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Ten-core versus 16-core transrectal ultrasonography guided prostate biopsy for detection of prostatic carcinoma: a prospective comparative study in Indian population

V. Surya Prakash, G. Chandra Mohan, S. Venkata Krishnaiah, V. Vijaykumar, G. Ramesh Babu, G. Vijaya Bhaskar Reddy, V. S. Mahaboob[1]

Department of Urology and Renal Transplantation, Narayana Medical College and Hospital, Nellore, India
[1]Advanced Research Centre, Narayana Medical College and Hospital, Nellore, India

Purpose: To compare the cancer detection rate in patients with raised serum prostate-specific antigen (PSA) or abnormal digital rectal examination (DRE) results between the 10-core and the 16-core biopsy techniques in an Indian population.
Methods: Between November 2010 and November 2012, 95 men aged >50 years who presented to the Urology Department with lower urinary tract symptoms, elevated serum PSA, and/or abnormal DRE findings underwent transrectal ultrasonography (TRUS)-guided prostate biopsy. A total of 53 patients underwent 10-core biopsy and 42 patients underwent 16-core biopsy.
Results: Of the 53 men in the 10-core group, 8 had cancer, whereas in the 16-core biopsy group, 23 of 42 men had cancer. Detection of prostate cancer was significantly higher in patients who underwent 16-core biopsy than in those who underwent 10-core biopsy ($P<0.001$). Among the 95 men, 44 men had abnormal DRE findings (46.3%), of whom 23 showed cancer (52.27%). Of 51 men with normal DRE findings and elevated PSA, 8 men had malignancy with a cancer detection rate of 15.68%. Among 20 men with PSA between 4.1 and 10 ng/mL, 2 (10%) had cancer. In 31 men with PSA between 10.1 and 20 ng/mL, 3 cancers (9.67%) were detected, and in 44 men with PSA >20 ng/mL, 26 cancers were detected (59.09%).
Conclusions: The cancer detection rate with 16-core TRUS-guided biopsy is significantly higher than that with 10-core biopsy (54.76% vs. 15.09%, $P<0.001$). In patients with both normal and abnormal DRE findings, 16-core biopsy has a better detection rate than the 10-core biopsy protocol. With increasing PSA, there is a high rate of detection of prostate cancer in both 10-core and 16-core biopsy patients.

Keywords: Prostate neoplasms, Prostate-specific antigen, Digital rectal examination, Transrectal ultrasonography, Prostate biopsy

INTRODUCTION

Prostate cancer has been the most common non cutaneous malignancy in United States men since 1984 and now accounts for one-quarter of all such cancers (American Cancer Society, 2008). Its incidence varies widely between countries and ethnic populations, with disease rates differing by more than 100-fold. The incidence is highest in African Americans (272 cases/100,000 men/yr) and lowest in Asian Chinese (1.9 cases/1,00,000) [1]. In the Indian population, the incidence ranges from 5.39 to 6.58/100,000 [2]. Use of serum prostate-specific antigen (PSA), digital rectal examination (DRE), and

Corresponding author: G. Chandra Mohan
Department of Urology and Renal Transplantation, Narayana Medical College and Hospital, Nellore-524003, Andhra Pradesh, India
Email: chandramohan_godala@yahoo.co.in / Tel: +918612317963 / Fax: +91-8612331763
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transrectal ultrasonography (TRUS)-guided biopsy of the prostate have led to increased detection of early-stage prostate cancer and a decrease in mortality. The method introduced by Hodge et al. [3] involving 6 systematic sextant TRUS-guided biopsies has been the gold standard protocol for this purpose. However, it is associated with a relatively high false-negative rate of 15% to 31% [4,5]. Because of concern about the possibility of missing clinically significant tumors, several investigators have considered different regimens involving more extensive sampling of the gland, particularly the far lateral aspects of the peripheral zone of the prostate [6,7]. Although it is evident that increased sampling of the peripheral zone increases the cancer yield, there is no universally accepted technique for prostate gland biopsy. Hence, we planned to study 16-core biopsy in a subset of our study population and compare it with 10-core biopsy.

MATERIALS AND METHODS

This prospective observational study was carried out in our department between November 2010 and November 2012. All male patients above 50 years of age presenting to the urology outpatient department with lower urinary tract symptoms were evaluated by DRE and serum PSA. Patients who had abnormal DRE findings or raised PSA were enrolled in the study (95 patients) and were further evaluated by TRUS-guided biopsy for diagnosing prostate cancer. In patients with normal DRE findings and PSA elevation, repeat PSA testing was done. If both PSA levels were above 4 ng/mL, the patient was subjected to TRUS-guided biopsy. In the initial consecutive 53 patients, a 10-core biopsy was done, and in the remaining 42 patients, a 16-core biopsy was performed. Patients unable or unwilling to give informed consent, patients with mental disorders, and patients with urinary tract infection or a history of previous prostate surgery were excluded from the study. Prior approval was obtained from the Institutional Ethics Committee.

1. TRUS biopsy procedure

TRUS-guided prostate biopsy is done as an outpatient procedure. A proctoclysis enema was given on the day of biopsy. Patients taking anticoagulants and anti-platelets were advised to stop medication 5 days prior to biopsy. Written informed consent was obtained for inclusion in the study. Local anaesthesia was given by per rectal instillation of Lignocaine jelly 5 to 10 minutes before the TRUS biopsy procedure. TRUS imaging of the prostate was done with the patient in the left lateral decubitus position with a Pro Focus UltraView-2202 (BK Medical ApS, Herlev, Denmark) using a biplane transrectal probe (6–12 MHz). Prostate imaging was done simultaneously in the longitudinal and transverse planes, prostate volume was calculated, and any abnormalities in the prostate were noted. The Pro-Mag Ultra automatic biopsy instrument (Angiotech Pharmaceuticals Inc., North Bend, WA, USA) with an 18-G, 20-cm needle was used for prostate biopsy.

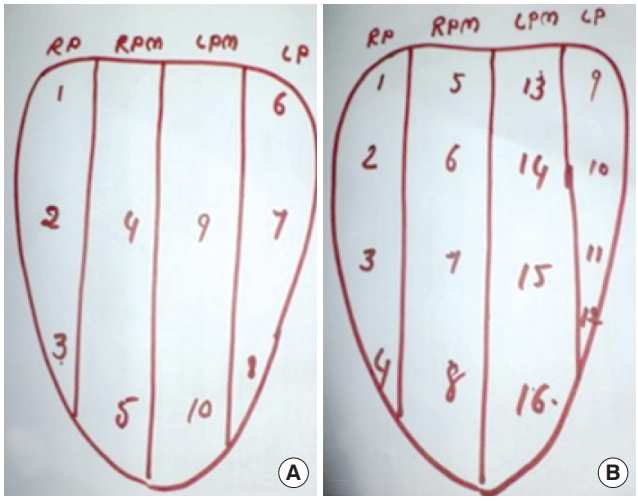

Fig. 1. Prostate biopsy sites. (A) 10 cores, (B) 16 cores. RP, right periphery; RPM, right paramedian; LP, left periphery; LPM, left paramedian.

The sites of the 10 cores (Fig. 1A) were as follows:

right periphery, 3 (1 base, 1 mid, 1 apex); right paramedian, 2 (1 mid, 1 apex); left periphery, 3 (1 base, 1 mid, 1 apex); left paramedian, 2 (1 mid, 1 apex).

The sites of the 16 cores (Fig. 1B) were as follows:

right periphery, 4 (1 base, 2 mid, 1 apex); right paramedian, 4 (1 base, 2 mid, 1 apex); left periphery, 4 (1 base, 2 mid, 1 apex); left paramedian, 4 (1 base, 2 mid, 1 apex).

On TRUS imaging of the prostate, any altered echotexture abnormalities of the prostate were noted and a systematic 10- or 16-core biopsy was done including the abnormal areas in the biopsy region. Tissue bits collected in 10- and 16-core biopsy procedures were placed in tissue paper bits and kept in 4% formalin. Each core was sent in a separate bottle to the pathology department for histopathological examination. Patients were advised to take oral antibiotics (levofloxacin 250 mg+ornidazole 500 mg twice daily) and analgesics (combination of tramadol 50 mg+paracetamol 500 mg twice daily) for 3 days starting from the day of biopsy. The results of the biopsy and the complications of the procedure were studied in the 10- and 16-core groups.

2. Statistical analysis

The statistical analysis was carried out by using SPSS ver. 16.0

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(SPSS Inc., Chicago, IL, USA). The data are summarized in tabular form. Continuous data are presented as means and standard deviations and between-group analysis was carried out by using Student *t*-test. Categorical data are presented as actual numbers and percentages. Categorical variables were analyzed with the chi-square test. For statistical significance, a probability (*P*) value of less than 0.05 was considered.

RESULTS

In this study, we analyzed the results of TRUS-guided prostate biopsy in men suspected of having prostate cancer on the basis of the results of the DRE or PSA measurement. Among 95 patients subjected to TRUS-guided prostate biopsy, prostatic adenocarcinoma was detected in 31 (32.6%), high-grade prostatic intraepithelial neoplasia in 12 (12.62%), fibroadenoleiomyomatous hyperplasia in 32 (32.58%), fibroadenoleiomyomatous hyperplasia with chronic prostatitis in 5 (5.20%), and chronic prostatitis in 15 patients (15.78%). The age range of all the patients was between 50 and 85 years. In patients between the ages of 51 and 60 years, 8 of 30 had cancer; in patients between 61 and 70 years, 11 of 38 had cancer; in patients between 71 and 80 years, 10 of 22 had cancer; and in patients older than 80 years, 2 of 5 had cancer, respectively. The cancer detection rate increased with increasing age. Of 53 men in the 10-core group, 8 had cancer on TRUS biopsy, whereas in the 16-core biopsy group, 23 of 42 had cancer (Table 1). Detection of prostate cancer was significantly higher in patients who underwent 16-core biopsy than in those who underwent 10-core biopsy ($P<0.001$) (Table 1). Among 95 men, 44 men had abnormal DRE findings (46.3%), of whom 23 had evidence of malignancy with a cancer detection rate of 52.27%. All these 44 patients with abnormal DRE findings had elevated serum PSA levels. Of 51 men with normal DRE findings and elevated PSA, 8 had evidence of malignancy on biopsy with a cancer detection rate of 15.68% (Table 2).

Among 22 patients with abnormal DRE findings in the 10-core group, 6 patients were found to have cancer, whereas in the 16-core group, 17 of 22 patients with abnormal DRE findings had cancer ($P=0.002$) (Table 2). In patients with normal DRE findings, 2 of 31 patients in the 10-core group had cancer positivity, whereas 6 of 20 patients in the 16-core group had cancer positivity ($P=0.04$) (Table 2).

All 95 patients had a serum PSA level of more than 4 ng/mL. Among the 20 men with a PSA value between 4.1 and 10 ng/mL, 2 (10%) had cancer. In 31 men with PSA between 10.1 and 20 ng/mL, 3 cancers (9.67%) were detected, and in 44 men with PSA >20 ng/mL, 26 cancers were detected (59.09%). The cancer detection rate with increasing PSA was statistically significant ($P<0.0013$) in the group of patients whose PSA was more than 20 ng/mL

In the 10-core group, 14 patients had a PSA value in the range of 4 to 10 ng/mL, 21 patients had a value in the range of 10.1 to 20 ng/mL, and 18 patients had a value of more than 20 ng/mL. Of them, 1 patient in the lowest range of PSA values had cancer, 2 patients in the middle PSA range had cancer, and 5 patients in the upper PSA range had cancer (Table 3). In the 16-core group, 1 of 6 patients with a PSA value in the range of 4 to 10 ng/mL, 2 of 9 patients with a PSA value in the range of 10.1 to 20 ng/mL, and 20 of 27 patients with a PSA value in the range of more than 20 ng/mL had cancer (Table 3).

We did not encounter any major complications in any of

Table 1. Overall cancer detection rate in the 10-core and 16-core groups

Group	Positive patients for cancer, n (%)	*P*-value
10 Cores (n=53)	8 (15.68)	
16 Cores (n=42)	23 (54.76)	0.001

Table 3. Cancer detection in comparison with PSA in the 10-core and 16-core groups

Group	PSA (ng/mL)	No. of patients	No. of cancers detected	Cancer detection rate (%)	*P*-value
10 Cores					0.09
	4–10	14	1	7.14	
	10.1–20	21	1	4.76	
	>20	18	6	33.34	
16 Cores					0.02
	4–10	6	1	16.60	
	10.1–20	9	2	22.23	
	>20	27	20	74.07	

PSA, prostate-specific antigen.

Table 2. Cancer detection rate in patients with abnormal DRE findings versus normal DRE findings in the 10-core and 16-core groups

Variable	Abnormal DRE			Normal DRE		
	10 Cores	16 Cores	*P*-value	10 Cores	16 Cores	*P*-value
No. of patients	22	22		31	20	
Positive patients for cancer	6	17	0.002	2	6	0.040

DRE, abnormal digital rectal examination.

the 95 patients. Minor complications such as mild hematuria, perineal pain, and transient rectal bleeding were comparable in both 10-core and 16-core groups of patients and were managed accordingly.

DISCUSSION

Prostate cancer is rarely diagnosed in men younger than 50, accounting for only 2% of all cases [8]. The median age at diagnosis is 68 years [9]. In our study, among men between 51 and 60 years of age, 8 cancers (26%) were detected on TRUS biopsy; among men aged 61 to 70 years, 11 cancers (28%) were detected; among men aged 71 to 80 years, 10 cancers (45%) were detected; and among men aged >80 years, 2 cancers (40%) were detected. The cancer detection rate increased with increasing age. The median age in our study was 69 years.

In our study, in the initial 53 consecutive patients, 10-core biopsy was done. In this group, the cancer detection rate was only 15.09%. Owing to the low detection rate, we felt that the gland was not adequately sampled by the 10-core method and hence a widespread sampling of the peripheral zone of the prostate was adopted by doing a 16-core biopsy in the later 42 patients. In the 16-core technique, the peripheral zone was divided into four quadrants, and 4 biopsies were taken from each quadrant (Fig. 1).

Matlaga et al. [10] reviewed the English literature for the current indications and methods of prostate biopsy. In that review, the most widely accepted indication for prostate biopsy was a PSA value of greater than 4.0 ng/mL apart from an abnormal DRE finding. The current literature describes a trend toward increasing the number of cores obtained and the sites biopsied beyond those of the standard sextant technique. The additional cores in many series are obtained from more lateral regions of the gland, and although several criteria are used as indications for initial prostate biopsy, all are based on PSA level and/or abnormal DRE findings. There is no universally accepted technique for prostate gland biopsy.

An abnormal DRE finding is an absolute indication for prostate biopsy. But DRE has only fair reproducibility in the hands of experienced examiners and misses a substantial proportion of early cancers [11]. Overall, the sensitivity of DRE in diagnosing prostate cancer in various studies ranges from 18% 68%. In our study, of a total of 95 patients, 44 had an abnormal DRE finding in the form of a nodule or induration of the prostate. All these 44 patients also had elevated serum PSA. Cancer was diagnosed in 23 patients (52.27%) with abnormal DRE findings (Table 2).

In patients with normal DRE findings, cancer was detected in 8 of 53 patients (15.68%), which emphasizes the fact that biopsy is necessary in patients with raised PSA with negative DRE findings. The cancer detection rate in the 16-core group was higher than in the 10-core group (6 out of 20 versus 2 out of 31), even in the patients with normal findings DRE (Table 2). In 1992, the cancer detection rate for patients with PSA levels of 4 to 10 ng/mL and a normal DRE finding was reported to be 5.5% [12]. Recent data suggest that the current cancer detection rate is 20% to 30% for patients with a PSA of 4–10 ng/mL [13,14]. This could be due to changing patterns of biopsy techniques, including extended biopsy protocols. Catalona et al. [15] found that increasing the PSA cutoff to 4.5 ng/mL among men aged 60 to 69 years would result in 15% fewer biopsy sessions but would miss 8% of organ-confined cancers [15].

In our study, among the patients with normal DRE findings, 1 of 14 patients (7.1%) with PSA of 4 to 10 ng/mL and 2 of 19 patients (10.52%) with PSA of 10.1 to 20 ng/mL had cancer. The low cancer detection rate in lower PSA ranges could be explained by the non malignant pathologies contributing to elevated PSA in our study population (Table 3).

Serum PSA levels greater than 20 ng/mL have been associated with cancer detection rates greater than 70%, and it is uncommon for BPH or chronic prostatitis to increase the PSA to these high levels without concurrent cancer in the gland [16-18]. In our study, in patients with PSA levels greater than 20.1 ng/mL, the cancer detection rate was 59.09% (Table 3).

Multiple *in vivo* studies have revealed that increasing the number of prostate biopsies enhances prostate cancer detection [19-21]. Eskew et al. [20] performed the first prospective study comparing the sextant biopsy method with a 13-core biopsy method. In that study, in addition to the traditional sextant regions (6 cores), 4 cores (2 from each side) from the far lateral regions ("anterior horn" or "lateral" biopsies) and 3 midline biopsies were taken. Those authors found a statistically significant advantage (35% greater detection) with the additional cores of the 5-region biopsy. Babaian et al. [22] investigated an 11-core biopsy method in 362 patients, which included sextant biopsies as well as 1 biopsy from the far lateral region (anterior horn), midline, and bilateral transition zones (adjacent and anterior to the urethra). That study revealed an overall increase of 33% in the prostate cancer detection rate, which was statistically significant. Presti et al. [23] evaluated systematic prostate biopsy in 483 patients. This biopsy scheme obtains 10 samples from the prostate, 6 samples from the traditional sextant regions, and 2 cores from each of the lateral regions (peripheral zones). This method is similar to the 5-region technique, with the exception that the midline

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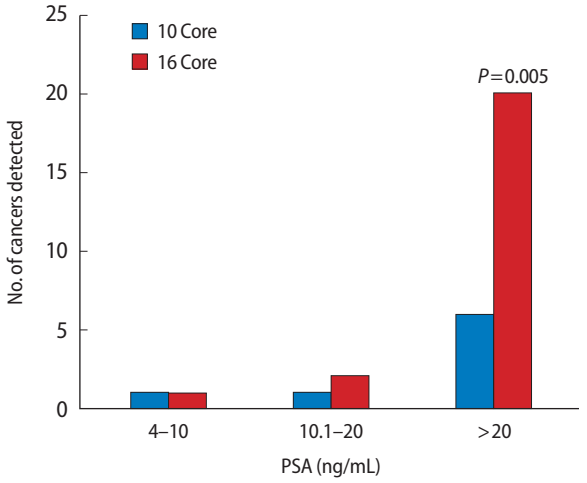

Fig. 2. Comparison of 10 cores with 16 cores on prostate cancer detection with rising prostate-specific antigen (PSA).

biopsies are eliminated. They found that systematic cores taken from the traditional sextant region and lateral base and lateral mid portion of the gland could detect 96% of the cancers diagnosed. Contrary to the above studies, Naughton et al. [24] in their randomized study of 244 patients found that the cancer detection rate in the 6- and 12-core groups was almost identical (26% and 27%, $P=0.9$) [24].

In our study, the overall cancer detection rate in both the 10- and 16-core groups was 32%, i.e., 31 of 95. In the 10-core group, the detection rate was 15.09% (8 of 53), whereas in the 16-core group it was 54.76% (23 of 42) (Table 1). The detection rate was significantly higher in the 16-core group than in the 10-core group ($P=0.001$). On evaluation, we found that there was no statistical significance in the detection of cancer among patients who underwent 10-core biopsy with rising PSA levels ($P=0.09$). However, in the 16-core biopsy group, we found a statistically significant difference in the detection of cancer with rising PSA levels ($P=0.02$) (Table 3). On further evaluation in patients having a PSA level >20 ng/mL, we found a significant increase in detection of cancer among patients who underwent 16-core biopsy compared with 10-core biopsy (6 patients out of 18 versus 20 patients out of 27; $P=0.005$) (Fig. 2).

The limitation of our study was that it was not a randomized study. Also, we did not include the follow-up data of patients who had a negative prostate biopsy result, which might have some bearing on the statistical analysis.

In conclusion, the results of our study support the available literature that the DRE and serum PSA are efficient tools in directing treating physicians whether to proceed for prostatic biopsy. The triad of PSA, DRE, and TRUS-guided prostatic biopsies increases the probability of prostate cancer detection. Also, the cancer detection rate is high when abnormalities are found in both the DRE and PSA (52.27%) compared with elevated PSA alone (15.68%). Our study is unique in that it compared the results of 10-core with those of 16-core prostate biopsy for the first time in an Indian population. The detection rate with 16-core TRUS-guided biopsy was significantly higher than with 10-core biopsy (54.76% vs. 15.09%, $P<0.001$). In patients with both normal and abnormal DRE findings, 16-core biopsy has a better detection rate compared with the 10-core biopsy protocol. With increasing PSA, there is a high rate of detection of prostate cancer in patients undergoing both 10-core and 16-core prostate biopsy, although the rate is significantly higher in the 16-core prostate biopsy group.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Klein EA. Prostate carcinoma: introduction. In: de la Rosette JJ, Manyak MJ, Harisinghani MG, Wijkstra H, editors. Imaging in oncological urology. London: Springer; 2009:211-9.
2. Yeole BB. Trends in the prostate cancer incidence in India. Asian Pac J Cancer Prev 2008;9:141-4.
3. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. J Urol 1989;142:71-4.
4. Singh H, Canto EI, Shariat SF, Kadmon D, Miles BJ, Wheeler TM, et al. Improved detection of clinically significant, curable prostate cancer with systematic 12-core biopsy. J Urol 2004;171:1089-92.
5. Durkan GC, Sheikh N, Johnson P, Hildreth AJ, Greene DR. Improving prostate cancer detection with an extended-core transrectal ultrasonography-guided prostate biopsy protocol. BJU Int 2002;89:33-9.
6. de la Taille A, Antiphon P, Salomon L, Cherfan M, Porcher R, Hoznek A, et al. Prospective evaluation of a 21-sample needle biopsy procedure designed to improve the prostate cancer detection rate. Urology 2003;61:1181-6.
7. Presti JC Jr, O'Dowd GJ, Miller MC, Mattu R, Veltri RW. Extended peripheral zone biopsy schemes increase cancer detection rates and minimize variance in prostate specific antigen and age related cancer rates: results of a community multi-practice study. J Urol 2003;169:125-9.
8. Jani AB, Johnstone PA, Liauw SL, Master VA, Brawley OW. Age and grade trends in prostate cancer (1974-2003): a Sur-

veillance, Epidemiology, and End Results Registry analysis. Am J Clin Oncol 2008;31:375-8.
9. SEER Cancer Statistics Review, 1975-2005 [Internet]. Bethesda (MD): National Cancer Institute; [c2013] [cited 2013 Mar 13]. Available from: http://seer.cancer.gov/archive/csr/1975_2005/.
10. Matlaga BR, Eskew LA, McCullough DL. Prostate biopsy: indications and technique. J Urol 2003;169:12-9.
11. Cooner WH, Mosley BR, Rutherford CL Jr, Beard JH, Pond HS, Terry WJ, et al. Prostate cancer detection in a clinical urological practice by ultrasonography, digital rectal examination and prostate specific antigen. J Urol 1990;143:1146-52.
12. Walsh P, Retik AB, Stamey TA, Vaughan ED. Campbell's urology. 6th ed. Philadelphia: WB Saunders; 1992.
13. Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. N Engl J Med 1991;324:1156-61.
14. Oesterling JE, Jacobsen SJ, Chute CG, Guess HA, Girman CJ, Panser LA, et al. Serum prostate-specific antigen in a community-based population of healthy men. Establishment of age-specific reference ranges. JAMA 1993;270:860-4.
15. Catalona WJ, Hudson MA, Scardino PT, Richie JP, Ahmann FR, Flanigan RC, et al. Selection of optimal prostate specific antigen cutoffs for early detection of prostate cancer: receiver operating characteristic curves. J Urol 1994;152(6 Pt 1):2037-42.
16. Labrie F, Dupont A, Suburu R, Cusan L, Tremblay M, Gomez JL, et al. Serum prostate specific antigen as pre-screening test for prostate cancer. J Urol 1992;147(3 Pt 2):846-51.
17. Orozco R, O'Dowd G, Kunnel B, Miller MC, Veltri RW. Observations on pathology trends in 62,537 prostate biopsies obtained from urology private practices in the United States. Urology 1998;51:186-95.
18. Heyns CF, Naude AM, Ahmed G, Stopforth HB, Stellmacher GA, Visser AJ. Serum prostate-specific antigen as surrogate for the histological diagnosis of prostate cancer. S Afr Med J 2001;91:685-9.
19. Alavi AS, Soloway MS, Vaidya A, Lynne CM, Gheiler EL. Local anesthesia for ultrasound guided prostate biopsy: a prospective randomized trial comparing 2 methods. J Urol 2001;166:1343-5.
20. 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.
21. Levine MA, Ittman M, Melamed J, Lepor H. Two consecutive sets of transrectal ultrasound guided sextant biopsies of the prostate for the detection of prostate cancer. J Urol 1998;159:471-5.
22. Babaian RJ, Toi A, Kamoi K, Troncoso P, Sweet J, Evans R, et al. A comparative analysis of sextant and an extended 11-core multisite directed biopsy strategy. J Urol 2000; 163:152-7.
23. Presti JC Jr, 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;163:163-6.
24. 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;164:388-92.

http://dx.doi.org/10.12954/PI.13025