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The Quest for the Optimal Prostate Biopsy Regime for the 21st Century

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The diagnostic landscape for prostate cancer has changed more rapidly over the last few years than ever before. Many of these new insights have developed from the very simple observation that the more samples you take from different areas of the prostate and knowing where to sample improves the accuracy of detection [1]. With these developments, the modern prostate diagnostician has to grapple with a multitude of new conundrums: transrectal versus transperineal, systematic plus targeted or targeted biopsies alone, “cognitive” or software-based image-fusion, the optimal number of biopsy cores, and how to use the biopsy results in pateint management. There are a plethora of papers exploring each of these notions and the dust is yet to settle on what is the optimal biopsy strategy for the future. It also remains to be seen if these new insights, approaches, and use of expensive technology will materially alter prognosis and survival [2].

In recent weeks, two multicentre trials have explored the broader question of systematic plus targeted versus targeted biopsies alone using cohorts of men who underwent both procedures [3,4]. The Dutch 4M study reported that an in-bore magnetic resonance imaging (MRI)-guided biopsy alone was as good as a systematic transrectal ultrasound (TRUS) biopsy in detecting clinically significant prostate cancer (csPC; grade group $\geq$2) [3]. In the same month, the French MRI-First group reported no difference in detection of csPC between MRI-guided biopsy and standard TRUS biopsies [4]. Here, using any one approach only would have missed csPC in 5–8% of cases. 11% of the patients with negative MRI findings harboured csPC, consistent with other published series [5]. Interestingly, the 4M study also found that 4% of csPCs were only detected by TRUS biopsy in men with negative MRI. It therefore falls to a clinician's opinion on whether there is an imperative need to reduce the number of biopsies taken during a procedure and willingness to risk missing some csPCs if only the target is sampled. Notably, both these studies used different types of image-guided biopsy methods..

In this issue of *European Urology*, Hamid et al. [6] add an interesting dimension to the debate by comparing the method via which a lesion is targeted. Using an in-house developed image guidance platform they performed both cognitive and fusion biopsies of the same lesion in a re-biopsy population. They concluded that image-fusion technology did not outperform cognitive biopsies and in fact the highest diagnostic yield was achieved by a combination approach. This suggests that the expertise of the clinician remains crucial despite the availability of advanced image-fusion technology. The extent to which non image-guided biopsies were or were not from a broader area (peritumoural) cannot be ascertained, but this issue feeds into the debate regarding the optimal number of target cores that need to be taken. Lesion size was also not reported, but, intuitively, smaller lesions are likely to need more cores to overcome targeting errors and may better benefit from fusion software, whereas larger lesion might only need cognitive sampling [7]. Although not addressed by this study, transperineal cognitive targeting based on a fixed grid may also be more reliable that a transrectal approach. Assuming that the correct grid position is

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selected, the main targeting error arises only from the *z*-direction, whereas with a transrectal approach, error in any of the three planes is possible.

So where does this leave the quest for the optimal biopsy strategy for the 21st century? Perhaps key to knowing where you are heading is knowing where you have come from. The primary outcome for all the papers mentioned above is detection of csPC. While there may be subtle differences in this interpretation, the generally accepted criterion is any grade group $\geq$2. The rate of csPC reported before the era of MRI and targeting using this definition is in the range 22–49%, depending on whether screening is used [8,9]. The UK National Prostate Cancer Audit (2014–2015) revealed that of 23 835 men with biopsy histology information, 46% had grade group 2 disease and 26% had grade group $\geq$3 [10]. Only 4405 of the entire cohort were known to have undergone prebiopsy MRI. The rate reported for men in recent series of image-guided biopsies is between 25% and 38%, rising to 49% if image-guidance is combined with template transperineal biopsies [4–6]. The underlying population prevalence and the point at which investigations occur in the natural history of the disease may hence have an important bearing on how much incremental benefit image-guided strategies may confer. It is not entirely clear, therefore, that a one-size-fits-all approach will be useful or cost-effective. It may be that image-guided diagnostics (with or without the use of imaging software) may have a role for cases in which prostate-specific antigen (PSA) is low or in the "grey zone", but standard biopsies might suffice for higher PSA or bulky disease. When a biopsy is needed, there is no consensus that a targeted (vs targeted + systematic) or use of fusion software (vs skilled cognitive biopsies) is best practice or whether transperineal or transrectal guided biopsies are equivalent. What does appear to emerge from the paper by Hamid et al. and the MRI-First group is that the optimal approach for diagnosis is probably a combination of lesion targeting (as opposed to image fusion-targeting) and systematic biopsies to get the best diagnostic yield [5,6].

In conclusion, the paper by Hamid et al. reinforces that there remains a strong need for high-quality clinician expertise in prostate diagnostics and technology is unlikely to replace this, at least in the near future. However, technology can augment clinician expertise if resources and capacity allow. The decision to perform MRI in the first place should be treated like the decision to check a PSA, with consideration of the patient's demographics and clinical findings. Similarly, whether or not to perform a biopsy needs individualisation to the clinical context, MRI findings, and equipment available. As it stands, urologists and radiologists should be reassured that their skill is the paramount factor in delivering an excellent diagnostic service that can be achieved even if resources are scarce and fusion technology unavailable.

Conflicts of interest: The authors have nothing to disclose.

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