Initial 6 and 8 cores transrectal ultrasound guided prostate biopsy techniques are inadequate compared to 10 or 12 cores in detecting prostate cancer

Prostat kanser tespitinde ilk seferde transrektal ultrason eşliğinde alınan 6 ve 8 kadran prostat biyopsi teknikleri 10 veya 12 kadrana göre yetersizdir

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Abstract

Objectives: Limited data exist regarding the comparison of 6, 8, 10 and 12 cores of transrectal ultrasound guided biopsy (TRUS-Bx) of the prostate in detecting prostate cancer (PCa). The purpose of this study was to compare the cancer detection rates of 6, 8, 10 and 12 cores TRUS-Bx of the prostate on the same cohort of patients.

Material and Methods: Between February 2005 and January 2011, 2033 men with serum PSA levels higher than 2.5 ng/mL and/or with an abnormal digital rectal examination underwent TRUS-Bx of the prostate. Of the patients, 1131 (55.6%) who underwent initial 12 cores TRUS-Bx of the prostate were included in the study. Patients' pathology results were re-evaluated if they had undergone 6, 8, and 10 cores biopsies rather than 12 cores. PCa detection rates of these techniques were compared.

Results: Overall, 20.9% (236 of 1131) of the patients had PCa detected on 12 cores biopsy. Cancer detection rates of 6 cores, 8 cores and 10 cores biopsies were calculated as 16.4%, 20.1% and 20.4%, respectively. No significant difference was detected between 10 and 12 cores biopsy techniques in detecting PCa ($P = 0.06$). However, 12 cores biopsy had significantly higher PCa detection rate compared to both 6 ($P < 0.0001$) and 8 ($P = 0.0039$) cores biopsies.

Conclusion: Standard 6 and 8 cores of prostate biopsy seem to be inferior compared to 10 or 12 cores of TRUS-Bx of the prostate in detecting PCa. Therefore, 12 cores should be included in the initial TRUS-Bx of the prostate.

Keywords: Biopsy, prostate, prostate neoplasm

Özet

Amaç: Prostat kanseri (PCa) tespitinde transrektal ultrason eşliğinde (TRUS-Bx) alınan 6,8,10 ve 12 kadran biyopsi tekniklerini karşılaştıran sınırlı sayıda veri vardır. Bu çalışmanın amacı aynı hasta kohortunda 6,8,10 ve 12 kadran prostat TRUS-Bx tekniklerinin kanser tespit oranı açısından karşılaştırmaktır.

Gereç ve Yöntemler: Şubat 2005 ile Ocak 2011 tarihleri arasında, serum prostat spesifik antijen (PSA) değeri 2.5 ng/mL üzeri ve/veya anormal tuşe bulguları olan 2033 erkeğe prostat TRUS-Bx uygulandı. İlk seferde 12 kadran prostat biyopsisi alınan 1131 (%55.6) hasta çalışmaya dahil edildi. Hasta patolojileri hastalara 12 kadran biyopsi yerine 6,8 ve 10 kadran alınmış gibi tekrar değerlendirildi. Bu tekniklerin PCa tespit oranları karşılaştırıldı.

Bulgular: Toplamda hastaların %20.9'unda (236/1131) 12 kadran biyopsi ile PCa tespit edildi. Altı kadran, 8 kadran ve 10 kadran biyopsilerin kanser tespit oranı sırasıyla %16.4, %20 .1 ve %20.4 olarak hesaplandı. On ve 12 kadran biyopsi teknikleri arasında PCa tespiti açısından anlamlı bir farklılık saptanmadı (p=0.006). Ancak 12 kadran biyopsinin PCa tespit oranı hem 6 kadran ($p < 0.0001$) hem de 8 kadran (p=0.0039) biyopsiye göre anlamlı olarak yüksekti.

Sonuç: Standart 6 ve 8 kadran prostat biyopsisi PCa tespitinde 10 yada 12 kadran prostat biyopsisine kıyasla değersiz görünmektedir. Bundan dolayı ilk prostat biyopsisi 12 kadranı içermelidir.

Anahtar Kelimeler: Biyopsi, prostat, prostat neoplazmı.

Introduction

Systematic sextant biopsy of the prostate under transrectal ultrasound (TRUS) guidance was introduced in 1989 and has revolutionized our ability to detect carcinoma of the prostate (PCa) (1). In order to increase the cancer detection rates, Presti et al (2). recommended 8 core biopsy, including the apex, mid lobar mid gland, lateral mid gland and lateral base. Several years later, Gore et al recommended 10 core biopsy that combined laterally directed cores at the base, mid gland and apex of the prostate with mid lobar biopsy cores at the base and apex (3). Although there has been a tendency to increase the number of cores in order to increase detection rates, 12 core biopsy protocols are widely accepted to be adequate because of having almost the same cancer detection as the saturation biopsy techniques with fewer complications (4). Since many clinics demonstrate almost the same cancer detection as the saturation biopsy techniques, with fewer complications, they are now using 12 core biopsy protocols (5) . To our knowledge, no single study has compared 6, 8, 10 and 12 core biopsy techniques in detecting PCa and we aimed to retrospectively evaluate our patient cohort who underwent initial 12 cores transrectal ultrasound guidance biopsy (TRUS-Bx) and determine detection rates if they had undergone 6, 8 and 10 cores biopsies rather than 12 cores.

Material and methods

Study population: Following an approval from our institutional ethical board, Ankara Ataturk Training and Research Hospital and written consent from the patients involved. Between February 2005 and January 2011, 2033 men with prostate specific antigen (PSA) levels greater than 2.5 ng/mL and/or abnormal digital rectal examination (DRE) findings underwent TRUS-Bx at our institution. Of the patients, 1131 (55.6%) who underwent 12 core initial prostate biopsy were included into the study. Patients' records including age, serum PSA level, anesthesia type, prostate volume and pathology result of each core were evaluated.

TRUS-Bx: All participants were administered a 5 to 7-day course of an oral floroquinolone antibiotic prophylaxis or an appropriate alternative if there was a floroquinolone allergy, starting the night before the biopsy procedure. A cleansing rectal enema was administered on the

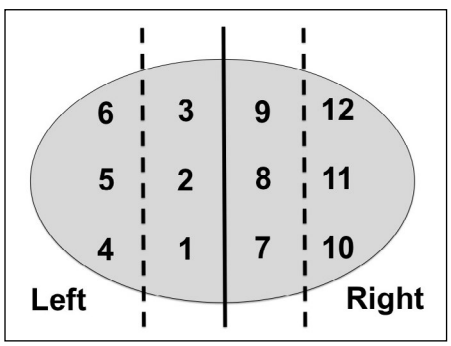


Figure 1. Prostate biopsy sites.

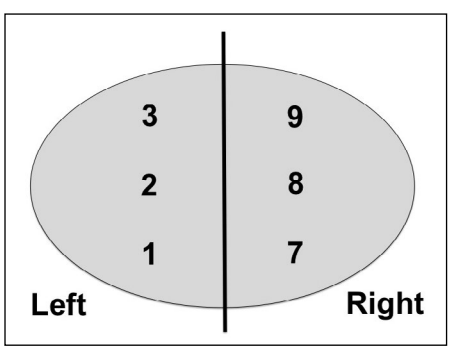


Figure 2. Prostate biopsy sites: 2a. 6 core prostate biopsy (1); 2b. 8 core prostate biopsy (2) and; 2c. 10 core prostate biopsy (3).
Figure 2a.

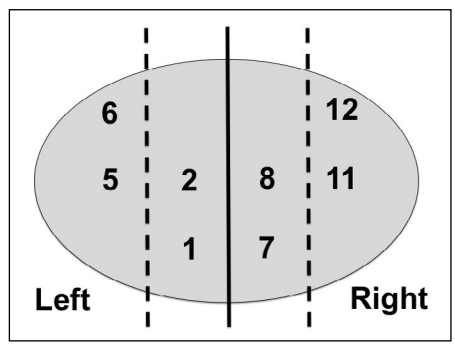


Figure 2b.

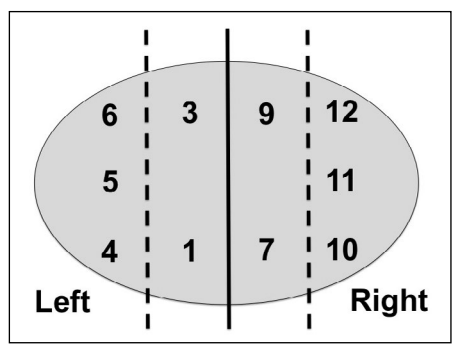


Figure 2c.

morning of the TRUS-Bx. Patients were instructed not to take any anticoagulant drugs for at least 7 days before TRUS-Bx. TRUS-Bx was performed on left lateral decubitus position with an automatic spring loaded with 18 gauge needle under TRUS guidance using a 7.5 MHz transrectal probe (Viking 2400, BK Medical, Denmark) following periprostatic lidocaine injection for local anesthesia. Procedures were well tolerated without any need for intravenous sedation.

Prostate volume was calculated using the formula for the volume of a prolate spheroid, $\pi/6 \times (\text{major axis}^2 \times \text{minor axis})$ (6). The sites of TRUS-Bx are demonstrated in Figure 1.

Transrectal ultrasound guidance biopsy specimens were referred to pathological examination separately. Thereafter, patients' pathological results were re-evaluated according to 6 core scheme (1), 8 core scheme (2) and 10 core scheme (3) (Figure 2). Cancer detection rates of each prostate biopsy scheme were compared.

Statistical analysis: Data including patients' age, serum PSA value, prostate volume and pathological results of each core were recorded. Mann-Whitney U Test was used for comparisons between prostate cancer groups. Twelve core biopsy technique accepted as a gold standard and sensitivity of 6, 8 and 10 core techniques was calculated. Statistical analyses of these variables were performed with SPSS 15.0 software program (Chicago, IL, USA) and significance level was set at 0.05.

Results

Prostate cancer was detected in 236 (20.9%) of the 1131 patients who initially underwent 12 core TRUS-Bx. Mean patient age and serum PSA value were higher wheras mean prostate volume was lower among patients diagnosed with PCa (Table 1).

Prostate cancer was detected in 236 (20.9%) patients

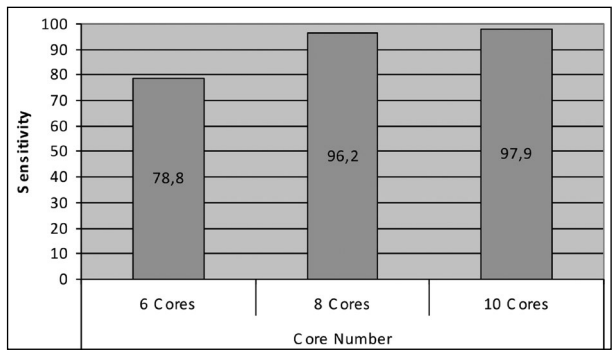


Figure 3. Sensitivities of 6, 8 and 10 core prostate biopsy techniques.

in our entire patient population with 12 core prostate biopsy technique. Our analyses revealed that if 6, 8 and 10 core biopsy technique had been performed instead of 12 core technique, PCa could have been detected in 186 (16.4%), 227 (20.1%) and 231 (20.4%) patients, respectively. Although PCa detection rate of 12 core scheme was significantly higher than 6 ($p < 0.0001$) and 8 core ($p=0.0039$), it was not statistically different compared to 10 core biopsy technique ($p=0.0625$). No significant difference was detected in PCa detection rates between 12 core and 10 core biopsy techniques ($p=0.0625$). Table 2 shows PCa detection rates of each biopsy technique.

Overall, PCa was detected in 1349 cores, 643 (47.7%) of which were within the standard sextant biopsy sites where as 706 (52.3%) cores with PCa were detected in lateral sites ($p < 0.001$). The distribution of cores with PCa according to PBx cores demonstrated on Table 3.

Sensitivities of 6, 8 and 10 core biopsy techniques were 78.8%, 96.2% and 97.9%, respectively (Figure 3).

Discussion

The most accurate way of searching for cancer in prostate is to remove it entirely and evaluate it histologically. However, this approach is not possible due to the significant morbidity associated with the operation

Table 1. Comparison of the characteristics of the patients diagnosed with and without PCa who underwent 12 core prostate biopsy .

	Overall	PCa (+)	PCa (-)	P*
Number of patients: n (%)	1131 (100)	236 (20.9)	895 (79.1)	
Mean patient age±SD (min-max)	64.62 ± 7.95 (40-85)	67.17 ± 7.47 (43 - 83)	63.94 ± 7.94 (40 - 85)	**P < 0.001**
Mean serum total PSA±SD (min-max) (ng/ml)	12.63 ± 24.01 (0.124 – 526)	25.34 ± 47.07 (1.190 - 526)	9.51 ± 11.22 (0.124 – 112)	**P< 0.001**
Mean prostate volume±SD (min-max) (mL)	62.57 ± 30.39 (11.8 - 220)	53.11 ± 25.36 (14.4 - 176)	65.07 ± 31.12 (11.8 - 220)	**P < 0.001**

* Mann-Whitney U Test.
PCa: Prostat cancer

Table 2. Prostate cancer detection rates of each biopsy technique.

Biopsy technique	Cancer detection rate (%)
6 Core	186/1131 (%16.4)
8 Core	227/1131 (%20.1)
10 Core	231/1131 (%20.4)
12 Core	236/1131 (%20.9)

Table 3. Number of cores and percentages with PCa detected in each prostate biopsy site.

Biopsy site	N	%
Right apex	93	6.9
Right middle	112	8.3
Right basis	117	8.7
Right far lateral apex	121	9
Right far lateral middle	122	9
Right far lateral basis	128	9.5
Left apex	115	8.5
Left middle	108	8
Left basis	98	7.3
Left far lateral apex	122	9
Left far lateral middle	107	7.9
Left far lateral basis	106	7.9
Total	**1349**	**100**

and organ loss. Therefore, we perform TRUS-Bx and try to identify cancer cells within the prostate. Since the amount of tissue taken from each core is approximately 15 mm^3, increasing the number of cores sampled during TRUS-Bx will improve the detection rate for PCa (7-11) . However, it is still not clear whether the location from which the cores have an impact on the detection rate.

Several investigators have reported their experiences with extended field biopsy. Eskew et al proposed a systematic 5 region biopsy protocol with additional biopsy cores obtained from the midline and lateral of the prostate (7). With this regimen, 40% of the patients were detected to have PCa. Moreover, the authors demonstrated that 35% of cancer would have been missed with the standart sextant biopsy technique. The base and apical region of the prostate regions are found to be important in computerized biopsy simulations (12). The laterally directed cores did not include these areas. Levine et al used standard sextant biopsy and detected 30% false negative rate, suggesting that consecutive 2 sets of sextant biopsy would increase the ability of PCa detection rate (9). Furthermore, to decrease false negative rate of TRUS-Bx, Eskicorapci et al recommended adding lateral peripheral cores to the standard sextant biopsy scheme, which would increase the detection rate by 14-35% (13). Presti et al utilized 10 core TRUS-Bx and demonstrated that PCa was detected 42% of the patients whereas 20% of cancers would have been missed with standard sextant biopsy alone (2). The authors also showed that there was no statistically significant difference between the cancer detection rates of 8 and 10 core technique and offered to take at least 8 cores. Similarly, Babaian et al advocated that 11 core technique is more effective compared to standard sextant biopsy, which misses 20-25% of cancer (14). Gore et al included bilateral mid apex and basis to laterally directed 6 core scheme and detected cancer in 40.3% of the patients (3).

In our study, cancer detection rate was 20.9% with 12 core biopsy technique. If 6, 8 or 10 cores were used rather than 12 cores, the cancer detection rates would have been 16.4%, 20.1% and 20.4%, respectively. Low rate of cancer detection in this study can be explained by our including patients with lower PSA levels. Presti et al detected PCa in 42% of their patients whose serum PSA levels were ≥ 4 ng/mL included in their study (2). Gore et al detected PCa in 40.3% of the patients and 28% of whom had prior negative biopsy, 5.3% were already diagnosed with PCa and biopsy performed for staging and 44.4% of those patients' PSA level was 4.0 – 10.0 ng/ml (3). In our study, patients with serum PSA levels > 2.5 ng/mL underwent TRUS-Bx and patients with a history of prior biopsy and PCa were excluded.

As the technology improved, new sonographic biopsy techniques was developed such as sonoelastography and contrast-enhanced ultrasound (15). However, currently there is not enough evidence for their routine use (16). Ultimately, multiparametric magnetic resonance imaging (mpMRI) was introduced to decrease the number of samples and increase the detection rate. However, studies showed that the detection rate of mpMRI decreased as the tumor volume and gleason score decreased (17). Furthermore, the detection of significant PCa via mpMRI was superior to TRUS in patients with repeat biopsy settings but not in men with an initial biopsy (18). On the other hand, the cost/benefit analysis of the mpMRI is still required for more widespread use of the technique (19).

To the best of our knowledge, no published study has compared cancer detection rates of 6, 8, 10 and 12 core biopsy techniques performed on the same patient cohort. Cancer detection rates were similar between 10 and 12 core biopsy schemes in our study which were superior to 6 and 8 core biopsy techniques in detecting PCa. This finding is in accordance with Gore et al (3). These results suggest that taking 10 or 12 core biopsies rather than 6 or 8 cores must be the standart approach in patients who have elevated PSA levels and/or suspicious DRE findings.

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