Comparison of 8, 10, 12, 16, 20 cores prostate biopsies in the determination of prostate cancer and the importance of prostate volume

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Abstract

Introduction: In this study, we evaluate the relationship between increasing core numbers and cancer detection rate.

Methods: We included 1120 patients with prostate-specific antigen levels ≤20 ng/mL and/or suspicious digital rectal examination findings in this study. All patients had a first-time prostate biopsy with 8, 10, 12, 16, and 20 core biopsies taken and examined in different groups during the study. Multiple logistic regression analysis was made to reach the factor affecting the cancer detection rate between the patients with and without cancer. A p < 0.05 was considered statistically significant.

Results: Out of 1120 patients, 221 (19.7%) had prostate cancer. Again of the total 1120 patients, 8 core biopsies were taken from 229 (20.4%); 10 core biopsies from 473 (42.2%); 12 core biopsies from 100 (8.9%); 16 core biopsies from 140 (12.5%); and 20 core biopsies from 178 (15.9%) patients. The increase in the core number increased the cancer detection rate by 1.06 times (p = 0.008).

Conclusions: As long as prostate volume increases, increasing the core number elevates the cancer detection rate. Thus, the rate of missed cancer will be reduced and the rates of unnecessary repetitive biopsy decreases.

Introduction

Transrectal ultrasound (TRUS)-guided prostate needle biopsy is the gold standard in the diagnosis of prostate cancer. Recently, the detection of localized prostate cancer has improved due to the development of various new biopsy methods.1,2 However, a standard biopsy method, including a number of cores, has not yet been established. In 1989, Hodge and colleagues proposed TRUS-guided sextant prostate needle biopsy.3 Since then, the random, systemic 6-core prostate biopsy has become the most popular biopsy method and has significantly improved prostate cancer detection. However, recent reports have indicated that systematic sextant biopsy might be inadequate for cancer detection.4 This approach is associated with a relatively high false-negative rate of 15% to 31%.5 Groups at many clinics perform extended prostate biopsy strategies consisting of 8 to 13 biopsies since this strategy has not been associated with an increase in morbidity and the number of clinically insignificant prostate cancers.6,7 In addition, Letran and colleagues reported that the sextant biopsy protocol was not appropriate in patients with a prostate gland volume greater than 55.6 cc.8

Several issues arise when considering what constitutes the optimal biopsy strategy for patients with suspected prostate cancer. How many biopsies should be taken to maximize cancer detection? In this study, we compared the cancer detection rates of 8, 10, 12, 16, and 20 core prostate biopsies in patients with suspected prostate cancer and prostate-specific antigen (PSA) ≤ 20 ng/mL.

Methods

Between January 2003 and August 2010, we retrospectively reviewed the charts of 1700 patients who underwent TRUS-guided biopsy of the prostate at the Türkiye Yüksek İhtisas Training and Research Hospital and Elazığ Training and Research Hospital. We excluded patients with previously known prostate cancer, PSA > 20 ng/mL, suspicion of acute prostatitis and a history of cystourethroscopy or urethra catheterization within 1 month. A total of 1120 patients with a serum PSA ≤ 20 ng/mL and/or suspicious digital rectal examination (DRE), who received TRUS-guided biopsy for the first time, were included in the analysis. All the patients in this study were Turkish.

Prostate biopsies were taken from only 1 urologist (CC). Ten minutes before the procedure, each patient was instilled with 20 mL of 2% lidocaine jelly rectally. Patients were
placed in the left decubitus position. Biopsies were done with 18-gauge Tru-cut biopsy needles during longitudinal scanning. All patients were given fluoroquinolone for 3 days, starting on the day of biopsy. Ages, prostate volumes, PSAs, free-total PSA rates, PSA densities (PSADs), numbers of core taken, DREs, Gleason scores of all patients were recorded. The patients were divided into 2 groups as those with cancer and without cancer according to biopsy results.

TRUS prostate volume was calculated using a computer-generated elliptical estimation of $0.52 \times \text{length} \times \text{width} \times \text{height}$. All procedures were performed using a diagnostic ultrasound machine with 7.5 mHz biplanar probe (EUB-420, Hitachi Medical Corp, Tokyo Japan).

In addition to classical sextant biopsy, 4 biopsies were taken laterally directed (lateral apex, lateral midgland, lateral base) (Fig. 1).

**Statistical analysis**

Data analysis was performed by using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL). To determine whether the continuous variables were normally distributed, we used the Shapiro Wilk test. Homogeneity of variances was evaluated by the Levene test. Data were shown as mean ± standard deviation or median (interquartile range) for continuous variables and number of cases and percentages for categorical ones.

Previously, the analyses of prostate volume were categorized by quartiles. The mean differences among prostate volume quartiles were analyzed by one-way ANOVA following post-hoc Tukey test; the Kruskal Wallis test was applied for comparisons of the median values. When the $p$-values from the Kruskal Wallis test statistics were statistically significant, the Conover’s non-parametric multiple comparison test was used to determine group differences.

We used the univariate logistic regression analyses to determine whether the associations between clinical character-

<table>
<thead>
<tr>
<th>Variables</th>
<th>Negative biopsy (n=899)</th>
<th>Positive biopsy (n=221)</th>
<th>$p$ value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.1 ± 7.5</td>
<td>67.1 ± 8.0</td>
<td>&lt;0.001</td>
<td>1.054 (1.033–1.075)</td>
</tr>
<tr>
<td>Volume</td>
<td>50 (31)</td>
<td>40 (24)</td>
<td>&lt;0.001</td>
<td>0.981 (0.974–0.988)</td>
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<tr>
<td>Volume quartiles</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>12–34 (cc)</td>
<td>180 (20.1%)</td>
<td>88 (39.8%)</td>
<td>&lt;0.001</td>
<td>3.352 (2.166–5.188)</td>
</tr>
<tr>
<td>35–47 (cc)</td>
<td>237 (26.4%)</td>
<td>60 (27.1%)</td>
<td>0.017</td>
<td>1.736 (1.103–2.733)</td>
</tr>
<tr>
<td>48–66 (cc)</td>
<td>240 (26.8%)</td>
<td>38 (17.2%)</td>
<td>0.744</td>
<td>1.086 (0.663–1.777)</td>
</tr>
<tr>
<td>67–253 (cc)</td>
<td>240 (26.8%)</td>
<td>35 (15.8%)</td>
<td>—</td>
<td>1.000</td>
</tr>
<tr>
<td>Total PSA (ng/mL)</td>
<td>6.9 (3.88)</td>
<td>8.6 (6.06)</td>
<td>0.002</td>
<td>1.041 (1.015–1.067)</td>
</tr>
<tr>
<td>Free PSA (ng/mL)</td>
<td>1.2 (0.83)</td>
<td>1.0 (0.86)</td>
<td>0.800</td>
<td>0.984 (0.869–1.114)</td>
</tr>
<tr>
<td>Free,total PSA (ng/mL)</td>
<td>0.18 (0.11)</td>
<td>0.15 (0.10)</td>
<td>&lt;0.001</td>
<td>0.021 (0.003–0.180)</td>
</tr>
<tr>
<td>PSA density</td>
<td>0.13 (0.10)</td>
<td>0.21 (0.20)</td>
<td>&lt;0.001</td>
<td>19.628 (7.123–54.091)</td>
</tr>
<tr>
<td>No. cores</td>
<td>11.8 ± 4.0</td>
<td>13.1 ± 4.6</td>
<td>&lt;0.001</td>
<td>1.072 (1.036–1.108)</td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: confidence interval; PSA: prostate-specific antigen.

**Results**

Prostate cancer was found in 221 (19.7%) of the 1120 patients. Of these total number of patients (n =1120), 8 core biopsies were taken from 229 (20.4%), 10 core biopsies from 473 (42.2%), 12 core biopsies from 100 (8.9%), 16 core
Prostate biopsies from 140 (12.5%), and 20 core biopsies from 178 (15.9%) patients. The mean age of patients with benign prostatic hyperplasia (BPH) was 64.1 ± 7.5, and the mean age of the group with cancer was 67.1 ± 8.0 (p < 0.001). While the median prostate volume in the BPH group was 50 cc (range: 12-253), the median volume in the cancer group was 40 cc (range: 14-156) (p < 0.001). While the number of cores taken in patients in whom prostate cancer was detected was 13.1 ± 4.6, it was 11.8 ± 4.0 in the BPH group (p < 0.001). The cancer detection rate decreased from 39% to 15% as long as prostate volume increases.

The cancer detection rates of 8, 10, 12, 16, and 20 core prostate biopsies were 18.3%, 14.8%, 24%, 22.1%, and 30.3%, respectively (Fig. 2). The highest cancer detection rate was achieved with a 20-core biopsy.

The mean prostate volumes and PSA values of the patients according to the number of core are seen in Table 2. The mean prostate volumes of the patients from whom 8, 10, 12, 16, and 20 core biopsies were found as 46.1 ± 18.8 cc, 56.6 ± 26.3 cc, 52.3 ± 29 cc, 49.4 ± 27.5 cc, and 55.1 ± 29.7 cc, respectively (p = 0.0001). A post-hoc analysis was done to determine the differences between groups. While the prostate volumes of the 8-core patients were lower than the 10- and 20-core patients (p < 0.0001), the mean prostate volume of the 10-core patients was higher than volume in the 16-core patients (p < 0.0001). The prostate volumes of the other groups were similar (Table 2).

The mean PSA values of the patients from whom 8, 10, 12, 16, and 20 core biopsies were taken were 8.4 ± 4.2 ng/mL, 6.5 ± 2.3 ng/mL, 8.7 ± 4.6 ng/mL, 8.8 ± 4 ng/mL, and 9.7 ± 8.8 ng/mL, respectively (p = 0.0001). Again, a post-hoc analysis was done to determine the differences between groups. While the 10-core patients had lower PSA values compared to the 8-, 12-, 16-, and 20-core patients, the PSA values of the other groups were similar.

Hematuria was observed in 25 (10.9%), 38 (8%), 12 (12%), 17 (12.1%), 22 (12.4%) of patients from whom 8, 12, 16, and 20 core biopsy were taken, respectively (p = 0.35) Fever (over 38°) and infection were found in 2 (0.9%) in 8-core, 10 (2.1%) in 12-core, 0.1 (0.7%) in 16-core, and 2 (1.1%) in 20-core patients (p = 0.36). Rectal bleeding was found in 3 (1.3%) 8-core, 7 (1.5%) 12-core, 0.1 (0.7%) 16-core, and 2 (1.1%) 20-core patients (p = 0.75). Urinary retention, epididymitis, and rectal bleeding were not observed in these patients.

We performed a multivariate analysis to find the most valuable variable to detect the possibility of cancer positivity in positive-biopsy patients. In doing so, we found that age increases the cancer detection rate by 1.05 times, prostate volume in the first quartile (12-34 cc) by 3.9 times, and the increasing number of cores by 1.06 times (Table 3).

### Discussion

The final diagnosis of prostate cancer is established by pathology. The sextant (bilateral specimen from apex, midgland, and base on the sagittal plane) biopsy described first by Hodge and colleagues in 1989 misses clinically important prostate cancers by 20% to 30%. Various biopsy methods in which additional biopsies were taken particularly from the lateral region of the prostate were developed to increase the cancer detection rate. Most researchers take more lateral zone samples to elevate the cancer detection rate. In the study by Yamamoto and colleagues, a 12-core transperineal prostate biopsy was taken from 300 patients with PSA 2.5 to 20 ng/mL and the cancer detection rate increased. In another study, 10, 12, and 13 core prostate biopsies increased the cancer detection rate by 25%, 22%, and 35%, respectively. In the study by Guichard and colleagues, the cancer detection rates of 6, 12, 18, and 21 core prostate biopsies were 31.7%, 38.7%, 41.5%, and 42.5%, respectively. In a study made on 1086 cases, a 12-core biopsy significantly increased the cancer detection rate in proportion to the 6-core biopsy. Eskicorapci and colleagues found that the cancer detection rate increased by 25.5% with the addition of the lateral peripheral zone biopsies to the sextant biopsy technique.
When Durkan and colleagues took a 2-core biopsy from the transitional zone and a 4-core biopsy from the peripheral zone in addition to a sextant biopsy, they found that the cancer detection rate alone increased by 19% in proportion to sextant biopsy. The logic of these studies is based on the increase in the possibility to detect cancer by increasing the samples. However, the situation is not always so simple. There are also many studies which show that increasing the core number does not affect the cancer detection rate. In one particular study, a 12-core extended biopsy was not superior to a sextant biopsy.16

Ung and colleagues took 6 to 18 core biopsies from 750 patients and reviewed the effect of the association of the increasing core number with prostate volume on the cancer detection rates. They showed that the cancer detection rate decreased from 40% to 27% as long as prostate volume increased; moreover, the cancer detection rate was not different as long as the number of cores increased (p = 0.77). Authors, however, had a very wide PSA range in this study (0.3 to 67 ng/mL).17

When Scattoni and colleagues compared 12 and 18 core prostate biopsy techniques, they found that the cancer detection rates were similar (p = 0.37). In this same study, the increasing core number and the cancer detection rate increased significantly when the prostate was larger than 55 cc.18 Similarly, Jones and colleagues found that saturation biopsy did not increase the cancer detection rate.19

Many studies show the effect of prostate volume on prostate cancer detection rate. Ficarra and colleagues suggest at least an 8-core biopsy if prostate volume is >30 cc.20 In a study performed in France, Guichard and colleagues divided the prostate into 3 groups: <35 cc, 35-55 cc, and >55 cc; cancer detection rates were 45%, 36%, and 28%, respectively, when a 12-core biopsy was taken. Moreover, in this study, the authors found that the prostate volume was significantly low in the positive biopsy (39.7 vs. 46.8 cc, p < 0.01).21 Uzzo and colleagues found that the cancer detection rate in prostates below 50 cc was significantly higher in proportion to those above 50 cc (38% vs. 23%).22

### Table 3. Multiple logistic regression analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.052</td>
<td>1.027–1.079</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Volume quartiles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12–34 (cc)</td>
<td>3.942</td>
<td>2.148–7.234</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>35–47 (cc)</td>
<td>2.071</td>
<td>1.141–3.756</td>
<td>0.017</td>
</tr>
<tr>
<td>48–66 (cc)</td>
<td>1.304</td>
<td>0.689–2.466</td>
<td>0.414</td>
</tr>
<tr>
<td>67–253 (cc)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free/total PSA (ng/mL)</td>
<td>0.105</td>
<td>0.011–0.996</td>
<td>0.047</td>
</tr>
<tr>
<td>PSA density</td>
<td>2.422</td>
<td>0.755–7.771</td>
<td>0.137</td>
</tr>
<tr>
<td>No. cores</td>
<td>1.067</td>
<td>1.017–1.119</td>
<td>0.008</td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: confidence interval; PSA: prostate-specific antigen.

### Conclusion

Although taking at least 8 core biopsies is recommended if the prostate gland is 30 to 40 cc, there is still no consensus on the core number required for large-volume prostates. We found that as the prostate volume increased, the core numbers increased; therefore, these factors elevated the cancer detection rate. Thus, the rate of missed cancers and the rate of unnecessary repetitive biopsy were decreased.

**Competing interests:** Dr. Ceylan, Dr. Doluoglu, Dr. Aglamis and Dr. Baytok all declare no competing financial or personal interests.
References


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