Original Research Article

Evaluation of breast lump using elastography, histopathology and its diagnostic accuracy

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ABSTRACT

Background: Current era has brought with it a dramatic climb in the incidence of malignancies especially breast carcinoma among females. It is known to be top most diagnosed life-threatening malignancy in females across the world. Thus, there is need for an imaging modality that helps in minimizing any delay in treatment initiation and avoids unnecessary biopsy. Elastography is a technique based on the concept that hardness of tissue increases proportionately with pathology developing within it compared to the tissue parenchyma surrounding it.

Methods: A prospective cross-sectional study was carried out at JSS Hospital, Mysuru enrolling 90 patients who consented for the study. Patients who gave history of breast lump were admitted and evaluated with detailed history, clinical examination, followed by radiological and pathological investigation. Statistical methods were applied and sensitivity and specificity of B-Mode USG and elastography were determined. The diagnosis was confirmed by histopathology of the specimen.

Results: Out of 90 patients, 46 lesions were benign and 44 were malignant. The sensitivity, specificity and diagnostic accuracy of B-mode USG was calculated to be 71.74%, 90.91% and 81.11% and that for elastography was 95.65%, 68.18% and 82.22% respectively.

Conclusions: In this study, elastography may complement conventional B-mode USG to improve the diagnostic performance.

Keywords: Breast lump, B-mode USG, Elastography, Histopathology

INTRODUCTION

Breast cancer is the most common female cancer worldwide representing nearly a quarter (25%) of all cancer. Earlier cervical cancer was most common cancer in Indian woman but now the incidence of breast cancer has surpassed cervical cancer and is leading cause of cancer death, although cervical cancer still remains most common in rural India.¹ Breast cancer is a non-existent entity for a majority of population till a near and dear one suffers from it. The most important reason being lack of

awareness and screening about breast cancer among rural population. More than 50% patients of breast cancer present in stages 3 and 4, and outcome is not as good as earlier stages, however aggressive the treatment may be.^{2,3} Hence, breast cancer awareness and early detection of cases will help in reducing morbidity and mortality.

Mammography is standard modality for breast imaging.⁴ It can be used as diagnostic tool which is used to evaluate women with abnormal findings such as breast mass or nipple discharge. Other use being screening

mammography which is used to detect unexpected breast cancer in asymptomatic women. With advent of technology digital breast tomosynthesis with 3D images has been introduced as an alternative to standard 2D mammography imaging that is limited by superimposition of breast parenchyma and breast density.⁵ However, not all breast cancers can be detected by the use of mammography. Studies have shown that imaging using ultrasound and magnetic resonance (MR) imaging can find small cancers not visible on the mammograms.⁶ Even though it is more sensitive, it is generally not applicable for initial breast screening.

Breast biopsy, the current method used to distinguish between benign and malignant breast abnormalities seen at imaging, yields a benign result in more than 75% of the patients, making it the costliest per capita component of breast cancer screening program.⁷ Thus ultrasonography was used to classify breast lesions.⁸ However, this was not reliably confirmed nor widely applied. To overcome this sono-elastography was developed whose sensitivity and specificity is higher than sono-mammography in differentiating benign from malignant breast lesions.

Breast sono-elastography is a non-invasive imaging technique which provides information on breast lesions. It quantifies the hardness of a breast lesion in relation to surrounding tissue, being useful in differentiating between benign and malignant tissue.⁹ Two techniques are now available for clinical use: strain (compression based) and shear wave elastography.¹⁰ This improvement may substantially reduce the number of benign biopsies performed. The type of elastography used in this study will be strain elastography.

Strain is computed as the rate of change in axial tissue displacement as a function of depth. Strain images are produced when the relative differences in tissue motion at each location in the breast are calculated and displayed. Harder areas of the breast (i.e., areas with less tissue displacement during compression) appear darker on strain images and softer areas of the breast (i.e., areas with more tissue displacement during compression) appear brighter.^{10,11}

METHODS

All patients with history of lump in the breast attending JSSH, Surgery OPD in the period of May 2016 to September 2018 with inclusion and exclusion criteria as described below were considered for the study.

The study was conducted at JSS Hospital, Mysuru from May 2016 to September 2018 (28 months) with sample size of 90 patients with breast lesions along with the inclusion and exclusion criteria were considered for the study.

Ultrasound- Phillips iU22: The high frequency linear probe (L 12-5) was used in this study, which was also

compatible for the real time tissue elastography and the histopathology of the specimen after surgery were taken. The images are captured and documented for the study.

A prospective and correlation study of 65 patients with palpable breast lesions were done to assess the type of lesion with histopathological correlation.

The patients with family history of breast lesion, who came to the Department of Surgery with history of lump in the breast and follow-up patients of known case/operated case of carcinoma in the opposite breast were included. The patients with acute inflammatory conditions of breast, pregnant and lactating women, patients not willing for the study and diagnosed and treated cases were excluded.

The investigations done were breast ultrasound-B mode and color doppler, sono-elastography, FNAC/core needle biopsy and histopathological report.

Procedure

This study was approved by JSS Academy of Higher Education and Research ethical committee and an informed consent was obtained by all 90 patients enrolled in the study. Author performed Sono-mammogram and real-time free hand sono-elastography in 90 consecutive women who presented to OPD of Department of General Surgery with history of lump in the breast. Sono-mammogram was performed and lesions scored according to BIRADS US Lexicon criteria. Following sono-mammogram, ultrasound elastography was performed and the elastography score along with strain ratio were obtained. The findings were then correlated with histopathological diagnosis. The additive role of ultrasound elastography and its accuracy over sono-mammogram were assessed in differentiating benign from malignant breast lesions.

Continuous variables in terms of Mean $\pm$ SD and categorical variables in terms of frequency and percentage. Chi square test (2*2) to compare data between two groups, Cramer's V test, sensitivity, specificity, PPV and NPV were done.

RESULTS

Present study composed of 90 patients with 44 benign and 46 malignant lesions on histopathology examination (Figure 1).

In relation to breast lesions age of the patient was an essential parameter. The patients from 15-74 years of age were included in this study. In this study, mean age was found to be 45.6 years (Figure 2). The majority of patients with malignant breast lesions were above the age of 45 years. In this study, author had used the Tsukuba scoring system for elastography scoring of breast lesions and classified the lesions accordingly: lesions in the

categories 1-3 were considered benign, whereas lesions in categories 4 and 5 were considered malignant and author

achieved a sensitivity of 95.65% and a specificity of 68.18% for elastography score (Table 1).

Figure 1: Surgical management.

Table 1: Sensitivity and specificity of elastography score.

Statistic	Sensitivity	Specificity	PPV	NPV	Accuracy
Value	95.65%	68.18%	75.86%	93.75%	82.22%
95% CI	85.16% to 99.47%	52.42% to 81.39%	67% to 82.95%	79.21% to 98.33%	72.74% to 89.48%

Table 2: Sensitivity and specificity of BI-RADS scoring on sono-mammogram.

Statistic	Sensitivity	Specificity	PPV	NPV	Accuracy
Value	71.74%	90.91%	89.19%	75.47%	81.11%
95% CI	56.54% to 84.01%	78.33% to 97.47%	76.10% to 95.53%	65.79% to 83.11%	71.49% to 88.59%

Figure 2: Distribution based on the age of the patient.

Present study showed an increase in sensitivity of elastography by 24% in comparison to BI-RADS characterization of lesions by B-mode ultrasonography (Table 2) and a difference of 20% in NPV respectively in differentiating benign from malignant breast lesions. The sensitivity results of this study were consistent with other published data on the use of real-time USG elastography score. Several studies have identified the cut-off value for strain ratio between 2.5 and 5. The priority in this study was to evaluate the diagnostic value of elastography method by comparing with histopathological results. The mean strain ratio of lesions according to the Tsukuba scoring in group 1 was 0, group 2 was 2.07, group 3 was 3.28, group 4 and group 5 was 4.6. The mean SR for benign lesions was 2.13 and for malignant lesions it was 4.34 (Table 3).

With the cut- off point being 3 on strain ratio, author achieved sensitivity of 82.61%, specificity of 81.82%,

PPV of 82.61% and NPV of 81.82%. With 2.5 as the cut-off value, author obtained sensitivity of 73.19%, specificity of 81.82%, PPV of 80.9% and NPV of 75% for SR. Thus, there was dropping in sensitivity and negative predictive value when the cut-off point was taken as 2.5 but however, the specificity level remained the same.

Table 3: Mean strain ratio for benign and malignant lesions.

	Histopathology	N	Mean	SD	P value
Strain ratio	Benign	46	2.1370	1.01874	<0.001
	Malignant	44	4.3409	1.75742	

In this study, the combined use of elastography and strain ratio showed an increase in the sensitivity by 17.39% in differentiating the benign from malignant breast lesions compared to B-mode ultrasonography imaging.

DISCUSSION

The interpretation of focal breast lesions detected on x-ray mammography and B-mode ultrasound mainly relies on morphological criteria. Breast ultrasound elastography is an emerging sonographic imaging technique which provides information on breast lesions in addition to conventional ultrasonography and mammography. Over the last decade, there has been increasing interest in imaging the elasticity of biological tissues to complement information from standard anatomical imaging. Recent studies showed that ultrasonographic-elastography (USE) provides higher diagnostic accuracy compared with B-mode ultrasonography during breast cancer diagnosis, which helps to reduce false-positive results and therefore is useful in avoiding unnecessary breast biopsy.

Present study incorporated the B-mode ultrasonography for characterization of focal breast lesions based on BI-RADS US criteria. The features of malignancy on USG like shape of the lesion, orientation to the skin, lesion boundary, architectural distortion, etc. were assessed accordingly. In this study, 43.2% of malignant lesions were found to be irregular in shape and 47.8% benign lesions had an oval shape. 84.8% benign lesions were parallel in orientation to the skin and 22.7% were not. The malignant lesions with non-parallel orientation were 77.3%. From this, author can reaffirm the BI-RADS criteria for suspicion of malignancy in non-parallel lesions.

Another BI-RADS criterion for suspicion for malignancy is the lesion boundary on sono-mammogram. If the lesion boundary is found to be having an abrupt interface, it suggests benign etiology and if there is an echogenic halo, there is high probability for malignancy. Similarly, in this study, author found that 60.9% benign lesions had an abrupt interface with the surrounding parenchyma and 40.9% malignant lesions had an echogenic halo. Surrounding architectural distortion on sono-

mammogram was absent in 95.7% benign lesions and present in 22.7% of malignant lesions. Thus, most of the malignant lesions are associated with surrounding architectural distortion.

Early studies investigating the use of colour, power and quantitative spectral doppler US in the breast reported that the presence of increased vascularity, as well as changes in the pulsatility and resistive indexes, showed that these Doppler findings could be used to reliably characterize malignant lesions. However, other investigators have demonstrated substantial overlap of many of these Doppler characteristics in both benign and malignant breast lesions. Gokalp G et al, also demonstrated that the addition of power doppler US and spectral analysis to BI-RADS US features of solid breast masses did not improve specificity.¹² While the current BI-RADS US lexicon recommends evaluation of lesion vascularity is not considered mandatory. Power doppler is generally more sensitive than colour doppler to low-flow volumes typical of breast lesions. Currently both power and colour doppler are complementary tools to gray-scale imaging and power doppler may improve sensitivity in detecting malignant breast lesions. Demonstration of irregular branching central or penetrating vascularity within a solid mass raises suspicion of malignant neovascularity. High-grade invasive cancer and metastatic lymph nodes may occasionally appear anechoic. Demonstration of flow within these lesions helps in differentiating these lesions from simple cysts. In this study vascularity was present in 93.2% of malignant lesions and 15.2% of benign lesions. Most of the malignant lesions showed vascularity on colour Doppler as compared to benign lesions.

Lymph nodes were also more commonly seen in malignant lesions. Likewise, in this study 72.7% malignant lesions showed presence of lymph nodes with necrotic changes and 41.3% benign lesions showed presence of lymph nodes with preserved fatty hilum.

As portrayed in the results and analysis, author considered BI-RADS 2 and 3 as benign and BIRADS 4 and 5 as malignant lesions. As this study considered BI-RADS 4a, 4b and 4c and 5 as malignant lesions, there was only change in the frequency of the lesions falling into the BI-RADS categories. But there was no change in the overall statistical data. However, this imaging modalities could detect 71.74% of true malignant lesions and 90.91% of true benign lesions. The observation that benign and malignant breast lesions have inherently different firmness has long been used by clinicians during palpation of the breast, harder and less mobile lesions are considered more likely to be malignant. This is the main principle behind elastographic imaging. Based on this principle ultrasonographic (US) strain imaging has been developed to measure the relative stiffness of lesions in contrast to the surrounding tissue. US strain imaging may allow the differentiation of benign from malignant solid masses on the basis of differences in stiffness. Results of

the clinical use of SE were initially published in 1997-2001 but it was only in 2003 that USG equipment was developed that had incorporated software for real-time processing of elastography images and routine USG examinations.

However, the Food and Drug Administration (FDA) granted approval for clinical research use only in 2006. The lesions contour, dimensions, colour, SR and appearance on elastography are some of the criteria used for differentiating benign from malignant lesions. In this study, author used the colour coded mapping method to demonstrate the strain pattern and obtained the elastography scores. Malignant lesions, which are very stiff, deform less and are displayed in blue on the elastography images, whereas benign lesions deform much more easily and are depicted in green colour. This is based on the colour coding preset used in the respective ultrasound system.

Previous studies mainly used the "strain pattern", which is a qualitative method in distinguishing malignant from benign breast masses. Garra BS et al, have used the "strain ratio", the quantitative measurement obtained by comparing the hardness of the target lesion and surrounding breast adipose tissue.¹³ It represents the relative compliance stiffness of lesions compared with surrounding tissues and it has been found in various earlier studies that the strain ratio of malignant lesions was found to be higher as compared to the strain ratio of benign lesions. In this study, author evaluated both of these elastographic findings i.e., colour coding (elastography score) and the strain ratio. Gheonea IA et al, also stated that application of strain ratio was useful for quantitative comparison of the elasticity of soft tissues with the elasticity of the lesion.¹⁴

Selection of the reference ROI is important to obtain the correct SR indicating the real stiffness of the tissue. In a previous study that evaluated the diagnostic performance of the fat to lesion strain ratio, the ROI for the reference was placed in the superficial fat tissue adjacent to the skin layer. One of the previous studies suggested that a reference ROI placed in the glandular tissue at the same depth as the lesion would indicate the lesion stiffness

correctly. However, glandular tissue showed various moduli depending on the compression level, whereas fat tissue shows a constant modulus over various compression loadings. In this study, the ROI for the reference was placed in the fat tissue at a depth similar to or as close as possible to the target mass to avoid stress decay, which is dependent on the depth of the lesion. The superficial layer under the transducer displaces more than the deep layer, so the strain value of a lesion in the superficial layer would be higher than that in the deep layer. Therefore, fat tissue located at the same depth as the target lesion would be the most adequate reference point. This was in agreement with Cho N et al.¹⁵

For characterization of breast lesions, two elasticity scoring systems have been proposed: the Tsukuba score (Figure 3) developed by Itoh A et al, color-elastography images are scored according to the scale described by Itoh et al. The higher the score, the higher the likelihood of invasive breast carcinoma and another designed by the Italian Research Group (Figure 4) after Rizzatto G et al.^{11,16}

Score 0, an elastography pattern seen with simple cysts is not shown.

Figure 3: Tsukuba score. Pathology 3a): Lipoma, 3b): fibroadenoma, 3c): fibroadenoma, 3d): lobular carcinoma, 3e): invasive ductal carcinoma.

Chromatic code	Elastosonographic score	Italian team of study
	Score 1: Presence of chromatic tri-stratification (blue/green/red).	Prevalently in the liquid forms.
	Score 2: Prevalence of green, within case some blue point, inconstant seat.	Prevalently elastic: prevalently in the benign forms.
	Score 3: Prevalently green, but with some blue spot.	
	Score 4: Almost completely blue, within case some green point, most of all in periphery.	Prevalently rigid: prevalently in the malignant forms.
	Score 5: Completely blue, also with a blue peripheral glow around the nodule.	

Figure 4: Elasticity score proposed by the Italian research group.

A recent study investigating sono-elastography with colour doppler US has focused on its potential in reducing the number of biopsies with benign results due to further discrimination of low suspicious lesions and its increased diagnostic performance in distinguishing benign from malignant breast masses.

On the other hand, Yerli H et al, mentioned that, the elasticity scoring and strain ratio methods seem to have similar diagnostic potential for differentiating between benign and malignant breast masses and that the combined use of B-mode sonography and qualitative 5-point scoring is a sufficient method that increases specificity when differentiating benign and malignant breast masses.¹⁷ Lee SH et al, reported that elasticity score alone showed the best diagnostic performance but a combination of B-mode US and elasticity score may have a predictive value for the differentiation of benign and malignant lesions <1cm.¹⁸

Most of the lesions classified as BI-RADS category 3 on B-mode sonography with an elastographic score of 3 or lower were cyto-pathologically and histo-pathologically benign. However, few cases of fibroadenoma were classified into grade 4, as they had a high strain ratio. Moreover, they had a predominantly blue pattern on elastogram due to presence of calcification. Few cases which had B-mode features of malignancy could be categorized into BI-RADS US 3 criteria with the help of elastography colour pattern and strain ratio.

The high degree of coincidence between elastography and histopathological assessment in the diagnosis of these lesions could reduce the number of unnecessary biopsies and would allow for management of these low-radiologic and sonographic risk patients with follow-up.

Regarding the size of the lesion, according to Giuseppetti GM et al, the diagnostic performance of elastography is better in lesions smaller than 2cm.¹⁹ However, in the series by Itoh A et al, the capacity of this technique to discriminate between benign and malignant lesions did not depend on the lesion size (between 0.4 and 3cm).¹¹

Likewise, Scaperrotta G et al, did not find statistically significant differences in the diagnostic performance between small lesions (up to 1cm) and larger lesions (1.1-2cm).²⁰ Similarly, in this study, author did not find statistically significant differences in the predictive value of the elastography to discriminate benign and malignant lesions based on size.

In summary, author found that US elastography and strain imaging features improves differentiation of malignant and benign breast lesions. The diagnostic accuracy improved when both the modalities were used. Therefore, author believed that US elastography and strain imaging has reduced the dilemma whether or not to perform the breast biopsy unnecessarily.

CONCLUSION

Strain elastography is widely available and easy to use in a clinical setting. It's a fact that SE is real-time and can be done bedside along with the B-mode evaluation. In breast cancer, SE has shown great potential and a good diagnostic performance in several studies.

The results of this study demonstrated that the use of elastography improved the sensitivity in differentiating benign from malignant lesions, which increased from 75.5% to 95.8%. The specificity of this method significantly dipped from 91.6% to 68.3%. There was a good correlation between elasticity score (qualitative) and strain ratio (quantitative) methods allowing more accurate differentiation of benign and malignant lesions when both are used. In this study, when the cut-off point being 3, sensitivity of 87.5% for SR was obtained. This result was consistent with other published data on the use of real-time USG elastography.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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