Core Length: An Alternative Method for Increasing Cancer Detection Rate in Patients with Prostate Cancer

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Purpose: We determined whether the lengths of benign and malignant cores affect cancer detection rates in patients with prostate cancer (PCa).

Materials and Methods: We evaluated retrospectively 512 patients in our clinic who had undergone 12 core transrectal ultrasound (TRUS)-guided prostate biopsies. The cores were divided into two groups: one with cancer (group 1) and one without cancer (group 2). We also classified Gleason scores as poorly differentiated (scores of 7-10) and moderately differentiated (scores of 5-6); these scores were compared with each other in terms of the core length. The core lengths of the groups were compared using a Student's *t*-test. A *P* value of less than .05 was considered to be statistically significant.

Results: Of the 512 patients, 76 (15%) had PCa. In total, we evaluated 912 cores of prostate biopsy samples from the 76 patients. Since 92 cores included insufficient tissue and rectal mucosa, we were not able to evaluate them. The remaining 820 cores were divided into two groups. Cancer was detected in 302 cores; 518 cores were benign in nature. The average core length in group 1 was 11.9 ± 4.4 mm, and the average core length in group 2 was 11.1 ± 5.1 mm (*P* = .015). The core lengths of poorly differentiated and moderately differentiated cancers were similar: 12.3 ± 4.2 mm and 11.7 ± 4.5 mm, respectively (*P* = .25).

Conclusion: Increasing cancer detection rates in cores may be related to core length in TRUS-guided prostate biopsies in PCa patients.

Keywords: biopsy; needle; standards; instrumentation; prostatic neoplasms; diagnosis; ultrasonography; prospective studies.

INTRODUCTION

Prostate needle biopsy, used for diagnosing prostate cancer (PCa), is usually performed using transrectal ultrasound guidance (TRUS). After Hodge and colleagues described the sextant biopsy method in 1989, TRUS-guided needle biopsy has played an important role in the diagnosis of PCa.[1] Although the random systematic six-core prostate biopsy method has significantly improved the cancer detection rate, some reports have demonstrated that 15-31% of PCa cases can be missed by this method.[2,3] Therefore, to enhance the cancer detection rate, various strategies were advised by clinicians, like increasing the number of cores and collecting more lateral cores.[4-6] Thus, sampling more prostate sites and consequently obtaining more prostate tissue can increase the cancer detection rate.

The length of the cores sampled during prostate biopsy can also affect the PCa detection rate.[7,8] The core lengths and quality of obtained prostate tissue are the main parameters for cancer diagnosis. On the other hand, few studies have assessed the effect of needle core length on cancer diagnoses. Some studies specified that core lengths need to be more than 10 mm for a correct histological evaluation;[8,9] otherwise, the accuracy of prostate needle biopsy may be questionable and have no diagnostic value.[9]

In this study, we analyzed the lengths of the needle cores sampled during 12-core TRUS-guided prostate biopsy in patients with cancer. Our aim was to detect whether there was a correlation between the lengths of benign and malignant cores and cancer detection. Secondly, we tried to find out any relationship between the core length, Gleason score, and percentage of tumors in the cores of PCa patients.

MATERIALS AND METHODS

Study Population

After obtaining the Institutional Review Board's approval for the study, we retrospectively evaluated 512 patients who underwent TRUS-guided prostate biopsy in our department between 2008 and 2012. Twelve cores were sampled in every patient (sextant biopsy from each the right and left prostate lobes).

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Biopsy Procedure

Biopsy was performed with the patient in the lateral decubitus position and, in all cases, an anesthetic block of the periprostatic plexus was performed by administering 0.2% prilocaine. A 25 cm 18 gauge, side-notch cutting (Tru-cut®) needle was used in each case (General Electric, LOG-13, 41123WS1 ultrasonography equipment with a 6.5 MHz biplane transrectal probe). Biopsies were obtained under TRUS guidance in the sagittal plane, by two urologists that specialized in this subject (TK, AD), using automatic gun biopsy (Maxicore MCS 01090026, Geotek Medical Devices, Ostim, Ankara, Turkey). Every specimen was removed from the needle carefully and the quality of the cores was observed macroscopically by the urologist. If we obtained inadequate specimens, like fragmented or small tissues or those of suspect quality, additional specimens were taken immediately from the same sites.

Sample Evaluation

Each sampled core was numbered, identified by site and prostate lobe, and then sent for pathological examination. The pathology report described the length of each core in millimeters (mm) and any percentage of cancer in the biopsy specimen. We recorded and analyzed the length of the longer core and disregarded the fragmented and smaller cores.The tumor's grade of differentiation was assigned with the Gleason grading and scoring system. For homogenization, patients with a prostate-specific antigen (PSA) level higher than 20 ng/mL, prior prostate biopsy, presence of any urinary tract infections, suspicious digital rectal examinations (DRE), pathology reports (including atypical small acinar proliferation and high-grade prostatic intraepithelial neoplasia), or specimens containing only periprostatic tissue or rectal mucosa were excluded from the study. All patients included in the study had normal DRE. All patients were diagnosed with PCa after 12-core biopsies were obtained with TRUS, which was performed due to high serum PSA levels (> 2.5 ng/dL).

The sampled biopsy cores were divided into two groups: cores including cancer (group 1) and those without cancer (group 2). We compared the benign and malignant core lengths of patients diagnosed with cancer and their effects on the cancer detection rate. We also determined tumor grade differentiation with the Gleason score system as poorly differentiated (scores of 7-10) or moderately differentiated (scores of 5 or 6) tumors.

Statistical Analysis

The data analysis was performed using Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 16.0. Descriptive statistics for variables with a normal distribution, non-normal distribution, and categorical variables were shown as mean ± standard deviation (SD), median (min-max), and the number of cases and (%), respectively. Student's *t*-test and the Mann-Whitney *U* test were used for the intergroup analyses of continuous variables. Categorical variables were analyzed with chi-square test. The *P* value < .05 was considered statistically significant.

Table 1. Comparison of core lengths with and without cancer in patients with prostate cancer.

Variables	Core Length	*P* Value
Cores with cancer (n = 302)	11.9 ± 4.4 mm	.015*
Cores without cancer (n = 518)	11.08 ± 5.1 mm	

*Statistically significant.

RESULTS

Biopsy was performed for 512 patients. The mean age of the patients diagnosed with cancer was 67.1 ± 7.5 years, the average core length was 12.9 ± 5 mm, and the average prostate volume was 36 ± 22 mL. The average serum PSA level was 9.4 ± 4.6 ng/mL. Pathology reports of the 512 patients revealed cancer in 76 (15%) men; the other 436 cases were benign. A total of 912 prostate biopsy cores were evaluated from 76 PCa patients. Ninety-two cores contained inadequate prostate tissue or rectal mucosa and were thus excluded from the analysis; the remaining of 820 cores were included in the study. Pathology reports revealed that out of 820 cores, cancer was detected in 302 cores and the other 518 cores were benign tissue. The average core lengths in groups 1 and 2 were 11.9 ± 4.4 mm and 11.08 ± 5.1 mm, respectively (*P* = .015) (**Table 1**). In the **Figure**, the lengths of cores with andwithout cancer are shown in PCa patients. Of the 76 patients with a cancer diagnosis, the needle core lengths of poorly differentiated (12.3 ± 4.2 mm) and moderately differentiated (11.7 ±4.5 mm) tumors were not statistically significantly different (*P* = .25).

Distribution of cancer cores along the prostate regions and the comparison of average core lengths with and without cancer are shown in **Table 2**. The only statistically significant difference was observed between the core lengths at the right lateral apex (*P* = .02). Addition-

Table 2. Distribution of cores with and without cancer according to prostate regions, average core lengths, and average tumor percentages in cores with cancer.

Variables	1	2	3	4	5	6	7	8	9	10	11	12
Core length with cancer (mm)	12.6 ± 3.3	12.9 ± 3.7	12.1± 4.1	10.3± 4.6	12 ± 4.6	11.3± 4.7	13.6± 5.07	12.6 ± 4.8	10.5 ± 3.3	11.6 ± 4.1	13.5 ± 4.1	10.9 ± 4.8
Core length without cancer (mm)	13.1 ± 5.9	12.1 ± 5.3	10.2 ± 5.08	9.9 ± 3.9	10.9 ± 4.5	8.8 ± 3.8	11.4 ± 5.08	12.4 ± 5.6	11.6 ±5.6	10.4 ± 5.2	12.1 ± 4.4	9.9 ± 4.5
P value	.57	.56	.09	.81	.62	.02*	.09	.82	.46	.31	.26	.40
Cancer percentage in core regions, n /%	29/9.6	25/8.2	22/7.2	33/10.9	13/4.3	30/9.9	29/9.6	29/9.6	26/8.6	24/7.9	11/3.6	31/10.2

1: Right base, 2: Right midgland, 3: Right apex, 4: Right lateral base, 5: Right lateral midgland, 6: Right lateral apex, 7: Left base, 8: Left midgland, 9: Left apex, 10: Left lateral base, 11: Left lateral midgland, 12: Left lateral apex.

*Statistically significant.

Table 3. Division of cores by lengths, <10 mm and >10 mm and comparison of average tumor percentages in cores.

Core Length with Cancer	Cancer Percentages in Cores	*P* Value
<10 mm	37 ± 28	.93
≥ 10 mm	37 ± 26	

ally, when the cores with cancer were divided by the lengths, into < 10 mm and >10 mm groups, the average percentages of cancer detected in the cores were 37% ± 28 vs. 37% ± 26, respectively, and no statistically significant difference was found (P = .93) (**Table 3**).

DISCUSSION

PCa is still a major health problem among males all over the world. Histopathological examination of the tissue obtained from prostate biopsy is significant for a definite diagnosis of PCa. So the question is, "How can urologists improve the prognostic capability of prostate biopsy for cancer detection?" From this point of view, the main concern is increasing the number of cores, which enables increased sampling of prostate sites and prostate tissue. Various efforts have been applied for this purpose, like sextant biopsy, 8-15 core collection, or saturation biopsies.[6,10-14] The diagnostic value of sextant prostate biopsy is 43% higher than that of two or fewer biopsies.[1,15,16] Biopsy of 12 sites identified 29% more cancers than the sextant approach.[10] After performing saturation biopsies (14 - 45 sites) on patients who previously had a negative sextant biopsy, cancer was identified in 34% of them.[14] Ultrasound-targeted biopsies and an additional four far-lateral peripheral zone or posterolateral biopsies have also optimized the diagnostic yield of prostate biopsy.[12,13] Guichard and colleagues found that the cancer detection rates of 6-, 12-, 18-, and 21-core biopsies were 31.7%, 38.7%, 41.5%, and 42.5%, respectively.[17] In a study including 1086 cases, 12-core biopsy was significantly superior to sextant biopsy.[18] Similarly, in the study by Ceylan and colleagues, the cancer detection rates of 8-, 10-, 12-, 16-, and 21-core prostate biopsies were 18.3%, 14.8%, 24%, 22.1%, and 30.3%, respectively.[6] Addition of the lateral peripheral zone to biopsies was 25.5% more advantageous than the sextant biopsy technique in determining PCa.[19] Although it seems that sampling more anatomic sites can enhance the cancer detection rate, this may not be a valid way of thinking every time; in the study by Naughton and colleagues, there was no diagnostic yield of a 12-core biopsy above that of a sextant biopsy.[20]

The lengths of sampled needle cores can also influence the PCa detection rate.[8] In the study by Baccon-Gibod and colleagues, an average of 10 mm of prostate tissue was accepted as the shortest available length for adequate prostate biopsy. From their point of view, core lengths shorter than 10 mm might be inadequate for a correct pathologic result and diagnosis.[9] Iczkowski and colleagues observed that the lengths of the cores obtained from the midgland and base of the prostate were much longer than the apex,[7] and when sampling longer single cores, cancers were better detected at the apex. Ficarra and colleagues revealed the advantage of a transperineal approach, which allowed better and more sensitive sampling at the prostate apex than at the midgland and base.[21] In our study, cores with cancer were much more longer in all regions of the prostate except the right base and left apex. We consider that the biopsy needle length and method of transferring the tissue to the container are the main factors that affected core lengths. However, when the cores were evaluated separately, significant differences were detected only in region 6; we believe this was due to the declining number of samples when the cores were divided into subgroups (type II error). Additionally, while obtaining cores from the right and left apexes in the lateral decubitus position, pushing the probe forward, a short apex, and the difficulty of curling the right wrist laterally may explain the shorter core lengths in this region than the other regions.In the present study, when cores were divided into two groups, <10 mm and >10 mm, we determined no difference in the percentages of tumors detected in the cores. A possible explanation could be that after the tumor was captured, much longer lengths may be required to show a large amount of core invasion. If we were able to obtain cores longer than 20 mm, increasing the core lengths would provide high tumor-detection percentages. For this reason, efforts should be focused on prospective randomized studies that include

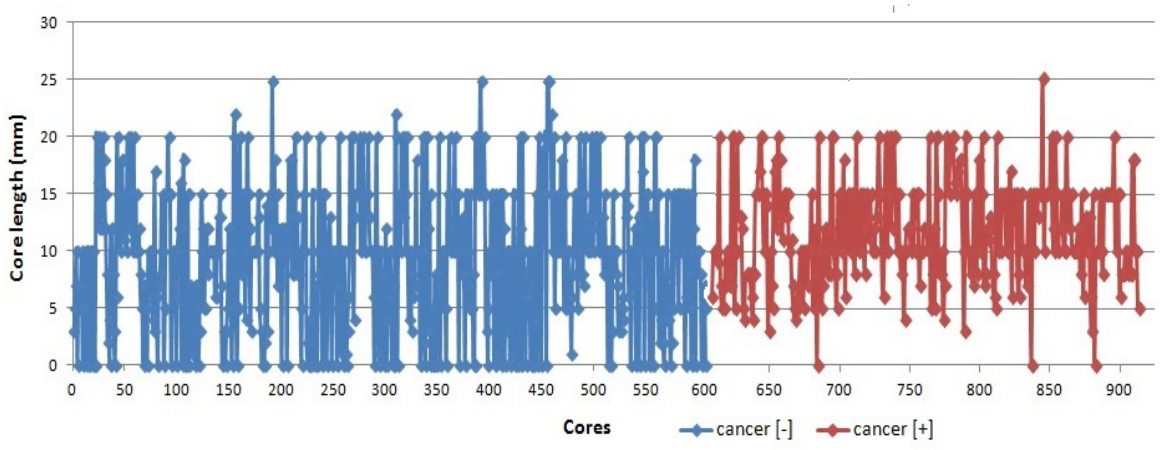

Figure: Length distribution of benign and malignant cores.

the evaluation of different core lengths.

Similar to our results, a newly published study by Öbekand colleagues demonstrated a significance between needle core length and cancer detection rate, including all biopsy cores and all prostate sites.[22] In cancer patients, we proved that the average length of the cores in groups showed a statistically significant difference ($P = .015$), meaning an increased cancer detection rate. In the present study, the mean length of the cores was longer than 10 mm, strongly supporting our findings. Öbek and colleagues determined that a core length greater than 11.9 mm was associated with a high possibility of cancer detection; they found cancer detection rates for cores under and over 11.9 mm of 23% and 39%, respectively. We did not try to find a cutoff value, but that might be necessary for obtaining more accurate results and increasing cancer detection. Our mean core lengths in groups 1 and 2 were close to the detected cutoff value, increasing the value of our study. Additionally, only PCa patients were included in our study and their cores were examined; this is different from the other studies in the literature. Even in patients with diagnosed cancer, the length of malignant cores was longer than benign ones, which suggests a strong correlation between core length and cancer detection. Reis and colleagues found that, among patients who underwent radical prostatectomy, the mean core length in those presenting an underestimated Gleason score upon biopsy was 11.61 mm (± 2.5, median 11.40), compared to 13.52 mm (± 3.2, median 13.70) in those with perfect Gleason score agreement between the biopsy and radical prostatectomy ($P < .001$).[23]

The lengths of cores might be influenced by several factors. The needle, transrectal, or transperineal biopsy procedures, sending the cores to the pathology department regularly, the techniques of pathological analysis, and the urologist who performs the biopsy may affect the diagnostic value of a prostate biopsy.[8,9] In our study, to reduce the impact of these factors, we made a standardized protocol that made every attempt to maximize the quality of the obtained prostate biopsy. All biopsies were performed transrectally by the same urologists (TK, AD) using the same ultrasound machine and biopsy needle. Our assistants transferred the specimens to the pathology department properly. The same uropathologist evaluated the histopathological result of the biopsy cores. From the beginning of the study, efforts were made to raise the power of the study and prevent missing any cancer cases.

The method of performing the biopsy can influence core lengths and the sampling of prostate anatomic sites. The transperineal prostate biopsy method is more effective and selective than the transrectal route when sampling the prostate peripheral and anterior zones.[24-26] In the study by Emiliozzi and colleagues, the core lengths obtained by transperineal and transrectal sextant biopsy overlapped.[25] Ficarra and colleagues found that the transperineal approach allows better sampling at the prostate apex than the other prostate sites.[19] Öbek and colleagues obtained effective results by transrectal biopsy and concluded that core length was an important indicator for the cancer detection rate. In our clinic, to support the quality of prostate biopsy, transrectal guidance is preferred. We try to obtain adequate prostate tissue; if not, a second attempt from the same anatomic site is done to avoid missing any PCa case.

Nevertheless, when we examined the biopsy records, 92 cores with insufficient tissue were excluded from the study. This may be due to fragmented tissues, not paying enough attention while removing each core from the biopsy needle properly, or a delay in sending biopsy specimens for pathological evaluation; the rest of the cores were suitable for the study. Reis and colleagues. reported that pathologists often receive more cores than the number sampled by the urologist, and suggested that these changes are due to core fragmentation. Fragmentation of biopsy cores may skew the interpretation of biopsy results. Therefore, we disregarded the fragmented and smaller cores in the present study.[27]

Although our study was retrospective and this seemed to be a limitation, it was one of the few studies that indicated the effect of core lengths on cancer detection. Even in PCa patients, the difference in core lengths between cores with and without cancer demonstrated the importance of core lengths as much as core numbers. Not assessing the whole prostate glandafter radical prostatectomy was the other limitation of our study. Multiple prospective studies should be done to determine adequate core lengths.

CONCLUSIONS

Our results suggest that needle core length is related with the cancer detection rate in cores of PCa patients. Biopsy tissue length is at least as influential as the number of sites sampled. All efforts should be focused on sampling longer tissue lengths.

CONFLICT OF INTEREST

None declared.

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