Diagnoses of breast masses with ultrasonography and elastography: A comparative study

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ABSTRACT

Context: Non-invasive diagnoses of breast masses remain a challenge to the clinician. Elastography, a new modality using elastic property of breast tissue can effectively differentiate between malignant and benign breast masses minimizing the need for aggressive unnecessary biopsy. Aim: The aim is to evaluate elastography to ascertain whether the differentiation and characterization of benign and malignant breast lumps could be done with it, comparing with the conventional sonography. Settings and Design: Single institutional prospective study. Materials and Methods: The study was conducted on 82 patients with palpable breast lumps. All these cases were subjected to a thorough clinical examination, sonography, elastography, and pathological diagnosis. Results of sonography and elastography were compared considering the pathological diagnosis as standard. Statistical Analysis: Statistical analysis was performed with the McNemar test. All data analysis was conducted using SPSS software (SPSS Inc.). Results: It was observed that the USG diagnosis of carcinoma tallied with the pathological diagnosis in only 88.9% of cases (i.e. 48 out of 54 cases) and the elastographic diagnosis of carcinoma tallied with the pathological diagnosis in 96.3% (i.e. 52 out of 54). On the other hand, out of 34 and 30 cases diagnosed as benign lesions on USG and elastography, respectively, only 28 cases were proved to be benign pathologically. Conclusion: Elastography was found to be more sensitive, specific, and accurate than sonography.

Key words: Breast lump, elastography, ultrasonography

INTRODUCTION

Breast cancer is the most common malignancy in women and the second-most common cause of cancer-related mortality.[1] Recent research on service screening programs suggests that participation in modern, organized service screening may well reduce the risk of death caused by breast cancer by 40% or more.[2] That is, early, sensitive and accurate diagnosis represents a better prognosis.

Non-invasive diagnosis of breast cancer remains a challenging task to the clinician. Mammography and sonography are currently the most sensitive modalities for detecting breast cancer. This is especially valuable for countries where women have relatively small, dense breasts,[3] which is one of the various factors leading to false-negative findings on mammography.[4] In practice, sonography is chosen as the primary workup tool in young age women. However, the sonographic features for benign and malignant lesions have been shown to over-ride each other substantially.[5,6]

Because of various limitations of mammography and sonography and the great desire not to miss a malignant lesion in the early stage of disease lead to aggressive biopsy, but only 10%-30% biopsy results are found to be malignant.[7,8] This means that 70%-90% of breast biopsies are performed for benign diseases leading to unnecessary patient anxiety in addition to increasing burden of costs to the patient. Therefore, it clearly denotes to a great need for the development of additional reliable methods in order to complement the existing diagnostic procedures to avoid unnecessary biopsy.
In the early 1990s, a technique called elastography was described by Ophir et al.[9] Elastography is a procedure of diagnostic imaging, similar to the ultrasound imaging, which helps doctors distinguish between malignant tumors and normal body tissue. Since 1990s, elastography has been utilized to detect the presence of cancerous tumors in breast tissue and elsewhere in the body on an outpatient basis within a short period of time.

Elastography is effective because it can clearly distinguish between elastic tissue and stiff cancerous lumps. Itoh et al.[10] first used the US elastography for the detection of breast lesions and a 5-point scoring system was proposed. When imaging scans reveal darker, harder spots among a lighter, flexible background, it is most likely to indicate a tumor. Images can usually be viewed in real-time on a computer monitor. Advances in the ultrasonic technology are making it possible for doctors to make confident diagnoses without the need for invasive tissue biopsies. The goal of this study was to evaluate whether the new method of ultrasound elastography could improve the differentiation and characterization of benign and malignant breast lesions in comparison with the conventional sonography.

**MATERIALS AND METHODS**

This prospective study was conducted on 82 patients with palpable breast lumps, who were admitted in the female surgical wards and came to out patient department between Nov 2008 and May 2011. The study was approved by the Ethics Committee of the Hospital and informed consent was taken from each patient. Patients under 15 years of age or with present or past history of radiotherapy or chemotherapy were excluded from the study.

All these cases were subjected to a thorough clinical examination besides sonography, elastography, and pathological diagnosis. The resected tissues in patients undergoing surgery were sent for histopathological examination for the confirmation of the diagnosis.

**Conventional USG of the breast lump**

Conventional US (ultrasonography) images of the breast were, primarily, taken and in the course of this conventional examination, obtaining B-mode images were given priority. Subsequently, in order to evaluate the vascularity of the mass, which was one of the BI-RADS criteria for US, color Doppler US was performed in the patients with breast lumps. Lesion size was defined as the diameter of the hypoechoic lesion at B-mode US.

Images were assigned to one of five categories according to the BI-RADS criteria for US: category 1, negative findings; category 2, benign findings; category 3, probably benign findings; category 4, findings suspicious for malignancy; and category 5, findings highly suggestive of malignancy [Figures 1-4].

**Elastography of the breast lump**

Next stage was to obtain elasticity images as motion images on the same day. It was performed on the patient in supine position, and with the stabilizer-equipped probe oriented perpendicular to the chest wall. The probe was applied to the breast and was moved slightly inferior and superior, and normal breast tissue was included to obtain the elasticity images. The probe was applied with just a light pressure in order to obtain the images, which were appropriate for analysis and a higher level of pressure was simply passed up.

Before and after soft compression of tissues, an image was taken in which color coding was used to evaluate deformation. Moderate vertical compressions were applied with the probe, three to five times, over the lump and elasticity images were displayed on a computer monitor. The lump was compressed manually.

**Color coding**

Red
Tissues with greatest strain (softest component).
Diagnoses of breast masses with ultrasonography and elastography

Akhtar, et al.: Blue
Tissues with no strain (hardest component).

Green
Tissues with average strain.

The color pattern of images were evaluated for classification of elasticity images both in the hypoechoic lesion [i.e. the area that was hypoechoic or isoechoic relative to the subcutaneous fat (except for echogenic halo) on B-mode images] and in the surrounding breast tissue. Each image was assigned an elasticity score on a five-point scale based on overall pattern.

A score of 1 indicates even strain for the entire hypoechoic lesion (i.e., the entire lesion was evenly shaded in green).

A score of 2 indicates strain in most of the hypoechoic lesion with some areas of no strain (i.e. the hypoechoic lesion had a mosaic pattern of green and blue).

A score of 3 indicates strain at the periphery of the hypoechoic lesion, with sparing of the center of the lesion (i.e., the peripheral part of lesion was green, and the central part was blue).

A score of 4 indicates no strain in the entire hypoechoic lesion (i.e. the entire lesion was blue, but its surrounding area was not included) [Figures 5-7].

A score of 5 indicates no strain in the entire hypoechoic lesion or in the surrounding area (i.e., both the entire hypoechoic lesion and its surrounding area were blue).

Pathological examination
Final diagnosis was made by pathological analysis of breast lump samples obtained with fine-needle aspiration cytology, needle biopsy, excision biopsy, or radical surgery.

Statistical methods
Statistical analysis was performed with the McNemar test. P < 0.05 was considered statistically significant. All data analysis was conducted using SPSS software (SPSS Inc.).

RESULTS
The study was performed on 82 patients with palpable breast lumps. Following results were obtained.

Age distribution
It was observed that the maximum numbers of cases of palpable breast lumps were seen in the fourth decade of life (40.2%) [Table 1]. It was also noted that maximum cases of malignant lesions were seen in the fourth decade of life, while majority of benign lesions were seen in the third decade of life [Table 2].

Side distribution
The number of incidents of the right-side breast lesions was 46 (56.1%), higher than the left-side breast lesions, which was 36 (43.9%) [Table 3].

Sonographic diagnosis of palpable breast lumps
Based on USG diagnosis, the incidence of malignant and benign lesions was 58.5%, and 41.5%, respectively. A diagnosis of fibroadenoma was made in 26 cases, phylloid tumor in four cases and fibroadenosis in four cases [Table 4]. Using statistical classifications, sensitivity, specificity, accuracy, and positive predictive value of sonography for the diagnosis of malignant lesions were found to be 77.8%, 70.0%, 75.7% and 87.5% respectively.

Elastographic diagnosis of palpable breast lumps
Based on elastographic diagnosis, the incidence of malignant and benign lesion was found 63.4% and 36.6%, respectively. Of 52 malignant lesions, 45 (86.5%) lesions had a score of 4 or 5 [Table 5]. All of the lesions in this group had a score of >3.0. Of the 30 benign lesions, 28 (93.3%) lesions had a score of >3.0.
of 1 or 2. All the lesions in this group had a score of <3.0. The mean elasticity score was significantly higher for malignant lesions (4.1 ± 1.0) than for benign lesions (1.9 ± 1.0) ($P < 0.001$).

Using statistical classifications, sensitivity, specificity, accuracy, and positive predictive value of elastography for the diagnosis of malignant lesions were 96.3%, 85.7%, 92.7%, and 92.9%, respectively.

**Correlation of sonographic diagnosis with elastographic diagnosis**

It was observed that the USG diagnosis of carcinoma tallied with the pathological diagnosis [Table 7] in only 88.9% of cases (i.e. 48 out of 54 cases, [Table 8]) and the elastographic diagnosis of carcinoma tallied with the pathological diagnosis in 96.3% (i.e. 52 out of 54, [Table 9]). On the other hand in 34 and 30 cases which were diagnosed as benign lesions on USG and elastography, respectively, only 28 cases were proved to be benign pathologically [Tables 6]. On statistical analysis elastography was found to be more sensitive and specific ($P < 0.05$).

**DISCUSSION**

Diagnosis of breast cancer with imaging modalities remains one of the major concerns. Currently, the use of...
mammography, ultrasound, and finally, the pathological diagnosis has markedly increased the accuracy of pre-operative diagnosis of breast diseases. A large number of aggressive biopsies for benign lesions is carried out that result in anxiety, discomfort, risk of infection, and burden of cost. In order to overcome these problems, a new procedure, called elastography, has come into existence. This procedure is based on displacement of breast tissue produced after tissue compression. This displacement (strain) is more in the softer tissue than in the harder one.[10]

In this series, we have compared the results of ultrasonography and elastography in the diagnosis of breast lumps. Our results suggest that elastography has more sensitive, specific and accurate means of differentiating benign and malignant breast lesions than sonography. True positive, True negative, False positive and False negative values for USG and elastography for the diagnoses of malignant lesion has been shown and Mc Nemar test has been applied for analysis [Tables 10-12].

In the present study [Table 13], it has been observed that the specificity of USG for the diagnosis of malignant lumps is 70.0%, sensitivity is 77.8% and accuracy is 75.7%. The results of this study are contrary to those of Guyer et al.,[11] who reports a sensitivity of 91.2% and a specificity of 97.2%. Leucht et al.,[12] reports about an accuracy rate of 91% for carcinomas and 74% for benign lesions.

The accuracy rate of USG for diagnosis of fibroadenosis is 100% which favorably compares with the observations of Kobayashi et al.,[13] who also reports a similar result.

**Diagnostic accuracy of elastography for malignant lesions**

Table 9 shows that elastography is able to diagnose 52 cases out of 54 pathologically proven carcinoma. In the present study, it has been observed that specificity of elastography for the diagnosis of malignant lesion is 85.7%, sensitivity is 96.3% and accuracy is 92.7% [Table 13]. The results of this study correspond well with those of Itoh et al.,[10] who reports about a sensitivity of 89.3% and specificity of 93.1%. They conclude that elastography has higher sensitivity than conventional US (P < 0.05). By using equivalence bands for noninferiority or equivalence, it is shown that the specificity of elastography is not inferior to that of conventional US and that the accuracy of elastography is equivalent to that of conventional US.

Thomas et al.,[14] evaluates the use of elastography in 108 patients and finds that specificity is improved from 78% for conventional sonography to 91.5% for US elastography.

Zhi H et al.,[15] had conducted their study in which ultrasound elastography was superimposed on conventional sonography. When they combined the two modalities together, they got the best results for detection of breast cancer. The sensitivity, specificity, accuracy, and positive
predictive value had improved to 89.7%, 95.7%, 93.9%, and 89.7%, respectively.

Llewelyn Simi et al.,[16] had conducted their study at Singapore general hospital in 99 women. They found that elastography detected all malignant lesions in the study compared with 88.5% by routine ultrasound.

### Diagnostic accuracy of elastography for benign lesions

In the present study, it has been observed that elastography is able to diagnose 30 cases as benign, of which 28 have been proven pathologically and misdiagnosed two cases as benign, which are pathologically malignant. Among 28 benign lesions, 20 (71.4%) have been proved pathologically fibroadenoma, four phyllloid and four fibroadenosis.

The results are not compared well with the study of Fleury EF et al.,[17] to show and correlate the imaging features of breast masses, especially fibroadenomas, using sonoeLASTography. Two hundred and thirty-five patients with 302 breast lesions, participated in the study, were referred for core needle biopsy. All lesions appearing as solid masses on conventional US were included. They found that out of the included lesions (270), 115 (42.6%) corresponded to histologically confirmed fibroadenomas and 155 (57.4%) to lesions with histologically confirmed diagnoses other than fibroadenomas.

In our study, for assessing breast lesions, the sensitivity and specificity of elastography is found to be more than USG ($P < 0.05$). This compares well with the results of Itoh et al., who concludes that, for assessing breast lesions, US elastography with the proposed imaging classification, which was simple compared with that of the Breast Imaging Recording and Data System (BI RADS) classification, had almost the same diagnostic performance as conventional US. They evaluated the diagnostic performance of real-time free-hand elastography by using the extended combined autocorrelation method (CAM) to differentiate benign from malignant breast lesions, with pathologic diagnosis as the reference standard. Conventional ultrasonography (US) and real-time US elastography with CAM were performed in 111 women (mean age, 49.4 years; age range, 27–91 years) who had breast lesions (59 benign, 52 malignant). Elasticity images were assigned an elasticity score according to the degree and distribution of strain induced by light compression. The area under the curve and cutoff point, both of which were obtained by using a receiver operating characteristic curve analysis, were used to assess diagnostic performance. Mean scores were examined by using a Student 't' test. Sensitivity, specificity, and accuracy were compared by using the standard proportion difference test or the $\Delta$-equivalent test.

In this study, the mean elasticity score is significantly higher for malignant lesions ($4.1 \pm 1.0$) than for benign lesions ($1.9 \pm 1.0$). This compares well with the study of Itoh et al., who finds that, for elasticity score, the mean ± standard deviation is $4.2 \pm 0.9$ for malignant lesions and $2.1 \pm 1.0$ for benign lesions ($P < 0.001$).

Krouskop et al.,[18] finds that various breast tissues differ in elastic stiffness. They show fatty tissue of the breast having the highest elasticity, followed by normal glandular breast tissue, fibrous tissue in the breast, noninvasive carcinoma, and invasive carcinoma in that order.

Itoh A et al., in their study conclude that the mean elasticity scores for fibroadenoma and ANDI are lower than those for carcinomas and that for scirrhous carcinoma is significantly higher than that for Ductal carcinoma in situ. Their findings correspond with experimental results for elastic moduli measured by Krouskop TA et al.[18]

One of the limitations of elastography is the overlap of the elasticity score between benign and malignant breast lesions.[19] In this study, two of 54 malignant lesions are missed by Elastography. Elastography gives false negative results in early stages of invasive ductal carcinoma, noninvasive carcinoma, and some invasive soft tissue carcinomas. Invasive soft tissue carcinoma, such as cystosarcoma phylloides having large central necrosis always, shows false negative findings on elastography impairing diagnostic assessment.[5,14] Due to decline in estrogen levels with aging, certain physiological changes occurs in the breast. A low level of estrogen leads to dryness of skin, thus, decreasing its elasticity.

By using off-line assessment, several researchers have performed free-hand US elastography in patients with breast lumps. They have compared the traced outlines of tumors on B-mode images with those on

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<th>Table 12: Comparison of elastography and USG for the diagnoses of malignant breast lump</th>
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USG: Ultrasonography, $P <0.05$

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<th>Table 13: Comparison of sensitivity, specificity, accuracy and PPV of USG and elastography</th>
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USG: Ultrasonography, PPV: Positive predictive value
In the clinical setting, grayscale US elastography uses the motor driven compression plates for imaging breast lesions keeping the patients in seated position.\textsuperscript{[23]}

During screening a lesion using US elastography, there are many things to be kept in mind. First, the area occupied in the region of interest of the target lesion should be less than one-third. The echo signals are captured on an external computer monitor and are used for calculation of tissue strain with the combined auto autocorrelation method.\textsuperscript{[22]} Region of interest should consist of both tissue types for the comparison of elasticity of the target lesion with that of normal breast tissue.\textsuperscript{[24]} Secondly, light pressure should be applied over the lesion with the probe manually. Applied pressure neither should be too high nor too low.

Since the invention of elastography, this concept has been utilized for elasticity imaging of a wide range of different applications including prostate,\textsuperscript{[25]} thyroid,\textsuperscript{[26]} and intravascular ultrasound.\textsuperscript{[27]}

Beside own limitations of elastography, we recognize some limitations of our study. These include the fact that the sample size is relatively small, and patients with present or past history of radiotherapy or chemotherapy are excluded from the study. Patients who had history of radiotherapy or chemotherapy did not undergo elastography or US which could have resulted in relatively fewer malignant masses in our study.

**CONCLUSIONS**

It was concluded that US elastography to be more sensitive, specific, and accurate than conventional ultrasonography. Using elastography, a more accurate preoperative diagnosis can be made, thereby, obviating the need for aggressive biopsy in cases of benign lesions.

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