-K, Neill C, et al. Detection of clinically significant prostate cancer following initial omission of biopsy in multiparametric MRI era. Prostate Cancer Prostatic Dis. 2025;28:795–801.
2. Zambon A, Nguyen T-A, Fourcade A, Segalen T, Saout K, Deruelle C, et al. Which protocol for prostate biopsies in patients with a positive MRI? Interest of systematic biopsies by sectors. Prostate Cancer Prostatic Dis. 2024;27:500–6.
3. Brisbane WG, Priester AM, Ballon J, Kwan L, Delfin MK, Felker ER, et al. Targeted prostate biopsy: umbra, penumbra, and value of perilesional sampling. Eur Urol. 2022;82. https://doi.org/10.1016/j.eururo.2022.01.008.
4. Noujeim JP, Belahsen Y, Lefebvre Y, Lemort M, Deforche M, Sirtaine N, et al. Optimizing multiparametric magnetic resonance imaging-targeted biopsy and detection of clinically significant prostate cancer: the role of perilesional sampling. Prostate Cancer Prostatic Dis. 2023;26. https://doi.org/10.1038/s41391-022-00620-8.
5. Guo S, Zhang J, Wang Y, Jiao J, Li Z, Cui C, et al. Avoiding unnecessary biopsy: the combination of PRIMARY score with prostate-specific antigen density for prostate biopsy decision. Prostate Cancer Prostatic Dis. 2024;27:288–93.
6. Ahdoot M, Wilbur AR, Reese SE, Lebastchi AH, Mehralivand S, Gomella PT, et al. MRI-targeted, systematic, and combined biopsy for prostate cancer diagnosis. N Engl J Med. 2020;382. https://doi.org/10.1056/nejmoa1910038.
7. Wei JT, Barocas D, Carlsson S, Coakley F, Eggener S, Etzioni R, et al. Early detection of prostate cancer: AUA/SUO guideline part II: considerations for a prostate biopsy. J Urol. 2023;210. https://doi.org/10.1097/JU.0000000000003492.
8. Gore JL, Shariat SF, Miles BJ, Kadmon D, Jiang N, Wheeler TM, et al. Optimal combinations of systematic sextant and laterally directed biopsies for the detection of prostate cancer. J Urol. 2001;165. https://doi.org/10.1016/s0022-5347(05)66347-1.
9. Rezaee ME, Macura KJ, Trock BJ, Herati A, Pavlovich CP, Han M, et al. Likelihood of sampling prostate cancer at systematic biopsy as a function of gland volume and number of cores. Prostate Cancer Prostatic Dis. 2025;28:112–6.
10. Deivasigamani S, Adams ES, Kotamarti S, Mottaghi M, Taha T, Aminsharifi A, et al. Comparison of procedural anxiety and pain associated with conventional transrectal ultrasound prostate biopsy to magnetic resonance imaging-ultrasound fusion-guided biopsy: a prospective cohort trial. Prostate Cancer Prostatic Dis. 2024;27. https://doi.org/10.1038/s41391-023-00760-5.
11. Novara G, Zattoni F, Zecchini G, Aceti A, Pellizzari A, Ferraioli G, et al. Role of targeted biopsy, perilesional biopsy, random biopsy, and their combination in the detection of clinically significant prostate cancer by mpMRI/transrectal ultrasonography fusion biopsy in confirmatory biopsy during active surveillance program. Prostate Cancer Prostatic Dis. 2024;27. https://doi.org/10.1038/s41391-023-00733-8.
12. Miano R, Manenti G, Orecchia L. TRexit is going one step further. Prostate Cancer Prostatic Dis. 2024;27. https://doi.org/10.1038/s41391-024-00819-x.
13. Hagens MJ, Ribbert LLA, Jager A, Veerman H, Barwari K, Boodt B, et al. Histopathological concordance between prostate biopsies and radical prostatectomy specimens—implications of transrectal and transperineal biopsy approaches. Prostate Cancer Prostatic Dis. 2024;27. https://doi.org/10.1038/s41391-023-00714-x.

14. Hogenhout R, Remmers S, van Leenders GJLH, Roobol MJ. The transition from transrectal to transperineal prostate biopsy without antibiotic prophylaxis: cancer detection rates and complication rates. Prostate Cancer Prostatic Dis. 2023;26. https://doi.org/10.1038/s41391-022-00641-3.
15. Diamand R, Peltier A, Albisinni S. Transrectal prostate biopsy: easy, effective and safe. Prostate Cancer Prostatic Dis. 2024;27:363–4.
16. Pradere B, Veeratterapillay R, Dimitropoulos K, Yuan Y, Omar MI, Maclennan S, et al. Nonantibiotic strategies for the prevention of infectious complications following prostate biopsy: a systematic review and meta-analysis. J Urol. 2021;205. https://doi.org/10.1097/JU.0000000000001399.
17. Lam W, Wong AHG, Chun S, Wong T, Hung WPL, Lie H, et al. Prostate cancer detection, tolerability and safety of transperineal prostate biopsy under local-anaesthesia versus standard transrectal biopsy in biopsy-naïve men: a pragmatic, parallel group, randomized-controlled study. Eur Urol. 2021;79. https://doi.org/10.1016/s0302-2838(21)01372-5.
18. Hu JC, Assel M, Allaf ME, Ehdaie B, Vickers AJ, Cohen AJ, et al. Transperineal versus transrectal magnetic resonance imaging–targeted and systematic prostate biopsy to prevent infectious complications: the PREVENT randomized trial. Eur Urol. 2024;86. https://doi.org/10.1016/j.eururo.2023.12.015.
19. Mian BM, Feustel PJ, Aziz A, Kaufman RP, Bernstein A, Avulova S, et al. Complications following transrectal and transperineal prostate biopsy: results of the ProBE-PC randomized clinical trial. J Urol. 2024;211. https://doi.org/10.1097/JU.0000000000003788.

AUTHOR CONTRIBUTIONS

AF: writing—original draft preparation, conceptualization; RL: writing—review and editing; CDN: supervision, conceptualization.

COMPETING INTERESTS

The authors declare no competing interests.