Use of Ultrasound Elastography in Characterization of Solid Breast Lesions

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Abstract

Purpose: To study the role of strain ultrasound elastography in diagnosis of solid breast lesions, and evaluate its capability in differentiating benign from malignant lesions, in comparison to histopathological diagnosis taken as the reference standard.

Patients and Methods: A total of eligible 28 female patients with solid breast masses, were subjected in our prospective study; sampled in a simple random manner. All patients underwent history taking, physical examination, conventional B-mode ultrasound examination which was evaluated according to the BIRADS (Breast Imaging Reporting and Data System) categories, and then subjected to ultrasound Elastography (Smart detect; S-detect and Elastoscan) in the same session which were evaluated according to Tsukuba elasticity score and the Strain Ratio (SR) method. All patients with breast lesions were biopsied by US guided interventional procedures using true cut needle biopsy or Fine Needle Aspiration Cytology (FNAC) or undergo surgical biopsy. Data from elasticity scoring and the strain ratios were compared with the histopathological diagnoses.

Results: It was found that conventional B-mode ultrasound examination and the Tsukuba color scoring system had the same sensitivity of 80%, specificity of 94.4% and accuracy of 89.3%. While, S-detect turned out to have sensitivity of 80%, specificity of 83.3% and accuracy of 82.1%. The addition of strain ratio parameter for evaluating the elastography images showed the highest sensitivity, specificity and accuracy (90%, 94.4% and 92.8% respectively) in differentiating benign from malignant breast lesions with the best SR cutoff point of 2.

Conclusion: Ultrasound elastography of the breast masses is a non invasive and easy procedure with high diagnostic performance which can be easily integrated with the B-mode ultrasound examination in the same session and improves its specificity in differentiation between benign and malignant breast lesions, also it has proven benefit in minimizing the number of unnecessary biopsies.

Key Words: Benign breast mass – Malignant breast mass – Ultrasound elastography – S-Detect – Elastoscan – Strain ratio.

Introduction

ULTRASOUND elastography is the most striking of the new technologies in recent diagnostic ultrasound systems. Cancer tissue is stiffer than normal breast tissue, and it is believed that the stiffening process begins in the early stage of cancer [1].

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 [2].

The principle of US elastography is that tissue compression produces strain (displacement) within the tissue and that the strain is smaller in harder tissue than in softer tissue. Therefore, by measuring the tissue strain induced by compression, we can estimate tissue hardness, which may be useful in diagnosing breast cancer [3].

The elastography strain images were scored according to the elasticity score in to five categories [4]. 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 elastogram [5].

Elastography has been used clinically to examine a variety of breast lesions in patients, and it has been concluded that this modality allows radiologists to accurately distinguish benign from malignant breast lesions and it could significantly reduce the number of breast biopsies required [6].
Elastography was found to be superior to B-mode US in evaluating BI-RADS 3 (Breast Imaging Reporting and Data System) benign lesions [7]. Prevention of unnecessary histopathological 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 BI-RADS 2. This may support the compliance of women, and also reduces costs in the health care system [8]. Elastography is a potentially attractive new technique for measuring the elastic properties of tissues [9].

The objective of this study was to study the role of strain ultrasound elastography in diagnosis of solid breast lesions, and evaluate its capability in differentiating benign from malignant lesions, in comparison to histopathological diagnosis taken as the reference standard.

Patients and Methods

This prospective study enrolled 28 female with solid breast lesions (age range 20-70 years, with a mean age of 41.5 years). They were sampled in a simple random manner, and referred from Surgery Department, Suez Canal University Hospital. Breast ultrasound and US elastography were performed in the Ultrasound and Doppler Unit, Diagnostic Radiology Department, Suez Canal University Hospital over a period from June to November 2015.

The inclusion criteria included all patients with positive breast ultrasound for presence of solid breast mass, while exclusion criteria involved patients with breast implants, superficial mass (<5mm deep to the skin surface), cutaneous lesions, and purely cystic lesions on conventional US.

All patients were subjected to clinical examination, breast lesion biopsy and histopathological diagnosis, B-mode US examination, and US Elastography (S-Detect and Elastoscan), comparison of conventional US and US elastography data with histopathological results, as the following:

I- Clinical examinations:

- Full history taking including clinical presentation and complaint (mass, nipple discharge, breast enlargement, pain and follow-up after surgical procedure), age, family history and past history.

- Physical examination by both the clinician and the radiologist.

II- Imaging study:

All patients had a conventional B-mode ultrasound examination and ultrasound elastography.

Equipment:

The study was performed using a digital ultrasound scanner (RS80A Samsung Medison Co., Ltd, Seoul, Korea) with real time tissue Elastography Unit, S-Detect software and volume linear transducer L3-12A gives Multi-dimensional volume data.

Position:

After palpation of both breasts to locate any obvious abnormality, the patient was asked to lie supine and turn slightly to the contra-lateral side with the ipsi-lateral arm raised over her head.

Techniques:

A- Conventional US:

First, breast lesions were evaluated by; conventional B-mode ultrasound after spreading acoustic coupling gel on to the skin. Radial scanning of the entire breast and axillary tail on both sides was performed. Longitudinal and transverse images of breast lesions were obtained.

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, category 6 lesions were pathologically proven to be malignant.

B- S-DetectTM for breast:

After making the final assessment, we applied S-DetectTM (Smart-DetectTM Samsung Medison Co., Ltd, Seoul, Korea) to the captured US images of the lesions and obtained the results.

This intelligent technology uses the standardized Breast Imaging-Reporting and Data System (BI-RADS) score for standardized analysis and classification of suspicious lesions. The user simply touches a seed point on the touch screen or simply clicking the suspected area and the S-Detect auto-
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matically draws the lesion’s boundary, providing multiple images. Then a recommendation on whether the lesion is benign or malignant is automatically displayed as possibly benign or possibly malignancy. Such technology assists in a more accurate diagnosis.

C- E-BreastTM (ElastoscanTM for breast):

On the same session, real time free hand US elastography examination was performed. The probe was applied to the breast with repeated compression and decompression in a sustained frequency in a direction perpendicular to the diagnosis area.

We choose a color map in which blue and green indicate softer areas, while red indicate harder areas. All lesions were studied using split image, displaying a B-mode image on one side and Elasto mode on the other side. To get a correct sonoelastographic map, the process was repeated until a stable image was obtained. We selected an image obtained in the early phase of compression because these images provide the best contrast according to [3].

- 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. [3], as the following:
  - 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 semi quantitative evaluation of the sonoelastographic images, the E-BreastTM calculates the strain ratio between the selected target and surrounding fatty tissues. Unlike conventional ultrasound elastography, we select only one ROI (the lesion) and the machine automatically set the reference area of the surrounding fatty tissue region. The strain ratio was automatically obtained as the reference strain ratio/the ROI strain ratio, as shown in Fig. (1).

III- Histopathological diagnosis:

Histopathological diagnoses of breast lesions samples were performed in the Pathologic Department of the Suez Canal University Hospital by group of well-trained expert pathologists. Samples were obtained with Fine Needle Aspiration Cytology (FNAC), core biopsy, surgical excision and radical surgery. Histopathological diagnoses of surgical specimens or biopsy specimens were obtained and served as reference standards. Data from elasticity scoring and the strain ratios were compared with the histopathological diagnoses.
Results

The demographic features of our study represented eligible 28 female patients with breast masses. The age ranged from 20 to 70 years (mean age 41.5 ± 13.320). The mean age was higher for patients with malignant lesions (47.5 ± 12.518) than for patients with benign lesions (38.16 ± 12.729) with a statistically significant difference as regard the age between the two groups (p > 0.05).

The histopathological results of the biopsied breast lesions revealed 18 benign breast lesions (64.3%), and 10 malignant breast lesions (35.7%). Detailed description for the number and percentage for each pathological entity within benign and malignant categories are illustrated in (Table 1).

Table (1): Detailed histopathological data of the biopsied breast lesions.

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
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<td>64.3</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>16</td>
<td>57.1</td>
</tr>
<tr>
<td>Complex cyst</td>
<td>1</td>
<td>3.6</td>
</tr>
<tr>
<td>Non specific granulomatous mastitis</td>
<td>1</td>
<td>3.6</td>
</tr>
<tr>
<td>Malignant</td>
<td>10</td>
<td>35.7</td>
</tr>
<tr>
<td>Infiltrating ductal carcinoma</td>
<td>7</td>
<td>25</td>
</tr>
<tr>
<td>Ductal carcinoma insitu</td>
<td>2</td>
<td>7.1</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>1</td>
<td>3.6</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>100</td>
</tr>
</tbody>
</table>

Conventional US data:

When considering US BI-RADS categories of 1, 2, 3 as benign and that of 4, 5 as malignant, there were 19/28 (67.86%) cases diagnosed as benign by conventional US, 17/19 (89.5%) of them were benign (true negative) by pathology, and 2/19 (10.5%) were malignant by pathology (false negative). On the other hand 9/28 (32.14%) lesions were diagnosed as malignant by US, out of which 8/9 (88.9%) lesions confirmed to be malignant by pathology (true positive) and 1/9 (11.1%) lesion were benign by pathology (false positive), as shown in (Table 2).

The calculated sensitivity of conventional US was 80%, specificity was 94.4%, and the total accuracy was 89.3%. The PPV and NPV were 88.9%, and 89.5% respectively.

Table (2): Number and percentage of breast lesions by conventional us compared to histopathological data.

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Benign No.</th>
<th>Benign %</th>
<th>Malignant No.</th>
<th>Malignant %</th>
<th>Total No.</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>17</td>
<td>89.5</td>
<td>1</td>
<td>11.1</td>
<td>18</td>
<td>64.3</td>
</tr>
<tr>
<td>Malignant</td>
<td>2</td>
<td>10.5</td>
<td>8</td>
<td>88.9</td>
<td>10</td>
<td>35.7</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>67.86</td>
<td>9</td>
<td>32.14</td>
<td>28</td>
<td>100</td>
</tr>
</tbody>
</table>

S-DetectTM data:

After revising pathology results, 17/28 (60.71 %) diagnosed as benign by S-detect, 15/17 (88.2%) were benign (true negative) by pathology and 2/17 (11.8%) were malignant by pathology (false negative). Meanwhile, 11/28 (39.29%) cases diagnosed as malignant by elastography scoring, 8/11 (72.7%) lesions confirmed to be malignant by pathology (true positive) and 3/11 (27.3%) lesion were proved to be benign by pathology (false positive), as shown in (Table 3).

The calculated sensitivity of S-detect was 80%, specificity was 83.3%, PPV and NPV were 72.7% and 88.2% respectively, the total accuracy was 82.1%.

Table (3): Number and percentage of breast lesions by S-detect compared to histopathological data.

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Benign No.</th>
<th>Benign %</th>
<th>Malignant No.</th>
<th>Malignant %</th>
<th>Total No.</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>15</td>
<td>88.2</td>
<td>3</td>
<td>27.3</td>
<td>18</td>
<td>64.3</td>
</tr>
<tr>
<td>Malignant</td>
<td>2</td>
<td>11.8</td>
<td>8</td>
<td>72.7</td>
<td>10</td>
<td>35.7</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>60.71</td>
<td>11</td>
<td>39.29</td>
<td>28</td>
<td>100</td>
</tr>
</tbody>
</table>

Elastoscore data:

The distribution of elasticity scores for malignant and benign breast lesions, as shown in (Table 4). Lesions that scored 1, 2, and 3 were considered benign, whereas lesions that scored 4 and 5 were considered malignant.

It was found that 19/28 (67.86%) diagnosed as benign lesions by elastography, 17/19 (89.5%) were benign (true negative) by pathology, and 2/17 (10.5%) were malignant by pathology (false negative). After revising pathology results of the 9/28 (32.14%) cases diagnosed as malignant by elastography scoring, 8/9 (88.9%) lesions confirmed to be malignant by pathology (true positive) and 1/9
(11.1%) lesion was proved to be benign by pathology (false positive), as shown in (Table 5).

The calculated sensitivity of elastography scoring was 80%, specificity was 94.4%, PPV and NPV were 88.9% and 89.5% respectively, and the total accuracy was 89.3%.

Table (4): Distribution of elastography scoring among examined breast lesions.

<table>
<thead>
<tr>
<th>Color scoring</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 1</td>
<td>4</td>
<td>14.3</td>
</tr>
<tr>
<td>Score 2</td>
<td>11</td>
<td>39.3</td>
</tr>
<tr>
<td>Score 3</td>
<td>4</td>
<td>14.3</td>
</tr>
<tr>
<td><strong>Benign scoring:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score 4</td>
<td>7</td>
<td>25.0</td>
</tr>
<tr>
<td>Score 5</td>
<td>2</td>
<td>7.1</td>
</tr>
<tr>
<td><strong>Malignant scoring:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score 6</td>
<td>9</td>
<td>32.1</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>100</td>
</tr>
</tbody>
</table>

Table (5): Number and percentage of breast lesions by elastoscore compared to histopathological data.

<table>
<thead>
<tr>
<th>Color scoring</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>17</td>
<td>89.5</td>
<td>1</td>
<td>5.6</td>
<td>18</td>
<td>64.3</td>
</tr>
<tr>
<td>Malignant</td>
<td>1</td>
<td>10.5</td>
<td>9</td>
<td>90</td>
<td>10</td>
<td>35.7</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>67.86</td>
<td>9</td>
<td>32.14</td>
<td>28</td>
<td>100</td>
</tr>
</tbody>
</table>

Strain ratio (SR):

The mean SR for both malignant and benign lesions was $1.798 \pm 0.821$ with a range of (0.89-3.4), it was found that the mean SR for malignant lesions ($2.63 \pm 0.69$; range, 2-3.4) was significantly greater than that for benign lesions (mean, $1.35 \pm 0.44$; range, 0.89-1.8) ($p$-value <0.001), as illustrated in (Table 6).

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Benign</td>
<td>17</td>
<td>89.5</td>
<td>1</td>
</tr>
<tr>
<td>Malignant</td>
<td>2</td>
<td>10.5</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>67.86</td>
<td>9</td>
</tr>
</tbody>
</table>

By applying a ROC curve, it was found that the true positive rate (sensitivity) was plotted against false positive rate (1-specificity) analysis with the area under the curve=0.903, as illustrated in Fig. (2).

It was found that; sensitivity was 100% when the cutoff point was 1.09, while the specificity was 27.8%. By increasing the cutoff point to 1.5 1, the sensitivity decreased to 90% and the specificity was 77.8%. Further increase in the cutoff point to 2 increased the specificity to 94.4% and the sensitivity remains unchanged. So it was found that the best cutoff point is 2 with a sensitivity of 90% and specificity of 94.4%.

When considering lesions with strain ratio less than 2 as benign and lesions with strain ratio more than or equal 2 as malignant, 18/28 (64.3%) lesions were benign by strain ratio, 17/18 (94.4%) of them were benign (true negative) by pathology, and 1/18 (5.6%) were malignant by pathology (false negative). 10/28 (35.7%) lesions seemed to be malignant by strain ratio. Out of which 9/10 (90%) lesions were confirmed to be by pathology (true positive) and 1/10 (10%) lesion were proved to be benign by pathology (false positive), as illustrated in (Table 7) & Figs. (3-6).

The previous results revealed sensitivity of 90% and specificity of 94.4%. The Negative Predictive Value (NPV) was 94.4%, and the Positive Predictive Value (PPV) was 90% respectively, the total accuracy was 92.85%.

Table (7): Number and percentage of breast lesions for SR compared to histopathological data.

<table>
<thead>
<tr>
<th>SR at 2.00 cut off</th>
<th>Histopathology</th>
<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Benign</td>
<td>17</td>
<td>94.4</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Malignant</td>
<td>1</td>
<td>5.6</td>
<td>9</td>
<td>90</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>64.3</td>
<td>10</td>
<td>35.7</td>
</tr>
</tbody>
</table>
Fig. (3): 27 years old female patient presented by Rt. breast mass. (A) B-mode breast US revealed a well defined macrolobulated hypoechoic solid mass at 11 o'clock measuring about 1.7 x 1.2 cm in diameter with no posterior acoustic shadowing (BIRADS 3). (B) S-Detect TM revealed possibly benign mass. (C) Elastogram revealed E2 score of the mass. (D) Strain ration was calculated (SR=1.32). Fine needle aspiration cytology (FNAC) was done and revealed benign fibroadenoma; complementary elastographic assessment confirmed the conventional ultrasound finding and highly raised the possibility of benignity which may reduce the need for biopsy in future.

Fig. (4): 41 years old female patient presented by Rt. breast mass. (A) B-mode breast US revealed a well defined hyperechoic solid mass with central liquefaction at 9 o'clock measuring about 2.5 x 1.3 cm in diameter with no posterior acoustic shadowing (BIRADS 3). (B) S-Detect TM revealed possibly benign mass. (C) Elastogram revealed E3 score of the mass. (D) Strain ration was calculated (SR=2.78). Fine needle aspiration cytology (FNAC) was done and revealed hypercellular fibroadenoma; conventional ultrasound and S-detect were superior to elastography in this case as elastography depended on the lesion elasticity only.
Fig. (5): 29 years old lactating female patient presented by Lt. breast tenderness and palpable lump. (A) B-mode breast US revealed an ill defined heterogenous hypoechoic solid mass with speculated borders at 12 o'clock measuring about 2.7 x 2.4cm in diameter, associated enlarged ipsilateral axillary lymph nodes with suspicious pattern were seen (thickened cortex and tethered fatty hilum) (BIRADS 5). (B) S-Detect TM revealed possibly malignant mass. (C) Elastogram revealed E5 score of the mass. (D) Strain ration was calculated (SR=2.43). Fine needle aspiration cytology (FNAC) was done and revealed infiltrating duct carcinoma, elastography and S-detect confirmed the findings of conventional ultrasound, both are highly suggestive of malignancy.

Fig. (6): 49 years old female patient presented by palpable Lt. breast mass. (A) B-mode breast US revealed a well defined lobulated heterogenous hypoechoic solid mass at 2 o'clock measuring about 2.5 x 1.7cm in diameter, no posterior acoustic shadowing (BIRADS 4b). (B) S-Detect TM revealed possibly malignant mass. (C) Elastogram revealed E2 score of the mass (mixed red & green pattern). (D) Strain ration was calculated (SR=2.23). Core biopsy of the mass was done and revealed invasive lobular carcinoma, conventional US, elastography and S-detect ultrasound findings correctly suggested the malignant nature of the lesion.
Correlation between elastoscopy, conventional ultrasound, and strain ratio:

The study evoked strong +ve correlation between elastoscopy and strain ratio (Spearman’s correlation=0.694), as well as with S-detect (Spearman’s correlation=0.600). Also S-detect is strongly correlated with conventional ultrasound (Spearman’s correlation=0.524) and strain ratio (Spearman’s correlation=0.657). Conventional ultrasound is moderately correlated with strain ratio (Spearman’s correlation=0.469), as well as with elastoscopy (Spearman’s correlation=0.399), as shown in (Table 8).

The diagnostic performance of the conventional sonography by the BI-RADS category, S-detect, Elastography score and strain ratio is shown in (Table 9). Strain ratio shows the highest sensitivity, specificity and accuracy. Elastography score and conventional sonography show same sensitivity and specificity, while S-detect showed the lowest specificity compared to conventional sonography, elastography score and strain ratio.

Table (8): Correlation between elastoscopy, conventional ultrasound, S-detect and strain ratio.

<table>
<thead>
<tr>
<th>Item</th>
<th>BIRADS:</th>
<th>Color scoring:</th>
<th>Strain ratio:</th>
<th>S-detect:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>BIRADS:</td>
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<td>.399*</td>
<td>.469*</td>
<td>.524**</td>
</tr>
<tr>
<td>p</td>
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<td>.012</td>
<td>.004</td>
<td>.004</td>
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<td>N</td>
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<td>.694**</td>
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<td>.657**</td>
</tr>
<tr>
<td>p</td>
<td>.012</td>
<td>.000</td>
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<td>.000</td>
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</table>

Table (9): Comparison between the diagnostic performance of the BI-RADS, elasticity score, strain ratio and s-detect.

<table>
<thead>
<tr>
<th>Item (at cut off 2.00)</th>
<th>TP</th>
<th>FN</th>
<th>TN</th>
<th>FP</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<th>-ve PV</th>
<th>Accuracy</th>
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<td>90.0</td>
<td>94.4</td>
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<td>BI-RADS</td>
<td>8</td>
<td>2</td>
<td>17</td>
<td>1</td>
<td>80.0</td>
<td>94.4</td>
<td>88.9</td>
<td>89.5</td>
<td>89.3</td>
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<tr>
<td>Color scoring</td>
<td>8</td>
<td>2</td>
<td>17</td>
<td>1</td>
<td>80.0</td>
<td>94.4</td>
<td>88.9</td>
<td>89.5</td>
<td>89.3</td>
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<tr>
<td>S-detect</td>
<td>8</td>
<td>2</td>
<td>15</td>
<td>3</td>
<td>80.0</td>
<td>83.3</td>
<td>72.7</td>
<td>88.2</td>
<td>82.1</td>
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Discussion

Elastography is a non invasive new imaging modality that detects tumors based on their stiffness (elasticity) compared to normal tissue. Generally breast cancer tissue is harder than normal breast tissue [7].

A combination of elastography and sonography had the best results in detecting cancer and potentially could reduce unnecessary biopsy [6].

According to the our study results the calculated sensitivity, specificity, total accuracy, PPV and NPV for conventional US were 80%, 94.4%, 89.3%, 88.9 and 89.5% respectivly. Our results showed higher sensitivity and lower specificity than those reported by Schaefer et al., 2011 [8] (sensitivity 57.8%, specificity 96.1% and total accuracy 49.2%), and Itoh et al., 2006 [3] (sensitivity 71.2%, specificity 96.6% and accuracy 84.7%). These difference are mainly attributed to the fact that they chose a higher cut-off BI-RADS category (BI-RADS 1, 2, 3, and 4 considered as benign, and BI-RADS 5 considered as malignant).

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 [11].

The calculated sensitivity of S-detect in our study was 80%, specifity was 83.3%, PPV and NPV were 72.7% and 88.2% respectively, the total accuracy was 82.1%. Our results were comparable to the results reported in the white paper done by Samsung medical center 2014 which shows a higher sensitivity of 84.6% and lower specificity (68.8%) than ours.

In our study the sensitivity of the conventional US was the same as S-detect, while the specificity of conventional US was higher than S-detect. The main cause which decreased specificity of S-detect
was irregular shaped fibroadenomas referred for biopsy; S-detect assessed them as possibly malignancy. The S-detect is a program that analyzes the US features of the lesion only and assesses the possibility of malignancy based on the BI-RADS US. Therefore, circumscribed malignant mass may be remained as limitation of S-detect. Moreover, radiologists try to find out any subtle suspicious feature when they perform breast US examination of patients with suspicious clinical findings, but S-detect is not available to do such performance.

According to Tsukuba scoring, lesions in our study were classified into 5 elasto-scores, as previously described. Where the lesions that scored E1 (4, 14.3%), E2 (11, 39.3%), and E3 (14, 3%) were considered benign (19/28 cases, 67.9%), whereas lesions that scored E4 (7, 25.0%), and E5 (2, 7.1%) were considered malignant (9/28 cases, 32.1%). In our study, we considered elastographic scoring of 1, 2, 3 as benign and that of 4, 5 as malignant. The mean elasticity score was significantly higher for malignant lesions (4) than for benign lesions (2). These results are identical to the study done by Itoh et al., [3] they reported that the mean elasticity scoring for benign lesions was (2) and for malignant breast lesions was (4), however, the study done by Tan et al., [4], reported that the mean elastoscoring for benign lesions was (2) and for malignant lesions was (5).

In our study, the calculated sensitivity of elastography scoring was 80%, specificity was 94.4%, PPV and NPV were 88.9% and 89.5% respectively, and the total accuracy was 89.3%.

Our results are close to the study done by Itoh et al., 2006 [8], that reported the best cutoff point is between 3 and 4 elasticity scores, showing higher sensitivity (86.5%), lower specificity (89.8%), and accuracy (88.3%) than ours and to the study done by Elsaid and Mohamed, [12], that showed sensitivity of (84%) and lower specificity of (84%).

Our study results were comparable to the results reported by Schaefer et al., [8], who stated a cutoff point of elastography scores between 3 and 4, but showed higher value for sensitivity 96.9%, lower values for specificity (76.0%) and accuracy (82.9%) than ours.

When comparing between conventional sonography (BI-RADS category) and elastography (Tsukuba scoring system), most studies have reported better specificity for elastography and higher sensitivity for conventional sonography, with the exception of the study done by Cho et al., [13], which reported same degrees of sensitivity (82%) and lowered specificity (84%) for strain ratio to differentiate between benign and malignant breast lesions. In our study, the calculated strain ratio revealed that the best cut off point is set between 3 and 4 elastography scores, and same degree of specificity values (94.4%).

As for us, we agree with most studies that elastography has better or same specificity values, but disagree with that the conventional sonography has better sensitivity values; we found that both modalities have a similar degree of sensitivity. Our study results show that sonographic elastography and conventional sonography have the same degree of sensitivity (80%) when the cutoff point is set between 3 and 4 elastography scores, and same degree of specificity values (94.4%).

Leong et al., [14] compared the diagnostic performance of breast elastography versus conventional ultrasound in the assessment of breast lesions in a prospective study involving 110 lesions. Sensitivity, specificity, and accuracy were 88.5%, 42.9% and 53.6%, respectively for conventional ultrasound, where 100%, 73.8%, and 80%, respectively, for elastography. 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.

Several studies were done on the strain ratio parameter to set a best cutoff point and to evaluate its diagnostic accuracy in differentiating benign from malignant lesions. In our study, the mean SR for both malignant and benign lesions was 1.798 ± 0.821 with a range of (0.89-3.4), it was found that the mean SR for malignant lesions (2.36±0.69; range, 2-3.4) was significantly greater than that for benign lesions (mean, 1.35±0.44; range, 0.89-1.8); p-value 0.001 was considered to indicate significant differences.

Our results are comparable to that reported by Thomas et al., [15], where the mean strain ratio for benign lesions was 1.6±1, and the mean strain ratio for malignant lesions was 5.1 ±4.2. Kumm and Szabunio, 2010 [10] reported higher values, where the mean ratios were 2.7 and 10.5, for benign and malignant lesions respectively.

Our results regarding Semi-Quantataive anlaysis of the elastography ultrasound with automatically calculated strain ratio revealed that the best cut off value for strain ratio to differentiate between benign and malignant breast entities was found to be at 2 level (AUC, 0.903) allowed significant differentiation (p<0.001) between malignant and benign breast lesions.
When considering lesions with strain ratio less than 2 as benign and lesions with strain ratio more than or equal to 2 as malignant, 18/28 (64.3%) lesions were benign by strain ratio, 17/18 (94.4%) of them were benign (true negative) by pathology, and 1/18 (5.6%) were malignant by pathology (false negative). 10/28 (35.7%) lesions seemed to be malignant by strain ratio. Out of which 9/10 (90%) lesions were confirmed to be by pathology (true positive) and 1/10 (10%) lesion were proved to be benign by pathology (false positive).

The previous results revealed sensitivity of 90% and specificity of 94.4%. The Negative Predictive Value (NPV) was 94.4%, and the Positive Predictive Value (PPV) was 90% respectively, the total accuracy was 92.85%. Our results agreed with the study done by Thomas and his colleagues who 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 < 0.001) 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 [15].

Another study done by Zhi et al., 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. The diagnostic performance of strain ratio based elastographic analysis was better than that of the five-point scoring system with ultrasound elastography (p < 0.05) [16].

Kumm and Szabunio, [10] evaluated 310 breast lesions. Sensitivity was 76% for Elastoscore (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.

The difference in the results between our study and that of Zhi et al., 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 utilized Hitachi medical system (Hitachi Medical, Tokyo, Japan), while in our study we used (RS80A Samsung Medison Co., Ltd, Seoul, Korea).

Regarding to our results, elastoscopy is strongly correlated with strain ratio (Spearman's correlation=0.694), as well as with S-detect (Spearman's correlation=0.600), also S-detect is strongly correlated with conventional ultrasound (Spearman's correlation=0.524) and strain ratio (Spearman's correlation=0.657), while conventional ultrasound is moderately correlated with strain ratio (Spearman's correlation=0.469), as well as with elastoscore (Spearman's correlation=0.399).

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 lesion pathology is one of the most important role of diagnostic imaging. 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 [6].

In our study, one lesion was considered to be positive by conventional ultrasound (BI-RADS 4) and yielded benign elastoscore and strain ratios. Pathological studies confirmed their benignity (fibroadenomas). Cases with these lesions could have been saved from biopsy, if elastographic results were put into consideration. On the other hand, 1 breast lesion with BI-RADS 4 by conventional US showed benign elastographic results and were proved to be malignant by pathology (ductal carcinoma insitu).

These results agreed with the study done by Itoh et al., 2006 [8] they reported that Ultrasound elastography may be used to down grade BI-RADS categorization of breast lesions especially those with BIRADS 3 and 4. This approach may reduce the number of false-positive results and unnecessary invasive diagnostic procedures.

Also Schaefer et al., [8], reported that the use of elastography in addition to conventional US may down grade some lesions categories BI-RADS 3 or 4 to BI-RADS 2. The study done by Cho et al., 2008 [10] for 100 women who had been scheduled for an US-guided core biopsy of 100 non palpable breast masses (83 benign, 17 malignant). Results of the study showed that for BI-RADS

Use of Ultrasound Elastography in Characterization of Solid Breast Lesions

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category 4a lesions, 44% (22 of 50) had an elasticity score of 1 and all were found to be benign. They concluded that BI-RADS category 4a lesions with an elasticity score of 1 probably do not require biopsy.

Regarding the previously mentioned data we suggest that elastographic evaluation including five point scoring system may prevent unnecessary biopsies however, we evaluate the case as a whole, regarding the history, clinical examination as well as conventional US findings in addition to the semi quantitative elastography evaluation to prevent false negative results that affect the diagnostic efficacy for malignant lesions.

Caution must be paid, before deciding to avoid a scheduled biopsy on the basis of a negative elastographic score, because of the considerable amount of false negative results. The combined use of conventional US, color coded SE and strain ratio may downgrade some lesions categories BI-RADS 3 or 4 to BI-RADS 2.

Conclusions:

Ultrasound elastography of the breast masses is a non invasive and easy procedure with high diagnostic performance which can be easily integrated with the B-mode ultrasound examination in the same session and improves its specificity in differentiation between benign and malignant breast lesions; also it has proven benefit in minimizing the number of unnecessary biopsies.

References

الملخص العربي

يعتبر قياس مطاطية الأنسجة باستخدام الموجات فوق الصوتية وسيلة تشخيصية بسيطة. وتتم هذه الطريقة على أن أنفسة الثدي الطبيعية تكون أكثر مرونة وأقل صلابة من أي أفق داخلها، وأيضا أن الأفاط الخبيثة أكثر صلابة من الأفاط الحميدة. من خلالها يمكن توفير معلومات حول صحة الثدي وذك الاختبارات. وتستخدم وسيلة تكميلية للموجات فوق الصوتية التقليدية التي تختص بالتقنيات المورفولوجية للورم.

وعلى الرغم من أن الفحص التقليدي بالموجات فوق الصوتية الذي يتمتع بنسبة جداسية عالية إلا أن له نسبة تحديدية منخفضة نسبيا مما يؤدي إلى زيادة أعداد الخزعات في حالات الأفاط الحميدة. وذلك أجريت الدراسات على قياس مطاطية الأنسجة على أمل زيادة كفاءة التشخيص بالموجات فوق الصوتية في التفقرة بين أفات الثدي الحميدة والخبيثة ومن ثم الحد من عدد الخزعات غير الضرورية.

وهي تعتبر طريقة سبيطة تتم في نفس جلسة الفحص التقليدي بالموجات فوق الصوتية وينسج الجهاز عند طريق إدراج برنامج بجهاز الموجات فوق الصوتية. تأخذ صور الأصل قبل وبعد اجراء ضغط بسيط على حسب مدى الإصابة الناتجة في طبقات الثدي لاستنتاج مقدار مرونة وصلابة أفق داخلها. ثم تترجم المعلومات ببيانات طريقة إضافية إذا بطريقة المقارن المحموم أو بطريقة عذبة الألوان. ومن ثم يمكن لهذا التكييف أن يقلل من احتمال الخزعات الثديية غير الضرورية وإن يقدم نتائج أفضل للتشخيص.