

Power doppler ultrasonography guided and random prostate biopsy in prostate cancer diagnosis — a comparative study

Shahzada Khalid Sohail,¹ Rahat Sarfraz,² Muhammad Imran,³ Naeem Ahmed Khan,⁴ Noshin Wasim Yusuf⁵

Abstract

Objective: To compare the diagnostic accuracy of power Doppler-guided targeted prostate biopsy and random sextant biopsy in the diagnosis of prostate cancer.

Methods: The prospective study was carried out at the Allama Iqbal Medical College and Jinnah Hospital, Lahore, Pakistan, from January to December, 2012, and comprised clinically suspected cases of carcinoma prostate. Power Doppler-guided biopsies using automatic biopsy gun were obtained from the suspected targeted site. One to three cores per suspected site were obtained. Subsequently random sextant biopsies were performed in the same sitting. Six cores were obtained from 6 random sites using the same gun. Biopsies from both sources were processed for routine haematoxylin and eosin stained sections for histopathological examination.

Results: Of the 50 patients in the study, 30(60%) were diagnosed with power Doppler-guided biopsy as malignant, whereas random sextant biopsy could pick up 22(44%) cases. For benign prostatic hyperplasia, random sextant biopsy labelled 28(56%) as benign, whereas only 20 (40%) were labelled as benign with power Doppler-guided biopsy. Discrepancy in the results between the two procedures was observed in 14(28%) cases, and of them, 11 (22%) were labelled as malignant on power Doppler-guided biopsy while histopathology of sextant biopsies labelled these as benign. The sextant biopsies rendered a specificity, sensitivity, negative predictive value, positive predictive value and diagnostic accuracy of 60.71%, 86.36%, 85%, 63.33% and 72% respectively.

Conclusion: Random sextant biopsy in combination with power Doppler-guided targeted biopsy increases the rate of detection of prostate cancer whereas both procedures in isolation have low sensitivity and specificity for cancer detection.

Keywords: Power Doppler ultrasonography, Random sextant biopsy, Adenocarcinoma prostate. (JPMA 65: 65; 2015)

Introduction

Prostate cancer is rated as the second most common cause of cancer-related death in men. Majority of these patients are diagnosed with prostate cancer at 60 years of age or above.

The modalities for diagnosing prostate cancer are limited which include digital rectal examination (DRE), significantly raised serum Prostate Specific Antigen (PSA) level, Trans-rectal Ultrasonography (TRUS), power Doppler Ultrasound (PDU) and finally the histopathological examination of biopsy tissue.^{1,2} The last one happens to be the gold standard.³ The PDU modality shows increased vascular flow in the cancerous area of the prostate and thus facilitates its localisation.⁴ It is relatively a new technique with a high sensitivity for picking up foci of prostate cancer.⁵⁻⁷ The procedure, however, is more time-consuming, needs special expertise and an expensive equipment. Power Doppler Trans-rectal

Ultrasonography (PD-TRUS) has an added advantage of having a high negative predictive value and may help to reduce the number of unnecessary biopsies.⁸

Since the specificity of PSA as a screening tool is low, the biopsy is imperative for a definite tissue diagnosis of prostate cancer. The area of enhanced vascular flow with PDU can therefore be subjected to targeted biopsy under ultrasound guidance. The other popular conventional biopsy procedure is the systematic sextant biopsy technique. It has been successfully used since its introduction in late 1980s for diagnosing carcinoma prostate.⁹

The present study was planned to evaluate the diagnostic efficacy of both PDU-guided target biopsy and random sextant biopsies in isolation and together, and we aimed at finding out the specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) of random sextant biopsy.

Patients and Methods

The prospective study was carried out at the Radiology and Urology Department of Allama Iqbal Medical College and Jinnah Hospital, Lahore, Pakistan, and comprised clinically suspected cases of carcinoma prostate. DRE,

.....
^{1-3,5}Department of Pathology, Allama Iqbal Medical College, ⁴Department of Radiology, Jinnah Hospital, Lahore, Pakistan.

Correspondence: Shahzada Khalid Sohail. Email: sks190@hotmail.com

raised PSA level >4ng/ml or radiological examination were included in the study.

Biopsies from suspected sites were obtained as PDU-guided targeted biopsy using automatic biopsy gun before obtaining systematic sextant biopsy. One to 3 cores were obtained from each suspicious site and were preserved in 10% buffered formalin. In the same sitting, Random sextant biopsy was performed on the patient. Six cores were taken randomly from prostate using the same gun from parasagittal plane midway between lateral border and midline; 3 cores each from right and left sides, including base, mid gland and apex.¹⁰ The biopsy cores were preserved in 10% buffered formalin. Biopsies from both sources were then processed for routine haematoxylin and eosin (H&E) stained sections for histopathological examination. Specificity, sensitivity, PPV, NPV and accuracy of the sextant random biopsy was calculated using the 2x2 table and PDU-guided biopsy taken as the gold standard.

Results

There were 50 patients with clinical features or DRE findings of prostatic enlargement and suspected carcinoma. The overall mean age was 70.44±9.88 years (range: 50-91 years). Among them, 19(38%) were in the 70-75 age bracket. The mean PSA value was 52.98±66.14ng/ml (range: 10-410ng/ml).

Histopathological examination of the random sextant biopsy was carried out to pick up cases of adenocarcinoma and benign prostatic hyperplasia (BPH). A diagnosis of adenocarcinoma prostate was made in 22(44%) patients whereas BPH was the diagnosis in 28(56%) (Table-1). In the same cohort of patients, the biopsy examination of the PDU-guided targeted biopsy revealed prostatic adenocarcinoma in 30(60%) patients

Table-1: Comparison of the two procedures.

Power	Random	Sextant Malignant	Biopsy Benign	Results Total
Doppler Guided Biopsy	Malignant	19(38%)	11(22%)	30 (60%)
	Benign	3(6%)	17(34%)	20 (40%)
	Total	22 (44%)	28 (56%)	50

Table-2: Random sextant biopsy.

Specificity	60.71%
Sensitivity	86.36%
Negative predictive value	85%
Positive predictive value	63.33%
Accuracy	72%

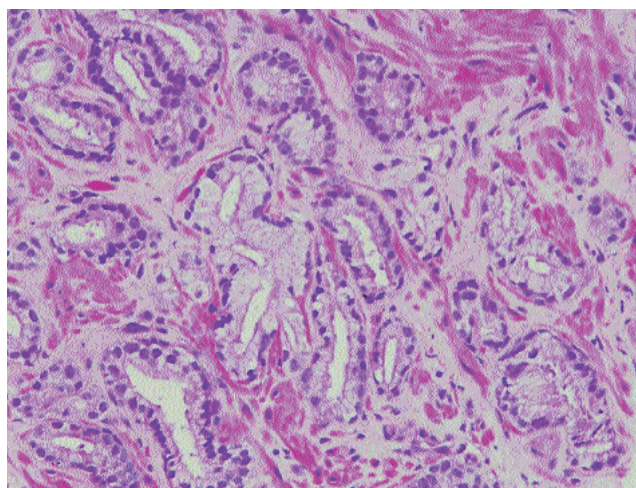


Figure-1: Photomicrograph of Adenocarcinoma Prostate showing Gleason Grade 3 (Score 3 + 3 = 6). Haematoxylin & Eosin stain (20x).

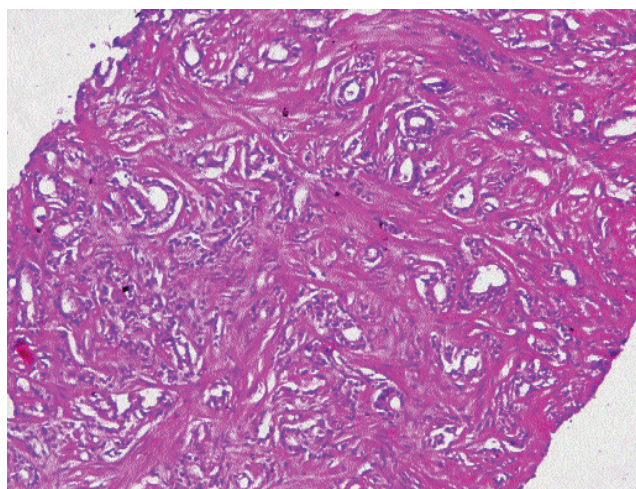


Figure-2: Photomicrograph of Adenocarcinoma Prostate showing Gleason Grade 4 (Score 4 + 3 = 7). Haematoxylin & Eosin stain (10x).

whereas in the remaining 20 (40%) the diagnosis was BPH. Furthermore, 14(28%) cases did not show the same biopsy diagnosis with the two procedures; 11(22%) of them were labelled as malignant on PDU whereas sextant labelled these as benign.

None of our patients had other associated pathologies as infarction, acute or chronic prostatitis and no case of Prostate Intraepithelial Neoplasia (PIN) was recorded either.

On comparing the results of histopathological examination of random sextant biopsies and PDU-guided biopsies for ability to correctly pick up malignant cases, 17(34%) were benign on both procedure; 11(22%) were

malignant on PDU-guided biopsy and benign on random sextant biopsy; 19(38%) were malignant on both procedures; and 3(6%) were benign on PDU-guided biopsy and malignant on random sextant biopsy.

The specificity, sensitivity, NPV, PPV and diagnostic accuracy of the sextant random biopsy was 60.71%, 86.36%, 85%, 63.33% and 72% respectively (Table-2).

Discussion

Prostatic adenocarcinoma, being a leading cause of morbidity and mortality and ranking second in the list of cancer deaths in men, needs to be addressed from every aspect, including its screening, early diagnosis and then the appropriate management. Early diagnosis of prostate cancer is a challenging issue for urologists and pathologists. Biopsy remains the gold standard for the diagnosis of prostate cancer. Various methods are used to procure the biopsy sample of prostate for diagnostic purposes. Random sextant biopsy and the PDU-guided targeted biopsy are the two widely used procedures.^{5,11} Site-directed prostate biopsy on the initial examination improves both sensitivity and specificity for early detection of prostate cancer. Peripheral hypoechoic lesion of prostate on TRUS is the most frequent radiological presentation of prostate cancer. However, lesions, including inflammation, infarction and fibrosis, also appear hypoechoic, resulting in low specificity of this technique.¹² Here, the PDU can enhance the diagnostic capability of TRUS by identifying the actual site for biopsy.

We hypothesised that random sextant biopsies can serve to diagnose prostate carcinoma as effectively as the more expensive procedure of PDU-guided biopsy and thus offer a cheaper and more familiar conventional technique for procuring diagnostic biopsy material.

The current study was therefore conducted to evaluate the efficacy of random sextant biopsy in the diagnosis of prostate cancer and to compare it with the diagnostic efficacy of PDU-guided targeted biopsy.

The mean age for prostate disease in our series was 70.44 ± 9.88 . A sharp increase in the incidence of prostate cancer with age is the hallmark of the disease and has been reported in several studies¹³⁻¹⁷ and our results showed the same trend.

The TRUS-guided prostate biopsy is more precise and less traumatic than the digitally-guided direct biopsy. The ultrasound guidance allows a more precise needle positioning, permitting the separate puncture of base and the mid of prostate apex.¹¹ Sextant biopsies were obtained in all our cases and the diagnostic efficacy was determined. Histologically, 22(44%) cases were diagnosed

as carcinoma prostate and 28(56%) as BPH. The various indices calculated for random sextant biopsy in our study revealed sensitivity for identifying carcinoma prostate to be 86.36%, specificity as 60.71%, PPV 63.33%, NPV 85% and the accuracy 72%. PDU-guided biopsy was taken as the gold standard. Similar results were reported by an earlier study.⁵ Accordingly, the random sextant biopsy had a sensitivity of 86.7%, specificity 61%, PPV 66.7%, NPV 83.6% and accuracy 73.2%.⁵ One study, however, reported 100% specificity and a much lower sensitivity of 60%.¹⁸ It later rose to 71.4% when cancers only in the peripheral zone were taken into account.

The standard sextant TRUS-guided prostate biopsy has its limitations. False negative results have been reported in a study where 20% patients with negative results initially, turned out to be positive with subsequent biopsy. Several studies have therefore strongly recommended repeat biopsies in patients with high clinical suspicion for prostate cancer and negative initial sextant biopsies.¹⁹

Several alternative biopsy approaches to improve prostate sampling have also been suggested. Increasing the number of cores and sampling the far lateral peripheral zones have been recommended.¹⁹ The addition of laterally directed core biopsy to the standard sextant approach has been reported to increase the diagnostic yield for cancer prostate.²⁰ Similarly TRUS-guided systematic 13-core prostate biopsy is reported to significantly increase the cancer detection rate.^{17,21} Presently, 8-12 cores of biopsy samples are being practised in different institutions.¹² In our study, the conventional procedure was carried out and in every case, 6 cores in random sextant biopsy and 3 cores in PDU-targeted biopsy were obtained.

PD-TRUS has been utilised in several studies in an attempt to improve the prostate cancer detection. It is used for guiding the specific site of biopsy in order to obtain targeted biopsy sample from the suspicious hyper-vascular area. In the present study, the PDU-guided biopsy detected 30(60%) cases of adenocarcinoma prostate whereas 20(40%) cases were diagnosed histologically as BPH. A study observed PD-TRUS-guided biopsy in 136 subjects with serum PSA levels between 4.1-10.5ng/ml. In the series, the sensitivity of the PDU-guided biopsy was 53.8%, specificity 59%, PPV 16.7% and NPV was 89.5%. Accordingly, it highlighted that PD-TRUS had a high NPV and therefore may help to reduce unnecessary biopsies when used as an additional tool during TRUS biopsies.¹³ A similar study on 108 men with elevated serum PSA levels reported an improved cancer detection rate since PDU could identify appropriate hyper-vascular sites for targeting the biopsy. However, the directed

biopsies did not have the sufficient diagnostic accuracy to replace or act as an alternative to the conventional systematic biopsy. Their recommendation was a combined use of the PDU-directed biopsies and random sextant biopsies for better results.⁷ Several workers have explored this aspect of diagnostic workup of prostate neoplasia to extensively analyse the efficacy of PDU.^{5-7,14} The results of these studies indicated that PDU was marginally better than random sextant biopsy. The overall cancer detection rate, however, was not significantly different for targeted biopsy and random sextant biopsy ($p=0.58$).¹⁵ Comparing the diagnostic power of PDU compared to sextant in picking up carcinoma cases, 28% cases did not show similarity of results. In 22% cases, PDU was able to pick up carcinoma but in these cases sextant failed to do so. It was only in 6% cases that sextant biopsy could pick up carcinoma but the diagnosis was BPH with PDU. This makes PDU a more sensitive tool with higher NPV compared to sextant. This observation has been highlighted in several studies.^{5-7,14}

The current study explored the diagnostic aspects of one of the very important neoplastic conditions encountered in men, ranking 6th in prevalence in our country. Worldwide, its incidence and prevalence vary, being the highest in American blacks and the lowest in Asians. Its early diagnosis has been facilitated by the popular screening tool of estimating serum PSA. This has led to increasing use of prostatic biopsy for tissue diagnosis in suspect cases. Exploring a method with high negative and positive predictive value as well as being economically and technically feasible is the need of the time. Our study tried to compare two prevailing methods of random sextant and PDU-guided prostate biopsies and explored their effectiveness for tissue diagnosis of prostate adenocarcinoma.

Conclusion

Either random sextant biopsy or PDU-targeted biopsy alone had low sensitivity and specificity for cancer detection. Using them in combination may increase the rate of detection of prostate cancer.

References

- Halpern EJ, Fraucher F, Strup SE, Nazarin LN, Kane P, Gomella LG. Prostate: high frequency Doppler US imaging for cancer detection. *Radiology* 2002; 225: 71 - 7.
- Quinlan MR, Teahan S, Mulvin D, Quinlan DM. Is digital rectal examination still necessary in early detection of prostate cancer? *Ir J Med Sci* 2007 ; 176: 161 - 3.
- Wilson NM, Masoud AM, Barsoum HB, Refaat MM, Moustafa MI, Kamal TA. Correlation of power Doppler with microvessel density in assessing prostate needle biopsy. *Clin Radiol* 2004 ; 59: 946 - 50.
- Sauvain JL, Palascak P, Bourscheid D, Chabi C, Atassi A, Bregon JM, et al. Value of power Doppler and 3D vascular sonography as a method for diagnosis and staging of prostate cancer. *Eur Urol* 2003; 44: 21 - 30.
- Kimura G, Nishimura T, Kimata R, Saito Y, Yoshida K. Random sextant biopsy versus power Doppler ultrasound guided target biopsy in the diagnosis of prostate cancer: Positive rate and clinicopathological features. *J Nippon Med Sch* 2005; 72: 262 -9.
- Okihara K, Kojima M, Nakanouchi T, Okada K, Miki T. Transrectal power Doppler imaging in the detection of prostate cancer. *BJU Int* 2000; 85: 1053 - 7.
- Takahashi S, Yamada Y, Homma Y, Horie S, Hosaka Y, Kitamura T. Power Doppler ultrasonography directed prostate biopsy in men with elevated serum PSA levels: An evaluation of the clinical utility and limitations. *Urology* 2002; 60: 248 - 52.
- Remzi M, Dobrovits M, Reissigl A, Ravery V, Waldert M, Wiunig C, et al. Can power Doppler enhanced transrectal ultrasound guided biopsy improve prostate cancer detection on first and repeat prostate biopsy? *Eur Urol* 2004; 46: 451 - 6.
- Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of prostate. *J Urol* 1997; 157: 199 - 203.
- Presti JC. Prostate Biopsy: Current Status and Limitations. *Rev Urol* 2007; 9: 93-8.
- Applewhite JC, Matlaga BR, McCullough DL, Hall MC. Transrectal ultrasound and biopsy in early diagnosis of prostate cancer. *Cancer control* 2001; 8: 141 - 50.
- Patel U. TRUS and prostate biopsy: Current status. *Prostate Cancer Prostatic Dis* 2004; 7: 208 - 10.
- Remzi M, Dobrovits M, Reissigl A, Ravery V, Waldert M, Wlunig C, et al. Can Power Doppler Enhanced transrectal ultrasound guided biopsy improve prostate cancer detection on first and repeat prostate biopsy? *Eur Urol*: 2004; 46: 451-6.
- Franco OE, Arima K, Yanagawa K, Kawamura J. The usefulness of power Doppler ultrasonography for diagnosing prostate cancer: histological correlation of each biopsy site. *BJU Int* 2000; 85: 1049 - 52.
- Frauscher F, Klauser A, Volgger H, Halpern EJ, Pallwein L, Steiner H et al. Comparison of contrast enhance color Doppler targeted biopsy with conventional systematic biopsy: Impact on prostate cancer detection. *J Urol* 2002; 167: 1648 - 52.
- Barakzi MA, Mubarak M, Kazi JI. Histopathological lesions in transrectal ultrasound guided biopsies of prostate with raised serum prostate specific antigen. *Nephrol Urol*. 2011; 3: 186-90.
- Rashid R, Mubarak M, Kazi JI. Frequency of Adenocarcinoma in Transrectal Ultrasound -guided Prostate Needle Biopsies in Men with raised Serum Prostate Specific Antigen. *Middle East J Cancer* 2013; 4: 73-8.
- Terris MK. Sensitivity and specificity of sextant biopsies in the detection of prostate cancer; preliminary report. *Urology* 1999; 54: 486 -9.
- Stamey TA. Making the most out of six systemic sextant biopsies. *Urology* 1995; 45: 2 - 7.
- Eichler K, Hempel S, Wilby J, Myers L, Bachmann LM, Kleijnen J. Diagnostic value of systemic prostate biopsy methods in the investigation of prostate cancer: a systematic review. *J Urol* 2006; 175: 1605 - 12.
- Yang L, Dang J, Zhong H, Hu J, Wei H, Wang L. Transrectal ultrasound guided systematic 13 core prostate biopsy to diagnose prostate carcinoma. *Chinese J Clin Oncol* 2005; 2: 849 - 51.