EDITORIAL

Standardizing targeted and perilesional biopsy: considerations and challenges

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We thank Dr. Jiang for the letter regarding our review. The specific considerations for focal therapy are beyond the scope of this reply, as they are extensively discussed in our review [1]. In their recent well-conducted prospective randomized-controlled trial on biopsy naïve patients, they demonstrated that regional saturation biopsy (RSB), defined as a 9-core sampling technique targeting mpMRI-identified lesion and perilesional area, outperformed targeted biopsy (TB) (2–4 cores obtained through software-driven MRI-US fusion TB (FUS-TB)) alone and systematic biopsy alone (SB) (12–16 cores, including ipsilateral and contralateral side). The respective clinically significant prostate cancer (csPCa) detection rates were 44.1% for RSB compared to 31.8% for TB ($p = 0.01$) and 34.1% for SB ($p = 0.03$). When comparing RSB to the conventional TB + SB strategy, they found a similar csPCA detection rate (44.1% vs. 40.7%, $p = 0.3$) between both groups [2].

The results of this study provide additional high-quality evidence supporting recent changes introduced in the EAU 2024 update, which recommends the use of TB combined with perilesional biopsy (PLB) while allowing for the omission of contralateral systematic biopsy in presence of a PI-RADS ≥ 4 lesion, or PI-RADS ≥ 3 lesions with high clinical suspicion of csPCA [3].

Several terms, that may be confounding due to their similarity yet contain distinct differences, are used in the literature to describe PLB, including "regional biopsy", "zonal biopsy", "regional saturation", "perilesional biopsy" and "ipsilateral systematic biopsy". All these terms describe the concept of sampling not only the region of interest (ROI) but also an additional extended tissue zone to account for underestimation of MRI findings and targeting errors during TB. Interest in the TB + PLB sampling has been increasing and a recent systematic review showed no difference in its csPCa detection rate compared to the previously widely accepted TB + SB strategy (44.2% vs. 46.1%, $p = 0.07$) while TB + SB was associated with a higher detection of insignificant prostate cancer (OR 1.18, $p = 0.008$). However, due to heterogeneity in practice, no standardized or preferred technique has yet emerged as the leading approach [4]. The sampling technique used by Jiang et al., was well standardized, utilizing a reproducible a 9-core template guided by a brachytherapy grid, tailored to the ROI location (transitional, peripheral zone and anterior zones), thereby providing a valuable framework for future research [2].

Several key challenges remain to be addressed to further standardize the TB + PLB approach using the transperineal technique. First, regarding equipment, many urologists do not employ a brachytherapy grid for biopsy. The transperineal freehand (FH) technique, which avoids a mechanical arm while still enabling FUS-TB, has been described as feasible under local anesthesia in large patient cohorts by Marra et al. [5] Interestingly, Urkmez et al. suggested that an FH technique combined with a needle-guide assistance system could achieve a similar csPCa detection rate compared to a brachytherapy grid while reducing the risk of urinary retention [6] The FH technique also offers the advantage of real-time needle direction adjustments, which can be beneficial in cases where symphysis collision occurs in patients with larger prostates or anterior lesions, making grid use challenging. Second, reproducibility remains a concern. The authors reported that 9-core RSB was performed using cognitive fusion by an expert who had conducted over 1000 biopsies. While a brachytherapy grid may enhance reproducibility, it remains unclear whether cognitive fusion alone is sufficient for less experienced urologists, particularly in patients with larger prostates or smaller lesions, or whether additional guidance such as FUS-TB is required. Third, the definition of the "penumbra" in PLB requires further clarification. It is uncertain whether the penumbra should be defined as a fixed distance from the ROI border or determined on a patient-specific basis using factors such as the PI-RADS score and PSA density. Conflicting results have been reported between Brisbane et al. and Noujeim et al. regarding the spatial distribution of csPCa and its correlation with PI-RADS scoring [7, 8].

Fourth, the optimal number of biopsy cores remains a subject of debate. A recent narrative review by the EAU-YAU Prostate Cancer Working Group, focusing on studies aimed at optimizing the number of cores in focal saturation biopsy, suggested that a minimum of five cores, comprising both TB and PLB, is necessary to achieve a 90% csPCa detection rate. However, multiple factors may influence the optimal number of cores, including MRI findings (number of foci), prostate volume, tumor diameter, PI-RADS score, clinical suspicion of prostate cancer, lesion location, prior biopsy history, and the experience of the urologist. Consequently, recommendations have varied between ≤3 and >5 cores [9]

With the adoption of new biopsy strategies, new challenges arise. One major challenge is the need for an adapted risk classification that accounts for the intensive regional sampling performed in these newer biopsy strategies. For example, the transition from the 2014 ISUP grading system (highest Gleason grade) to the 2019 ISUP recommendations (aggregate Gleason grade) has been associated with lower rates of downgrading at radical prostatectomy and improved grade concordance, thus reducing overgrading during initial staging [10]. Another challenge involves developing new nomograms to evaluate the need for extended pelvic lymph node dissection based on unilateral sampling. Finally, omitting contralateral biopsy may complexify operative strategy, especially when intra-fascial nerve-sparing surgery is considered.

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OW: writing of the manuscript. MV and JDLR: critical revision.

COMPETING INTERESTS

The authors declare no competing interests.