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Is the Transitional Zone Biopsy Specimen Significant for Prostate Cancer Detection?

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ABSTRACT

INTRODUCTION: Reports of prostate cancer (PCa) detected from biopsies obtained from the transitional zone (TZ) have become more common. However, TZ prostate biopsies have the potential to cause infectious complications, and questions remain about their value. The purpose of the study was to investigate the detection of PCa from biopsies taken from the TZ and peripheral zone (PZ), individually and in combination.

METHODS: Retrospective data were collected from 482 men who underwent sextant PZ plus TZ biopsy (2 cores, 1 from each lobe) for suspected PCa. The data were analyzed for the relationships between the presence of PCa from TZ or PZ biopsies, prostate-specific antigen (PSA) levels, and Gleason scores (GSs).

RESULTS: PCa was detected on biopsy in 192 (39.8%) patients. PCa was detected only in the TZ for 10 patients (5.2%), only in the PZ for 69 patients (35.9%), and in both the TZ and PZ for 113 patients (58.9%). Obtaining a biopsy only from the TZ resulted in a significantly lower cancer detection rate than obtaining the biopsy only from the PZ or from the combined PZ and TZ ($P < .05$). High GSs (≥ 7) were found in 3 of 10 patients (30%) with PCa detected in the TZ, 29 of 69 patients (42%) with PCa detected in the PZ, and 90 of 113 patients (79.6%) with PCa detected in the combined TZ and PZ. Among the patients with PSA levels < 10 ng/mL, none of the 4 patients with PCa detected only in the TZ had GSs ≥ 7; however, 14 of 41 patients (34.1%) with PCa detected only in the PZ and 18 of 32 patients (56.3%) with PCa detected in the combined TZ and PZ had GSs ≥ 7. Patients with a biopsy only from the TZ had significantly fewer GSs ≥ 7 than patients with a biopsy only from the PZ or from the combined PZ and TZ in this PSA range ($P < .05$).

CONCLUSIONS: It may be possible to omit a prostate biopsy from the TZ for patients with serum PSA < 10 ng/mL.

KEYWORDS: Prostate biopsy; Transitional prostate zone; Gleason scores

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Abbreviations and Acronyms

GS = Gleason score
PBx = prostate biopsy
PCa = prostate cancer
PSA = prostate-specific antigen
PZ = peripheral zone
RP = radical prostatectomy
TRUS = transrectal ultrasound
TZ = transitional zone

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INTRODUCTION

Prostate biopsies (PBx) are an essential tool for prostate cancer (PCa) diagnosis. A variety of methodologies and techniques are employed. For example, although the choice between the transperineal or transrectal approach remains controversial [1], some authors have found that the transperineal PBx helps avoid infectious adverse events and provides an easier method for sampling the abdominal aspect of the prostate [2,3]. Other authors prefer transrectal PBx for both pain control for patients and ease of use for physicians [4]. In terms of the number of core samples taken in PBx, many investigators have added several specimens bilaterally to sextant biopsies [5,6]. Miyake et al [7] reported the efficacy of adding transitional zone (TZ) PBx to sextant biopsies, and Shigemura et al [8] found that lateral (far lateral) biopsies combined with sextant PBx showed better cancer detection than the sextant PBx alone, especially in patients with serum prostate-specific antigen (PSA) ≤ 10 ng/mL. The authors contributing to the *Campbell-Walsh Urology* textbook [9] support the efficacy of lateral PBx.

Unfortunately, TZ PBx (including locations around the urethra) have the potential to cause more infectious complications such as acute bacterial prostatitis, especially when the transrectal approach is chosen. Some cases of septic infection and death after PBx have been reported [10], and some of the methods included TZ PBx. Recently, antibiotic-resistant strains such as fluoroquinolone-resistant *Escherichia coli* have spread [11]. Physicians need to pay attention to this problem to prevent unnecessary PBx or specimens taken by PBx.

Clinically significant PCa is thought to involve tumor volume > 0.5 cc and a Gleason score (GS) > 7 because insignificant PCa is defined by tumor volume < 0.5 cc and GS 6 [12]. Therefore, it is necessary to detect clinically significant evidence of PCa in order to determine the patient's prognosis.

In the past, TZ PCa was usually diagnosed after transurethral resection of the prostate (TURP) [13]. After several reports described the increased detection of TZ PCa, the idea of taking samples from the TZ became more widespread [2,14]. However, several authors have reported that TZ cancer was not significant, meaning that it can be observed without any treatment and with strict PSA checking [15].

Questions about the value of TZ prostate biopsy remain. Therefore, the purpose of the present study was to investigate the detection of PCa from biopsies taken from the TZ and PZ, individually and in combination.

METHODS

Patients

Between May 2004 and October 2008, data were collected retrospectively and uniformly from 482 referred patients who underwent PBx at the Akashi Municipal Hospital. All patients had suspected PCa based on high serum PSA, abnormal digital rectal examination (DRE), or abnormal transrectal ultrasound (TRUS). The median patient age was 71 years (range, 44-95 years). The median serum PSA level was 8.53 ng/mL (range, 1.17 - 3181 mg/mL).

TRUS and Prostate Biopsy Procedures

Acetylsalicylic acid or oral anticoagulant agents were stopped appropriately before PBx with the approval of the prescribing physician. All biopsies were performed with a 16-gauge Bard Max Core disposable biopsy instrument biopsy needle (CR Bard Inc, Convington, Georgia, USA) in conjunction with a medical ultrasound console (Aloka SSD-2000, Aloka Co Ltd, Tokyo, Japan). Sextant biopsies with TZ biopsy (ie, 8 [sextant PZ + 2 TZ] cores) were taken from each patient. All cases of PBxs were performed via the transrectal approach.

No preparatory cleansing enemas were used. The PBx procedure was performed with only sacral anesthesia with 1% lidocaine and transrectal povidone iodine sterilization just before the PBx. Prophylactic medications for infectious complications were isepamicin (400 mg, administered 1 time intravenously or intramuscularly) and levofloxacin (300 mg, administered orally for 3 days).

Data Analysis

There was a complete set of data from all patients for statistical analysis. Patient data included serum PSA, the presence and location of cancer, and GS.

Statistical analyses were performed using the chi-square test. Patients were divided into 2 groups: 1) those with serum PSA ≥ 10 ng/mL, and 2) those with serum PSA < 10 ng/mL. The authors analyzed the relationships between the presence of PCa from TZ or PZ biopsies (individually and combined) and PSA levels or GSs. All tests were done using Stata® (StataCorp LP, College Station, Texas, USA). Statistical significance was set at $P < .05$.

RESULTS

Table 1 contains the number of patients with PCa according to PSA levels. PCa was detected on biopsy in 192 (39.8%) of the total 482 patients. There were 278 patients with serum PSA levels < 10 ng/mL; of these, 77 (27.7%) had PCa detected on biopsy. There were 204 patients with serum PSA levels ≥ 10 ng/mL; of these, 115 (56.4%) had PCa detected on biopsy.

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Table 1. Number of Patients With Prostate Cancer According to Prostate-Specific Antigen Levels (N = 482).
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PSA Level	Number Positive for PCa	n	% n
≥ 10 (ng/mL)	115	204	56.4
< 10 (ng/mL)	77	278	27.7
Total	192	482	39.8

Abbreviations: PSA, prostate-specific antigen; PCa, prostate cancer

Table 2 contains the number of patients with PCa detected in the TZ or PZ, individually and combined, and the probability of significant differences between paired comparisons. Out of the 192 patients with PCa, the cancer was detected only in the TZ for 10 patients (5.2%), only in the PZ for 69 patients (35.9%), and in both the TZ and PZ for 113 patients (58.9%). Obtaining a biopsy only from the TZ resulted in a significantly lower cancer detection rate than obtaining the biopsy only from the PZ or from the combined PZ and TZ ($P < .05$). These results were verified in all PSA level comparisons.

Table 3 contains the number of patients with PCa that was detected in the TZ, PZ, and combined TZ and PZ, and the number of patients with GS ≥ 7. The table also includes the probability of significant differences between paired comparisons. High GSs (≥ 7) were found in 3 of 10 patients (30%) with PCa detected in the TZ, 29 of 69 patients (42.0%) with PCa detected in the PZ, and 90 of 113 patients (79.6%) with PCa detected in the combined TZ and PZ. Among those patients with PSA levels < 10 ng/mL, none of the 4 patients with PCa detected only in the TZ had GSs ≥ 7; however, 14 of 41 patients (34.1%) with PCa detected only in the PZ and 18 of 32 patients (56.3%) with PCa detected in the combined TZ and PZ had GSs ≥ 7. Patients with a biopsy only from the TZ had significantly fewer GSs ≥ 7 than patients with a biopsy only from the PZ or from the combined PZ and TZ in this PSA range ($P < .05$).

DISCUSSION

Prostate cancer is one of the most common male cancers worldwide, and its reported incidence has been increasing [16]. A variety of approaches (ie, routes), specimen core numbers, and prophylactic medications to prevent adverse infectious events may be used for PBx [4]. Even if the PBx is limited to the transrectal route, there are debates about the number of core

Table 2. Number of Patients With Prostate Cancer Detected in the Transitional Zone, Peripheral Zone, or Combined Transitional and Peripheral Zones (n = 192; N = 482); Probability of Significant Differences.
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Biopsy Area	n	% n	P^a	P^b
Transitional Zone				
PSA ≥ 10 (ng/mL)	6	3.1		
PSA < 10 (ng/mL)	4	2.1		
Total	10	5.2		
Peripheral Zone				
PSA ≥ 10 (ng/mL)	28	14.6	<.05	
PSA < 10 (ng/mL)	41	21.4	<.05	
Total	69	35.9	<.05	
Transitional Zone and Peripheral Zone				
PSA ≥ 10 (ng/mL)	81	42.2	<.05	<.05
PSA < 10 (ng/mL)	32	16.7	<.05	<.05
Total	113	58.9	<.05	

Abbreviation: PSA, prostate-specific antigen
[a]Comparison with transitional zone only outcomes
[b]Comparison with peripheral zone only outcomes

Table 3. Number of Patients With Prostate Cancer Detected in the Transitional Zone, Peripheral Zone, or Combined Transitional and Peripheral Zones (n = 192; N = 482) and Number with Gleason Scores ≥ 7; Probability of Significant Differences.
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Biopsy Area	n	% PSA n	P^a	P^b
Transitional Zone				
PSA ≥ 10 (ng/mL)	6			
GS ≥ 7	3	50		
PSA < 10 (ng/mL)	4			
GS ≥ 7	0	0		
Peripheral Zone				
PSA ≥ 10 (ng/mL)	28			
GS ≥ 7	15	53.6		
PSA < 10 (ng/mL)	41			
GS ≥ 7	14	34.1	<.05	
Transitional Zone and Peripheral Zone				
PSA ≥ 10 (ng/mL)	81			
GS ≥ 7	72	88.9	<.05	<.05
PSA < 10 (ng/mL)	32			
GS ≥ 7	18	56.3	<.05	<.05

Abbreviations: PSA, prostate-specific antigen; GS, Gleason scores
[a]Comparison with transitional zone only outcomes
[b]Comparison with peripheral zone only outcomes

specimens and the problem of infectious complications [10]. Kawakami et al [17] reported that taking more core specimens may lead to higher cancer detection rates, but various results have been reported depending on where the cores were taken [2,7,8]. Miyake et al [7] reported that including the TZ for the PBx yielded higher PCa detection rates than using the PZ alone.

It is generally well known from previous literature that TZ PCa is low grade and has low GSs. However, these studies were performed in the USA and Europe, where patients with PCa have characteristics different from men in East Asia [18]. The present study investigated the significance of TZ PCa in Japanese men. The study had core numbers and methodologies that differed from the Miyake et al study [7]. Results of the present study showed a significantly lower rate of cancer detection when the PBx was taken only from the TZ, when compared with the rate of PCa detection from PBx taken from only the PZ or from both the TZ and PZ, combined.

The GS is the best-known index of PCa aggressiveness and patient prognosis [19,20]. GSs ≥ 7 are considered an indication of more aggressive cancer when compared with GSs < 7 [20] and may suggest unfavorable prognosis for the patient's life. The present data showed that none of the 4 patients with PCa detected only in the TZ with serum PSA levels < 10 ng/mL had GSs ≥ 7. PCa detection for these patients was significantly lower than for comparable patients with PBx from the PZ alone or from the TZ and PZ, combined. These findings suggest that TZ biopsy may not be necessary for patients with PSA < 10 ng/mL.

A study by Grignon and Sakr [21] conducted in the USA reported that PCa detected in the PZ had higher proliferative rates than PCa detected in the TZ. This finding is consistent with the lower GSs and cancer detection rates found in the patients with TZ PBx in the present study. This finding also suggests that there may be a similarity in rates of TZ PCa between men from the USA and Japan.

Buhmeida et al [22] studied prognostic factors in PCa. They stated that nuclear morphometry and GSs are the most highly significant progression-associated prognosticators in advanced PCa. Erbersdobler et al [23] stated that TZ PCa may reveal lower Gleason scores as well as lower expression of markers related to tumor growth, which might contribute to a less malignant clinical behavior when compared with PZ PCa. The results from these studies support the present finding that TZ PCa with low GSs may not be significant. This also suggests that, in specific patients such as those with low PSA, PBx from the TZ could be omitted.

Yoshizako et al [24] showed that adding diffusion-weighted magnetic resonance imaging (DW-MRI) to the T2-weighted image (WI) with fat saturation (FST2-WI) increased the diagnostic accuracy of TZ PCa. The addition of dynamic contrast-enhanced MRI may be an option for better diagnosis of TZ PCa. This kind of imaging study may be the future work of the present authors.

One limitation of the present study is that there are sometimes discrepancies in the pathological findings between PBx specimens and specimens taken by radical prostatectomy (RP) [25]. The authors are planning future studies to confirm the association between TZ PBx and RP specimens and to compare TZ PCa directly with PZ PCa using RP specimens from the Japanese population.

In conclusion, the present PBx data revealed that patients with TZ PCa may have significantly lower GSs and lower cancer detection ratios, especially if the serum PSA is < 10 ng/mL. These results suggest that TZ PBx may not be necessary for patients with low PSA.

Conflict of Interest: none declared

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