

RESEARCH

Open Access



The diagnostic accuracy of diffusion-weighted magnetic resonance imaging and shear wave elastography in comparison to dynamic contrast-enhanced MRI for diagnosing BIRADS 3 and 4 lesions

Rasha Wessam Abdel Rahman^{1,2*}, Reham Mohammed Abd ElHai Refaie^{1,2}, Rasha Mohammed Kamal^{1,2}, Shaimaa Farouk Lasheen³ and Dalia Salaheldin Elmesidy^{1,2}

Abstract

Background: Breast cancer is one of the leading causes of female morbidity and mortality. Management options vary between lesions of BIRADS categories 3 and 4. Therefore, reliable differentiation would improve outcome. Although sonomammography and contrast-enhanced breast magnetic resonance imaging (CE-MRI) remain the cornerstone for assessment of breast disease, additional, non-invasive techniques can be used to increase the efficiency of evaluation such as shear wave elastography (SWE) and diffusion-weighted magnetic resonance imaging (DW-MRI). This prospective study included 66 breast lesions that were categorized as BIRADS 3 or 4 by ultrasound \pm mammography. All lesions were evaluated by SWE, CE-MRI and DW-MRI. For SWE, lesions were evaluated by both qualitative and quantitative methods. For CE-MRI, both morphological and kinematic evaluations were done and for DW-MRI, both qualitative and quantitative assessments were studied. Results of all imaging modalities were correlated to histopathology.

Results: Thirty-seven out of the examined 66 lesions (56.06%) were categorised as BIRADS 3, out of which 1 (2.7%) turned out to be malignant on histopathology and 36 (97.29%) were proved benign. Twenty-nine (43.93%) were categorized as BIRADS 4, out of which 2 (6.89%) turned out to be benign on pathology and 27 (93.1%) were proved malignant. Morphological and kinematic evaluations of CE-MRI showed 92.59% and 92.86% sensitivity, 94.74% and 84.21% specificity, 92.59 and 81.25% PPV, 94.74 and 94.12% NPV, and 93.85% and 87.88% accuracy respectively. Color-coded scoring of SWE showed indices of 89.29%, 68.42%, 67.57%, 89.66%, and 77.27% respectively. The calculated cut-off value for E_{max} differentiating benign from malignant was 65.15 kpa, resulting in indices of 96.43%, 57.89%, 95.65%, 62.79%, and 74.24% respectively. For E_{ratio} , the calculated cut-off value was 4.55, resulting in indices of 71.43%, 68.42%, 76.47%, 62.50% and 69.70% respectively. For qualitative evaluation of DW-MRI, indices were 78.57%, 65.79%, 62.86%, 80.65%, and 71.21% respectively. For ADC, the calculated cut-off value was $1.25 \times 10^3 \text{ mm}^2/\text{s}$, which resulted in indices of 75.00%, 84.21%, 82.05%, 77.78%, and 80.30% respectively.

*Correspondence: rashakao@yahoo.com

¹ Department of Diagnostic and Interventional Radiology, Faculty of Medicine, Cairo University, 1 Kasr Elainy Street Fom Elkalig, Cairo, Egypt
Full list of author information is available at the end of the article

Conclusion: CE-MRI showed the best diagnostic performance indices. While, SWE and DW-MRI present variable diagnostic performance, both techniques can be used as an adjunct to other imaging modalities to aid the clinical decision and increase its diagnostic confidence.

Keywords: Shear wave elastography, Diffusion weighted magnetic resonance imaging, Contrast enhanced magnetic resonance imaging

Background

Breast cancer is a major cause of female morbidity and mortality [1]. Sonomammography (SMG) is the gold standard for evaluation of breast cancer. However, adding other non-invasive modalities to the assessment may improve the efficiency of evaluation of breast disease.

Elastography (either shear wave or strain) is one of the technical advances of ultrasound (US) that can be utilised to non-invasively evaluate the stiffness of a certain lesion and consequently assess its potential of malignancy [2]. Shear wave elastography (SWE) records the velocity of a shear wave during the excitation of an acoustic radiation force, producing both an elastography color-coded map and a quantitative measurement of the stiffness of tissues [3].

Diffusion-weighted magnetic resonance imaging (DW-MRI) is a non-contrast enhanced technique of magnetic resonance imaging that utilizes water molecule microscopic motion to produce an image and is reported to have the potential of differentiating malignant from benign tissue, both qualitatively (via visually detecting the signal of a lesion) or quantitatively (via measuring apparent diffusion coefficient-ADC) [4].

The objective of this study was to evaluate the additive value of using either SWE or DW-MRI in differentiating lesions categorized as BIRADS 3 or 4, both being non-invasive techniques that can be utilized in the preoperative setting in the clinical decision making. BIRADS 3 and 4 lesions are of particular clinical concern where they commonly present a clinical dilemma due to the considerable overlap of some of their radiologic features, especially that management options differ greatly between both categories.

Methods

This study included 66 lesions from 66 female patients who presented to the breast clinic of our institution during the period from January 2018 to January 2020 with variable breast complaints, including palpable lumps (either breast or axillary), mastalgia and nipple discharge. Their ages ranged from 30 to 68 years (mean age = 44.76 ± 11.52 SD). For each patient, we included a single lesion that was characterised as either BIRADS 3 (probably benign) or BIRADS 4 (probably malignant) based on US \pm mammography. We excluded breast

lesions that were categorized as BIRADS 1, 2 and 5 on SMG. We also excluded those with contraindications to contrast media administration (such as pregnancy or major renal impairment) and those with a general contraindication to magnetic resonance imaging (such as pacemakers, cochlear implants, claustrophobia, etc.).

All patients provided informed written consent to participate in the study and our institutional ethics committee approval was obtained. Patients were subjected to demographic and clinical data collection including name, age, marital status, number of offsprings, residence, phone number, duration of illness, past history and family history.

Patients were primarily examined by SMG (59 patients) or conventional US only (7 patients) if they were below 35 years of age. All patients were then subjected to evaluation by SWE, contrast-enhanced magnetic resonance imaging (CE-MRI) of the breast and DW-MRI.

Technique of SWE examination

The study was carried out using a GE LOGIQ E9 XDclear ultrasound machine that has a linear multi-frequency probe that operates at 9 and 15.8 MHz.

A clear B-mode image was acquired. The examined lesion was assessed for SWE color-coded images utilizing a modulated scoring system that relies on the percentage of stiff areas within it [5]. Scores for SWE were recorded on a scale of 1–4 according to the patterns of the elastogram. Lesions almost totally occupied by blue colour scored as 1, those with blue colour occupying more than 50% scored as 2, those with red colour occupying more than 50% scored as 3, while those almost totally occupied by red colour scored as 4. Lesions scoring 1 or 2 were considered as benign whereas those scoring 3 or 4 were considered as malignant. Results were then correlated to those of the final histopathology.

The maximum value for elasticity (E_{max}) (in kilopascals) and the ratio between the mean value of elasticity in the lesion to that in the surrounding fat (E_{ratio}) were automatically calculated. Cut-off values that differentiate benign from malignant lesions for both E_{max} and E_{ratio} were calculated and correlated to the results of histopathology.

Technique of CE-MRI and DW-MRI

A Siemens Magnetom Aera machine (1.5 Tesla field strength) was utilized to conduct this study. Patients were put in the prone position and a double breast coil was used.

Image acquisition

T1-weighted (TR=537 ms, TE=10 ms), and T2-weighted (TR=4123 msec, TE=120 ms) fast spin echo sequences (FSE) were taken in the axial plane. Short tau inversion recovery (STIR) images were acquired (TR=4007 ms, TE=70 ms) in the axial and sagittal planes. Post contrast sequences were obtained, including 7 dynamic acquisitions, one before and the rest after intravenous injection of 0.1 mmol/kg of body weight of gadolinium-diethylene triamino-penta-acid (Gd DTPA), using the dynamic sequence T1 high-Resolution Isotropic Volumetric Examination (THRIVE) (TR/TE=5/2 ms).

Image analysis of CE-MRI

Lesions were classified on CE-MRI based on their morphology into 4 categories: 'benign', 'probably benign', 'probably malignant', and 'malignant'. To calculate the statistical indices, both the 'benign' and 'probably benign' groups were considered as benign, while both the 'malignant' and 'probably malignant' groups were considered as malignant. Kinematic curve evaluation (rising, plateau or washout curves) was also done for each lesion when applicable.

DW-MRI was done using the single-shot echo planar imaging along with fat suppression. The following parameters were utilized; 5000 ms/75 ms (TR/TE), 5 mm (section thickness), 256 × 256 (matrix), 30 × 30 cm field of view (FOV) and 3 mm (section gap).

Regarding b values in the current study, three b values were used, at 0, 400 and 800 s/mm².

Image post processing of DW-MRI

For Qualitative assessment visual evaluation of the signal intensity of a lesion on diffusion-weighted images (DWI) (at b values of 400 and 800 s/mm²) and on the corresponding ADC maps. Facilitated diffusion was defined as intermediate or high signal intensity on DWI without signal drop on the corresponding ADC map. On the other hand, restricted diffusion was defined as intermediate or high signal intensity on DWI with complete signal loss on the corresponding ADC map.

For Quantitative assessment ADC values were calculated by manually drawing a region of interest (ROI) in the most hypointense (most restricted) part of a lesion on the ADC map. This was done more than one time and the mean value was calculated.

All examinations were conjointly read by two consultant breast imaging radiologists, having more than ten years of experience in the field of breast imaging. Finally, findings of SWE, CE-MRI and DW-MRI were compared to the final histopathological results.

Statistical analysis

Data were coded utilizing the Statistical Package for the Social Sciences (SPSS) version 26 (IBM, Armonk, NY, USA). Quantitative data was summarized using mean, standard deviation (SD), median, minimum and maximum whereas for categorical data, frequency (count) and relative frequency (percentage) were used. Standard diagnostic indices including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic efficacy were calculated as described by Galen [6]. Receiver operating characteristics curve (ROC) curve was constructed with analysis of the area under the curve (AUC) to determine the best cut-off value of a certain parameter for detection of malignancy. Comparisons between quantitative variables were carried out utilizing the non-parametric Mann–Whitney test [7]. For comparing categorical data, Chi square test was done. Exact test was utilized instead when the expected frequency was less than 5 [8]. A p value less than 0.05 was considered as statistically significant. To calculate the sample size for the current study, Epi-calc 2000 was used. Assuming 80% power, 0.05 level of significance, 63% null hypothesis value and estimated proportion of 80%, the resultant sample size was 56. Therefore, this study included 66 patients having BIRADS 3 or 4 lesions presenting to our institution during the time frame from January 2018 to January 2020.

Results

This prospective study included 66 female patients having breast lesions categorized as BI-RADS 3 (probably benign) or BIRADS 4 (probably malignant) who were examined by ultrasound ± mammography (according to the patient's age), SWE, CE-MRI and DW-MRI. The ages of the patients ranged from 30 to 68 years (mean age 44.76 years ± 11.52 SD) where a statistically significant correlation was found between older ages and malignant pathology (p value: 0.003).

According to the BIRADS categorization of cases, 37 out of the examined 66 lesions (56.06%) were probably benign (BIRADS 3), and 29 (43.93%) were suspicious (BIRADS 4). One out of the 37 (2.7%) considered BIRADS 3 lesions turned out to be malignant on histopathology and 36 (97.29%) were proved truly benign. On the other hand, 2 out of the 29 considered BIRADS 4 lesions (6.89%) turned out to be benign on histopathology and 27 (93.1%) were proved malignant (p value < 0.01).

According to the results of the histopathology examination of the biopsied cores and surgical specimens, 38 out of the 66 studied lesions (57.6%) were benign, and 28 (42.4%) were malignant. Out of the 38 benign cases, we had 25 fibroadenomas (37.87%), 4 intraductal papillomas (6%), 2 cases of fibrocystic changes (3%), 3 cases of adenosis (4.54%) and 4 cases of other pathologies including a hamartoma, a hematoma, a fat necrosis and an atypical ductal hyperplasia (ADH) (6%). Out of the 28 malignant cases, we had 19 cases of infiltrating ductal carcinoma (IDC) (28.78%), 2 cases of infiltrating tubular carcinoma (ITC) (3%), 3 cases of infiltrating lobular carcinoma (ILC) (4.54%), 2 cases of papillary carcinoma (3%) and 2 cases of ductal carcinoma insitu (DCIS) (3%).

Shear wave elastography (SWE) results

The distribution of lesions according to the color-coded map scoring (qualitative assessment)

Scores of 1 and 2 were considered as benign and those of 3 and 4 were considered as malignant, resulting in a calculated sensitivity of 89.29%, a specificity of 68.42%, a PPV of 67.57%, a NPV of 89.66%, and an accuracy of 77.27%.

The distribution of SWE scoring in correlation to the final histopathology results is shown in (Table 1).

Within the BIRADS 3 group lesions, color-coded map scoring had a sensitivity of 100%, a specificity of 66.67%, a PPV of 7.69%, a NPV of 100% and an accuracy of 67.57%. Whereas within the BIRADS 4 group lesions, it had a sensitivity of 88.89%, a specificity of 100%, a PPV of 100%, a NPV of 40% and an accuracy of 89.66%.

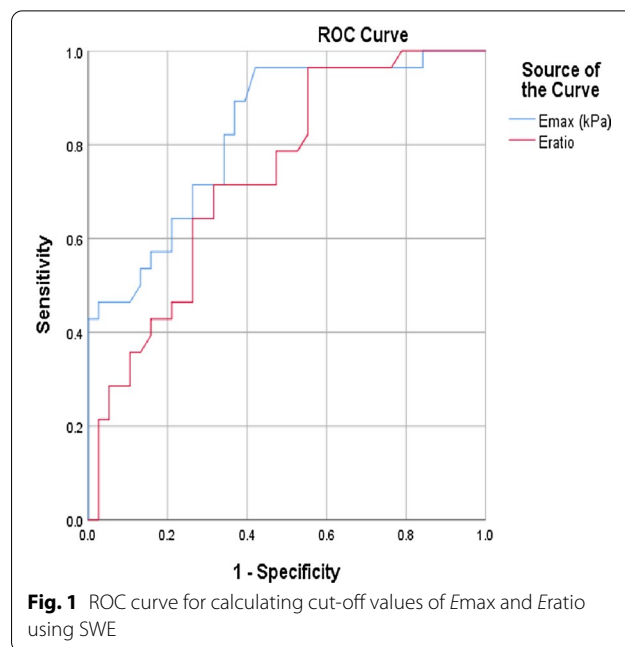
The distribution of lesions according to maximum elasticity (Emax) and elasticity ratio (Eratio) (quantitative assessment)

The obtained Emax values for all examined lesions ranged from 3.00 to 204.20 kPa (mean 94.61 ± 58.52) (mean = 94.61, SD = 58.52, median = 102.00, minimum = 3.00, maximum = 204.20).

By analysing the ROC curve of Emax (Fig. 1) by plotting the true positive rate (sensitivity) against the false positive rate (specificity), the AUC = 0.828 and the cut-off point to differentiate benign from malignant lesions was 65.15 (Table 2).

Table 1 The distribution of the SWE score in relation to the final pathology

Shear wave elastography colour map score	Benign		Malignant	
	Count	%	Count	%
Benign = score 1	21	55.3	1	3.6
Probably benign = score 2	5	13.2	2	7.1
Probably malignant = score 3	9	23.7	10	35.7
Malignant = score 4	3	7.9	15	53.6



When considering the calculated cut off value of Emax which differentiates benign and malignant lesions as 65.15, 23 out of the examined 66 (34.84%) lesions were categorized as benign, out of which 1/23 turned out to be malignant by histopathology (false negative). On the other hand, 43 out of the examined 66 (65.15%) lesions were considered to be malignant, out of which 16/43 proved to be benign on histopathology (false positive) (Fig. 2).

According to the previous results, the calculated value for sensitivity was 96.43%, for specificity was 57.89%, for NPV was 95.65%, for PPV was 62.79% and for accuracy was 74.24%.

Within the BIRADS 3 group, Emax had a sensitivity of 100%, a specificity of 55.56%, a PPV of 5.88%, a NPV of 100% and an accuracy of 56.76%. Whereas within the BIRADS 4 group of lesions, it had a sensitivity of 96.3%, a specificity of 100%, a PPV of 100%, a NPV of 67.67% and an accuracy of 96.55%.

As for Eratio, the resulting AUC for ROC curve analysis = 0.735 (Fig. 1), and the calculated cut-off point to differentiate benign from malignant lesions was 4.55 (Table 3).

When considering the calculated cut-off value of Eratio which can differentiate between benign and malignant lesions as 4.55, 34 out of the examined 66 lesions (51.51%) were considered as benign, out of which 8/34 turned out to be malignant by histopathology (false negative). And 32 out of the examined 66 lesions were considered to be malignant (48.48%), out of which 12/32 proved to be benign (false positive) (Figs. 3, 4).

Table 2 The calculated *E*_{max} cut-off point to differentiate benign from malignant lesions

	AUC	<i>p</i> value	95% confidence interval		Cut-off	Sensitivity	Specificity
			L bound	U bound			
<i>E</i> _{max} (kPa)	0.828	<0.001	0.730	0.927	65.15	96.4	57.9

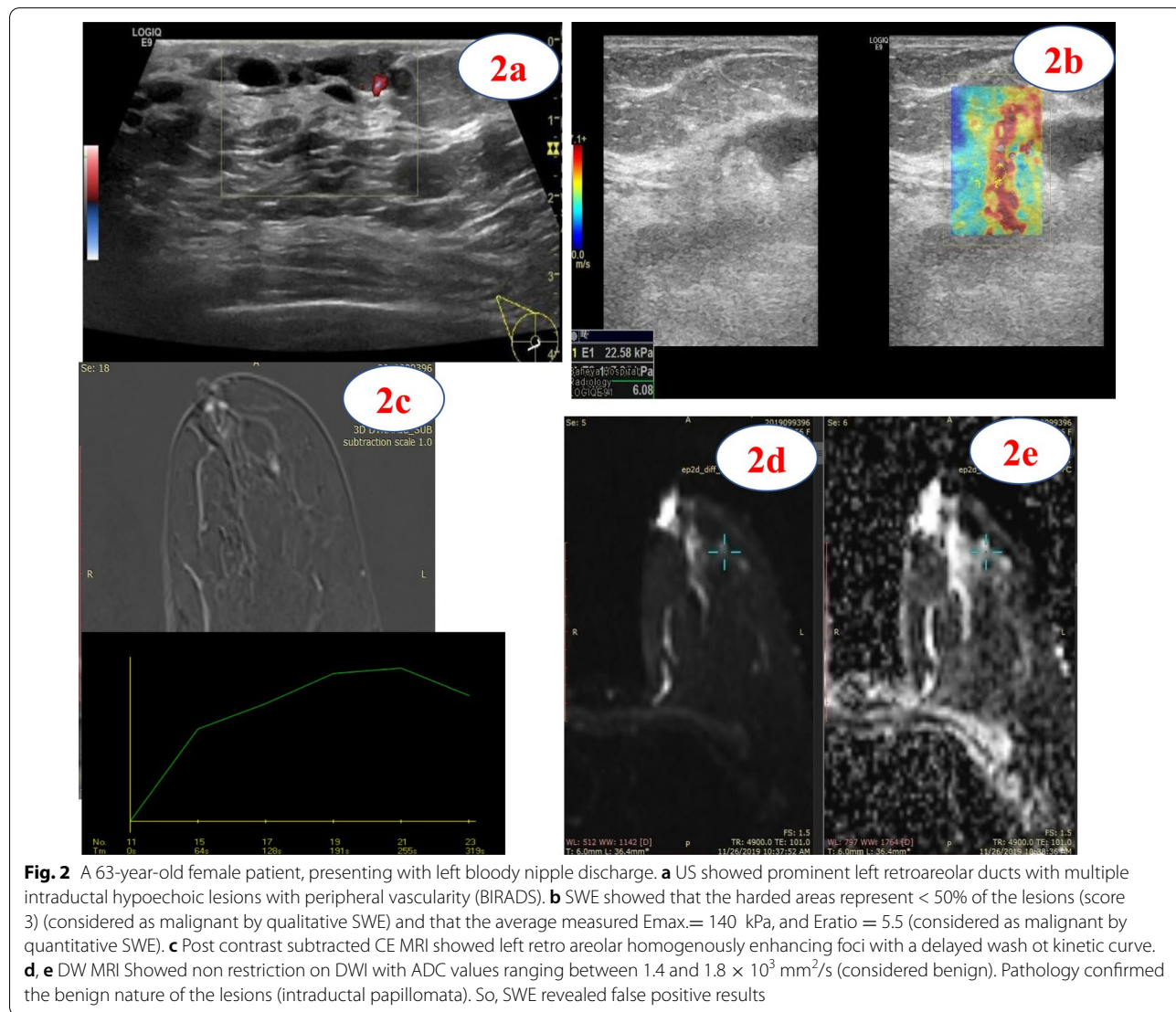


Table 3 The calculated *E*_{ratio} cut-off point to differentiate benign from malignant lesions

	AUC	<i>p</i> value	95% confidence interval		Cut off	Sensitivity %	Specificity %
			LBound	UBound			
<i>E</i> _{ratio}	0.735	0.001	0.616	0.855	4.55	71.4	68.4

According to the previous results, the calculated sensitivity for *Eratio* was 71.43%, the specificity was 68.42%, the NPV was 76.47%, the PPV was 62.50% and the accuracy was 69.70%.

Within the BIRADS 3 group, *Eratio* had a specificity of 69.44%, a NPV of 96.15% and an accuracy of 67.57%. Whereas within the BIRADS 4 group of lesions, it had a sensitivity of 74.07%, a specificity of 50%, a PPV of 95.24%, a NPV of 12.5% and an accuracy of 72.41%.

Contrast-enhanced magnetic resonance imaging (CE-MRI) results

Morphological assessment of CE-MRI

The 66 lesions included in the current study were classified on CE-MRI based on their morphology into 4 categories according to the BIRADS lexicon for breast MRI [9]. These categories are: 'benign' (32 lesions-48.5%), 'probably benign' (6 lesions-9.1%), 'probably malignant' (5 lesions-7.6%), and 'malignant' (23-34.8%).

To calculate the statistical indices, we considered both the 'benign' and 'probably benign' groups as benign, while we considered the 'malignant' and

'probably malignant' groups as malignant. A statistically significant correlation was found between the CE-MRI categories and final pathology (p value 0.003) (Table 4).

The calculated sensitivity, specificity, PPV, NPV and accuracy were 92.59%, 94.74%, 92.59%, 94.74%, and 93.85% respectively.

Kinematic curve assessment of CE-MRI

Out of the included 66 lesions, 34 (51.5%) showed a benign (rising) kinematic curve (out of which 2 turned out to be malignant by pathology). On the other hand, 12 lesions (18.2%) showed a plateau curve, and 20 lesions (30.3%) showed a washout curve. A statistically significant correlation (p value < 0.001) was found between malignant curves and pathologically proven malignant lesions, and between benign curves and benign lesions (Table 5).

The calculated sensitivity, specificity, PPV, NPV and accuracy were 92.86%, 84.21%, 81.25%, 94.12%, and 87.88% respectively.

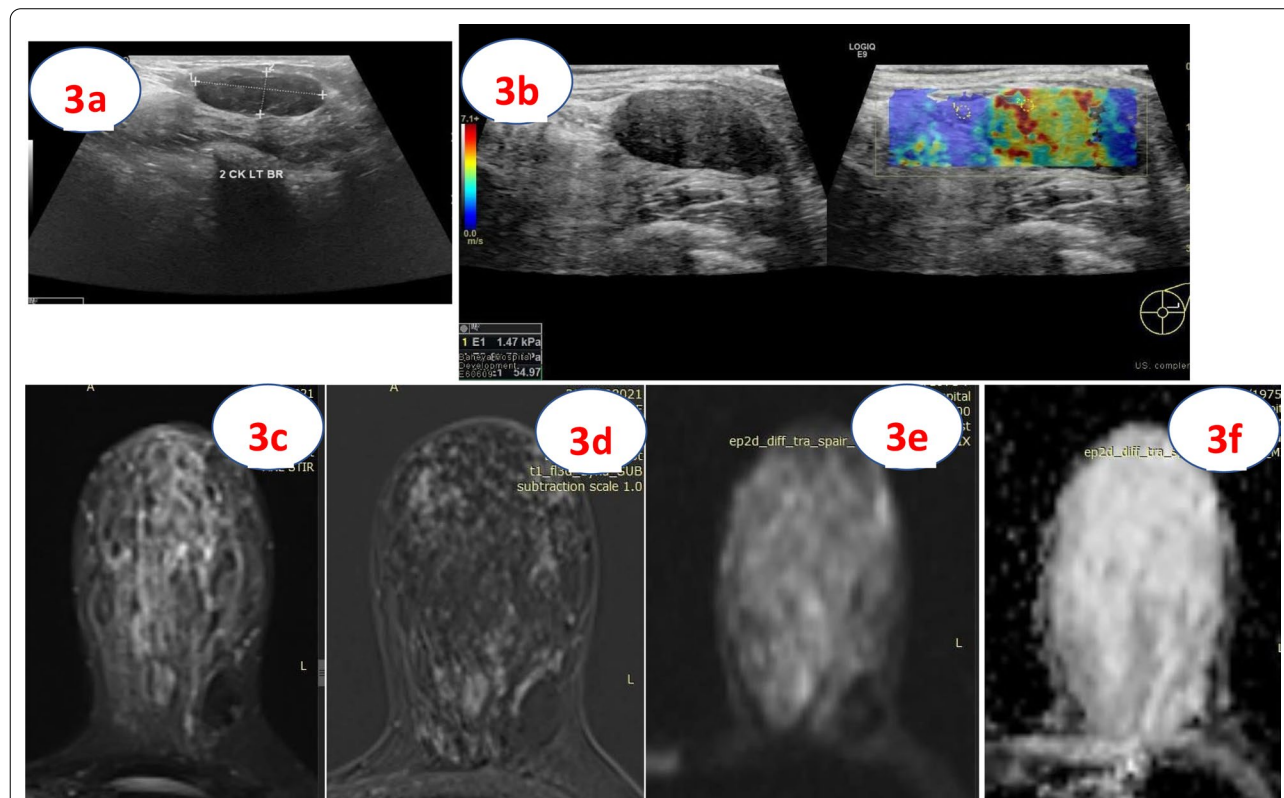


Fig. 3 A 44-year-old female presenting with a left breast lump. **a** US showed a left upper outer quadrant, well-circumscribed, ovoid, hypoechoic mass lesion (BI-RADS 3). **b** SWE showed that the hard/red areas represent less than 50% of the lesion (score 2, considered as probably benign). The measures $E_{max} = 80.7$ kPa and $E_{ratio} = 54.9$ (considered as suspicious). **c, d** CE-MRI showed no contrast uptake within the lesion of concern (and consequently no kinematic curve). **e, f** DW-MRI showed non-restriction with and ADC value of $1.8 \times 10^{-3} \times \text{mm}^2/\text{s}$ (considered as benign). This lesion was proved benign (quantitative SWE showed false positive results)

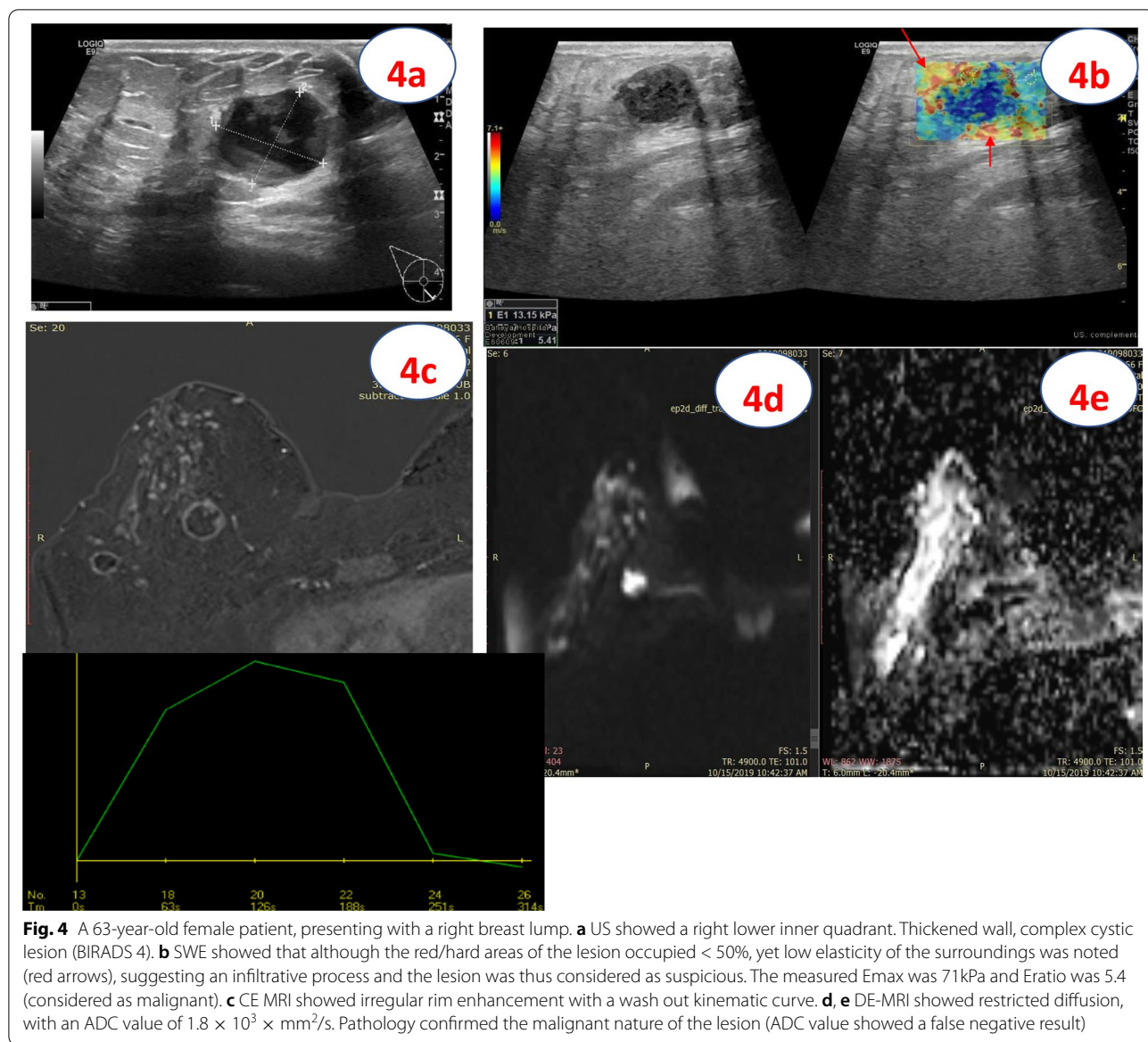


Fig. 4 A 63-year-old female patient, presenting with a right breast lump. **a** US showed a right lower inner quadrant. Thickened wall, complex cystic lesion (BIRADS 4). **b** SWE showed that although the red/hard areas of the lesion occupied < 50%, yet low elasticity of the surroundings was noted (red arrows), suggesting an infiltrative process and the lesion was thus considered as suspicious. The measured Emax was 71kPa and Eratio was 5.4 (considered as malignant). **c** CE MRI showed irregular rim enhancement with a wash out kinematic curve. **d, e** DE-MRI showed restricted diffusion, with an ADC value of $1.8 \times 10^3 \times \text{mm}^2/\text{s}$. Pathology confirmed the malignant nature of the lesion (ADC value showed a false negative result)

Table 4 CE-MRI categorization of lesions based on their morphology in correlation to the final histopathology results

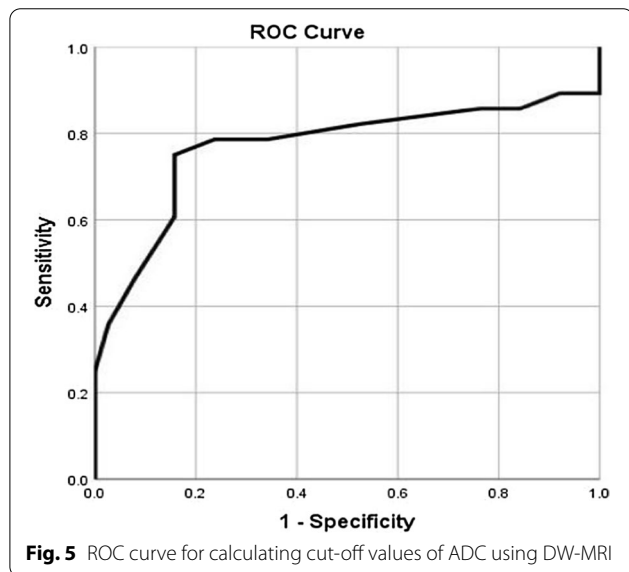
	Final pathology				p value
	Benign		Malignant		
	Count	%	Count	%	
Benign	36	94.7	2	7.1	<0.001
Malignant	2	5.3	26	92.9	

Table 5 Performance of CE-MRI kinematic curves and their correlation to the final histopathology results

Kinematic curve	Final histopathology				p value
	Benign = 38		Malignant = 28		
	Count	%	Count	%	
Type 1: rising	32	84.2	2	7.1	<0.001
Type 2: plateau	6	15.8	6	21.4	
Type 3: washout	0	0.0	20	71.4	

Table 6 Distribution of breast lesions according to the pattern of diffusion and its correlation to the final pathology results

MR diffusion	Final pathology				p value
	Benign = 38		Malignant = 28		
	Count	%	Count	%	
Restricted	13	34.2	22	78.6	< 0.001
Not restricted	25	65.8	6	21.4	



Diffusion-weighted magnetic resonance imaging (DW-MRI) results

Qualitative assessment of DW-MRI

Out of the examined 66 lesions, 35 (53.0%) showed a restricted pattern of diffusion, while 31 (47.0%) showed a facilitated pattern. A statistically significant correlation was found between malignant lesions and restricted pattern of diffusion with a *p* value < 0.001 (Table 6).

This resulted in a calculated sensitivity of 78.57%, a specificity of 65.79%, a PPV of 62.86%, a NPV of 80.65%, and an accuracy of 71.21%.

Within the BIRADS 3 group of lesions, qualitative DW-MRI showed a specificity of 63.89%, a NPV of 95.83% and an accuracy of 62.16%. Whereas within the BIRADS 4 group, it showed a sensitivity of 81.48%, a specificity of 100%, a PPV of 100%, a NPV of 28.57% and an accuracy of 82.76%.

Quantitative assessment of DW-MRI (ADC values)

The obtained ADC values for all examined lesions ranged from 0.4 to 7.70×10^{-3} mm²/s (mean: 1.49 ± 1.19 SD, median: 1.40).

By applying ROC curve analysis of the obtained ADC values (AUC=0.769), it was found that the best cut-off

value to differentiate benign from malignant lesions is 1.25×10^{-3} mm²/s (Fig. 5).

By applying this value as a cut-off point, 39 out of the examined 66 lesions (59.05%) were considered as benign. Out of these 7 (25.0%) proved to be malignant by pathology (false negative). On the other hand, 27 out of the examined 66 (40.90%) lesions were considered to be malignant out of which 6/27 (15.8%) proved to be benign by pathology (false positive) (Figs. 6, 7).

This resulted in a sensitivity of 75.00%, a specificity of 84.21%, a NPV of 82.05%, a PPV of 77.78% and an accuracy of 80.30% (*p* value < 0.001).

Within the BIRADS 3 group of lesions, quantitative DW-MRI showed a sensitivity of 100%, a specificity of 86.11%, a PPV of 16.67%, a NPV of 100% and an accuracy of 86.49%. Whereas within the BIRADS 4 group, it showed a sensitivity of 74.07%, a specificity of 50%, a PPV of 95.24%, a NPV of 12.5% and an accuracy of 72.41%.

Comparison of the diagnostic performance of different modalities included in the study is shown in (Table 7).

Discussion

Breast cancer remains a public health problem [10]. Conventional SMG and CE-MRI are the cornerstones for the management of breast cancer where CE-MRI offers rather high sensitivity for the depiction of malignancy [11]. DW-MRI relies upon the microscopic mobility of water molecules to differentiate malignancy and can be quantified by evaluating its ADC [4]. Elastography can help increase the confidence of diagnosis of malignancy by evaluating tissue stiffness [12].

The aim of this study was to evaluate the additive role of SWE and DW-MRI in predicting malignancy in breast lesions categorized as BIRADS 3 or 4.

Using SWE

Breast lesions were evaluated both by a qualitative method (color-coded map scoring) and a quantitative one (*E*_{max} and *E*_{ratio}).

By using color-coded map scoring

The current study had 12 false positive results which included 7 fibroadenomata that were either very deeply seated, creating an incorrect impression of a more solid lesion due to compression against a rib or were rather heterogeneous and of a large size. Four other cases were intraductal papillomata which were reported by previous researchers [13] to be liable to show a false positive scoring of elasticity. The remaining false positive case was that of an ADH presenting as a hard palpable lesion. There were 3 false negative results. One of them was a low-grade, small sized (< 1 cm) IDC. Elasticity values for malignant lesions were reported to vary according

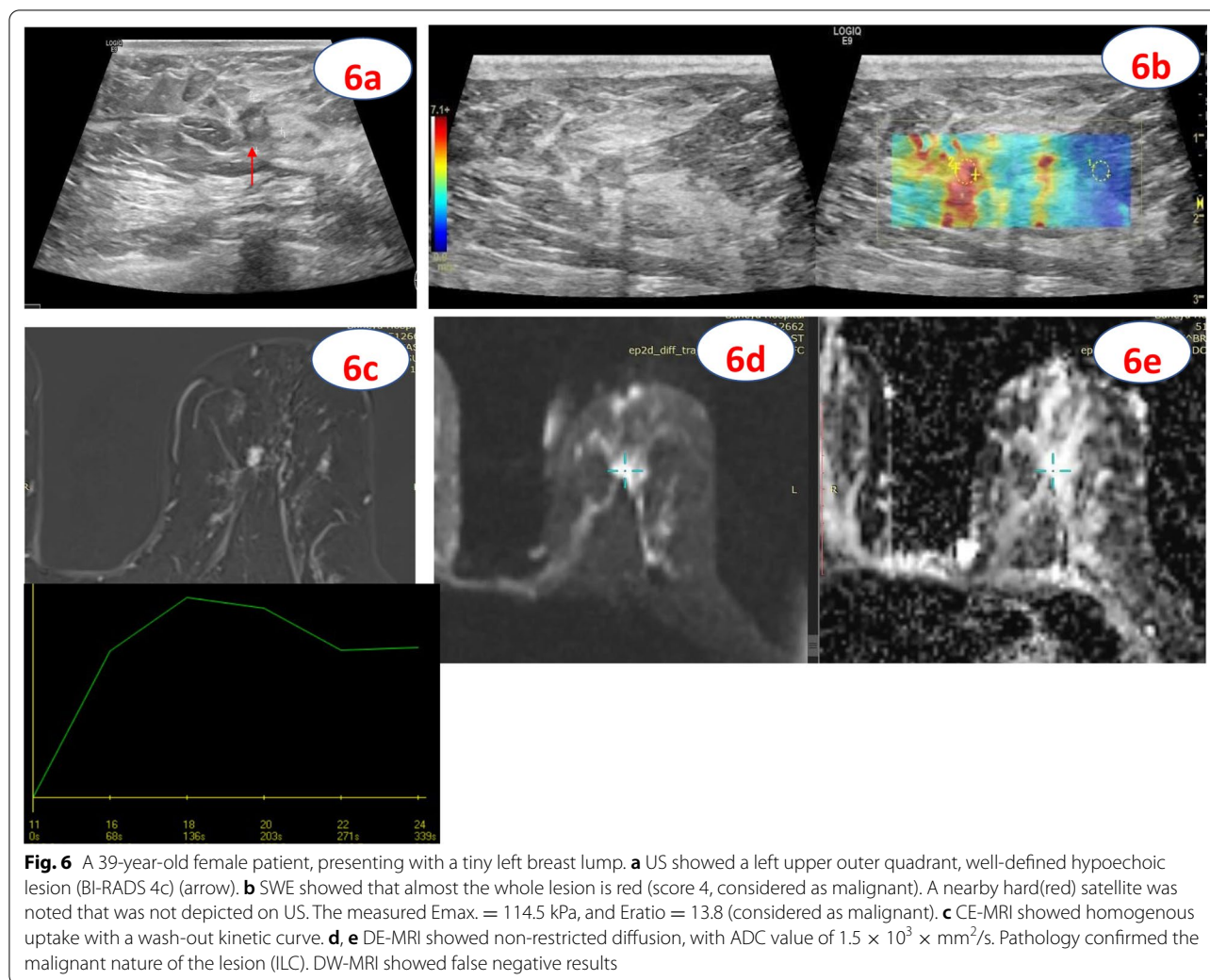


Fig. 6 A 39-year-old female patient, presenting with a tiny left breast lump. **a** US showed a left upper outer quadrant, well-defined hypoechoic lesion (BI-RADS 4c) (arrow). **b** SWE showed that almost the whole lesion is red (score 4, considered as malignant). A nearby hard (red) satellite was noted that was not depicted on US. The measured E_{max} = 114.5 kPa, and E_{ratio} = 13.8 (considered as malignant). **c** CE-MRI showed homogenous uptake with a wash-out kinetic curve. **d, e** DE-MRI showed non-restricted diffusion, with ADC value of $1.5 \times 10^3 \times \text{mm}^2/\text{s}$. Pathology confirmed the malignant nature of the lesion (ILC). DW-MRI showed false negative results

to their grade of malignancy [10]. The other 2 false negative cases were invasive papillary carcinomas. Papillary lesions of the breast were reported to be influenced by both breast thickness and lesion depth and may consequently give a false interpretation [14].

In the current study, qualitative SWE showed relatively lower specificity (68.42%). This is comparable to the results of a previous study [14] that gave lesion heterogeneity and large size as an explanation for the relatively lower specificity, where it renders applying even pressure rather uneasy. However, another study [15] used a different scoring system and concluded higher specificity (93.24%) but lower sensitivity (73.96%).

The calculated cut-off value for E_{max} in the current study affording the maximal predictive accuracy for the differentiation between benign and malignant lesions was 65.15 kPa whereas the cut-off value for E_{ratio} was 4.55.

In the current study, E_{max} showed higher sensitivity (96.43%) and accuracy (72.24%), but lower specificity

(57.89%), if compared to E_{ratio} (71.43%, 69.70% and 68.42% respectively). The calculated cut-off value in the current study may be a reason for the relatively higher sensitivity at the expense of a lower specificity. In the present study, there were 16 false positive results, out of which 10 were deeply seated fibroadenomas, mostly in large sized breasts. Other potential reasons include increased heterogeneity of tissues and uneven skin surface which exert an impact upon the reliability of SWE, as reported in a previous study [11]. Another 4 false positive results were intraductal papillomata which may elicit relatively higher values for elasticity, as reported by a previous study [16]. The remaining 2 cases were ADH and fat necrosis presenting as hard palpable lesions and thus gave false positive results.

These results match those of a previous study [14] that reported that E_{max} (with a cut-off value = 82.8 kPa) had a better diagnostic performance if compared to E_{ratio} (with a cut-off value = 5.5). However, another

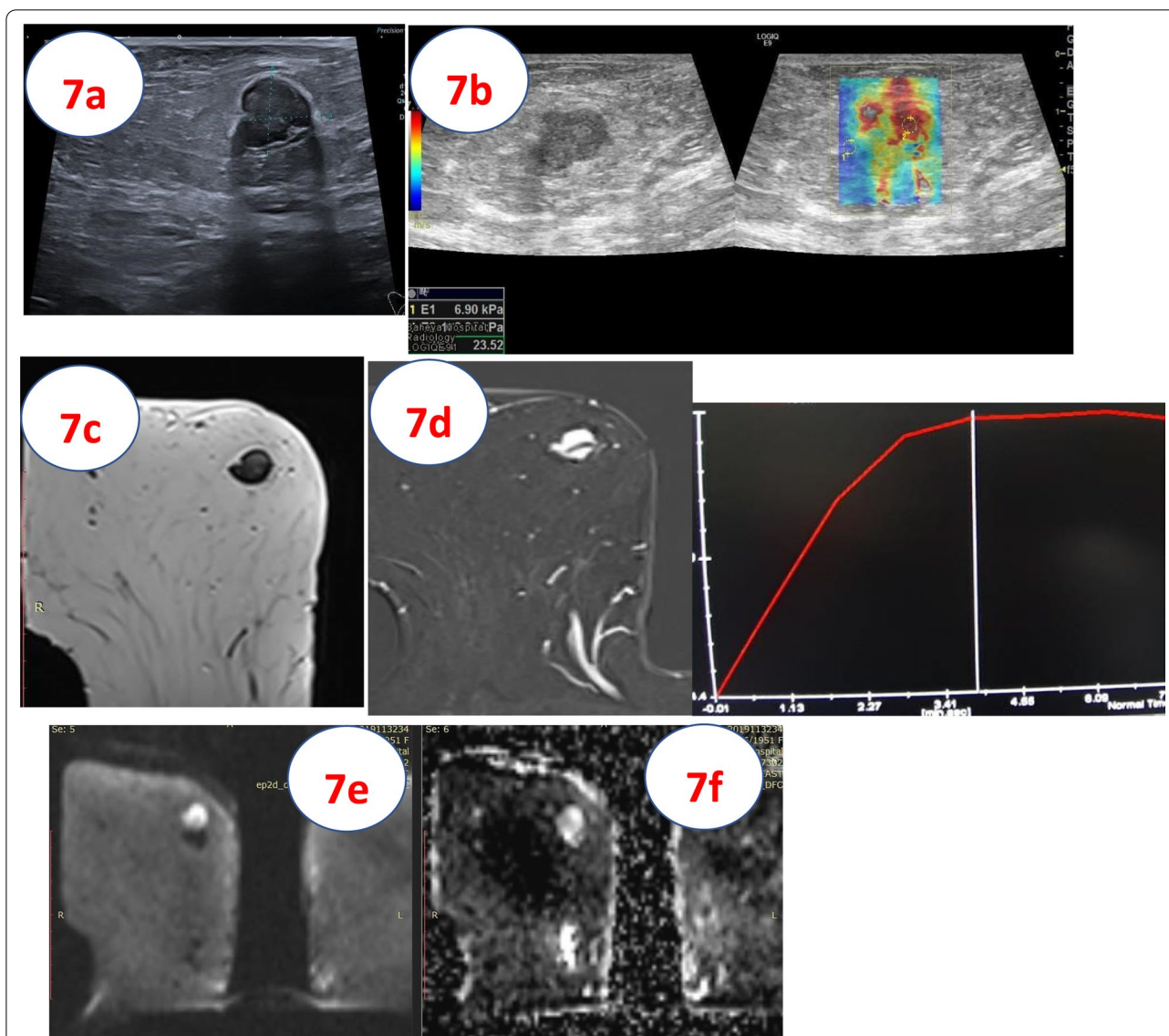


Fig. 7 A 68-year-old patient, presenting with a right breast lump. **a** US showed a right upper outer quadrant macrolobulated hypoechoic mass lesion (BI-RADS 3). **b** SWE showed that the hard area/red represent < 50% (score 3, considered as malignant). The measured E_{max} = 162.3 kPa, and $Eratio$ = 23.5 (considered as malignant). **c, d** DW-MRI showed restricted diffusion, with ADC value of $0.7 \times 10^{-3} \times \text{mm}^2/\text{s}$ (considered as malignant) Pathology confirmed the malignant nature of the lesion (both quantitative DW-MRI and SWE revealed false negative results)

study [10] that concluded that $Eratio$ (with a cut-off value = 4.70) showed higher diagnostic indices if compared to E_{max} (with a cutoff value = 54.25 kPa).

In the current study, there was a complex cystic lesion in which the actual lesion showed red areas less than 50%. Yet, significant low elasticity in the surrounding nearby parenchyma had to be considered and consequently scoring was upgraded to 4. Another case was categorized as a single BIRADS 4 lesion by conventional US and was modified into a multifocal breast cancer when nearby

satellite lesions were noted by SWE and confirmed by CE-MRI.

Contrast-enhanced MRI showed the highest diagnostic indices among other modalities included in the study, which may be justified by the superiority of combining both morphological and functional data. A statistically significant correlation was found between malignant descriptors and pathologically proven malignant lesions and vice versa (p value 0.003). Also, a statistically significant correlation (p value < 0.001) was found between the malignant curves and pathologically proven malignant

Table 7 Diagnostic performance of different modalities included in the study

Item	TP	FN	TN	FP	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Shear wave color coded map score	25	3	26	12	89.29	68.42	67.57	89.66	77.27
Contrast MRI	26	2	36	2	92.59	94.74	92.59	94.74	93.85
MRI Diffusion (restricted/non restricted)	22	6	25	13	78.57	65.79	62.86	80.65	71.21
E _{max}	27	1	22	16	96.43	57.89	62.79	95.65	74.24
E _{ratio}	20	8	26	12	71.43	68.42	62.50	76.47	69.70
ADC value	21	7	32	6	75.00	84.21	77.78	82.05	80.30

lesions with no false negative results, and between the benign curves and benign lesions. Those results go in accordance with the results of several other studies [17, 18].

Regarding the qualitative assessment of DW-MRI

There were 13 false positive results and 6 false negative cases. Two of the thirteen false positive cases were sclerosing adenosis where cellular variations accompanied with secondary changes in sclerosing adenosis may affect the diffusion pattern, as reported by a previous study [19]. Other 4 cases were intra-ductal papillomata which, as stated by previous investigators [20], often show mammary ductal papillary proliferation and secondary changes such as haemorrhage, infarction, or fibrosis that may result in false diffusion restriction. The remaining 7 cases were relatively large sized fibroadenomas with internal heterogeneity.

On the other hand, two of the six false negative results presenting with a false non-restricted diffusion pattern were invasive papillary carcinomas; one of which was very small in size measuring less than 1 cm. This may be justified by the fact that the inaccuracy of DWI in lesions less than 1 cm may be due to poor inherent and low spatial resolution, as postulated in a previous study [4]. Another one was a malignant lesion presenting with central necrosis where according to a previous study [21] done on 200 patients, false negative results were encountered in lesions showing central necrosis. Two lesions were ILC, where, as explained by previous researchers [22], ILC has a different morphology that invades the stroma individually with interposed normal fibroglandular tissue inbetween the lesions which renders radiological detection rather difficult. This is also the reason why ILC is commonly underestimated on DWI leading to false negative results. The remaining 2 cases were IDC where, as stated in a previous study [19], IDC is

commonly pathologically heterogenous, showing a mixture of cells.

A statistically significant correlation (p value < 0.001) was found between malignant lesions and restricted pattern of diffusion which goes in accordance with the results of other researchers [4].

Regarding the quantitative assessment of DW-MRI in the current study, the obtained ADC values were generally lower for malignant lesions than for benign ones, yet with an overlap between both groups.

The calculated cut-off ADC value for differentiating benign from malignant lesions was 1.25×10^{-3} mm²/s with resultant statistical indices comparable to the results of several previous studies [4, 23, 24].

Six cases showed false positive results, out of which 3 were fibroadenomas, 2 were sclerosing adenosis and 1 was a hamartoma. All had the same criteria being of heterogeneous texture. There were 7 false negative results. These were 2 cases of DCIS, 2 cases of low-grade IDC, 2 cases papillary carcinoma and a case of ILC.

For benign (BIRADS 3) lesions, both color-coded mapping and E_{max} had excellent sensitivity (100% each), however with moderate specificity (66.67% for color-coded mapping and 55.56% for E_{max}). This moderate specificity was reported in a previous study to be ameliorated by combining both conventional US and color-mapping or E_{max} for the evaluation [25]. However, for BIRADS 4 lesions, both had excellent specificity (100%) along with rather very good sensitivity (88.89% for color-coded mapping and 96.3% for E_{max}). Both had better overall accuracy with BIRADS 4 lesions as compared to BIRADS 3 ones (89.66% and 96.55% versus 67.57% and 56.76%). E_{ratio} had moderate overall performance for both BIRADS 3 and 4 lesions (67.57% and 72.41%). Yet, the rather smaller number in both subgroups of the current study represents a major limiting factor and further detailed studies with a larger sample size for each subgroup may be advisable. However, in a previous study,

it was reported that utilising visual colour stiffness to upgrade BIRADS 3 lesions or absence of stiffness to downgrade BIRADS 4 lesions improved the specificity from 61.1 to 78.5% and utilising maximum elasticity values improved specificity to 77.4%, without a change in sensitivity [26]. Comparable findings were also reported in several other studies [27, 28].

As for DW-MRI, its qualitative method showed better specificity for BIRADS 4 lesions if compared to BIRADS 3 ones (100% vs. 63.89% specificity). On the other hand, quantitative DW-MRI showed better overall performance for BIRADS 3 lesions if compared to BIRADS 4 ones (100% sensitivity, 86.11 specificity and 86.49 accuracy vs. 74.07% sensitivity, 50% specificity and 72.41% accuracy). However, the paucity of candidates within each of the subgroups in the current study represents a limiting factor. It was reported in previous studies that ADC values differ between benign and malignant lesions and it was confirmed that DW-MRI has the potential to ameliorate the differential diagnosis of suspicious breast lesions and can be potentially used to limit the number of unnecessary sampling [29, 30].

Limitations

As for the limitations of the current study, we were faced with movement of some patients which represented a source of misregistration of images on DW-MRI. Moreover, as a result of the lower spatial resolution of DWI, smaller foci of cancer (less than 1 cm) were rather difficult to detect (such as those of DCIS or scattered foci of ILC). We were also faced by the overlap of ADC values between benign and malignant conditions which may be justified by the fact that ADC values are generally more sensitive to other histopathologic conditions such as cellularity, fibrosis or necrosis. On the other hand, we were also faced with inconsistent results for *E*_{max}, resulting from pressure difference applied, which may affect the recorded values of a certain lesion. *E*_{ratio} should be less affected by this, because shear wave values should alter in both the lesion and its surrounding tissue. Regarding the separate analysis of both BIRADS 3 and 4 categories, the rather smaller number of lesions included in each subgroup represented a limiting factor which renders further detailed studies with a larger sample size for each subgroup advisable.

Conclusion

Our results show that CE-MRI is still superior in the diagnosis and evaluation of breast cancer which is the result of combining both morphological and kinetic data. SWE shows variable diagnostic performance, however, can be used clinically to increase the diagnostic

confidence when suggesting or ruling out malignancy within a breast lesion, especially in cases of radiological overlap, such as BIRADS 3 or 4 categories. DW-MRI is a non-contrast-enhanced technique that can aid the differential diagnosis of equivocal/suspicious breast lesions. Both techniques can be used as an adjunct to standard imaging of the breast to increase reliability and confidence of diagnosis.

Abbreviations

ADC: Apparent diffusion coefficient; ADH: Atypical ductal hyperplasia; AUC: Area under curve; BIRADS: Breast imaging reporting and database system score; CE-MRI: Contrast-enhanced magnetic resonance imaging; DCIS: Ductal carcinoma insitu; DWI: Diffusion-weighted image; DW-MRI: Diffusion-weighted magnetic resonance imaging; *E*_{max}: Maximum elasticity value; *E*_{ratio}: Ratio between the mean value of elasticity in a lesion to that; FSE: Fast spin echo; Gd-DTPA: Gadolinium-diethylene triamino-penta-acid; IDC: Infiltrating ductal carcinoma; ILC: Infiltrating lobular carcinoma; ITC: Infiltrating tubular carcinoma; NPV: Negative predictive value; PPV: Positive predictive value; ROC curve: Receiver operating characteristics curve; ROI: Region of interest; SD: Standard deviation; SE: Strain elastography; SMG: Sonomammography; STIR: Short tau inversion recovery; SWE: Shear wave elastography; TE: Time to echo; THRIVE: T1 high-resolution isotropic volumetric examination; TR: Time to repetition; US: Ultrasonography.

Acknowledgements

No Acknowledgements.

Authors' contributions

DE wrote the manuscript. RR collected patient data. RA worked on image processing and collection of patient images. RK participated in the design of the study and performed the statistical analysis. RR and DE conceived the study, and participated in its design and coordination and helped to draft the manuscript. RK was responsible of revision of the draft from clinical point of view. SL collected the clinical and pathological data. All authors have read and approved the manuscript.

Funding

No funding sources.

Availability of data and material

The data sets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of "Faculty of medicine, Cairo University" with ethical committee approval number and date not available. An informed written consent was taken from all subjects.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

No financial or non-financial competing interests.

Author details

¹Department of Diagnostic and Interventional Radiology, Faculty of Medicine, Cairo University, 1 kasr Elainy Street Fom Elkalig, Cairo, Egypt. ²Department of Diagnostic and Interventional Radiology, Baheya Foundation, Allouba Street, Haram, Cairo, Egypt. ³Department of Clinical Oncology, Faculty of Medicine, Cairo University, 1 kasr Elainy Street Fom Elkalig, Cairo, Egypt.

Received: 20 April 2021 Accepted: 21 July 2021
Published online: 29 July 2021

References

- Liu Q, Xing P, Dong H, Zhao T, Jin F (2018) Preoperative assessment of axillary lymph node status in breast cancer patients by ultrasonography combined with mammography. *Medicine (Baltimore)* 97(30):e11441. <https://doi.org/10.1097/MD.00000000000011441>
- Imtiaz S (2018) Breast elastography: a new paradigm in diagnostic breast imaging. *Appl Radiol* 47(3):14–19
- Youk JH, Gweon HM, Son EJ (2017) Shear-wave elastography in breast ultrasonography: the state of the art. *Ultrasonography* 36(4):300–309. <https://doi.org/10.14366/usg.17024>
- Lekshmy R, Sandya CJ, Moorthy S, Sekhar R (2017) Value of diffusion-weighted MRI in BIRADS 3 and 4 breast lesions. *J Evol Med* 6(31):2557–2562. <https://doi.org/10.14260/Jemds/2017/553>
- Xu Y, Bai X, Chen JL, Hu B, Hu B, Yu L (2018) Application of real-time elastography ultrasound in the diagnosis of axillary lymph node metastasis in breast cancer patients. *Sci Rep* 8(1):10234. <https://doi.org/10.1038/s41598-018-28474-y>
- Galen RS (1980) Predictive values and efficiency of laboratory testing. *Pediatr Clin N Am* 27(4):861–869. [https://doi.org/10.1016/s0031-3955\(16\)33930-x](https://doi.org/10.1016/s0031-3955(16)33930-x)
- Chan YH (2003) Biostatistics 102: quantitative data—parametric and non-parametric tests. *Singap Med J* 44(8):391–396
- Chan YH (2003) Biostatistics 103: qualitative data—tests of independence. *Singap Med J* 44(10):498–503
- Rao AA, Feneis J, Lalonde C, Ojeda-Fournier H (2016) A Pictorial Review of Changes in the BI-RADS fifth edition. *Radiographics* 36(3):623–639. <https://doi.org/10.1148/rq.2016150178>
- Cebi Olgun D, Korkmaz B, Kilic F, Dikici AS, Velidedeoglu M, Aydogan F, Kantarci F, Yilmaz MH (2014) Use of shear wave elastography to differentiate benign and malignant breast lesions. *Diag Interv Radiol* 20(3):239–244. <https://doi.org/10.5152/dir.2014.13306>
- Satake H, Nishio A, Ikeda M, Ishigaki S, Shimamoto K, Hirano M, Nagawa S (2011) Predictive value for malignancy of suspicious breast masses of BI-RADS categories 4 and 5 using ultrasound elastography and MR diffusion-weighted imaging. *AJR* 196(1):202–209. <https://doi.org/10.2214/ajr.09.4108>
- Chang W, Jia W, Shi J, Yuan C, Zhang Y, Chen M (2018) Role of elastography in axillary examination of patients with breast cancer. *J Ultrasound Med* 37(3):699–707. <https://doi.org/10.1002/jum.14538>
- Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, Yamakawa M, Matsumura T (2006) Breast disease: clinical application of US elastography for diagnosis. *Radiology* 239(2):341–350. <https://doi.org/10.1148/radiol.2391041676>
- Yoon JH, Ko KH, Jung HK, Lee JT (2013) Qualitative pattern classification of shear wave elastography for breast masses: how it correlates to quantitative measurements. *EJR* 82(12):2199–2204. <https://doi.org/10.1016/j.ejrad.2013.08.047>
- Suvannarerg V, Chitchumngong P, Apiwat W, Lertdamrongdej L, Tretipwanit N, Pisarnurakit P, Sitthinamsuwan P, Thiravit S, Muangsomboon K, Korpraphong P (2019) Diagnostic performance of qualitative and quantitative shear wave elastography in differentiating malignant from benign breast masses, and association with the histological prognostic factors. *Quant Imag Med Surg* 9(3):386–398. <https://doi.org/10.21037/qims.2019.03.04>
- Ng WL, Rahmat K, Fadzli F, Rozalli FI, Mohd-Shah MN, Chandran PA, Westerhout CJ, Vijayanathan A, Abdul Aziz YF (2016) Shearwave elastography increases diagnostic accuracy in characterization of breast lesions. *Medicine (Baltimore)* 95(12):e3146. <https://doi.org/10.1097/md.00000000000003146>
- Yasin R, Abd El Ghany E (2019) BIRADS 4 breast lesions: comparison of contrast-enhanced spectral mammography and contrast-enhanced MRI. *EJRN* 50:34. <https://doi.org/10.1186/s43055-019-0043-6>
- Łucznińska E, Heinze-Paluchowska S, Hendrick E, Dyczek S, Rys J, Herman K, Blecharz P, Jakubowicz J (2015) Comparison between breast MRI and contrast-enhanced spectral mammography. *Med Sci Monit* 21:1358–1367. <https://doi.org/10.12659/msm.893018>
- Kuroki Y, Nasu K, Kuroki S, Sekiguchi R, Nawano S, Satake M (2010) Diffusion-weighted imaging (DWI) for breast cancers: challenging to diagnose ductal carcinoma in situ (DCIS) and invasive lobular carcinoma (ILC). In: IWDW: digital mammography. pp 213–218
- Yabuuchi H, Matsuo Y, Sunami S, Kamitani T, Kawanami S, Setoguchi T, Sakai S, Hatakenaka M, Kubo M, Tokunaga E, Yamamoto H, Honda H (2011) Detection of non-palpable breast cancer in asymptomatic women by using unenhanced diffusion-weighted and T2-weighted MR imaging: comparison with mammography and dynamic contrast-enhanced MR imaging. *Eur Radiol* 21(1):11–17. <https://doi.org/10.1007/s00330-010-1890-8>
- Palle L, Reddy B (2009) Role of diffusion MRI in characterizing benign and malignant breast lesions. *Indian J Radiol Imaging* 19(4):287–290. <https://doi.org/10.4103/0971-3026.57209>
- Woodhams R, Ramadan S, Stanwell P, Sakamoto S, Hata H, Ozaki M, Kan S, Inoue Y (2011) Diffusion-weighted imaging of the breast: principles and clinical applications. *Radiographics* 31(4):1059–1084. <https://doi.org/10.1148/rq.314105160>
- Yilmaz E, Sari O, Yilmaz A, Ucar N, Aslan A, Inan I, Parlakliic UT (2018) Diffusion-weighted imaging for the discrimination of benign and malignant breast masses; utility of ADC and relative ADC. *J Belg Soc Radiol* 102(1):24. <https://doi.org/10.5334/jbsr.1258>
- Bostan BT, Koc G, Sezgin G, Altay C, Gelal MF, Oyar O (2016) Value of apparent diffusion coefficient values in differentiating malignant and benign breast lesions. *Balkan Med J* 33(3):294–300. <https://doi.org/10.5152/balkanmedj.2016.141007>
- Hari S, Paul SB, Vidyasagar R, Dharmija E, Adarsh AD, Thulker S, Mathur S, Sreenivas V, Sharma S, Srivastava A, Seenu V, Prashad R (2018) Breast mass characterization using shear wave elastography and ultrasound. *Diagn Interv Imaging* 99(11):699–707. <https://doi.org/10.1016/j.diii.2018.06.002>
- Berg WA, Cosgrove DO, Dore CJ, Schafer FKW, Svensson WE, Hooley RJ, Ohlinger R, Mendelson EB, Balu-Maestro C, Locatelli M, Tourasse C, Cavanaugh BC, Juhan V, Stavros AT, Tardivon A, Gay J, Henry J, Cohen-Backrie C (2012) Shear-wave elastography improves the specificity of breast US: the BE1 multinational study of 939 masses. *Radiology* 262(2):435–449. <https://doi.org/10.1148/radiol.11110640>
- Youk JH, Son EJ, Gweon HM, Kim H, Park YJ, Kim JA (2014) Comparison of strain and shear wave elastography for the differentiation of benign from malignant breast lesions, combined with B-mode ultrasonography: qualitative and quantitative assessments. *Ultrason Med Biol* 40(10):2336–2344. <https://doi.org/10.1016/j.ultrasmedbio.2014.05.020>
- Gweon HM, Youk JH, Son EJ, Kim JA (2013) Clinical application of qualitative assessment for breast masses in shear-wave elastography. *Eur J Radiol* 82(11):e680–e685. <https://doi.org/10.1016/j.ejrad.2013.08.004>
- Maltez de Almeida JR, Gomes AB, Barros TP, Fahel PE, Rocha MS (2017) Diffusion-weighted imaging of suspicious (BI-RADS 4) breast lesions: stratification based on histopathology. *Radiol Bras* 50(3):154–161. <https://doi.org/10.1590/0100-3984.2015.0224>
- Rahbar H, Zhang Z, Chenevert TL, Romanoff J, Kitsch AE, Hanna LG, Harvey SM, Moy L, DeMartini WB, Dogan B, Yang WT, Wang LC, Joe BN, Oh KY, Neal CH, McDonald ES, Schnall MD, Lehman CD, Comstock CE, Partridge SC (2019) Utility of diffusion-weighted imaging to decrease unnecessary biopsies prompted by breast MRI: a trial of the ECOG-ACRIN Cancer Research Group (A6702). *Clin Cancer Res* 25(6):1756–1765. <https://doi.org/10.1158/1078-0432.CCR-18-2967>

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.