Role of diffusion weighted images combined with breast MRI in improving the detection and differentiation of breast lesions

Waleed Hetta

Radiodiagnosis Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Received 6 September 2014; accepted 25 October 2014
Available online 17 November 2014

Abstract  Purpose: To assess the impact of diffusion-weighted images as a complementary tool to conventional breast MRI in the evaluation of various breast lesions.

Materials and methods: From November 2013 to June 2014 thirty patients referred from breast clinic by breast symptoms and abnormal sono-mammography lesions have been included in this study. All patients underwent breast DCE-MRI combined with DWI and the results were compared with the histopathological examination which was used as the standard diagnostic method.

Results: The study included thirty patients complaining of breast lesions, 35 lesions were detected, according to the histopathological analysis, there were 20 malignant lesions (57.14%) and 15 benign lesions (42.86%). DCE-MRI had a sensitivity of 80%, a specificity of 73.33%, PPV of 80%, NPV of 73.3% and accuracy of 77.14%. The malignant lesions showed a mean ADC value of 1.03 ± 0.35. Alternatively, the benign lesions showed a mean ADC value of 1.38 ± 0.26. Among the 20 malignant lesions, 17 lesions showed an ADC value ≤1.20 mm²/s and 3 lesions showed an ADC value >1.20 mm²/s. While among the 15 benign lesions, 14 lesions showed ADC value >1.20 mm²/s and 1 lesion showed an ADC value ≤1.20. The ROC curve showed that the best ADC cut-off value to differentiate between benign and malignant lesions was 1.2 mm²/s (P < 0.001) with sensitivity, specificity, PPV, NPV and accuracy of 85%, 93.33%, 94.4%, 82.4% and 90.3% respectively.

Conclusion: DWI had a higher sensitivity and specificity than DCE-MRI with ADC cut off value 1.20. This value was a sensitive and specific parameter in differentiating benign and malignant breast lesions.

1. Introduction

Breast cancer is the most common female neoplasm (31% of tumors in females), and the second-leading cause of death among women. Breast lesions were first classified as malignant or benign categories (1). Further, the increasing rate of breast...
cancer continues to be a major area of concern for both clinicians and researchers. Increased awareness in the affected population leads to more frequent physical examinations and diagnostic imaging procedures which results in earlier diagnosis and hence improved prognosis (2).

Mammography has been proven to detect breast cancer at an early stage; other screening technologies also may contribute to the earlier detection of breast cancer, particularly in women under the age of 40 years for whom mammography is less sensitive such as breast ultrasound or MRI (3).

Breast ultrasound examination has been used for years as an adjunct to mammography for evaluating palpable or mammographically detected breast masses to determine if a lesion represents a cyst or a solid mass (4).

Conventional mammography and ultrasound are known to have high false positive rates in the detection of breast malignancy (60–80%), resulting in unnecessary biopsies being performed. So, MR techniques have shown strong potential to improve the sensitivity and specificity in the diagnosis of breast cancer (5).

Breast MRI has become an important tool for breast cancer detection and characterization. Dynamic contrast-enhanced MRI is highly sensitive for breast cancer, allowing detection of malignancy that is occult on physical examination, mammography, and sonography (6).

Breast MRI may be used to distinguish between benign and malignant areas, this may reduce the number of breast biopsies done to evaluate a suspicious breast mass. Although MRI can detect tumors in dense breast tissue, it cannot detect tiny specks of calcium (micro calcifications), which account for half of the cancers detected by mammography (7).

Typical breast MRI exams involve a contrast-enhanced scan to highlight tissue with increased vascularity, very sensitive for detecting malignancies but also producing many false-positives (8).

DWI is a technique that involves the exchange of water molecules (diffusion) between breast tissue compartments. Diffusion rates vary between normal and pathologic tissue. The value of diffusion of water in tissues is called apparent diffusion coefficient (ADC) and it is calculated in the MRI machine by using ADC mapping. The studies showed that the ADC varies between malignant and benign breast masses. So application of DW sequence to the breast MRI will improve the specificity of the MRI (9).

So using diffusion-weighted imaging (DWI) combined to MRI is helpful to distinguish malignant versus benign breast lesions and it also may reduce the number of unnecessary breast biopsies (10).

2. Patients and methods

From November 2013 to June 2014, thirty patients have been included in this study, the patients’ age ranges from 24 to 76 years with mean age of 47 ± 10.5.

2.1. Inclusion criteria

1. Female gender.
2. Age more than 18 years old.
3. Patients with newly discovered breast symptoms.
4. Patients with recurrent breast cancer following chemotherapy or radiotherapy sessions.

2.2. Exclusion criteria

1. Male gender.
2. Patient with recent breast trauma in the same diseased breast within the last 6 months.
3. Contraindication to perform MRI examination. These include:
   - Cardiac pacemaker.
   - Metallic aneurysm clips.

The patients underwent full history taking and dedicated general and local examination. All patients underwent breast MRI examination and the results of breast MRI were compared with the histopathological examination which was used as the standard diagnostic method.

2.3. MR imaging protocol

Dynamic contrast enhanced MRI was performed with high field strength 1.5 Tesla MR Systems using dedicated double breast coil. DWI was performed before the DCE-MRI acquisition using a diffusion-weighted echo-planar imaging (EPI) sequence with parallel imaging. A bolus of gadolinium was injected intravenously by a pump at a dose of 0.1 mmol/kg. Dynamic T1 WIs were then performed using gradient echo T1 weighted image with fat suppression (STIR).

2.4. Image post processing on the workstation

A region of interest was defined for each DCE-MRI-detected lesion at the corresponding location on the combined DWI (SDWI) series. The mean ADC of the voxels in the ROI was calculated for each lesion. Quantitative analysis was done presented in automatically created time/signal intensity curve.

2.5. MRI image interpretation

STIR images were first examined to detect the presence or absence of lesion enhancement.

In case of lesion enhancement the corresponding non subtracted pre-contrast and post contrast images in each time point were viewed together and lesion interpretation took place whether it a focus, mass or non mass like enhancement.

In case of mass enhancement evaluation was carried out as follows:

- Its shape (regular or irregular).
- Its border (well defined, ill defined, speculated).
- Pattern of enhancement (homogenous, heterogeneous or ring enhancement).
- Dynamic behavior of the mass with evaluation of the initial enhancement as well as the shape of time/signal intensity curve (type I, type II or type III) was studied.

Diffusion-weighted images are then examined regarding the signal intensity and the mean ADC of each lesion.

MRI BI-RADS classification was applied for each lesion based on the combination of morphologic and kinetic criteria.
described by Fischerl et al. (11) and Sardanelli et al. (12). Findings were correlated with histopathological result.

2.6. Data analysis

Data were statistically described in terms of range, mean ± standard deviation (±SD), frequencies (number of cases) and percentages when appropriate. Accuracy was represented using the terms sensitivity and specificity. All statistical calculations were done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results

The present study included 30 patients with mean age of 47 ± 10.5 and age range of 24–76 years. The mean age of patients with benign lesions was 49 ± 5.7, whereas, the mean age of patients with malignant lesions was 47 ± 12.1, (Table 1 and Fig. 1).

Among the included 30 patients, 26 patients (86.67%) presented with a single lesion and 4 patients (13.33%) presented with multiple lesions.

The study is formed of 12 patients (40%) who came with first time breast symptoms while the remaining 18 patients (60%) were in follow up following breast cancer surgery and management.

Regarding the site of the detected lesions, the malignant lesions were retro-areolar in 5 patients (25%), deeply seated in 7 patients (35%), upper outer quadrant in 4 patients (20%), at operative bed in 1 patient (5%), lower outer quadrant in 1 patient (5%) and lower inner quadrant in 2 patients (10%).

Alternatively, the benign lesions were retro-areolar in 1 patient (6.67%), deeply seated in 3 patients (20%), upper outer quadrant in 6 patients (40%), all the breast in 2 patients (13.33%), lower outer quadrant in 1 patient (6.67%) and axillary bed in 2 patients (13.33%) (Table 2 and Fig. 2).

According to the histopathological analysis, there were 20 malignant lesions (57.14%) and 15 benign lesions (42.86%). The histopathological types are presented in Table 3 and Fig. 3.

3.1. MRI BI-RADS of benign and malignant lesions

The detected 35 breast lesions classified according to MRI BI-RADS scoring were: 7 lesions assigned for MRI BI-RADS 2 were benign lesions, 8 lesions were assigned for MRI BI-RADS 3; 4 lesions were malignant and 4 lesions were benign, 13 lesions were assigned for MRI BI-RADS 4; 9 lesions were malignant and 4 lesions were benign, 7 lesions assigned for MRI BI-RADS 5 were malignant lesions (Table 4 and Fig. 4).

Regarding appearance of lesion in MRI T2 weighted image, the lesions were low signal in 12 malignant lesions and 8 benign lesions, intermediate signal in 6 malignant lesions and 3 benign lesions and high signal in 2 malignant lesions (Phyllodes cystosarcoma and inflammatory carcinoma) and 3 benign lesions.

Regarding the shape of the lesion, the shape was diffuse in 6 malignant lesions and 2 benign lesions, oval in 4 malignant lesions and 6 benign lesions. In addition the shapes were round, irregular in (7) (2), (3) (5) malignant lesions and benign lesions respectively.

Considering the margin of the lesions detected, ill-defined margin was seen in 21 lesions (60%); 14 lesions (66.67%) were malignant and 7 lesions (33.33%) were benign. On the other hand, well-defined margin was noted in 14 (40%) lesions; 6 (42.86%) lesions were malignant and 8 (57.14%) lesions were benign.

Considering the pattern of contrast enhancement, Rim enhancement was noted in 7 lesions; 5 lesions were malignant and 2 lesions were benign. On the other hand, heterogeneous enhancement was noted in 11 lesions; 10 lesions were malignant and 1 lesion was benign. In addition, homogenous enhancement was noted in 12 lesions; 5 lesions were malignant and 7 lesions were benign, and non enhancement in 5 benign lesions.

Regarding the type of dynamic curve (time/signal intensity curve), type 3 (wash out) was noted in 13 malignant lesions. Type 2 (plateau) was noted in 7 malignant lesions and 7 benign lesions while type 1 (progressive rising) was noted in 8 benign lesions (Table 5 and Fig. 5).

DCE-MRI had a sensitivity of 80%, a specificity of 73.33%, PPV of 80%, NPV of 73.3% and accuracy of 77.14% (Fig. 6).

The malignant lesions showed a mean ADC value of 1.03 ± 0.35.

Alternatively, the benign lesion showed a mean ADC value of 1.38 ± 0.26, (Table 6 and Fig. 7). This table shows highly statistically significant ADC difference between benign and malignant lesions, with p-value < 0.001 HS.

The ROC (receiver operating characteristic) curve showed that the best ADC cut-off value to differentiate between benign and malignant lesions was 1.2 mm²/s (P < 0.001) with

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison between histopathological results as regards age.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Min.</td>
</tr>
<tr>
<td>Malignant</td>
<td>24.00</td>
</tr>
<tr>
<td>Benign</td>
<td>45.00</td>
</tr>
</tbody>
</table>

Fig. 1 Comparison between histopathological results as regards age.
sensitivity, specificity, PPV, NPV and accuracy of 85%, 93.33%, 94.4%, 82.4% and 90.3% respectively (Fig. 8).

Among the 20 malignant lesions, 17 lesions showed an ADC value ≤1.20 mm²/s and 3 lesions showed an ADC value >1.20 mm²/s. While among the 15 benign lesions, 14 lesions showed ADC value >1.20 mm²/s and 1 lesion showed an ADC value ≤1.20 (Table 7 and Fig. 9).

4. Discussion

We conducted a study of 30 patients (12 patients with first time breast lesions and 18 patients post operative recurrent breast lesions) with 35 breast lesions (20 malignant and 15 benign lesions) to evaluate the role of DWI in the detection of primary or recurrent breast lesions.

In this study, deep sited region was the most frequent site of malignant lesions (35.00%), followed by retro areolar site and upper outer quadrant with 25.00% and 20.00% respectively. The upper outer quadrant was the most frequent site of benign lesions (40.00%), followed by deep sited region and axillary site with 20.00% and 13.33% respectively.

This is comparable with Harirchi et al. who reported that upper-outer quadrant was the most frequent site of malignant lesions (39.9%), followed by peri-areolar region (18.4%), while the most frequent site of benign lesions was upper-outer quadrant (32.75%), followed by axillary bed (15.3%) (13).

According to our study, the two most frequent malignant lesions were invasive ductal carcinoma and invasive lobular carcinoma which represented 17.14% and 14.29% respectively while the two most frequent benign lesions were fibroadenoma and fibrotic scar which represented 17.14% and 17.14% respectively.

On the other hand, Li et al. showed in their breast lesions survey that invasive ductal carcinoma account for 56%, fibroadenoma in 20% and invasive lobular carcinoma in 10% only (14).

Appearance of the lesions in T2 weighted image in this study was almost either low or intermediate signal intensity which is similar to the result of a study conducted by Kuhl et al. who found that 87% of lesions in their study were either low or intermediate signal to the adjacent glandular tissue (15).

Shape of the malignant lesions in this study was variable with a predominant round and diffuse pattern in 7 and 6 lesions respectively, while benign lesions were oval and irregular in shape in 6 and 5 lesions respectively.

Al-Khawari et al. and Tozaki et al. showed in their studies that most malignant lesions had diffuse and irregular shape while benign lesions had round or oval shape (16,17).

In our study, we found ill defined & speculated margins in 21 mass lesions, 7 of them were benign and 14 lesions were
malignant, there were 14 well defined mass lesions; 8 of them were benign and 6 lesions were malignant.

This is comparable with Al-Khawari et al. who reported that most malignant lesions showed ill defined margin while benign lesion showed well defined margin. They also reported that the value of morphologic criteria in the form of shape and margin of the lesion to describe MRI-detected breast lesions has been limited by the lack of a definitive classification scheme (16).

In our study regarding pattern of enhancement, heterogeneous enhancement was seen in 11 lesions, rim in 7 lesions, homogenous in 12 lesions and non enhancement in 5 lesions.

However, Tozaki et al. reported that the most frequent morphological finding among the lesions was heterogeneous and rim internal enhancement with a percentage of 45% and 30% respectively (17).

In our study, the sensitivity and specificity of DCE-MRI examination were 80% and 73.33% respectively, this was based on the combination of morphologic and kinetic criteria described by Fischerl et al. (18) and Sardanelli et al. (12).

We disagree with Gianfelice et al. who reported that sensitivity and specificity of DCE-MRI were 90% and 67% respectively (19).

Drew et al. reported that sensitivity and specificity of DCE-MRI were 90% and 76% respectively (20).

Table 4 MRI BI-RADS of benign and malignant breast lesions.

<table>
<thead>
<tr>
<th>BIRADS</th>
<th>Malignant</th>
<th>Benign</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>II</td>
<td>0</td>
<td>0.00</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>4</td>
<td>20.00</td>
<td>4</td>
</tr>
<tr>
<td>IV</td>
<td>9</td>
<td>45.00</td>
<td>4</td>
</tr>
<tr>
<td>V</td>
<td>7</td>
<td>35.00</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>100.00</td>
<td>15</td>
</tr>
</tbody>
</table>

Fig. 3 Pie chart shows the histopathological diagnoses of the 35 examined breast lesions.

Fig. 4 Pie chart shows the histopathological diagnoses of the 35 examined breast lesions.
Table 5  The type of curve & distribution of the detected breast lesions in correlation with histopathological results.

<table>
<thead>
<tr>
<th>Type</th>
<th>Groups</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant</td>
<td>Benign</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>I</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
<td>35.00</td>
</tr>
<tr>
<td>III</td>
<td>13</td>
<td>65.00</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>100.00</td>
</tr>
</tbody>
</table>

$\chi^2 = 20.71$

$p$-Value $<0.001$ (HS)

Fig. 5  Pie chart shows the type of curve & distribution of the detected breast lesions in correlation with histopathological results.

Table 6  Comparison between histopathological results as regards ADC.

<table>
<thead>
<tr>
<th>Histopathological</th>
<th>ADC</th>
<th>$t$-Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Min.</td>
<td>Max.</td>
</tr>
<tr>
<td>Malignant</td>
<td>0.50</td>
<td>1.80</td>
</tr>
<tr>
<td>Benign</td>
<td>1.13</td>
<td>1.95</td>
</tr>
</tbody>
</table>

Fig. 6  A receiver operating characteristic (ROC curve) for DCE-MRI to differentiate between benign and malignant breast lesions.

Fig. 7  Bar chart shows the mean ADC values of benign and malignant lesions.

Fig. 8  A receiver operating characteristic (ROC curve) analysis for the ADC value to differentiate between benign and malignant breast lesions.
In our study after evaluating the morphologic characteristics of each lesion, we assessed the dynamic behavior using quantitative analysis of signal intensity [measured by means of computer manipulated region of interest (ROI)] as well as type of the time/signal intensity curve.

Among benign lesions, type 1 curve was obtained in 8 lesions; type 2 curve in 7 lesions while no lesion had been detected showing type 3 curves.

Among malignant lesions, type 1 curve was not obtained in any malignant lesion, type 2 in 7 lesions and type 3 in 13 lesions.

This is in agreement with many studies that reported the importance of the curve shape in differentiating between malignant and benign lesions. Type III curve is more suspicious for malignancy (21), whereas progressive rising curves are associated with benign lesions (21). Plateau curves are indicative of either malignant or benign lesions (22).

In this study, DWI had a sensitivity of 85% and specificity of 93.33%, whereas, DCE-MRI had a sensitivity of 80% and a specificity of 73.33%.

Kul (2011), reported 94.4% sensitivity and 84.4% specificity of DWI in the characterization of lesions with ADC cut off 0.90 mm$^2$/s (23). Tozaki and Maruyama achieved a specificity of 67% and sensitivity of 97% for lesions with ADC cut off 1.10 mm$^2$/s (24).

Our findings for lesions showed that the best ADC cut off value to differentiate between benign and malignant lesions was 1.20 mm$^2$/s. Malignancy exhibited lower mean ADC values compared with those of benign lesions being 1.03 $\times 10^{-3}$ mm$^2$/s and 1.38 $\times 10^{-3}$ mm$^2$/s respectively.

Comparable with Rubesova et al. in their study, they found that the threshold between malignant and benign lesions for highest sensitivity and specificity (both 86%) was around 1.13 $\times 10^{-3}$ mm$^2$/s (25).

Similarly, Imamura et al. reported that the most feasible ADC value to depict malignant lesions was found to be less than 1.10 $\times 10^{-3}$ mm$^2$/s. Using this threshold sensitivity & specificity were 68.8 and 72.7 respectively (26).

Also, Yabuuchi et al. demonstrated an ADC value less than 1.30 $\times 10^{-3}$ mm$^2$/s as the strongest indicator of malignancy (27).

This difference in ADC threshold can be explained by difference in many technical variables that can affect the ADC values, such as different MRI units, pulse sequences, or b-values (26).

Palle and Reddy (2009) found that the ADC value obtained with low b-values (0 and 150 s/mm$^2$) is higher than that obtained with higher b-values (499 and 1500 s/mm$^2$) for all lesion types due to contribution of main perfusion effects to the ADC. Therefore, we calculated the ADC value with high b-values (800) to avoid the signal attenuation caused by perfusion effects at low b-values (28).

We also agree with Liu et al., who reported that DWI has higher sensitivity and specificity than those of DCE-MRI in the characterization of breast lesion enhancement (29).

Conflict of interest

None.

Appendix A. Cases

A.1. Case (1)

History: A 47 years old female complained of right breast tenderness with No history of previous breast surgeries (Fig. A.1).

This lesion is associated with marked skin thickening with No malignant axillary lymph node enlargement seen.

MRI diagnosis: Using MRI scoring system, the findings are keeping with BI-RADS 4; suspicious for malignancy.

Histopathological diagnosis: Invasive ductal carcinoma.

<table>
<thead>
<tr>
<th>Table 7</th>
<th>The distribution of benign and malignant lesions according to the best cut off value.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC</td>
<td>Malignant, $n$ (%)</td>
</tr>
<tr>
<td>Below cut off $\leq 1.2$ mm$^2$/s</td>
<td>17 (85%)</td>
</tr>
<tr>
<td>Above cut off $&gt;1.2$ mm$^2$/s</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Total</td>
<td>20 (100%)</td>
</tr>
</tbody>
</table>

![Fig. 9 Bar chart shows distribution of benign and malignant lesions according to the best ADC cut off value.](image-url)
Fig. A.1 The right breast shows bilobed, ill-defined margin mass (arrowed) is seen in the retro-areolar region. The lesion exhibits isointense signal intensity in T2 (a), high signal intensity in STIR (b) and irregular rim post contrast enhancement (c). The lesion displays restricted diffusion apart from its centre with measured ADC value of $0.5 \times 10^{-3}$ (d). The dynamic initial enhancement is medium and the dynamic post contrast curve is of type 2 (e).
Most of the right breast parenchyma is seen replaced by a diffuse non-mass lesion (arrowed) with ill-defined margin. The lesion extends deeply. The lesion exhibits low signal at T2 (a), inhomogeneous post contrast enhancement (b). The lesion displays restricted diffusion with measured ADC value of $1.1 \times 10^{-3}$ (c). The dynamic initial enhancement is medium and the dynamic post contrast curve is of type 3 (d).
Fig. A.3  As regards the right breast small simple cyst is seen at about 6 o’clock position with diffusion restriction and ADC value $1.82 \times 10^{-3}$ cm/s (d), yielded type 1 curve (e).
A.2. Case (2)

History: A 51 years old female complained of right breast lump with No history of previous breast surgeries (Fig. A.2). This lesion is associated with marked skin thickening with No malignant axillary lymph node enlargement seen.

MRI diagnosis: Using MRI scoring system, the findings are keeping with BI-RADS 4: Highly suggestive for malignancy.

Histopathological diagnosis: Invasive lobular carcinoma.
A.3. Case (3)

**History:** A 47 year old female a known case of left breast cancer underwent lumpectomy followed by CTH (Fig. A.3).

As regard the left breast: 2 fat containing lesions are seen.

One at about 1 o’clock position near surgical scar with peripheral rim irregular enhancement (c) yielded type 1 curve (f), with no diffusion restriction (d).

The other one is seen at axillary tail which shows heterogeneous appearance (c) with no diffusion restriction and ADC value $1.32 \times 10^{-3}$ cm/s (d).

Normal skin and subcutaneous tissue, with no abnormal L.N.

**MRI Dx:** using MRI scoring system, right breast small simple cyst BIRADs (2).

Left breast benign looking 2 fat containing focal lesions likely representing fat necrosis BIRADs (3).

**Histopathological Dx:** Left breast fat necrosis.

A.4. Case (4)

**History:** A 55 years old female complain of right breast lump with no history of previous surgery (Fig. A.4).

The lesion display normal skin and subcutaneous tissue thickness with no evidence of abnormal L.N.

**MRI Dx:** using MRI scoring system, it is of BIRADs (3).

**Histopathological Dx:** Fibroadenoma.

References


