Diffusion weighted MRI in the characterization of solitary breast mass

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Abstract  MRI is becoming an essential tool for assessment of breast pathology. Diffusion weighted imaging (DWI) provides quantitative and qualitative information reflecting the changes in tissue cellularity and integrity of cell membranes.

Objective: To assess the diagnostic importance of ADC numerical value and ratio in the differentiation between benign and malignant breast masses.

Patients and methods: The study included 37 patients with solitary solid breast mass. DWI was acquired at b-value 0–600. ADC value and ADC ratio were calculated and the values were correlated to histopathology.

Results: Sixteen out of 37 detected masses were malignant and 21 were benign. Malignant lesions showed lower ADC values than benign lesions. The ROC study revealed that a cutoff ADC value of 1.175/C210/C0 3 mm2/s had high sensitivity of 95.2% and specificity of 93.8% in the differentiation between benign and malignant breast masses. Malignant lesions showed lower ADC ratio than benign lesions. A cutoff value for ADC ratio of 0.9 had moderate sensitivity of 73.7% and high specificity of 100% in the differentiation between benign and malignant lesions.

Conclusion: DWI can differentiate between benign and malignant breast lesions with high sensitivity and specificity.


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motion in tissues (Brownian motion) which in fact is closely related to the tumor cellularity and integrity of cell membranes. Both qualitative and quantitative assessment can be made, and the latter is achieved through measuring the apparent diffusion coefficient (ADC), that is directly proportional to the water diffusion in the tissue (8). We aimed in this study to assess the diagnostic importance of ADC numerical value and ratio in the differentiation between benign and malignant breast masses.

2. Patients and methods

2.1. Study design and sample

A prospective study was conducted at the MRI unit at AL-Emamain Alkadhimain medical city/Baghdad during the period from May 2014 through December 2014. Initially a total of 44 female patients were examined by MRI. Later on 7 patients were excluded and only 37 patients constituted the study sample. The patients were recruited from the breast clinic at the same medical center following the detection of breast mass by other imaging modalities (ultrasound (US), mammography (MG)). Written informed consent was obtained from all patients to participate in the study. Only those patients who were found to have solitary breast mass were further evaluated by conventional MRI and DWI. Lesions were included in the study if benign or malignant outcome could be definitively confirmed through tissue acquisition or the lesions confirmed to be of benign nature by previous examinations (US, MG and/or MRI) with no significant modification in the size or characters for more than 1 year duration. The demographic criteria and relevant clinical history were recorded as well as current and prior breast imaging findings (US/MG mammography and BIRADS category). Then the patients were referred to the MRI unit (after exclusion of any contraindications for the examination). Conventional DWI was performed and the findings were analyzed. The histopathological results for the lesions under study were obtained later. Seven patients out of 44 patients were excluded from the study after MRI either because the mass found to be complicated cyst, nonvisualization of the lesion by DWI mainly related to its small size (less than 1 cm), or because the DW-MRI sequences did not have diagnostic quality due to motion artifact, nonmass like enhancement due to diffuse tumor spread and difficult to obtain ROI measurement due to partial volume effect or due to loss of follow-up, leaving only 37 patients to represent the study sample.

2.2. MRI protocol and data analysis

The images were acquired with a 1.5-T MRI scanner (PHILIPS ACHIEVA MEDICAL SYSTEM) using bilateral single breast coil. The conventional MRI sequences performed included T1 W sequence axial section and T2 W sequence axial section, and five continuous dynamic Ethrive contrast-enhanced acquisitions in axial sections were performed using Magnaevid 0.5 mmol/ml (dimeglumine gadopentetate), and the dose given was 0.2 mmol/kg body weight administered by intravenous route. All the diffusion weighted images were obtained by echoplanar imaging (EPI) sequence with single shot at b value (0, 600), TR/TE: 1000/82, FOV: 340 mm, slice thickness: 3 mm, and total scan duration: 3:24:1 min. The images were transferred to a workstation for processing. The ADC values were calculated automatically by placing the region of interest (ROI) within the confines of the lesions. The reference image was obtained from the contrast-enhanced images as the latter had better resolution. The enhanced part of the lesion was selected for evaluation on the corresponding DW-MRI. The scanner software provides the mean value within the ROI, which equals the ADC value (multiplied by $10^{-3}$). The area of the ROI ranged from 24 to 88 mm$^2$ (the mean: 53.38 $\pm$ 10.87 SD) according to the size of the lesions. Apparent necrotic or cystic components were avoided by referring to conventional MR images. For lesions less than 2 cm in diameter, one circular region was measured as the ROI and for lesions larger than 2 cm three areas were measured in different places and their average values were obtained.

Measurement of ADC ratio was obtained after measuring the ADC value of the fibroglandular tissue at the normal contralateral side, which is equal to lesion ADC/fibroglandular ADC.

3. Statistical analysis

T-test statistical study was used for statistical analysis of the data comparing the mean ADC values and ADC ratio between benign and malignant breast masses with reference to the Histopathological or follow-up data. A $p$ value <0.05 was considered significant. Receiver operating characteristic (ROC) curve statistical study used for presentation of data and the optimal cutoff levels for differentiating benign versus malignant lesions were determined by identifying the points where the sensitivity and specificity were equal on the ROC curves. According to ROC analyses, the sensitivities and specificities of ADC value and ADC ratio were obtained.

4. Results

A total number of 37 patients were enrolled in this study, and the age range was 17–83 years (mean = 42 years $\pm$ 17.49). Twenty-one of the masses were benign and 16 were malignant. The histopathological types of malignant masses ($N = 16$) are represented in Table 1. Seventeen out of 21 benign masses were proved by histopathology, and the other 4 lesions were classified as BI-RADS 2 category by U/S and/or mammography.
with no significant change in the imaging patterns of these lesions over one year period of follow-up with mammography and/or sonogram (Table 1).

The range of ADC values for malignant breast lesions (N = 16) was 0.65–1.46 × 10⁻³ mm²/s and the median was 0.93 × 10⁻³ mm²/s. The range of ADC value for benign breast lesions was 1.11–1.86 × 10⁻³ mm²/s and the median was 1.51 × 10⁻³ mm²/s (Fig. 1).

The ADC values obtained from malignant breast lesions range from 0.65 to 1.46 × 10⁻³ mm²/s, and mean was 0.94 ± 0.2 × 10⁻³ mm²/s with 15 lesions having ADC value equal or less than 1.1 × 10⁻³ mm²/s; these values were significantly lower than those observed in benign lesions which ranged from 1.11 to 1.86 × 10⁻³ mm²/s, and mean was 1.5 ± 0.17 × 10⁻³ mm²/s with 20 lesions showing ADC values equal or more than 1.3 × 10⁻³ mm²/s, p value <0.0001 (Table 2).

Only one of 16 malignant lesions (malignant Paget’s disease) showed high ADC value (1.46 × 10⁻³ mm²/s); on the other hand one of the 21 benign lesions (papilloma) showed low ADC value measures (1.1 × 10⁻³ mm²/s). Regarding malignant lesions minimum ADC value was obtained in invasive ductal carcinoma stage 3 and the highest ADC value was obtained in malignant Paget’s disease. For benign lesions minimum ADC value was noted for papilloma while the highest ADC value was reported for tuberculous granuloma. Comparing the malignant breast tumors, ductal carcinoma (no = 15) had significantly higher ADC value range (1.5–1.7 × 10⁻³ mm²/s, mean 1.58 ± 10⁻³ mm²/s ± 0.08) than ductal and lobular carcinoma (no = 15). Comparing the malignant breast tumors, ductal carcinoma (no = 8) was found to have mildly lower ADC value range (0.65–1.08 × 10⁻³ mm²/s, mean 0.84 ± 10⁻³ mm²/s ± 0.14) than lobular carcinoma (no = 7) (range 0.77–1.15 × 10⁻³ mm²/s, mean 1.00 ± 10⁻³ mm²/s ± 0.12).

ROC statistical analysis study was used for presentation of data and measure of cutoff point ADC value between benign and malignant breast lesions. The ROC study reveals that a cutoff ADC value (1.175 × 10⁻³ mm²/s) had high sensitivity of 95.2% and specificity of 93.8% in the differentiation between benign and malignant breast lesions (p value <0.001) (Fig. 2).

The mean ADC values for normal fibroglandular tissue were 1.363 mm²/s ± 0.3 SD, and range was 1.24–1.79 × 10⁻³ mm²/s. Malignant masses showed ADC ratio range of 0.46–0.91 and the mean was 0.7 ± 0.18; these results were significantly lower than those of benign masses that showed ADC ratio range of 0.67–1.25 and the mean was 1.02 ± 0.15, p value <0.0004 (Table 3).

ROC study revealed that a cutoff ADC ratio 0.9 had a high sensitivity and specificity in the differentiation between benign and malignant breast lesions that is 73.7% and 100% respectively (Fig. 3).

By comparing ADC value and ADC ratio for all the lesions, the current study showed that in both methods of measurement there are significant differences between benign and malignant lesions, p value <0.0001 and 0.0004 respectively. In addition both ADC ratio and ADC value had high sensitivity and specificity in the differentiation between benign and malignant breast lesions (p value <0.001 for both). The ADC ratio had more specificity but lower sensitivity than ADC value.

5. Discussion

Despite the improvement in the detection of breast cancer with the widespread application of mammography and ultrasound, breast lesions still remain difficult to diagnose and characterize, especially in dense fibroglandular breasts. The main advantage of MRI in the breast is that they can improve the detection and characterization of multiple and/or small lesions even in the dense fibroglandular breasts (9). However, the moderate specificity of conventional MRI remains a problem (3,4).

In recent years, the DWI has been extensively applied in evaluating cerebral tumors and the correlation between the ADC value and the cellular density has been verified. Briefly, the higher the cellular density is, the lower the ADC value will be in DWI, and vice versa (10). For malignant tumors, they have a relatively high cellular density and therefore will produce a low ADC value in DWI, while for benign lesion, its density is generally low and thus will produce a high ADC value in DWI. Application of DWI in the diagnosis of breast lesions has been reported recently (11–14).

In the current study the mean ADC value of malignant breast tumors (higher cellularity tumors) was significantly lower than that of benign breast tumors (lower cellularity tumors), using a cutoff value of 1.175 × 10⁻³ mm²/s and the sensitivity and specificity of as high as 95.2% and 93.8% respectively (p value <0.001) in the differentiation between benign and malignant breast lesions. These results were in agreement with those of Pereira et al. (15) who showed that the mean ADC value of breast tumors correlates well with tumor cellularity and that malignant breast tumors have a higher cellularity and a lower ADC value than benign breast tumors, and they proposed that a cutoff ADC value of 1.24 × 10⁻³ mm²/s had sensitivity and specificity of as high as 92% and 96%, respectively, for the differentiation between benign and malignant lesions.

Other Prior studies with breast MRI and DWI have shown promising results in differentiating benign and malignant lesions, with sensitivity ranging from 81% to 93% and specificity from 80% to 88.5% (16–20).
In current study, the ADC ratio (lesion/fibroglandular ADC) also had high sensitivity and specificity (73.7% and 100% respectively) in the differentiation between benign and malignant breast lesions, p value <0.001 and in comparison with same lesions sample ADC value which revealed sensitivity and specificity of 95.2% and 93.8% respectively, p value <0.001, we noted that the ADC ratio is less sensitive but more specific than ADC value, so that adding ADC ratio to ADC value can increase the specificity of the breast DWI in the diagnosis; however, measurement of ADC ratio has some limited application when dealing with fatty breast where no fibroglandular tissue can be recognized. Our results were in agreement with Hirano et al. (21), who showed the sensitivity and specificity of ADC ratio in the diagnosis of benign and malignant lesions to be 70.1% and 70.1% respectively while Sahin & Aribal (22) showed that a threshold ADC ratio of 0.8 had 91.4% sensitivity and 100% specificity in the diagnosis of breast lesions.

In the current study, one out of 16 malignant lesions (malignant Paget’s disease) showed high ADC value measures 1.46 × 10^{-3} \text{mm}^2/\text{s}. The possible explanation may be related to the histopathologic features of the lesion which showed abundant pale cytoplasm that often contains mucinous material so more the molecular motion and higher the ADC value. On the other hand the only case of duct papilloma from benign lesions encountered in this study showed low ADC value of 1.1 × 10^{-3} \text{mm}^2/\text{s} and this was possibly due to high cellularity of the tumor so more the restriction in the molecular motion and lower the ADC value. Kawashima et al. (23) and Hatakenaka et al. (24) concluded that a carcinoma with a very high signal intensity on T2-weighted images such as mucinous colloid carcinoma resulted in misleading ADC values because of a lower cell density and higher extracellular water content.

Furthermore Guangwei et al. (25) and Woodhams et al. (26) also reported that most intraductal papilloma had low ADC values.

Pereira et al. (15) showed that a malignant tumor with low cellularity, such as the malignant phyllodes tumor with cystic areas shows high ADC value, consequently was misdiagnosed as benign. Conversely, a benign tumor with high cellularity, such as the papilloma showed low ADC and led to the misdiagnosis of malignancy.

According to the ADC values, all fibroadenomas and invasive carcinomas were appropriately classified. These indicate that ADC would be effective in the distinction between fibroadenomas and invasive carcinomas. This should be helpful in lesion characterization because fibroadenomas are known to have characteristics that overlap with malignant lesions in both ultrasound and dynamic contrast-enhanced MRI studies (27–29).

Pereira et al. (15) also showed that there is significant difference in ADC value of fibroadenoma and invasive carcinoma.

In the current study it has been found that even different types of malignant breast lesions had low but different ADC values, and invasive ductal carcinoma showed lower ADC value than lobular carcinoma that probably related to degree of invasiveness and cellularity as the more invasiveness of the tumor, the more the cellularity, the more the restriction and the lower the ADC value. Hatakenaka et al. reported an inverse correlation between ADC value and tumor cellularity (24).

In conclusion, DW MRI of the breast and ADC value are sensitive and specific parameters that can help to differentiate benign and malignant breast lesions. DWI of the breast provides additional information to characterize focal breast lesions.

### Table 2
Comparison of ADC value between benign and malignant lesions by t test.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Benign N = 21 range</th>
<th>Benign mean ± SD</th>
<th>Malignant N = 16 range</th>
<th>Malignant mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC (×10^{-3} \text{mm}^2/\text{s})</td>
<td>1.11–1.86</td>
<td>1.5 ± 0.17</td>
<td>0.65–1.46</td>
<td>0.94 ± 0.2</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

### Table 3
Comparison of ADC ratio between benign and malignant lesions by t test.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Benign N = 21 range</th>
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</tr>
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</table>
lesions in a fast and easy way and will hopefully help to reduce invasive procedures.

Conflicts of interest

The authors declare that there are no conflicts of interests.

References