MRI to Ultrasound Cognitive Targeted Prostate Biopsy Provides All the Benefit of Ultrasound Fusion Without the Increased Resources

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A Diagnostic Dilemma

In 2013, the American Urological Association (AUA) set out to maximize the clinical utility of the diagnostic prostate biopsy[1]. Goals included maximizing detection of clinically significant prostate cancer (csPCa), minimizing over-detection of clinically insignificant prostate cancer (ciPCa), and decreasing cost to the patient and the system. Historically, systematic template biopsies resulted in over-detection and overtreatment of ciPCa. The goal of prostate biopsy has shifted from merely identifying prostate cancer towards diagnosing only csPCa. Use of MRI to risk-stratify patients before biopsy and targeting regions of interest identified on MRI increases detection of csPCa, while minimizing detection of ciPCa[2]. MRI targeted biopsies have been developed in 3 different modalities: cognitive targeted biopsy (COG-TB), MRI to ultrasound fusion targeted biopsy (FUS-TB) and in-bore. The most common modalities are FUS-TB and COG-TB. Despite multiple studies attempting to answer this question, debate remains over which method yields superior results.

FUS-TB is expensive, time-consuming, and resource-limited, and has not been definitively shown to improve diagnostic accuracy over COG-TB. Arguments for FUS-TB include a shorter operator learning curve, and a trend toward improved detection of csPCa. There is no or low-quality evidence supporting these claims. FUS-TB creates a significant burden on the health care system, while COG-TB is a simple and low-cost procedure. This commentary presents an argument for COG-TB to remain standard of care when completing diagnostic prostate biopsy.

A Brief Literature Summary

In the seminal PROFUS trial by Wysock et al., cancer detection rates of FUS-TB were compared with COG-TB. Men with suspicious lesions on MRI (n = 125) underwent transrectal FUS-TB, then had 2 COG-TB cores collected with standard template 12-core biopsy. Detection of cancer and csPCa was not significantly different between FUS-TB and COG-TB (32.0% and 20.3%; 26.7% and 15.1%, respectively)[3]. FUS-TB did show increased detection of csPCa in the anterior transition zone and in small lesions detected on MRI. The study was not powered to detect differences in tumor location or size; therefore, interpretation of results must be made with caution.

In 2019, the SmartTarget Biopsy Trial assessed concordance between COG-TB and FUS-TB. Patients with a discrete lesion of PI-RADS 3-5 were enrolled, and 129 patients had both biopsies performed. Each modality detected 86% of csPCa[4]. Notably, each missed 14% of csPCa that was detected by the alternate modality.

In 2020, a systematic review and meta-analysis by Watts et al. identified 9 studies (N = 1714) undergoing MRI targeted biopsy[5]. Studies included transperineal and transrectal biopsies, although findings were unchanged when transperineal biopsies were removed from the analysis. They did not find a statistically significant difference in odds

ratios for overall and csPCa detection (OR 1.11, 95% CI 0.91 to 1.36, $P = 0.30$ and OR 1.13, 95% CI 0.89 to 1.44, $P = 0.32$, respectively)[5]. The authors of this meta-analysis were unable to stratify their data based on user experience and did not assess the detection of ciPCa.

In a recent study by Izadpanahi et al., FUS-TB was compared with COG-TB in a randomized controlled trial (n = 199)[6]. This trial showed a significantly higher detection of overall and csPCa for FUS-TB (44.4% and 33.3%, respectively) compared with COG-TB (31.0% and 19.0%, respectively)[6]. However, a higher detection rate of BPH was reported in the COG-TB versus the FUS-TB group (66.0% versus 47.5%). No subsequent analysis was completed on prostate size despite a known inverse correlation between size and cancer detection[7]. This critical methodological flaw again limits interpretation and generalizability of the results.

Putting the Numbers into Context

No strong evidence exists suggesting FUS-TB is superior to COG-TB. COG-TB is simple and cost-effective, whereas FUS-TB is cumbersome and costly. Operation of FUS-TB requires significant infrastructure including equipment maintenance, image acquisition/segmentation, data processing, and device operation.

The PROFUS study suggests distinct situations (anterior transition zone and smaller lesions) in which FUS-TB may be beneficial. However, this study was not powered to make such conclusions. Regarding size, targeting accuracy for FUS-TB has been studied, claiming accuracy for lesions ≥ 3 mm. The authors recognize that the study's ex vivo prostate models do not fully represent critical in vivo conditions, given the model's sharper image contours, and the lack of tissue movement and deformation seen during in vivo biopsy[8]. Further, prostate cancer may exist within 10 mm of a lesion detected on MRI, allowing a larger target for small radio-graphic lesions for FUS-TB and COG-TB alike[9]. Press et al. showed that targeting hypoechoic regions in close proximity to an MRI identified region of interest independently predicts detection of csPCa[10]. Hypoechoic regions can be identified and directly applied to the COG-TB technique, improving biopsy success rates. With a mean target size of 12 mm (IQR 8 to 15mm)[2], 75% of lesions are greater than or equal to 8 mm. This suggests FUS-TB might provide benefit for only a minority of cases, and certainly should not be widely adopted as standard of care for all MRI identified prostate lesions.

The SmartTarget Biopsy Trial showed both modalities missed an equal number of csPCa[4]. The meta-analysis by Watts et al. showed no significant difference between the 2 modalities, and no conclusions can be drawn about the benefits of a faster learning curve for FUS-TB[5]. One study does compare operator learning curves between FUS-TB and COG-TB. The authors show that an experience plateau is reached more quickly with FUS-TB than with COG-TB[11]. However, only 3 operators were compared in a retrospective manner, introducing selection bias. Further, transrectal approach was used for all COG-TB, whereas transperineal was used in 55% of FUS-TB, introducing significant heterogeneity into the sample, risking confounding the results. Finally, the randomized controlled trial by Izadpanahi et al. shows a difference between FUS-TB and COG-TB. This study is significantly limited by its discrepant BPH findings and lack of prostate size reporting, despite a known inverse correlation between prostate size and cancer detection rates[6].

Returning to the AUA's 2013 mandate, data suggest that FUS-TB does not maximize detection of csPCa, minimize over-detection of ciPCa, or decrease cost to the patient and the system. Therefore, COG-TB should remain the standard of care for targeted diagnostic prostate biopsy until clear evidence suggests otherwise.

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