Role of Sonoelastography in the Differentiation between Benign and Malignant Breast Lesions

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ABSTRACT

Purpose: To prospectively evaluate the accuracy of real time elastography (ultrasound strain imaging) for distinguishing between benign and malignant solid breast lesions with the pathologic results as the reference standard. We also evaluated if the fat/lesion ratio could semi-quantitatively evaluate the stiffness of breast lesions.

Patients and Methods: Conventional ultrasonography (US) and real time elastography were performed in 100 women with breast masses with the mean age is 50 years. Elasticity images were given an elasticity score according to the degree and distribution of the strain induced by light compression with 1-3 is benign and 4-5 is malignant. We also calculated the ratio of the normal breast tissue to that of the lesion (fat/lesion ratio) of the different breast lesions with the fat as the reference. The cutoff point was 4.8 with ratio below this level is considered benign and above this level is considered malignant.

Results: For elasticity score, the mean standard deviation was 4.1 for malignant lesions and 2.1 for benign lesions ($p<.001$). When a cutoff point between 3 and 4 was used, elastography had 87.2% sensitivity, 90.6% specificity and 90% accuracy. The fat/lesion ratio (F/L ratio) of the benign lesions was different from that of the malignant ones.

Conclusion: US strain imaging can facilitate improved classification of benign and malignant breast masses and has the potential to aid their diagnosis. By using the F/L ratio, the stiffness of breast lesions could be semi-quantitated and this method may provide another diagnostic method in addition to the scoring system.

Key Words: Breast – Sonoelastography – Strain imaging – Fat-lesion ratio.

INTRODUCTION

Breast cancer remains the most common cancer in women worldwide [1].

Percutaneous image-guided core biopsy has been shown to be an economical and accurate alternative to the surgical biopsy of suspicious breast lesions [2-4].

However, there are disadvantages and complications for ultrasound guided core biopsy. Masses smaller than 5mm are problematic, as biopsy can obscure or remove the lesion making subsequent localization difficult [5]. Radiologists are often reluctant to perform biopsy in patients with breast implants because of concern about rupturing the implant. Inadequate sample with repeating the biopsy is another disadvantage [6]. Contraindications common to all percutaneous large-core needle procedures include allergy to local anesthetics and a history of bleeding diathesis [7]. Major complications are unusual, with infection or hematoma in approximately 0.2% of patients. Minor complications, occurring in up to 50% of patients; include bruising, breast tenderness, and psychological stress [8]. In addition, breast biopsy yields a benign result in more than 75% of patients, making it the most costly per capita component of a breast cancer screening program [9].

A decade ago, physicians found that the imaging features on (US) images could be used to classify benign and malignant solid breast masses and thus decrease the numbers of biopsies performed [10]. The successes of these investigators, however, have been neither reliably confirmed nor widely applied [11].

For these reasons, an experimental ultrasound technique (elastography) has been developed to determine instantly whether a woman has cancer or not without doing a biopsy. Elastography could save thousands of women from...
the waiting, cost, discomfort and anxiety of a biopsy [12].

This technique exploits the theory that benign and malignant breast lesions have inherent differences in firmness [13]. This property serves as the basis for some examinations, such as palpation, that are currently being used in the clinical assessment of breast abnormalities [14]. US strain images are produced by comparing the US echo data obtained prior to and after slight axial compression of the breast [15]. Strain images display the relative stiffness of lesions by compression compared with the stiffness of surrounding tissue. Stiffer areas deform less easily than do their surroundings and are depicted as dark on strain images, whereas softer areas deform more easily than do their surroundings and are depicted as light. Malignant masses typically appear dark and have higher contrast with background breast tissue during deformation [16]. Benign masses typically appear light and have lower contrast with background breast tissue during deformation [17]. In addition, malignant lesions tend to be larger on US strain images than on corresponding B-mode US images, perhaps because of the desmoplastic reaction commonly associated with malignancy [18].

A novel motion-tracking algorithm has been developed and implemented on a clinical US system [19]. Phase-sensitive (I-Q) echo data are processed internally in real time on this system to estimate displacement and strain. The system displays B-mode and strain images side by side on the normal system display at about seven frames per second. A region of interest (ROI) is displayed in the B-mode image, and displacement and strain are estimated for tissue within that ROI [20]. When scanning, the normal freeze and cine capabilities of the system are available. When a sequence of data is acquired and stored (frozen), online post processing capabilities allow the ROI location and size to be modified, and other common tools such as modifying the gray-scale mapping are available [21]. Using the strain ratio measurement (F/L ratio), stiffness of breast lesions could be semi-quantitated with the fat of breast tissue as the reference [22].

**PATIENTS AND METHODS**

Female patients with newly discovered breast masses, without previous surgery or treatment, were studied at the National Cancer Institute, Cairo University between April 2008 and February 2009.

**Patient population:**

One hundred patients with a mean age of 50 years (age range 25-70 years) were included in our study. Histopathologic results of percutaneous or excisional biopsy or radical surgery were considered as the reference standard. We excluded patients without pathology. Purely cystic lesions were also excluded from the study.

Ultrasound examination of the breast lesions:

**A- Equipment:**

Conventional US was performed by using a digital electronic scanner with a frequency of 7.5-13 MHz (EUB-7500; Hitachi Medical Corporation, Tokyo, Japan). All elasticity images were obtained with a system that consisted of a digital US scanner that was remodeled exclusively for this study. The elasticity software includes a scale for pressure monitoring. Optimally; the pressure should not be more than 3 on the scale.

**B- Conventional US imaging technique:**

The orientation (transverse or longitudinal) that best depicted the lesion was chosen for display on the B-mode image. The lesion size was also measured.

**C- US strain imaging technique:**

The elasticity images obtained with the probe were moved slightly inferior and superior. Importantly, to obtain images that were appropriate for analysis, we applied the probe with only light constant pressure which does not exceed 3 on the scale. We avoided using higher levels of pressure as the pattern of the elasticity image started to change drastically as the pressure increased.

In the machine we used, elastography acquisition should be considered correct when the value of the reference LEDs on the monitor is constant and with a value of at least 2 or 3 color homogeneity through all the scanning area surrounding the lesion. This indicates a good technical approach.

Multiple frames of elasticity images were acquired, and many elasticity images were generated by comparing two adjacent frames

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during compression and relaxation by continuously moving the probe. In addition, the process of detecting strain was equivalent to the compensation of the displacement. Consequently, elasticity images were produced by comparing an almost identical area on the two images (Fig. 1).

The echo signals acquired by using the US scanner were captured by the external computer and were used to calculate the tissue strain.

The strain distribution was then reconstructed as an elasticity image and was displayed on the computer monitor. The scale of the elasticity images ranged from red for components with greatest strain (i.e., softest components) to blue for those with no strain (i.e., hardest components). Green indicated average strain in the ROI. Color images were constructed automatically with the same image processing settings throughout the study.

B-mode and strain images were displayed in a side-by-side format within the individual frames that were contained within a cine-loop sequence of approximately 100 frames.

The radiological results were compared to the pathological results.

After obtaining the strain image, we used the strain ratio (fat/lesion ratio) measurement method, which the US machine was equipped with, to measure the strain ratio of the lesion and breast tissue, which reflected the lesion stiffness. We first contoured the target lesion as A, then selected the breast tissue as B, and obtained the strain ratio of B/A as the strain index, which reflected the lesion stiffness. In our study, we used the fat as a reference. The fat/lesion ratio is obtained by dividing the strain of the fatty tissue by that of the tumor. The cutoff = 4.8. The measurement of fat/lesion ratio adds only 2-5 minutes to the time of the examination.

Statistical analysis:

We first compared malignant and benign lesions by (a) comparing the mean elasticity scores for real-time US elasticity images between malignant and benign lesions to determine the score for differentiating between these lesions and (b) comparing the elasticity scores between the three groups within each lesion size category (i.e., 4-10mm, 11-20mm, and 21-30mm) to assess the usefulness of this modality for various lesion sizes. All comparisons were made by using the Student $t$-test. For the indices that did not show a statistically significant difference, we examined equivalence or noninferiority by using the $\Delta$ equivalent test. All

Fig. (1): Images present general appearance of lesions for elasticity scores of (a) 1, (b) 2, (c) 3, (d) 4, and (e) 5. Black circle indicates outline of hypoechoic lesion (i.e., border between lesion and surrounding breast tissue) on B-mode images [18].
statistical tests were performed by using commercially available software (Stat Mate 2000, version 3.01, ATMS, Tokyo, Japan and PASS 2002, NCSS, Kaysville, Utah). For all tests, a \( p \)-value of less than 0.05 was considered to indicate a statistically significant difference.

**RESULTS**

All breast cancers were diagnosed histologically by means of radical surgery, excisional biopsy or needle biopsy.

The mean elasticity score was significantly higher for malignant lesions (4.1) than for benign lesions (2.1) \( (p<0.001) \).

In our study, 47 cases were malignant and 53 cases were benign. The malignant cases included different pathological types as invasive ductal carcinoma, non scirrhous, scirrhous and mucinous carcinomas and ductal carcinoma in situ. The benign pathological types were fibroadenomas, intraductal papilloma and benign phylloides tumors.

The distributions of elasticity scores for the 47 malignant lesions (shown in Table 1) were 22 cases (46.8%) having a score of 5, 17 cases (36.2%) having a score of 4, 5 cases (10.6%) with a score of 3 and 3 cases (6.4%) with a score of 2. None of the lesions in this group had a score of 1.

The distributions of elasticity scores for the 53 benign lesions (shown in Table 2) were 19 cases (35.9%) having a score of 1, 17 cases (32.1%) having a score of 2, 12 cases (22.6%) with a score of 3 and 4 cases (7.5%) had a score of 4 and 1 case (1.9%) with a score of 5.

One (4.3%) of the 23 lesions with a score of 5 and four (19%) of the 21 lesions with a score of 4 were benign. Two (11.8%) of 17 lesions with a score of 3 and four (20%) of 20 lesions with a score of 2 were malignant.

The mean elasticity scores according to lesion size on B-mode images are shown in Table (3). For each lesion size category, the mean score was significantly higher for malignant lesions than for benign lesions \( (p<0.001) \).

The diagnostic performance of elastography at various cutoff points is shown in Table (4). For elastography, sensitivity (87.2%), specificity (90.6%), and accuracy (90%) are shown, with the best cutoff point between elasticity scores of 3 and 4.

The cutoff point for the fat/lesion ratio was 4.8. Below this level is considered benign and above this level is considered malignant. The differences of the strain indexes of benign and malignant lesions were statistically significant \( (p<0.001) \). The ratio of 5 benign lesions was higher than 4.8, which was the minimum index of the malignant lesions. Of the 5 lesions, 2 lesions had calcifications which could explain the high index.
Fig. (2): Invasive duct carcinoma in a 50-year old patient. The right image shows the conventional B-mode appearance of the lesion. The left image is the elasticity image of the lesion with score of 4; the entire lesion is blue (no strain in the entire lesion). Note the scale on the right lower corner of the elasticity image which measures the strength of the pressure. For the pressure to be optimal, the reading should not be more than 3.

Fig. (3): Fibroadenoma in a 33 year-old-patient. Right: Conventional B-mode image. Left: On elasticity image, the lesion shows mosaic pattern of green and blue; score 2. The strain index (F/L ratio) of the lesion was 3.28.

Fig. (4): Non scirrhous carcinoma in a 45-year old patient. The right image is the conventional B-mode image. On elasticity image (the left one), the entire lesion was blue which indicates score 4. The F/L ratio of the lesion was 35.14.

Fig. (5): Fibroadenoma in a 40-year old patient. The left image shows the elasticity picture of the lesion, the hypoechoic lesion shows mosaic pattern of green and blue; score 2. The strain index of the lesion was 2.51.
DISCUSSION

Elastography is found to be useful for differentiation between malignant and benign lesions [16,21]. Investigators have reported that elastography allowed differentiation of cancers from fibroadenomas, and that the width of the cancers was greater on elasticity images than on B mode images [18]. Our results correspond with theirs.

Although all the studies done on elastography are not yet able to precisely quantify elasticity, they have arrived at a point where semi quantitative assessment in the clinical setting is possible. Our finding of a significant difference between mean elasticity scores for malignant and benign lesions in patients suggests that elastography may be useful in diagnosing breast lesions in the clinical setting. Although the study done by Itoh et al. [18], tried to characterize the distribution of elasticity scores according to the histologic type of the malignant lesions, as ductal carcinoma in situ and invasive duct carcinoma, and to that of benign lesions, as fibroadenomas and papilloma; we did not do so in our study as we believe that once malignant lesion is suspected, surgery will be done and once benign lesion is highly suggested, follow-up is advised whatever the subtype of the lesion.

Our findings were similar to that of Itoh et al. [18] that an elasticity score of 5 indicates infiltration of cancer cells into the interstitial tissues (e.g., in scirrhous carcinomas) or into an intraductal component (e.g., in DCIS), both of which are characteristics of carcinoma. An elasticity score of 4 seems to be characteristic of tumors such as solid tubular carcinomas that are circumscribed and homogeneously harder than the adjacent normal breast tissue. Elasticity score of 3 was mainly found in benign lesions. We recommend that all lesions with elasticity scores of 3 or higher be examined by means of aspiration cytology or needle biopsy. Elasticity scores of 2 indicate lesions that are soft yet somewhat harder than normal breast tissue. False negative results were found in 3 patients with malignant lesion but showed score 2. This could be due to lack of enough experience in this newly practiced technique.

We believe that an elasticity score of 1 indicates that lesions have almost the same compressibility as the surrounding breast tissue. In our study, no malignant lesions had a score of 1. Although our findings will require confirmation, this result suggests that invasive diagnostic procedures, such as histologic examination, may be omitted for patients who have lesions with a score of 1.

In the study done by Itoh et al. [18], it was found that all of the invasive ductal carcinomas with a score of 2 were classified as BI-RADS category 4 or 5, a finding that supports the combined use of elastography and conventional US to avoid misdiagnosing an invasive carcinoma as a benign lesion. They also found that when radiologists integrate US strain imaging features with conventional US characteristics, the differentiation of malignant and benign solid breast masses improves. Therefore, strain imaging has the potential to improve the decision of whether to perform breast biopsy.

Although most images clearly resemble one of the five distinct patterns used for classification, the selection is currently made by the examiner and is not yet automated.
There is an overlap of elasticity between the benign and malignant lesions in the breast that could interfere with UE diagnosis. In our study, 5 benign lesions were stiffer than the minimum stiffness indexes of the malignant lesions. Two lesions had calcification, which changed the stiffness of the lesions and interfered with the results of UE.

In a study done by Martegani et al. [23], the sensitivity and specificity were 97.7% and 86.4% respectively considering 3-5 score as a cutoff value.

Conclusion:
Elastography can complement conventional US and make it easier to diagnose breast lesions. Elastography is promising, and we expect that with future improvements in the technology (e.g., approaches for quantitative assessment), this imaging modality will become an invaluable tool for the diagnosis of breast diseases in the clinical setting.

We also found that the fat lesion ratio could semi-quantitatively reflect the stiffness of solid lesions in the breasts. Although limited by the current sample size, we were not able to elicit the standard criteria in distinguishing either benign or malignant lesions precisely for clinical use; we believe this method could be a more objective predictor than the 5-point scoring method for determining breast malignancy with UE.

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