



## Editorial

# Prostate Biopsy and Optimization of Cancer Yield

David G. Bostwick\*, Isabelle Meiers

Bostwick Laboratories, Richmond, Virginia, USA

It is hard to imagine practicing urology and urologic pathologic today without prostate-specific antigen (PSA) and multiple thin-bore needle biopsies, yet these advances only became available in the past 18 years. The old large-bore needles provided considerably more tissue for the pathologist to examine, but suffered from compression artifact on the edges and a small but significant risk of needle tracking of cancer; both problems are circumvented with the smaller-bore biopsy needles used today.

### 1. Burden of the pathologist

A greater number of prostate biopsies are obtained now and more biopsy cores are submitted than ever before and create a huge interpretive burden for the pathologist. More than one million biopsies are performed annually in the United States; each contains an average of 10 cores. This creates an estimated 10 million tissue samples for the pathologist to interpret.

This burden is compounded by a number of factors that have increased the difficulty of prostate interpretation: (1) many patients undergo biopsy for elevated serum PSA with no other evidence of cancer, which results in an enormous number of biopsies that often contain only a microscopic suspicious focus; (2) numerous diagnostic pitfalls of prostate cancer, including atypical adenomatous hyperplasia, post-atrophic hyperplasia, and pro-

static intraepithelial neoplasia, have recently been described, and the high number of prostate biopsy specimens magnifies the risk of encountering rare or unusual lesions and the potential for misinterpreting small foci; and (3) 10 or more biopsies (five or more from each side) have largely replaced the bilateral cores of 15 years ago.

In this issue of *European Urology*, Montironi and colleagues describe the diagnostic and prognostic findings derived from prostate needle biopsies. Their practical approach to biopsy handling and evaluation, which represents centers in Italy and Spain, is virtually identical to that of their counterparts elsewhere in Europe and the United States. This universal agreement by pathologists on diagnostic criteria and results reporting optimizes patient care by allowing valid comparison of results among institutions; it represents the culmination of more than a decade of multidisciplinary cooperation. The report summarizes current areas of controversy that continue to provide fodder for academic exchanges. This paper should be required reading for all students of prostate biopsy use or interpretation and serves as a point of reference on which future discussions can build.

### 2. Detecting cancer: factors that influence diagnostic yield in biopsies

How can we improve the yield of cancer from prostate needle biopsies beyond that described by

DOI of original article: 10.1016/j.eururo.2005.11.022

\* Corresponding author. Bostwick Laboratories, 4355 Innslake Drive, Richmond, Virginia, 23060, USA. Tel. +1 804 967 9225; Fax: +1 804 288 6568.

E-mail address: [bostwick@bostwicklaboratories.com](mailto:bostwick@bostwicklaboratories.com) (D.G. Bostwick).

0302-2838/\$ – see front matter © 2006 Elsevier B.V. All rights reserved. doi:10.1016/j.eururo.2005.12.052

**Table 1 – Factors that influence the detection rate of cancer in contemporary prostate needle biopsies**

Uncontrolled factors
Patient risk factors
Patient population (e.g., screening population vs. urologic practice)
Patient symptoms
Serum PSA
Clinical stage
Patient age
Patient race
Prior biopsy findings (e.g., PIN, ASAP)
Prostate-related factors
Prostate volume
TRUS and other imaging findings
Controlled factors
Urologist-controlled factors
Number of needle cores obtained
Method of biopsy (e.g., random, ultrasound guided, etc.)
Location of biopsy (e.g., laterally-directed biopsies vs. midline, etc.)
Amount of tissue obtained (e.g., biopsy “gun” employed; operator skill)
Pathologist-controlled factors
Histotechnologist’s skill in processing and cutting prostate biopsies
Number of needle cores embedded per cassette
Number of tissue cuts obtained per specimen
Pathologist’s skill in prostate biopsy interpretation

Montironi et al.? Table 1 describes the known variables that influence the diagnostic yield of prostate biopsies. Uncontrollable factors include patient- and prostate-related factors. Controllable factors are invariable biopsy method-related factors that can be modified by the urologist or pathologist to increase the diagnostic yield, and thus deserve additional consideration.

### 2.1. Number of needle cores obtained

The increase from six to 12 cores improved prostate cancer detection by 29% [1]. Eskicorapci et al. noted that 10, 12, and 13 core biopsy strategies increased the cancer detection rate by 25.5%, 22% and 35%, respectively [2]. Mathematical models demonstrate that more biopsy cores increase the chance of prostate cancer detection [3].

### 2.2. Method of biopsy

Technical aspects of prostate biopsy are not standardized. The diagnostic yield of biopsy is improved by ultrasound-targeted biopsies, but the magnitude of the increase in accuracy remains controversial. Fink et al. found that using a 29-mm cutting length increased cancer yield 18% over a 19-mm cutting

length [4]. Watanabe et al. reported that the combination of six transperineal and six transrectal biopsies in the same patient resulted in cancer detection of 48.5%, and the detection rate significantly increased 7.2% and 8.5% compared to the transperineal and transrectal groups alone, respectively [5].

### 2.3. Location of biopsy

Lateral midgland and lateral base biopsy cores had the highest cancer detection rates for all prostate volumes, perhaps because of the extensive sampling of the peripheral zone by lateral biopsies. However, midgland and base biopsy cores had a lower yield in small prostates, probably because of sampling of the central zone in these prostates where the prostate cancer incidence is known to be low [2]. A computer-based model suggests that the cancer detection rate increases 23% with a modified sextant protocol by only directing the needles into the more lateral aspect [3]. Conversely, ultrasound-directed lesion biopsies may be omitted when 10 core biopsy protocols are used, since the yield of these biopsies is less than 2% [2].

### 2.4. Amount of tissue obtained

The detection rate of cancer in sextant needle biopsies is higher as longer single cores are sampled, particularly at the apex [6]. For example, a 20-mm core from the right apex provided a 27% probability of cancer detection versus 18% for a 10-mm core. The amount of tissue obtained by biopsy varies widely, and we found an overall tissue sample (likely to be an inadequate sample) smaller than 50 mm in up to 4% of biopsies [6].

### 2.5. Histotechnologist’s skill in processing and cutting prostate biopsies: prostate

biopsies are particularly difficult to embed and cut because they are small and tend to fragment and curve. Flat embedding of the biopsy cores enhances the amount of tissue that is examined by the pathologist. Laboratories that process prostate biopsies with other tissues of differing density and consistency (for example, breast biopsies with abundant fatty tissue) usually handle all specimens the same way, which often results in prostate biopsies that are overstained or too thick to interpret. Similarly, overstained sections (the most common problem in our consultation practice) contain obscured nuclear chromatin without recognizable nucleoli. These problems are compounded

in biopsies with small foci that are suspicious for malignancy.

### 2.6. Number of needle cores embedded per cassette

Multiple needle biopsies submitted in one or two containers tend to entangle and fragment and are difficult to embed in a single plane during processing. The resulting loss of tissue surface area makes a definitive diagnosis difficult in many cases, and results in equivocal pathology reports [7]. If multiple cores are embedded in one cassette, all must be separated from each other.

### 2.7. Number of tissue cuts obtained per specimen

There is variation between laboratories in the number of serial tissue cuts obtained from each needle core for routine examination. To avoid undersampling, we routinely obtain six cuts (two adjacent sections from three separate levels) from the paraffin block for routine staining; additional intervening sections are placed on another slide and saved for immunohistochemical stains or special studies. In our experience, recutting the block for additional levels with small suspicious foci is useful in only about half the cases.

### 2.8. Pathologist's skill in prostate biopsy interpretation

Pathologists with special interest in urologic pathology have a higher level of accuracy in needle biopsy interpretation and Gleason grading. Interobserver reproducibility of Gleason grading among urologic pathologists was considered "acceptable,"; the greatest differences of interpretation result from low-grade cancer, cancer with small cribriform pattern, and cancer whose histology was on the border between Gleason patterns [8]. The false-negative rate (missed prostate cancer) was 0.6–1.0%, and the false-positive rate (overdiagnosis of prostate cancer) was 0.3%. These numbers indicate a small but significant error level that could be avoided by secondary pathology review [9].

## 3. The future of prostate biopsies

A sample of future trends in prostate biopsy handling and clinical significance is presented in

**Table 2 – Select future trends in prostate needle biopsy reporting and clinical application**

Location of Prostate Cancer
Site-specific labeling
3D mapping
Focal therapy
Quality Assurance in Urology
Quality of biopsies
Number of biopsies
Quality assurance in urologic pathology
Personal Outcome Predictions
Use of neural networks and advanced measures of outcome
Improved understanding of "clinically insignificant" cancer
Molecular Diagnostics from Needle Biopsies

**Table 2.** These anticipated advances should provide a substantial amount of new information from the tiny threads of tissue obtained by biopsy.

## References

- [1] Elabbady AA, Khedr MM. Extended 12-core prostate biopsy increases both the detection of prostate cancer and the accuracy of Gleason score. *Eur Urol* 2006;49:49–53.
- [2] Eskicorapci SY, Guliyev F, Akdogan B, Dogan HS, Ergen A, Ozen H. Individualization of the biopsy protocol according to the prostate gland volume for prostate cancer detection. *J Urol* 2005 May;173(5):1536–40.
- [3] Zeng J, Bauer J, Zhang W, et al. Prostate biopsy protocols: 3D visualization-based evaluation and clinical correlation. *Comput Aided Surg* 2001;6(1):14–21.
- [4] Fink KG, Hutarew G, Pytel A, Schmeller NT. Prostate biopsy outcome using 29 mm cutting length. *Urol Int* 2005;75(3):209–12.
- [5] Watanabe M, Hayashi T, Tsushima T, Irie S, Kaneshige T, Kumon H. Extensive biopsy using a combined transperineal and transrectal approach to improve prostate cancer detection. *Int J Urol* Nov 2005;12(11):959–63.
- [6] Iczkowski KA, Casella G, Seppala RJ, et al. Needle core length in sextant biopsy influences prostate cancer detection rate. *Urology* 2002 May;59(5):698–703.
- [7] Gupta C, Ren JZ, Wojno KJ. Individual submission and embedding of prostate biopsies decreases rates of equivocal pathology reports. *Urology* 2004;63(1):83–6.
- [8] Allsbrook Jr WC, Mangold KA, Johnson MH, et al. Interobserver reproducibility of Gleason grading of prostatic carcinoma: urologic pathologists. *Hum Pathol* 2001 Jan;32(1):74–80.
- [9] Oxley J. Reviewing negative prostatic core biopsies for the multidisciplinary team meeting. *Histopathology* 2005 Dec;47(6):643–4.