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The Specific Choice of Transrectal Ultrasound-Guided Prostate Biopsy Scheme Based on Prostate Specific Antigen and Prostate Specific Antigen Density

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Although magnetic resonance imaging (MRI)-targeted biopsy and saturation biopsy can improve the accuracy of prostate biopsy, transrectal ultrasound (TRUS)-guided prostate biopsy is still the cornerstone for diagnosis of prostate cancer. However, it is not clear whether it is necessary to perform the same TRUS-guided biopsy scheme for patients with different prostate specific antigen (PSA) or prostate specific antigen density (PSAD) levels. The purpose of this study was to evaluate the optimal core number for specific suspected prostate cancer patients.

Material/Methods: There were 398 patients who underwent 12-core biopsy scheme, who were included in this retrospective analysis. The 12-core scheme incorporated a classic sextant scheme and 4-core biopsies from the base and middle regions bilaterally. The cancer detection rates of patients with different PSA or PSAD levels between the 12-core, sextant, 4-core, and 2-core biopsy were compared.

Results: The differences in cancer detection rates between the 12-core biopsy scheme and the sextant biopsy scheme were significant in patients with PSA <20 ng/mL or PSAD <0.3. There were no differences in the cancer detection rates between the 12-core biopsy scheme and the 4-core biopsy scheme in patients with PSA ≤50 ng/mL or PSAD ≤1.0. There were significant differences between 12-core and 2-core scheme when PSA ≤70 ng/mL or PSAD ≤1.5.

Conclusions: We recommend that the 12-core biopsy should be used for patients with PSA <20 ng/mL or PSAD <0.3. The biopsy scheme in patients with PSA 20–50 ng/mL or PSAD 0.3–1.0 should be considered in combination with DRE and MRI. For patients with PSA >50 ng/mL or PSAD >1.0, we recommend 6-core or 4-core biopsy by comprehensively considering multiple factors. The 2-core biopsy is recommended for patients with PSA >70 ng/mL or PSAD >1.5.

MeSH Keywords: Biopsy • Prostate-Specific Antigen • Ultrasound, High-Intensity Focused, Transrectal

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Background

In recent years, with the advent of multiparametric magnetic resonance imaging (MRI)-targeted biopsy and transperineal temple mapping saturation biopsy, the accuracy of prostate biopsy has been increased [1,2]. Although MRI-targeted biopsy and saturation biopsy have both been shown to have similar or higher rates of detection of clinically significant prostate cancer [3,4], transrectal ultrasound (TRUS)-guided prostate biopsy is still considered the cornerstone and standard diagnostic approach in suspicion of prostate cancer [5]. Therefore, in consideration of anesthesia, hospital stays, and hospitalization cost, the systematic biopsy scheme with 12 cores has been used in several hospitals.

Systematic sextant biopsy was the classical protocol for diagnosing prostate cancer, but now the systematic 12-core scheme has become the dominating TRUS-guided prostate biopsy approach [6]. However, controversy exists concerning the use of this extended prostate biopsy scheme for all suspected prostate cancer patients. A greater possibility of prostate biopsy complications has been reported after increasing the number of biopsy cores performed; complications reported included rectal bleeding, hematuria, and urinary tract infection [7]. Thus, limiting the number of prostate biopsy cores according to different patient criteria might have clinical significance in decreasing the potential complications without affecting the detection rate.

Nowadays, although tests for screening and early detection have been stressed, many patients still have prostate specific antigen (PSA) levels over 20 ng/mL before biopsy, sometimes even much higher. It is unknown whether it is necessary to perform the same TRUS-guided biopsy scheme for patients with different PSA or PSA density (PSAD) levels. In addition, the most suitable core number of prostate biopsies is also not clear. It is advantageous to design individual biopsy schemes for different patients. In this study, we evaluated the indications for various biopsy schemes for detecting prostate cancer. Moreover, the goal of our work was to determine the optimal core biopsy number for specific patients with suspected prostate cancer.

Material and Methods

Patients

A retrospective analysis from January 2007 to December 2017 showed that 398 patients who were suspected of having prostate cancer underwent 12-core TRUS-guided prostate biopsy scheme for the first time in our department. The indications for performing prostate biopsy were PSA >10 ng/mL or abnormal digital rectal examination (DRE) or PSA between 4 ng/mL and 10 ng/mL plus abnormal PSAD level. The serum PSA detection and DRE of all patients were conducted before prostate biopsy.

Procedure

Prostate biopsies were performed using an ultrasound scanner with a 5–10 MHz TRUS probe. An 18-gauge biopsy needle and a spring-loaded biopsy gun were used to perform each biopsy, producing 15 mm long tissue samples. Patients were prescribed 500 mg tinidazole orally once daily and 200 mg norfloxacin twice daily for 3 days before the biopsy, and intravenously 2 g cefodizime twice daily and 500 mg ornidazole twice daily after the procedure. An enema was given to each patient 2 hours before the biopsy. All patients adopted the left lateral decubitus position with knees flexed at 90 degrees. Ultrasonograms of the prostate were observed by TRUS and the prostate volumes were calculated according to the solid ellipse formula (length×width×height $\pi/6$). The 12-core prostate biopsy scheme incorporated the sextant scheme and another 6 core biopsies by targeting the needle towards the basal, middle, and apical regions of the prostate bilaterally (Figure 1A , 1B). The biopsy specimens were preserved separately in labeled containers filled with 10% formalin. The histopathological examination was performed by a single experienced pathologist according to the current diagnostic criteria.

Statistical analysis

All statistical analyses were performed using SPSS software (version 17.0). The Mann-Whitney U test was used to evaluate the differences of age, PSA, and PSAD between positive biopsy patients and negative biopsy patients. The McNemar test was used to compare the pathological results between the 12-core biopsy scheme and the 2-core, 4-core, and sextant biopsy schemes. Statistical significance was set at $P<0.05$.

Results

Clinical characteristics of patients

All prostate biopsies were performed successfully, and pathological results were obtained. In total, 176 patients (44.2%) were determined to have prostate cancer. Table 1 lists the clinical characteristics of the positive biopsy patients and the negative biopsy patients. Mean age, mean PSA, and mean PSAD were significantly higher in positive biopsy patients compared to negative biopsy patients. The mean age, mean PSA and mean PSAD of the positive biopsy patients were 72.32 years, 43.58 ng/mL, and 1.35, respectively. Table 2 shows the biopsy characteristics of the 176 prostate cancer patients according to different PSA ranges. With the increase of PSA levels, more patients had age ≥70 years, positive core number ≥7, Gleason score >6, and bi-lobar disease. Higher PSA level was associated with increased cancer detection number.

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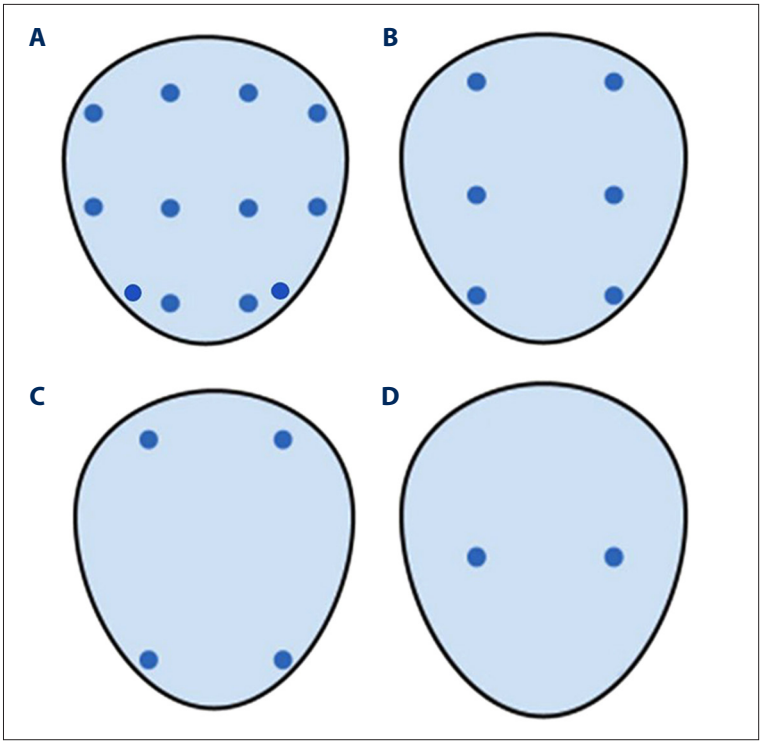

Figure 1. Different prostate biopsy schemes. (**A**) 12-core scheme: bilateral para-sagittal basal, middle, apical and bilateral base, middle, apical biopsy; (**B**) sextant scheme: bilateral para-sagittal basal, middle and apical biopsies; (**C**) 4-core scheme: bilateral para-sagittal basal and apical biopsies; (**D**) 2-core scheme: bilateral para-sagittal middle biopsies.

Table 1. Comparison of clinical data of positive biopsy patients and negative biopsy patients.

	Negative		Positive		P value
Number of patients (%)	222	(55.8%)	176	(44.2%)	
Mean age	61.18	(46-81)	72.32	(51-88)	<0.001
Mean PSA (ng/mL)	17.24	(0.58–104)	43.58	(0.36–120)	<0.001
Mean PSAD	0.74	(0.02–12.64)	1.35	(0.01–18.0)	<0.001

PSA – prostate specific antigen; PSAD – prostate specific antigen density.

Table 2. Biopsy characteristics of prostate cancer patients.

PSA (ng/mL)	Age				Extent of tumor		Positive core number			Gleason score		
	<60	60–69	70–79	≥80	One-lobar	Bi-lobar	≤2	3–6	≥7	≤6	7	≥8
<20	3	12	13	5	16	17	13	14	6	14	12	7
20–50	5	17	34	11	19	48	11	35	21	13	36	18
>50	5	14	38	19	8	68	9	26	41	1	33	42

PSA – prostate specific antigen.

Comparison of cancer detection rate between sextant and 12-core biopsy scheme

The influences of PSA and PSAD levels on the prostate cancer detection rates are listed in Table 3. The cancer detection rate of the 12-core biopsy scheme was 44.2% (176 out of 398 patients), and the sextant scheme resulted in cancer detection rate of 35.7% (142 out of 398 patients). In total, the 12-core biopsy scheme increased the cancer detection rate by 19.3% (34 out of 176 patients) compared with the sextant scheme ($P<0.05$). As shown in Table 3, the advancement in cancer detection rate of the 12-core biopsy reduced significantly with the rise of PSA or PSAD level. The differences of cancer detection rate between the 12-core scheme and sextant scheme

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Table 3. Comparison of cancer detection rate between sextant biopsy scheme and 12-core biopsy scheme.

	Biopsy positive rate (%)		Increase in positive rate (%)	*P* value
	Sextant scheme	12-core scheme		
	142/398 (35.7)	176/398 (44.2)	34/176 (19.3)	<0.05
PSA range (ng/mL)				
<20	10/136 (7.4)	33/136 (24.3)	23/33 (69.7)	<0.001
20–50	56/177 (31.6)	67/177 (37.8)	11/67 (16.4)	>0.05
>50	76/85 (89.4)	76/85 (89.4)	0	
PSAD range				
<0.3	12/135 (8.9)	36/135 (26.7)	24/36 (66.7)	<0.01
0.3–1.0	52/174 (29.9)	62/174 (35.6)	10/62 (16.1)	>0.05
>1.0	78/89 (87.6)	78/89 (87.6)	0	

PSA – prostate specific antigen; PSAD – prostate specific antigen density.

Table 4. Comparison of cancer detection rate between 4-core biopsy scheme and 12-core biopsy scheme.

	Biopsy positive rate (%)		Increase in positive rate (%)	*P* value
	4-core scheme	12-core scheme		
PSA range (ng/mL)				
≤50	55/313 (17.6)	100/313 (31.9)	45/100 (45.0)	<0.01
>50	73/85 (85.9)	76/85 (89.4)	3/85 (3.5)	>0.05
PSAD range				
≤1.0	56/309 (18.1)	98/309 (31.7)	42/98 (42.9)	<0.01
>1.0	72/89 (80.9)	78/89 (87.6)	6/89 (6.7)	>0.05

PSA – prostate specific antigen; PSAD – prostate specific antigen density.

Table 5. Comparison of cancer detection rate between 2-core biopsy scheme and 12-core biopsy scheme.

	Biopsy positive rate (%)		Increase in positive rate (%)	*P* value
	2-core scheme	12-core scheme		
PSA range (ng/mL)				
≤70	39/336 (11.6)	118/336 (35.1)	79/118 (66.9)	<0.001
>70	57/62 (91.9)	58/62 (93.5)	1/58 (1.7)	>0.05
PSAD range				
≤1.5	37/334 (11.1)	116/334 (34.7)	14/116 (68.1)	<0.001
>1.5	59/64 (92.2)	60/64 (93.8)	1/60 (1.7)	>0.05

PSA – prostate specific antigen; PSAD – prostate specific antigen density.

were significant in the patients with PSA <20 ng/mL or PSAD <0.3. Moreover, in the patients with PSA >50 ng/mL or PSAD >1.0, the sextant scheme and 12-core scheme could detect the same number of prostate cancer patients.

Comparison of cancer detection rate between 4-core and 12-core biopsy scheme

The 4-core biopsy scheme in our study included the bilateral para-sagittal basal and apical biopsies used in the 12-core scheme (Figure 1C). The cancer detection rate of the 4-core biopsy scheme was 32.2% (128 out of 398 patients). Table 4

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shows the significant differences of the biopsy positive rates between the 12-core scheme and the 4-core scheme in the patients with PSA ≤50 ng/mL or PSAD ≤1.0 (P<0.01). However, there were no differences in the cancer detection rates of these 2 schemes when PSA >50 ng/mL or PSAD >1.0 (P>0.05).

Comparison of cancer detection rate between the 2-core and the 12-core biopsy scheme

The 2-core biopsy scheme in this study consisted of the bilateral para-sagittal middle biopsies as used in the 12-core scheme (Figure 1D). The positive rate of the 2-core biopsy scheme was 24.1% (96 out of 398 patients). As illustrated in Table 5, there were significant differences in the cancer detection rates of the 12-core scheme and the 2-core scheme when PSA ≤70 ng/mL or PSAD ≤1.5 (P<0.001). Nevertheless, in comparison with the 2-core biopsy scheme, the 12-core scheme did not improve the cancer detection rate in the patients with PSA >70 ng/mL or PSAD >1.5 (P>0.05).

Discussion

The scheme for initial TRUS-guided prostate biopsy remains controversial, although it is the standard pathway in the diagnosis of prostate cancer [8]. Multiple studies from developed countries have reported that the extended biopsy schemes are superior to the sextant biopsy scheme in prostate cancer detection rate [6,9]. Because of different economic and social conditions, delays in seeing a doctor often happens in men with PSA >50 ng/mL, even in men with PSA levels of more than 100 ng/mL. Moreover, there are also some patients who present suffering from lymph nodes or distant metastasis before definite diagnosis. Our study found 65.8% of the patients had PSA levels more than 20 ng/mL (262 out of 398 patients) and 21.4% of the patients had PSA >50 ng/mL (85 out of 398 patients). Dai et al. [10] reported that higher PSA levels were associated with increased prostate cancer detection rates. In our study, the biopsy positive rates of the 12-core scheme for different PSA levels were 24.3% (<20 ng/mL), 37.8% (20–50 ng/mL), and 89.4% (>50 ng/mL). Philip et al. [11] found that patients with higher PSA had larger volume, bi-lobar disease, more positive core numbers, and higher Gleason score. Our results were consistent with their conclusions.

PSAD is a predictor of tumor volume, extracapsular extension, and pathologic characteristics [12]. Prostate volume is relevant to the planning for the optimal core number in the first biopsy [13]. According to our data, the 12-core scheme only increased the biopsy positive rate by 16.1% over the sextant scheme in the patients with PSAD between 0.3 and 1.0. However, when PSAD >1.0, the cancer detection rates were identical for the 12-core scheme and the sextant scheme, and there was no significant difference between the 12-core scheme and 4-core scheme. Additionally, for the patients with PSAD >1.5, the 12-core scheme did not improve the biopsy positive rate compared with the 2-core scheme. Our studies demonstrated that cancer detection increased with elevated PSAD levels and higher PSAD levels were associated with decreased biopsy core number.

Recently, some studies have reported that MRI-targeted prostate biopsy or saturation biopsy could improve prostate cancer detection and localization [14,15]. In addition, increasing the biopsy core sample number can also predict the tumor volume, extracapsular invasion, and Gleason score for patients with lower PSA levels [16,17]. Nevertheless, for older patients with higher PSA levels and lymph nodes or distant metastasis, radical prostatectomy cannot be performed, and the purpose of biopsy is only to establish the pathologic diagnosis. Furthermore, fewer biopsy core samples can reduce the surgical risk and decrease the expense of diagnosis, which is extremely important for these patients.

TRUS-guided prostate biopsy might cause pain, hematuria, urinary tract infection, rectal bleeding, hematospermia, and other complications. The most common complication is minor bleeding, and some patients might occasionally suffer from lower urinary symptoms or hematospermia [18]. Infectious complications might be the primary reason for sepsis or hospitalization after biopsy. The risk factors for infection mainly include older age, antimicrobial resistance, and pre-existing diseases [18]. In our study, there were 2 cases of patients with serious infections, and they recovered through emergency treatment. Studies have reported significantly greater complications after increasing the biopsy core number [19]. Moreover, some studies have indicated that further increase of core number at initial biopsy did not significantly improve the diagnostic rate [20,21]. Our study showed that for patients over 70 years old, the percentage for different PSA levels was 15.0% (<20 ng/mL), 37.5% (20–50 ng/mL), and 47.5% (>50 ng/mL), and the cases of patients diagnosed with prostate cancer increased with the rise of PSA levels for this older group of men. Furthermore, the possibility of suffering from various diseases was higher in older men. For instance, the risk of prostate biopsy was increased in many patients who were using aspirin. Additionally, patients who were sensitive to TRUS probe could not tolerate the whole biopsy procedure. Therefore, we think that limiting the biopsy core number for specific patients could reduce the complications and risks of biopsy, alleviate pain, and facilitate the procedure without decreasing cancer detection rate.

Conclusions

Currently, due to various reasons, urologists in many medical institutions have been performing the traditional systematic

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10- to 12-core biopsy schemes regardless of PSA level. Based on our data, we individually designed the biopsy schemes based on PSA and PSAD levels. For the patients with PSA <20 ng/mL or PSAD <0.3, the 12-core biopsy scheme increased the cancer detection rate by 69.3% over the sextant scheme; thus, we recommend the 12-core biopsy should be applied. The 12-core biopsy scheme only increased cancer detection by about 16% compared with the sextant scheme for Chinese patients with PSA level of 20–50 ng/mL or PSAD level of 0.3–1.0. We thus recommend that the choice of biopsy scheme for these patients should consider combining the results of DRE and prostate MRI. For those patients with PSA >50 ng/mL or PSAD >1.0, we recommend the 6-core biopsy or the 4-core biopsy after comprehensively considering multiple factors, such as PSA, PSAD, age, prostate MRI, cost, and health condition of the patient. In particular, for patients having higher age, weak tolerance, extracapsular extension or lymph nodes metastasis, we recommend adopting the 4-core biopsy scheme. The 2-core biopsy scheme is strongly recommended for the patients with PSA >70 ng/mL or PSAD >1.5.

Conflicts of interest

None.

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