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Dinesh Maharjan

Lecturer, Patan Academy of
Health Sciences, Nepal.

Comparison of conventional B mode ultrasound with elastography for differentiation of benign and malignant breast mass

Dinesh Maharjan

Abstract

Introduction: Breast cancer is the most common cancer in female worldwide. Imaging plays important role in early diagnosis of breast cancer. Deaths due to breast cancer are decreasing in developed countries due to early detection and treatment. Although mammography is modality of choice for screening breast cancer, in developing countries ultrasonography is commonly used for evaluation of breast disease. Conventional B mode ultrasound has good sensitivity and specificity in differentiating the benign and malignant breast lesion. However there has been significant increase in number of fine needle aspiration or biopsy even for benign nodule when only B mode evaluation was used for evaluation of lesion. Elastography is newer development in ultrasonography which can detect the hardness of lesion qualitatively and quantitatively. Elastography findings can be used in differentiating benign breast lesion from malignant lesion.

Methodology: This was a prospective crosssectional study done in 54 patients with sonographically proven solid breast lesion. Conventional B-mode sonography was performed and lesions were characterized as benign and malignant depending upon various characteristics of lesion. Following that elastography was performed and lesions were evaluated with elastography 5-point score and strain ratio of lesions measured. Lesions were then evaluated pathologically. Sample for pathological examination was obtained by ultrasound guided FNAC or core biopsy. Conventional sonographic findings and elastography findings were correlated with pathological diagnosis and accuracy of conventional sonography and elastography for differentiating benign and malignant breast lesions were assessed and compared.

Results: Out of 54 breast lesions 31 lesions were benign and 23 were malignant. Conventional Sonography showed sensitivity, specificity and accuracy of 86.9%, 87.1%, and 87.0% respectively, in differentiating benign and malignant breast lesion. Elastography 5-point score system showed better sensitivity specificity and accuracy than conventional Sonography (95.6%, 96.7%, and 96.2% respectively). Strain ratio measurement of lesions showed when cut off value of 3.9 was used, sensitivity and specificity were 96.8% and 91.3%. ROC curve analysis showed area under curve for conventional sonography, elastography 5-point score system and strain ratio measurements were 0.870 ± 0.054 , 0.962 ± 0.031 and 0.969 ± 0.026 respectively.

Conclusion: Elastography provides more precise differentiation between malignant breast lesions from benign breast lesions. No significant differences were noted between Elastographic 5 point score system and strain ratio measurements in differentiating benign and malignant breast lesions.

Keywords: breast, benign, elastography, malignant, nodule, ultrasonography.

Introduction

Breast cancer is the most common cancer in women. Breast cancer comprise 16% of all female cancers. It is estimated that 519,000 women died in 2004 due to breast cancer, and although breast cancer is thought to be a disease of the developed world, a majority (69%) of all breast cancer deaths occurs in developing countries. The incidence of breast cancer is increasing in the developing world due to increasing life expectancy, increasing urbanization and adoption of western lifestyles.¹

Mammography and physical examination are the recommended modalities for breast-cancer screening for women. Mammography, however, cannot detect lesions in dense breast tissue. Dense breasts conceal small masses in mammary glands. Some breast cancers might be

Correspondence:

Dinesh Maharjan

Lecturer, Patan Academy of
Health Sciences, Nepal.

missed if screening involves only mammography and physical examination.²

Ultrasound has become increasingly important in the diagnosis and management of breast disease. The main reasons are its ability to distinguish between cystic and solid lesions, its special advantages in examining the dense breast, and the absence of potential radiation hazard.³ Sonography is a diagnostic method that can also help establish the differentiation between benign and malignant solid tumors.⁴ However, higher detection rate of lesion by sonography has led to increase in rate of percutaneous biopsy of even benign breast lesions. It is estimated that 80% of breast lesions currently biopsied prove to be benign. Reducing that percentage is advantageous to both patients and the imaging community. Adding elastography may improve specificity in differentiating benign from malignant lesions.⁵

Breast elastography is a new sonographic technique that provides additional characterization information on breast lesions over conventional sonography and mammography. This technique provides information on the hardness of a lesion, similar to a clinical palpation examination. Three different modes are currently available in tissue elastography. Free-hand ultrasound elastography, Acoustic Radiation Force Impulse (ARFI) technique and Shear-wave elastography (SWE). Among these free-hand ultrasound elastography common mode available in commercially available elastosonography machines. In this method light compression is applied and released on the region of interest with the ultrasound probe. Signals are obtained before and after the compression as tissue shows displacement with compression. Depending upon stiffness of tissue displacement varies.⁶

These data obtained with compression can be analyzed by two methods. First method displays strain data into color scale images superimposed on B-mode images called elastogram. Color coding is done with blue being stiff tissue without displacement, green being softest tissue with marked displacement and red being intermediate. Elastogram obtained can be interpreted with 5-point scoring system. A score of 1 indicates even strain throughout the lesion (entirely green lesion), a score of 2 indicates strain in most of the lesion, with some strain free areas (a mosaic pattern of green and blue), a score of 3 indicates strain at the periphery of the lesion, with sparing of the center of the lesion (the peripheral part of the lesion in green, and the central part in blue), a score of 4 indicates no strain throughout the lesion (the entire lesion in blue, but the area surrounding it is not included), a score of 5 indicates no strain in the entire lesion or in the surrounding area (both the lesion and surrounding area are blue). The risk of malignancy increases from score 1 (a benign lesion) to score 5 (malignant lesion). Five point scoring system represents qualitative assessment of elasticity of the lesion.^{7,8}

Second method is semiquantitative evaluation of elasticity. Strain of tissue in region of interest i.e. both the lesion and surrounding normal tissue can be measured with ultrasonography machine. Strain index or ratio is then calculated as ratio of strain in normal tissue to strain in the lesion. Malignant lesions tend to have higher strain index. Initial evaluation of these techniques in clinical trials suggests that they may substantially improve the characterization of breast lesions as benign or malignant.

This improvement may substantially reduce the number of benign biopsies performed.⁹

This study is aimed at exploring potential use of elastographic examination of breast lesions to differentiate benign and malignant lesions.

Methodology

This was a cross-sectional prospective study carried out in Department of Radiodiagnosis, Bir Hospital, National Academy of Medical Sciences (NAMS) from Nov 2012 to October 2013. Total of 54 patients who had sonographically proven solid lesion in breast were included in this study. All patients were evaluated with Toshiba Aplio 400 machine. First conventional B-mode ultrasonography was used for characterization of the lesion. High frequency linear probe (8-10 MHz) was used for the conventional B-mode imaging of breast. Lesions were evaluated for shape, size (width and height), echogenicity, margins and calcifications. Depending upon above mentioned characteristics of lesion, they were categorized as benign or malignant lesions. Following conventional B-mode examination lesions were further evaluated with free hand elastography. For elastography image plane with best visualization of lesion and adjacent normal tissue was identified. Then light compression and release with the linear transducer over the lesion was applied. Compression and release was controlled and repeated till a good sine wave curve was noted. With good sine wave curve elastogram image was captured. Color coded elastogram was obtained with blue color representing the hard tissue and red being the soft. Obtained color coded elastogram was evaluated for color pattern and 5 point scoring was done as described by Itoh et al. (Fig 1)¹⁰

Score 1: entirely green lesion (even strain throughout the lesion)

Score 2: a mosaic pattern of green and blue (strain in most of the lesion, with some strain free areas)

Score 3: peripheral part of the lesion in green, and the central part in blue (strain at the periphery of the lesion, with sparing of the center of the lesion)

Score 4: entire lesion in blue, but the area surrounding it is not included (no strain throughout the lesion)

Score 5: both the lesion and surrounding area are blue (no strain in the entire lesion or in the surrounding area)

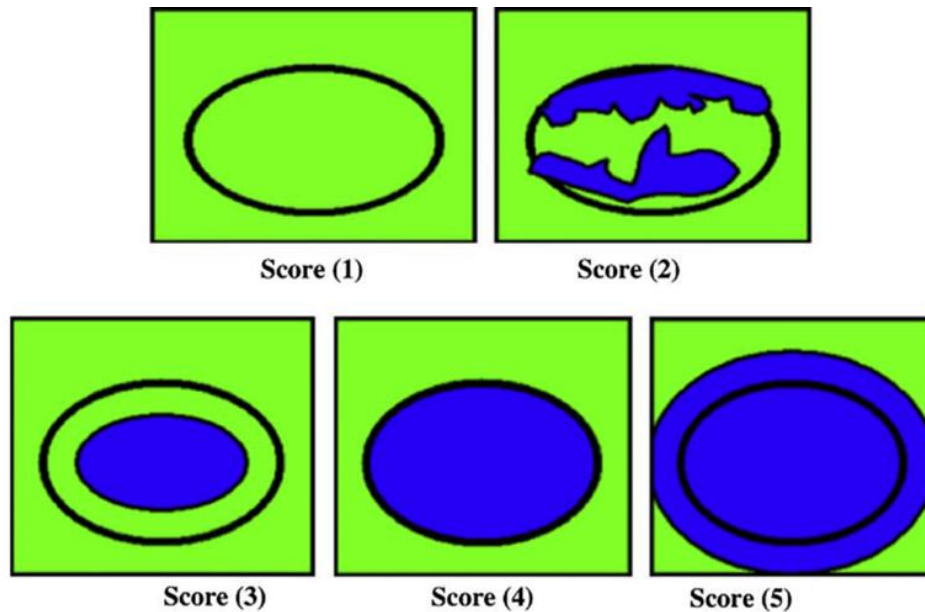


Fig 1: Elasticity score quoted from Itoh.¹⁰

Lesions with score of 1 and 2 were classified as benign lesions and those with 3 and above were classified as malignant.

After 5 point scoring, elastograms were subjected to semiquantitative measurement of strain ratio of lesion was done. For this an elliptical or round ROI was drawn with electronic calipers over the lesion in elastogram. Similar sized ROI was drawn in adjacent soft tissue preferably at same depth as that of lesion for reference. Strain ratio automatically calculated by US scanner was recorded. Three recordings of strain ratio was measured and average strain ratio was recorded.

When multiple masses of similar sonographic features were observed close to each other the largest lesions was selected for study. In cases where sonographically different types of lesions encountered the lesion with malignant looking features were evaluated.

After completing percutaneous fine needle aspiration was done under sonographic guidance. Obtained sample were sent to department of pathology for evaluation. In cases where FNAC reports were non conclusive due to inadequate sample, repeat FNAC was done. And when repeat FNAC was still inconclusive core biopsy of lesion was done for pathological diagnosis.

Correlation between sonographic feature and pathological diagnosis was analysed and their statistical significance tested by chi square test. P value of <0.05 was taken as criteria for significance. Correlation between elastography score and pathological diagnosis was also tested with chi square test. Mean strain ratio values for benign and malignant lesion were calculated and significance of difference between two values were tested with independent t-test. P value of <0.05 taken as criteria for statistical significance. Finally, receiver operating

characteristic (ROC) curve was calculated for conventional B- mode diagnosis, elastography 5 point score system and strain ratio measurement. Area under curve(AUC) for each methods of diagnosis were calculated and compared with each other. With ROC curve, cut off value for 5 point score system and strain ratio for differentiating benign and malignant lesions were calculated and sensitivity and specificity of individual test with derived cut off value were calculated.

Results

Mean age of the study population was 37 years and standard deviation (SD) was 14.7.

Out of 54 patients with breast lumps pathological diagnosis of benign disease was made in 31 cases and malignant disease in 23 cases.

All 9 cases under the age of 20 years had benign breast lump. Only one of the patient in age group 20-29 years, out of 8, had malignant breast lesion. All patients above age of 60 years (2) had malignant breast lesion.

The mean age of benign breast lesion was 30 years (± 12.5) and for malignant lesion was 47 years (± 11.6) (CI=95%, $p < 0.01$).

Among the 31 benign lesions the mean diameter of lesion was 23.7 mm (± 12.7) and for malignant lesions mean diameter of lesion was 43.7 mm (± 19.1). There was significant difference between the mean diameter size of benign and malignant lesion in our study (CI=95%, $p < 0.01$).

Out of 54 lesions in our study 43% (31 cases) were pathologically diagnosed as benign and 57% (23 cases) were pathologically proven as malignant.

B-Mode findings

Table 1: Taller than wider on B-mode.

	Pathological Category				Total
	Benign		Malignant		
	Number	Percent	Number	Percent	
Taller than wider	1	3%	7	30%	8
Wider than taller	30	97%	16	70%	46
Total	31	100%	23	100%	54

Table 2: Calcifications in breast masses.

Calcification	Benign		Malignant		Total
	Number	Percent	Number	Percent	
Present	4	13%	12	52%	16
Absent	27	87%	11	48%	38
Total	31		23		54

Calcifications within the breast mass was seen in 12 out of 23 malignant lesions and only 4 cases out of 31 benign lesions had calcifications. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of calcification as criteria for diagnosing malignant breast lesion was 52%, 87%, 75%, 71% and 72% respectively (p=0.002)

Table 3: Margins of breast lesions (B-mode).

Margin	Benign		Malignant		Total
	Number	Percent	Number	Percent	
Regular	25	81%	0	0%	25
Spiculated	1	3%	8	35%	9
Angular	0	0%	2	9%	2
Irregular	5	16%	10	43%	15
Microlobulation	0	0%	3	13%	3
Total	31	100%	23	100%	54

Among 31 benign breast lesions 81% (25) had regular margins. One of the benign lesions showed spiculated margin which on histopathological report was found to be granulomatous lesion. 16% of benign lesions (5) had irregular margins. Likewise among 23 malignant lesions in our study, 43% (15) of them had irregular margin, 35% (9) cases had spiculated margins, 13% (3) cases showed microlobulation and 9% (2) cases showed angular margin. When spiculated margins of lesion was used as the criteria for predicting malignancy the sensitivity, specificity, PPV, NPV and accuracy of conventional ultrasound were 34.7%, 96.8%, 88.9%, 66.7% and 70.4% respectively. Hence spiculated margin of lesion shows high specificity and PPV

for malignant lesion but has very poor sensitivity. Similarly angular margins of lesions as predictor of malignancy in conventional ultrasound showed specificity and PPV of 100% but has very poor sensitivity of 8.7%, NPV of 59.6% and accuracy of 61.1%. Microlobulation of margins of lesions also showed 100% specific and PPV for malignancy. However, it also had poor sensitivity of 13.0% and NPV and accuracy of 60.7% and 62.9 % respectively. Irregular margin of lesion as criteria for malignancy showed specificity of 83.8% but sensitivity, PPV, NPV and accuracy were only 43.5%, 66.7% and 66.7% and 66.7% respectively

Table 4: Acoustic shadowing of lesions (Conventional B-mode).

Acoustic Shadowing	Pathological Category				Total
	Benign		Malignant		
	Number	Percent	Number	Percent	
Present	2	6%	12	52%	14
Absent	29	94%	11	48%	40
Total	31	100%	23	100%	54

Acoustic shadowing was present in only in 14 lesions out of which 12 were malignant and 2 were benign lesions. Ninety four percent of benign lesions showed no acoustic

shadowing while 52% of malignant lesions demonstrated acoustic shadowing.

Table 5: Diagnosis by conventional B-mode sonography.

Convention B-mode diagnosis	Pathological Category		Total
	Benign	Malignant	
Benign	27	3	30
Malignant	4	20	24
Total	31	23	54

Total 30 cases were diagnosed as benign lesions and 24 were diagnosed as malignant by convention B mode. Three lesions diagnosed by B-mode only were cytopathologically proven as malignant and 4 of malignant diagnosed lesions

were proven to be benign. Sensitivity, specificity, PPV, NPV and accuracy of conventional B-mode ultrasound for diagnosing malignant lesion were 86.9%, 87.1%, 83.3%, 90% and 87.0% respectively.

Table 6: Elastography 5-point score and pathological correlation.

Elastography Score	Benign		Malignant		Total
	Number	Percent	Number	Percent	
1	13	42%	0	0%	13
2	17	55%	1	4%	18

3	0	0%	10	43%	10
4	1	3%	7	30%	8
5	0	0%	5	22%	5
Total	31	100%	23	100%	54

Thirteen lesions had elastography score of 1. All of these lesions were benign. Eighteen lesions had elastography score of 2 among which 17 were benign and 1 was pathologically proven as malignant.

Ten lesions had elastography score of 3 all of which were pathologically proven as malignant. Elastography score of 4 was observed in 8 lesions which were found malignant except for 1. Finally 5 lesions had elastography score of 5 and all were malignant lesions on pathological

examination. With elastography score of 1 and 2 as criteria for benign lesion and 3,4, and 5 as malignant lesion, 31 lesions were diagnosed as benign lesions out of which single lesion was pathologically proven to be malignant and 23 lesions were diagnosed as malignant among which 1 lesion was proved to be benign. Hence the sensitivity, specificity of 5 point elastography scoring system was 95.6% and 96.7% respectively. PPV, NPV and accuracy was 95.6%, 96.7% and 96.2% respectively

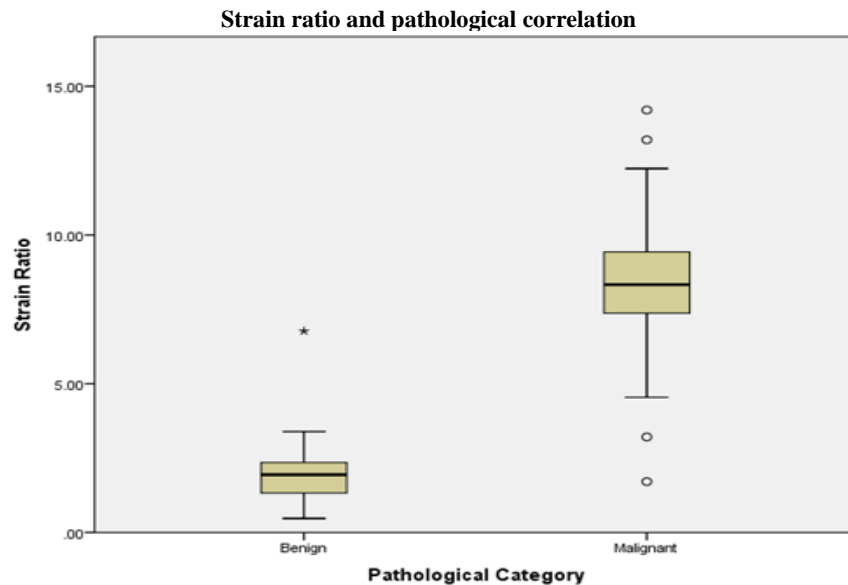


Fig 2: Distribution of strain ratios of benign and malignant breast lesions.

In our study the mean strain ratio of benign lesions were found to be 2.05 ± 1.16 , which was significantly lower than

mean strain ratio 8.45 ± 2.89 observed in malignant lesions ($p < 0.001$).

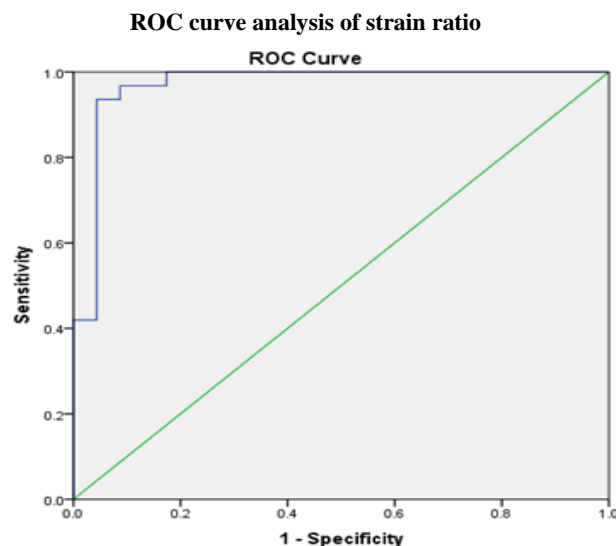


Fig 3: ROC curve for strain ratio in diagnosis of malignant breast lesion.

Receiver operating characteristic (ROC) curve analysis was done for strain ratio values of benign and malignant curve. ROC curve showed excellent accuracy of strain ratio to differentiate the benign breast lesions from malignant breast lesions. Area under the curve was 0.97 ± 0.026

($p < 0.001$, CI = 95% 0.918 – 1.0).

Comparison between 5-point elastography scoring and strain ratio and conventional B mode sonography

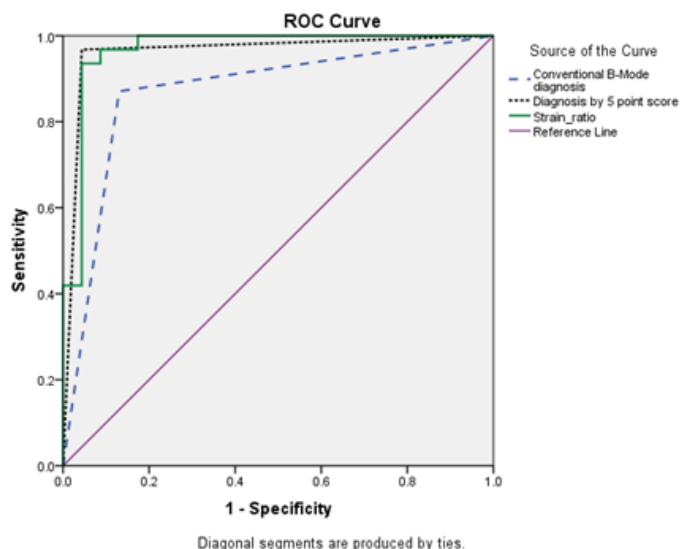


Fig 4: Comparison of ROC curves for different modalities in differentiating benign and malignant breast lesions.

Table 7: Area under curve for different modality.

Modality	AUC	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Conventional B-Mode diagnosis	.870	.054	.000	.765	.976
Diagnosis by 5 point score	.962	.031	.000	.902	1.000
Strain_ratio	.969	.026	.000	.918	1.000

Discussion

In this study among 54 cases, largest age group were in age group of 30-39 years and 50-59 years, each with total 13 (24%) no of cases. the most frequent age group to have diagnosed breast cancer was between 50 to 59 years age group. The youngest patient with malignant lesion of breast was 21 years in this study. The mean age of patients with malignant lesion was 47 years and for benign lesions was 30 years.

This study included the lesions of size ranging from 6mm to 79mm. Mean lesion size in the study population was 32.3 mm (± 18.5). Mean size of benign lesion was 23.7 mm (± 12.7) and for malignant lesions mean diameter of lesion was 43.7 mm (± 19.1). There was significant difference between the mean diameter size of benign and malignant lesion in our study (CI=95%, $p < 0.01$).

The sonographic criteria of taller than wider lesion when used as the predictor of malignancy, showed high specificity of 96.5% and PPV of 87.5% in this study. But the sensitivity was only 30.4% and accuracy was 68.1%. Similar specificity and PPV of 98.1% and 81.2 % was shown in study by Stavros et al. but with slightly better sensitivity of 41.6% and accuracy (88.7%).¹¹

Calcifications within the breast mass was seen in 12 out of 23 malignant lesions and only 4 cases out of 31 benign lesions had calcifications. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of calcification as criteria for diagnosing malignant breast lesion was 52%, 87%, 75%, 71% and 72% respectively ($p = 0.002$) Findings of this study showed better specificity and sensitivity but poorer NPV and accuracy, than those of findings of study by Stavros et al. Their study conducted in 1995 among 750 breast lesions showed calcification as predictor as malignancy had sensitivity, specificity, PPV, NPV and accuracy of 27.2%, 96.3%, 59.6%, 86.9% and 84.8% respectively.¹¹

Among 31 benign breast lesions 81% (25 cases) had regular margins. One of the benign lesions showed spiculated margin which on histopathological report was found to be granulomatous lesion. 16% (5 cases) of benign lesions had irregular margins. Likewise among 23 malignant lesions in our study, 43% (15 cases) of them had irregular margin, 35 % (9 cases) had spiculated margins, 13% (3 cases) showed microlobulation and 9% (2 cases) showed angular margin.

Spiculated margin of lesion shows high specificity and PPV for malignant lesion but has very poor sensitivity. In our study spiculated margins of lesion when used as the criteria for predicting malignancy the sensitivity, specificity, PPV, NPV and accuracy of conventional ultrasound were 34.7%, 96.8%, 88.9%, 66.7% and 70.4% respectively. These findings were consistent with findings of study by Stavros et al. which showed sensitivity, specificity, PPV, NPV and accuracy of 36.0%, 99.4%, 91.8%, 88.6% and 88.8% respectively.¹¹ Another study by Hong, A.S. et al. in 2004 also showed similar PPV of 86%, of spiculated margin as predictor of malignancy.¹²

Microlobulations was another sonographic criterion that we evaluated as predictor of malignancy. Among total 54 cases only 3 cases had microlobulation of margins and all of them were pathologically proven to be malignant lesion. Microlobulation of margin showed 100% specific and 100% PPV but sensitivity and accuracy of this criteria was only 13% and 62% respectively. Higher sensitivity, and accuracy of 75% and 82% was demonstrated in study by Stavros et al. specificity and PPV in their study was 83.8% and 48.2%.¹¹

Posterior acoustic shadowing seen in 52% (12) of malignant cases and 6% (2) benign cases in this study. Specificity and PPV of this characteristics is 93.55% and 85.7% but has low sensitivity (52.2%) and NPV (72.5%).

The overall diagnostic performance of convention B-mode

ultrasonography in differentiating benign and malignant breast lesions was also studied. This study showed 4 cases diagnosed as malignant by B-mode were false positive and 3 cases diagnosed benign were false negative. Sensitivity, specificity, PPV, NPV and accuracy of the B-mode ultrasound was found to be 86.9%, 87.1%, 83.3%, 90% and 87.0% respectively.

Study by Chen et al in 1203 solid breast lesions, reported that conventional Sonography had sensitivity of 79.3%, specificity of 89.3%, PPV of 78.1%, NPV of 90% and accuracy of 86%. Findings of their study and our study are comparable.¹³

Stavros et al. in their study however reported slightly higher sensitivity of 98.4% and NPV of 99.5%. but specificity (67.8%), NPV (38.0%) and accuracy (72.9%) was slightly lower than our study¹¹. Another study by Yerli, H et al also reported lower sensitivity and specificity of 87.5% and 72.6% for B-mode Sonography.⁸

Elastography 5-point scoring system

In our study 97 % of benign lesions (30) had elastography score between 1 and 2. Only 1 (3%) benign lesion had higher elastography score of 4. Similarly, 96% of malignant lesion had elastography score of 3 and above and 1 malignant lesion (4%) had score of 2. Mean elastography score of benign lesions was 1.6 ± 0.6 and for malignant lesion was 3.7 ± 0.9 . When elastography score of 2 was set as cut off value for differentiating benign and malignant lesion overall sensitivity, specificity, PPV, NPV and accuracy of 5-point scoring system was high (95.6%, 96.7%, 95.6%, 96.7% and 96.2% respectively). ROC curve analysis of 5-point scoring system in differentiation of benign and malignant lesion showed area under curve of 0.962 ± 0.026 ($p < 0.001$). When cut off value between 2 and 3 selected the sensitivity and specificity of 5-point score si 96.8% and 96.7% respectively.

Yerli H et al in study of 78 breast lesions by elastography reported the mean scores \pm SD on elastography of 2.69 ± 0.59 for benign lesions and 3.75 ± 0.68 for malignant lesions. The areas under the curves was 0.864 for 5-point scoring system. Reported sensitivity and specificity in their study for 5 point scoring system were 80% and 95%, respectively.⁸

Another study by Itoh, A. et al. mean elasticity scores of benign and malignant lesions were reported as 2.1 ± 1.0 and 4.2 ± 0.9 respectively ($P < 0.001$). The ROC curve analysis showed area under curve was 0.919. These values were comparable with our study as well.¹⁰ Similar specificity of 95.7%, accuracy of 88.2% and PPV of 87.1% was reported by Zhi H et al in their study of 267 solid breast lesions in 2007.¹⁴

Strain ratio

This study showed significant difference between the strain ratio of benign and malignant lesions. The mean strain ratios for benign and malignant lesions were 2.05 ± 1.16 and 8.44 ± 2.89 respectively (CI 95% and $p < 0.001$). ROC curve analysis showed area under curve to be 0.969 ± 0.026 . when strain ratio value of 3.9 as cut off value for differentiating benign and malignant lesion sensitivity and specificity were 96.8% and 91.3% respectively.

Study done by Farokh A et al. in 2011 reported mean strain ratios for benign and malignant lesions to be 1.87 and 7.9 respectively. ($P < 0.0001$). When a cutoff point of 3.54 was used, SR had a sensitivity of 94.6%, a specificity 94.3%, a PPV of 95.1%, an NPV of 93.7% and an accuracy of 94.4%. The area under curve was reported 0.96 for the strain ratio.¹⁵ Another study done by Yerli H et al reported mean strain ratio values were 2.03 ± 2.67 for benign lesions and 5.97 ± 4.45 for malignant lesions. Area under curve was 0.840 and sensitivity and specificity of 80% and 93% were reported with cut off value of strain ratio as 3.52.⁸

Case figures:

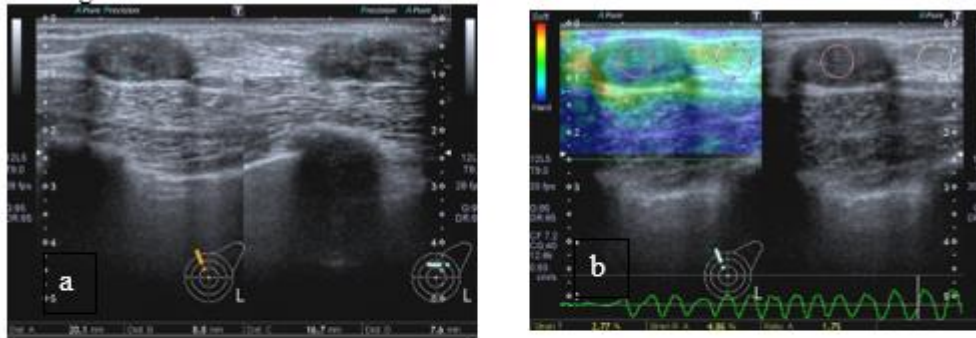


Fig: a) B-mode scan of left breast lesion with oval, wider than taller hypoechoic lesion with smooth regular margin s/o benign lesion. b) elastography of same lesion demonstrating mosaic of green and blue (elastography score 2) and strain ratio measuring 1.75 s/o benign lesion. (Pathological diagnosis: Fibroadenoma)

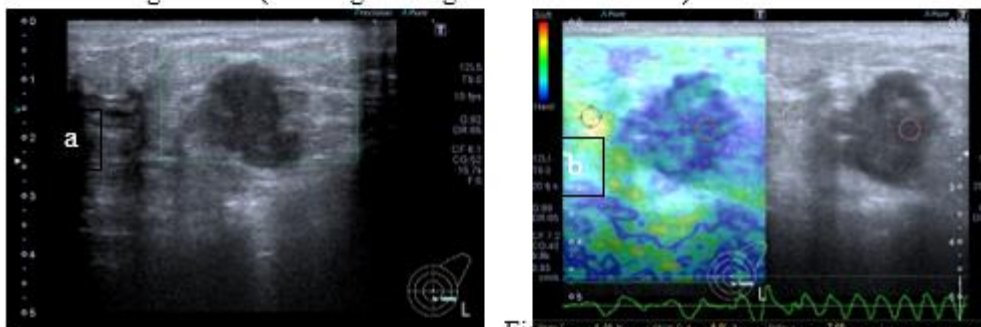


Fig. a) Convention B-mode scan irregularly margined hypoechoic lesion with taller than wider configuration and microlobulation s/o malignant lesion. b) elastography images showing predominantly blue color over lesion not extending beyond margin (elastography score of 4) and strain ratio of 7.9. (Pathologically proven to be malignant)

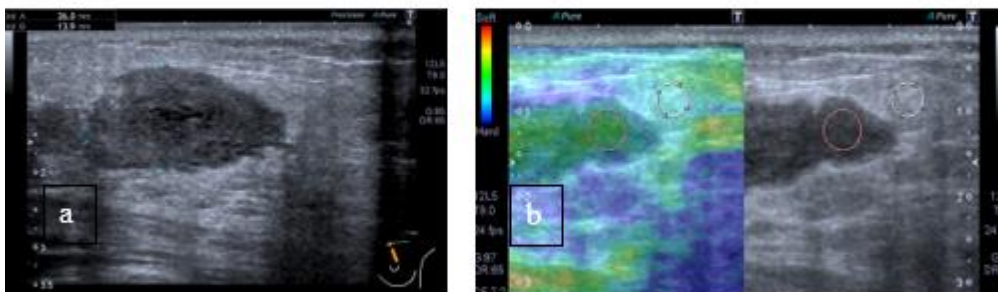


Fig: a) B-mode image of left breast lump showing hypoechoic irregularly margined and few spiculated margin suspicious of malignant lesion. b) Elastography image of same patient showing mosaic pattern with predominantly green color (elastography score 2) and strain ratio measuring 1.94 s/o benign lesion. (pathological diagnosis- benign granulomatous lesion)

Conclusion

Conventional B mode ultrasonography is used as an imaging modality to diagnose and characterize the breast lesions as malignant or benign. Addition of elastography to conventional ultrasound will increase the diagnostic performance of the ultrasound and hence can help in minimizing unnecessary biopsy rates in benign breast lesions.

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