Original Article

Prospective of 18-Core TRUS Biopsy and Detection Rate of Prostate Cancer

Chinnawat Wattana MD[1], Charoen Leenanupunth MD[1], Yada Phengsalae MSc[1], Premsant Sangkum MD[1], Suchin Worawichawong MD[1], Wisoot Kongchareonsombat MD[1], Chinnakhet Ketsuwan MD[1]

[1] Division of Urology, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background: A systematic 12-core transrectal ultrasound (TRUS)-guided prostate biopsy is currently recommended for prostate malignancy detection modalities. However, there is limited data about the diagnostic yield of increasing the core number to 18.

Objective: To assess the effectiveness of cancer detection and clinical advantages between 12- and 18-core TRUS biopsies.

Materials and Methods: The authors conducted a prospective, single-group trial of TRUS biopsies specifically for patients with prostate-specific antigen (PSA) levels between 4.0 and 20.0 ng/mL. Sixty-two consecutive patients were enrolled and received a 12- or an 18-core TRUS biopsy under local anaesthesia. The patients and prostate cancer characteristics, such as serum PSA, free PSA, prostate volume, PSA density, D'Amico risk classification, and Gleason grade group were recorded and analysed.

Results: The prostate cancer detection rate using 12 cores for the initial TRUS biopsy was 22.6% (14 patients), while using 18 cores was 24.2% (15 patients). The results were not statistically different (p=0.83). Postoperative complications were two cases of gross haematuria and two case of acute urinary retention, which did not require admission. Infection occurred in two patients and no serious morbidities or mortalities.

Conclusion: The present study did not find any significant benefit in increasing the number of biopsy cores from 12 to 18 for the diagnosis of prostate cancer in men with serum PSA levels between 4.0 and 20.0 ng/mL.

Keywords: Transrectal prostate biopsy; 12-core; 18-core; Prostate cancer; Cancer detection

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In men, prostate cancer is the second most common malignancy worldwide. The global incidence of prostate cancer is 1,276,106 persons, accounting for approximately 3.8% of all deaths caused by cancer in men in 2018[1]. In Thailand, the reported incidence rates of prostate cancer are much lower than in most Western developed countries, with prostate cancer being the fourth most common cancer affecting men[2]. Transrectal ultrasound (TRUS)-guided prostate biopsy is the main investigation used to diagnose prostate cancer. The original 6-core (sextant) biopsy technique, as described by Hodge, was proposed in 1989 with a true-positive rate of 20% to 30% and a false-negative rate of 15% to 35%[3]. Nonetheless, a 12-core systematic biopsy that includes apical and far-lateral cores in the template distribution is the standard at the present time, as it increases cancer detection rates by 19.4% relative to those of a sextant biopsy[4].

Theoretically, increasing the number of sample cores should improve the detection rate of prostate cancer[5]. The objective of the present study was to determine the differences in clinical efficacy and safety of 12- and 18-core biopsies in the diagnosis of prostate cancer. The present study was the first prospective study to evaluate the outcome of an 18-core biopsy in Asian patients with serum prostate-specific antigen (PSA) cutoffs between 4.0 and 20.0 ng/mL.

Correspondence to:

Ketsuwan C.

Division of Urology, Department of Surgery, Ramathibodi Hospital, Faculty of Medicine, Mahidol University, 270 Rama VI Road, Toong Phayathai, Ratchathewi, Bangkok 10400, Thailand.

Phone: +66-2-2011315, **Fax**: +66-2-2794704

Email: chinnakhet.ket@mahidol.ac.th

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Materials and Methods

Trial design

The present study was a prospective, single-centre, single-group cohort study conducted in agreement with the Good Clinical Practice guidelines

and the principles of the Declaration of Helsinki and approved by the Ramathibodi Hospital Institutional Review Board (COA. MURA2020/591). The present study was also registered at the clinicaltrials.in.th (TCTR20210929005). All participants received the necessary information and signed informed consent forms before enrolling. All data were kept safe and secure.

Participants

The participants were all new patients presenting with elevations in PSA levels or abnormal digital rectal exams that matched the inclusion criteria. Men were eligible for the present study if they were 18 years old or older and had serum PSA concentrations between 4.0 and 20.0 ng/mL. The exclusion criteria included patients who exhibited absolute contraindications for TRUS biopsy, were receiving ongoing anticoagulant medication, refused to participate, or were diagnosed with acute prostatitis.

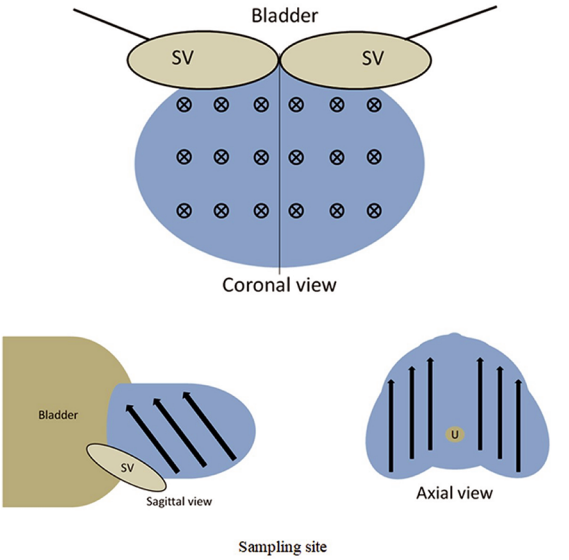

Figure 1. Sampling sites in 12- and 18-core prostate biopsy.

Settings, protocol, and interventions

The present study was performed between November 2017 and September 2021 at the Cystoscopy and Transrectal Ultrasound-Guided Prostate Biopsy Office at the Faculty of Medicine Ramathibodi Hospital. The patients were managed as an outpatient basis by an unaffiliated resident and urological staff and underwent a TRUS-guided biopsy (Flex Focus 1202; BK Medical, Germany). Each sample was obtained using an 18-gauge 25-cm Max-Core® biopsy needle in a spring-loaded biopsy gun.

The patients received a routine fleet enema a night before the procedure and an antibiotic prophylaxis regimen with one tablet of oral levofloxacin (500 mg) at the time of the TRUS biopsy and then continued therapy for seven days. First, the patient was positioned in a dorsal lithotomy position and instilled with povidone plus KY jelly rectally. This was followed by a periprostatic injection of 5 mL of 2% lidocaine without adrenaline into each patient's neurovascular bundle. An ultrasound transducer was subsequently introduced to estimate prostate volume and PSA density.

Registered nurses handled all aspects of the study protocol and methods, providing data during follow-up contact with the patients. Patients who met the inclusion criteria were enrolled in the present study. Groups 1 and 2 were made up of the same patients. Group 1 underwent 12-core TRUS biopsies, during which the prostate was divided into six segments on either side of the prostate, including the base, mid-gland, and apex, obtaining two biopsy specimens from the base and apex segments, two specimens in the mid-gland segments, one medially including the peripheral zone and inner gland, and one laterally as pure peripheral zone, as shown in Figure 1. Group 2 consisted of patients who underwent 18-core TRUS biopsies by adding three extra cores in the lateral peripheral zone of each lobe.

Measures

Using volumetric ultrasound imaging, the prostate size was calculated using the ellipsoid formula [(height × length × width) × π/6](6). PSA density was the serum PSA level divided by the volume of the prostate gland. The Gleason grading system was used to help determine how aggressive the prostate cancer was. Tissue samples were examined under low magnification, and the two most common gland architectural patterns were assigned a grade from 1 to 5 and reported as the Gleason score[7]. Cancer detection rates were compared directly between the groups. Adverse events were assessed according to the Clavien-Dindo classification[8].

Statistical analysis

Data analysis was performed by using Stata, version 14.1 (StataCorp LP, College Station, TX, USA). The record was analysed among the groups. Categorical variables were evaluated using the chi-square test or Fisher's exact test, when appropriate.

Data reported as number and percentages. For continuous variables and normal distribution were compared using Paired t-test. Data was reported as mean ± standard deviation. For continuous variables and non-normal distribution, the Wilcoxon signed-rank test was used. Data was reported as median (interquartile range, IQR). Difference was statistically significant when p-value was less than 0.05 (2-sided).

Results

Sixty-seven patients were eligible but five or 7.4%, were excluded, because they met the exclusion criteria. The remaining 62 male subjects were enrolled. Thus, the experimental and control groups consisted of 62 subjects each. Patient demographics and characteristics are listed in Table 1. The mean patient age was 69.1±6.5 years, the median BMI was 24.9 kg/m² (IQR 22.4 to 27.4 kg/m²), the median pre-TRUS biopsy PSA was 8.7 ng/mL (IQR 5.5 to 11.3 ng/mL) and the median free PSA was 1.2 ng/mL (IQR 1.0 to 2.8 ng/mL). At the time of procedure, the median volumetric prostate volume was 45.7 mL (IQR 36.0 to 67.0 mL) and the median PSAD was 0.1 ng/mL² (IQR 0.1 to 0.2 ng/mL²).

The overall number of patients diagnosed with prostate malignancy in each of the groups was 14 (22.6%) in those who underwent 12-core biopsy and 15 (24.2%) in those who underwent 18-core biopsy. Significant differences in cancer detection were not observed (p=0.832). The other histopathology outcomes derived from the 12-core TRUS-guided prostate biopsies demonstrated that 14.5% and 9.7% had positive biopsy results for high-grade prostatic intraepithelial neoplasia and atypical small acinar proliferation, respectively, compared with 20.9% and 9.7% for patients who underwent 18-core biopsies. Patients in the 18-core group had higher Gleason scores and grade groups than those in the 12-core group, although the differences were not statistically significant (Table 2).

Significant complications required a surgical, endoscopic, or radiological intervention as a sequence of the biopsy did not occur. Clavien-Dindo classification grade II was found postoperatively. Two patients (3.2%) had urosepsis from the biopsy and were treated with intravenous antibiotics and improved. Patients with urinary retention required urinary catheterization but had prior large prostate glands. Two patients had prostate gland larger than 100 mL and one patient had a history of recurrent urinary retention before biopsy. Patients having gross haematuria did not need blood transfusions.

Table 1. Demographic data (n=62)

Variables	Measure
Age (year); mean±SD	69.1±6.5
BMI (kg/m^2); median (IQR)	24.9 (22.4 to 27.4)
PSA (ng/mL); median (IQR)	8.7 (5.5 to 11.3)
PSA density (ng/mL^2); median (IQR)	0.1 (0.1 to 0.2)
Free PSA (ng/mL); median (IQR)	1.2 (1.0 to 2.8)
Percentage of free PSA (%); median (IQR)	19.3 (15.5 to 23.6)
Prostate volume (mL); median (IQR)	45.7 (36 to 67)
Abnormal DRE; n (%)	9.0 (14.5)

BMI=body mass index; DRE=digital rectal examination; PSA=prostate-specific antigen; IQR=interquartile range; SD=standard deviation

Table 2. Cancer detection rates according to different parameters

Variables	12 core (n=62); n (%)	18 core (n=62); n (%)	p-value
Cancer detection	14 (22.6)	15 (24.2)	0.832
Gleason score			
≤6	52 (83.9)	51 (82.3)	0.972
7	6 (9.7)	6 (9.7)	
8	3 (4.8)	4 (6.5)	
9 to 10	1 (1.6)	1 (1.6)	
Grade group			
1	6 (37.5)	6 (37.5)	0.976
2	2 (12.5)	2 (12.5)	
3	4 (25.0)	4 (25.0)	
4	3 (18.8)	4 (25.0)	
5	1 (6.3)	1 (6.3)	
ASAP	6 (9.7)	6 (9.7)	>0.999
HGPIN	9 (14.5)	13 (20.9)	0.347

ASAP=atypical small acinar proliferation; HGPIN=high-grade prostatic intraepithelial neoplasia

Discussion

Today, the diagnosis of prostate cancer is a challenge because the patient has easy access to the health system and thus high expectations. The result of an excellent diagnostic test is an essential tool in clinical practice since it assists urologists in establishing whether a patient has a malignancy condition. TRUS-guided prostate biopsy is described as the mainstay for the diagnosis of prostate cancer[9]. However, some locations within the prostate are not considered during the biopsy, either in the latero-anterior part of the peripheral zone, in the anterior part of the transitional zone, or in the anterior fibromuscular stroma[10]. Thus, various new strategic biopsy techniques in which additional lateral biopsies at the mid and apical regions were developed to improve the cancer detection rate[11].

Although increasing the number of cores beyond six has become commonplace, the optimum number of biopsy cores that yields the highest effectiveness remains unclear. The number of cores for saturation varies widely in published studies, with a range from 20 to 24 to as high as 139 cores[12]. The overall cancer detection rate using saturation prostate biopsy ranges from 19% to 35%[13,14]. In a study of 1,000 consecutive prostate biopsy cases, Guichard et al[15] obtained detection rates of 31.7%, 38.7%, 41.5%, and 42.5% for 6-, 12-, 18-, and 21-core biopsy samples, respectively. Lane et al[16] reported an office-based saturation prostate biopsy range of 20 to 33 cores to detect cancer in 110 of 257 men (42.8%). Stewart et al[17] revealed a detection rate for prostate cancer of 34% in men biopsied using a range of 14 to 45 cores in a saturation technique under anaesthesia in an outpatient surgical setting.

In contrast, other studies reported that increasing the number of cores does not yield a higher detection rate. Scattoni et al[18] demonstrated that 18-core prostate biopsy did not improve the overall prostate cancer detection rate compared with 12-core prostate biopsy at 39.9% and 38.4%, respectively (p=0.37). Similarly, Jones et al[19] compared 10-core with 24-core biopsies and reported that the saturation biopsy did not improve the rate of diagnosis of prostate cancer at 51.7% and 44.6%, respectively (p>0.9). In the present study, using 12 cores revealed a cancer detection rate of around 22.6%, and performing 18-core biopsies increased the detection rate by only 1.6%, which was not statistically significant (p=0.832), suggesting little benefit in increasing the number of cores from 12 to 18.

The possible complications encountered after TRUS biopsy are haematuria, urinary tract infections, rectal bleeding, and acute retention of urine. The incidence of serious adverse events that warranted hospitalization was 0.5% to 6.6% in different studies[20]. In the present study, minor complications such as urinary retention and hematuria occurred in four patients (6.45%), two patients had urinary retention that was treated by urinary catheterization, and two patients had haematuria that did not require admission or blood transfusion. Infection occurred in two patients (3.22%). There was no serious morbidities or mortalities. The authors assume that the rise in the number of biopsy cores did not affect postoperative adverse events.

The present study had limitations. The surgeon who performed the TRUS biopsy was not the same for all patients, which might have biased the results due to the different levels of experience of each surgeon. Moreover, the present study was conducted by only one institution. Therefore, it might not be possible to generalize the findings to general community urologic practice. Additional multicentre studies with a larger sample size are necessary to confirm the effectiveness of the present study and the generalizability of the results to other populations.

Conclusion

In terms of prostate cancer diagnosis for patients with PSA levels between 4.0 and 20.0 ng/mL, 18-core TRUS biopsy is probably not required for the first biopsy. A 12-core sampling should suffice in this group. Therefore, an 18-core TRUS biopsy is not recommended.

What is already known on this topic?

Due to the concerns about possibly missing clinically significant tumours, an extended, 18-core TRUS-guided prostate biopsy procedure was developed to achieve higher sensitivity in detecting prostate cancer.

What this study adds?

The authors proved that increasing the number of biopsy cores to 18 for diagnosing prostate malignancies did not provide any benefit.

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Conflicts of interest

The authors have no relevant financial or non-financial interests to disclose.

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