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Editorial

Saturation Biopsy of the Prostate: Why Saturation Does Not Saturate

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Currently, the adoption of extended, laterally directed, systematic templates for transrectal ultrasound (TRUS)-guided prostate biopsy (PBx) including at least 10 cores is considered the gold standard, since it significantly enhances the diagnosis of prostate cancer (PC) compared to conventional sextant protocols [1,2]. Superextended, equivalently termed *saturation*, schemes have recently been proposed with the aims of further increasing the PC detection rate and, at the same time, of identifying potentially clinically insignificant tumours [3].

The term *saturation PBx* was first coined by Stewart et al [4] to describe the technique developed almost simultaneously with Borboroglu et al [5] in patients with previous negative sextant PBx. These authors obtained up to 45 cores (Stewart et al [4] mean: 23 cores; Borboroglu et al [5] mean: 22.5 cores), and found that the additional value of taking >20 cores in terms of PC detection rate was limited. Thus, a threshold of 22–24 cores for a saturation PBx was arbitrarily set and is still adopted by most contemporary protocols, even in the absence of an univocal quantitative definition. The lack of a semantic standardisation so far likely reflects the inappropriateness of the chosen term.

In physics and chemistry, *saturation* refers to a condition or state in which a substance has reached its plateau concentration. The term implies the concepts of *maximisation* or *optimisation* in that the maximum either possible or desirable quantity is reached and can no longer be affected by additional external influences [6]. To determine this quantity, or, translated into strict mathematical terms, to solve an optimisation problem, specific algorithmic functions can be used to integrate experimental data with

so-called *decisional* variables that need to be calculated in such a way that the solution of the function is eventually maximised [7].

When applied to the field of PBx, saturation should theoretically define a sampling technique aimed at optimising the PC detection rate. This goal should be attained by optimising the basic determinants of the diagnostic yield, that is, the total number of cores to take and the location in the prostate from which to take them. As far as the two factors are concerned, the concept of saturation remains unfulfilled at present. Recent data have, in fact, shown that PC detection rate is high (up to 25%) on repeat PBx, even when superextended 21- or 24-core templates are adopted on initial PBx [8,9]. This finding suggests that this sampling strategy is far from optimal. Moreover, the PC detection rate is apparently similar when an extended template and a saturation template are compared [10].

Some considerations can be advanced to explain this inadequacy.

The first consideration is the number of cores. For a long time, prostate volume has been recognised as one of the main determinants of PBx diagnostic yield [11–13]. The intuitive assumption has definitively been proven that, for a given index cancer volume, the larger the prostate, the higher the number of cores to be taken to diagnose that cancer. The key question, however, still remains unaddressed: How many cores are needed to adequately sample—that is, to saturate—a given amount of prostate tissue to accurately diagnose a focus of PC, if any? It may well be that a given 30-core template is subsaturated or nonsaturated for a 90-cm³ prostate but is supersaturated for a 30-cm³ gland.

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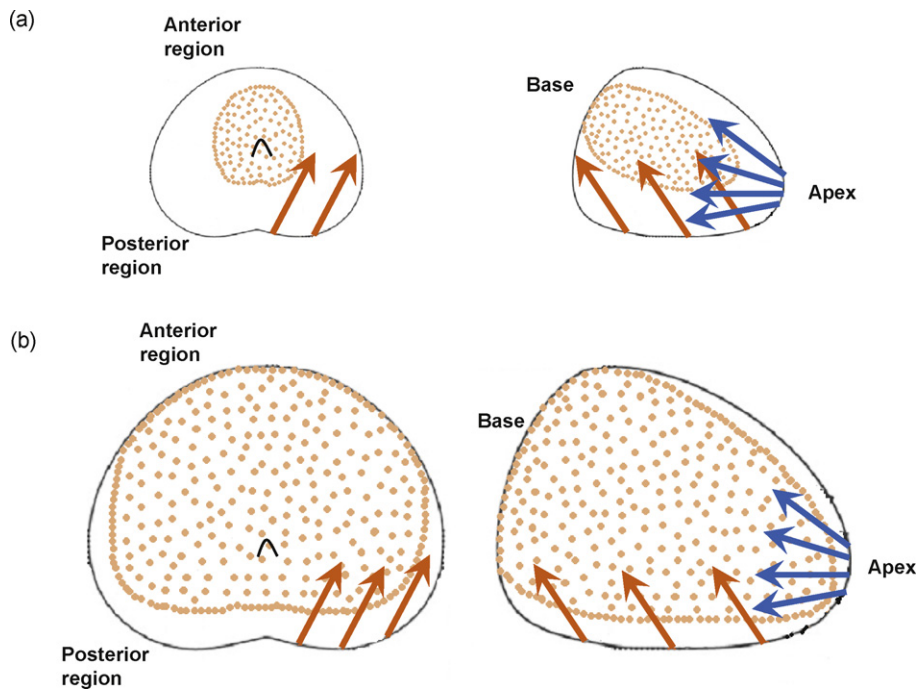


Fig. 1 – Transverse and sagittal view of the prostate showing the course of the needle during sampling of (a) a normal-sized and (b) an enlarged gland. Transrectal route is depicted in orange, and transperineal route is blue. In (b), the peripheral zone (white) is posteriorly compressed and laterally displaced by the enlarged transition zone (orange dots) in such a way that the needle inevitably harvests only a (small) fraction of peripheral zone at most puncture sites. Modified with permission of Elsevier [15].

Furthermore, when the prostate grows—a process solely sustained by transition zone enlargement—the peripheral zone, which predominantly harbours PC, is typically posteriorly compressed and laterally displaced. Consequently, sampling accuracy tends to progressively decrease, not only due to the larger volume itself but also because of the more dispersed and thin distribution of the peripheral zone tissue. These characteristics make a precise directing of the needle at times extremely difficult or simply impossible, even with numerically aggressive sampling (Fig. 1). Apparently, these anatomic and stereotactic issues have received no attention so far.

The second consideration is the location of cores. From repeat PBx studies, it emerges that PC tends to locate more frequently in the lateral and anterior apical regions than in the transition zone [3]. Geometric considerations would dictate that the apex and the anterior region of the prostate are best sampled via the transperineal route, whilst the base is best sampled via the transrectal approach [14,15] (Fig. 2). Almost universally, physicians performing PBx use only one of the two routes. We have convincing, albeit not yet replicated, data showing that a combination of transrectal and transperineal sampling with the intent of saturating all prostate regions may result in an optimisation of PC diagnosis [15]. In other words, a given 30-core transrectal-only (or transperineal-only) template may provide a lower diagnostic yield than a 30-core template in which half of the cores are taken transrectally and half are taken transperineally.

Admittedly, even with improvements in these two areas, certain prostate locations are likely to remain excluded from adequate sampling, possibly due to the inherent limitations of the equipment and technology currently adopted to perform PBx. To circumvent this theoretical

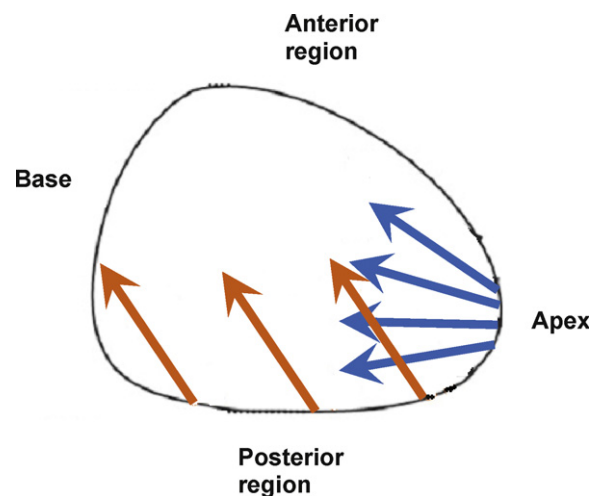


Fig. 2 – Sagittal view of the prostate showing the course of the needle when cores are taken via a transrectal (orange) and a transperineal (blue) route. The base and posterior region are marginally sampled with transperineal punctures, whilst the apex and anterior region are partially excluded with transrectal punctures. Modified with permission of Elsevier [15].

shortcoming, alternative options worth exploring could be, for instance, coupling the firing of the TRUS probe with variable angles of needle firing to better direct sampling or simply using longer sampling needles to obtain a larger amount of tissue (up to 3 cm in length) per single core [16].

It remains understood that if the intention is an optimisation of the PC detection rate, statistical analyses based on the aforementioned mathematical optimisation functions, such as the recursive partitioning models, are the most appropriate tools to gain advances in the field. Moreover, it is imperative that data from autopsy prostates are gathered to learn the true prevalence of the disease [17,18].

When a real saturation template is eventually conceived, then the question will arise: How can the required number of cores be uniformly spaced in the desired locations of the prostate during sampling? Initial data lend support to the speculation that grid-like devices constructed with the aid of three-dimensional computer simulation programmes will be required to automatically guide the needle with precision [19].

A further matter of debate will complicate this scenario: To what extent will the real saturation template help us diagnose potentially biologically indolent PC? This is hardly predictable, since the current definition of clinically insignificant PC at PBx will almost certainly decay once this optimised template is introduced into clinical practice. In this context, we share with great conviction the view expressed by Dr Jones in his recent editorial in the *Platinum Journal* [20]. The real issue with PC screening is not overdiagnosis, since there exists only diagnosis or misdiagnosis, but potential overtreatment. Consequently, we believe that urologists should make all efforts to diagnose PC when faced with this task, but at the same time, they should identify and treat only the harmful cancers.

In conclusion, further research is warranted to maximise the diagnostic yield of TRUS-guided PBx. Individualising the sampling template to the size, shape, and zonal anatomy of the gland seems like the right path to pursue. Only when such a protocol is devised can the term *saturation PBx* be rightfully used.

Conflicts of interest: The authors have nothing to disclose.

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