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Original Article

Different T-PSA and prostate volume detection of prostate cancer by using 13-core and theoretical 10-core transrectal ultrasound-guided needle biopsies scheme

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Abstract: This study aims to compare efficiency between 13-core and theoretical 10-core transrectal ultrasound guided needle biopsies scheme to detect prostate cancer. From January 2001 to January 2010, 409 patients who underwent 13-core biopsy were analyzed. We further defined a theoretical 10-core biopsy to be performed by reducing 3 midline punctures in prostate. Then we compared positive detection rates and percentages of positive cores (PPCORE) in patient groups with different T-PSA and prostate volume between 13-core biopsy scheme and 10-core biopsy scheme. The results indicated that hematuria incidence after 13-core biopsy was 53.3%. Thirteen- and 10-core systematic biopsies had similar positive detection rates (45.2% and 44.3%, P = 0.439). There was statistical difference in positive detection rate among different T-PSA level groups (4-20 ng/ml, 20-100 ng/ml and > 100 ng/ml) for same puncture scheme (P = 0.000). Thirteen- and 10-core biopsies were not different in positive detection rate in same T-PSA level group (P = 0.566). Similarly, there was significant difference in positive detection rate among different groups of prostate volume (< 40 ml, 40-60 ml and > 60 ml) (P = 0.000), whereas no difference could be observed between 13-and 10-core biopsies in positive rate within same groups of prostate volume (P = 0.354). The average PPCORE was 0.282 ± 0.380 for 10-core biopsy and 0.286 ± 0.382 for 13-punctures biopsy, respectively (P > 0.05). In conclusion, ten- and 13-core biopsies were comparable in positive rate and PPCORE for detection of prostate cancer, with 10-core biopsy bears a much lower risk of hematuria complication.

Keywords: Prostate cancer, positive detection rate, percentages of positive core, prostate volume, complication

Introduction

The prostate cancer is the most frequently diagnosed malign tumor and the second most common cause of death among men in the East, supplanted only by lung cancer [1]. However, many men with prostate cancer do not display symptoms and undergo no therapy. The only test that can fully confirm the diagnosis of prostate cancer is a biopsy, the removal of fragments of prostate gland which are then subjected to histological evaluation.

The most common technique for prostate biopsy is transrectal ultrasound (TRUS)-guided needle prostate biopsy. During the procedure, a biopsy needle is passed through the ultrasound probe placed in the rectum and into parasagittal midline of both prostatic lobes, in basal, mid-gland and apical portions (the sextant or 6-puncture scheme), with the addition of punctures directed to ultrasonographic suspicious areas. This technique was first described by Hodge et al. in 1989, who demonstrated that ultrasound-guided random systematic biopsy combined with additional directed biopsies of the rare hypoechoic areas not included in the pattern of systematic sampling was able to provide a highly accurate means to diagnose prostate cancer [2]. It was then accepted at the time as the standard of care and helped to emphasize TRUS as a more useful tool for biopsy than for imaging. However, after the establishment

of efficacy for this technique to diagnose prostate cancer, the number of samples and the locations of biopsy are still a matter of debate in the urologic literature and no consensus can be achieved.

Further adding to this puzzle, a new challenge was posed since the 90's when prostatic specific antigen (PSA) measurement was used to screen for early prostate cancer. The percentage of detected tumors and false negative results are inconsistent in literature owing to lack of stratification according to different PSA levels as well as the prostate volume. As a result, patients presenting bulky prostate tumors, which are easily sampled, were compared to patients presenting minimal disease, which was difficult to detect. Similarly, conclusions were drawn after comparison of different biopsy schemes for detecting prostate cancer in a heterogeneous patient sample with PSA measures ranging from slightly elevated to highly elevated. Resulting in a high rate of false negative findings described in literature ranging from 1% to 35% [3, 4].

To avoid these potential limitations seen in previous studies, we retrospectively investigated the efficiency of 13-core TRUS-guided biopsies to detect prostate cancer from our 10-year clinical experience. The study was also carried out with the aim of assessing and comparing the efficacy of different puncture schemes, as well as categorizing the optimal choice for patients stratified by different groups of T-PSA level and prostate volume.

In these ten years, in order to ensure stability, coherence and comparability in punctures operation and pathological process, prostate puncture biopsy was carried out by a designated operator in ultrasound department, and pathological observation of diagnosis was carried out by a designated pathologist.

Materials and methods

Patients

In Guangzhou First People's Hospital, 409 patients took 13 punctures TRUS-guided biopsy from January 2001 to January 2010 were included in this study. Study inclusion criteria were abnormal digital rectal examination and/or T-PSA $\geq$ 4 ng/ml, and no previous biopsy. Their median age was 73 (41-90) years. The median T-PSA level for these 409 patients was 19.0 ng/ml, and their prostate volume was 54.5 ± 38.3 ml.

Methods

PSA level measurement PSA level was detected using the testing kit developed by Roche Diagnostics (Mannheim, Germany) as per manufacturer's instructions.

Patient preparation

Patients should have normal prothrombin level and discontinue anticoagulant therapy 7 days before the operation. All patients received routine cleaning enema before the operation and continuous intravenously infused or orally administered fluoroquinolones or cephalosporin (bacteriostatics that combat the bacterial overgrowth in the rectum) combined with metronidazole 0.2 g t.i.d. 3 days before and after the operation, respectively. Routine cleansing enema was also carried out 2 hours before the operation, which included drainage with 500 ml to 800 ml soapsuds (concentration 0.1% to 0.2%) 2 hours before the biopsy, slow and low-pressure drainage with 300 ml to 400 ml liquor hibitane (0.05‰) 1 hour before the biopsy, and a final requirement on the patients to release the stool 3 to 5 minutes after the drainage. Regular food was permitted before the biopsy.

Puncture schemes

ESAOTE AU4-Idea transrectal biplane probe with transducer frequencies ranging from 5.5 to 7.5 MHz (average: 6.5 MHz, Italy), ALOKA α10 color ultrasonic diagnostic system UST-9118 with TRUS head scanning probe (Japan), Logic7 e8c transrectal probe (GE, USA) and 18G automatic puncture biopsy needle (Bard, USA) were used for the biopsy procedure. Patients were asked to lie down on their left side. After routine perineum and crissum disinfection and the towel sheet being spread, a 20G puncture needle was inserted by 3 mm in depth under the guidance of the above-mentioned probes. Then 5 ml lidocaine (2%) was injected into the capsule cavity on both sides of prostate apex. Five minutes later, an 18G Trocut needle was preceded under color ultrasonic guidance. The 13-core biopsy followed the procedure that in addition to the standard 6-punctures biopsy, 3 separated punctures were placed in the midline and 2 punctures in the lateral line of each prostatic lobe (**Figure 1**). These 13 punctures (3 midline punctures, 6

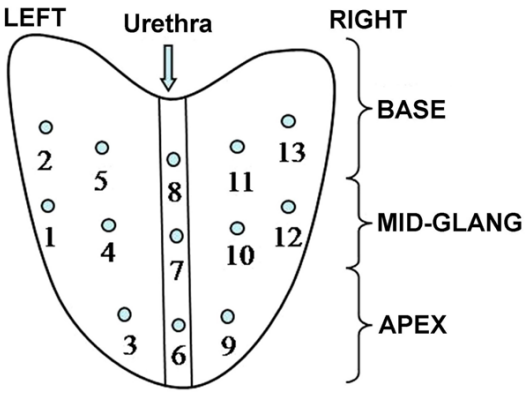

Figure 1. Demographics showing the longitudinal distribution of the 13 punctures for biopsy (numbers indicate the locations of the punctures). The 13 punctures (3 midline, 6 parasagittal, and 4 lateral) were grouped into 3 horizontal portions (base, mid-gland and apex).

parasagittal midline punctures, and 4 lateral punctures) were grouped into 3 horizontal portions (base, mid-gland and apex, **Figure 1**) or 5 longitudinal regions (**Figure 2A-E**). The specimens were obtained from the rim tissues as near as possible to the prostatic capsule and sent for pathological examination.

10-core biopsy

In this study 10-core biopsy was used for detecting prostate cancer. The 10-core biopsy comprises one core from the base, one core from the mid gland, two cores from the apex and one core from the transition zone (TZ) on both sides of the gland. The examiners taking the repeat biopsies were unaware of the location of the previous HGPIN on initial biopsies.

Statistical analysis

The "gold standard" for diagnosis was based on the pathological results. SPSS 17.0 software was used for the analysis. All data were inspected by chi-square analysis of 2 × 2 or R × C tables. Independent samples *t*-test was used to compare the percentages of positive core (PPCORE) of different puncture scheme. A $P < 0.05$ was considered statistically significant.

Results

Complications

Bleeding: This included hematuria and bloody stools. Altogether 218 (53.3%) of the 409 patients who received 13-core biopsy were found with hematuria; and 61 (14.9%) patients were found with bloody stools.

Infection: Six (1.5%) of the 409 patients who received 13-core biopsy were found with infectious complication within 3 days after the operation. One of these 6 patients was found with shivering (0.2% in all) and 5 were found with sepsis (1.2% in all). Among these 5 patients, 1 manifested pyemia and septic shock. Hemoculture identified the pathogenic bacteria to be Escherichia coli. The patient had negative urine culture result and recovered after anti-infection treatment. None of these 409 patients was found with complication of prostate abscess.

Pain: The severity of the pain during the prostate puncture biopsy was rated on a scale of 0 (no pain) to 10 (unbearable pain) and reported by the patients. Four degrees of intensity were established according to the visual analog scale (VAS) scores achieved: 0 stands for no pain, 1-3 for mild pain, 4-5 for moderate pain and 6-10 for severe pain. In the 409 patients who received 13-core biopsy, 308 (75.3%) were found with no pain, 97 (23.7%) were with mild pain, and only 4 (1.0%) were with moderate pain. No patient reported severe pain.

Vasovagal reactions: The vasovagal reactions included perspiration, dizziness and elevated blood pressure, etc. In serious cases, a drop of blood pressure accompanied by nervous system reactions could be witnessed. In the 409 patients who received 13-core biopsy, 11 (2.7%) were found with vasovagal reactions. The vasovagal reactions in these 11 patients were all mild in severity and patients simultaneously recovered soon after the suspension of the operation.

Comparison of positive rates between 13-and 10-core biopsies

In the 409 patients who received 13-core biopsy, 185 (45.2%) were found to be positive for prostate cancer. If the standard 10-core biopsy was applied, there would be 181 (44.3%) patients to be positive, and 4 (0.9%) patients would have a missed diagnosis. Thus the positive rate of 13-core biopsy was only 0.9% higher than that of 10-core biopsy, and no statistical difference in positive rate could be observed between these two groups ($P = 0.439$).

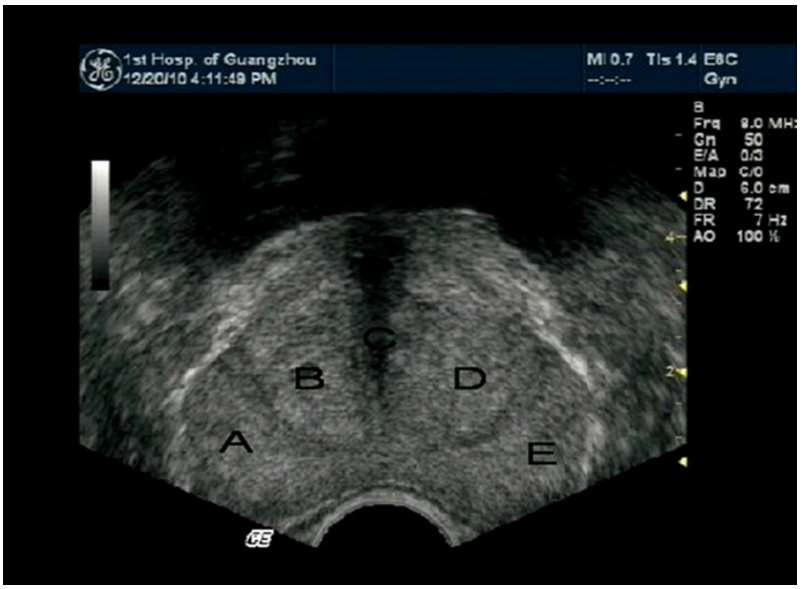

Figure 2. Cross-section and inferior-posterior view of the prostate after 13-punctures biopsy under TRUS-guidance. The 13 punctures were grouped into 5 longitudinal regions (A-E).

Comparison of positive rate among different T-PSA level groups

There was significant statistical difference in positive rate among the different T-PSA groups (4-20, 20-100 and > 100 ng/ml, P = 0.000). No statistical difference was observed between 13-and 10-core biopsies for patients in the same T-PSA level group (P = 0.566) (**Table 1**).

Comparison of positive rate among groups with different prostate volume

There was significant statistical difference in positive rate among groups with different prostate volume (< 40, 40-60 and > 60 ml, P = 0.000). Thirteen- and 10-core biopsies were comparable in positive detection rate among groups with the same prostate volume (P = 0.354) (**Table 2**).

Comparison of PPCORE between 10- and 13-core biopsies

The mean PPCOREs for 10- and 13-core biopsies were 0.380 ± 0.282 and 0.382 ± 0.286, respectively, and there was no statistical difference between these two groups (P = 0.865).

Discussion

Although puncture biopsy and pathological examination hold the key for correct diagnosis of prostate cancer, there is no consensus regarding the choice of optimal puncture scheme. It is reported that adding the number of punctures can increase the detection rate effectively as compared with the standard 6-punctures biopsy [5]. Previous analysis on patients who received prostate puncture biopsy demonstrated that the detection rate of 13-core biopsy was 21% higher than that of 6 -punctures biopsy [6].

The overall positive rate of prostate puncture biopsy in previous investigations has been reported to be around 40% [7, 8]. Our present data showed that the total positive rate of 13-core biopsy was 45.2% from January 2001 to January 2010 in our hospital, which is consistent with previous studies demonstrating that extended biopsy schemes result in an increased detection rate for prostate carcinoma. Notably, it was shown that biopsy locations outside of the standard 6-punctures location are more likely to be positive [9, 10].

It is reported that the complication rates of transrectal type-B ultrasound prostate punctures biopsy are as follows: 4.1%-36.3% for hematuria, 5%-45% for hemospermia, 0.9%-37% for rectal bleeding, 1.7%-7.3% for pyemia, 25% for obvious pain, and 2.7% for vasovagal reaction [11-14]. In our study, the incidence of hematuria, bloody stools and infection after 13-core biopsy occurred in 53.3%, 14.9% and 1.5%, respectively, of the patients, with that of hematuria being higher than previously reported. We propose the mechanism to be that, during 13-core biopsy, the 3 punctures along the prostate midline (region C) locate in close proximity beneath the urethra, so punctures along prostate midline in this region are more likely to hurt the urethra and serve as the main cause of hematuria incidence after the operation.

In this study, there was marked difference in positive detection rate in different T-PSA levels (P = 0.000) and the detection rate of prosta-

Table 1. Comparison of positive rate in different T-PSA level groups

Puncture scheme	Total cases	Positive cases	Positive cases N (%)			Chi-square value	P
			4-20 ng/ml	20-100 ng/ml	> 100 ng/ml		
13-punctures	409	185	55 (29.7)	74 (40.0)	56 (30.3)	99.802	0.000
10-punctures	409	181	52 (28.7)	73 (40.3)	56 (30.1)	104.294	0.000

Table 2. Comparison of positive rate among patients with different prostate volume

Puncture scheme	Total cases	Positive cases	Positive cases N (%)			Chi-square value	P
			< 40 ml	40-60 ml	> 60 ml		
13-punctures	409	185	71 (38.4)	54 (29.2)	60 (32.4)	19.781	0.000
10-punctures	409	181	70 (38.7)	51 (28.2)	60 (33.1)	18.574	0.000

te cancer increased with rising T-PSA levels. However, a comparison between 13-and 10-core biopsies yielded no statistical difference in detection rate within the same T-PSA level, indicating that the addition of 3 punctures along the prostate midline was ineffective in improving the detection rate of prostate cancer.

No consensus has yet been reached as to whether it is necessary to add more punctures for patients with larger prostate volume. It is recommended that individualized puncture scheme can be applied to patients according to their prostate volume [15]. Specifically, it was believed to be advisable to use 8-punctures biopsy for patients with prostate volume less than 40 ml, 10-core biopsy for those with a volume from 40 ml to 60 ml, and 12-punctures biopsy for those with a volume more than 60 ml [15]. However, other literature does not support increasing the number of biopsy punctures for patients with larger prostate [16]. As was shown in **Table 2**, positive detection rate differed significantly among groups with different prostate volumes P = 0.000) and was decreased with increasing prostate volume. It should therefore be considered to increase the number of punctures for patients with larger prostate volume, especially for those with prostate volume more than 100 ml. For patients with similar prostate volume, 13-and 10-core biopsies were comparable in the detection rate of prostate cancer (P = 0.354). Therefore, increasing the number of punctures from 10 to 13 should not be advised, especially when considering the increased hematuria complication in the 13-core scheme.

No matter in groups with different T-PSA level or with different prostate volume, 10-core biopsy was equally efficient to 13 -punctures biopsy in the detection rate of prostate cancer. If the 409 patients in our study took 10- instead of 13-core biopsy, only 4 of them would have experienced a missed diagnosis, which only accounted for 0.9%. That is to say, 13-core biopsy was only 0.9% more efficient than 10-core biopsy in positive detection rate. However, this puncture scheme carries an increased hematuria risk given the close proximity in location of the additional 3 punctures to the urethra and therefore should be avoided in clinical practice.

In conclusion, detection rate of prostate cancer enhances with increasing PSA level, whereas it decreases with accruing prostate volume. An individualized puncture scheme of TRUS-guided biopsy should be advised for patients with prostate cancer, taking into consideration the PSA level, the volume of the prostate, and the clinical stage of the disease, as well as the efficacy and safety profiles of the specific puncture scheme to be applied.

We show in the present study that 10- and 13-core biopsies have similar yield in both positive detection rate and PPCORE, but 10-core biopsy bears a much lower risk of hematuria complication as compared with 13-core biopsy. Our clinical data show 13-punctures transrectal ultrasound-guided needle biopsies scheme should not be advised to detect Prostate Cancer.

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Disclosure of conflict of interest

None.

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References

[1] Qiao L, Liang Y, Lin N, Hu X, Luo D, Gu J, Lu Y, Zheng Q. Endothelin-A receptor antagonists in prostate cancer treatment-a meta-analysis. Int J Clin Exp Med 2015; 8: 3465-3473.

[2] Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. J Urol 1989; 142: 71-74.

[3] Naughton CK, Miller DC, Mager DE, Ornstein DK, Catalona WJ. A prospective randomized trial comparing 6 versus 12 prostate biopsy cores: impact on cancer detection. J Urol 2000; 164: 388-392.

[4] Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. J Urol 1997; 157: 199-202.

[5] Nesrallah L, Nesrallah A, Antunes AA, Leite KR, Srougi M. The role of extended prostate biopsy on prostate cancer detection rate: a study performed on the bench. Int Braz J Urol 2008; 34: 563-570.

[6] Zhong H, Yang L, Deng J, Huang P, Hu J, Wei H, Wang L. Transrectal ultrasound guided systematic 13 core prostate biopsy for diagnosing prostate carcinoma. Chin J Ultrasound Med 2003; 19: 294-296.

[7] Mortimer AM, Ridley N, Cook JL. The influence of ultrasound probe orientation on prostate cancer detection rate during transrectal ultrasonography-guided prostate biopsy. J Endourol 2010; 24: 2075-2081.

[8] Emiliozzi P, Corsetti A, Tassi B, Federico G, Martini M, Pansadoro V. Best approach for prostate cancer detection: a prospective study on transperineal versus transrectal six-core prostate biopsy. Urology 2003; 61: 961-966.

[9] Presti JC, Chang JJ, Bhargava V, Shinohara K. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: results of a prospective clinical trial. J Urol 2000; 163: 163-166.

[10] Gore JL, Shariat SF, Miles BJ, Kadmon D, Jiang N, Wheeler TM, Slawin KM. Optimal combinations of systematic sextant and laterally directed biopsies for the detection of prostate cancer. J Urol 2001; 165: 1554-1559.

[11] Lee SH, Chen SM, Ho CR, Chang PL, Chen CL, Tsui KH. Risk factors associated with transrectal ultrasound guided prostate needle biopsy in patients with prostate cancer. Chang Gung Med J 2009; 32: 623-627.

[12] Hori S, Sengupta A, Joannides A, Balogun-Ojuri B, Tilley R, McLoughlin J. Changing antibiotic prophylaxis for transrectal ultrasound-guided prostate biopsies: are we putting our patients at risk? BJU Int 2010; 106: 1298-1302.

[13] Simsir A, Kismali E, Mammadov R, Gunaydin G, Cal C. Is it possible to predict sepsis, the most serious complication in prostate biopsy? Urol Int 2010; 84: 395-399.

[14] Zaytoun OM, Anil T, Moussa AS, Jianbo L, Fareed K, Jones JS. Morbidity of prostate biopsy after simplified versus complex preparation protocols: assessment of risk factors. Urology 2011; 77: 910-914.

[15] Liang H, Qiu S, Zheng K, Wu R. Individualization of transrectal ultrasonograhpy-guided prostate biopsy for prostate cancer detection. Chin J Cancer 2007; 26: 552-554.

[16] Chepurov AK, Vladimirov VG, Zarinskaia SA, Meshkov VV, Kobaladze KM, Iremashvili VV. On extended biopsy of the prostatic gland. Urologiia 2010; 2010: 52-55.