



Editorial – referring to the article published on pp. 266–271 of this issue

## Systematic Prostate Biopsies Are More And More Often Becoming Saturation Biopsies

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The transrectal ultrasound (TRUS) prostate biopsy techniques have changed drastically over the years from the original Hodge sextant biopsy protocol. Before the end of the second millennium, several authors had already shown limitations in cancer detection with sextant biopsy and had reported high rates of false-negative biopsies. Thus, Hodge's scheme became soon obsolete. In the last 5 yr, different prostatic schemes with 8 or 10 or 12 biopsies have been proposed as a new standard of reference, as emerging evidence suggested that taking >6 biopsies might have significantly increased the rate of cancer detection [1].

Nevertheless, prostate cancer detection is still an area currently fraught with many unanswered questions and much controversy. The optimal number of biopsies needed to identify all patients with prostate cancer at the earliest stage possible for optimal treatment, outcome, and survival is still not known. Prostate volume is one of the factors that may influence the prediction of cancer at first biopsy. There is a significant inverse relationship between the cancer detection rate and prostate volume and it has been shown that the yield of sextant biopsy decreases with increasing prostate volume. Mathematical models and computer simulation of prostatic biopsies demonstrate that it is necessary to increase the number of biopsies according to prostate volume especially in younger patients [1]. However, it is not clear how many

additional cores should be taken beyond the extended approach in larger prostates to increase the cancer detection rate. Recently, Ficarra et al. demonstrated that a scheme with eight cores turned out to be appropriate in patients with prostates smaller than 30 cc. On the other hand, in prostates >50 cc, an extended procedure with >12–14 cores is mandatory, even if the authors were not able to define the exact number of cores [2].

The role of biopsy of the transition zone (TZ) is still controversial [3]. The literature reports some evidence that the benefit of TZ biopsy for cancer detection at the time of first biopsy seems to be of low value, whereas others support the use of TZ biopsies only in patients with prior negative biopsies and a persistently elevated serum prostate-specific antigen (PSA) level [4]. When performing TZ biopsies, the detection rate may increase from 0% to 4.2%. In selected cases with a high PSA value (>10 ng/ml) without clinical suspicion of positive nodules on digital rectal examination (DRE), TZ biopsies may be useful at initial biopsy [5]. On the contrary, Pelzer et al. do not support the use of TZ biopsies even in patients with prior negative biopsies [3].

To increase accuracy of prostatic biopsy, new imaging techniques, such as contrast-enhanced imaging, power Doppler imaging, tissue harmonic imaging, computer-assisted determination of gray-scale images, and four-dimensional imaging can be

successfully adopted, but their routine use is still controversial. With the intensive use of PSA testing, the majority of prostate cancers are detected without any abnormalities on conventional TRUS and it also unlikely that new imaging techniques will be able to detect microscopic alterations.

For all these reasons, there is a worldwide tendency to perform prostatic biopsies with an increasing number of cores. The concept of saturation biopsy (from 15 to 45 cores) under general anesthesia has been introduced and widely adopted in cases of rebiopsy. The recent introduction and refinement of local anesthesia has allowed application of the concept of saturation biopsy in the outpatient setting and to increase, even more, the number of biopsies taken (from 10 to 18 or 20) without increasing the discomfort and pain of the patients. To date, two local anesthesia techniques are currently available during TRUS-guided biopsy: local anesthesia with 2% lidocaine gel and periprostatic nerve block. Topical anesthesia with lidocaine gel (2%) in the rectum has been reported to have controversial results versus placebo and, in randomized studies, topical anesthesia was reported to be inferior to periprostatic lidocaine injection [6,7]. Periprostatic nerve block during TRUS prostate biopsies has been reported to guarantee the best pain control in several studies since the first report by Nash et al. in 1996. Despite the variability of dosage and location of infiltration, the periprostatic lidocaine injection is currently the most effective method to reduce pain during TRUS biopsy [7].

Given the worldwide use of local anesthesia in the outpatient setting, extended TRUS prostatic biopsies with 14–18 cores are now becoming the standard technique in most urologic departments. Although it has been emphasized that more extensive biopsy approaches may also detect clinically insignificant cancers, it is considered that the benefit of a higher cancer detection rate might be better than the risk of detecting an insignificant cancer.

Moreover, the increase of sampled tissue may certainly achieve a more complete picture of the disease burden. The diagnosis can be quite difficult for the pathologist given the small samples and the fact that there are many benign histologic lesions that can mimic cancer. Using the multisite protocol, biopsy core information has been evaluated to predict both tumor volume and the presence of extracapsular extension. The number of positive cores, the percentage of positive cores, tumor length, and the percentage of tumor are considered important factors that may predict tumor volume and pathologic outcome. Last but not least, extended prostate needle biopsy has been demon-

strated to improve the concordance of Gleason score between prostate biopsy and radical prostatectomy.

The concept of extended biopsies has been equally applied to the transperineal approach, which has proved to provide the same results as those achieved with the transrectal one.

This issue has been successfully discussed by Ficarra et al. in their paper [8]. They have analyzed the length of the needle cores sampled as a quality indicator, adopting a transperineal approach with 14 cores per patient. Interestingly, the authors have routinely used a multisite approach with 14 cores (12 peripheral biopsies and 2 biopsies of the TZ) since October 2002 when extended transperineal biopsies with >10 cores were not widespread. The authors have demonstrated that the mean length of the cores obtained with a transperineal approach fulfills the quality parameters required by pathologists, that is, a mean length of the biopsy core, measured on the glass slide, longer than 10 mm. Ficarra et al. [8] have concluded that the transperineal approach provides the same quality of tissue than the transrectal procedure. It is also interesting to note that they have routinely performed TZ biopsies with a detection rate of single-sampled prostate needle cores of 7.3% (right) and 9.7% (left), which is half of what they have obtained with the peripheral cores (~18%). Recently, Demura et al. have explored the distribution of carcinoma cores within the prostate and the potential impact of a systematic ultrasound-guided transperineal template biopsy (mean number of cores = 20.1; range, 9–38) on improving detection rates [9]. They have reported that in patients with negative DRE the carcinoma core rate in the anterior region (7.2%) did not differ from that in the posterior region (7.3%). Differences in detection rates between the two studies may be due to patient selection bias but both papers suggest that prostate carcinoma grows throughout the entire prostate in a similar proportion.

Two considerations about the study of Ficarra et al. should be mentioned. First, the authors have shown that the transperineal approach allows correct sampling of the whole gland, but, comprehensively, the transperineal approach allowed a greater sampling of the apex compared to the mid-gland and prostate base. Furthermore, Furuno et al. have shown that, in those patients undergoing repeat biopsy, a template perineal biopsy resulted in a higher detection rate in the anterior region of the prostate [10]. Because most of the patients initially undergo a transrectal biopsy that selects for tumors in the posterior region of the prostate, the transperineal approach might provide a higher detection rate in repeat biopsies than a transrectal one. The value of

such an approach would increase considerably if these results were confirmed in other studies.

Second, Ficarra et al. [8] have shown that the whole mean length of the six samples from the right lobe was higher than the mean corresponding value of the six samples from the left lobe. The authors have explained these results by the fact that the operators extracting the sample, all right-handed, must perform the sampling in the opposite direction to the natural way. Nevertheless, these histologic data did not influence the detection rate, which overlapped in each prostate lobe. These results are very similar to our data adopting a transrectal approach with an extended scheme of 12-16 cores performed clockwise from the right apex to left apex. In our series we have recorded a slight difference between the mean length of the cores of the right lobe compared to that of the left lobe (unpublished data). These results might suggest that the ability of the operator might influence the detection rates, but, at present, no studies have analyzed if other factors, such as experience and skill of the operator to detect suspected area at ultrasound, might have an impact on cancer detection. A template-assisted prostate biopsy (saturation biopsy), recently proposed as initial biopsy, might have the merit of taking cores more evenly from the whole prostate and the outcome might not be too influenced by the skill of the operators.

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