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Platinum Opinion

Transperineal Prostate Biopsy Is the New Black: What Are the Next Targets?

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1. Introduction

The latest European Association of Urology (EAU) recommendations (https://uroweb.org/guideline/prostate-cancer/) advocate the use of transperineal (TP) biopsies as the preferred technique for diagnosis of localized prostate cancer (PCa). The lower rates of infectious complications [1] and hospital readmission [2] for sepsis after TP prostate biopsy support the switch from transrectal (TR) biopsy to the TP approach. This change in practice raises many challenges that the urology community will need to address in the coming years.

2. Biopsy quality

High-quality data evaluating the accuracy of TP biopsy versus TR biopsy are scarce. One meta-analysis summarizing the finding from four studies revealed that the TP route detected more clinically significant PCa (csPCa) than the TR route on magnetic resonance imaging (MRI)-targeted biopsy (62% vs 41%, especially in detecting tumors located in the anterior zone of the gland) [3]. These results were confirmed by Ber et al. [4], who reported that TP fusion biopsies were noninferior to TR fusion biopsies in detecting csPCa within MRI-visible index lesions. However, no randomized controlled trial comparing the two routes has been published to date. Moreover, beyond biopsy accuracy, measured as the detection rate for csPCa, other objective and reproducible metrics for assessing biopsy quality remain to be defined. Further studies comparing the upgrading and downgrading rates for TP and TR targeted biopsy would be helpful for better assessment of biopsy accuracy. Nevertheless, recent studies tend to show that MRI-targeted TP biopsies may be at least as effective as TR biopsies, but may also be superior in the case of anterior lesions, as a first-line choice and as a requalification tool in cases of discordance between TR biopsies and MRI features [5].

3. Change of sampling plane

While TR biopsies sample the prostate in an axial plane because of the orientation of the needle and the probe, TP biopsies allow coronal sampling, parallel to the rectum. In the case of small glands, a single biopsy core will probably recover prostatic tissue from the apex to the base. Lack of orientation of the biopsy core may lead to uncertainty regarding the exact cancer location. This may lead to inaccurate orientation and suboptimal management when focal therapy is planned, particularly for modalities with a TR route, such as high-intensity focused ultrasound. This shortcoming could be overcome by anchoring the core to provide orientation for pathological analysis. Otherwise, the pathologist would not be able to provide a detailed location of the PCa and the clinician would have to rely solely on MRI to locate it. Conversely, a large prostate can be troublesome in terms of adequate access to the anterior areas of the gland because of potential interference from the pubic arch [6], which has mostly been described in the setting of TP prostate seed brachytherapy with TR ultrasonography. This hurdle can be overcome by increasing the pelvic rotation from the supine to the lithotomy position, as well as upward orientation of the needle tip, resulting in less inter-

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ference from the pubic arch [7]. However, such a maneuver may be challenging in cases performed under local anesthesia.

4. The issue of systematic biopsy template

Systematic biopsy combined with targeted biopsy remains the gold standard for PCa diagnosis in biopsy-naïve patients. However, the axial sampling pattern for the prostate gland, with six biopsies on each side for sampling of the medial and lateral parts of the apex, middle, and base of the prostate, is not transferable in its current format to the TP approach. To date, there is no consensus regarding validation of a TP systematic biopsy template, mainly because the number of biopsies needed to reach the same detection level is unclear. Beyond the questions related to feasibility, tolerance, and the higher risk of urinary retention, this high number of systematic biopsies also raises the issue of the risk of detecting insignificant cancers and therefore of overtreatment. There is also an increasing use of peri-objective saturation biopsies in the urology community to ensure sampling of the index lesion without increasing overdiagnosis of invisible foci of insignificant PCa.

However, the actual trend for the MRI pathway is to limit systematic sampling of the gland to biopsy-naïve patients in a screening setting [8]. In the future, urologists will have to define the key prebiopsy factors for selection of patients for a targeted-only biopsy protocol. In this setting, many drawbacks of the TP route, such as time, pain, and the risk of urinary retention, would be minimized.

5. Cost-effectiveness

Costs associated with the management and prevention of pain during biopsy have long precluded widespread adoption of TP biopsy by urologists. The duration of the procedure and the need for general anesthesia have been the main drawbacks, driving up the cost of TP biopsy compared to TR biopsy. However, it has recently been shown that TP biopsy is feasible under local anesthesia, with minimal pain and a mean procedure time of 15.9 min [9]. Finally, the added cost of a slightly longer procedure is likely to be offset by the lower need for hospital readmission to treat sepsis. Cost-effectiveness studies including the cost associated with readmission and complications for TP versus TR biopsy should be useful in assessing the real costs and to prompt insurers to provide reimbursement for the full cost of TP biopsy.

6. Infectious challenge

The latest EAU guidelines favoring use of the TP route are mainly based on a meta-analysis of seven randomized studies [1]. Although there was a clear trend towards lower rates of postbiopsy sepsis with TP biopsy, these randomized studies were not designed to evaluate postoperative complications and sepsis, and the antibiotic prophylaxis protocol was not standardized. A multicenter study involving several countries with a wide range of *Escherichia coli* resistance to fluoroquinolones and using a standardized antibiotic protocol would be needed to assess the true benefit of TP biopsy in terms of postoperative complications and readmissions. Moreover, such a study could also assess the need for antibiotic prophylaxis in the TP biopsy population. A recent meta-analysis suggests that antibiotic prophylaxis might not reduce the rate of postprocedural sepsis after TP biopsy [10].

7. Risk of urinary retention

In a recent nationwide population-based study including 73 630 patients, Berry et al. [2] found that use of the TP route would prevent readmission for sepsis for 278 patients at the expense of three additional patients readmitted for urinary retention. In addition, patients who underwent TP biopsy were more likely to have stayed overnight immediately postoperatively than those who underwent TR biopsy (12.3% vs 2.4%; $p < 0.001$). The higher risk of developing urinary retention eventually leading to an overnight stay or readmission might be related to the use of general anesthesia or the greater number of cores retrieved. Recent studies proving the feasibility of TP biopsy under local anesthesia [9] and the tendency to reduce biopsy cores within the MRI pathway [8] should be helpful in minimizing urinary retention and the associated rates of prolonged hospital stay and readmission. However, these hypotheses remain to be validated in future studies.

Conflicts of interest: Morgan Rouprêt is an advisory board member for Arquer Diagnostics, Cepheid, Merck Sharp & Dohme, Nucleix, and Roche. Pierre Mozer has patents for a targeted biopsy device and has been involved in licensing of the Koelis UroStation system. The remaining authors have nothing to disclose.

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