Case Report

Cognitive Fusion-Guided Transperineal Biopsy Leading to the Diagnosis of Early Prostate Adenocarcinoma After Repeated Negative Evaluations: A Case Report

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ABSTRACT: Background: Prostate cancer remains one of the most frequently diagnosed malignancies in men, where early detection is key to curative treatment. Conventional biopsy techniques can miss small or focal lesions, especially in cases with persistently elevated prostate-specific antigen (PSA) levels and uncertain imaging, risking delayed diagnosis. Case Report: We present the case of a 69-year-old male who initially presented in 2022 with lower urinary tract symptoms and an elevated PSA level of 26.17ng/ml. He was diagnosed with acute prostatitis and responded favourably to targeted treatment. Over the following two years, his PSA levels remained in the "gray zone" (7.24-8.68ng/ml), raising continued clinical suspicion despite normal findings on digital rectal examination (DRE), PIRADS 3 lesions on serial multiparametric magnetic resonance imaging (mpMRI), and two previous transperineal prostate biopsies, including a saturation biopsy-both with benign histopathology. In July 2025, the patient presented for the first time to our center. A new mpMRI again showed a PIRADS 3 lesion in the transitional zone of the right prostatic lobe. Given the persistent suspicion and previous negative results, a transperineal cognitive fusion-guided biopsy was performed, combining MRI-targeted and systematic sampling. Histopathological evaluation identified a 0.55 mm focus of acinar adenocarcinoma with a Gleason score of 7 (3+4). Conclusion: This case illustrates how cognitive fusion-guided biopsy can detect clinically significant prostate cancer in patients who have undergone prior negative standard biopsies. The technique improves diagnostic detection rates and represents a valuable, accessible alternative for centers without computer-assisted fusion platforms.

KEYWORDS: *Prostate cancer, cognitive fusion biopsy, multiparametric MRI, PSA, Gleason score, transperineal.*

Introduction

Across Europe, prostate cancer has become the most frequently diagnosed cancer in men, with around 71,000 lives each year and affecting more than 340,000 new patients and even in regions with advanced screening and healthcare, this disease remains a major public health challenge [1].

Serum Prostate-Specific Antigen (PSA) remains the key element of prostate cancer screening, serving as a simple yet highly useful biomarker that enables early detection of men at increased risk for the disease.

Large randomized trials, including the European Randomized Study of Screening for Prostate Cancer (ERSPC) [2], have demonstrated that PSA-based screening can reduce prostate cancer mortality by up to 21%, and more recent analyses confirm that regular, structured PSA testing further enhances early detection of clinically significant cases, potentially lowering mortality by as much as 40% under optimal screening conditions [3].

Prostate biopsy remains an essential procedure in the diagnostic pathway of prostate cancer, enabling clinicians to confirm malignancy and distinguish it from benign conditions, while recent advances in imaging and biopsy techniques have improved the accuracy and reliability of diagnosis [4].

The introduction of mpMRI has significantly reduced the risk of prostate cancer underdiagnosis by enabling more precise lesion localization and guiding targeted biopsies toward clinically significant tumours that might otherwise remain undetected [5].

This paper presents a clinical case of prostate adenocarcinoma diagnosed through transperineal cognitive fusion-guided biopsy after multiple previous negative prostate biopsies performed using conventional techniques.

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Case Report

A 69-year-old male with a medical history of grade II arterial hypertension under treatment and previous nasal septum deviation surgeries (2010 and 2017) was evaluated in another medical centre in February 2022 for lower urinary tract obstructive symptoms.

Laboratory tests revealed a PSA level of 26.17ng/ml. DRE showed a diffusely enlarged, elastic prostate, and the diagnosis of acute prostatitis was established.

The patient received antibiotic, anti-inflammatory, and alpha-blocker therapy, with favourable clinical evolution. At that time, no suspicion of malignancy was raised.

In July 2024, during a routine evaluation at the same medical centre, PSA was 7.24ng/ml, with a prostate volume of 65cm³ and a PSA density of 0.11.

DRE revealed no findings suggestive of malignancy, but given the persistently elevated PSA in the "gray zone," a mpMRI of the prostate was performed.

The result described a PIRADS 3 lesion located in the transitional zone of the right prostatic lobe.

A transperineal systematic biopsy was performed, showing benign prostatic hyperplasia with adenomatoid proliferation.

A six-month PSA follow-up was recommended.

In February 2025, the patient presented with a PSA of 8.08ng/ml, prostate volume of 69cm³, and PSA density of 0.11.

Considering the increased PSA velocity, a transperineal saturation biopsy was performed, again revealing benign prostatic hyperplasia.

Another six-month follow-up was advised.

In July 2025, the patient presented to our outpatient department, at the Emergency County Hospital of Craiova, with a PSA of 8.68ng/ml, prostate volume of 69cm³, and PSA density of 0.12. DRE revealed no suspicious areas.

A new mpMRI, interpreted by a different radiologist, showed a similar PIRADS 3 lesion in the transitional zone of the right lobe.

Given the PSA trend and stable imaging findings, a transperineal cognitive fusion-guided prostate biopsy (Figure 1) combined with systematic sampling was performed, with samples processed in separate batches.

Figure 1. Procedure-Transperineal cognitive fusion biopsy.

Histopathological examination of the cognitively targeted fragments revealed high-grade prostatic intraepithelial neoplasia (HGPIN) and partial glandular atrophy on the lesion from the right lobe.

The pathologist recommended immunohistochemical testing for differential diagnosis.

The final report, issued on October 29, 2025, confirmed a 0.55mm focus of acinar adenocarcinoma with a Gleason score of 7 (3+4), corresponding to International Society of Urological Pathology (ISUP) grade group 2.

A definitive diagnosis of acinar prostate adenocarcinoma was thus established-the first malignant finding after multiple negative biopsies performed in other centres.

The patient was referred for robotic-assisted radical prostatectomy with curative intent.

Discussion

Prostate biopsy has evolved significantly over the past century, adapting to advances in imaging and diagnostic precision [6,7].

Early finger-guided and open transperineal approaches were gradually replaced by ultrasound-guided systematic transrectal

biopsy, which became the diagnostic standard after the work of Hodge and colleagues in 1989 [8].

Although this technique improved detection rates, it remained limited by sampling errors, infection risk, and poor access to anterior and transitional zones.

The reintroduction of the transperineal route, refined through modern imaging guidance, has provided safer access to all prostate regions and reduced post-biopsy complication.

Today, continuous technical improvements-particularly the integration of mpMRI and fusion-based targeting-have transformed prostate biopsy into a precise, minimally invasive procedure for prostate cancer diagnosis [9].

The concept of cognitive fusion biopsy, also described by Sonn et al. in 2014, introduced a practical approach that relies on the operator's ability to mentally correlate MRI-identified lesions with real-time ultrasound images, offering a cost-effective alternative to software-based fusion systems.

This technique is particularly valuable for centres that lack access to computer-assisted fusion platforms, which remain limited by their high acquisition and maintenance costs [10].

Traditional transrectal ultrasound-guided prostate biopsy (TRUS-B) has long been the standard diagnostic approach, yet its limitations in accurately detecting clinically significant prostate cancer are well established.

In the landmark PROMIS study, TRUS-B demonstrated a sensitivity of only 48% for clinically significant disease, missing more than half of such cancers when compared to the reference standard of transperineal template mapping biopsy [11].

This underlines that many patients with aggressive prostate cancer remain underdiagnosed, while others undergo unnecessary biopsies or receive a diagnosis of clinically insignificant tumours.

Several studies have demonstrated that conventional transrectal ultrasound-guided prostate biopsy (TRUS-B) frequently underdetects clinically significant prostate cancer while overdetecting indolent disease.

In a comprehensive meta-analysis including 16 studies and 1926 men, Schoots et al. reported that MRI-targeted biopsy detected a higher proportion of clinically significant cancers compared with TRUS-B (91% vs. 76%), while the detection of insignificant tumours was substantially lower (44% vs. 83%).

These findings highlight the diagnostic limitations of the standard systematic approach, which may miss up to one quarter of clinically relevant cancers despite extended sampling protocols.

Consequently, the integration of mpMRI and targeted biopsy pathways offers a more accurate and balanced method for identifying significant prostate cancer while minimizing unnecessary interventions [12].

In our case, the cognitive fusion-guided biopsy made the crucial difference.

The patient had undergone several standard biopsies, including a saturation biopsy, all of which failed to detect any malignancy despite a persistently elevated PSA.

When the cognitive fusion approach was finally applied, matching MRI findings with real-time ultrasound, a small focus of adenocarcinoma was identified in an area repeatedly missed by conventional sampling.

This case shows how cognitive fusion can uncover clinically significant cancers that remain hidden with traditional techniques and proves its practical value, especially in centres without access to computer-assisted fusion systems.

If the procedure had been further postponed based on the previous negative results, the disease could have progressed to a non-curable stage, emphasizing how essential it is to maintain clinical suspicion and pursue advanced diagnostic methods when PSA levels remain high.

The outcome of this case also reinforces the conclusions of our previous research on transperineal cognitive fusion-guided biopsy, published in 2023.

In that study, we demonstrated that cognitive fusion significantly improved the detection rate of clinically significant prostate cancer compared with systematic biopsy alone, while maintaining a favourable safety profile.

The present case mirrors those findings in everyday clinical practice, confirming that even without access to computer-assisted fusion devices, cognitive fusion can reliably identify small, early lesions that might otherwise remain undiagnosed-allowing patients to benefit from timely curative treatment [13].

Conclusions

This case shows how cognitive fusion-guided biopsy can make a real difference when standard techniques fail.

By combining mpMRI information with real-time ultrasound, it allowed us to detect a

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small but clinically important cancer that previous biopsies had missed.

The method is simple, affordable, and can help doctors in any centre reach a timely and accurate diagnosis, giving patients a better chance at curative treatment.

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Author Contributions

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Conflicts of interest

The authors declare no competing interests.

Institutional Review Board

The study was conducted according to the guidelines of the Declaration of Helsinki.

Consent Statement

The patient provided written informed consent during hospitalization, as well as an additional signed consent for the publication of medical data related to his case. The report was conducted in accordance with the principles of the Declaration of Helsinki.

All data presented in the manuscript are available from the authors upon request.

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