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Can Strain Elastography is Used As An Adjunct To Conventional imaging in Differentiating Benign And Malignant Breast Lesions?

KEYWORDS Breast, ultrasound, mammography, strain index and elastography.

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ABSTRACT *Aims and Objectives:*

- *To compare mammography, ultrasound and strain elastography in differentiating solid breast lesions into benign and malignant lesions.*
- *To assess the sensitivity, specificity, Positive predicative value(PPV), Negative predictive value(NPV) and Accuracy of ultrasound and combined ultrasound and strain elastography in BIRADS category III and IV lesions.*

Study design: Mammography, ultrasound and strain elastography were done in 69 lesions(66 patients).

Results:

The mean strain index value on elastography was 2.49 ± 1.49 for benign and 6.45 ± 2.68 for malignant lesions with a sensitivity and specificity of 89.8% and 75% respectively.

The sensitivity, specificity, accuracy, PPV and NPV for ultrasound were 94%, 73.68%, 88.4%, 90.38%, 82.35% which improved on adding strain elastography to 96%, 84.21%,92.75%,94.11%, 88.88 % respectively.

Sensitivity, Specificity, Accuracy, PPV and NPV were 80%,85.71%,80%,85.71% and 83.33 respectively for combined ultrasound and elastography in category III and IV lesions.

Conclusion:

- *Strain index cut off value of 3.37 enabled the best distinction between benign and malignant lesions on elastography.*
- *Adding strain elastography to ultrasound improved sensitivity, specificity, PPV, NPV and Accuracy when compared to ultrasound or Mammography used alone.*

Introduction

Breast cancer is the most common malignancy in women all over the world [1]. The single most important factor in reducing mortality from breast cancer is early detection through screening [2]. The incidence of breast cancer is rising in India and its effective management is heavily dependent on early detection.

Mammography is used as a screening modality in older age group whereas in younger women with dense breasts, it often yield false-negative results. In younger women ultrasound is done [3,4] and though its sensitivity is higher in detection of lesions, its specificity is poor in characterizing them into benign or malignant. Since breast cancer in Indian population is seen in a younger population as compared to the west, hence there is a need for additional reliable methods to establish a diagnosis and avoid unnecessary biopsies.

Elastography is an emerging modality which is non-invasive and depicts relative tissue stiffness in response to an external force. The principle used in Elastography is : Stiff tissues deform less and exhibit less strain as compared to compliant tissues in response to an applied external force[5,6]. The two most frequently used elastography techniques are compressive/strain elastography and shear wave elastography.

Strain elastography: Stress is applied by repeated manual compression of the transducer, and the amount of lesion deformation relative to the surrounding normal tissue is measured and displayed.

Shear wave elastography: Uses an acoustic radiation force impulse created by a focused ultrasound beam, which allows measurement of the propagation speed of shear waves with in the tissue to locally quantify its stiffness in kilopascals/meters per sec.

AIMS AND OBJECTIVES:

To compare mammography, ultrasound and strain elastography in differentiating solid breast lesions into benign

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and malignant lesions.

To assess the sensitivity, specificity, Positive predicative value(PPV), Negative predictive value(NPV) and Accuracy of ultrasound and combined ultrasound and strain elastography in BIRADS category III and IV lesions.

MATERIALS AND METHODS:
A prospective study done in Department of Radiodiagnosis in a tertiary health care hospital, from September 2014 to august 2015.

A total of 69 solid breast lesions were studied in 66 patients after obtaining Institutional ethical committee (IEC) clearance and informed consent from patient.

The lesions were evaluated by mammography, ultrasound and strain elastography .Final diagnosis was confirmed by Histopathology / Imaging follow up at one year.

Statistical analysis was done using SPSS statistical software version 16.

INCLUSION CRITERIA:
Patients with solid breast lesions > 1cm and < 5 cm on ultrasound who also underwent mammography and elastography.

Patients with histo-pathological diagnosis/imaging follow up at one year.

EXCLUSION CRITERIA:

Cystic breast lesions.
Patient who were not evaluated by all the three imaging modalities (mammography, ultrasound and strain elastography).

Patients without histo-pathological diagnosis and or imaging follow up.

IMAGING:
Standard medio-lateral oblique (MLO) and cranio-caudal (CC) views were done on WIPRO GE – DMR PLUS mammography unit. Additional views (coned-down compression and magnification views) were done when required.

Ultrasound and Strain Elastography were done on Aplio XG (Toshiba medical systems corp., JAPAN)

Ultrasound technique : Ultrasound of breast was done in radial/anti radial planes using 8-13 MHz linear transducer with patient in supine position .

Elastography technique- Semi quantitative strain elastographic image box was fitted to cover the lesion and a compressive and decompressive force was applied vertically, keeping the lesion in the field of view. Care was taken to stabilize the lesion to avoid lateral movement.

The compression and relaxation waveforms were seen as sinusoidal waveforms and Strain index (SI) values were obtained from an appropriate relaxation wave. Strain index was measured by selecting ROI (region of interest) in lesion and a corresponding ROI in adjacent normal parenchyma. Using the Breast Elastography software, SI values were displayed on a static image as the ratio of tumor-adjusted ROI and the ROI placed in adjacent tissue. Multiple values with in the lesion were recorded and the average of two highest values was taken as strain index (SI).

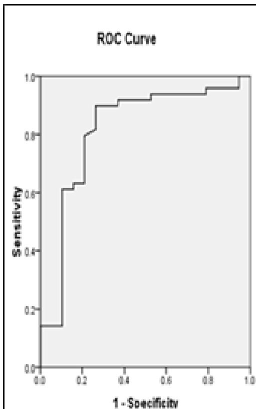
RESULTS:
A total of 69 lesions (66 patients) were included in the study and all patients underwent mammography, ultrasound and strain elastography.

The age of the patients ranged from 26 to 83 years, with majority of patients between 41-50 years ; mean age of the sample being 54.3 years.

Mammograms were assessed for shape, margin, and density of masses, calcifications, architectural distortion, asymmetric densities and axillary lymphnodes.

Ultrasound features assessed were antero- posterior width ratio, shape, margin, internal echogenicity, internal echotexture, and posterior acoustic phenomena. The benign lesions were between 10- 20 mm in size with a mean size of 14 mm and malignant lesions were between 21-30 mm in size with a mean size of 33 mm.

Strain index values of all 69 lesions were compared with histopathological findings and using ROC curves, the diagnostic performance of strain index method was evaluated(Figure 1).



Test Result Variable(s): strainindex

Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
-.8500	1.000	1.000
.3350	1.000	.947
.5300	.980	.947
.6400	.959	.947
.7800	.959	.895
1.0400	.959	.842
1.2800	.959	.789
1.4000	.939	.789
1.5150	.939	.737
1.5600	.939	.684
1.5950	.939	.632
1.6250	.939	.579
1.6650	.939	.526
1.7900	.918	.526
2.0500	.918	.474
2.3250	.918	.368
2.5950	.898	.368
2.8950	.898	.316
➡ 3.3750	.898	.263
4.0000	.878	.263
4.3500	.816	.263
4.4500	.796	.211
4.5500	.735	.211
4.6350	.714	.211
4.6850	.694	.211
4.7500	.653	.211
4.8500	.633	.211
5.0000	.633	.158

Figure 1: ROC curve and coordinate table for strain index values.

On applying independent T test, 2 tailed p value was 0.001(statistically significant). The mean strain index values ± SD on elastography were 2.49 ± 1.49 for benign lesions and 6.45 ± 2.68 for malignant lesions. Sensitivity and specificity for malignant lesions were 89.8% and 75% when a cutoff point of 3.37 was used.

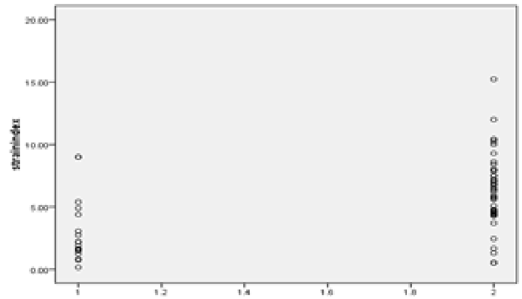


Figure 2: Scatter plot of strain indices(distribution of strain indices left side – benign and right side – malignant):

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Strain index values of most of malignant lesions were clustered between 4 to 12, whereas for benign lesions it was between 1 to 4(Figure 2). Highest strain index value in malignant lesions was 15.23, lowest value was 0.54, whereas highest strain index value in benign lesions was 8.9, and lowest value was 0.38.

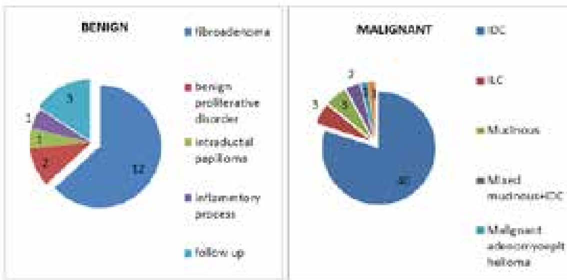

Figure 3 : Histopathology/Follow up of benign and malignant lesions

The final histopathology/ Follow up diagnosis was as shown above (Figure 3).Comparison of mammography, Ultrasound and Strain elastography findings was done with histopathology.

A result was classified as false-negative when a diagnostic method classified histopathologically confirmed cancer as benign and as false-positive when a diagnostic method classified a histologically confirmed benign lesion as cancer.

Imaging modality	Sensitivity%	Specificity%	Accuracy%	PPV%	
Mammography	94	57.89	84.05	94	78.57
Ultrasound	94	73.68	88.4	90.38	82.35
US+ELASTO	96	84.21	92.75	94.11	88.88

Figure 4: Comparison of Mammography, Ultrasound, and Strain Elastography in differentiation of breast lesions.

Combined ultrasound and elastography showed improvement in all statistical parameters(sensitivity, specificity, accuracy, PPV and NPV) as compared to mammography or ultrasound used alone(Figure 4).

Imaging modality	Sensitivity%	Specificity%	Accuracy	PPV%	
Ultrasound	80	85.71	83.33	80	85.71
US+ELASTO	90	92.85	91.66	90	92.85

Figure 5: Comparison of Ultrasound and Combined Ultrasound plus Elastography in BIRADS category III and IV lesions.

There is often a diagnostic dilemma in categorizing BIRADS III and IV lesions. Addition of strain elastography to ultrasound improved all statistical parameters(sensitivity, specificity, accuracy, PPV and NPV) and may help in reducing the number of lesions which need to be biopsied. (Figure 5).

DISCUSSION:

Solid breast lesions in present study were evaluated by mammography, ultrasound and strain elastography to differentiate benign from malignant lesions.

Mammography showed a high positive predictive value (94%) as compared to ultrasound (90%) as the number of malignant lesions in present study (Figure 4) were more. The specificity of mammogram (57.89%) was significantly less than ultrasound(73.68 %) as five lesions could not be seen on mammogram due to high breast density and were assigned BIRADS category 0. The accuracy of mammography was 84.05% and ultrasound was 88.4%.

Imaging Modality	Sensitivity %	Specificity %	Accuracy	PPV %	NPV %
present study	72.4/94	87.1/57.89	82.7/84.05	70.0/94	88.3/78.57
present study	71.2/94	73.2/73.68	72.6/88.4	52.5/90.38	86.0/82.35

Figure 6: Comparison of mammography and ultrasound in the diagnosis of solid breast lesions". Hui et al[7]. vs present study.

As compared to study done by Hui et al, Sensitivity and positive predictive values of both mammography and ultrasound were higher in present study, while the specificity and negative predictive values were lower(Figure 6). This can be attributed to inclusion of more number of malignant lesions (50/69) in the present study.

	present study	Ioana Andreea et al.	
SI Cut off	3.37	3.67	2.24
Mean SI benign	2.49 ± 1.49	2.08	2.63 ± 4.57
Mean SI malignant	6.45 ± 1.49	6.28	6.57 ± 6.62
Sensitivity	89.8	93.3	95
Specificity	73.68	92.9	75

Figure 7: Differentiation of benign and malignant lesion using strain elastography – Study done by Ioana Andreea et al.[8] and Nariya cho et al[9].vs present study.

Mean strain indices for benign and malignant lesions and sensitivity(at cut off of 3.37) of present study were in agreement with the values obtained in the study done by Ioana Andreea et al. and slightly high as compared to Nariya cho et al(Figure 7).

At a cut off of 3.3.7 we found a specificity of 73.68 % whereas Ioana Andreea et al found a specificity of 92.9% at a cut off of 3.67 and Nariya cho et al found a specificity of 75 % at a cut off of 2.24. This may be attributed to a relatively smaller number of benign cases.

On strain elastography, five histopathologically diagnosed benign lesions showed high strain index values(> 3.37) – out of which three lesions were fibroadenomas, one lesion was intraductal papilloma and another one lesion was inflammatory process with giant cell reaction. The three fibroadenomas had calcifications that increased the stiffness

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of the lesion, which in turn affected the assessment on elastography and showed high strain index values . Since inflammatory process with giant cell reaction is a chronic inflammatory condition it may have increased the stiffness of lesion.

Out of five histopathologically diagnosed malignant lesions showing low strain index values(< 3.3.7) - two lesions were mucinous carcinomas, two were infiltrating ductal carcinomas and one lesion was invasive lobular carcinoma. Mucinous carcinomas and early stages of infiltrating ductal carcinoma are known to be relatively soft (10) and hence can give low strain index values. The necrotic component in invasive ductal carcinoma can account for low strain index values(< 3.37).

The results are in agreement with study done by Krouskop et al (10). in 1998, which showed that various breast tissues had differing elastic stiffness, invasive carcinoma having the lowest elasticity, followed by noninvasive carcinoma, fibrous tissue in the breast, normal glandular breast tissue, and breast fat tissue in that order.

Combined ultrasound and elastography allows evaluation of two important features of a lesion, morphology and stiffness.

Morphological characteristics includes shape, margin, internal echogenicity, echotexture, and posterior acoustic shadowing which are important in differentiating benign and malignant breast lesions according to Stavros et al(11). According to stiffness criteria(10), malignant tissue is usually harder than normal breast tissue (10) and gives high strain index values. Hence, combining ultrasound with elastography assesses both morphology and stiffness at the same time thereby improving the specificity and negative predictive value.

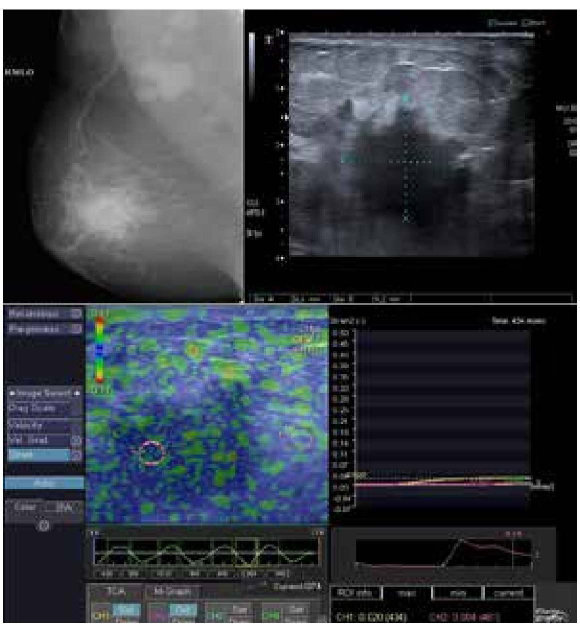

Figure 8: A 63 year old woman with palpable lump in right breast A) MLO view on mammography, B) B-mode ultrasound, C) strain elastography image showed high SI value (6.14) and was categorized as BIRADS V. Histopathology was suggestive of infiltrating ductal carcinoma

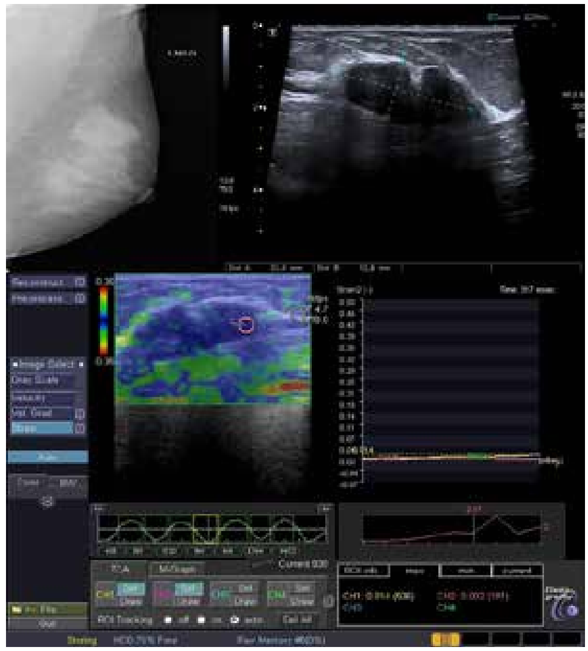

Figure 9: A 46 year old woman with palpable lump in left breast. A) MLO view on mammography, B) B-mode ultrasound and C) strain elastography image showed low SI value (2.47) and was categorized as BIRADS III – histopathology suggestive of fibroadenoma

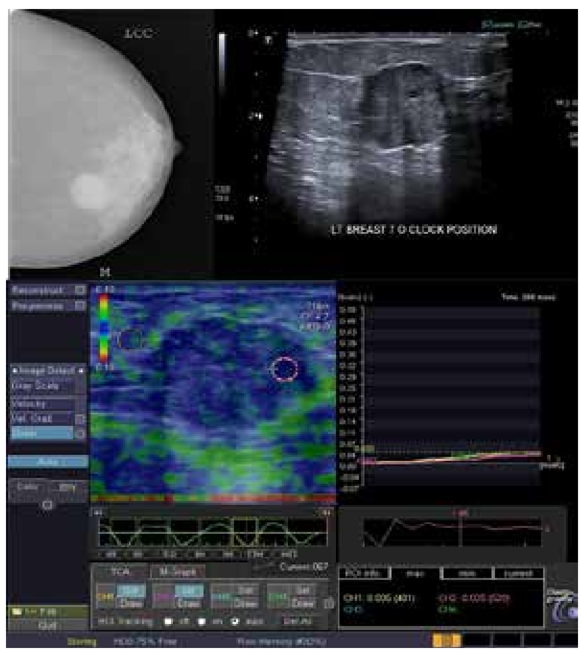

Figure 10: A 48 year old woman with palpable lump in left breast. A) CC view on mammography, B) B-mode ultrasound and C) strain elastography image showed low SI value (1.48) and was categorized as BIRADS IVA – Histopathology was suggestive of mucinous carcinoma

LIMITATIONS:

- Small sample size
- Less number of benign lesions.
- Subjective variability of compression during elastography.

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CONCLUSION:

- There is a significant difference in the mean strain index values on strain elastography for benign and malignant lesions (2.49 ± 1.49 for benign lesions and 6.45 ± 2.68 for malignant lesions).
- Strain index cut off value of 3.37 enabled the best distinction between benign and malignant breast lesions by using ROC curve.
- Combined ultrasound and elastography improved all statistical parameters [sensitivity, specificity, PPV, NPV and Accuracy] which were significantly higher when compared to mammography or ultrasound performed individually.

References:

1) Jemal A1, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, Feuer EJ, Thun MJ. Cancer statistics, 2005. CA Cancer J Clin. 2005;55(1):10-30.
2) Pavel Crystal 1,2 Selwyn D. Strano2,3 Semyon Shcharynski 2 Michael J. Koretz2 Using Sonography to Screen Women with Mammographically Dense Breasts. AJR 2003;181:177–182
3) Lehman CD, Lee CI, Loving VA, Portillo MS, Peacock S, Demartini WB. Accuracy and value of breast ultrasound for primary imaging evaluation of symptomatic women 30-39 years of age. Am. J. Roentgenol. 2012. 5:1169-77.
4) Devolli-Disha E1, Manxhuka-Kërliu S, Ymeri H, Kutllovci A. Comparative accuracy of mammography and ultrasound in women with breast symptoms according to age and breast density.Bosn J Basic Med Sci 2009 ;9(2):131-6.
5) Krouskop TA, Wheeler TM, Kallel F, et al., Elastic moduli of breast and prostate tissues under compression.Ultrason Imaging 1998, 20:260-274.
6) Itoh A., Ueno E., Tohno E., Kamma H., Takahashi H., Shiina T. Breast disease: clinical application of US elastography for diagnosis. Radiology. 2006;239(2):341-50. Epub 2006 Feb 16.
7) Hui Zhi, MD, Bing Ou, MD, Bao-Ming Luo, MD, Xia Feng, MD, Yan-Ling Wen, MD, Hai-Yun Yang, MD. Comparison of Ultrasound Elastography, Mammography, and Sonography in the Diagnosis of Solid Breast Lesions. J Ultrasound Med 2007; 26:807–815.
8) Ioana Andreea Gheonea, Zoia Stoica, Simona Bondari. Differential diagnosis of breast lesions using ultrasound elastography. Indian J Radiol Imaging. 2011; 21(4): 301–305.
9) Cho N1, Moon WK, Kim HY, Chang JM, Park SH, Lyou CY. Sonoelastographic strain index for differentiation of benign and malignant nonpalpable breast masses. J Ultrasound Med. 2010 ;29(1):1-7.
10) J Ophir , S K Alam , B Garra , F Kallel , E Konofagou , T Krouskop , T Varghese Elastography: ultrasonic estimation and imaging of the elastic properties of tissues (1999). Proc Inst Mech Eng H. 1999;213(3):203-33.
11) Stavros AT1, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. Radiology. 1995;196(1):123-34.