



## Diagnosis of Carcinoma Prostate Based on Transrectal Ultrasound Doppler Findings Validated Against Transrectal Ultrasound Guided Biopsy

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### ABSTRACT

**Background:** Prostate cancer is the fifth leading cause of death from cancer in men, accounting for about 6.6% of the total deaths in men. Mortality rates are generally high in predominantly black populations and very low in Asia<sup>[1]</sup>. However, according to recent studies based on National Cancer Registry, the incidence of carcinoma prostate is on the rise in India<sup>[2]</sup>. The study aims at validating Transrectal ultrasound Doppler findings in patients clinically diagnosed to have prostatic malignancy, using Transrectal ultrasound guided biopsy findings as reference standard.

**Materials and Methods:** Diagnostic test evaluation was done by validating Transrectal ultrasound Doppler findings with histopathology, which is taken as reference standard. All patients between the age of 40 –75 years clinically suspected to have carcinoma prostate by the urologist, referred to Department of Radiodiagnosis, were taken as study subjects. Transrectal ultrasound (TRUS) guided 12 core sextant biopsy was performed in all 166 of the study subjects with additional cores from suspicious lesions identified by Doppler pattern criteria defined in the study. Malignant lesions were graded by Gleason scoring after histopathological evaluation.

**Results:** The lesion characterisation by the defined Doppler criteria, was found to have a high sensitivity of 74.68% and a positive predictive value of 73.75% while retaining an equally high specificity of 75.86% and a negative predictive value of 76.34%. Doppler was found to be particularly useful for evaluation of isoechoic lesions which were missed by gray scale.

**Conclusion:** From this study, TRUS Doppler patterns for lesions likely to be malignant were identified. Thus TRUS guided targeted biopsies of suspicious lesions may be recommended in selected patients (elderly, patients with comorbidities), in whom, invasive multicore sextant biopsies may be avoided.

**Keywords:** Transrectal ultrasonography, prostate cancer, TRUS guided biopsy.

### INTRODUCTION

Carcinoma prostate is a common malignancy of males in old age. It has a long course, about 10

years from asymptomatic diagnosis to cause specific death<sup>[1]</sup>. Only a few develop clinically significant carcinomas in their lifetime.

### Diagnosis of Carcinoma Prostate

Current tools for evaluation include measuring serum prostate specific antigen (PSA) levels, digital rectal examination (DRE) and transrectal ultrasound (TRUS) scanning and biopsy<sup>[3]</sup>. The prostate cancer detection rate when the PSA value is < 4ng/ml is less. At PSA values more than 10 ng/ml; cancer detection rate is increased. Diagnosis based on PSA alone can lead to over treatment of the patients subjecting them to unnecessary surgical interventions. Combining DRE and PSA can increase the rate of clinically significant carcinoma prostate case detection in patients with symptoms. But there is likelihood of missing the lesions even with extensive sampling. Thus by validating TRUS Doppler findings with TRUS guided biopsy findings, one could identify TRUS Doppler patterns by which clinically significant lesions of carcinoma prostate can be diagnosed with an acceptable sensitivity and specificity. This could avoid biopsies, especially in elderly patients with comorbidities.

### MATERIALS AND METHODS

The study was a descriptive study with Diagnostic test evaluation conducted during a period of January 2014 to June 2015 in the Department of Radiodiagnosis. All male patients between 40-75 years of age attending Urology outpatient department and referred to Department of Radiodiagnosis who were clinically suspected to have carcinoma prostate by the urologist on the basis of elevated PSA values(>4ng/ml) or suspicious DRE findings (hard irregular gland/hard nodule) irrespective of the symptoms, during the study period were included in the study. Previously diagnosed cases, patients with no rectal access, patients with a previous prostate biopsy, patients with abnormal haemostasis or other medical contraindications and those who were not willing to participate were excluded from the study.

### Study Procedure and Analysis

The study was commenced after the approval of the Ethical committee of the institute. A total of

171 patients (men between 40-75 years of age) were included in the study. However 2 patients were lost in the process of follow-up and in 3 patients, the 12 core biopsy criteria could not be fulfilled. Hence these five patients were excluded from the analysis. A 7.5 MHz transrectal probe (model CB10-4P, biplane-convex) of Mindray Z6 was used and scanning was done by the same examiner.

In all the 166 subjects, prostate was scanned from apex to base on either side. The peripheral zone echogenicity was taken as standard for echogenicity in the prostate and was defined to be isoechoic. Focal hypoechoic /hyperechoic lesions, with well-defined/ill-defined or irregular borders, isoechoic prostatic parenchyma with focal contour bulge/ capsular irregularity for lesions in peripheral zone were considered malignant.

Vascularity of entire glandular parenchyma as well as suspicious lesions on gray scale was evaluated using colour and power Doppler. Vascularity was particularly useful for evaluation of isoechoic lesions.

### Doppler patterns were graded as:

**Pattern 1:** Regular, strip-shaped flow in peripheral and /or transitional zones

**Pattern 2:** Focal increased vascularisation in any zone of prostate

**Pattern 3:** Diffusely increased flow with vascular disorganisation in the peripheral and transitional zones.

**Pattern 4:** Any other patterns noted

Pattern 1 was considered normal and patterns 2, 3 and 4 were considered malignant.

Prostate biopsies were taken using a 20 cm spring-loaded 18-gauge biopsy needle (BARD MAGNUM Core Biopsy System) after adequate precautions and preparations. A biopsy guide was used for guiding the needle to the required site. Each suspicious lesion was biopsied, followed by a systematic 12 core biopsy<sup>[4]</sup>. Sites of the 12 core biopsy included: 6 cores from the base, mid and apex of bilateral peripheral zones (standard sextant biopsy) with additional biopsies from

more laterally directed peripheral base, mid-gland, and apex regions.

Histological analysis were done by a pathologist with standard procedures and biopsy report given as-

- Normal
- Prostatitis
- Benign prostatic hyperplasia

- Malignancy (Gleason score was given for each of the samples which were positive for carcinoma.)

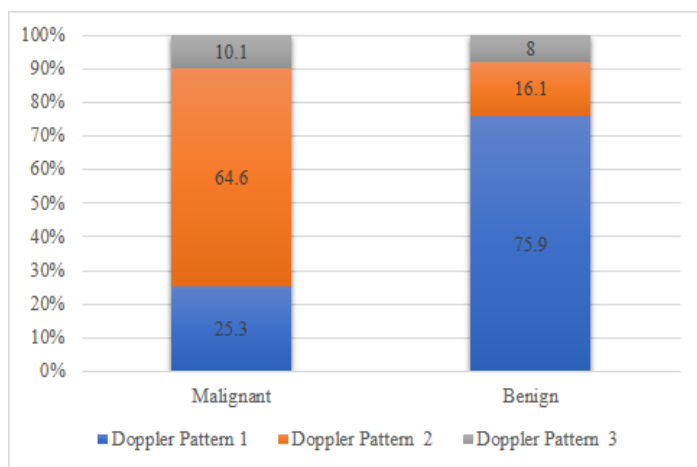
**STATISTICAL EVALUATION, RESULTS AND INTERPRETATION**

After the completion of the study, the following observations were made from the analysis of the study variables from 166 study subjects.

**Table 1:** Relation of Doppler Patterns with Histopathology

Doppler	HPE				Total	
	Malignant		Benign			
	No:	%	No:	%	No:	%
Regular strip-shaped flow in peripheral and transitional zones (Pattern 1)	20	25.3	66	75.9	86	51.8
Focal increased vascularisation in any zone of prostate(Pattern 2)	51	64.6	14	16.1	65	39.2
Diffusely increased flow with vascular disorganisation in the peripheral and transitional zones(Pattern 3)	8	10.1	7	8	15	9
<b>Total</b>	79	100	87	100	166	100

No: - number of cases

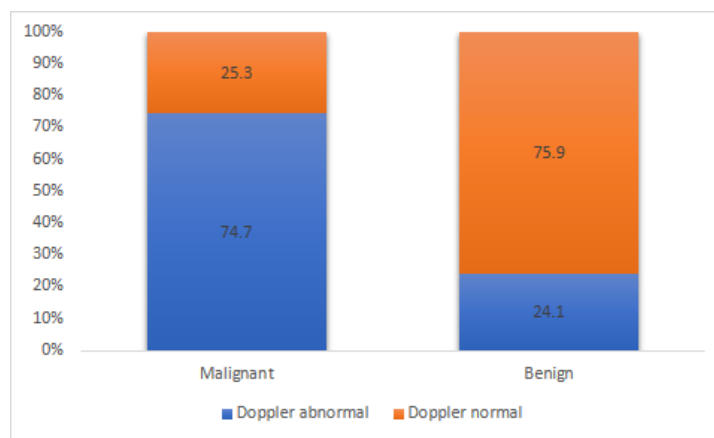


**Figure 4:** Bar chart showing relation of Doppler patterns with histopathology

**Table 2:** Relation of Doppler Findings with Histopathology

Doppler	HPE				Total	
	Malignant		Benign			
	No:	%	No:	%	No:	%
Abnormal	59	74.7	21	24.1	80	48.2
Normal	20	25.3	66	75.9	86	51.8
<b>Total</b>	79	100	87	100	166	100

No: - number of cases



**Figure 5:** Bar chart showing relation of Doppler findings with histopathology

Doppler findings had sensitivity of 74.68%, specificity of 75.86%, positive predictive value of 73.75% and negative predictive value of 76.34%. Of the imaging characters described, focal increased vascularity in any zone of prostate was the most common imaging finding consistent with malignancy on correlation with histopathology. There were 25.3% of false negative cases, which were detected in regular sextant biopsy. Besides

the described patterns of vascularity, no other specific patterns could be elicited in the study. Of the 59 malignant lesions identified by defined Doppler criteria, Doppler could identify 9 isoechoic malignant lesions which were missed by gray scale.

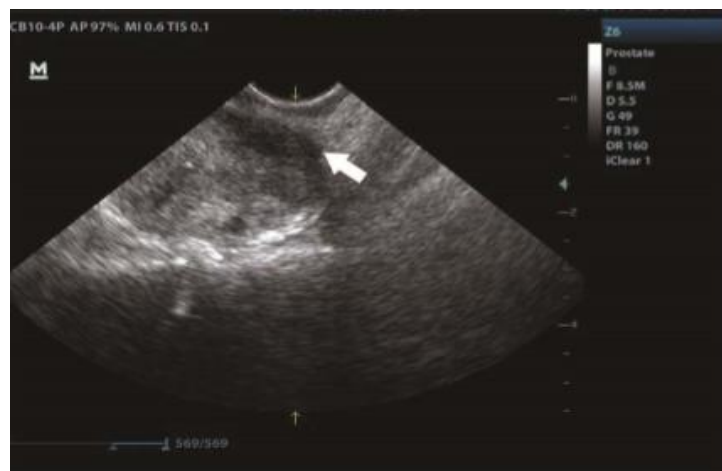


Fig 1a

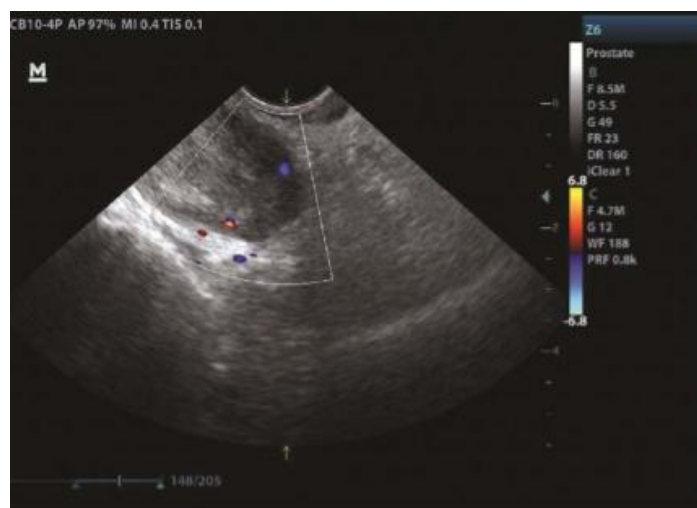


Fig 1b

**Fig 1A,1B:** Axial TRUS image: Hypoechoic lesion in peripheral zone showed focal increased vascularity in colour Doppler (pattern 2 vascularity). The lesion was proved to be malignant in histopathology with a Gleason score 7



Fig 2a



Fig 2b

**Fig 2A,2B:** Axial TRUS image: A hypoechoic lesion (arrow) with ill defined borders noted predominantly in the peripheral zone of prostate, partly extending into central gland, showing focal increased vascularity with an area of vascular disorganisation (pattern 2 vascularity).

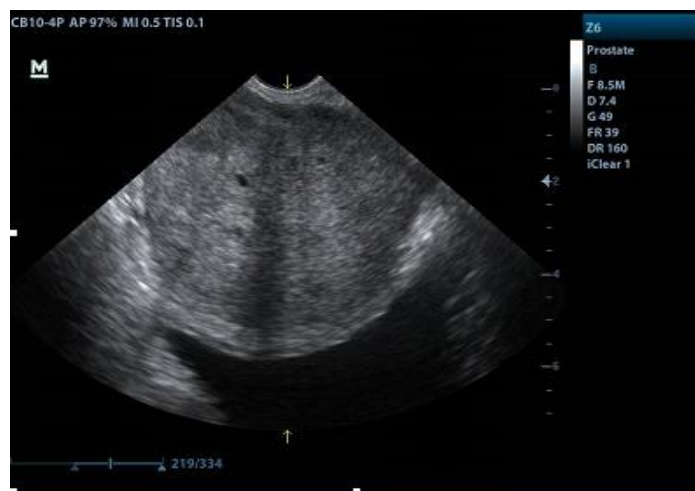


Fig 3a



**Fig 3b**

**Fig 3A,3B:** Axial TRUS image: A hyperechoic lesion (arrow) in the central gland showing diffusely increased vascularity (pattern 3 vascularity). Lesion was proved to be of Gleason score 7 by histopathology.

## DISCUSSION

This study shows that of all the Doppler characters described, focal increased vascularisation in any zone of prostate was the most common imaging finding consistent with malignancy on correlation with histopathology. The sensitivity of Doppler studies in detecting malignancy was found to be 74.68% and specificity, 75.86%. Positive predictive value of Doppler imaging in the study was 73.75% and negative predictive value, 76.34%. The study results are in agreement with studies done by Okihara et al<sup>[5]</sup> which reported that power Doppler studies showed a sensitivity of 97.5%, specificity of 78.3%, positive predictive value of 58.8% and a negative predictive value of 99%.

In the study, Doppler identified 9 isoechoic malignant lesions which were missed by gray scale. The study by Okihara et al<sup>[5]</sup> also have demonstrated the advantage of power Doppler in identification of isoechoic lesions.

Doppler imaging missed 25.3% of the malignant cases in this study. These false negative cases were of lower grade of malignancy and included lesions with scores 6 and 7 in Gleason Scoring system. The study by Okihara et al<sup>[5]</sup>, missed only

2.4% malignant cases by Doppler imaging which is lower than this study.

Several studies showed that, even though there was increased angiogenesis in malignant lesions of prostate when compared to benign lesions or normal prostatic tissue, the vessels of neoangiogenesis were of smaller calibre and were uniformly distributed. This makes these microvessels below the limit of resolution of color or power Doppler and hence missing these malignant lesions in the imaging. Only the large feeder vessels would be identified which supply similar volume of vascular beds in the benign and malignant lesions. Besides, the total volume of intravascular blood may be only mildly elevated in malignant lesions when compared to benign lesions<sup>[6],[7],[8]</sup>.

Hence the study indicates that Doppler imaging findings alone are not sufficient for excluding malignancy and that malignant foci may be missed (especially low grade), if only targeted biopsies are performed based on Doppler patterns. This observation was in agreement with the study of Halpern and Strup<sup>[9]</sup> which showed that a significant number of malignant lesions were missed by targeted biopsies, which were identified in sextant biopsies.

The 21 false positives of the study included prostatitis (acute and chronic) and benign prostatic hypertrophy.

## CONCLUSIONS

From this study, TRUS Doppler patterns for lesions likely to be malignant were identified. Doppler findings were also found to be invaluable in evaluation of isoechoic lesions. Hence it may be suggested that TRUS Doppler findings may be used in screening of debilitated and elderly patients clinically suspected to have carcinoma prostate who cannot tolerate the much invasive sextant biopsy, so that targeted biopsy may be undertaken. However it is not a replacement of the regular sextant biopsy.

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