

Contents lists available at [ScienceDirect](http://ScienceDirect.com)

## The Egyptian Journal of Radiology and Nuclear Medicine

journal homepage: [www.sciencedirect.com/locate/ejrn](http://www.sciencedirect.com/locate/ejrn)

# The role of magnetic resonance imaging in early detection of recurrent breast cancer

Ola I. Saleh <sup>\*</sup>, Mohammad S.A. Attia, Howida A. Ahmed

Radiodiagnosis Department, Faculty of Medicine, Alazhar University, Egypt

## ARTICLE INFO

### Article history:

Received 25 January 2016

Accepted 27 September 2016

Available online xxxx

### Keywords:

Dynamic contrast enhanced MRI (DCE-MRI)

Magnetic resonance mammography (MRM)

Breast conservation therapy (BCT)

Magnetic resonance spectroscopy (MRS)

Neoadjuvant chemotherapy (NAC)

## ABSTRACT

**Purpose:** The purpose of this work was the evaluation of new advances of magnetic resonance imaging (MRI) in diagnosis of recurrent breast cancer after conservative surgery, chemotherapy and radiotherapy. **Introduction:** Breast conservation surgery followed by breast radiotherapy and chemotherapy produces changes on both physical examination and on post-treatment breast imaging. Distinguishing these normal treatment-related findings from breast cancer recurrence in the original lumpectomy site or elsewhere in the breast (new primary tumors) is challenging.

**Introduction:** Our prospective study is done on fifty female patients who had undergone breast-conserving therapy at least 6 months since the end of radiation therapy. All cases were suspected for either recurrence or post-operative complications by clinical examination in conjunction with mammography and/or US. Confirmation of different lesions was achieved by fine needle aspiration biopsy, core or excisional biopsy. All patients were examined by dynamic contrast enhanced MRI (DCE-MRI). If one of imaging modalities suspected recurrence, all of the imaging modalities were performed. From our study we concluded that MRI is useful examination that can provide very valuable information in patient with suspected recurrence. It is a technique that offers not only information on lesion cross sectional morphology but also on functional lesion features such as tissue perfusion and enhancement kinetics.

© 2016 The Egyptian Society of Radiology and Nuclear Medicine. Production and hosting by Elsevier. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

A close follow up of patients after breast conserving therapy (BCT) is necessary because tumor recurrence ranges between 1% and 2% per year. It typically occurs 3–7 years after BCT. Early detection of local recurrence of breast cancer has been shown to significantly improve long-term survival [1].

Breast conservation surgery followed by breast radiotherapy produces changes on both physical examination and post-treatment breast imaging. Detection of local tumor recurrence, as well as evaluation of the remainder of the breast tissue by conventional methods can be difficult due to post treatment alteration, especially within dense breasts; hence, repeated biopsy is often required [2].

The breast conservative surgery including lumpectomy, partial mastectomy, and segmentectomy is aiming at surgical excision of

the breast cancer with a surrounding margin of histologically normal breast parenchyma while conserving the patient's breast appearance and form. Breast conservative surgery is the most common surgical option for patients with early stages of breast cancer, typically T1 or T2 [3].

Chemotherapy leads to necrosis and fibrosis, which appear as persistent density on mammogram. Similarly, calcifications associated with a carcinoma can persist even when the viable tumor cells are no longer present. Both persistent density and calcification can be incorrectly identified as carcinoma on mammogram, resulting in false positive results [4]. Moreover mammographic evaluation within the 1st 12 months after radiation is frequently impaired by radiation induced changes.

Ultrasound (US) may be of limited ability in detection of neoplastic recurrence, as it is operator dependent, and the hypoechogenicity with posterior acoustic shadowing at the site of scarring tissue can limit the proper evaluation due to their similarity to patterns seen with recurrent tumors. There is also diminished reliability of US for detection of small and non-invasive cancers, even in the untreated breasts. Extensive scarring after multiple operations or complicated healing can cause diagnostic

Peer review under responsibility of The Egyptian Society of Radiology and Nuclear Medicine.

<sup>\*</sup> Corresponding author.

E-mail address: [oismail08@yahoo.com](mailto:oismail08@yahoo.com) (O.I. Saleh).

<http://dx.doi.org/10.1016/j.ejrn.2016.09.018>

0378-603X/© 2016 The Egyptian Society of Radiology and Nuclear Medicine. Production and hosting by Elsevier.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Please cite this article in press as: Saleh OI et al. The role of magnetic resonance imaging in early detection of recurrent breast cancer. Egypt J Radiol Nucl Med (2016), <http://dx.doi.org/10.1016/j.ejrn.2016.09.018>

problems making the exclusion or the demonstration of neoplastic recurrence too difficult [5].

DCE-MRI has been shown to aid significantly in detection and characterization of primary and recurrent breast cancers. The sensitivity of breast MR imaging for detection of residual and recurrent tumors in the post-operative breast is over 90%. Breast MR imaging has been shown to be useful in differentiating scar tissue from tumor recurrence regarding the non-enhancing areas which have a high negative predictive value for malignancy (88–96%) [1].

It is also a valuable technique and more specific in differentiation of post irradiation changes from recurrent carcinoma in patients who had undergone breast irradiation [4].

DCE-MRI together with MR spectroscopy is known to enable the most accurate assessment of tumor response in breast cancer after neoadjuvant chemotherapy (NAC) in comparison with other conventional techniques. It is able to monitor complete, partial and poor response [6].

## 2. Patients and methods

Fifty female patients were subjected to this prospective study, their ages ranged from 27 to 67 years with mean of 47 years, the study was done at Alazhar University Hospitals in the period between June 2014 and October 2015, the patients were referred to the Radio-diagnosis Department from the general and oncology surgery units. Also outpatients were included. All cases had undergone BCT with at least 6 months spare period since the end of irradiation therapy. All cases were suspected for either recurrence or post-operative complications by the clinical examination in conjunction with mammography and US. Confirmation of different lesions was achieved by fine needle aspiration cytology, core or excisional biopsy.

All patients were instructed to come whenever possible during the 1st half of the cycle to avoid the associated prominent enhancement of the breast parenchyma due to the physiological hormonal effect that may obscure or mimic the malignancy.

All patients had undergone one of the different approaches of BCT with or without post-operative irradiation and chemotherapy.

Forty-one patients were submitted to post-operative radiation and chemotherapy; the remaining 9 patients were submitted to surgery alone.

An irradiation therapy and NAC were mainly given after surgery in cases with +ve axillary lymph nodes, large 1ry tumor (>2 cm), 1ry cancer of high grade (III) or if cancer cells were negative for hormone receptors.

Inclusion criteria at MRI examination consisted of history of BCT with suspicion of neoplastic recurrence either clinically or in mammography and ultrasound. Exclusion criteria were the recent irradiation therapy (up to 6 months after termination of therapy) and usual contraindications for performing MRI such as claustrophobia, marked obesity, metal devices in the body, and pacemaker.

All patients were examined by MRI ± Mammograms and Ultrasound. If one of the imaging modalities suspected neoplastic recurrence, in such cases all of the imaging modalities were performed.

Specific breast history was taken regarding the patient breast risk factors, family history, breast lumps, scars, or other areas of complaint. The patient details are regarding the location, date, and the results of previous breast biopsy. The patient also documented any use of exogenous hormonal therapy and the phase of the menstrual cycle or menopause.

### 2.1. Technique of mammography

The mammogram was mainly performed to grossly confirm or exclude the presence of a lesion and detect micro-calcifications. The machine used was Stephanix 800S.

The mammographic views were done including cranio-caudal and medio-lateral views and specific views such as magnified and localization views for more proper evaluation of a suspicious lesion were also done.

### 2.2. Technique of ultrasound examination

The ultrasound was performed for specification and evaluation of mammographically detected opacities and for exclusion of post operative collections, residual or recurrent lesions. All ultrasound examinations were performed on GE logiq S6 (using a high frequency linear 12 L transducer with frequency range 4.5–13 MHz) and Toshiba Xario SSA-660A (using a high frequency linear probe, PLT 805 AT transducer with frequency range 6.2–12 MHz).

### 2.3. Technique of magnetic resonance imaging

Before MRI scanning, the patient fulfilled an MRI safety form to exclude contraindications of entering the strong magnetic field, such as ferromagnetic vascular clips, metallic ocular fragments, pacemakers, and implanted electromechanical devices. A qualified person reviewed the standardized MRI safety forms before scanning.

The qualified nurse placed MRI-compatible markers on the patient's breast to indicate lumps location or areas of concern and annotated them on the history form; All MRI studies were performed on a superconducting magnet system (1.5 T. Philips Achieva, class II a, USA). All patients were placed in prone position using a dedicated double phased array breast coil. The majority of patients were comfortable for the duration of the entire scan with both arms at their sides. The patients were instructed to "hold still" during the scan time in order to obtain the best imaging quality. IV catheter, was placed before scanning and continuously flushed by normal saline solution.

The imaging protocol consisted of bilateral simultaneous axial and coronal images of both breast, as well as sagittal images of the diseased side.

An axial T1-weighted localizer sequence through both breasts was initially taken, and precontrast T1W frames with and without fat saturation were acquired in the axial plane (TSE; parallel imaging; flip angle = 90; TR = 9.9 ms; TE = 4.2 ms; NEX, 1; 2–4 mm slice thickness with no gap; matrix 512 × 192, FVO = 35) and also T2WI (TSE; parallel imaging with TE 80–120 ms and TR at least 3000 ms. 2–4 mm slice thickness with no gap; matrix 512 × 192, FVO = 35). For post contrast and dynamic series, intravenous injection of 0.1 mmol per/kg of gadopentetate dimeglumine (Gd-DTPA, Magnevist) was done at flow rate 2 ml/s, followed by 20 ml flush (normal saline) at the start of the acquisition. Imaging time with this frame was approximately 80 s. Axial T1 WIs with fat suppression and subtracted images acquisition were done after the DCE-series. For kinetic analysis and acquisition of time-signal intensity curve, Axial fast 2D GRE acquisition was planned. Five 2D image sets with fat suppression were performed within the first 7 min following intravenous administration of contrast agent. A small region of interest (ROI < 3 pixels) was placed selectively over the most intensely enhancing area of the lesion. Signal intensity/Time curves were constructed. Diffusion-weighted imaging (DWI) was performed before the DCE-MRI acquisition in an axial plane using a 2D spin echo-echo planar imaging (SE-EPI) sequence with a parallel acquisition technique using the signal intensity and two different B-values. To assess ADC value the region of interest (ROI) was manually drawn avoiding the necrotic or cystic components by referring to DCE-MRI and T2-weighted images; The ADC value was calculated as the mean of the voxels within the ROI of the tumor. For 1H spectroscopy, used for assessment of choline peak,

Single-voxel choline spectroscopy was done with voxel size of less than  $1 \times 1 \times 1$  cm.

#### 2.4. Histopathological correlation

US guided core biopsy was used for confirmation of different lesions suspected by the performed imaging modalities. Informed consent was obtained after patient discussion about the risks and benefits of the procedure and alternatives to the procedure. The patient lied supine on an examination table with the ipsilateral arm resting above the head. In cases of large breast, an oblique position was used. The lesion was localized with US guidance. The skin was sterilized by povidone iodine. The transducer was also cleaned with an antiseptic solution. A high-frequency electronically focused linear-array transducer was used. An automated 18-gauge, long-throw core biopsy needle was used.

The qualitative assessment of morphologic features of the suspected lesion was recorded regarding the site, size, margins, detection of multifocality, unifocality, skin involvement or lymph node involvement and type of enhancement as well as restricted or free diffusion on DWI. The evaluation also included search for acute post-operative changes (changes occurring during 1st several weeks up to 6 months post-operative) including skin thickening, hematoma, seroma, edema, granulation tissue formation and tissue disruption. Chronic post-operative changes (occurring following 6 months post operative) including scar tissue formation, nipple retraction, development of dystrophic calcifications, fat necrosis and architectural distortion.

Data collected were reviewed, and coding and statistical analysis of collected data were done by using SPSS program (statistical package of social science; SPSS Inc., Chicago, IL, USA) version 18 for Microsoft Windows. Frequency of occurrence was calculated

to describe qualitative data and chi-square-test ( $\chi^2$ ) was used to find the difference between two qualitative variables. The level of significance was taken at p-value of  $<0.05$  with confidence level 95%. The results are represented in tables.

### 3. Results

The patients were divided into two groups according to their menstrual status. Thirty were premenopausal (age 27–47 years) and twenty were postmenopausal (age 47–67 years).

Eleven cases with pathologically proven recurrence was noted among the premenopausal group, while the postmenopausal group showed only five recurrent cases (Table 1).

First and second degree positive family history was present in twenty-two cases from which there were nine cases with pathologically proven recurrence while among the remaining twenty-eight cases with negative family history there were seven cases with pathologically proven recurrence (Table 2).

Number and ratios of the postoperative recurrent cases among each group are illustrated in Table 3.

Forty-one patients were submitted to postoperative radiation therapy and chemotherapy while the remaining nine patients were not, and number and ratios of the recurrent cases among each group are illustrated in Table 4.

Mammographic findings suspected recurrence in twenty-four cases, of them fourteen cases were confirmed by pathological examination and proved to be true recurrence, while the remaining ten false positive cases were likely caused by irregular scarring tissue, dystrophic calcifications and seromas with no evidence of malignancy. Two pathologically proven recurrent cases were missed by mammography. These two cases were ductal carcinoma in situ and invasive ductal carcinoma located adjacent to the

**Table 1**

Age distribution of the studied group with the ratios of the recurrent cases among each group.

Age of the patient	Pathologically proven recurrence						Chi-square	
	Negative		Positive		Total		$\chi^2$	P-value
	N	%	N	%	N	%		
27–47 (premenopausal)	19	55.88	11	68.75	30	60.00	0.310	0.577
47–67 (postmenopausal)	15	44.12	5	31.25	20	40.00		
Total	34	100.00	16	100.00	50	100.00		

**Table 2**

Family history of breast cancer among the studied group with the ratios of the recurrent cases among each group.

Family history of breast cancer	Pathologically proven recurrence						Chi-square	
	Negative		Positive		Total		$\chi^2$	P-value
	N	%	N	%	N	%		
Present	13	38.24	9	56.25	22	44.00	0.577	0.372
Absent	21	61.76	7	43.75	28	56.00		
Total	34	100.00	16	100.00	50	100.00		

**Table 3**

Types of operation done among the studied group with the ratios of the recurrent cases among each group.

Types of operation done	Pathologically proven recurrence						Chi-square	
	Negative		Positive		Total		$\chi^2$	P-value
	N	%	N	%	N	%		
Lumpectomy	4	11.76	4	25.00	8	16.00	1.430	0.489
Lumpectomy with axillary dissection	23	67.65	9	56.25	32	64.00		
Quadrantectomy with axillary dissection	7	20.59	3	18.75	10	20.00		
Total	34	100.00	16	100.00	50	100.00		

**Table 4**

Submission to postoperative radiation therapy and chemotherapy among the studied group with the ratios of the recurrent cases among each group.

Postoperative radiation therapy and chemotherapy	Pathologically proven recurrence						Chi-square	
	Negative		Positive		Total		X <sup>2</sup>	P-value
	N	%	N	%	N	%		
Given	29	85.29	12	75.00	41	82.00	0.239	0.624
Not given	5	14.71	4	25.00	9	18.00		
Total	34	100.00	16	100.00	50	100.00		

operative scar, in relatively dense breasts. The mammographic sensitivity, specificity, accuracy as well as positive and negative predictive value are represented in Table 5.

The ultrasound examinations agreed with mammography in twenty cases only. The remaining four cases suspected by mammography were proved to be three cases with seroma and one case with dystrophic calcifications within the postoperative scar (appeared as suspicious calcifications on mammogram). The US findings suspected recurrence in five false positive cases and missed the diagnosis (revealed no suspicious findings) in one false negative case. The maximum diameters of tumors noted by US ranged from 13 mm to 26.5 mm and the mean maximum diameters of the tumors were about 22.5 mm. The ultrasound sensitivity, specificity, accuracy as well as positive and negative predictive value are represented in Table 6.

The magnetic resonance mammography (MRM) revealed suspicious morphological and kinematic findings for recurrence in eighteen cases, of them sixteen recurrent cases were confirmed pathologically. The remaining two false positive cases were pathologically proved to be granulomatous reaction with no evidence of malignancy, both cases showed regional non mass enhancement at the operative bed with type II time-signal intensity curves on kinetic analysis. The maximum diameters of tumors noted by MRI ranged from 16.5 mm to 32 mm and the mean maximum diameters of the tumors were about 27.5 mm. The MRM sensitiv-

ity, specificity, accuracy as well as positive and negative predictive value are represented in Table 7.

In correlating the site of the suspicious findings in MRM to the operative tumor bed, twelve cases were noted at the operative bed (including the two false positive cases). Four cases were seen away from the operative bed in the same breast and two cases at the contralateral breast (Table 8).

Of the eighteen cases suspected by MRM, eleven cases were noted as enhancing mass lesion with suspicious morphology, while the remaining seven cases presented as focal, regional or linear areas of non-mass enhancement (Table 9).

On kinetic analysis eleven cases showed type III time-signal intensity curves with rapid wash in and delayed wash out. The remaining seven cases showed type II time-signal intensity curves with rapid wash in and delayed plateau (Table 10).

Quantitative diffusion weighted imaging of the 18 cases suspected by DCE-MRI (including the two false positive cases) revealed low ADC values in the range of  $0.8-1.45 \times 10^{-3} \text{ mm}^2/\text{s}$ , with a mean ADC of  $1.2 \times 10^{-3} \text{ mm}^2/\text{s}$  and cut off value of  $1.3 \times 10^{-3} \text{ mm}^2/\text{s}$ . 17 cases were below and only one case above this limit ( $1.45 \times 10^{-3} \text{ mm}^2/\text{s}$ ). 1H MRS analysis of the eighteen cases suspected by DCE-MRI, revealed high choline peak in fifteen cases. Fourteen cases of them were positively correlated with the histopathological data. Absent choline peak were noted in three cases including one of the false positive cases suspected by DCE-MRI.

**Table 5**

Correlation between mammographic and pathological findings among the studied group. PPV positive predictive value, NPV negative predictive value, sensitivity and specificity.

Mammography	Pathologically proven recurrence						Chi-square		
	Negative		Positive		Total		X <sup>2</sup>	P-value	
	N	%	N	%	N	%			
Negative	24	70.59	2	12.50	26	52.00	12.473	0.0004*	
Positive	10	29.41	14	87.50	24	48.00			
Total	34	100.00	16	100.00	50	100.00			
ROC curve	Sensitivity		Specificity		PPV		NPV		Accuracy
	87.50		70.59		58.33		92.31		76.00

\* P-value  $\leq 0.05$ .**Table 6**

Correlation between ultrasound and pathological findings among the studied group. PPV positive predictive value, NPV negative predictive value, sensitivity and specificity.

U/S	Pathologically proven recurrence						Chi-square		
	Negative		Positive		Total		X <sup>2</sup>	P-value	
	N	%	N	%	N	%			
Negative	29	85.29	1	6.25	30	60.00	25.126	<0.001*	
Positive	5	14.71	15	93.75	20	40.00			
Total	34	100.00	16	100.00	50	100.00			
ROC curve	Sensitivity		Specificity		PPV		NPV		Accuracy
	93.75		85.29		75.00		96.67		88.00

\* P-value  $\leq 0.05$ .

**Table 7**

Correlation between MRM and pathological findings among the studied group. PPV ositive predictive value, NPV negative predictive value, sensitivity and specificity.

MRM	Pathologically proven recurrence					Chi-square		
	Negative		Positive		Total		X <sup>2</sup>	P-value
	N	%	N	%	N	%		
Negative	32	94.12	0	0.00	32	64.00	37.845	<0.001 <sup>*</sup>
Positive	2	5.88	16	100.00	18	36.00		
Total	34	100.00	16	100.00	50	100.00		

ROC curve	Sensitivity	Specificity	PPV	NPV	Accuracy
	100.00	94.12	88.89	100.00	96.00

<sup>\*</sup> P-value ≤ 0.05.**Table 8**

The location of the MRM suspicious findings in relation to the operative tumor bed.

Location	MRI (n = 18)	
	N	%
Tumor operative bed	12	66.67
Same breast away from the operative bed	4	22.22
Contralateral breast	2	11.11
Total	18	100.00

**Table 9**

Different types of enhancement of the MRM suspicious lesions.

Type of lesion	MRI (n = 18)	
	N	%
Enhancing mass lesions	11	61.11
Non-mass enhancement	7	38.89
Total	18	100.00

**Table 10**

Different types of time-signal intensity curves obtained after kinetic analysis of the MRM suspicious lesions.

Type of curve	MRI (n = 18)	
	N	%
Type III curve	11	61.11
Type II curve	7	38.89
Total	18	100.00

After addition of quantitative diffusion weighted imaging and 1H MRS analysis of the suspected lesions, the overall MRM specificity increased to 97%.

Post-operative fibrosis in the operation bed was noted by the MRM, showing no enhancement in twenty-one cases. In twenty-seven cases the scarring tissue presented with mild enhancement with type I curve on kinetic analysis. Only two cases showed regional non mass enhancement that were non separable from the scarring tissue at the operative bed and revealed type II time-signal

**Table 11**

The presentation of post-operative scarring tissue on dynamic MRI examination.

	Post-operative scarring	
	N	%
Non enhancing scarring tissue	21	42.00
Mildly enhancing scarring tissue with type I time-signal intensity curve	27	54.00
Mildly enhancing with type II time-signal intensity curves	2	4.00
Total	50	100.00

**Table 12**

Types of skin thickening among the studied cases.

	Skin thickening	
	N	%
Focal	15	30.00
Diffuse	35	70.00
Total	50	100.00

**Table 13**

Histopathological types of the recurrent masses.

	Histopathological types	
	N	%
Invasive ductal carcinoma	11	68.75
Invasive lobular carcinoma	4	25.00
Ductal carcinoma in situ	1	6.25
Total	16	100.00

intensity curves on kinetic analysis; both cases were biopsied and revealed granulomatous reaction (Table 11).

Focal skin thickening was found among fifteen cases while diffuse thickening was found in thirty-five cases represented in Table 12.

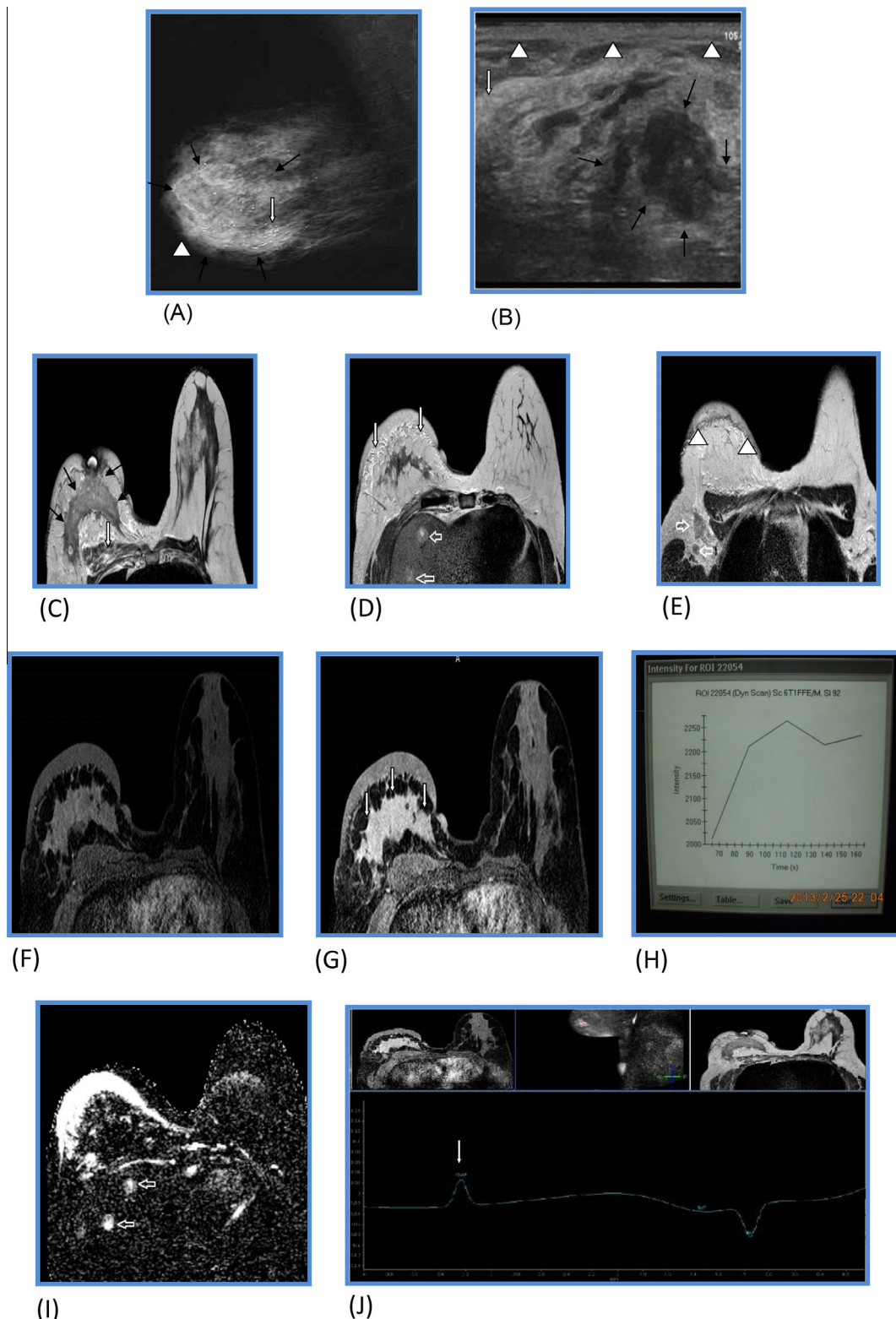
The histopathological types of the pathologically proven recurrent masses are represented in Table 13.

#### 4. Discussion

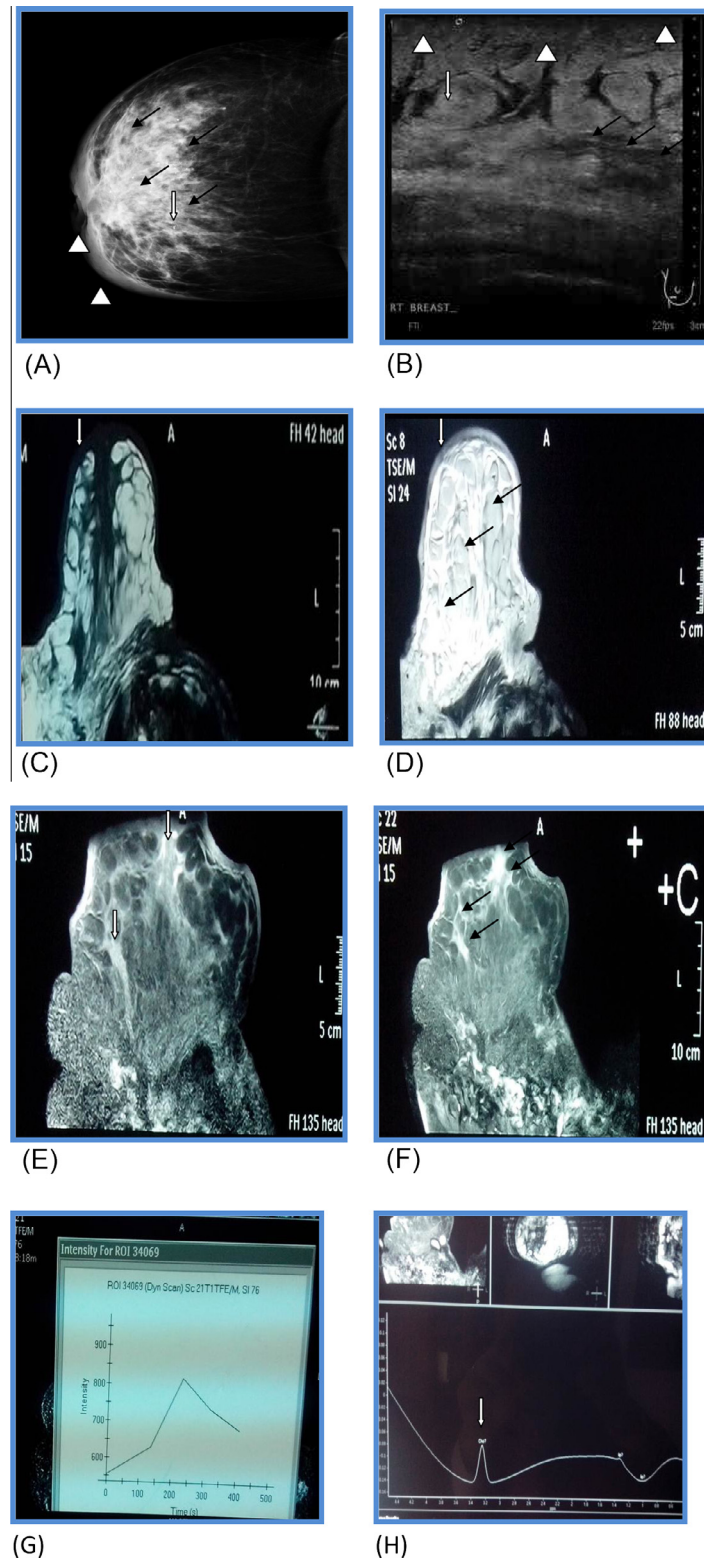
The recurrence of the tumor in a conservatively treated breast usually occurs at the lumpectomy bed, adjacent to the operative margin. However it may recur elsewhere in the breast. The majority of true local recurrences arise close to the original primary site, while the new primaries are most often seen outside the original quadrant [7]. On mammography, commonly encountered benign post treatment changes include skin thickening and edema, focal fluid collections representing hematoma or seroma, developing coarse or dystrophic calcifications in or near the surgical bed, and scarring. These changes usually result in increased density and surgical bed deformity which are in conjunction with dystrophic benign calcifications and dense breasts of young patients, compromise the ability of mammography to show the tumor in the treated breast. All of the previously described issues are the reasons for relatively decreased mammographic sensitivity, and specificity in our study which is 87.5% and 70.59%, respectively [2].

In our study, microcalcifications are noted only in three recurrent cases (Fig. 1) while dystrophic benign calcifications are seen in one case with no corresponding suspicious abnormalities on the US or MRI. The low prevalence of microcalcifications in this





**Fig. 1.** 43 years old patient presented with history of right breast ductal carcinoma and was submitted to quadractomy and axillary dissection with postoperative radiation and chemotherapy. (A) Mammogram shows heterogeneous ill-defined increased density (black arrows) at the retro-areolar region with irregular outline and multiple foci of microcalcifications (white arrow), thickened skin and retracted nipple (arrow head) are noted. (B) Ultrasonography shows heterogeneous ill-defined soft tissue mass lesion at retro-areolar region (black arrows) showing mainly hypochoic texture and irregular outline. Thickened skin (arrow heads) and parenchymal edema (white arrow) were seen. (C, D, E) Axial T2 WI MRI revealed large infiltrative ill-defined soft tissue mass lesion (black arrows) at the retro-areolar region showing heterogeneous intermediate signal alteration and irregular outlines. Diffuse edema of the breast parenchyma and pectoralis major muscle (white arrows) are seen. Thickened skin and retracted nipple (arrow heads) are also noted. Right axillary rounded lymph nodes and hepatic focal lesions are seen (open arrows). (F, G) Axial T1WI MRI with fat suppression before and after IV contrast administration revealed moderate homogenous post contrast mass enhancement (white arrows). (H) Kinetic analysis revealed type III time-signal intensity curve with rapid wash in and delayed wash out (indicative of malignancy). (I) Corresponding diffusion WI revealed low ADC value ( $1.1 \times 10^{-3}$  mm/s) seen as hypointense signal (denoting diffusion restriction of malignancy) at the site of the lesion while hyperintensity (denoting no restriction and benignity) is seen at the site of edema. Hepatic focal lesions are also seen on DWI (open arrows). (J) MRS analysis revealed high choline peak at 3.2 ppm (white arrow) indicative of malignancy.



**Fig. 2.** 60 years old patient presented with history of left breast lobular carcinoma that was treated by radical mastectomy, the patient developed a contralateral right breast carcinoma later on and the patient was treated by lumpectomy and axillary dissection with postoperative radiation and chemotherapy. (A) Right breast mammogram shows prominent regional increased breast density and heterogeneous ill-defined speculated opacity (black arrows) seen at the retro-areolar region showing irregular outlines and foci of microcalcifications (white arrow). Marked diffuse skin thickening and retracted nipple (arrow heads) are also seen. (B) Ultrasonography shows retro-areolar soft tissue mass lesion with heterogeneous hypoechoic texture and ill-defined irregular outlines (black arrows), marked glandular tissue edema (white arrow) and thickened skin (arrow heads) are seen. (C, D) Axial T1 & T2W MRI shows marked edema of the breast parenchyma (black arrows), thickened skin (white arrows) and retracted nipple. (E and F) Axial T1WI with fat suppression before and after IV contrast administration show irregular ill-defined soft tissue mass lesion at retro-areolar region with marked post contrast enhancement (black arrows). Linear areas of high signal on pre-contrast images (white arrows) are likely related to lactiferous ducts filled with proteinaceous material or blood. (G) Kinetic analysis revealed type III time-signal intensity curve with rapid wash in followed by wash out (indicative of malignancy). (H) Corresponding MRS revealed high choline peak (white arrow). Diffusion WI (not shown) revealed low ADC value ( $0.8 \times 10^{-3}$  mm/s) indicative also of malignancy.

study group may be explained by limited existence of ductal carcinoma in situ among pathologically proven cases.

Assessment by US is known and valuable tool when recurrent masses are suspected. Hasan et al. [9] in their study carried on fifty-seven breast cancer patients, stated that the accuracy of US for residual lesion around the previous scar is even higher than that of MRI. However, its sensitivity considerably lower.

On the other hand problems encountered with US include hypoechoic areas, posterior acoustic shadowing within the scar tissue, and fat necrosis which had a similar appearance to that of breast lumps as well as other distinct lesions from the primary cancer and multifocal lesions [9].

In our study, US was a reliable test if the mammogram result is negative. US recorded sensitivity and specificity of 93.75% and 85.29% respectively which were higher than those of mammography. Mammographic false positive results caused by seroma, abscess and dystrophic calcifications were easily identified by ultrasonography.

All previously mentioned reasons made the DCE-MRI a useful additional examination in patient with suspected recurrence. It has known and well established advantages over conventional breast imaging for the detection of malignancy. These advantages are as follows absence of ionizing radiation, all imaging planes are possible, capability of imaging the entire breast volume and chest wall, images are reproducible and non-operator dependent, 3-D mapping of the lesion with techniques such as maximum intensity projection slab 3-D reconstruction, higher sensitivity to invasive carcinoma and accurate estimation of its size, detection of occult, multi-focal or residual malignancies and its ability to image regional lymph nodes.

Dynamic contrast enhanced DCE-MR in our study detected the recurrence and differentiated it from non-enhanced scar tissue with high sensitivity and specificity. The true recurrent cases detected were sixteen out of a total eighteen suspected cases. Recurrence away from operative bed in multifocal and multicentric lesions is detected by MRI in six cases (4 cases in the same breast away from operative bed and 2 cases in the contra lateral breast) (Fig. 2). This is one of the advantages of the MRI over the US which usually misses these multifocal and multi-centric lesions [8].

Two false positive cases are found presented as focal areas of non-mass enhancement with type II time-signal intensity curve on kinetic analysis, after US guided true cut biopsy of the suspicious lesions, both were reported pathologically as a granuloma with no evidence of malignant cells infiltration. Hyunkyung et al. [11] stated seven false positive cases among a total number of sixteen cases showing suspicious MRM features and claimed it due to short post radiation period (12 month). The scarring tissue enhanced after the operation by 6 month without radiation and up to 18 month after the radiotherapy.

One of these two false positive cases showed relatively high ADC value ( $1.4 \times 10^{-3} \text{ mm}^2/\text{s}$ ) on quantitative DWI. Also, the lesional 1H MR spectroscopic analysis revealed no choline peak, meaning that specificity of the MRM is increased when additional DWI and 1H MRS are planned. Among the studies that examined the role of diffusion weighted imaging on improving the MRM sensitivity and specificity, Jiang et al. [17] also concluded that combination of quantitative kinetic parameters and ADC showed higher diagnostic performance for predicting malignancy than each parameter alone for the evaluation of patients with breast cancer. Kaplan et al. [4] stated that when applying an ADC cut off value of 1.33 the specificity and PPV of DCE-breast MRI increased from 59.5% and 75–78.5% and 83.3%, respectively. The diagnostic performance of Magnetic resonance spectroscopy (MRS) in recurrent breast masses following BCT was also evaluated by Khattab et al. [13] and achieved a sensitivity of 94.7%, specificity of 85.7% and overall accuracy of 92.3%.

Significant difference between US and MRI in the size and extension of the recurrent disease was noted in this study. The mean maximum diameter of tumors by US was about 22.5 mm while on the corresponding MRI the mean maximum diameter of tumors was about 27.5 mm. There is a statistically significant difference of 5 mm.

The overall sensitivity of the DCE-MRM in our study was 100%. The specificity and accuracy were 94.12% and 96%, respectively. With addition of quantitative diffusion weighted imaging and 1H MRS analysis of the suspected lesions, the overall MRM specificity increased to 97%.

Our results support the increased prevalence of local recurrence among younger age group. As 11 recurrent cases were noted among a total number of thirty cases aged 27–47 years while among the group aged 47–67 years (20 cases) only 5 recurrent cases were noted which was also proved by another study carried on 209 premenopausal women [14], stated that the age remains the first prognostic factor for regional breast cancer recurrence in women treated with breast conserving surgery with the relative risk of local recurrence increased by 7% for every decreasing year of age.

The first and second degree positive family histories are present in twenty-two cases from which there were nine cases with pathologically proven recurrence. Among the remaining twenty-eight cases with negative family history there were seven cases with pathologically proven recurrence. The impact of positive family history on local recurrence after breast-conserving therapy was performed within a better framework of a large, multicenter matched case-control study [16] establishing that the local recurrence risk after BCT for patients with a positive family history was similar to or less than that of patients without a family history of breast cancer.

Post-operative radiation and chemotherapy were given for forty one cases with recurrence noted in 12 cases of them (accounting for a percentage of 29.2%) while post-operative radiation and chemotherapy were not given for the remaining nine cases among which four recurrent cases were noted (accounting for a percentage of 44.4%). These results are suggestive of increased recurrence rates in case of avoidance of post-operative irradiation and chemotherapy. Similar results were obtained from similar previous study (18) establishing that the avoidance of radiotherapy and tamoxifen after breast-conserving surgery increases the rate of local recurrences substantially by about three times.

## 5. Conclusion

From our study we concluded that MRI is useful examination that can provide very valuable information in patient with suspected recurrence. Compared to mammography and breast ultrasonography. The DCE-MRI is a technique that offers not only information on lesion cross sectional morphology but also on functional lesion features such as tissue perfusion and enhancement kinetics. It was able to detect residual or recurrent disease of previously treated breast cancer, differentiating them from post treatment changes with the greatest sensitivity and specificity. Addition of quantitative diffusion weighted imaging and 1H MRS analysis of the suspected lesions to the routine MRM protocol is recommended as both are suggested to increase the overall MR specificity, preventing unnecessary invasive procedures or surgical interventions.

## Conflict of interest

The authors declare that there are no conflict of interests.



## References

- [1] Drukteinis JS, Gombos EC, Raza S, Chikarmane SA, et al. MR imaging assessment of the breast after breast conservation therapy: distinguishing benign from malignant lesions. *RadioGraphics* 2012;32:219–34.
- [2] Gutierrez R, Horst KC, Dirbas FM, Ikeda DM. Breast imaging following breast conservation therapy. In: Dirbas FM, Scott C, editors. *Breast surgical techniques and interdisciplinary management*. USA: Springer; 2011. p. 975–95 [chapter 81].
- [3] Neal CH, Yilmaz ZN, Noroozian M, Klein KA, Sundaram B, et al. Imaging of breast cancer related changes after surgical therapy. *AJR* 2014;202:262–72.
- [4] Kaplan JB, Dershaw DD. Post therapeutic magnetic resonance imaging. In: Morris Elizabeth A, Liberman Laura, editors. *Breast MRI diagnosis & intervention*. USA: Springer Company; 2005. p. 227–37.
- [5] Vilar VS, Goldman SM, Ricci MD, Pincerato K, et al. Analysis by MRI of residual tumor after radiofrequency ablation for early stage breast cancer analysis by MRI of residual tumor after radiofrequency ablation. *AJR* 2012;198:W285–91.
- [6] Yi An Y, Kim SH, Park YH. Response evaluation to neoadjuvant chemotherapy in advanced breast cancer: comparison of MRI and PET/CT. *J Kor Soc Radiol* 2014;71(2):89–96.
- [7] Whipp E, Beresford M, Sawyer E, Halliwell M. True local recurrence rate in the conserved breast after magnetic resonance imaging-targeted radiotherapy. *Int J Radiat Oncol Biol Phys* 2010;76(4):984–90.
- [8] Oh SD, Lee JS. A comparison of residual tumor accuracy prior to re-excision between breast magnetic resonance imaging and ultrasonography. *J Breast Dis* 2014;2(1):8–15.
- [9] Hasan DI, Mazrouh MA, Tantawy IM. The value of dynamic MRI in the evaluation of the breast following conservative surgery and radiotherapy. *Egypt J Radiol Nucl Med* 2010;41:469–73.
- [11] Hyunkyung Y, Shin HJ, Baek S, Cha JH, Kim H, Chae EY, et al. Diagnostic performance of apparent diffusion coefficient and quantitative kinetic parameters for predicting additional malignancy in patients with newly diagnosed breast cancer. *Magn Reson Imag* 2014;32:867–74.
- [13] Khattab EM, Abdulmonaem G, Al-Attar AZ. Magnetic resonance spectroscopy in recurrent breast masses following conservative surgery and radiation therapy. *Egypt J Radiol Nucl Med* 2012;43:19–24.
- [14] Bollet MA, Sigal-Zafranib B, Mazeauc V, Savignonic A, Rochefordière ADL, Vincent-Salomonb A, et al. Age remains the first prognostic factor for loco-regional breast cancer recurrence in young (<40 years) women treated with breast conserving surgery first. *Radiother Oncol* 2007;82:272–80.
- [16] Winzera KJ, Sauerbreib W, Braunc M, Lierschd T, Dunste J, Guskif H, et al. Radiation therapy and tamoxifen after breast-conserving surgery: updated results of a 2 × 2 randomised clinical trial in patients with low risk of recurrence. *Eur J Cancer* 2010;46:95–101.
- [17] Jiang L, Zhou Y, Wangc Z, Lud X, Chena M, Zhou C. Is there different correlation with prognostic factors between “non-mass” and “mass” type invasive ductal breast cancers? *Eur J Radiol* 2013;82:1404–9.