Detection of Significant Prostate Cancer According to Anatomical Areas of Sampling Cores Obtained with Transrectal Systematic 12-Core Biopsy

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Key Words

Prostate cancer • Biopsy • Radical prostatectomy • Significant cancer

Abstract

Background: To analyze the diagnostic performance of 12-core biopsy in detecting significant prostate cancer (PCa).

Patients and Methods: This study included 206 PCa patients who underwent transrectal 12-core biopsy followed by radical prostatectomy. Radical prostatectomy specimens were anatomically divided into 12 areas according to the sampling cores, and the existence of significant cancer, defined by a tumor volume > 0.5 ml, was investigated. The detection rate of significant cancer in each area was calculated as follows: the number of positive core biopsies/the number of areas containing significant cancer × 100. **Results:** The overall detection rate of significant cancer in all areas was 53.6%. The detection rate was significantly higher in the standard sextant cores than in the additional 6 cores in patients with prostate-specific antigen ≥ 10 ng/ml, clinical stage ≥ T2, or biopsy Gleason score ≥ 7, but not in those with prostate-specific antigen < 10 ng/ml, clinical stage T1c, or biopsy Gleason score ≤ 6. **Conclusions:** Approximately half of the significant cancers were not accurately detected, and the detection rates in biopsy cores other than the sextant cores appeared to be significantly lower in PCa patients with aggressive features.

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Introduction

Prostate cancer (PCa) is the most frequently diagnosed malignancy and second leading cause of cancer-specific deaths in men in Western industrialized countries [1]. The introduction of a serum prostate-specific antigen (PSA) assay combined with a digital rectal examination as a screening tool for PCa has resulted in a marked increase in the number of patients subsequently undergoing transrectal ultrasound (TRUS)-guided needle biopsy, which is regarded as a mainstay in the diagnosis of PCa [2]. The sextant technique, which targets the peripheral zone (PZ), including the apex, middle, and base of the bilateral lobe, has become the standard method used for prostate biopsies and has significantly improved the detection of PCa [3]. However, this procedure has been shown to underestimate the presence of malignant disease, with false-negative rates ranging from approximately 10 to 30% [4]. Therefore, alternative prostate biopsy schemes, intended to perform more extensive systematic sampling, have been considered in order to improve PCa detection rates [4–7]. Twelve cores have routinely been taken from each patient undergoing TRUS-guided biopsy at our institution; 8 cores from the PZ, including the standard sextant cores and 2 cores from the anterior lateral horns (ALHs), 2 cores from the transition zones (TZs), and an additional 2 cores from the dorsal apex (DA). Taking 12 cores was shown to result in a comparatively satisfactory outcome in the cancer detection rate [8].

A number of studies have so far assessed the significance of prostate biopsy in the detection of PCa in each patient [2–8]; however, investigating the diagnostic ac-

Table 1. Patient characteristics

Item	Value
Age (years)*	67.5 ± 5.9
Serum PSA (ng/ml)*	10.3 ± 7.7
Clinical stage (%)	
T1c	68 (33.0)
T2	138 (67.0)
Biopsy Gleason score (%)	
≥ 6	74 (35.9)
7	108 (52.4)
≥ 8	24 (11.7)
Pathological stage (%)	
pT2	154 (74.8)
pT3	52 (25.2)
Gleason score (%)	
≥ 6	61 (29.6)
7	130 (63.1)
≥ 8	15 (7.3)

PSA = Prostate-specific antigen. *, values are expressed as the mean ± SD.

curacy of all malignant foci present in the prostate has become important gland in several situations associated with the treatment of patients with PCa [9–12]. For example, the recent introduction of robotic techniques has allowed for the precise preservation of the neurovascular bundles, resulting in a significant increase in the proportion of patients undergoing nerve-sparing radical prostatectomy (RP), which is commonly indicated in consideration of the anatomical localization of tumor foci in the prostate [10]. The implications for focal therapies targeting the affected side have also been determined by the localized pattern of PCa foci based on the pathological outcomes of positive biopsy cores [11]. Considering these findings, it would be of interest to investigate the detection rate of PCa according to anatomical areas in the prostate; therefore, we performed a mapping evaluation of RP specimens obtained from patients diagnosed following 12-core systematic biopsies in the present study, and assessed the detection rate of significant PCa in each area from which the biopsy core was taken.

Patients and methods

Patients

This study included a total of 206 patients who were diagnosed with clinically localized PCa by systematic 12-core biopsies and subsequently underwent RP without any neoadjuvant therapies

Table 2. Cancer detection rate according to the anatomical area of sampling cores

	No. of positive cores/ No. of significant cancers	Cancer detection rate (%)
Standard sextant cores		
Apex	93/153	60.8
Middle	101/176	57.4
Base	51/94	54.3
Total	245/423	57.9
Other biopsy cores		
ALH	50/114	43.9
TZ	52/104	50.0
DA	70/137	51.1
Total	172/355	48.5
Overall biopsy cores	417/778	53.6

ALH = Anterior lateral horn; TZ = transition zone; DA = dorsal apex. *, significantly higher than the cancer detection rate in other biopsy cores ($p = 0.0081$).

at our institution between January 2008 and December 2012. Informed consent to perform this study was obtained from all patients, and the study design was approved by the Research Ethics Committee of our institution.

TRUS-Guided Prostate Biopsy

The prostate biopsy procedure performed in this series has been described previously [8]. Briefly, after a sacral block, transrectal biopsies of the prostate were taken with a spring-loaded biopsy gun (Biopty, CR Bard, Covington, GA) and 18-gauge Tru-cut biopsy needle under TRUS guidance using a model 1846 console with a multiplane transducer (Model 8551; Bruel & Kjaer, Naerum, Denmark). Our 12-core based biopsy strategy was as follows: specimens were obtained from 8 cores from the PZ consisting of the apex, middle, and base of the PZ, and ALH, which represented the extreme lateral and anterior PZ surrounding the TZ, in each lobe, 2 cores from the TZ, and additional 2 cores from the DA.

Assessment of RP Specimens

RP and bilateral pelvic lymphadenectomy were performed based on the surgical procedure described by either Walsh [13] or Patel et al. [14]. Resected prostate specimens were prepared using the whole-mount technique, in which the surface was inked and fixed in neutral formalin solution. After fixation, the apex and base were amputated and then serially sectioned along the vertical parasagittal plane. The seminal vesicles were sectioned parallel to their junction with the prostate and entirely submitted for evaluation. The remaining specimen was serially sectioned perpendicularly to the long axis of the gland from the apex to the base at 3-mm intervals. Each section was stained with hematoxylin and

Table 3. Cancer detection rate according to several clinical parameters

	Standard sextant cores		Other biopsy cores		p
	No. of positive cores/ No. of significant cancers	Cancer detection rate (%)	No. of positive cores/ No. of significant cancers	Cancer detection rate (%)	
Serum PSA (ng/ml)					
< 10	130/249	52.2	101/213	47.4	0.30
≥ 10	115/174	66.1	71/142	50.0	0.0042
Clinical stage					
T1c	55/123	44.7	38/105	36.2	0.19
≥ T2	190/300	63.3	134/250	53.6	0.021
Biopsy Gleason score					
6	52/109	47.7	40/96	41.7	0.39
≥ 7	193/314	61.5	132/259	51.0	0.012

PSA = Prostate-specific antigen.

eosin, and examined for the location of cancer, capsular penetration, and seminal vesicle invasion. All pathological specimens were examined in the present study under the guidance of a single pathologist according to the 2002 TNM classification system.

Calculation of the Cancer Detection Rate

Each tumor volume detected in the mapping study of RP specimens was determined as described previously [15]. Briefly, the maximum tumor area of the single tumor focus was determined using a digital planimeter (Uchida Yoko, Tokyo, Japan), and the tumor volume was calculated as the sum of surface areas for that tumor multiplied by the thickness of the prostate slice. Clinically significant cancer was regarded as a tumor greater than 0.5 ml according to the criterion advocated by Stamey et al. [16]. RP specimens were anatomically divided into 12 areas according to the sampling cores of the prostate biopsy, and the existence of significant cancer, defined by a tumor volume > 0.5 ml, was examined. The detection rate of significant cancer in each area was calculated as follows: the number of positive core biopsies/the number of areas containing significant cancer × 100.

Statistical Analysis

All statistical analyses were performed using Statview 5.0 software (Abacus Concepts, Inc., Berkeley, California), and p values less than 0.05 were considered significant. Differences in the cancer detection rates between 2 categories were analyzed using the chi-square test.

Results

The clinicopathological characteristics of the 206 patients included in this study are summarized in table 1. As shown in table 2, pathological examinations of the 12 core-biopsy specimens identified a total of 417 cancer-positive cores, while the mapping study of RP specimens detected 778 areas containing significant cancer-

ous foci. Therefore, the overall cancer detection rate in all 12 areas was 53.6%. Furthermore, the detection rate of significant cancer was significantly higher in the standard sextant cores than in the additional 6 cores.

We then investigated the relationship between the detection rate of significant cancer and major clinical parameters available prior to RP. As shown in table 3, the cancer detection rate was significantly higher in the standard sextant cores than in the additional 6 cores in patients with PSA ≥ 10 ng/ml, clinical stage ≥ T2, or biopsy Gleason score ≥ 7, but not in those with PSA < 10 ng/ml, clinical stage T1c, or biopsy Gleason score ≤ 6.

Discussion

The most accurate way to detect cancer foci inside the prostate gland is surgical removal followed by a pathological examination of the entire gland. Since it is impossible to clinically apply this approach to each patient suspected of PCa, prostate biopsy is accepted as the best diagnostic technique to detect PCa [4]. TRUS-guided sextant biopsy, introduced by Hodge et al. [3], was the traditional method used in the diagnosis of patients with PCa. However, this procedure has been replaced over the past 2 decades by strategies that intend more extensively sampling from alternative areas of the prostate because many studies reported improved rates of PCa detection with an increase in the number of biopsy cores [4–7]. Therefore, TRUS-guided biopsy targeting 10–18 cores has become a common approach for diagnosing PCa in many high volume centers [4]. Systematic biopsies that

take 12 cores from each patient are routinely performed at our institution, and have yielded a comparatively favorable outcome with a cancer detection rate of 35.0% [8].

Most studies that have evaluated the significance of prostate biopsy have focused on the detection of PCa in each patient [2–8]; however, it is also important to assess whether each cancerous lesion is exactly diagnosed considering the recent trend in therapeutic options for patients with early localized PCa. In fact, information on the anatomical localization of tumor foci in the prostate has had crucial effects on decision-making in several clinical situations [9–12]. In this study, therefore, we precisely mapped PCa in RP specimens from PCa patients diagnosed by 12-core systematic biopsies, and analyzed the detection rate of significant PCa according to 12 anatomical areas divided by the distribution of biopsy cores in the prostate.

We identified 778 areas containing significant PCa by mapping RP specimens; however, only 417 biopsy cores were diagnosed with PCa by pathological examinations. This outcome showed that the overall detection rate of significant PCa in all 12 anatomical areas was 53.6%. Few studies have evaluated the ability of prostate biopsies to detect PCa after the presence of malignant lesions has been pathologically confirmed in the prostate [17, 18]. For example, Fink et al. [17] performed ex-vivo sextant biopsy on removed prostate specimens with biopsy-proven cancer, and showed that approximately 10% of all cancers, most of which were clinically significant, were not diagnosed, even though 20-core biopsy cores were taken. However, these studies did not address the diagnostic accuracy of each cancerous lesion; hence, to the best of our knowledge, this study is the first to report cancer detection rates calculated based on the finding of an individual significant PCa.

It is of interest to compare cancer detection rates according to the 12 anatomical areas divided by the sampling manner of prostate biopsy. In this study, the cancer detection rate was shown to be significantly higher in the sextant biopsy cores than in the additional 6 cores. In fact, the cancer detection rates in the apex, middle, and base of the PZ were all > 50%, whereas those in the ALH, TZ, and DA were all ≤ 50%. The lower detection rates of significant PCa in areas other than the sextant cores can be explained as follows: it is technically difficult to obtain optimal biopsy specimens from the ALH and DA through a transrectal approach in some patients [8, 19], while, the number of cores taken from the TZ may be insufficient, particularly in patients with larger

prostates, considering a sample amount with 2 biopsy cores of approximately 30 mm³ [18]. These findings suggest that it might be a promising approach to combine the transperineal approach with the transperineal approach and /or increase the number of biopsy cores targeting the TZ in order to improve the detection rate of significant PCa.

Another point of interest is the relationship between the cancer detection rate according to the anatomical areas and the major clinical parameters. The cancer detection rate was significantly higher in the standard sextant cores than in the additional 6 cores in patients with higher serum PSA, more advanced clinical stage, or greater biopsy Gleason score. Although it is difficult to explain the reason for this trend, these findings suggest that tumor foci with features characteristic to aggressive phenotypes are likely to be misdiagnosed in cores other than those obtained using the sextant biopsy procedure; therefore, it is of importance to further evaluate the presence of tumor foci using alternative diagnostic tools, such as magnetic resonance imaging, in patients with PCa characterized by aggressive features.

There were several limitations to this study. Firstly, this was a retrospective study, and the sample size of 206 men in such a common disease as PCa was not large enough to draw definitive conclusions on the issues assessed in this study. Secondly, preoperative TRUS-guided 12-core prostate biopsies were not performed by a single physician, which may have influenced the current results. Thirdly, this study included only men with positive prostate biopsies and excluded men with false-negative initial biopsies; hence, the actual cancer detection rate may be much lower, and further studies are required to resolve this problem. Fourthly, despite the comparable concordance rates between biopsy and RP Gleason scores to those in previous studies [20, 21], the impact of inaccurate Gleason grading, particularly that of downgrading of the biopsy Gleason score 8, on the present findings should be considered. Finally, although an investigation on the significance of additional parameters, such as patient age and prostate volume, was conducted, there was no significant association between the cancer detection rate and these factors (data not shown). However, it remains important to further examine the impacts of factors that may be potentially associated with the cancer detection rate in order to more clearly understand the diagnosis of each tumor foci using systematic biopsies.

In conclusion, the results of the present study suggest that approximately half of the significant cancers were not accurately detected by systematic TRUS-guided 12-

core biopsies, and the detection rates of significant PCa in cores other than those of traditional sextant biopsy were significantly lower in patients with PCa having aggressive features. Therefore, a novel strategy needs to be

developed to sample biopsy cores from areas different to those obtained with the sextant biopsy procedure in order to improve the detection rate of significant PCa.

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