Role of diffusion weighted imaging and dynamic contrast enhanced MR mammography to detect recurrence in breast cancer patients after surgery

Safaa Ibrahim Saif El-nasr a,*, Rasha Wessam Abdel Rahman a, Sherif Fathy Abdelrahman a, Maha Hussein Helal b, Soha Talaat Hamed a

a Radiology Department, Faculty of Medicine, Cairo University, Egypt
b Radiology Department, National Cancer Institute, Cairo University, Egypt

Received 10 October 2015; accepted 10 April 2016
Available online 2 May 2016

Abstract  Objective: To assess role of Diffusion weighted imaging (DWI) in addition to dynamic contrast-enhanced magnetic resonance mammography (DCE-MRM) in detection of breast cancer recurrence after surgery.

Patients and methods: Sixty female patients who underwent breast surgery were included in this prospective study. Patients were examined by sonomammography followed by DCE-MRI to exclude recurrence. DWI was performed using $b$ values of 0, 50, and 850 s/mm². Patients with suspected recurrence were subjected to histopathological confirmation.

Results: Twenty seven patients had pathologically proven recurrence and thirty three patients showed spectrum of post operative changes. DCE-MRI was superior to DWI with 2 false positive (FP) cases and no false negative (FN) cases, while DWI showed 3 (FN) cases and 4 (FP) cases. DCE-MRI & DWI showed sensitivity (100%, 88.9%), specificity (93.9%, 87.9%), positive predictive value (PPV) (93.1%, 88.9%), negative predictive value (NPV) (100%, 90.6%) & accuracy (96.7%, 88.3%) respectively.

Conclusion: Our study showed better diagnostic performance for DCE-MRI compared to DWI in post operative breast assessment. However, DWI can provide an alternative diagnostic tool to contrast administration “if interpreted in association with conventional MR sequences” thus can be used when contrast media is contraindicated.

© 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

Breast cancer is the most frequent cancer in women, where it accounts for 27% of all female cancers. It is considered to be the second after lung cancer as the most prevalent cause of...
death due to cancer in women (1). After surgical treatment of breast cancer and radiation, the incidence of local recurrence is between 1% and 2% per year, with most of the recurrences occurring in the first 5 years (2).

Early detection and proper treatment of recurrent disease is of high importance as it still may present without distant metastases. Also, second ipsilateral primary carcinomas in the treated breast can occur at every site and develop on average 7 years after the first primary tumor (3).

For many years, magnetic resonance imaging (MRI) examination has been widely accepted as a diagnostic tool for evaluation of breast cancer (4). One of its indications, is the differential diagnosis between cancer recurrence and surgical scar in surgically treated patients (5). Both breast surgeries and radiotherapy can produce scarring with architectural distortion. Thus differentiating those expected post operative and related treatment changes from true recurrence on physical examination as well as on post-treatment breast imaging can be sometimes challenging (6).

Over the past decade, many new MR techniques and interpretation strategies have been developed aiming to improve the specificity and positive predictive value (PPV) of breast MRI. Of these diffusion weighted imaging (DWI) (7) is an unenhanced MRI sequence that measures the random motion of free water protons (Brownian motion) and characterizes different tissue properties, and thus can provide complementary information to dynamic contrast enhanced MRI (DCE-MRI) (8,9).

2. Patients and methods

2.1. Patients

Our study was a prospective one, approved by the Faculty of Medicine Ethics committee of the Cairo University; cases had given informed consents for their used data. The study was performed at least 6 months after the operation on sixty breast cancer female patients who underwent CBS (n = 29) or MRM (n = 31) where two of them had reconstructive surgery. The study was conducted at radiology department of Kasr El Aini hospital and National Cancer institute – Cairo University in the period from March 2013 until March 2015. The patients underwent full history taking and clinical examination. Digital mammography, US and MRI examinations were performed for all patients.

Patient preparation: Renal laboratory function tests were done for all patients before contrast enhanced MRI. An I.V. cannula was inserted in the patients’ contralateral arm to the side of breast surgery whenever possible. After lying in prone position with a dedicated bilateral breast coil, Magnevist (gadopentetate dimeglumine) was injected as 0.2 mL/kg (0.1 mmol/kg) intravenously by power injector.

2.2. Methods

MR imaging was performed for all cases with high field strength 1.5 T (Gyroscan Intera Phillips, medical system Netherlands) with the following protocol:

- Precontrast sequences: T1 weighted fast spin echo sequence (TR = 500 ms, TE = 5.3 ms) in axial orientation with slice thickness = 4 mm, matrix = 512 x 192, flip angle = 90° and FOV = 34–37 cm. T2 weighted fast spin echo sequence (TR = 120 ms, TE = 4.9 ms) in axial & sagittal orientation with slice thickness = 4 mm, matrix = 512 x 192, flip angle = 90° and FOV = 34–37 cm. T2-weighted inversion recovery (IR) (TR = 80, TE = 6.5 ms) in axial orientation with slice thickness = 4 mm, matrix = 512 x 192, flip angle = 90° and FOV = 34–37 cm.

![Fig. 1](image1.png)

**Fig. 1** Receiver operating characteristic (ROC) curve of ADC value in the studied group.

![Fig. 2](image2.png)

**Fig. 2** Shown is the diagnostic performance for DCE-MRI & DWI.
• **STIR sequence:** TR = 80, TE = 6.5 ms) in axial orientation with slice thickness = 4 mm, matrix = 512 × 192, flip angle = 90° and FOV = 34–37 cm.

• **DW sequences** in axial orientation with TR = 5000, TE = 77 ms, slice thickness = 5 mm, 1 mm interslice gap, matrix = 124 × 100 and b-values (0, 50 and 850 s/mm²).

• **Dynamic post contrast** series were performed using six series of 3D ‘T1 High Resolution Isotropic Volumetric Examination’ THRIVE acquisition. One sequence before & five after contrast injection (nearly at 1.5, 3, 4.5, 6 and 7.5 min) with parameters TR = 2.8, TE = 9 ms and slice thickness = 1.5 mm.

• Rate of injection was 10 mL per 15 s followed by saline flush.

**Image interpretation:** Data analysis and interpretation were performed by two experienced radiologists as follows:

**Interpretation of dynamic contrast MRI:** Subtraction images were first examined followed by examination of the rest of the sequences. Cases that showed pathological enhancement ‘masses/non mass enhancement’ were analyzed concerning the following: side of the lesion, whether on the ipsilateral or contralateral side of the previous surgery, number of lesions (multifocal or multicentric), size, morphology of the lesion “shape and margin”, patterns of enhancement, kinetic analysis with drawing of region of interest (ROI) on the lesion and performing the corresponding time intensity curves with calculating maximum relative enhancement and time to peak. Associated findings as edema, skin thickening and nipple retraction were also reported. DCE-MRI was considered positive in cases that showed suspicious enhancement and patients were further sent for pathological confirmation. MRI was considered negative in the absence of suspicious enhancement and patients were sent for follow-up (3–6 months). Suspicious enhancement includes heterogeneous, ring or non mass enhancement of the lesion.

**Interpretation of DWI:** DWI is assessed both qualitatively and quantitatively in all patients.

**Qualitatively:** By the visualization of signal intensity that corresponds to the lesion of concern in the conventional images and observing its signal character with increasing b-values and in the corresponding Apparent Diffusion Coefficient (ADC) maps. The ADC map for each lesion was calculated using the different b-values (0, 50 and 850 s/mm²). In order to avoid contamination by adjacent structures, an oval region of interest (ROI) was chosen with average diameter of 4-6 mm and drawn over the lesion with exclusion of areas of breaking down whenever possible.

**Quantitatively:** By measuring ADC values on ADC maps for the positive cases at the site of suspected recurrence and for the negative cases at the site of the post operative changes.

We considered $1.24 \times 10^{-3}$ mm²/s to be our cutoff ADC value in differentiating benign from malignant breast lesions according to Pereira et al. (10).

---

**Fig. 3** Female patient 36 year old underwent right CBS 2 years ago: (a) MR subtraction sequence shows stippled enhancement at the operative bed (red arrow), (b) time-signal intensity curve shows delayed peak of contrast uptake with continuous rising (type I) curve, (c) DWI & (d) ADC map with ROI at the operative bed (red circle) showed facilitated diffusion with ADC value of $1.4 \times 10^{-3}$ mm²/s. Findings are consistent with post operative sequel (post operative scar) with no recurrence.
DWI positive lesions showed abnormal bright signal intensity ‘restriction’ that remains enhanced with increasing b values and showed intermediate/low signal intensity on the corresponding ADC map with ADC values lower than or equal to our cutoff point.

We did not perform FNA in our study and pathological confirmation was obtained using tissue core biopsy.

Statistical analysis: We used software SPSS computer program (version 16 windows) for data analysis.

3. Results

Sixty female patients were included in our final statistical analysis. The patients’ mean age was 49.3 ± 9.95 (range from 35–68 y). Twenty-nine patients underwent Conservative Breast Surgery (CBS) and 31 underwent MRM, 2 of them had reconstructive surgery “Transverse Rectus Abdominis Myocutaneous” (TRAM). Pathology was done for 32 cases: 27 were pathologically confirmed to have recurrence while recurrence was excluded in the remaining 5 cases. The rest of cases (n = 28) showed spectrum of post-operative changes and were considered negative for malignancy by imaging and no newly developed lesions on follow-up.

Recurrent lesions were detected in the positive group (27 cases) in a period of 9–60 months (mean 28 months) after operation. Twelve cases showed recurrence at the operative bed (ipsilateral recurrence). Eleven cases showed recurrence/newly developed malignant lesions on the contralateral side. Three cases had bilateral malignancy while one case showed metastasis in the chest wall (new lesion centered on the manubrium sterni).

Dynamic sequence in our study showed pathological enhancement in 29 cases (48.3%). They showed early peak of contrast uptake (in first two minutes) with high maximum

![Image](https://example.com/image)

**Fig. 4** Female patient 65 year old underwent right MRM 1.5 years ago: (a) T2WI shows high signal oval shaped cavity at the operative bed with low signal capsule, (b) subtraction sequence shows marginal enhancement of the cavity, (c) time-signal intensity curve shows delayed peak of contrast uptake with rising curve (type I), (d) DWI shows faint marginal high signal and (e) ADC map shows high signal and after drawing ROI, the ADC value was $1.34 \times 10^{-3}$ mm$^2$/s. Diagnosis was operative bed chronic seroma.
relative enhancement and either early wash out type III curve \( (n = 18) \) or type II plateau curve \( (n = 11) \). Those 29 cases represent 27 TP cases (pathologically proven) and 2 FP cases (one case was foreign body granuloma & the other was borderline phyllodes tumor). The remaining 31 cases (51.7\%) showed no suspicious enhancement and were diagnosed as TN cases (their follow-up showed no changes).

According to DWI, 28 cases (46.7\%) showed high signal ‘restricted diffusion’ on high b value 850 mm\(^2\)/s and corresponding low/intermediate signal on the ADC maps. Those 28 cases included 24 TP cases and 4 FP cases (2 cases were fat necrosis and 2 cases were atypical hyperplasia). In the remaining 32 cases (53.3\%), 29 were TN cases (did not show low signal on the ADC maps), while the remaining 3 cases were FN cases (two cases with tumoral breaking down showed high signal on the ADC maps and one case had small lesion that was not appreciated on the ADC map).

The mean ADC value of the negative group \([1.50 \pm 0.45 \text{ (range = 0.5–2.6} \times 10^{-3} \text{ mm}^2/\text{s}]\) was statistically higher than the mean ADC value of the positive group (pathologically proven) \([0.81 \pm 0.23 \text{ (range = 0.3–1.2} \times 10^{-3} \text{ mm}^2/\text{s}]\) with \( p \) value = 0.001 \( (p < 0.01 = \text{highly significant}) \).

The ROC curve indicated a good statistical performance of the ADC values to predict the presence of malignant lesions (area under the curve = 0.941) Fig. 1.

Pathological confirmation was done for thirty-two patients; ‘IDC’ was found in twenty-six (43.3\%) patients (Fig. 5), ‘ILC’ in one patient (1.7\%) with a total of twenty-seven positive patients and five patients showed no recurrence and their pathology revealed atypical hyperplasia in two cases, borderline phyllodes tumor in one case, foreign body granuloma in one case and fat necrosis in one case (Fig. 6). So the latter five cases as well as the rest of patients [they were twenty-five patients (41.7\%) who had post operative scarring (Fig. 3), one patient (1.7\%) had fat necrosis and two patients (3.3\%) had seromas (Fig. 4) represent the negative cases in our study \( (n = 33) \).

After calculating the sensitivity, specificity, PPV, NPV and accuracy for dynamic and DWI, dynamic sequence showed better diagnostic performance than DWI as shown in Fig. 2.

### 4. Discussion

Breast cancer is a disease that carries a risk of recurrence whether at the lumpectomy bed, adjacent to its margin or elsewhere in the breast (11).

DCE-MRI has been accepted as a highly significant diagnostic tool that can aid in detection and characterization of primary as well as recurrent breast cancers (12).

Having a high sensitivity that sometimes can exceed all other breast imaging modalities, DCE-MRI showed a somehow limited specificity, that required searching for additional techniques aiming to improve its specificity (13).

DWI is an unenhanced MRI sequence that reflects the random thermal motion of water molecules. DWI can give an important information about tissue cellularity thus can be a
useful technique for the discrimination between benign and malignant breast lesions (2,14).

Our study aimed to evaluate the diagnostic role of DWI in addition to DCE-MRM in assessing the postoperative patients and thus to discriminate between true cancer recurrence from accepted benign post operative sequelae.

The DCE-MRI in our study diagnosed 29 patients as positive for recurrence compared to 31 negative cases. After pathological results were obtained for 32 as well as follow-up images for the rest of cases, all were compared to DCE-MRI results and revealed 27 patients as TP cases, 31 as TN cases, 2 as FP cases and no FN. As a result DCE-MRI showed 100% sensitivity, 93.9% specificity, 93.1% ‘PPV’, 100% ‘NPV’ and 96.7% accuracy.

On the other hand, DWI diagnosed 28 cases positive for recurrence and 32 negative for recurrence. DWI showed 24 TP cases, 29 TN cases, 4 FP cases and 3 FN cases. The diagnostic performance of DWI showed 88.9% sensitivity, 87.9% specificity, 88.9% ‘PPV’, 90.6% ‘NPV’ and 88.3% accuracy.

As a result our study showed that diagnostic performance of dynamic sequence was higher than that of the DWI.

Our results disagree with Rinaldi et al. (2) & Mansour and Behairy (15) results. Both studies showed that DWI was higher in the specificity than the dynamic MRI. This can possibly be explained as DWI in our study showed higher number of FP & FN cases (compared to dynamic sequence) decreasing its specificity and sensitivity respectively. Also in our study we compared the results obtained from DWI to that of dynamic

---

**Fig. 6** Female patient 39 year old underwent right mastectomy 14 months ago. Post operative scar tissue that elicits low signal on (a) T1WI and high signal on the (b) STIR sequence with central focal area of fat signal intensity. Associated skin thickening, retraction and edema are also noted. (c) MR subtraction images show marginal enhancement at the operative bed focal area. (d) Time intensity curve shows continuous rising curve. (e) High signal is seen in DWI with b value (850) and (f) low value on ADC map (0.49 × 10^{-3} mm^2/s). Tissue core biopsy showed focal area of fat necrosis with no malignant cells.
images, unlike Mansour and Behairy study which combined the conventional sequences ‘T1WI & T2STIR’ in the diagnoses of some cases through DWI by raising its diagnostic accuracy. This was better appreciated in cases of fat necrosis that can give a FP appearance on dynamic as well as on DWI (as happened in our study) and thus were diagnosed correctly as TN cases.

In our study, the mean ADC value of benign lesions (1.50 ± 0.45 SD) was statistically higher than the mean ADC value of malignant lesions (0.81 ± 0.23SD), [p value = 0.001]. One exception in our study is the 2 cases of fat necrosis, as they showed low ADC values mimicking recurrence (mean ADC of fat necrosis was 0.695 ± 0.21). Fortunately those two cases were diagnosed by detection of fat signal in the conventional sequences; presence of high signal in the lesion in T1WI showed signal drop in T2 STIR. This result matched Mansour and Behairy (15) results as their mean ADC value of the benign lesions (1.2 ± 0.34 × 10⁻³ mm²/s) was statistically higher than that of the malignant lesions (0.83 ± 0.15 × 10⁻³ mm²/s) also with 2 exceptions in cases of fat necrosis as in our study and in cases of fibrosis. Both have low values (fibrosis was = 0.77 ± 0.2 × 10⁻³ mm²/s, and fat necrosis was = 0.56 ± 0.1 × 10⁻³ mm²/s).

Our study also matched Rinaldi and co-authors (2) study, where the mean ADC value of their local recurrence patients was 1.25 ± 0.29 × 10⁻³ mm²/s, while the mean ADC value for benign post operative sequelae was 1.84 ± 0.24 × 10⁻³ mm²/s. Another study was conducted by Abdulghaffara and Tag-Aldeinb (16) that concluded that all cases of local tumor recurrence showed lower ADC values [mean ADC = (0.95 ± 0.37 × 10⁻³ mm²/s)] than benign post operative changes [mean ADC = (1.69 ± 0.16 × 10⁻³ mm²/s)] which also matched our results. However, one exception of the benign sequela was a case of hematoma that showed lower ADC value (0.34–0.56 × 10⁻³ mm²/s) and was diagnosed by conventional MRI. We did not have any cases of hematomas in our study to compare with.

Although DWI has the advantage of being an easy, contrast free imaging sequence, it poses some limitations. Some of them appeared in our study as in cases of small lesions (lesions are difficult to elicit on the ADC maps so difficult to be measured) and in cases of fat necrosis (can give low ADC values so interpreted as FP lesions). Also fibrosis and hematomas can give false positive appearance on DWI as stated by other authors (15,16) respectively.

Based on our study we can recommend patients with suspicious tiny lesions which are difficult to be diagnosed by DWI; dynamic sequences can be satisfactory for diagnosis. Also in cases with suspected fat necrosis which is a frequent finding in the post operative breast, conventional sequences are superior in detection of fat signal intensity within the lesion to avoid diagnostic dilemmas caused by interpretation of DWI or dynamic sequences alone in many cases.

5. Conclusion

Although DWI is a safe, fast, contrast free sequence that can be easily added to all MRI machines, it can possess some limitations. Based on our study, dynamic sequence showed better diagnostic performance than DWI in the setting of the post operative breast assessment. DWI can be however, a good alternative imaging technique if combined with conventional MR sequences in patients where contrast media is better avoided as in renal impairment and during pregnancy.

Conflict of interest

The authors declare that there are no conflict of interests.

References