Targeted Prostate Biopsies: The Complexity Behind a Simple Concept

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The price for the reduction in prostate cancer mortality brought about by prostate-specific antigen (PSA) screening [1] is the increase in overdiagnosis of indolent cancers, with the associated risk of exposure to overtreatment. PSA has taken the brunt of the criticism, but equally to blame is our current nontargeted, random, transrectal ultrasound (TRUS) biopsy. Random sampling at biopsy affects diagnosis and treatment planning. Biopsy Gleason score is upgraded in up to 40% of cases at radical prostatectomy [2], and because therapeutic management is dependent on accurate biopsy Gleason assignment, this could potentially result in undertreatment due to incorrect risk attribution. Technological and software developments in the past 10 yr have finally given prostate specialists the ability to identify cancerous lesions, with good diagnostic performance using multiparametric magnetic resonance imaging (mp-MRI). The sensitivity and negative predictive values of mp-MRI are >90% when assessing large and poorly differentiated cancers [3].

With the ability to pinpoint highly suspicious areas at mp-MRI, the next logical step would be the targeted biopsy. As shown by Pokorny and colleagues [4] in the current issue of European Urology, targeted prostate biopsies outperform standard ultrasound-guided strategies. Overall, fewer cancer diagnoses were made, but almost all of them consisted of identifying intermediate- or high-risk disease. Similar results were recently reported by Siddiqui and colleagues [5], who, instead of conducting in-bore magnetic resonance imaging (MRI)-targeted biopsies, relied on real-time MRI-TRUS fusion performed in a clinic setting.

To further support the use of MRI-guided biopsies, a recent modeling study in Europe estimated the cost of this strategy to be just 31 euros more expensive than the standard method [6]. In addition, implementing MRI to identify biopsy targets could potentially prove cheaper when accounting for a reduction in the rate of overdiagnosis and overtreatment.

Facing a novel and potentially better diagnostic strategy, we need to emphasize certain critical aspects if the reader is considering starting such a program. First, targeted biopsies are image-based procedures, thus acquisition and interpretation of mp-MRI must be optimized, standardized, and performed by experienced prostate radiologists. Attaining high-quality images is strongly dependent on the machinery (ideally, 3 tesla with an endorectal coil [3]) and the acquisition protocols utilized. Great interreader variability exists between radiologists, and dedicated training can reduce such heterogeneity in interpretations [7].

Second, is the in-bore targeted biopsy approach better than the TRUS-MRI fusion technique? Both require experience and training because targeted biopsy is truly an art as much as it is a science. In-bore biopsies have the advantage of visualizing the actual target imaged by MRI without distortion of the image or registration mismatch, as can occur with fusion biopsies. In-bore biopsies consume more “magnet” time and hence reduce the available time for revenue-generating diagnostic scans. In contrast, MRI-TRUS fusion systems depend on accurate segmentation and registration, potentially inducing several other variables that may contribute to targeting error, especially when pursuing smaller lesions. MRI-TRUS fusion machines theoretically allow any trained urologist to perform targeted biopsies, provided that an appropriate mp-MRI has been conducted and reasonable targets have been delineated. Fusion biopsies are quicker, allow for additional random biopsies,
and may increase wider adoption of the technique by urologists. Indeed, machine availability and access, prices of mp-MRI and fusion systems, and third-party reimbursement vary greatly among countries and health care systems and may account for practice preferences.

Third, patient selection is fundamental. For example, high-risk patients who present with high PSA values and advanced clinical stage might benefit simply from conventional biopsies, whereas men with elevated PSA and prior negative TRUS biopsies or patients interested in organ-sparing procedures or active surveillance might need more comprehensive assessment of their tumor burden. Furthermore, new definitions of significant cancer obtained by targeted biopsy need to be determined. Targeted biopsies will most likely result in an increase in positive cancer cores, and the percentage of involvement may be related to criteria different from those applied to cores from random sampling. Pokorny and colleagues proposed a novel classification of risk-stratifying biopsy results (Supplemental Fig. 1 in their study) [4], but this needs to be further validated.

Finally, when developing a diagnostic mp-MRI and targeted biopsy program, the urologist and the radiologist need to foster cooperation at all stages of the process, including target identification and patient counseling and, importantly, postbiopsy analysis based on histopathology. Radiologists need to report regions of interest in a standardized format, such as the Prostate Imaging Reporting and Data System (PI-RADS) scoring system [8], so that the urologist and the patient have realistic expectations, including understanding the implications of a negative targeted biopsy. As clearly reported by Pokorny et al. [4], lesions with lower PI-RADS scores are less likely to harbor significant disease or cancer at all.

We are currently witnessing the dawn of a new era of prostate cancer diagnosis, thanks to the implementation of mp-MRI. If targeted biopsies become the gold standard, we need to ensure that they have a standardized technique, are advantageous in economic terms, and are readily available. Only then can we can state that prostate cancer diagnosis has truly improved and can be embraced in the general community setting.

Conflicts of interest: Thomas J. Polascik is a member of the board of the COLD registry and a consultant for Endocare. He is also an investigator for a clinical trial on Nanoknife (Angiodynamics). Niccolò M. Passoni has nothing to disclose.

References