The Egyptian Journal of Hospital Medicine (April 2018) Vol. 71 (7), Page 3655-3666

Impact of Ultrasound Elastography in The Diagnosis of Solid Breast Lesions

Ahmed M. Monib, Amr M. AbdelSamad, Amany A. AbdElhakam
Department of Radiodiagnosis, Faculty of Medicine Ain Shams University
Corresponding author: Amany A. AbdElhakam; Mobile: 01069551758, Email:mony_elhenawy@yahoo.com

ABSTRACT

Background: Ultrasound scanning is noninvasive, usually painless procedure that used as the main adjuvant modality with mammography for depiction of the breast lesions nature. It is easy-to-use and less expensive than other imaging modalities. Besides lacking the exposure risk to ionizing radiation as in mammography, it also provides real-time imaging, and can easily detect lesions in women with dense breasts. Conventional ultrasound however is not free from limitation. It cannot replace annual mammography and careful clinical breast examination. Being an operator dependent, US needs experienced radiologists as well as good equipment to avoid misinterpretation of the lesions, and to decrease the number of false positive and false negative results. **Aim of the Work:** is to detect the impact of ultrasound elastography in diagnosis of solid breast lesions, and to evaluate its capability in differentiating benign form malignant lesions, with special focus on: A-Evaluation of sensitivity and specificity of sonoelastography, with cyto-histological diagnosis taken as the reference. B-Detection of the ability of sonoelastography to provide additional information on tissue elasticity in the event of equivocal mammographic and/or sonographic findings in order to guide the diagnostic workup towards biopsy or follow-up. **Patients and methods:** The present study is a prospective research work that included 39 patients with breast lesions where elastographic ultrasound was performed following screening or diagnostic mammography and breast ultrasound to evaluate its possible impact on accurate diagnosis and consequent guidance for management planning. This study was performed at a private center in the period from September 2017 to March 2018. The patients' age ranged between (24 - 72 years) with a mean of 48 years. **Results:** The elastography scores for different breast lesions was:Lesions that scored 1, 2, and 3 were considered benign(30/39 cases, 77 %), whereas lesions that scored 4 and 5 (9/39 cases, 23%) were considered malignant. After revising pathology results of the 30 cases diagnosed as benign by elastography scoring 26/30(87%) were benign (true negative) by pathology and 4/30(13%) were malignant by pathology (false negative).After revising pathology results of the 9 cases diagnosed as malignant by elastography scoring 7/9(82.8%) lesions confirmed to be malignant by pathology (true positive) and 2/9(17.2%) lesions were proved to be benign by pathology (false positive).The calculated sensitivity of elastography score was 80%, specificity was 88.9%, PPV and NPV were 82.8% and 87% respectively, and the total accuracy was 85.3%.**Conclusion:** Sonoelastography is a simple, non-invasive diagnostic technique that provides information about the stiffness of a breast masses, thus completing the morphological assessment of B-mode ultrasound. **Recommendations:** Other studies are recommended to be performed on axillary lymph nodes, to evaluate the elastographic efficacy in differentiating between reactive and malignant pathologically enlarged axillary lymphadenopathy.

Keywords: ultrasound elastography, solid breast lesion.

INTRODUCTION

Breast cancer is the most common female neoplasm (31% of tumors in females), and the second-leading cause of death among women. Breast lesions were first classified as malignant or benign categories [(1)].

The most prevalent malignant lesions were further subdivided into three subgroups including: ductal carcinoma in situ (DCIS), invasive ductal carcinoma of nonscirrhous type, and invasive ductal carcinoma of scirrhous type [(2)]. Similarly, the most prevalent benign lesions were divided into three subgroups, including intraductal papilloma, fibroadenoma, and aberrations of normal development and involution (ANDI) [(2)].

There have been marked advances in the quality of ultrasound imaging over the past 2 decades [(3)]. However the breast nodule is still a daily challenge for the radiologist in the setting of US diagnosis. This created the need for new diagnostic approaches including ultrasound elastography (UE)[(1)].

The principle of elastography is that tissue compression produces strain (displacement) within the tissue, and that the strain is smaller in harder tissue than in softer tissue [(2)]. Therefore, by measuring the tissue strain induced by compression, ultrasound elastography (UE) can make the hardness of the tissue "visualize", display its texture, and reflect the biological characteristics of the mass. It shows promising

Received:20 / 3 /2018 DOI: **10.12816/0047689**
Accepted30: /3 /2018

prospects in differentiating benign from malignant breast tumor [4].

Today, real time elastographic systems that allow freehand scanning and provide excellent spatial resolution with less noise are integrated into commercially available US units. Benign tumors show even strain, whereas breast cancers show no strain in lesions or in surrounding areas [5]. Elastography could also be used to distinguish an area of shadowing due to fibrosis from that due to carcinoma [6].

The elastography strain images were scored according to the elasticity score in to five categories [6]. Elasticity of breast tissue is affected by both physiological and pathological processes that cause structural changes as well as histological type of the mass being examined. Other factors that may affect the elasticity score are lesion size and depth. The more superficial the lesion, and the smaller its size, the more the sensitivity and specificity of yielded elastograms [7].

Elastography allows for differentiation of malignant lesions from benign lesions (even among lesions smaller than 10 mm) [2].It also has the potential to evaluate the nature of the lesions detected at screening mammography and associated with microcalcifications, whether benign or malignant [8].

Axillary lymphadenopathies are the single most important prognostic factor for operable breast cancer [1]. Elastography can provide useful information about the nature of lymph nodes and the quantitative technique of the elastography further makes the diagnosis more accurate than B-mode, color and power Doppler sonography alone [4].

Frequently cystic alterations of the breast are interpreted as indeterminate nodules by the conventional approach, particularly those with a thick fluid content, fine debris in suspension, or complex cysts with mural nodules [9].

Combination between UE, conventional sonography, and mammography facilitates detection of two features of a lesion, morphologic characteristics and hardness, which reflect the properties of the lesion, facilitating differentiation between benign and malignant tumors, and thus elevating the sensitivity, specificity, accuracy, and the positive predictive value, augmenting the diagnostic capability of sonomammography [3].

UE is better than sonomammography for detecting breast cancer in small sized breasts [3]. Also elastography has a higher sensitivity compared with B-mode US in the presence of breast lipomatous involution [10]. However, when using UE, one should pay attention to all the factors that would affect the stiffness of lesions such as large-scale necrosis, coarse calcifications, or organized hemorrhage, which may increase the hardness of the lesion, and cause misleading results [3].

Elastography was found to be superior to B-mode US in evaluating BI-RADS 3 (Breast Imaging Reporting and Data System) benign lesions [10]. Prevention of unnecessary histopathologic confirmation of breast lesions of BI-RADS 3 or 4 corresponding with elasticity scores 2, is one of the most important advantages. Additionally, a 6-month follow-up is not necessary in case of BI-RADS 3 in conventional B-mode US and elasticity scores 2. Both situations provide a downgrading of the lesion to category BIRADS 2. [11]This may support the compliance of women, and also reduces costs in the health care system [12].

Sonoelastography is not, however, free of limitations. These include high level of operator dependency, subjective interpretation of elastograms and sensitivity to slight changes in patient position [7]. In summary, recent improvements in breast ultrasound equipment technology have occurred including the introduction of UE, which is very promising complementary diagnostic tool. Breast ultrasound is still being developed further, and this will lead to further better diagnostic approaches [13].

Aim of work

The aim of this study is to detect the impact of ultrasound elastography in diagnosis of solid breast lesions, and to evaluate its capability in differentiating benign form malignant lesions, with special focus on:

A- Evaluation of sensitivity and specificity of sonoelastography, with cyto-histological diagnosis taken as the reference.

B- Detection of the ability of sonoelastography to provide additional information on tissue elasticity in the event of equivocal mammographic and/or sonographic findings in order to guide the diagnostic workup towards biopsy or follow-up.

PATIENTS AND METHODS

***Patients:**

The present study is a prospective research work that included 39 patients with breast lesions where elastographic ultrasound was performed following screening or diagnostic mammography and breast ultrasound to evaluate its possible impact on accurate diagnosis and consequent guidance for management planning.

This study was performed at a private center in the period from September 2017 to March 2018.

The patients' age ranged between (24 - 72 years) with a mean of 48 years.

- ***Inclusion Criteria:***

- Patients who have positive ultrasound and/or MRI findings of breast masses.

- ***Exclusion Criteria:***

- Cases with breast implants.
- Cases with superficial (<5 mm deep to the skin surface), and cutaneous lesions.
- Cases with purely cystic lesions on conventional ultrasound examination.

Image Analysis:

Imaging analysis including mammogram reading, ultrasound performance (both gray scale and elastographic ultrasound) was performed under the guidance of two qualified consultants of radiology, M.D. certified (Professor and lecturer- 20 and 10 years experience in breast imaging and interventional procedures respectively). Imaging-guided biopsy for the detected masses was performed by the consultants. The authors were blinded to each other's analysis as well as to the pathology results at the time of initial evaluation. At the stage of final evaluation, there was a multidisciplinary discussion of cases with the referring physician.

***Methods:**

- ***Full-Field Digital mammography***

Mammographic studies were performed using ***Hologic Selenia Dimentions instrument.*** Standard cranio-caudal and medio-lateral oblique views were obtained.

- ***Ultrasound Examination***

All patients were examined with B-mode ultrasound. Examinations were performed using a high-end ultrasound system ***(Toshiba Aplio XG Medical Systems, Japan)*** that includes a multifrequency linear probe operating at 5 to 10 MHz software and a combined autocorrelation method.

The scanning protocol included transverse and longitudinal real-time imaging of masses of concern. A split-screen imaging mode (twin images) was used for conventional US and US elastography so as to obtain identical images optimal for accurate application for region of interest (ROI) and strain ratio (SR) measurement later on.

On ***B-mode sonography***, lesions were evaluated regarding, shape, boundary, orientation, margin, echo pattern, and posterior acoustic features, + calcifications. Surrounding tissue condition was also included in the final assessment. Lesions were classified according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) for B-mode sonography as follows: ***category 2*** lesions were classified as benign; ***category 3*** as probably benign; ***category 4*** as suspicious for malignancy; ***category 5*** as highly suggestive of malignancy and ***category 6*** lesions were pathologically proven to be malignant.

- ***Sonoelastography***

All patients were examined with ultrasound elastography. ***Sonoelastographic images*** were obtained by placing the transducer with coupling gel on the skin and then the considered mass is focused upon.

After activating the sonoelastographic function, images were obtained by applying repeated compression and decompression in a sustained frequency. Color coding is superimposed on the translucent B-mode images. To get a correct sonoelastographic map, the process was repeated until a stable image was obtained. The sonoelastographic images were obtained in a 256-color scale ranging from red to blue. The softest component of the lesion was depicted in red, showing the greatest strain, whereas the hardest component with no strain was depicted in blue; while green indicated intermediate elasticity. We selected an image obtained in the early phase of compression because these images provide the best contrast according to **Itoh *et al.*** [2].

- ***In the qualitative (color coded) evaluation*** of the sonoelastographic images, lesion classification was performed on the basis of a 5-point scoring method (Tsukuba scoring system) proposed by **Itoh *et al.*** [2].
- ***Score 1*** indicated even strain for the entire lesion (i.e., the entire lesion was evenly shaded in green).
- ***Score 2*** indicated strain in most of the lesion, with some areas of no strain (i.e., the lesion had a mosaic pattern of green and blue).
- ***Score 3*** indicated strains at the periphery of the lesion, (i.e., the peripheral part of lesion was green, and the central part was blue).
- ***Score 4*** indicated no strain in the entire lesion (i.e., the entire lesion was blue, but its surrounding area was not included
- ***Score 5*** indicated no strain in the entire lesion or in the surrounding area (i.e. the entire lesion and its surrounding area were blue).

In the semiquantitative evaluation of the sonoelastographic images, the strain indices of the lesions were calculated. For each case, normal - appearing breast region approximately at the same level of the concerned lesion was elicited as an internal reference (channel 1) and the region of interest including the lesion was selected as (channel 2), to correctly determine the difference in hardness of the lesion compared with the

surrounding normal area. The strain ratio was automatically obtained as the strain measured via channel 1/ the strain measured via channel 2 ratio.

***Histopathologic Diagnoses:**

Histopathologic diagnoses of surgical specimens or biopsy specimens were obtained and served as reference standards. Diagnoses from elasticity scoring and the strain ratios were compared with the histopathologic diagnoses.

Statistical Analysis

- The statistical software SPSS version 17.0 (Chicago, ILI) was used for analysis of the data.
- Logical tests (true or false) were applied to assess the accuracy of the elastographic measurements compared with the gold standard of histology, The mean strain ratio calculated by **using student T test**. Diagnostic sensitivity, specificity, and positive and negative predictive values were calculated on the basis of pathologic results, at different cut off points, regarding the five point elastographic scoring system, the best cut off point was attained where the summation of the sensitivity and specificity was maximum.
- Different Cutoff values of SRs were optimized using receiver-operating characteristic (ROC) curve analysis.
- Mean values and standard deviations were calculated for both benign and malignant lesions using the pathology as a gold standard.
- The diagnostic performances of conventional US and US elastography with respect to the differentiation of benign and malignant breast masses were compared by calculating, areas under ROC curves for both methods.
- The Mean elastoscores, and mean strain ratios, for different benign and malignant pathological entities were calculated.
- Correlation between elastoscoring, conventional ultrasound and strain ratio was performed, (Pearson correlation is considered week when it measures less than 0.250, fair between (0.250: 0.500), moderate between (0.500: 0.750), and strong if more than 0.750.

RESULTS

Pathological Diagnoses

All solid breast lesions were diagnosed histologically by means of radical surgery, excisional, true cut biopsy, or fine needle aspiration cytology. The final pathologic diagnoses including the total number of benign and malignant lesions are illustrated in the following table

Table (1): Final pathologic diagnoses of breast lesions.

Pathology	Number	Percentage
Benign	30	77%
Malignant	9	23%

Detailed description for the number and percentage for each pathological breast entity within benign and malignant categories are illustrated in the following tables.

Table (2): Final pathologic diagnosis of benign breast lesions

	Number and percentage
Fibroadenoma	10 (25.64%)
Focal adenosis	6 (15.38%)
Postoperative scar	2 (5.12%)
Breast abscess and mastitis.	4 (10.26%)
Complicated cyst	3 (7.69%)
Fat necrosis	2 (5.12%)
Intracystic papilloma	1 (2.56%)
lactating adenoma	2 (5.12%)
Infiltrating ductal carcinoma (IDC)	4 (10.26%)
Ductal carcinoma in situ (DCIS)	2 (5.12%)
Inflammatory carcinoma	1 (2.56%)
Medullary carcinoma	1 (2.56%)
Metastatic undifferentiated carcinoma of unknown origin	1 (2.56%)
Total	9 (23.08%)

Table (3): Detailed description of sonographic findings

		Number	*Percentage*
Borders	***Ill defined***	***16***	***41.02%***
	Well defined	***14***	***35.9%***
	Lobulated	***9***	***23.07%***
Shape	***Regular***	***20***	***51.2%***
	Irregular	***19***	***48.8%***
Acoustic shadowing	***No***	***26***	***66.7%***
	yes	***13***	***33.3%***
Acoustic	***No***	***27***	***69.2%***
enhancement	***yes***	***12***	***30.8%***
Calcifications	***No***	***31***	***79.5%***
	yes	***8***	***20.5%***
pattern	***Homogenous***	***20***	***51.3%***
	Heterogenous	***19***	***48.7%***
Echogenicity	***Hypoechoic***	***22***	***56.4%***
	Isoechoic	***11***	***28.2%***
	Hyperechoic	***6***	***15.4%***
Orientation	***Parallel***	***25***	***64.1%***
	Vertical	***14***	***35.9%***

Elasticity Scores

The elastography scores for different breast lesions was: Lesions that scored 1, 2, and 3 were considered benign (30/39 cases, 77 %), whereas lesions that scored 4 and 5 (9/39 cases, 23%) were considered malignant. After revising pathology results of the 30 cases diagnosed as benign by elastography scoring 26/30(87%) were benign (true negative) by pathology and 4/30(13%) were malignant by pathology (false negative).

After revising pathology results of the 9 cases diagnosed as malignant by elastography scoring 7/9(82.8%) lesions confirmed to be malignant by pathology (true positive) and 2/9(17.2%) lesions were proved to be benign by pathology (false positive).

The calculated sensitivity of elastography score was 80%, specificity was 88.9%, PPV and NPV were 82.8% and 87% respectively, and the total accuracy was 85.3%.

Table (4): Analysis of false positive and false negative diagnosis by elastographic scoring when considering E1,2,3 as benign and E 4,5 as malignant

	Pathologic Diagnosis	**Number**
False Negative		6
	Ductal carcinoma in situ (DCIS)	2
	Infiltrating ductal carcinoma(IDC)	1
	Colloid (mucinous carcinoma)	1
False Positive		5
	Fibroadenoma	1
	Breast abscess	1

As suggested by the relatively high number of cases along the diagonal of the table, the scores of the two methods tended to be positively correlated.

Strain ratio:

The mean strain ratio calculated for benign lesions was 2.44, while the mean strain ratio for malignant lesions was calculated as 8.14, by **using student T test**. The standard deviation for benign lesions was 1.2776, and the standard deviation for malignant lesions was 5.4212 as illustrated in the following table.

Table (5): Mean, number and standard deviation of strain ratio regarding different pathological entities

Group Statistics

Pathology	N	Mean	Std. Deviation	p value
Strain ratio Benign	**30**	**2.442**	**1.2776**	
Malignant	**9**	**8.138**	**5.4212**	**< 0.001**

Elastography and Lesion diameters

The elastographic scoring showed the maximum sensitivity and NPV(84.6%, and 92.6 % respectively), for lesions less than 20 mm in diameter, however, for lesions more than or equal 20 mm in diameter, the specificity, and PPV were higher and calculated as 93.8% and 92.9% respectively. On the other hand, the strain ratio rendered higher, sensitivity, specificity, PPV for lesions more than or equal 20 mm in diameter, where they were (82.4%, 93.8%, and 93.3%, respectively) as shown in table 6.

Table (6): Sensitivity, specificity, PPV, NPV of elastography and SR, for lesions < 20 mm and >20mm

	Sensitivity	Specificity	PPV	NPV
Elastography scoring among lesions (< 2cm) (42)	84.6%	86.2%	73.3%	92.6%
Elastography scoring among lesions (> 2 cm) (33)	76.5%	93.8%	92.9%	78.9%
SR among lesions (< 2cm) (42)	76.9%	69%	52.6%	87%
SR among lesions (> 2 cm)(33)	82.4%	93.8%	93.3%	83.3%

Comparison between Receiver operating characteristic curves for, elastoscoring, conventional ultrasound, and strain ratio

It was found that the diagnostic performances of conventional US, US elastography, and the strain ratio with respect to the differentiation of benign and malignant breast masses were similar. Moreover, areas under ROC curves showed no statistically significant difference for the three methods.

Table (7): Areas under ROC curves, for conventional ultrasound, elastoscoring and strain ratio methods

Test Result Variable(s)	Area	Asymptotic 95% Confidence Interval	
		Lower Bound	Upper Bound
Conventional US	**0.888**	**.814**	**.962**
Elasto scoring	**0.846**	**.742**	**.949**
Strain ratio	**0.876**	**.790**	**.962**

Correlation Between Elastoscoring. Conventional Ultrasound and Strain Ratio

The following table illustrate the correlation between elastoscoring, conventional ultrasound and strain ratio, where conventional US is fairly correlated with elastoscoring (Pearson correlation=0.469), strain ratio is moderately correlated with elastoscoring (Pearson correlation=0.658) as well as with conventional ultrasound (Pearson correlation=0.512).

Table (8): Correlation between elastoscoring, conventional ultrasound and, strain ratio

		Elastoscore	ConvectionalUS	Strainratio
Elasto score	Pearson correlation	1	469.	.658
Conventional US	Pearson correlation	.469	1	.512
Strain ratio	Pearson correlation	.658	.512	1

When correlation was made between elastoscoring and log. strain ratio (its logarithmic value), the correlation changed from moderate to strong correlation (Pearson correlation=0.803).

CASE 1

Clinical background:

Thirty two-year-old female patient presented with right breast UOQ palpable lump.

Ultrasound Findings:

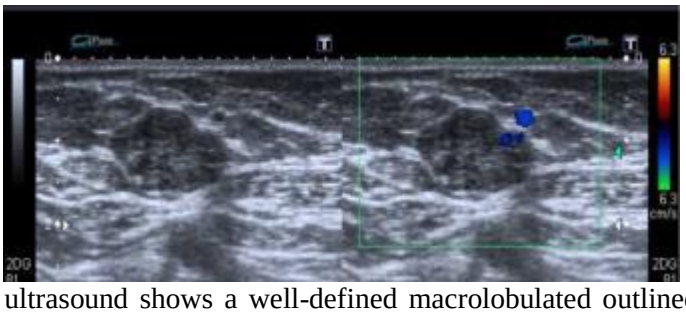

Fig. (1) B-mode ultrasound shows a well-defined macrolobulated outlined hypoechoic solid mass (BI-RADS 3).

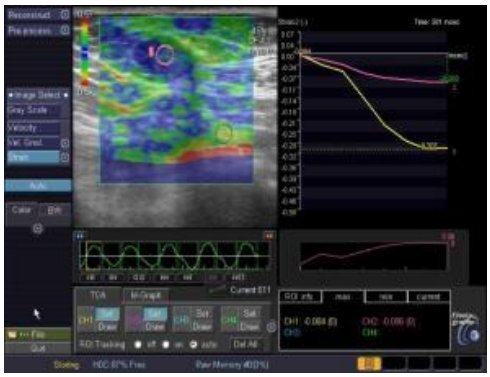

Fig. (2) Elastography image, shows the scoring was E3, and the yielded SR was 3.26. The elastography category was (BI-RADS 3).

Ultrasound elastography confirmed the data supplied by the conventional US.

Pathology: Fibroadenoma

CASE 2

Clinical background:

Twenty nine-year-old female patient presented with right lower inner quadrant (LIQ) breast palpable lump.

Ultrasound Findings: B-mode ultrasound shows a well-defined outlined hypoechoic solid mass with distal acoustic enhancement as illustrated in (Fig. 3) (BI-RADS 2).

On elastographic images, the scoring was E4 and the yielded SR was 1.41(Fig. 3) (BI-RADS 3). Elastography scoring upgraded the BI-RADS categorization of the case from BI-RADS 2 (benign) to BI-RADS 3 (probably benign).

Pathology: Highly Cellular Fibroadenoma.

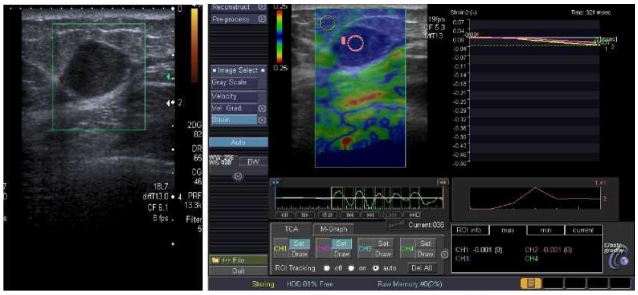

Fig. (3) B-mode ultrasound shows a well-defined outlined hypoechoic solid mass with distal acoustic enhancement as illustrated in.

DISCUSSION

Breast cancer is the most common female neoplasm (31% of tumors in females), and the

second-leading cause of death among women. Breast lesions were first classified as malignant or benign categories [(1)].The current research work is a prospective study where 39 solid breast lesions had been evaluated by means of conventional ultrasound as well as elastography mode. For each lesion strain ratio was calculated. From such evaluation we aimed to check the ability of elastography ultrasound to upgrade or downgrade the BI-RADS category of such lesions elicited by B-mode ultrasound, in order to seek more proper guidance for management.

Ultrasound scanning is noninvasive, usually painless procedure that is used as the main adjuvant modality with mammography, for characterization of the breast lesions nature. It is easy-to-use and less expensive than other imaging modalities. Besides lacking the exposure risk to ionizing radiation as in mammography, it also provides real-time imaging, and can easily detect lesions in women with dense breast [(14)].

Ultrasound is not free from limitation. It cannot replace annual mammography and careful clinical breast examination. Being an operator dependent, US needs experienced radiologists as well as good equipment to avoid misinterpretation of the lesions and to decrease the number of false positive and false negative results [(14)].

The previous limitation warranted additional diagnostic tools, like elastography, to be evolved. Elastography added a complementary role besides conventional sonography in assessing breast masses based on palpation concept as the standard clinical procedure for the detection of breast abnormalities, where cancer tissue is usually harder than adjacent normal tissue [(3)].**Ophir *et al.*[(15)]** described the elastography, in early 1990s. With this technique, the tissue is compressed, and the tissue strain resulting from this compression is imaged.

According to Tsucuba scoring, lesions in our study were classified into 5 elasto-scores, as previously described. In our results, lesions that scored E1 (6, 8%), E2 (16, 21.3%), and E3 (24, 32%) were considered benign, whereas lesions that scored E4 (17,22.7%), and E5 (12,16%) were considered malignant.

In our study, we considered elastographic scoring of 1,2,3 as benign and that of 4, 5 as malignant. After revising pathology results of the 30 cases diagnosed as benign by elastography scoring, 26/30(87%) were benign (true negative) by pathology, and 4/30(13%) were malignant by pathology (false negative). After revising pathology results of the 9 cases diagnosed as malignant by elastography scoring, 7/9 (82.8%) lesions confirmed to be malignant by pathology (true positive) and 2/9(17.2%) lesion were proved to be benign by pathology (false positive).

The calculated sensitivity of elastography scoring was 80%, specificity was 88.9%, PPV and NPV were 82.8% and 87% respectively, and the total accuracy was 85.3%. While considering elastographic scoring of E1,2,3,4 benign and that of E5 as malignant, the calculated sensitivity was 33.3%, specificity was 95.6%, PPV and NPV were 83.3%, and 68.3% respectively. The total accuracy was 70.7%.

Our results were comparable to the results reported by **Schaefer *et al.*[(12)]**, who stated a cut-off point of elastography scores between 3 and 4, with a sensitivity of 96.9%, a specificity of 76.0% and an accuracy of 82.9%.

Scaperrotta *et al.* [(16)] evaluated the diagnostic utility of sonoelastography in differentiating benign from malignant non-palpable breast lesions. A total of 293 BI-RADS 3-5 impalpable breast lesions in 278 women were evaluated with B-mode ultrasound (US) and subsequently with sonoelastography (SE) before performing US-guided biopsy. Among the 293 lesions (size up to 2 cm), 110 (37.5%) were histologically malignant and 183 (62.5%) were benign. Overall performance of SE was lower than US, with SE sensitivity and specificity of 80% and 80.9% respectively, as compared with 95.4% and 87.4% for US.

In spite of the previously mentioned data, ***Scaperrotta* and his colleagues[(16)]** finally stated that the joint use of SE and US in breast masses evaluation is over the use of US alone. The authors noted that SE is a simple, fast and non-invasive diagnostic method that may be a useful aid to US for less experienced radiologists in the assessment of solid non-palpable breast lesions.

Leong *et al.*[(17)] compared the diagnostic performance of breast elastography versus conventional ultrasound in the assessment of breast lesions in a prospective study involving one hundred and ten lesions. Sensitivity, specificity, and accuracy were 88.5%, 42.9% and 53.6%, respectively, for conventional ultrasound, 100%, 73.8%, and 80%, respectively, for elastography. Whereas there was no statistically significant difference between the two methods. The investigators concluded that ultrasound breast elastography was more specific and more accurate than conventional ultrasound. They concluded that combining elastography with ultrasound improved specificity and accuracy of ultrasound and can potentially reduce the number of false positive results.

Raza *et al.*[(18)],prospectively assessed the performance of real-time tissue elastography in

the evaluation of 200 breast masses and correlate it, and (BI-RADS) assessments with pathologic findings. Of the malignant lesions, 84% had ES of 5 and 4, whereas 76% of benign lesions had ES of 1 and 2. The sensitivity of real time elastography was 92.7%, and specificity was 85.8%, with 4 false-negative and 16 false-positive results. The difference in results between ours, and those derived by Raza and his colleagues[18] may be related to the fact that we used static elastography evaluation, rather than real time imaging.

Semi-Quantitative analysis of the elastography ultrasound was performed using automatically calculated strain ratio. In our study, the best cut off value for strain ratio to differentiate between benign and malignant breast entities was found to be at 3.13 level (AUC, 0.876). It allowed significant differentiation between benign, and malignant lesions ($p < 0.001$). When considering lesions with strain ratio less than 3.13 as benign and lesions with strain ratio more than or equal 3.13 as malignant.

In our study, the mean strain ratio for benign lesions was 2.44, with standard deviation equals 1.2776, while the mean SR for malignant lesions was 8.14 with standard deviation equals 5.4212, these results are comparable to those reported by **Kumm and Szabunio**[19]where the mean ratios were 2.7 and 10.5, for benign and malignant lesions respectively. **Thomas and his colleagues**[10]reported lower values, where the mean strain ratio for benign lesions was 1.6 with standard deviation equals 1.0, and the mean strain ratio for malignant lesions was 5.1 with standard deviation equals 4.2.

Kumm and Szabunio[19] evaluated310 breast lesions. Sensitivity was 76% for ES and 79%for SR. Specificity was 81% for ES and 76% for SR. Positive predictive value was 60% for ES and 57% for SR and negative predictive value was 90% for both ES and SR. The investigators concluded that although the initial clinical performance of elastography imaging showed potential to reduce biopsy of low-risk lesions, however, a large-scale trial addressing appropriate patient selection, diagnostic parameters, and practical application of this technique is necessary prior to widespread clinical use.

Thomas and his colleagues[11] evaluated 227 lesions, and reported that the sensitivity and specificity were 96% and 56% for B-mode scanning, 81% and 89% for elastography, and 90% and 89% for SRs. A SR cutoff value of 2.45 (area under the curve, 0.949) allowed significant differentiation ($P < .001$) of malignant and benign breast lesions. The quantitative method of SR calculation was superior to subjective interpretation of sonoelastograms and B-mode scans, with a positive predictive value of 89% compared to 68% and 84% for the other two methods.

When another study for **Zhi *et al.*** [3]was performed upon 559 solid lesions, the strain ratios of benign lesions (mean, 1.83) and malignant lesions (mean, 8.38) were significantly different ($P < 0.001$). When a cutoff point of 3.05 was introduced, SR method had 92.4% sensitivity, 91.1% specificity, and 91.4% accuracy. The area under the curve for strain ratio-based elastographic analysis was 0.944, and the area under the curve for the five-point scoring system was 0.885. The diagnostic performance of strain ratio-based elastographic analysis was better than that of the five-point scoring system with ultrasound elastography ($P < .05$).

In our study, the area under the curve for strain ratio was calculated as 0.876 with standard error 0.044 (95% confidence interval, 0.790-0.962), and the area under the receiver operating characteristic curve for the five-point scoring system was 0.846.

The difference in the results between our study and that of **Zhi *et al.*** [3] probably was related to the difference in the number of lesions being evaluated, as well as the different type of device used as **Zhi and co-workers**[3]utilized Hitachi medical system (Hitachi Medical, Tokyo, Japan), while in our study we used Toshiba Aplio XG Medical Systems, Japan.

Some authors [3,7,20]suggest that the diagnostic efficacy of elastography may be influenced by the lesion size. We divided our cases into two groups in respect to lesion size; the first group, lesions that are less than or equal 2 cm, and the second group, lesions that measured more than 2 cm. Our study revealed, that for lesions more than 2 cm in diameter, the SR had a greater sensitivity, specificity, and PPV (82.4%, 93.8% and 93.3%) respectively, than for smaller lesions, where the sensitivity, specificity and PPV were (76.9%, 69% and 52.6%) respectively, however the NPV was higher among lesions (<2cm) (87%) than among lesions (> 2 cm), where it was 83.3%. These results were comparable to those of **Zhi and his colleagues** [3]. Whereas when evaluating the performance of five point scoring system, it rendered a higher specificity and PPV of 93.8%, 92.9%, for lesions larger than or equal 2 cm and a higher sensitivity and NPV of 84.6% and 92.6% for lesions smaller than 2 cm.

In a similar study performed by **Regini *et al.*[7],**they reported sensitivity of 96.2% and

specificity of 90.9% for lesions up to 2 cm. The sensitivity and specificity were 84.6%, and 80.0% respectively for lesions more than 2 cm in diameter.

Our work showed conventional ultrasound to yield the highest sensitivity (90%) for detecting malignant cases, whereas sono-elastogarphic scoring rendered the highest specificity (88.9%), however, the diagnostic performance of the three diagnostic modalities (conventional ultrasound, five point elastoscoring system, and the strain ratio method) revealed no statistically significant difference, because areas under the ROC curve overlapped. It was 0.846 for elasto-scoring and 0.888 for conventional ultrasound, and 0.876 for strain ratio method. Our results were comparable to those derived by **Cho and his colleagues**, where areas under ROC curves were almost the same for both conventional US and elastography (0.901 and 0.916, respectively), which was not significantly different [(5)].

Schaefer *et al.*[(12)]reported that the area under the ROC the curve was slightly higher for elastography (0.884) than for conventional US (0.820).

Zhi *et al.*[(3)]reported that the AUC for the strain ratio assessment method was 0.944, and the AUC for the five-point scoring system was 0.862. The difference in their diagnostic performance was statistically significant. **Itoh *et al.*[(2)]** reported that ROC curves for elastography and conventional US were almost the same (0.9185 and 0.9153 for elastography and conventional US, respectively), but statistical comparison was not possible because the number of lesions was insufficient.

Regarding to our results, conventional US was fairly correlated with elastoscoring (Pearson correlation coefficient=0.469). Strain ratio was moderately correlated with elastoscoring (Pearson correlation coefficient=0.658) as well as with conventional ultrasound (Pearson correlation coefficient=0.512).

When correlation was made between elastoscoring and log. strain ratio, the correlation changed from moderate to strong correlation (Pearson correlation coefficient=0.803).

Detection of the pathology of breast lesions is a major factor which influence the way of management and treatment, so depiction and anticipation of the lesional pathology is one of the most important role of diagnostic imaging [(3)].

In our study the mean elastoscoring for benign breast lesions was 3, the mean SR was 2.44, and the mean BIRADS category was 3. **Itoh *et al.*[(2)]** reported that the mean elasticity scoring for benign lesions was 2. These results are identical to that reported by **Tan *et al.*[(6)]**, where the mean elastoscoring for benign lesions was 2.

Breast fibroadenomas are the most common cause of breast lumps among women. It is considered the commonest benign solid tumor of the female breast especially in those women aged 20 to 35 years [(20)].Fibroadenoma is usually presented by elasticity score of 2, for which parts of the hypoechoic lesion did not show strain at B-mode US, indicate lesions are soft yet somewhat harder than normal breast tissue [(2)].

In our study, the mean elasto-scoring for ***fibroadenoma*** was 2.68 ~ 3, this was comparable to the results derived by **Fleury *et al.*[(20)]** where they reported that the mean elastoscore for fibroadenoma was ranging from 2.5:2.6**.** The mean strain ratio in our study was 2.45 in comparison to 1.79 reported by **Zhi and his colleagues[(3)]**. In our study, three fibroadenomas were faulty reported as malignant lesions by elastographic scoring (false positive) (and falsely upgraded their BIRADS categorization), and seven fibroadenomas misdiagnosed as malignant by SR calculation, this may be because of the great variability in fibroadenomas histological presentation, which consist of a combination of proliferation of fibrous stroma and increases in epithelial ductal structures, including fibroadenomas with exuberant stromal collagen content, fibroadenomas associated with fibrocystic changes, hyaline fibroadenomas, high-cellularity fibroadenomas, and complex fibroadenomas. The high cellularity fibroadenomas with high levels of stromal fibrosis or complex fibroadenomas tend to be harder [(20)].

Regarding other benign entities presented in our work, we reported the mean elastographic scoring for breast abscess, adenosis, and for complicated cysts as 2, and for mastopathic nodules as 3. The mean SR for breast abscess was 3, that of adenosis was 1.87, for complicated cysts was 1.68, and for mastopathic nodules was 2.15. The latter pathology showed SR value of 1.7 according to [(3)].

In our study the mean elastoscoring for malignant breast lesions was 4, the mean SR was 8.14, and the mean BI-RADS category was 4. Our results were comparable to that reported by **Itoh *et al.*[(2)],** where the mean elasticity scoring for malignant lesions was 4, while **Tan and his colleagues[(6)]**reported it as 5.

Elasticity score of DCIS is between those of benign and invasive cancers [(8)]. In our study, we had 5 pathologically proved lesions as DCIS. Two of these showed low elastoscores that falsely downgraded their BIRADS categories with resultant mean elastoscore for DCIS as 3, which is

not compatible with the pathology category. This is may be attributed to the fact that DCIS is usually softer than invasive ductal carcinoma. These results were comparable to those derived by **Thomas and co-workers**[11] where DCIS lesions were found to be softer in the subjective interpretation of the elastograms. This may be related to the fact that DCIS has different elastic modulus from other breast malignant masses. The elastic moduli of DCIS are usually less than those of IDC [8].

The mean SR for DCIS was 5.39 in our results. There were 2 cases DCIS that showed benign elastoscores (1 and 3). Conventional ultrasound BI-RADS was category 4 and warranted biopsy, in such situations, the conventional US suspicious findings, as well as the relatively high strain ratio may guard against lesion follow up, and postponing biopsy.

All the factors that would affect the stiffness of lesions and cause misleading results, e.g. calcifications and organized hemorrhage can lead to false positive results and might affect the diagnosis on UE [3].

Some of cystic lesions are hardly differentiated from solid nodules, particularly those with a thick fluid content, sometimes with fine debris in suspension, being classified as indeterminate nodules, like cysts with inflammatory content and ductal ectasia [9]. Elastography was utilized in our study for differentiating solid from complicated cystic lesions (e.g.breast abscess with highly turbid pyogenic contents), considering that the cyst elasticity is higher than the adjacent parenchyma, while solid masses that could be misinterpreted as complicated cysts (e.g.lactating adenoma) has lower strain than the surrounding breast tissue.

Additionally, this method can be useful as an adjuvant in the evaluation of complex cysts, especially in the presence of mural nodules whose elasticity can be determined e.g.intracystic papilloma versus intracystic papillary carcinoma.

Fleury and his colleagues[9]performed a study to evaluate the efficacy of elastography for diagnosing cystic lesions e.g. cysts, duct ectasia, inflammatory lesions, and cystic papillary lesions and concluded that elastography was a useful and easily applicable method for differentiating benign complicated from malignant complex cystic breast lesions.

Ultrasound elastography may be used to down grade BI-RADS categorization of breast lesions especially those with BI-RADS 3 and 4. This approach may reduce the number of false-positive results and unnecessary invasive diagnostic procedures [2]. **Schaefer and his colleagues**[12], reported that the use of elastography in addition to conventional US may downgrade some lesions categories BI-RADS 3 or 4 to BI-RADS 2.

In our study, there were five lesions that were considered to be positive by conventional ultrasound (BI-RADS4), and yielded benign elastoscore and strain ratios. Pathological studies confirmed their benignity (one abscess lesion, two cases with fibroadenomata, one lesion of focal adenosis and one postoperative scarring). Cases with these lesions could have been saved from biopsy, if elastographic results were put into consideration.

On the other hand, 4 breast lesions with BI-RADS 4 and 5 by conventional US showed benign elastogarphic results and were proved to be malignant by pathology as follows: two lesions of DCIS (E1, and BI-RADS 4), and two lesions of IDC (E3, and BI-RADS 4, and 5).

CONCLUSION

Sonoelastography is a simple, non-invasive diagnostic technique that provides information about the stiffness of a breast masses, thus completing the morphological assessment of B-mode ultrasound. Elastography can provide useful additive tool to conventional ultrasound for detecting the nature of solid breast lesions and the semi-quantitative technique of the elastography (strain ratio method) further makes the diagnosis more easy and standardized. Meanwhile, the history and the clinical data should also be taken into consideration. This combination could potentially reduce unnecessary biopsy and render better diagnostic results.

RECOMMENDATIONS

We recommend other studies to be performed on axillary lymph nodes, to evaluate the elastographic efficacy in differentiating between reactive and malignant pathologically enlarged axillary lymphadenopathy. Also other studies may be needed to depict the elastographic role in diagnosing mammographically diagnosed indeterminate microcalcifications, as the number of studies performed for these two purposes were so limited.

REFERENCES

1) **Catalano O, Nunziata A, and SianiA (2009):** The breast,in Fundamentals in Oncologic Ultrasound.Sonographic Imaging and Intervention. Springer-Verlag Italia,1st edn.:145-179.
2) **Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, Yamakawa M, and Matsumura T (2006):** Breast Disease: Clinical Application of US Elastography for Diagnosis. Radiology, 239:341-350.

3) **Zhi H, Ou B, Luo B, Feng X, Wen YL, and Yang HY (2007):** Comparison of Ultrasound Elastography, Mammography, and Sonography in the diagnosis of Solid Breast Lesions. J Ultrasound Med., 26 (6):807-815.

4) **Zhang Y, Lv Q, Yin Y, Xie M, Xiangl F, Lu1 C, Yan1 T, Wei LI1, Xul H, and Huangl Y (2009):** The value of ultrasound elastography in differential diagnosis of superficial lymph nodes. Front. Med. China, 3(3): 368-374.

5) **Cho N, Moon WK, Park JS, Cha JH, Jang M, and Seong MH (2008):**Nonpalpable Breast Masses: Evaluation by US Elastography. Korean J Radiol., 9:111-118.

6) **Tan SM, Teh HS, Mancer JF, Poh WT, Mancer JF and PohWT (2008):** Improving B mode ultrasound evaluation of breast lesions with real-time ultrasound elastography. A clinical approach. The Breast, 17(3):252-257.

7) **Regini E, Bagnera S, Tota D, Campanino P, Luparia A, BarisoneF,Durando M (2010):**Mariscotti G., and GandiniG..Role of sonoelastography in characterizing breast nodules.Preliminary experience with 120 lesions. Radiol Med., 115(4):551-62.

8) **Cho N, Moon W K, and Park J-S (2009):** Real-time US elastography in the differentiation of suspicious microcalcifications on mammography. EurRadiol., 19: 1621-1628.

9) **Fleury EF, Rinaldi JF, Piato S, Fleury JC V and Junior DR (2008):** Features of cystic breast lesions at ultrasound elastography. Radiol Bras., 41(3):167-172.

10) **Thomas A, Kummel S, Fritzsche F, Warm M, Ebert B, Hamm B, and Fischer T (2006):** Real-Time Sonoelastography Performed in Addition to B-Mode Ultrasound and Mammography: Improved Differentiation of Breast Lesions?-AcadRadiol., 13:1496-1504.

11) **Thomas A, Degenhardt F, Farrokh A, Wojcinski S, Slowinski T, and Fischer T (2010):** Significant differentiation of focal breast lesions calculation of strain ratio in breast sonoelastography.AcadRadiol., 17:558-563.

12) **Schaefer FKW, Heer I, Schaefer PJ, Mundhenke C, Osterholz S, Order BM, Hofheinz N, Hedderich J, Heller M, Jonat W and Schreer I (2011):** Breast ultrasound elastography—Results of 193 breast lesions in a prospective study with histopathologic correlation-Eur J Radiol., 77(3):450-6.

13) **Tohno E and Ueno E (2008):** Current improvements in breast ultrasound, with a special focus on elastography. Breast Cancer, 15:200204.

14) **Madjar H (2002):** Advantages and limitations of breast ultrasound. GynakolGeburtshilflicheRundsch., 42(4):185-90.

15) **Ophir J, Cespedes I, Ponnekanti H, Yazdi Y and Li X (1991):** Elastography: a quantitative method for imaging the elasticity of biological tissues. Ultrason Imaging, 13 (2): 111-134.

16) **Scaperrotta G, Ferranti C, Costa C, Mariani L, Marchesini M, Suman L,Folini C and Bergonzi S (2008):**Role of sonoelastography in non-palpable breast lesions. Eur Radiol.,18 (11):2831-2839.

17) **Leong LC, Sim LS, and Lee YS (2010):** A prospective study to compare the diagnostic performance of breast elastography versus conventional breast ultrasound. ClinRadiol., 65(11):887-94.

18) **Raza S, Odulate A, Ong EM, Chikarmane S, and Harston CW (2010):** Using real-time tissue elastography for breast lesion evaluation: our initial experience. J Ultrasound Med., 29(4):551-63.

19) **Kumm TR, and Szabunio M (2010):** Elastography for the Characterization of Breast Lesions: Initial Clinical Experience Cancer Control, 17(3): 156-161.

20) **Fleury EF, Rinaldi CJ, Piato S, Fleury JCV, and Junior DR (2009):** Appearance of breast masses on sonoelastography with special focus on the diagnosis of fibroadenomas. EurRadiol., 19: 1337-1346.