

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

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## Role of sonoelastography and MR spectroscopy in diagnosis of solid breast lesions with histopathological correlation



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Received 10 June 2015; accepted 25 July 2015 Available online 7 August 2015

#### **KEYWORDS**

Ultrasound; Elastography; Breast; Dynamic contrast; MRI breast **Abstract** *Objective:* To demonstrate the role of ultrasound elastography and magnetic resonance spectroscopy in diagnosis of solid breast lesions with histopathological correlation.

*Patients and methods:* This study included 40 female patients, and their ages ranged from 17 to 73 years with mean age of 43.18 years. Patients were referred on the basis of suspected breast lesion and/or nipple discharge. All patients underwent elastography in addition to conventional ultrasonography and MR spectroscopy and the radiological results were correlated with histopathological examination for achieving confirmed final diagnosis.

*Results:* All benign lesions were 17 on the basis of elastography, while the malignant lesions were 18. Fifteen malignant lesions (93.7%, 15/21) had an elastography score 5, while Thirteen benign lesions (86.7%, 13/19) had an elastography score 3. On the basis of DCE-MRI, benign lesions were 16, while the malignant lesions were 19. Sixteen malignant lesions (94.1%) were diagnosed as BI-RADS 5, while fourteen benign lesions (93.3%) were diagnosed as BI-RADS 3. On the basis of MR spectroscopy, benign lesions were 17, while the malignant lesions were 19. Nineteen malignant lesions (90.5) had positive choline peak while seventeen benign lesions (89.5%) had negative choline peak. The study showed conventional ultrasound sensitivity, specificity, PPV, NPV and accuracy as 85%, 80%, 80.9%, 84.2% and 82.5% respectively, and sono-elastography sensitivity, specificity, PPV, NPV and accuracy as 90%, 85%, 85.7%, 89.4% and 87.5% respectively. Dynamic contrast enhanced MRI sensitivity, specificity, PPV, NPV and accuracy were 85.7%, 84.2% and 85% respectively, while MR spectroscopy sensitivity, specificity, PPV, NPV and accuracy were 90.4%, 89.4%, 90.4%, 89.5% and 80.5% respectively.

Conclusion: The study showed that sono-elastography and MR spectroscopy are valuable noninvasive diagnostic imaging techniques in diagnosis of early breast malignancy than any other diagnostic tools, consequently help to avoid nondesirable invasive surgical biopsy of the breast lesions.
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Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

http://dx.doi.org/10.1016/j.ejrnm.2015.07.010

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#### 1. Introduction

In the past, ultrasound was only considered useful for the diagnosis of cysts, meanwhile, diagnosis of breast cancer has been widely improved since the development of high resolution ultrasound equipments. It improves the differential diagnosis of benign and malignant lesions, local preoperative staging and guided interventional diagnosis (1). Ultrasound has long been used to distinguish between cysts and solid masses. However, solid masses are not always malignant; for example, both fibroadenomas and scirrhous carcinomas are solid and stiff, but only the latter are malignant (2). Breast elastography is a new sonographic imaging technique which provides information on breast lesions in addition to conventional ultrasonography (US) and mammography as it provides a noninvasive evaluation of the stiffness of a lesion (3). Elastography has integrated the diagnostic ability of palpation into an ultrasound instrument with a compressive probe and reflects the tissue stiffness (hardness) and elasticity in response to pressure, even in lesions that are not palpable by hand (4). Magnetic resonance imaging has shown promise in characterizing breast lesions and evaluating local extent of disease (5). Magnetic resonance spectroscopy shows excellent specificity in the detection of breast lesions. Choline is generally undetectable in normal breast tissue, and increased levels of choline compounds in a tumor are thought to be an indicator of the activity of that tumor, suggesting that it is malignant. This eliminates the need for biopsy, reduces patient morbidity, and saves unnecessary cost and time for both the patient and the medical staff (6).

The aim of the work was to demonstrate the role of ultrasound elastography and magnetic resonance spectroscopy in diagnosis of solid breast lesions with histopathological correlation.

#### 2. Patients and methods

This prospective study was performed during the period from September 2012 to January 2014 at Radiodiagnosis Department, Al-Azhar University Hospital (New Damietta) and included 40 female patients, and their ages ranged from 17 to 73 years with mean age of 43.18 years. The patients were referred from General Surgery Department, Damietta Oncology Center and also from outpatient clinics on the basis of suspected breast lesion and/or nipple discharge. Inclusion criteria were as follows: patients with solid breast lesions, and exclusion criteria were as follows: 1. Patients with nonsolid breast lesions and 2. Neoadjuvant chemotherapy or biopsy before MR examination. This study was approved by the local Ethics Committee, informed consent was taken from all patients, and then they were subjected to the following.

#### 2.1. History taking and clinical examination

#### 2.1.1. Radiological examinations

2.1.1.1. Sonoelastography examination of the breast. Using Ultrasonix, SP, Canada with a convex probe 2–5 MHz and linear probe 5–10 MHz.

The lesions were characterized using BI-RADS ultrasound descriptors of mass margin (circumscribed, obscured, microlobulated, ill-defined/indistinct or spiculated), shape

(oval, round, lobular or irregular), orientation (parallel or not parallel to the skin), matrix echogenicity and homogeneity (anechoic, hypoechoic or hyperechoic; homogeneous or heterogeneous) and attenuation (indifferent, shadowing or enhancement). Additionally, any associated findings (e.g. architectural distortion) or axillary lymphadenopathy was noted.

Elastographic diagnostic criteria were as follows: hardness of tissue is displayed in color tone, with increasing hardness presented in ascending order of red, yellow, green and blue. The hardness is scored on a scale of 1–5. Score 1 is defined as an overall green tone, whereas score 2 consists of a mosaic of green, blue and red and score 3 is presented by a blue center and green periphery. Scores 1–3 represent benign findings. Score 4 is defined as an almost blue color consistent with a hypoechoic region and score 5 as a definite blue color beyond that of a hypoechoic region. Malignant findings are represented by score 4 and score 5.

### 2.1.1.2. Dynamic MRI and MRS of the breast. Using MRI machine (Philips, Achieva 1.5 Tesla-XR-Netherlands 2010).

Technical considerations of dynamic MRI for the breast scanning protocol:

- 1. Patient preparation and position
  - The patients were instructed not to have any metallic objects such as cardiac pace makers and ocular implants.
  - Patients were instructed to avoid motions.
  - Patients were imaged in prone position with breasts hanging dependently within phased array breast coil.
  - The ideal time for examination was 4–17 days from first day of menstrual cycle "less dense stroma and lower breast water content" and the average scan time was 30–45 min.

#### 2. MRI imaging protocol

A. Initial scout views in axial, coronal and sagittal planes of both breasts to verify the precise position of the lesion.

*B. T1-weighted pulse sequence:* Nonfat saturated T1 WI was obtained by turbo spin echo (TSE) with the following parameters: Repetition time (TR): 450 ms, Echo time (TE): 14 ms, Number of signal averages (NSA): 1, slice thickness/interslice gap: 3 mm/0.0, field of view (FOV): 300-360 mm, flip angle:  $90^\circ$ , matrix was  $307 \times 512$  and acquisition time: 1.43 min.

*C. T2-weighted pulse sequence:* Nonfat saturated T2 WI was obtained by TSE with the following parameters: TR: 4 ms, TE: 120 ms, NSA: 1, slice thickness/interslice gap: 3 mm/0.0, FOV: 300–360 mm, flip angle: 90°, matrix was  $307 \times 512$  and acquisition time: 1.17 min.

D. Spectral attenuated inversion recovery (SPAIR) (Fat Sat.): SPAIR was obtained with the following parameters: TR: 13 ms, TE: 70 ms, inversion delay: 80 ms, NSA: 2, slice thickness/interslice gap: 3 mm/0.0, FOV 300–360 mm, flip angle: 90°, matrix was  $307 \times 512$  and acquisition time: 2.32 min.

*E. Dynamic study*: This study was obtained using a T1 weighted sequence with fat suppression dynamic. The dynamic imaging consisted of 6 individual dynamic series each lasting for 1:25–1:27 min; one was obtained before and five after rapid bolus intravenous injection of gadopentetate dimeglumine at a

**Table 1**Dynamic breast MRI pulse sequence parameters.

| Parameters              | Sequences        |                  |                  |                                 |  |  |  |
|-------------------------|------------------|------------------|------------------|---------------------------------|--|--|--|
|                         | T1 WI            | T2 WI            | SPAIR            | Dynamic<br>(THRIVE)             |  |  |  |
| Repetition<br>time (TR) | 450 ms           | 4 ms             | 13 ms            | 8 ms                            |  |  |  |
| Echo time<br>(TE)       | 14 ms            | 120 ms           | 70 ms            | 2 ms                            |  |  |  |
| Field of view (FOV)     | 320 × 320        | 320 × 320        | 320 × 320        | 320 × 320                       |  |  |  |
| Slice<br>thickness      | 3 mm             | 3 mm             | 3 mm             | 2 mm                            |  |  |  |
| Interslices gap         | 0 mm             | 0 mm             | 0 mm             | 0 mm                            |  |  |  |
| Matrix                  | $307 \times 512$ | $307 \times 512$ | $307 \times 512$ | 307 × 512                       |  |  |  |
| Flip angle              | 90°              | 90°              | 90°              | 20–25°                          |  |  |  |
| NSA                     | 1                | 1                | 2                | 3                               |  |  |  |
| Acquisition<br>time     | 1.43 min         | 1.17 min         | 2.32 min         | 1.25 min/1<br>individual series |  |  |  |

 Table 2
 Distribution of patients regarding lactation.

| State of patient   | Count | Percent (%) |
|--------------------|-------|-------------|
| Nonlactating cases | 37    | 92.5        |
| Lactating cases    | 3     | 7.5         |
| Total              | 40    | 100         |

| Table 3 1   | Distribution | bution of patients regarding menopausal state |             |  |  |  |  |
|-------------|--------------|-----------------------------------------------|-------------|--|--|--|--|
|             |              | Count                                         | Percent (%) |  |  |  |  |
| Perimenopa  | usal         | 6                                             | 15          |  |  |  |  |
| Postmenopa  | ausal        | 21                                            | 52.5        |  |  |  |  |
| Childbearin | ıg           | 13                                            | 32.5        |  |  |  |  |
| Total       |              | 40                                            | 100         |  |  |  |  |

**Table 4**Distribution of patients regarding hormonal replacement therapy (HRT) intake.

|             | Count | Percent (%) |  |  |
|-------------|-------|-------------|--|--|
| Without HRT | 30    | 75          |  |  |
| With HRT    | 10    | 25          |  |  |
| Total       | 40    | 100         |  |  |

dose of 0.1 mmol per kilogram of body weight, followed by a 20 mL sterile saline solution flush. After the dynamic series, image subtraction was done to suppress the signal from fat. The used MRI pulse sequence parameters are detailed in Table 1 (see Tables 2–5).

F. MRS acquisition: A single-voxel <sup>1</sup>H MRS was performed using a point-resolved spectroscopy sequence (PRSS), and the proton signals are converted into frequency information on the spectrum. According to the American College of Radiology BI-RADS-MRI lexicon, suspicious malignant lesions were diagnosed on the basis of the morphological features of the mass such as spiculated borders, microlobulated margins, irregular masses and breast stroma architectural distortion. Benign breast lesions were diagnosed based on their morphological feature (smooth masses of well defined borders and absence of surrounding breast stroma architectural distortion). Time-signal intensity plots of dynamic images were generated using console software. A small region of interest (ROI > 3 pixels) was placed selectively over the most intensely enhancing area of the lesion. The evaluation of enhancement kinetic curve was based on initial phase (within the first 2 min or when the curve starts to change), and late phase (after 2 min or after the change). The initial enhancement phase was categorized into fast, medium, and slow. The late enhancement phase was described as persistent, plateau, and washout. A spectrum was considered "positive" for choline if there was a well-defined peak at 3.2 ppm. The MRS result was considered "negative" if there was no peak at 3.2 ppm with appearance of adequate lipid suppression and shimming.

#### 2.2. Histopathological study

The definitive diagnosis was provided by histopathological examination of the biopsied tissue using fine needle, core or surgical biopsies or surgical excision. All radiological

 Table 5 Distribution of patients regarding complaint and clinical signs.

| Patient complaint            | Count | Percent (%) |
|------------------------------|-------|-------------|
| Painless breast lump         | 28    | 70          |
| Painful breast lump          | 6     | 15          |
| Nipple discharge             | 4     | 10          |
| Palpable axillary lymph node | 2     | 5           |
| Total                        | 40    | 100         |

examination results were compared with histopathological results, and the latter was regarded as the standard reference.

#### 2.3. Statistical analysis

The collected data were organized, tabulated and statistically analyzed, using statistical package for social science (SPSS) version 19 (SPSS Inc, Chicago, USA), running on IBM compatible computer with Microsoft Windows 7 operating System. Mean, standard deviation, frequency and percentage were used as descriptive; Chi square test ( $\chi^2$ ) was used for testing significance of observed differences between studied patients. The level of significance was adopted at p < 0.05%. Sensitivity, specificity, positive predictive value, negative

| Diagnosis          | Ultras | Ultrasound BI-RADS classes |         |        |           |            |                        |  |
|--------------------|--------|----------------------------|---------|--------|-----------|------------|------------------------|--|
|                    | 1      | 2                          | 3       | 4      | 5         | US results | Histopathology results |  |
| Benign, n (%)      | 0      | 0                          | 16 (80) | 2 (40) | 1 (6.7)   | 16         | 19                     |  |
| Malignant, $n$ (%) | 0      | 0                          | 4 (20)  | 3 (60) | 14 (93.3) | 17         | 21                     |  |
| Total              | 0      | 0                          | 20      | 5      | 15        |            | 40                     |  |

Table 6 Distribution of benign and malignant solid breast lesions for each ultrasound BI-RADS class compared with histopathological results.

**Table 7** Distribution of benign and malignant solid breast lesions for each elastography color scoring compared with histopathological results.

| Diagnosis          | Elast | Elastography score |           |        |           |                    |                        |  |  |
|--------------------|-------|--------------------|-----------|--------|-----------|--------------------|------------------------|--|--|
|                    | 1     | 2                  | 3         | 4      | 5         | Elastography score | Histopathology results |  |  |
| Benign, n (%)      | 0     | 4 (80)             | 13 (86.7) | 1 (25) | 1 (6.3)   | 17                 | 19                     |  |  |
| Malignant, $n$ (%) | 0     | 1 (20)             | 2 (13.3)  | 3 (75) | 15 (93.7) | 18                 | 21                     |  |  |
| Total              | 0     | 5                  | 15        | 4      | 16        |                    | 40                     |  |  |

Table 8 Distribution of benign and malignant solid breast lesions for each DCE-MRI BI-RADS class compared with histopathological results.

| Diagnosis        | DCE | DCE-MRI BI-RADS classes |           |        |           |                 |                        |  |  |
|------------------|-----|-------------------------|-----------|--------|-----------|-----------------|------------------------|--|--|
|                  | 1   | 2                       | 3         | 4      | 5         | DCE-MRI results | Histopathology results |  |  |
| Benign, $n$ (%)  | 0   | 2 (66.7)                | 14 (93.3) | 2 (40) | 1 (5.9)   | 16              | 19                     |  |  |
| Malignant, n (%) | 0   | 1 (33.3)                | 1 (6.7)   | 3 (60) | 16 (94.1) | 19              | 21                     |  |  |
| Total            | 0   | 3                       | 15        | 5      | 17        |                 | 40                     |  |  |

| Table 9  | Choline | results | compared | with | histopathological |  |
|----------|---------|---------|----------|------|-------------------|--|
| results. |         |         |          |      |                   |  |

| Diagnosis          | Choline results |           |                             |                                       |  |  |
|--------------------|-----------------|-----------|-----------------------------|---------------------------------------|--|--|
|                    | Negative        | Positive  | Total<br>choline<br>results | Total<br>histopathological<br>results |  |  |
| Benign, n (%)      | 17 (89.5)       | 2 (9.5)   | 17                          | 19                                    |  |  |
| Malignant, $n$ (%) | 2 (10.5)        | 19 (90.5) | 19                          | 21                                    |  |  |
| Total              | 19              | 21        |                             | 40                                    |  |  |

predictive value and accuracy were used as measurements of validity for MRI regarding histopathological results.

#### 3. Results

Forty female patients were included in this study, their ages ranged from 17 to 73 years (mean age 43.18 y), three patients were lactating and 37 patients were non-lactating. Twenty-eight cases presented clinically by painless breast lump (70%), six cases with painful breast lump (15%), four cases with nipple discharge (10%) and two cases with palpable axillary lymph nodes (5%).

In this study, there were 30 cases with no history of hormonal intake but 10 cases received oral HRT. Among them, 8 patients postmenopausal received oral HRT in the form of estradiol and 2 cases received oral contraceptive pills.

Twenty-eight cases presented clinically by painless breast lump (70%), six cases with painful breast lump (15%), four cases with nipple discharge (10%) and two cases with palpable axillary lymph nodes (5%).

On the basis of sonographic BI-RADS categorization, our cases were classified as follows: (20 cases) class 3, (5 cases) class 4 and (15 cases) class 5. No case was assigned to class 0, 1, 2 or 6 (Table 6).

All benign lesions diagnosed by ultrasound were 16, while the malignant lesions were 17. Fourteen malignant lesions (14/21, 93.3%) were diagnosed BI-RADS 5, and sixteen benign lesions (16/19, 80%) were diagnosed BI-RADS 3.

On the basis of elastographic color scoring categorization, our cases were classified as follows: 5 cases (score 2), 15 cases (score 3), 4 cases (score 4) and 16 cases (score 5) (Table 7) (see Tables 8–10).

All benign lesions diagnosed by elastography were 17, while the malignant lesions were 18. Fifteen malignant lesions (15/21, 93.7%) had an elastography score 5. Thirteen benign lesions (13/19, 86.7%) had an elastography score 3 (see Figs. 1–3).

On the basis of MRI BI-RADS categorization, our cases were classified as follows: (3 cases) class 2, (15 cases) class 3,

Table 10Conventional ultrasound, ultrasound elastography, DCE-MRI and MRS sensitivity, specificity, PPV, NPV and accuracy indiagnosis of solid breast lesions.

| Examination                             | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|-----------------------------------------|-----------------|-----------------|---------|---------|--------------|
| Conventional ultrasound                 | 85              | 80              | 80.9    | 84.2    | 82.5         |
| Ultrasound elastography                 | 90              | 85              | 85.7    | 89.4    | 87.5         |
| Dynamic contrast enhanced MRI (DCE-MRI) | 85.7            | 84.2            | 85.7    | 84.2    | 85           |
| MRI spectroscopy                        | 90.4            | 89.4            | 90.4    | 89.5    | 80.8         |



Fig. 1 Chart represents the included patients according to complaints/clinical signs.

(5 cases) class 4 and (17 cases) class 5. No case was assigned to class 0, 1 or 6 (Fig. 4) (see Figs. 5–7).

All benign lesions diagnosed by DCE-MRI were 16, while the malignant lesions were 19. Sixteen malignant lesions (94.1%) were diagnosed BI-RADS 5, while fourteen benign lesions (93.3%) were diagnosed BI-RADS 3.

All benign lesions diagnosed by MRI spectroscopy were 17, while the malignant lesions were 19. Nineteen malignant lesions (90.5) had positive choline peak, while seventeen (89.5%) benign lesions had negative choline peak.

In this study the conventional ultrasound sensitivity, specificity, PPV, NPV and accuracy were 85%, 80%, 80.9%, 84.2% and 82.5% respectively. Ultrasound elastography sensitivity, specificity, PPV, NPV and accuracy were 90%, 85%, 85.7%, 89.4% and 87.5% respectively. Dynamic contrast enhanced MRI sensitivity, specificity, PPV, NPV and accuracy were 85.7%, 84.2%, 85.7%, 84.2% and 85% respectively. MRS sensitivity, specificity, PPV, NPV and accuracy were 90.4%, 89.4%, 90.4%, 89.5% and 80.5% respectively.

#### 4. Discussion

Regarding the patients demography, there were 40 patients included in our study. The mean age of the patients was 43.18 years (range of age, 17–73 years).

Many studies showed that the age at diagnosis of breast cancer in Arab countries is a decade younger than that in Western countries. In the United States, the median age at presentation for breast cancer is 61 years, compared to 50– 54 years in Egypt (7). Boivin et al. (8) stated that sonography remains efficient in the diagnosis of masses. In addition to their diagnosis and characterization, it allows indispensable guided biopsies or monitoring of their evolution during neoadjuvant chemotherapy. The sonographic semiology of the masses does not seem to change during lactation. The MRI has its own semiology during lactation, related to the physiological changes. Even so, it remains efficient, allowing satisfactory detection according to the BI-RADS classification of tumors by the American College of Radiology (ACR). Also Iman et al. (9) mentioned that MRI breast should be used for



Fig. 2 Chart showing ultrasound BI-RADS correlated to histopathological results.



Fig. 3 Chart showing elastography score correlated to histopathological results.

undetermined cases and for staging of malignancy. Among the patients in this study, 3 cases (7.5%) were lactating.

Age at menopause has long been identified as a risk factor for breast cancer (10). Early menarche and late menopause are known to increase women's risk of developing breast cancer (11). The menopausal state is an important differentiating factor in the classification of patients with breast cancer. Instead of classifying by age, women with breast cancer are separated into either pre- or postmenopause (12). Among the patients of this study, 21 cases (52.5%) were postmenopausal.

In our study, ten patients received hormonal therapy (HT). Several studies have shown that the prognosis of HRT associated breast cancers is more favorable than that without HRT. This may be due to their greater hormone dependency, earlier diagnosis, lower tumor grades, better cooperation and surveillance of the patients or other yet unidentified factors. Although the studies showed an increased risk of breast cancer among women taking HRT, the same patients survived longer than women with breast cancer who did not take HRT (13).

The risk of breast cancer depends on duration of hormonal therapy (HT) use, and is reduced after cessation of use, leveling off after 5 years since quitting HT (14). The most presenting complaint was painless breast lump which represented 28 cases (70%) as breast mass was the most commonly reported first symptom. Furthermore, the development or increase in breast



Fig. 4 Dynamic MRI breast BI-RADS correlated with histopathological results.

mass size was the main cause for seeking medical care in threequarters of the patients (15).

Introduction of BI-RADS has provided a standardized ultrasound categorization system for lesion morphology. It has been successfully established in the interpretation of ultrasonography. Because the sonographic features of benign and malignant lesions have been shown to over-ride largely with each other, there are many false-negative and false-positive findings. These limitations of BI-RADS, and great desire not to miss a malignant lesion in the early stage of disease lead to an aggressive biopsy. The biopsy rate for cancer is only 10-30%. This means that 70-90% of breast biopsies are performed with benign diseases, which induce unnecessary patient discomfort and anxiety besides increasing financial cost of the patient. Clearly, there is a great need for the development of additional reliable methods to complement the existing diagnostic procedures to avoid unnecessary biopsy. Elastography is a new modality in addition to US to detect and identify the breast lesions. It can show another characteristic stiffness of the lesion to the investigator and give some help in diagnosis of breast lesions by US (16).

On the basis of sonographic BI-RADS categorization, our cases were classified as follows: (20 cases) class 3, (5 cases) class 4 and (15 cases) class 5. The conventional ultrasound sensitivity in diagnosis of solid breast lesions was 85% and it was lower than results of the literature by Leong et al. (17) in which the sensitivity was 88.5%, while the specificity and accuracy were 80% and 82.5% respectively and they were higher than the results of the literature by Leong et al. (17) in which specificity and accuracy were 42.5% and 53.6% respectively. The histopathological results revealed 19 benign lesions and 21 malignant lesions.

On the basis of elastography score categorization, our cases were classified as follows: (5 cases) score 2, (15 cases) score 3, (4 cases) score 4 and (15 cases) score 5. In this study, the ultrasound elastography sensitivity, specificity, PPV, NPV and accuracy were 90%, 85%, 85.7%, 89.4% and 87.5% respectively. Sonoelastography was useful for differentiating between benign and malignant lesions by evaluation of tissue elasticity and hardness.

Generally, the elasticity of pathological tissue changes and most of malignant tumors are constituted with hard lesion,



(G) Dynamic THRIVE (Subtraction)

(H) Time Intensity Curve

(I) MRI spectroscopy

**Fig. 5** 62 years-old female with right breast lumps. US showed multiple speculated lesions with heterogeneous hypoechogenicity (A). Elastography showed the lesions and the surrounding area blue with elastography score 5 (B). MRI showed multicentric ill-defined speculated lesions, low signal in T1 and T2 WIs (C), (D) and (E). Asymmetrical enlargement of right pectoralis muscle with abnormal intrasubstance signal (C) and (D). Dynamic study showed heterogenous enhancement of all lesions with type III intensity curve pattern (rapid washout) (F), (G) and (H). Single voxel MRS revealed positive choline peak (I). MRI diagnosis: multicentric malignant lesions (BI-RADS V). Histopathological result: Multicentric Intraductal Carcinoma (IDC).

adhered to adjacent structure, which decreases activity and elasticity and therefore increases hardness (18). Based on the results of this study, we can estimate the diagnostic value of elastography because a good correlation was found between the elastography scores and the histology results. In our study, the PPV of elastography was 85.7%, lower than results from the literature by Houelleu et al. (19) who showed PPV 91.9%, and higher than results from the literature by Sahar

and Omar (20) who showed PPV 70.6%. The NPV of elastography was 89.4%, higher than results found in a study by Houelleu et al. (19) in which the NPV was 61.3%.

The sensitivity of elastography in diagnosis of solid breast lesions was 90%, lower than results from the literature by Leong et al. (17) in which sensitivity was 100%, and slightly lower than results from the literature by Sahar and Omar (20) in which the sensitivity was 92.3%. The sensitivity of



(D) T2 WI

(E) T2 SPAIR



(F) Dynamic THRIVE (contrast)



(G) Dynamic THRIVE (Subtraction)

(H) Time Intensity Curve

(I) MRI spectroscopy

38 years-old female with right breast well defined oval shaped lesion. US showed homogeneous hypoechoic echo pattern with no Fig. 6 calcification or cystic degeneration (A). Elastography showed the lesion has mosaic pattern of green, blue and red, giving an elastography score 2 (B). MRI showed low signals in T1 and intermediate signals in T2 WIs (C) and (D). Dynamic study showed homogeneous enhancement of the lesion with type I intensity curve pattern (persistent curve) (F), (G) and (H). Single voxel MRS showed no evidence of choline peak detected at the spectrum (I). MRI diagnosis: benign lesion (BI-RADS III). Histopathological result: Myxoid Fibroadenoma.

elastography was also higher than results from the literature by Houelleu et al. (19), Yerli et al. (21) and Qiao et al. (18) in which sensitivity were 73.9%, 80% and 84.2% respectively.

The specificity of elastography was 85% and looks lower than results from the literature by Yerli et al. (21) in which specificity was 95%, and slightly lower than results from the literature by Houelleu et al. (19) in which the specificity was 86.4%. The specificity of elastography was also higher than results from the literature by Sahar and Omar (20), Leong et al. (17) and Qiao et al. (18) in which specificity was 74.1%, 73.8% and 84.6% respectively. The accuracy of elastography was 87.5%, higher than results from the literature by Leong et al. (17) in which accuracy was 80%.

Dynamic contrast enhanced (DCE) magnetic resonance imaging (MRI) is an established technique for detection, diagnosis and staging of breast cancer. However, it has an



(G) Dynamic THRIV (Subtraction)

**Fig. 7** 32 years-old female with right breast lesion. US showed heterogeneous hypoechoic pattern (A). Elastography showed the lesion in blue with score 4 (B). MRI showed ill-defined speculated lesion, low signals in T1 and intermediate signals in T2 WIs (C), (D) and (E). The lesion showed invasion of suspensory ligament with subsequent nipple retraction and subjacent focal skin thickening. Focal bulge in the pectoralis major muscle suspected infiltration. Dynamic study showed heterogenous enhancement of the lesion with type III intensity curve pattern (F), (G) and (H). Single voxel MRS revealed positive choline peak (I). MRI diagnosis: malignant lesion with pectoralis muscle infiltration (BI-RADS V). Histopathological result: intraductal carcinoma (IDC) with muscle invasion.

inherently high sensitivity but only moderate specificity for characterization of breast lesions. The standard breast imaging protocol enables the analysis of the morphological and kinetic patterns of benign and malignant breast lesions detected at MRI (Tan et al. (22)).

On the basis of MRI BI-RADS categorization, our cases were classified as follows: (3 cases) class 2, (15 cases) class 3, (5 cases) class 4 and (17 cases) class 5, and showed DCE-MRI sensitivity, accuracy, PPV and NPV of 85.7%, 85%, 85.7% and 84.2% respectively, which is lower than results of the literature by Pinker et al. (23) in which the sensitivity, accuracy, PPV and NPV were 97.6%, 89.8%, 89.1% and 92.3% respectively. The specificity was 84.2% and it was higher than results of the literature by Pinker et al. (23) in which specificity was 70.6%. Regarding MRI spectroscopy, there were 19 malignant lesions with positive choline peak in contrast with 17 benign lesions with negative choline peak.

Suppiah et al. (24) stated that, in a study conducted using 1.5 T MR systems reported the presence of the resonance of total choline (tCho) containing compounds at 3.2 parts per million (ppm), which includes contributions from choline, phosphocholine, glycerophosphocholine and taurine as reliable biomarkers of breast cancer. This is because choline-containing metabolites detected in breast lesions are an indicator of the increased cellular metabolism noted in malignant breast tumors. In our study the sensitivity of MRI spectroscopy was 90.4%, which is lower than results from the literature by Suppiah et al. (24) and Naglaa et al. (25) in which sensitivity was 95.2% and 96.7% respectively. The sensitivity of MRI spectroscopy was also higher than results from the literature by Katerina et al. (26) and Pascal et al. (27) in which sensitivity was 80% and 62% respectively.

In this study the specificity of MRI spectroscopy was 89.4%, which is lower than results from the literature by Suppiah et al. (24) and Naglaa et al. (25) in which specificity was 93.3% and 95.5% respectively. The specificity of MRI spectroscopy was also higher than results from the literature by Katerina et al (26) and Pascal et al. (27) in which specificity was 81.8% and 86% respectively. The PPV of MRI spectroscopy was 90.4%, so it is lower than results from the literature by Suppiah et al. (24) in which PPV was 97.6%, and slightly higher than results from the literature by Pascal et al. (27) in which the PPV was 90%. The NPV of MRI spectroscopy was 89.5.4% and looks higher than results from the literature by Suppiah et al. (24) in which PPV was 87.2%. The accuracy of MRI spectroscopy was 80.8% and looks slightly higher than results from the literature by Katerina et al. (26) in which accuracy was 80.7%.

Regarding our study, there were a few limitations of elastography as follows:

First, this was a relatively small study where the number of malignant cases was small. A larger pool of malignancies is required to assess "soft" tumours, such as mucinous carcinomas, cancers that do not incite significant desmoplastic reaction (e.g. invasive lobular carcinoma), and tumors with central necrosis or solid-cystic complex appearance, all of which can elicit a benign appearance on elastographic scoring system because of their soft interiors.

Second, ultrasound elastography, as with most ultrasound applications, is user-dependent. The amount of pressure to be applied on the breast when performing elastography, the recognition of the various elastographic patterns and the measurement techniques were some of the areas that were subjective and these limitations were also mentioned by Leong et al. (17).

As regards MRS limitations, some lesions that had erratic spectra due to technical problems (i.e. patient breathing/movement artefacts, susceptibility artefacts due to field inhomogeneity, and inability to perform proper high-order shimming for certain lesions) were also excluded. It would have also been better to perform MRS for normal tissue on the non-lesion containing breast, as the peritumoral environment could influence the tCho measurements and this was in accordance with Suppiah et al. (24).

#### **Conflict of interest**

No conflict of interest.

#### References

- Madjar H. Role of breast ultrasound for the detection and differentiation of breast lesions. Breast Care J 2010;5(2):109–14.
- (2) Selvan S, Kavitha M, Shenbagadevi S, Suresh S. Feature extraction for characterization of breast lesions in ultrasound echography and elastography. J Comput Sci 2010;6(1):67–74.
- (3) Goddi A, Bonardi M, Alessi S. Breast elastography: a literature review. J Ultrasound 2012;15(3):192–8.
- (4) Sadigh G, Carlos RC, Neal CH, Dwamena BA. Ultrasonographic differentiation of malignant from benign breast lesions: a metaanalytic comparison of elasticity and BIRADS scoring. Breast Cancer Res Treat 2012;133(1):23–35.
- (5) Gavenonis SC, Roth SO. Role of magnetic resonance imaging in evaluating the extent of disease. Magn Reson Imag Clin North Am 2010;18(2):199–206.
- (6) Mitsushiro T, Proton MR. Spectroscopy of the breast. J Breast Cancer 2008;15(3):218–23.
- (7) Nelly HA, Omnia MA, Dalia B, Salem ES, Eman G, Magda E, et al. Age at diagnosis in women with non-metastatic breast cancer: is it related to prognosis? J Egypt Natl Cancer Inst 2014;26(1):23–30.
- (8) Boivin G, de Korvin B, Marion J, Duvauferrier R. Is a breast MRI possible and indicated in case of suspicion of breast cancer during lactation? Diagn Interv Imag 2012;93(11):823–7.
- (9) Iman AH, Lamia AS, Hamed SE. Radiological evaluation of palpable breast masses during pregnancy and lactation. Egypt J Radiol Nucl Med 2011;42(2):267–73.
- (10) Rosner B, Colditz GA. Age at menopause: imputing age at menopause for women with a hysterectomy with application to risk of postmenopausal breast cancer. Ann Epidemiol 2011;21(6):450–60.
- (11) Beral VE, Bull DJ, Pirie KL, Reeves GK, Peto R. Menarche menopause and breast cancer risk individual participant meta analysis including 118964 women with breast cancer from 117 epidemiological studies. J Lancet Oncol 2012;13(11):1141–51.
- (12) Moffat RE, Eichholzer M, Myrick ME, Schmid SM, Raggi A, de Geyter C, et al. Menopausal state in breast cancer: how reliable is the data? Clin Breast Cancer 2011;11(6):390–4.
- (13) Manfred D. Hormone replacement therapy (HRT), breast cancer and tumor pathology. Maturitas J 2010;65(3):183–9.
- (14) Claudio P, Fabio L, Carlo LV. The rise and fall in menopausal hormone therapy and breast cancer incidence. Breast 2010;19(3):198–201.
- (15) Shimaa MM, Ibrahim AS, Ahmed H, Eman SE, Amr SS. Patterns of seeking medical care among Egyptian breast cancer patients: relationship to late-stage presentation. Breast 2011;20(6):555–61.
- (16) Zhi H, Xiao XY, Ou B, Zhong WJ, Zhao ZZ, Zhao XB, et al. Could ultrasonic elastography help the diagnosis of small (≤2 cm) breast cancer with the usage of sonographic BI-RADS classification? Eur J Radiol 2012;81(11):3216–21.
- (17) Leong LC, Sim LS, Lee YS, Ng FC, Wan CM, Fook-Chong SM, et al. A prospective study to compare the diagnostic performance of breast elastography versus conventional breast ultrasound. Clin Radiol 2010;65(11):887–94.
- (18) Qiao LZ, Li TR, Hua Z, Yi MY, Shao XD. Diagnosis of solid breast lesions by elastography 5-point score and strain ratio method. Eur J Radiol 2012;81(11):3245–9.

- (19) Houelleu ML, Monghal C, Bertrand P, Vildé A, Brunereau L. An assessment of the performance of elastography for the investigation of BI RADS 4 and BI-RADS 5 breast lesions: correlations with pathological anatomy findings. Diagn Interv Imag 2012;93(10):757–66.
- (20) Sahar MM, Omar SO. Elastography ultrasound and questionable breast lesions: does it count? Eur J Radiol 2012;81(11):3234–44.
- (21) Yerli H, Yilmaz T, Kaskati T, Gulay H. Qualitative and semiquantitative evaluations of solid breast lesions by sonoelas-tography. J Ultrasound Med 2011;30(2):179–86.
- (22) Tan SL, Rahmat K, Rozalli FI, Mohd-Shah MN, Aziz YF, Yip CH, et al. Differentiation between benign and malignant breast lesions using quantitative diffusion weighted sequence on 3 T MRI. Clin Radiol 2014;69(1):63–71.
- (23) Pinker K, Bickel H, Helbich TH, Gruber S, Dubsky P, Pluschnig U, et al. Combined contrast-enhanced magnetic resonance and diffusion weighted imaging reading adapted to the "Breast Imaging Reporting and Data System" for multiparametric 3-T imaging of breast lesions. Eur Radiol 2013;23(7):1791–802.

- (24) Suppiah S, Rahmat K, Mohd-Shah MN, Azlan CA, Tan LK, Aziz YF, Yip CH, et al. Improved diagnostic accuracy in differentiating malignant and benign lesions using single-voxel proton MRS of the breast at 3 T MRI. Clin Radiol 2013;68(9):e502–10.
- (25) Naglaa MA, Amr OA, Omar SO, Hussein OS. Role of proton MR spectroscopy in the high field magnet (3T) in diagnosis of indeterminate breast masses (BIRADS 3 & 4). Egypt J Radiol Nucl Med 2012;43(4):657–62.
- (26) Katerina V, Ioannis T, Evanthia K, Marianna V, Evaggelos A, Kiriaki T, et al. Application value of 3T 1H-magnetic resonance spectroscopy in diagnosing breast tumors. Acta Radiol 2013;54(4):380–8.
- (27) Pascal A, Baltzer T, Alexander G, Matthias D, Reinhard R, Mieczyslaw G, et al. Effect of contrast agent on the results of in vivo 1H MRS of breast tumors – is it clinically significant? NMR Biomed 2011;25(1):67–74.