Original Research Article

Contemporary techniques aiding in the transrectal ultrasound evaluation of the prostate

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Abstract

Prostate cancer is the second most common cause of cancer and the sixth leading cause of cancer death among men worldwide. There are many common imaging modalities to detect prostate cancer like PSA screening, B-mode transabdominal ultrasound, transrectal ultrasound and MRI. However, each of these modalities faces its own demons when it comes to being the gold standard modality to image prostatic lesions and aid in their biopsies. Transrectal elastosonography and histogram analysis of the prostate are upcoming, inexpensive and dexterous imaging modalities that can localize and characterize the prostatic lesions better. The supremacy of TRES lies in its ability to detect lesions efficiently that are invisible to the routine B-mode ultrasound. Histogram evaluation is another B-mode quantitative analysis technique in modern prostatic imaging. The aim of this article is to establish the role of TRES and histogram analysis as useful auxiliary techniques in detecting prostate lesions. This article also correlates TRES results with the corresponding histopathological diagnoses.

Key Words: TRES, Histogram, PSA, MRI, Elastography.

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INTRODUCTION

Prostate cancer is the second most common cause of cancer and the sixth leading cause of cancer death among men worldwide[1]. It is known to cause more morbidity than mortality. Attempts to establish a gold standard screening protocol have been futile, thus far. For the past three decades, abnormal digital rectal examination (DRE) and elevated serum prostate-specific antigen (PSA) have been the smoke signal to warn the clinicians about any prostatic afflictions, which warranted further investigations[2]. B-mode transabdominal ultrasound, transrectal ultrasound and MRI have been the radiologists' means to detect prostatic lesions. However, the shortcomings of these modalities have been well recognized lately, as elaborated below[2,3]. Serum PSA measurement is widely known to have low sensitivity, relatively poor specificity and high false negative rate[8,9,10,14]. This leads to countless unnecessary biopsies in patients who have neither cancer nor any other prostatic lesions. MRI is superior to most other imaging modalities when it comes to soft tissue imaging. However, when it comes to imaging of prostate gland, the superiority of MRI in detecting high-grade prostate cancers and extension into the nearby structures is annulled by its poor capability to detect low grade or indolent lesions[3]. MRI tends to have low specificity[7,14,15] and high false positive rate and quite often requires contrast agents for low-grade lesions. Also, MRI is known to confound the normal vascularity of normal inner gland and benign hyperplastic nodules with low-grade prostatic cancers[3]. It is to be noted that dynamic imaging using contrast and diffusion sequences[16] does help to improve the specificity of MRI however, this cannot be used as the first-line screening test for practical reasons[12]. B-mode TRUS is highly operator dependent. Routine TRUS has a diminished sensitivity and specificity for the detection of

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http://www.medpulse.in/Radio%20Diagnosis/

cancerous lesions (around 50%)[2,3,11,13]. Moreover, it fails to provide information about the composition of the tissue per se, as to whether it is benign or malignant. Due to the drawbacks of the aforementioned imaging modalities, extended multisite biopsy schemes have been recommended to maximize the cancer detection rate. Prostatic biopsy complications are many and include hematuria, hematospermia, rectal bleeding, genitourinary tract infection, etc[1]. Hence, biopsy protocols should be optimized to accurately detect PCa while also reducing the number of prostate biopsy specimens and biopsy-related patient morbidity[11]. According to Jones *et al*, the prostate cancer detection rate cannot be increased even with 24 cores, unless a better imaging modality takes precedence over the existing ones. And so, the radiologists were biding their time for the advent of a novel technique that solves all their problems. Ultrasound elastography is a pristine technique that uses a completely new parameter - tissue stiffness. It takes into account the fact that cancer / inflamed tissue has greater cell and vessel density, which results in greater tissue stiffness. It is used most commonly used to assess organs like prostate, breast, and thyroid. TRES of prostate provides greater sensitivity for detecting prostate cancer and exhibits a high negative predictive value[2,3], ensuring that few cancers are missed in the peripheral zone of the prostate. The sensitivity of elastography for PCa diagnosis can reach or exceed 90%, which clearly hammers down the sensitivities of PSA, DRE or TRUS[2]. TRES is best utilized when its results are supplemented with those of TRUS and MRI, instead of competing with them. The supremacy of TRES in prostate imaging lies in its ability in improving the localization of abnormal foci and in guiding the interventionist to sample limited targeted biopsies of suspicious areas. Real-time ultrasound elastography (RTE) and shear wave elastography (SWE) are the two most commonly used variants of elastography. Many researchers concur that SWE performs better than RTE because, RTE is highly operator dependant as it requires manual compression of the prostate, unlike SWE. According to Sang *et al*, SWE had a pooled sensitivity of 84.4% and specificity of 86.0% for the detection of PCa[4]. Barr *et al* reported that SWE showed a high sensitivity of 96.2%, specificity of 96.2%, positive predictive value (PPV) of 69.4%, and negative predictive value (NPV) of 99.6% for the detection of PCa[12]. These values are both higher than those derived for traditional TRUS and real-time elastography for the diagnosis of patients with prostatic lesions[4]. Histogram analysis is another contemporary aiding tool which quantitatively assesses the returning ultrasound echoes and classifies the nature of the tissues. This helps in differentiating prostatic simple cysts, abscesses, calcification, malignant lesions, etc. Histogram analysis is a special real time B-mode ultrasound technique, that requires a dedicated software installed in the ultrasound machine. A histogram is a simple graph that displays all the brightness levels contained in the region of interest (ROI), from the darkest to the brightest. The histograms represent the echo-distribution intensity in the ROI area. The horizontal axis represents the different shades of gray, and the vertical axis the distribution ratio of each shade. Here the number of picture elements (pixels) of the most common shade in the ROI areas were assumed to be 100%. All data were expressed as mean ± SD. As per research conducted worldwide, histogram analysis is assumed to have a definite role as an adjunct to TRUS in modern imaging.

MATERIALS AND METHODS

Included in our study were 26 in-patients who were admitted for various lower urinary tract symptoms. The indications of prostate biopsy were abnormal DRE, raised PSA (>4ng/ml) and detection of any pathological lesion during trans-abdominal sonography. Mean age of the patients was 65.6 years (range 48 to 85). Exclusion criteria were patients who did not consent and patients with bleeding tendencies. The methodology comprised of TRUS, SWE, histogram analysis and sextant biopsy in order. The patient was positioned in left lateral decubitus position and a thorough TRUS examination was performed to assess the prostate volume and the presence of any focal lesion. This was followed by elastography imaging for the qualitative analysis of the pathological lesion and to guide the systematic sextant biopsy of the prostate. An endocavitary transducer (model PVT-781VT) was used to scan the prostate. As the small-sized field of view is one of the limitations of SWE, each sextant is visualized separately. Round region of interest (ROI) is used for all measurements, as a standard. Measurements are taken in all the quadrants, with at least 8 values on the lesion of interest. Following SWE, histogram analysis was done, to quantitatively assess the nature of the lesion. The values were recorded for correlation. Proceeding further, TRUS-guided sextant biopsy was conducted including the areas deemed to be suspicious. Gleason's scoring system (scale of 2-10) was used in our institute, to stage the biopsies. At the end of each study, the young modulus (kPa) and the histopathology results are compared by generating the receiver operating characteristic (ROC) curve.

OBSERVATIONS AND RESULTS

A total of 26 patients participated in our study. Mean age was 65.6 years (range 48 to 85). Mean PSA value was 6.4 ng/ml. Figure 1 shows the ROC curve generated using the

young modulus values of SWE and histopathology results. Table 1 illustrates the positive correlation of the acquired SWE values and the HPE results. Based on this, a value of 59.9 kPa was derived from the ROC curve as the cut-off between benign and malignant lesions. In accordance with this value, our study produced a sensitivity of 78.6% (11/14), specificity of 66.7% (8/12), PPV of 73.3% (11/15), NPV of 72.7% (8/11). The mean young modulus values of benign lesions was 58.5 kPa. The mean young modulus value of malignant lesions was 81.6 kPa. Following the TRES study, real time histogram analyses of the prostatic lesions were conducted. The mean gray values observed in the histogram analyses from the region of interests were correlated with histopathology. Table 2 shows the observations of the histogram analyses. From the sample of 26 cases, the mean histogram values of benign lesions were observed to be less than 100 whereas, those of malignant lesions ranged between 100 and 200. In this study, HPE results of 9 cases were benign prostatic hyperplasia, 14 were malignant and 3 were acute on chronic inflammation. 25 of the cases showed positive correlation between the acquired histogram values and the histopathology results, with 1 case showing an equivocal result.

DISCUSSION

Transrectal elastosonography using the contemporary techniques (SWE and histogram) is very promising to assess the prostatic lesions and to guide the interventionist in making targeted biopsies. The strong backbone of our study is the availability of HPE results to compare and confirm our SWE and histogram findings. Our study has produced statistically significant results in TRES analyses (sensitivity of 78.6%, specificity of 66.7%, PPV of 73.3%, NPV of 72.7%). 14 out of 26 patients were histopathologically proven to be malignant, of which only 11 had young modulus values above the cut-off. This lead to a sensitivity of 78.6%. The presence of inflammation acted as a confounding factor for specificity because, inflamed prostate despite being benign, has a high young modulus value, simulating malignant lesions. 3 out of 12 benign samples had evidence of inflammation in our study. This was the cause for relatively low specificity 66.7% obtained from this study when compared to the sensitivity. One factor that could be improved upon our study was conducting the same on a larger scale with increased sample size. On retrospective analyses, the 3 inflammatory cases despite having high histogram values, showed no focal nodular (malignant) lesions in the routine B-mode TRUS imaging. Besides, the TRES-SWE value was well below the acquired cut-off value. This reinforces the concept that B-mode TRUS, TRES and histogram analyses complement each other and augments the overall diagnostic accuracy. Apart from attempting to differentiate benign from malignant pathologies, these contemporary techniques have a definite role in the field of image-guided-biopsies. Many trials have shown an increased rate of positive samples when biopsies are done from the areas deemed to be suspicious by these techniques. The overall yield of the biopsy samples is good even with fewer samples (6-core). Thereby, avoiding unnecessary extensive sampling of the prostate leads to better patient care.

CONCLUSION

Transrectal Elastosonography and histogram analyses are novel, non-invasive and inexpensive techniques which detect indolent lesions of the prostate and aid in the biopsy of the same. They are reputed to have very high specificity and negative predictive value, making sure that very few cancers are missed out. These techniques have the potential to guide the interventionists precisely to acquire better biopsy sampling and also reduce the number of core samples. However, it should be noted that "not all cancers are stiff, and all stiff lesions are not cancerous (fibrosis, calcifications, etc)". The potentials of TRES and histogram analysis are best tapped, when their results are supplemented with those of DRE, TRUS, and MRI, leading to the best possible patient care.

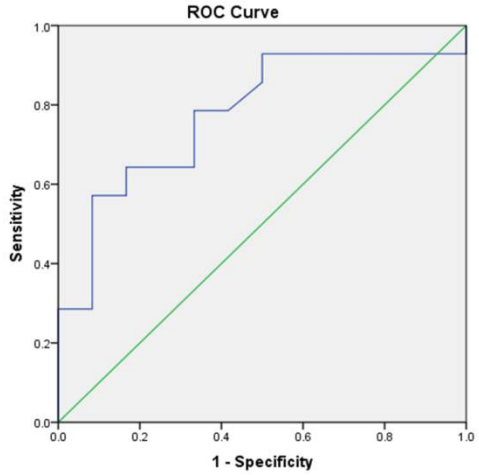
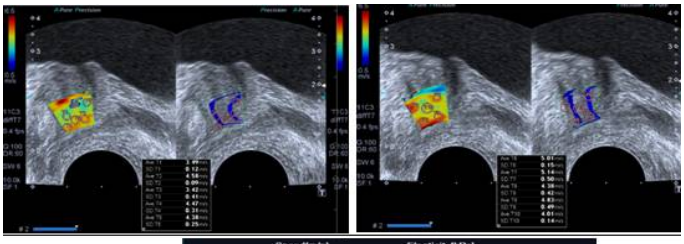
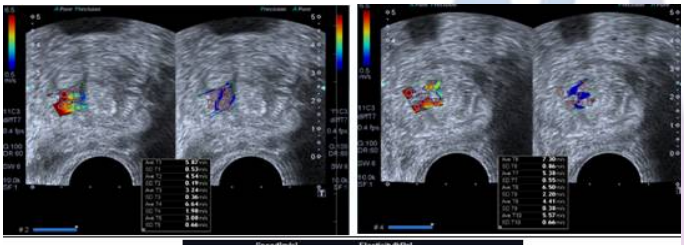


Figure 1: The ROC curve for kPa measurements between malignant and benign prostate lesions. With a value of 59.9 kPa as cutoff, the sensitivity is 78.6%, the specificity is 66.7%, PPV is 73.3%, NPV is 72.7%.



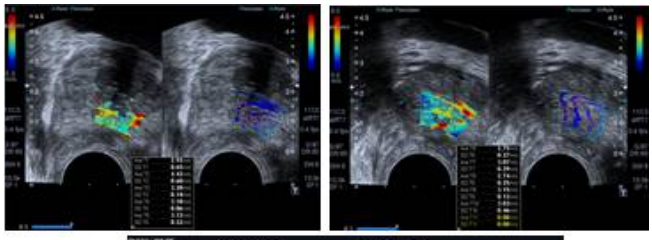
	Speed[m/s] Average	SD	Elasticity[kPa] Average	SD	Depth[cm]
1	3.49	0.12	36.6	2.5	1.3
2	4.58	0.09	63.2	2.6	1.0
3	3.42	0.41	35.6	9.1	1.5
4	4.47	0.31	60.3	8.2	0.9
5	4.38	0.25	57.8	6.6	1.1
6	5.01	0.15	75.5	4.6	1.0
7	5.14	0.50	80.2	15.6	1.5
8	4.38	0.42	58.4	11.1	1.5
9	4.83	0.49	70.9	14.2	0.9
10	4.01	0.14	48.2	3.4	1.3
Mean	4.37		58.7		
SD	0.55		14.3		
Median	4.43		59.3		
IQR	0.82		22.6		

Figure 2: Selected SWE images from a 62 year old man complaining of dysuria, round ROIs were placed on a heterogeneous (predominantly hypoechoic) lesion in the base of the prostate gland. On SWE, his median value of Young modulus was 59.3 kPa. On histogram analysis, the mean value was 42, indicating the benign nature of the lesion. Following image guided biopsy, the histopathology result revealed acute on chronic inflammation.



	Speed[m/s] Average	SD	Elasticity[kPa] Average	SD	Depth[cm]
1	5.87	0.53	104.5	18.7	2.1
2	4.54	0.19	62.3	5.1	2.0
3	3.24	0.36	32.1	5.1	1.9
4	6.64	1.98	113.7	44.2	2.5
5	3.08	0.66	30.4	8.6	2.3
6	7.30	0.86	132.8	43.4	2.5
7	5.38	0.55	88.0	18.3	2.0
8	6.50	2.20	146.2	50.1	2.0
9	4.41	0.38	58.9	9.9	2.5
10	5.57	0.66	94.8	22.4	1.8
Mean	5.25		86.3		
SD	1.35		37.8		
Median	5.47		91.4		
IQR	2.09		54.8		

Figure 3: Selected SWE images from a 71 year old man complaining of low back ache, he presented with serum PSA level of 18.5 ng/ml. B-mode TRUS showed multiple heterogeneous nodules in the right para-median lobe. On SWE imaging, his median value of young modulus is 91.4 kPa. On histogram analysis, the mean value was 125, indicating a probable malignancy. The histopathology result was adenocarcinoma of prostate, Gleason's score 4+4.



	Speed[m/s] Average	SD	Elasticity[kPa] Average	SD	Depth[cm]
1	2.92	0.65	27.9	6.6	1.6
2	4.42	0.60	61.3	9.2	1.3
3	3.20	0.18	30.8	3.5	1.1
4	3.10	0.06	28.8	1.2	1.1
5	3.12	0.22	29.3	4.2	1.4
6	2.75	0.27	22.9	4.8	1.7
7	3.07	0.29	28.6	5.5	1.7
8	2.74	0.25	22.6	4.0	1.2
9	3.15	0.12	29.8	2.2	1.6
10	3.03	0.46	28.2	8.9	1.1
Mean	3.15		31.0		
SD	0.45		10.4		
Median	3.09		28.7		
IQR	0.23		1.9		

Figure 4: Selected SWE images from a 61 year old man complaining of hematuria, he presented with a serum PSA value of 4.2 ng/ml. B-mode TRUS showed heterogeneous echotexture in the left para-median lobe. On SWE imaging, median value of Young modulus was 28.7 kPa. On histogram analysis, the mean value was 49, indicating the benign nature of the imaged lesion. The histopathology result was benign prostatic hyperplasia.

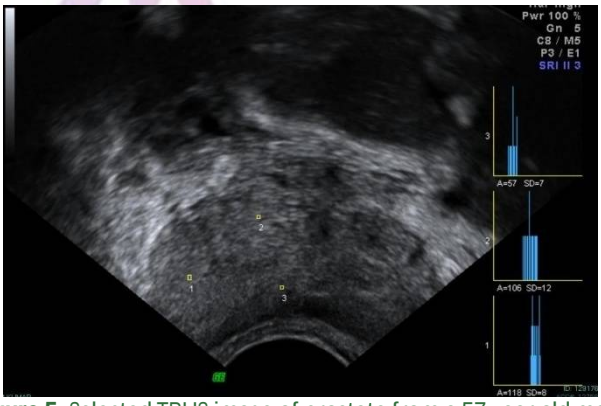


Figure 5: Selected TRUS image of prostate from a 57 year old man complaining of LUTS, he presented with a serum PSA value of 0.8 ng/ml. On SWE imaging, median value of Young modulus was 32.1 kPa. ROI [square 1] for histogram analysis was placed on the lesion. On histogram analysis, the mean value was 118 and the histopathology was benign prostatic hyperplasia with chronic inflammatory changes.

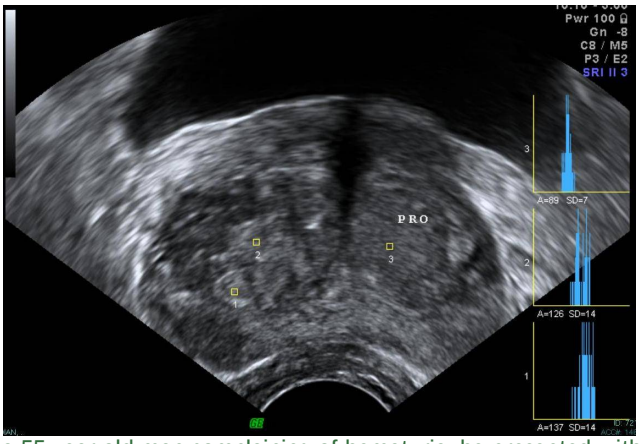


Figure 6: Selected TRUS image from a 55 year old man complaining of hematuria, he presented with a serum PSA value of 5.5 ng/ml. B-mode TRUS showed multiple heterogeneous foci in the central zone. On SWE imaging, median value of Young modulus was 108 kPa. ROI [square 1] for histogram analysis was placed on the one of the lesions. On histogram analysis, the mean value was 137 and the histopathology came out as adenocarcinoma of the prostate

Table 1: Shear wave elastography as an aiding technique in transrectal ultrasound evaluation of the prostate - correlation of kPa values with HPE results. As per the ROC curve generated in our study, 59.9 kPa is the cut-off value between the benign and malignant lesions in this study [Benign - kPa value is less than the derived cut-off value; Malignant - kPa value is greater than the derived cut-off value].

Sample case	SWE values (in kPa)	Nature of the disease as per the acquired SWE value	Histopathology	Correlation
1 (Figure 2)	59.3	Benign	Acute on chronic inflammation	Positive
2 (Figure 3)	91.4	Malignant	Adenocarcinoma of the prostate	Positive
3 (Figure 4)	28.7	Benign	Benign prostatic hyperplasia	Positive
4 (Figure 5)	32.1	Benign	Benign prostatic hyperplasia with chronic inflammatory changes	Positive
5 (Figure 6)	108	Malignant	Adenocarcinoma of the prostate	Positive

Table 2: Histogram analysis as an aiding technique in transrectal ultrasound evaluation of the prostate - correlation of histogram mean values with HPE results. As per our study, range of histogram values of benign lesions was 0- 100 and the range of malignant lesions was 120-200

Sample case	Histogram mean value	Nature of the disease as per the acquired histogram value	Histopathology	Correlation
1 (Figure 2)	42	Benign	Acute on chronic inflammation	Positive
2 (Figure 3)	125	Malignant	Adenocarcinoma of the prostate	Positive
3 (Figure 4)	49	Benign	Benign prostatic hyperplasia	Positive
4 (Figure 5)	118	Benign	Benign prostatic hyperplasia with chronic inflammatory changes	Intermediate
5 (Figure 6)	137	Malignant	Adenocarcinoma of the prostate	Positive

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