Combined sonoelastographic scoring and strain ratio in evaluation of breast masses

Amani Ezzat Mousa, Mohamed Aboelatta, Khaled Zalata

Diagnostic Radiology Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt
Pathology Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt

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Abstract  Aim of the work: To detect the diagnostic performance of the combined use of sonoelastographic scoring and strain ratio in differentiation of benign and malignant breast masses with the histopathology as the standard reference.

Patients and methods: One hundred and seventy-two women with 190 breast masses were enrolled in this prospective study. Conventional US (B-mode and color Doppler US) and sonoelastography (elasticity score “ES” and calculation of strain ratio “SR”) were performed. B-mode images were classified according to the Breast Imaging Recording and Data System. The hardness was determined with 5-point scoring method and SRs of the lesions were calculated. Receiver operating characteristic (ROC) curves were performed and the cutoff point for differentiation of benign and malignant masses was detected.

Results: There was a significant difference ($P=0.02$) in the mean SRs between benign and malignant breast masses. The area under the curve (AUC) for combination of ES and SR (0.964) was higher than for ES alone (0.852) and B-mode US (0.823). A cutoff value of 3.6 for the SR allowed the best differentiation of benign and malignant breast lesions.

Conclusion: The combined use of elasticity score and strain ratio of sonoelastography increased the diagnostic performance in distinguishing benign from malignant breast masses.

1. Introduction

It is well known that breast cancers are generally harder than normal breast tissue, which is one of the important findings in clinical evaluation by palpation. Breast biopsy, the current method used to distinguish between benign and malignant breast abnormalities, yields a benign result in more than 75% of patients, making it the most costly of a breast cancer screening program. Thus, a reliable method to differentiate benign from malignant breast masses on US images would be
valuable. US strain imaging (also known as elastography) may aid in the differentiation of benign from malignant solid breast masses (1–5).

Elasticity is one of the important characteristics of live tissues. To create elastic deformation in a tissue, a certain amount of force must be applied. Elasticity is defined as the spatial rate of tissue displacement as a result of certain amount of pressure on tissue. Sonoelastography is a sonographic technique that directly reveals the elasticity features of tissue and enables to determine changes in tissue hardness qualitatively and semiquantitatively. Malignant breast masses are harder and show less strain compared to benign lesions following compression. Strain images display the relative stiffness of lesions compared with the stiffness of surrounding tissues. Therefore, by measuring the tissue strain induced by compression, we can estimate tissue hardness, which may be useful in diagnosing breast cancer (6,7).

1.1. Aim of the work

To detect the diagnostic performance of the combined use of sonoelastographic scoring method and strain ratio in differentiation of benign and malignant breast masses with the histopathology is the standard reference.

2. Patients and methods

A total of 172 consecutive women with 190 breast masses were enrolled in this prospective study from September 2010 to October 2011. The mean age was 39.7 years (range 22–69 years). All patients had palpable breast masses. Ultrasound-guided core needle biopsy, fine-needle aspiration of sonographically visible breast masses, or excision biopsy were performed for all patients. For lesions with subsequent surgical excision, the final histology was based on the surgical specimens. Histopathology was used as the standard reference. Written informed consent for ultrasonography and biopsy was obtained from all patients prior to enrollment. All patients were examined with conventional ultrasonography (US) and sonoelastography. Mammographic examinations were available in 143 patients.

2.1. Equipment

Conventional US and sonoelastography were performed with a digital US scanner (EUB-7500, Hitachi Medical corporation, Tokyo, Japan). The US probe was 7–12 MHz linear electronic probe used for all the conventional ultrasound examinations as well as for freehand compression sonoelastography. Both the conventional and elastographic studies were performed by two radiologists (M.A.E. and A.M.) with 17 and 23 years of experience in breast imaging, respectively.

2.2. Technique of examination

Conventional US examination was performed first followed by elastography. The conventional examination included B-mode images and color Doppler US for all lesions. Sonoelastography included scoring method and calculation of strain ratio. The patient was examined in supine position with the arm elevated and the upper side of the affected side in an oblique position. Lesions detected at conventional B-mode US were evaluated for: shape, boundary, orientation, margin, echo pattern, posterior acoustic features, and calcification, together with evaluation of the surrounding tissues. Breast lesions included masses (solid or cystic) and architectural distortions. B-mode ultrasound images were classified according to the Breast Imaging Reporting and Data System (BI-RADS) criteria for US (8) for each of the breast masses. BIRADS scores of 2 and 3 were considered benign, whereas scores of 4 and 5 were considered malignant.

Elastography images were obtained as motion images. Both B-mode and elastographic images were simultaneously displayed on the same image divided into two panels with the right-sided showing the B-mode image and the left-sided showing the elastographic image with superimposed color-coded elasticity features. The region of interest (ROI) used for obtaining elasticity images included subcutaneous fat at the top and pectoral muscle at the bottom of the breast. The lateral borders were set more than 5 mm from the lesion’s boundary. The probe oriented perpendicular to the chest wall and was moved slightly inferior and superior with repeated compression using light pressure, the pressure indicator bar showed a value of 3, followed by decompression until uniform images of green were obtained. Examination started in the normal region then moved to the region of lesion with the same compression. 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; green indicated intermediate elasticity. The hardness is scored on a scale of 1–5 according to the elasticity scoring classification system proposed by Itoh et al. (9) (Fig. 1). Score 1 is defined as an overall green pattern of the mass, whereas score 2 consists of a mosaic pattern of green, blue and red. Score 3 is presented by a blue center and green periphery. Score 4 is defined as blue color confined to the mass, and score 5 is defined as blue color including the entire mass and its surrounding area. Scores 1–3 represent benign lesions while scores 4 and 5 represent malignant lesions. For the 5-point elasticity scoring classification, all of the sonoelastographic images were evaluated by consensus of the two radiologists. To obtain strain ratio (SR): the first ROI (A) for the lesion’s strain was manually drawn and placed to be bounded by the inner margin of the mass. The second ROI (B) for the fat strain was placed in the fat tissue at a depth similar or as close as possible to the depth of the mass to avoid stress decay with the depth. The second ROI for the fat strain was placed in the fat tissue encoded green because it represented intermediate stiffness in the chosen area. The strain index, defined as the fat to mass strain ratio (B/A ratio) that indicated mass stiffness, was calculated automatically by the software program in the ultrasound unit.

2.3. Statistical analysis

The differences between elasticity scores (ES) and mean SR values for the benign and malignant breast lesions were assessed with the Student’s t test. Two-tailed P value of less than 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curves were used to detect and compare the diagnostic performances of B-mode, ES and combination of ES and SR methods. The areas under the ROC curves were calculated and compared for these techniques. The best cutoff
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3. Results

This study included 172 patients with 190 breast lesions: 87 malignant and 103 benign lesions. All benign and malignant lesions were confirmed by histopathology. The final pathologic diagnosis for all breast lesions is illustrated in Table 1. The elasticity scores (ES) for benign and malignant lesions are listed in Table 2. BIRADS classification of different benign and malignant lesions is illustrated in Table 3. Sensitivity, specificity, and accuracy of B-mode, ES and combined ES and SR in the diagnosis of breast lesions are illustrated in Table 4.

Of the malignant lesions, 76 out of 87(87.4%) lesions had elasticity of score 4 ($n=39$) and score 5 ($n=37$). The remaining 11 (12.6%) lesions had score 2 ($n=5$) and score 3 ($n=6$) which confirmed by histopathology to be malignant. Six of these 11 lesions showed high strain ratios (range 6.85–17.36) denoting their malignant nature which increased the sensitivity of elastography into 94.3%. These 11 lesions with false negative results had BIRADS scores of 4 ($n=8$) and 5 ($n=3$).

None of the malignant lesions had elasticity of score 1. Figs. 2–6 show malignant masses with different ESs and SRs.

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 the lesion (the border between lesion and surrounding breast tissues) on B-mode images (9).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Final pathological diagnosis in 190 breast lesions.</th>
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<tr>
<td>Pathological diagnosis</td>
<td>No. of lesions (%)</td>
</tr>
<tr>
<td><strong>(A) Malignant lesions</strong></td>
<td></td>
</tr>
<tr>
<td>- Invasive ductal carcinoma:</td>
<td>63 (33.2%)</td>
</tr>
<tr>
<td>*Nonschirrus type</td>
<td>45 (23.7%)</td>
</tr>
<tr>
<td>*Schirrus type</td>
<td>18 (9.5%)</td>
</tr>
<tr>
<td>- Ductal carcinoma in situ</td>
<td>11 (5.8%)</td>
</tr>
<tr>
<td>- Mucinous carcinoma</td>
<td>5 (2.6%)</td>
</tr>
<tr>
<td>- Colloid carcinoma</td>
<td>5 (2.6%)</td>
</tr>
<tr>
<td>- Invasive lobular carcinoma</td>
<td>3 (1.6%)</td>
</tr>
<tr>
<td><strong>(B) Benign lesions</strong></td>
<td></td>
</tr>
<tr>
<td>- Fibrocystic changes</td>
<td>29 (15.3%)</td>
</tr>
<tr>
<td>- Fibroadenoma</td>
<td>41 (21.6%)</td>
</tr>
<tr>
<td>- Cyst</td>
<td>17 (8.9%)</td>
</tr>
<tr>
<td>- Papilloma</td>
<td>9 (4.7%)</td>
</tr>
<tr>
<td>- Abscess</td>
<td>7 (3.7%)</td>
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<th>Table 2</th>
<th>Elasticity scores in 190 benign and malignant breast lesions.</th>
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<td>Pathological diagnosis</td>
<td>Elasticity score</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td><strong>Benign lesions</strong></td>
<td>37</td>
</tr>
<tr>
<td><strong>Malignant lesions</strong></td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>37</td>
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</table>

<table>
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<tr>
<th>Table 3</th>
<th>BIRADS scores of benign and malignant breast lesions.</th>
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<tr>
<td>Pathological diagnosis</td>
<td>Conventional US</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>Benign lesions</strong></td>
<td>27</td>
</tr>
<tr>
<td><strong>Malignant lesions</strong></td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>27</td>
</tr>
</tbody>
</table>

3.1. Diagnostic performance

The receiver operating characteristic (ROC) curves for B-mode US, ES and combination of ES and SR in differentiation of benign and malignant lesions are shown in Fig. 10. The area under the curve (AUC) for combination of ES and SR (0.964) was...
higher than for ES alone (0.852) and B-mode US (0.823). The combined use of both ES and SR had a high significant difference ($P = 0.003$) compared to B-mode US alone or ES alone.

4. Discussion

Breast sonography has proved to be useful in the differentiation between not only solid and cystic masses but also benign and malignant masses. However, the sonographic features for benign and malignant lesions have been shown to have a substantial overlap with each other (10). Therefore, biopsy is presently used to supplement other diagnostic methods in the evaluation of breast lesions, but the rates of cancer detection in biopsies are only 10–30% (11). A reliable, noninvasive imaging method that can be used for breast cancer detection has to be established. Sonoelastography, a noninvasive method of revealing the physical properties of a tissue, has been devel-
Fig. 3  A 47-year-old woman with left breast mass (A) Mammogram shows an irregular mass in the lower inner quadrant. (B) Sonoelastography and B-mode image on split screen mode. The right B-mode image shows an irregular, hypoechoic solid mass that categorized as BI-RADS 5. The left image with elastography shows the entire lesion is blue, indicating no strain and ES of 4. The SR is very high (29.76). (C) Enlarged axillary lymph node showing the same criteria as the breast mass with high SR (15.67). Histopathology yielded invasive ductal carcinoma.

Fig. 4  A 51-year-old woman with right breast mass. (A) Sonoelastography: the right B-mode image shows an irregular, hypoechoic solid mass that categorized as BI-RADS 4. The left image with elastography shows the entire lesion is blue (ES of 4). The SR between the mass and the surrounding tissue is high (4.34). (B) Histopathology yielded invasive lobular carcinoma.
opposed as an alternative to breast biopsy. The interpretation criteria in elastography consist of the qualitative parameter “elasticity score” (ES) and the quantitative parameter “strain ratio” (SR). The most frequently used qualitative classifications that differentiate between five elastography patterns are that where patterns 4 and 5 indicate malignant breast lesions and patterns 1–3 indicate benign breast lesions. The SR is the ratio between the lesion and the reference area, which is the fat region (12).

In the current study, we used both ES and SR of sonoelastography to detect the diagnostic performance of their combined use in differentiation of benign and malignant breast masses. Among the 103 benign lesions, ES correctly diagnosed 88 lesions compared to 65 out of 103 lesions based on B-mode alone denoting better results when ES was added to B-mode. This was in agreement with several studies (13–16). Moreover, with the addition of SR more lesions were correctly diagnosed (97/103) lesions. This was in concordance with Zhi et al. (17) who reported that the diagnostic performance of strain ratio-based elastographic analysis was better than that of the five-point scoring system \( P < 0.05 \) with the AUC for SR (0.944) was higher than that for ES (0.885). They concluded that SR can provide a new and more reliable diagnostic tool in comparison to a five-point scoring system.

Among the 87 malignant lesions, ES correctly diagnosed 76 lesions and the addition of SR improved the diagnosis to 82 out of 87 lesions compared to 79 out of 87 lesions based on B-mode alone. In a study that compared the diagnostic performance of sonoelastography SR alone to the B-mode sonography, found that the area under the curve had a low significant difference \( P = 0.490 \) between the SR (AUC = 0.879) and B-mode sonography (AUC = 0.835) (18). In the present study the combined use of both ES and SR had a high significant difference \( P = 0.003 \) and higher AUC (0.964) compared to ES (AUC = 0.852) or B-mode sonography (AUC = 0.823) in differentiation of benign and malignant breast lesions. Thomas et al. (19), Zhao et al. (20) and Landoni et al. (21), found that the quantitative method of SR calculation was superior to subjective interpretation of ES and B-mode scans, with a positive

**Fig. 5** A 57-year-old woman with right breast mass. (A) Mammogram shows a well-defined mass with speculated margin. (B) Sonoelastography: the right B-mode image shows an irregular, hypoechoic solid mass that categorized as BI-RADS 5. The left image with elastography shows both the entire hypoechoic lesion and its surrounding area appear blue (ES of 5). The SR is very high (21.07). (C) Histopathology yielded colloid carcinoma: malignant epithelial cells floating in mucin.
predictive value of 89% compared to 68% and 84% for the other two methods. They reported that calculation of SR contributes to the standardization of sonoelastography with high sensitivity and allows significant differentiation of benign and malignant breast lesions. Quantitative measurement of the SR has been reported also in studies regarding cervical lymph nodes, in which the strain index was helpful in differentiation of benign and metastatic cervical lymph nodes (22,23).

In our study, SR cutoff value of 3.6 showed a statistically significant difference ($P = 0.02$) in differentiation of benign and malignant breast lesions with sensitivity of 94.3% and specificity of 94.2%. This was comparable to SR cutoff value defined by Yerli et al. (24). Different SR cutoff values were reported in researches. Zhi et al. (17) reported that when a cutoff point of 3.05 was introduced, elastography had sensitivity of 92.4%, specificity of 91.1%, and accuracy of 91.4%. In another recent study (25), the authors applied the same cutoff point of SR that was used by Zhi et al. (17) and recorded sensitivity of 80.1%, and specificity of 97.1%. Cho et al. (18) found that the best SR cutoff point to achieve the maximal sum of the sensitivity (95%) and specificity (75%) was 2.24 while Thomas et al. (19) found that SR cutoff value of 2.45 allowed significant differentiation of malignant and benign lesions. On the other hand, Ueno et al. (26) reported a higher SR cutoff point of 4.8.

In our study the combined use of ES and SR increased the diagnostic performance of sonoelastography in differentiation of benign and malignant breast masses. This was in agreement with Zhi et al. (17) and Thomas et al. (19). Also Athanasiou et al. (27) used quantitative sonoelastography with supersonic

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**Fig. 6** A 66-year-old woman with two breast masses. B-mode US (right) depicts well-defined hypoechoic solid masses (BI-RADS 4). Elastography (left) shows that most of the left lesion is blue with green periphery (ES of 3) and low SR (3.10). Pathology yielded invasive ductal carcinoma.

**Fig. 7** Two fibroadenomas in different patients. B-mode US (right in A & B) depicts homogeneously hypoechoic oval solid masses (BI-RADS 2). Sonoelastography (left in A & B) shows almost homogeneous green appearance of both masses (ES of 1) with low SR (0.53) of the first mass in A and high SR (5.8) of the second mass in B.
shear imaging to assess lesion stiffness and were able to differentiate between benign and malignant breast lesions. A recent study investigating sonoelastography with color Doppler US has focused on its potential in reducing the number of biopsies with benign results due to further discrimination of low suspicious lesions and its increased diagnostic performance in distinguishing benign from malignant breast masses (28). On the other hand Yerli et al. (24) mentioned that, the elasticity scoring and strain ratio methods seem to have similar diagnostic potential for differentiating between benign and malignant breast masses and that the combined use of B-mode sonography and qualitative 5-point scoring is a sufficient method that increases specificity when differentiating benign and malignant breast masses. Lee et al. (29) reported that elasticity score alone showed the best diagnostic performance, but a combination of B-mode US and elasticity score may have a predictive value for the differentiation of benign and malignant lesions < 1 cm.

Selection of the reference ROI is important to obtain the correct SR indicating the real stiffness of the tissue. In a previous study that evaluated the diagnostic performance of the fat to lesion strain ratio, the ROI for the reference was placed in the superficial fat tissue adjacent to the skin layer (26). This study found that 4.8 was the best cutoff value for differentiating benign and malignant masses that was higher than detected in our study and also in other studies. Another study suggested that a reference ROI placed in the glandular tissue at the same depth as the lesion would indicate the lesion stiffness correctly.

Fig. 8  Breast abscess in a 31-year-old lactating woman. B-mode US (right) depicts a well-defined multilocular lesion. Sonoelastography (left) shows green appearance of the lesion with blue foci (ES of 2) with low SR (0.25).

Fig. 9  Two cystic lesions in different patients. B-mode US (right) depicts homogeneously hypoechoic lesions without posterior acoustic enhancement with regular margins, (BI-RADS 2). Sonoelastography (left) shows the characteristic trilaminar (blue–green–red “BGR”) appearance of the cystic lesions (score 1).
However, glandular tissue shows various moduli depending on the compression level, whereas fat tissue shows a constant modulus over various compression loadings (31). In our study, the ROI for the reference was placed in the fat tissue at a depth similar to or as close as possible to the target mass to avoid stress decay, which is dependent on the depth of the lesion. The superficial layer under the transducer displaces more than the deep layer, so the strain value of a lesion in the superficial layer would be higher than that in the deep layer. Therefore, fat tissue located at the same depth as the target lesion would be the most adequate reference point. This was in agreement with Cho et al. (18).

The limitation of the current study is that the wide range of SR values where some malignant lesions showed low SR while some benign lesions showed high SR. This caused overlapping in the diagnoses of some benign and malignant breast lesions. However, the use of ES together with SR and also the B-mode US allowed the correct diagnosis.

5. Conclusion

Sonoelastography is a non-invasive technique with high sensitivity and specificity. The combined use of elasticity score and strain ratio of sonoelastography increased the diagnostic performance in distinguishing benign from malignant breast masses and it is recommended to be routinely applied in the evaluation of breast masses.

References


