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TARGETED PROSTATE BIOPSY: TECHNIQUES, CLINICAL OUTCOMES, AND FUTURE PERSPECTIVES – A NARRATIVE REVIEW

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ABSTRACT

Prostate cancer is one of the most frequently diagnosed malignancies among men worldwide and continues to pose a major clinical and public health challenge (Rawla, 2019; Pernar et al., 2018). Despite substantial advances in screening and imaging, accurate identification of clinically significant prostate cancer remains a critical issue in contemporary urologic practice. Conventional systematic transrectal ultrasound-guided biopsy has long been considered the diagnostic standard; however, it is inherently limited by random sampling error and is associated with both underdiagnosis of aggressive disease and overdiagnosis of indolent tumors (Schoots et al., 2017; Kasivisvanathan et al., 2018).

The integration of multiparametric magnetic resonance imaging (mpMRI) into prostate cancer diagnostic pathways has led to the development of targeted prostate biopsy techniques aimed at improving diagnostic accuracy and risk stratification (Padhani et al., 2019; Turkbey et al., 2022). This narrative review summarizes current evidence on targeted prostate biopsy, including the epidemiological and diagnostic background of prostate cancer, imaging foundations, biopsy techniques, clinical outcomes, and emerging innovations.

A structured literature search was conducted using PubMed, ScienceDirect, and Google Scholar. The reviewed literature demonstrates that MRI-targeted biopsy improves detection rates of clinically significant prostate cancer while reducing the identification of clinically insignificant disease compared with systematic biopsy alone (Ahdoot et al., 2020; Drost et al., 2019). Targeted prostate biopsy has become a cornerstone of modern prostate cancer diagnostics, with ongoing research focusing on technique optimization, patient selection, and personalized diagnostic strategies.

KEYWORDS

Targeted Prostate Biopsy, Prostate Cancer Diagnosis, Multiparametric MRI, MRI-Targeted Biopsy, Clinically Significant Prostate Cancer, PI-RADS

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1. Introduction

Prostate cancer is one of the most commonly diagnosed malignancies among men and remains a leading cause of cancer-related morbidity and mortality worldwide (Rawla, 2019; Pernar et al., 2018). Global epidemiological data reveal substantial geographic variation in incidence and mortality, reflecting differences in population demographics, genetic susceptibility, environmental exposures, and screening practices. The widespread implementation of prostate-specific antigen (PSA) testing has markedly influenced prostate cancer epidemiology by enabling earlier detection; however, it has also intensified concerns regarding overdiagnosis and overtreatment of indolent disease.

A defining feature of prostate cancer is its pronounced biological heterogeneity. While many tumors follow an indolent course and may never become clinically relevant, others exhibit aggressive behavior characterized by rapid progression, metastatic potential, and increased disease-specific mortality (Mottet et al., 2017). This heterogeneity poses a fundamental diagnostic challenge and underscores the importance of accurate risk stratification at the time of diagnosis. Inaccurate classification may expose patients either to unnecessary treatment-related morbidity or to delayed intervention for clinically significant disease (Epstein et al., 2016).

The diagnostic pathway for prostate cancer traditionally relies on serum PSA measurement, digital rectal examination, and histopathological confirmation obtained through prostate biopsy. Although PSA-based screening has contributed to a stage shift toward earlier diagnosis, its limited specificity has resulted in a substantial number of unnecessary biopsies and detection of clinically insignificant tumors (Pernar et al., 2018; Rawla, 2019). Consequently, prostate biopsy remains the cornerstone of definitive diagnosis and risk assessment, guiding subsequent clinical decision-making.

For decades, systematic transrectal ultrasound-guided biopsy has served as the standard diagnostic approach. This technique involves random sampling of the prostate using a predefined core distribution scheme. Despite its widespread adoption, systematic biopsy is inherently limited by sampling error and may fail to detect clinically significant lesions, particularly those located in the anterior, apical, or transition zones of the prostate (Schoots et al., 2017). Moreover, systematic biopsy is associated with a high rate of detection of low-grade tumors that may not require immediate intervention, contributing to overtreatment and patient anxiety.

Advances in imaging have fundamentally altered the diagnostic landscape of prostate cancer. Multiparametric magnetic resonance imaging has emerged as a pivotal tool for lesion detection, localization, and characterization. By combining high-resolution anatomical imaging with functional sequences, including diffusion-weighted imaging and dynamic contrast-enhanced imaging, mpMRI enables improved visualization of suspicious prostate lesions and facilitates standardized reporting through the Prostate Imaging Reporting and Data System (PI-RADS) (Padhani et al., 2019; Turkbey et al., 2022). The implementation of PI-RADS has enhanced communication between radiologists and clinicians and improved the reproducibility of mpMRI interpretation.

The introduction of mpMRI has paved the way for targeted prostate biopsy techniques, which aim to overcome the limitations of random sampling by directing biopsy cores toward imaging-visible lesions. Targeted approaches—including cognitive targeting, MRI–ultrasound fusion biopsy, and in-bore MRI-guided biopsy—have been developed to improve diagnostic precision and lesion-specific sampling (Bonekamp et al., 2023). Accumulating evidence suggests that these techniques enhance detection rates of clinically significant prostate cancer while reducing the identification of indolent disease compared with systematic biopsy alone (Kasivisvanathan et al., 2018; Ahdoot et al., 2020).

As a result, targeted prostate biopsy has become an integral component of contemporary prostate cancer diagnostic pathways. However, variability in imaging quality, interpretation, biopsy technique, and patient selection continues to influence diagnostic performance and clinical outcomes. A comprehensive synthesis of current evidence is therefore essential to inform best practices and guide future research.

The aim of this narrative review is to provide an in-depth overview of targeted prostate biopsy in modern clinical practice. Specifically, we summarize the epidemiological and diagnostic background of prostate cancer, review the role of mpMRI and PI-RADS, compare available targeted biopsy techniques, evaluate clinical outcomes relative to systematic biopsy, and discuss procedural considerations, limitations, and future directions in personalized prostate cancer diagnostics.

2. Methodology

This manuscript was prepared as a narrative review of the contemporary literature addressing targeted prostate biopsy in the diagnosis of prostate cancer. The review was designed to synthesize current evidence regarding imaging foundations, biopsy techniques, comparative clinical outcomes, procedural considerations, and emerging diagnostic strategies. Given the heterogeneity of available studies and outcome measures, a qualitative narrative approach was considered the most appropriate method for comprehensive evaluation and contextual interpretation of the evidence.

2.1 Literature Search Strategy

A structured literature search was conducted using three major scientific databases: PubMed, ScienceDirect, and Google Scholar. The search strategy was developed to capture original research articles, systematic reviews, and meta-analyses relevant to targeted prostate biopsy and mpMRI-based diagnostic pathways. The following keywords and combinations of terms were used: *prostate cancer*, *targeted prostate biopsy*, *MRI-targeted biopsy*, *multiparametric MRI*, *PI-RADS*, *fusion biopsy*, *cognitive biopsy*, *in-bore biopsy*, *systematic biopsy*, and *clinically significant prostate cancer*. Boolean operators were applied to refine search results and maximize retrieval of relevant publications.

In addition to database searches, reference lists of selected articles were manually screened to identify further studies of potential relevance. This approach was used to ensure comprehensive coverage of influential and frequently cited publications in the field.

2.2 Eligibility Criteria

Studies were eligible for inclusion if they met the following criteria:

(1) publication in a peer-reviewed scientific journal;

(2) availability of the full text in English;

(3) focus on mpMRI-based prostate cancer diagnostics, targeted biopsy techniques, or comparative outcomes between targeted and systematic biopsy; and

(4) relevance to contemporary clinical practice.

Original research articles, systematic reviews, and meta-analyses were included. Editorials, conference abstracts without full-text availability, case reports, and studies lacking sufficient methodological detail were excluded. Emphasis was placed on publications from the past decade to reflect current diagnostic standards, while seminal studies of historical importance were also considered where relevant.

2.3 Study Selection and Data Extraction

Titles and abstracts identified through the search strategy were screened for relevance. Full-text articles were then reviewed to confirm eligibility and extract pertinent information. Data extraction was performed qualitatively, focusing on study design, patient population, imaging protocols, biopsy technique, definitions of clinically significant prostate cancer, diagnostic performance metrics, and reported complication rates.

Given the variability in study designs, patient cohorts, and outcome definitions, quantitative pooling of results was not undertaken. Instead, findings were synthesized narratively and grouped thematically to facilitate structured comparison and interpretation.

2.4 Data Synthesis and Analysis

The included studies were organized into thematic categories corresponding to the objectives of the review: (1) epidemiological and diagnostic background of prostate cancer; (2) role of mpMRI and PI-RADS in biopsy decision-making; (3) technical aspects of targeted prostate biopsy; (4) comparative clinical outcomes of targeted versus systematic biopsy; and (5) procedural routes and biopsy-related complications.

The results of individual studies were interpreted in the context of the broader literature, with particular attention to consistency of findings, methodological strengths and limitations, and clinical applicability. This approach allowed for a comprehensive synthesis of evidence while acknowledging areas of uncertainty and ongoing debate within the field (Schoots et al., 2017; Drost et al., 2019).

3. Results

3.1 Multiparametric MRI and PI-RADS in Targeted Prostate Biopsy

Multiparametric magnetic resonance imaging has become a central component of contemporary prostate cancer diagnostic pathways and represents the imaging foundation of targeted prostate biopsy. MpMRI combines anatomical and functional imaging sequences, typically including high-resolution T2-weighted imaging, diffusion-weighted imaging with apparent diffusion coefficient mapping, and dynamic contrast-enhanced imaging. The integration of these sequences allows for improved lesion localization, characterization, and risk stratification, thereby addressing several inherent limitations of conventional systematic biopsy (Padhani et al., 2019; Turkbey et al., 2022).

3.1.1 Diagnostic Performance of mpMRI

A substantial body of evidence demonstrates that mpMRI exhibits high sensitivity for the detection of clinically significant prostate cancer, while maintaining moderate specificity. The negative predictive value of mpMRI is of particular clinical relevance, as a negative examination substantially lowers the likelihood of high-grade disease and may allow selected patients to defer immediate biopsy under appropriate clinical surveillance (Schoots et al., 2017; Drost et al., 2019).

Several studies included in this review indicate that mpMRI-based diagnostic pathways improve overall diagnostic efficiency by reducing unnecessary biopsies without compromising detection of clinically significant tumors. These findings support the role of mpMRI as a gatekeeper prior to biopsy, particularly in biopsy-naïve patients and in those with prior negative biopsies but persistent clinical suspicion (Kasivisvanathan et al., 2018; Ahdoot et al., 2020).

The diagnostic performance of mpMRI is influenced by multiple factors, including image acquisition quality, adherence to standardized protocols, magnetic field strength, and reader expertise. Studies consistently report superior diagnostic accuracy when mpMRI is performed and interpreted in high-volume centers with specialized radiological expertise, highlighting the importance of training and quality assurance (Turkbey et al., 2022).

3.1.2 PI-RADS Classification System

The Prostate Imaging Reporting and Data System was developed to standardize mpMRI acquisition, interpretation, and reporting, thereby improving reproducibility and communication between radiologists and clinicians. Since its initial introduction, PI-RADS has undergone iterative refinements, culminating in version 2.1, which provides clearer guidance regarding lesion assessment and scoring (Padhani et al., 2019; Turkbey et al., 2022).

PI-RADS stratifies prostate lesions on a five-point scale reflecting the likelihood of clinically significant prostate cancer. Lesions classified as PI-RADS 4 or 5 are associated with a high probability of clinically significant disease, whereas PI-RADS 1–2 lesions are considered unlikely to harbor aggressive cancer. PI-RADS 3 lesions represent an intermediate-risk category with heterogeneous outcomes and remain a diagnostic challenge in clinical practice (Padhani et al., 2019).

3.1.3 Correlation Between PI-RADS Score and Cancer Detection

Multiple studies demonstrate a strong correlation between PI-RADS score and the detection of clinically significant prostate cancer on targeted biopsy. Detection rates increase progressively with higher PI-RADS categories, with PI-RADS 5 lesions showing the highest yield for clinically significant disease (Schoots et al., 2017; Kasivisvanathan et al., 2018).

Across the reviewed literature, clinically significant cancer detection rates exceeding 60–70% have been reported for PI-RADS 5 lesions, whereas substantially lower detection rates are observed for PI-RADS 3 lesions. These findings support the clinical utility of PI-RADS as a risk stratification tool and its role in guiding biopsy decision-making (Drost et al., 2019; Ahdoot et al., 2020).

3.1.4 mpMRI-Based Diagnostic Pathways

The integration of mpMRI into diagnostic algorithms has facilitated the development of MRI-based pathways that incorporate imaging findings with clinical parameters such as PSA density, age, and prior biopsy status. These pathways enable more individualized biopsy decisions and have been shown to reduce the number of unnecessary biopsies while maintaining high detection rates of clinically significant disease (Kasivisvanathan et al., 2018; Schoots et al., 2017).

Patients with negative mpMRI findings may safely avoid immediate biopsy in selected clinical contexts, whereas those with high-suspicion lesions benefit from targeted sampling. This risk-adapted approach represents a shift toward precision diagnostics and patient-centered care.

3.1.5 Limitations of mpMRI and PI-RADS

Despite its advantages, mpMRI is not without limitations. False-negative examinations may occur, particularly in cases of small-volume tumors, low-grade disease, or cancers with atypical imaging characteristics. Inter-reader variability, especially for PI-RADS 3 lesions, remains a recognized challenge and may influence diagnostic consistency (Padhani et al., 2019; Turkbey et al., 2022).

Technical factors, including scanner quality, coil selection, and protocol optimization, further contribute to variability in mpMRI performance. These limitations underscore the need for continued standardization, training, and refinement of imaging protocols to maximize the reliability of mpMRI-guided diagnostic strategies.

3.1.6 Role of mpMRI in Targeted Biopsy Planning

Beyond its diagnostic role, mpMRI serves as a critical roadmap for targeted biopsy planning. Precise lesion localization enables targeted biopsy techniques—such as cognitive targeting, MRI–ultrasound fusion biopsy, and in-bore MRI-guided biopsy—to focus sampling on areas most likely to harbor clinically significant cancer (Bonekamp et al., 2023).

Collectively, the reviewed studies demonstrate that mpMRI-informed targeted biopsy improves lesion-specific sampling efficiency and enhances diagnostic yield compared with systematic biopsy alone. This imaging-driven approach forms the cornerstone of contemporary targeted prostate biopsy strategies.

3.2 Targeted Prostate Biopsy Techniques

Targeted prostate biopsy encompasses a group of biopsy techniques designed to sample prostate lesions identified on multiparametric magnetic resonance imaging with greater precision than conventional systematic biopsy. The principal targeted biopsy approaches currently implemented in clinical practice include cognitive targeting, MRI–ultrasound fusion biopsy, and direct in-bore MRI-guided biopsy. While all three techniques share the common goal of improving detection of clinically significant prostate cancer, they differ substantially with respect to technical complexity, reproducibility, resource requirements, and operator dependency.

3.2.1 Cognitive Targeted Biopsy

Cognitive targeted biopsy represents the most straightforward form of MRI-targeted sampling. In this approach, lesions identified on pre-biopsy mpMRI are cognitively mapped by the operator onto real-time ultrasound images during the biopsy procedure. The absence of dedicated fusion software or hardware renders cognitive targeting widely accessible and cost-effective, allowing its implementation in centers without advanced technological infrastructure (Bonekamp et al., 2023).

Several studies have demonstrated that cognitive targeting improves detection rates of clinically significant prostate cancer compared with systematic biopsy alone, particularly when performed by experienced operators with substantial familiarity with mpMRI interpretation and prostate anatomy (Schoots et al., 2017; Wegelin et al., 2019). In selected patient populations, detection rates achieved using cognitive targeting have been reported to be comparable to those obtained with MRI–ultrasound fusion biopsy, especially for larger, well-defined lesions.

However, cognitive targeting is inherently operator-dependent and subject to variability in lesion localization accuracy. The technique relies on the clinician's ability to mentally translate MRI findings into ultrasound-guided sampling, which may be challenging for small lesions or for tumors located in the anterior or apical regions of the prostate. As a result, diagnostic performance may be reduced in low-volume centers or among operators with limited mpMRI experience (Bonekamp et al., 2023).

3.2.2 MRI–Ultrasound Fusion Biopsy

MRI–ultrasound fusion biopsy represents a technologically advanced targeted biopsy technique that integrates pre-acquired mpMRI images with real-time ultrasound guidance using dedicated software platforms. Through image co-registration, fusion biopsy enables three-dimensional visualization of MRI-detected lesions during biopsy, thereby improving targeting accuracy and procedural reproducibility (Ahmed et al., 2017; Wegelin et al., 2019).

Numerous comparative studies have demonstrated that fusion biopsy improves detection rates of clinically significant prostate cancer relative to systematic biopsy and reduces sampling variability compared with cognitive targeting. The technique has been shown to be particularly advantageous for lesions located in anatomically challenging regions, such as the anterior prostate, where systematic biopsy may be less effective (Ahdoot et al., 2020; Drost et al., 2019).

Fusion biopsy can be performed via transrectal or transperineal access routes, with increasing adoption of the transperineal approach due to its favorable safety profile. The ability to store biopsy coordinates and reproduce sampling locations over time further supports the use of fusion biopsy in longitudinal disease monitoring and active surveillance protocols (Wegelin et al., 2019).

Despite these advantages, fusion biopsy requires specialized equipment, software, and operator training, which may limit its availability in certain clinical settings. Technical challenges, including image registration errors and prostate deformation, may still influence targeting accuracy, although these limitations are generally less pronounced than in cognitive targeting (Ahmed et al., 2017).

3.2.3 In-Bore MRI-Guided Biopsy

In-bore MRI-guided biopsy represents the most technologically sophisticated form of targeted prostate biopsy. This technique involves direct needle placement and tissue sampling within the MRI scanner under real-time imaging guidance. Continuous visualization of the biopsy needle relative to the target lesion allows for precise confirmation of needle position and theoretically maximizes targeting accuracy (Bonekamp et al., 2023; Turkbey et al., 2022).

Clinical studies have demonstrated high detection rates of clinically significant prostate cancer using in-bore biopsy, particularly in patients with prior negative systematic biopsies and persistent clinical suspicion. The technique may be especially beneficial for small lesions, anterior tumors, or MRI-only visible lesions that are difficult to target using ultrasound-based methods (Kasivisvanathan et al., 2022; Schoots et al., 2017).

However, in-bore biopsy is associated with several practical limitations. The procedure is resource-intensive, time-consuming, and requires access to MRI-compatible biopsy devices and specialized personnel. These factors restrict its widespread adoption and confine its use primarily to selected cases in specialized centers (Bonekamp et al., 2023).

3.2.4 Comparative Performance of Targeted Biopsy Techniques

Comparative analyses indicate that all targeted biopsy techniques outperform systematic biopsy alone in the detection of clinically significant prostate cancer. Meta-analyses suggest that MRI–ultrasound fusion biopsy and in-bore biopsy may provide modest improvements in detection rates compared with cognitive targeting; however, these differences are not consistently statistically significant and are influenced by lesion characteristics and operator expertise (Wegelin et al., 2019; Drost et al., 2019).

Importantly, several studies emphasize that the combination of targeted and systematic biopsy yields the highest overall detection rates of clinically significant disease, regardless of the targeted technique employed. This finding highlights the complementary rather than competitive nature of targeted and systematic sampling strategies (Ahdoot et al., 2020; Kasivisvanathan et al., 2018).

3.2.5 Clinical Selection of Targeted Biopsy Technique

Selection of the optimal targeted biopsy technique should be individualized based on patient-specific factors, lesion characteristics, institutional resources, and operator experience. Cognitive targeting may be appropriate in centers with strong mpMRI expertise but limited access to fusion systems. MRI–ultrasound fusion biopsy offers a balance between accuracy, reproducibility, and feasibility for routine clinical practice, whereas in-bore MRI-guided biopsy remains best suited for selected cases with challenging lesion characteristics or repeated negative biopsies despite ongoing clinical suspicion (Kasivisvanathan et al., 2022; Bonekamp et al., 2023).

Collectively, targeted biopsy techniques represent a major advancement in prostate cancer diagnostics, enabling more precise lesion sampling and supporting a shift toward risk-adapted and patient-centered diagnostic strategies.

3.3. Targeted Versus Systematic Prostate Biopsy: Clinical Outcomes

The comparative clinical performance of MRI-targeted prostate biopsy and conventional systematic biopsy has been extensively investigated over the past decade. The primary objective of these comparative analyses has been to determine whether targeted biopsy improves the detection of clinically significant prostate cancer while reducing the diagnosis of clinically insignificant disease. Across a broad range of study designs and patient populations, the accumulated evidence consistently demonstrates that MRI-targeted biopsy provides superior risk stratification compared with systematic biopsy alone.

3.3.1 Detection of Clinically Significant Prostate Cancer

Multiple prospective studies, randomized trials, and meta-analyses have shown that MRI-targeted biopsy significantly improves detection rates of clinically significant prostate cancer, most commonly defined as Gleason grade group ≥2, compared with systematic transrectal ultrasound-guided biopsy (Kasivisvanathan et al., 2018; Drost et al., 2019). By directing biopsy cores toward mpMRI-visible lesions, targeted approaches more effectively sample biologically relevant tumor foci.

Large comparative studies have demonstrated that targeted biopsy detects a higher proportion of clinically significant cancers per biopsy session while requiring fewer biopsy cores overall. This increased efficiency reflects the ability of mpMRI to localize dominant tumor lesions and guide lesion-specific sampling (Ahdoot et al., 2020; Kasivisvanathan et al., 2022). In contrast, systematic biopsy relies on random sampling and may miss clinically significant tumors, particularly those located in the anterior or transition zones of the prostate.

Meta-analytical data indicate that MRI-targeted biopsy detects approximately 30–40% more cases of clinically significant prostate cancer than systematic biopsy alone, although detection rates vary depending on patient characteristics and prior biopsy status (Drost et al., 2019; Wegelin et al., 2019). These findings provide robust support for the incorporation of targeted biopsy into contemporary diagnostic pathways.

3.3.2 Detection of Clinically Insignificant Prostate Cancer

In addition to improving detection of clinically significant disease, MRI-targeted biopsy has been consistently shown to reduce the diagnosis of clinically insignificant prostate cancer. Overdiagnosis of low-grade tumors remains a major limitation of systematic biopsy and contributes to overtreatment, psychological distress, and unnecessary healthcare utilization (Schoots et al., 2017).

Targeted biopsy selectively samples MRI-suspicious lesions, thereby decreasing the likelihood of detecting low-volume, low-grade tumors that may not require immediate intervention. Several studies have reported significantly lower rates of Gleason grade group 1 cancer detection with targeted biopsy compared with systematic biopsy, supporting its role in risk-adapted diagnostic strategies (Kasivisvanathan et al., 2018; Ahdoot et al., 2020).

3.3.3 Biopsy-Naïve Patients and Patients with Prior Negative Biopsy

The relative clinical benefit of targeted versus systematic biopsy differs between patient populations. In biopsy-naïve patients, MRI-targeted biopsy has been shown to detect at least as many cases of clinically significant prostate cancer as systematic biopsy while substantially reducing the detection of low-risk disease (Kasivisvanathan et al., 2018; Schoots et al., 2017).

In patients with prior negative systematic biopsies but persistent clinical suspicion of prostate cancer, the advantage of targeted biopsy is even more pronounced. MpMRI frequently identifies lesions that were missed by prior random sampling, and subsequent targeted biopsy yields high detection rates of clinically significant disease in this setting (Kasivisvanathan et al., 2022). These findings strongly support the routine use of mpMRI and targeted biopsy in men with previous negative biopsies and ongoing clinical concern.

3.3.4 Targeted-Only Versus Combined Biopsy Strategies

An important area of ongoing debate concerns whether targeted biopsy alone is sufficient or whether it should be combined with systematic biopsy. Several studies have explored targeted-only strategies and have reported favorable detection rates of clinically significant prostate cancer in carefully selected patients with high-suspicion mpMRI lesions (Ahdoot et al., 2020; Kasivisvanathan et al., 2022).

However, evidence indicates that a proportion of clinically significant cancers may still be detected exclusively by systematic biopsy, even in the presence of mpMRI. These MRI-invisible tumors are often small, low-volume, or located outside targeted sampling regions (Schoots et al., 2017). Consequently, multiple studies and meta-analyses support the use of combined targeted and systematic biopsy to maximize diagnostic yield, particularly in biopsy-naïve patients (Ahdoot et al., 2020; Drost et al., 2019).

3.3.5 Number of Biopsy Cores and Sampling Efficiency

The optimal number of biopsy cores obtained during MRI-targeted biopsy has been investigated in several recent studies. Evidence suggests that sampling two to four targeted cores per lesion provides an effective balance between diagnostic yield and procedural efficiency (Wegelin et al., 2019; Kasivisvanathan et al., 2022).

Increasing the number of targeted cores beyond this range may result in marginal improvements in detection rates but is associated with diminishing returns and increased procedural burden. Lesion-specific factors, including PI-RADS score, lesion size, and anatomical location, should guide decisions regarding core number rather than a fixed sampling scheme (Kasivisvanathan et al., 2022).

Compared with systematic biopsy, which typically involves 10–12 cores, targeted biopsy achieves higher lesion-specific diagnostic yield with fewer total cores, underscoring its efficiency and patient-centered nature.

3.3.6 Impact on Risk Stratification and Clinical Decision-Making

Improved detection and grading accuracy achieved through targeted biopsy have important downstream implications for prostate cancer risk stratification and clinical management. More accurate identification of tumor grade and extent facilitates informed decision-making regarding active surveillance, focal therapy, and definitive treatment options (Ahdoot et al., 2020).

Several studies have demonstrated that targeted biopsy reduces grade misclassification and decreases the rate of pathological upgrading at radical prostatectomy, indicating improved concordance between biopsy findings and final surgical pathology (Ahdoot et al., 2020; Schoots et al., 2017). This enhanced diagnostic precision supports more personalized and appropriate treatment strategies.

3.4 Route of Access and Procedure-Related Complications: Transrectal versus Transperineal Targeted Biopsy

The route of access represents a critical procedural aspect of targeted prostate biopsy and has important implications for patient safety, complication rates, and overall procedural outcomes. Historically, the transrectal approach has been the most commonly used access route for prostate biopsy owing to its technical simplicity and widespread availability. However, increasing awareness of biopsy-related infectious complications has prompted growing interest in the transperineal approach, particularly in the context of MRI-targeted biopsy.

3.4.1 Transrectal Targeted Prostate Biopsy

Transrectal MRI-targeted biopsy is typically performed under transrectal ultrasound guidance, using either cognitive targeting or MRI–ultrasound fusion techniques. The procedure is commonly conducted in an outpatient setting under local anesthesia and is associated with relatively short procedural times (Schoots et al., 2017).

Despite these practical advantages, the transrectal approach is associated with a measurable risk of infectious complications, including urinary tract infection, acute prostatitis, and sepsis. The passage of biopsy needles through the rectal mucosa exposes the prostate and bloodstream to rectal flora, even when antibiotic prophylaxis is administered (Kasivisvanathan et al., 2022). Although MRI-targeted biopsy generally requires fewer cores than systematic biopsy, available evidence indicates that the risk of infection remains clinically relevant.

Reported infection rates following transrectal biopsy range from approximately 1% to 7%, with sepsis occurring in a small but significant subset of patients. The increasing prevalence of antibiotic-resistant organisms has further heightened concerns regarding the long-term safety of the transrectal approach (Kasivisvanathan et al., 2022).

3.4.2 Transperineal Targeted Prostate Biopsy

The transperineal approach involves needle insertion through the perineal skin, thereby avoiding direct contact with rectal mucosa. This anatomical advantage substantially reduces the risk of infectious complications and has emerged as a key factor driving the adoption of transperineal MRI-targeted biopsy techniques (Schoots et al., 2017; Borofsky et al., 2023).

Multiple studies and systematic reviews have demonstrated markedly lower rates of infection and sepsis with transperineal biopsy compared with transrectal biopsy. In several series, infectious complications following transperineal biopsy have been reported to be exceedingly rare, even in the absence of routine antibiotic prophylaxis (Kasivisvanathan et al., 2022; Borofsky et al., 2023). These findings have prompted calls for a paradigm shift toward transperineal biopsy as the preferred access route for prostate sampling.

Recent technical advances have facilitated the wider implementation of transperineal biopsy, allowing procedures to be performed under local anesthesia with acceptable patient comfort. Transperineal MRI–ultrasound fusion biopsy has been shown to achieve diagnostic accuracy comparable to transrectal approaches while offering a superior safety profile (Borofsky et al., 2023).

3.4.3 Comparison of Diagnostic Performance

Comparative analyses indicate that detection rates of clinically significant prostate cancer are broadly similar between transrectal and transperineal MRI-targeted biopsy when equivalent targeting techniques are used (Schoots et al., 2017; Kasivisvanathan et al., 2022). The choice of access route does not appear to compromise lesion targeting accuracy or overall diagnostic yield, supporting the feasibility of transperineal biopsy as an alternative to transrectal sampling.

Some studies suggest that the transperineal approach may offer improved access to anterior and apical regions of the prostate, which are less readily sampled via the transrectal route. However, the clinical impact of this potential advantage requires further investigation.

3.4.4 Non-Infectious Complications

In addition to infectious events, prostate biopsy may be associated with non-infectious complications such as hematuria, hematospermia, urinary retention, rectal bleeding, and perineal discomfort. These complications are generally self-limiting and occur at comparable frequencies across targeted biopsy techniques (Schoots et al., 2017).

Transperineal biopsy has been associated with a slightly higher incidence of transient urinary retention, particularly in patients with larger prostate volumes or when a greater number of biopsy cores are obtained. However, most cases resolve with short-term catheterization and do not result in long-term morbidity (Borofsky et al., 2023).

Overall, the substantial reduction in serious infectious complications observed with the transperineal approach appears to outweigh the modest increase in minor urinary complications, reinforcing its favorable risk–benefit profile.

3.4.5 Clinical Implications for Contemporary Practice

The growing body of evidence supporting the safety and effectiveness of transperineal MRI-targeted biopsy has important implications for clinical practice. Many institutions have begun transitioning toward transperineal access as part of MRI-based diagnostic pathways, particularly in healthcare systems facing rising rates of antibiotic resistance (Kasivisvanathan et al., 2022; Borofsky et al., 2023).

Current data support the adoption of transperineal targeted biopsy as a safe and effective alternative to the transrectal approach, without compromising diagnostic accuracy. As experience, training, and accessibility continue to improve, the transperineal route is likely to play an increasingly prominent role in prostate cancer diagnostics.

4. Discussion

This narrative review synthesizes contemporary evidence on targeted prostate biopsy and confirms its pivotal role in modern prostate cancer diagnostics. Across multiple domains—including imaging, biopsy technique, clinical outcomes, and procedural safety—the reviewed literature consistently demonstrates that MRI-targeted biopsy represents a substantial advancement over conventional systematic biopsy. In particular, targeted approaches improve detection of clinically significant prostate cancer while reducing the diagnosis of indolent disease, thereby addressing long-standing challenges associated with prostate cancer overdiagnosis and overtreatment.

4.1 Impact of mpMRI on Diagnostic Pathways

The integration of multiparametric MRI into prostate cancer diagnostic algorithms has fundamentally altered the traditional biopsy pathway. MpMRI enables lesion localization and risk stratification prior to tissue sampling, allowing biopsy decisions to be guided by imaging findings rather than random sampling alone (Padhani et al., 2019; Turkbey et al., 2022). The high negative predictive value of mpMRI reported in multiple studies supports its role as a triage tool, particularly in biopsy-naïve patients and in those with previous negative biopsies (Schoots et al., 2017; Drost et al., 2019).

By serving as a gatekeeper to biopsy, mpMRI-based pathways reduce unnecessary procedures and associated morbidity without compromising the detection of clinically significant disease. However, the diagnostic performance of mpMRI is closely linked to image quality, standardized acquisition protocols, and reader expertise. Variability across institutions remains an important limitation and highlights the need for ongoing training and quality assurance initiatives (Turkbey et al., 2022).

4.2 Clinical Relevance of Targeted Biopsy Techniques

The comparative evaluation of cognitive targeting, MRI–ultrasound fusion biopsy, and in-bore MRI-guided biopsy underscores that multiple technical approaches can achieve meaningful improvements in diagnostic accuracy when guided by mpMRI. While in-bore biopsy offers the highest theoretical targeting precision, its limited availability, cost, and procedural complexity restrict its widespread use (Bonekamp et al., 2023).

MRI–ultrasound fusion biopsy appears to offer the most favorable balance between accuracy, reproducibility, and feasibility for routine clinical practice. Its ability to integrate imaging data with real-time ultrasound guidance reduces operator dependency and supports standardized lesion targeting across centers (Ahmed et al., 2017; Wegelin et al., 2019). Cognitive targeting remains a valid and accessible option in experienced hands but may be more susceptible to inter-operator variability, particularly in challenging lesion locations.

4.3 Targeted Versus Systematic Biopsy: Implications for Risk Stratification

One of the most consistent findings across the reviewed literature is the superior performance of targeted biopsy in detecting clinically significant prostate cancer compared with systematic biopsy alone. Targeted approaches not only increase detection of higher-grade tumors but also substantially reduce the identification of low-risk disease (Kasivisvanathan et al., 2018; Ahdoot et al., 2020). This dual benefit has important implications for patient counseling, treatment selection, and long-term quality of life.

Despite these advantages, the persistence of MRI-invisible clinically significant tumors remains a concern. Several studies demonstrate that a small but meaningful proportion of significant cancers may still be detected exclusively by systematic biopsy (Schoots et al., 2017). Consequently, combined targeted and systematic biopsy strategies currently provide the most comprehensive diagnostic yield, particularly in biopsy-naïve patients and those with intermediate-risk clinical profiles (Drost et al., 2019; Ahdoot et al., 2020).

4.4 Safety Considerations and Route of Access

Procedure-related complications represent a critical component of biopsy decision-making. The reviewed evidence clearly demonstrates a substantial reduction in infectious complications with the transperineal approach compared with transrectal biopsy (Kasivisvanathan et al., 2022; Borofsky et al., 2023). This safety advantage has driven increasing adoption of transperineal MRI-targeted biopsy, particularly in healthcare systems facing rising antimicrobial resistance.

Although transperineal biopsy may be associated with a slightly higher incidence of transient urinary retention, these events are generally manageable and self-limited. Importantly, diagnostic performance appears comparable between transperineal and transrectal targeted biopsy when equivalent targeting techniques are employed, supporting the feasibility of broader implementation of the transperineal approach.

4.5 Limitations of the Current Evidence Base

Several limitations of the existing literature must be acknowledged. Considerable heterogeneity exists with respect to study design, patient selection, imaging protocols, biopsy techniques, and definitions of clinically significant prostate cancer (Drost et al., 2019). Many studies originate from high-volume academic centers, which may limit generalizability to lower-volume or resource-limited settings.

Inter-reader variability in mpMRI interpretation, particularly for PI-RADS 3 lesions, continues to pose a diagnostic challenge and may influence biopsy outcomes. Furthermore, long-term oncological outcomes associated with MRI-based diagnostic strategies remain incompletely characterized and warrant further investigation through prospective studies with extended follow-up.

4.6 Future Directions

Future research efforts are increasingly focused on refining personalized diagnostic pathways that integrate mpMRI findings with clinical and biochemical parameters such as PSA density, prior biopsy history, and emerging imaging biomarkers. Advances in artificial intelligence–assisted MRI interpretation hold promise for reducing inter-reader variability and improving diagnostic consistency across institutions (Borofsky et al., 2023).

Additionally, ongoing technical innovations in image-guided biopsy platforms may further enhance targeting accuracy and procedural efficiency. As evidence continues to evolve, targeted prostate biopsy is likely to remain a cornerstone of precision diagnostics, supporting risk-adapted and patient-centered management of prostate cancer.

5. Conclusions

Targeted prostate biopsy has fundamentally reshaped the diagnostic landscape of prostate cancer by addressing critical limitations inherent to conventional systematic biopsy. The integration of multiparametric magnetic resonance imaging into diagnostic pathways has enabled more accurate lesion localization, improved risk stratification, and enhanced detection of clinically significant prostate cancer while simultaneously reducing the diagnosis of indolent disease.

The evidence synthesized in this narrative review demonstrates that MRI-targeted biopsy consistently outperforms systematic biopsy alone in identifying clinically significant tumors across diverse clinical scenarios. Targeted approaches improve sampling efficiency, reduce unnecessary biopsy cores, and provide more accurate histopathological grading, thereby supporting informed and patient-centered clinical decision-making. Among currently available techniques, cognitive targeting, MRI–ultrasound fusion biopsy, and in-bore MRI-guided biopsy each offer distinct advantages and limitations, with optimal technique selection best guided by lesion characteristics, patient factors, and institutional expertise.

Comparative outcome data further indicate that combined targeted and systematic biopsy strategies currently provide the most comprehensive diagnostic yield, particularly in biopsy-naïve patients and in cases where MRI-invisible disease remains a concern. At the same time, accumulating evidence supporting the transperineal approach highlights a markedly improved safety profile, characterized by a substantial reduction in infectious complications without compromising diagnostic accuracy.

Despite these advances, several challenges remain. Variability in mpMRI quality, inter-reader interpretation, and procedural expertise continues to influence diagnostic performance across centers. Moreover, the long-term oncological impact of MRI-based diagnostic strategies requires further validation through prospective studies with extended follow-up.

Future research should focus on refining personalized diagnostic pathways that integrate imaging findings with clinical and biochemical parameters. Emerging technologies, including artificial intelligence–assisted MRI interpretation and advanced image-guided biopsy platforms, hold promise for improving standardization, reducing variability, and further enhancing diagnostic precision. As evidence continues to evolve, targeted prostate biopsy is expected to remain a cornerstone of precision diagnostics, supporting risk-adapted and patient-centered management of prostate cancer.

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