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ORIGINAL ARTICLE

Role of quantitative diffusion weighted imaging in characterization of breast masses

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KEYWORDS

Breast cancer;
Diffusion weighted imaging (DWI);
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Abstract *Purpose:* To evaluate the diagnostic accuracy of diffusion-weighted imaging (DWI) in differentiating benign from malignant breast lesions.

Patients and methods: Forty patients with positive diagnoses at mammography or breast ultrasound were included in this study. Patients were imaged with dynamic contrast enhanced MRI and DWI before biopsy of their breast tumors. Apparent diffusion coefficient (ADC) map was utilized to select the region of interest (ROI) for ADC calculation. DWI was performed using three sets of b value (0, 400, and 800 s/mm^2).

Results: The final analysis comprised 40 breast lesions, 18 of which were malignant and 22 were benign. Significant results were obtained between ADC values of benign and malignant lesions ($p < 0.001$). The cut-off ADC value for benign and malignant lesions was 1.25×10^{-3} mm^2/s.

Conclusion: The present study provides consistent evidence to support DWI as a diagnostic tool for breast lesion characterization and as a useful adjunct to standard breast MRI protocols in aiding the diagnosis of breast cancer.

1. Introduction

Conventional MRI of the breast is mainly based on the combined analysis of the morphological data and enhancement kinetics of the lesions. This gives information about tumor physics, vascularity, and vascular permeability. It provides high sensitivity yet with moderate specificity for breast cancer (1), with overlap between benign and malignant lesions (2–6).

Due to the low specificity of the conventional MRI, an additional feature is needed to characterize suspicious lesions in order to decrease the number of invasive breast procedures. Prior studies with breast MRI and DWI have already addressed this question and show promising results (7–9).

Diffusion weighted imaging is a novel technique in magnetic resonance imaging and has a high sensitivity in the detection of changes in local biological environment .A significant advantage of diffusion weighted MR imaging is its high

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sensitivity to changes in microscope cellular environment without the need for intravenous contrast material injection (10).

The diffusion of water in tissue is quantified by the apparent diffusion coefficient (ADC). Based on the diffusion-weighted images, an ADC map can be calculated which shows the ADC value of each voxel in every slice. Restricted water movement in tumors with high cellularity leads to smaller ADC values (7).

The objective of this study was to evaluate the role of DWI with ADC value measurement in differentiating benign from malignant breast lesions.

2. Patients and methods

Forty patients with positive diagnoses at mammography or breast ultrasound were included in this study which was conducted over a period of 10 months. Patients were imaged with dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) and diffusion weighted imaging (DWI) before biopsy of their breast tumors. Lesions greater than 1 cm in size were selected for this study because smaller lesions are hardly identifiable on the DWI images. Lesions less than 1 cm in size or purely cystic lesions were excluded as the latter show no diffusion restriction. Approval for the study was obtained from the local ethical committee and informed consent was obtained from all the study subjects. In all patients, MRI was performed bilaterally, and results were correlated with histopathology. The age of the patients ranged from 12 to 50 years (mean age 36.5 ± 9.6).

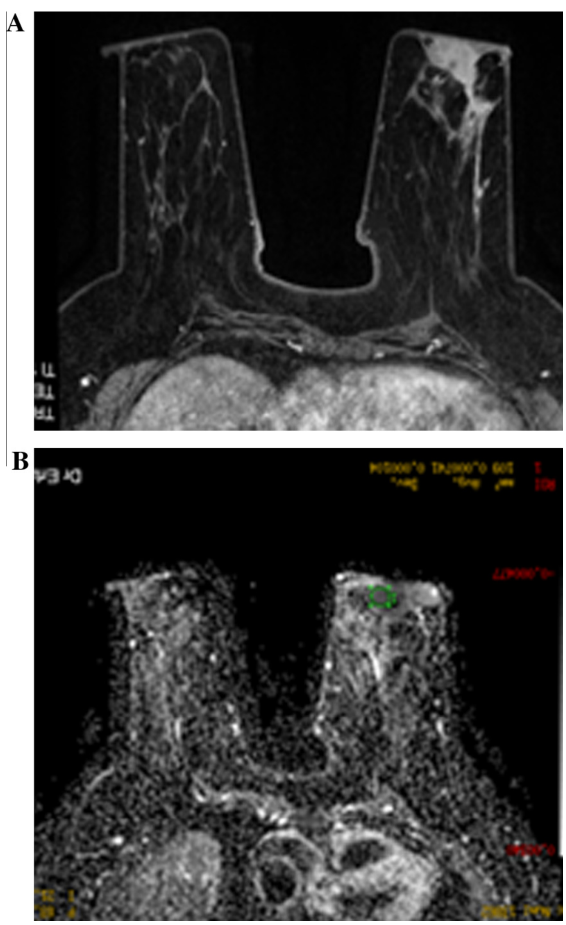

Fig. 1 A – DCE-MRI shows an inhomogeneously enhancing retroareolar mass lesion with spiculated margins. B – ADC map revealed restricted diffusion with a low mean ADC value of 0.7×10^{-3} mm^2/s.

2.1. MRI protocol

All patients were examined using a 1.5-T MR unit (Achieva, Philips Medical Systems, Best, The Netherlands) and a dedicated double breast coil. Imaging was performed within days 7–14 of the menstrual cycle for premenopausal women. Patients were placed in the prone position.

The conventional MRI protocol included the following:

- T2W axial sequence (TR/TE: 4800/120), number of excitation (NEX): 1, slice thickness: 3 mm with no gap, and field of view (FOV): ranged from 280 to 340 mm depending on the breast size, matrix = 256×160 or 256×192.

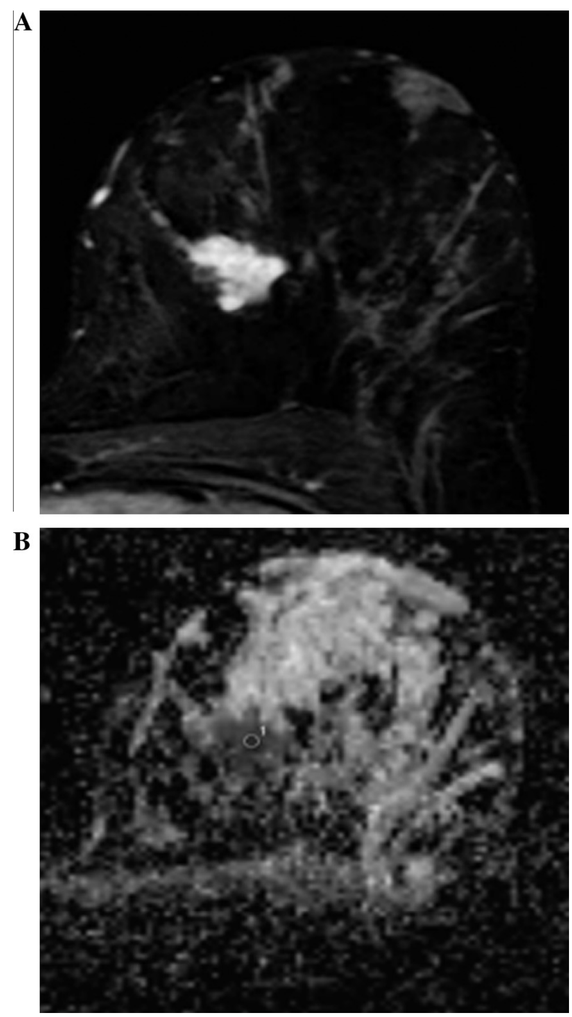

Fig. 2 A – DCE-MRI shows an intensely enhancing irregularly outlined mass lesion in the upper inner quadrant of the left breast with a curvilinear tail of abnormally enhancing tissue seen directed anteromedially. B – ADC map revealed restricted diffusion with a low mean ADC value of 0.81×10^{-3} mm^2/s.

- T1W axial sequence (TR/TE: 540/10), number of excitation (NEX): 1, slice thickness: 3 mm, and field of view (FOV): ranged from 280 to 340 mm depending on the breast size, matrix = 256 × 160 or 256 × 192.
- Axial/sagittal STIR (TR/TE: 2000–7500/55–170), number of excitation (NEX): 1, slice thickness: 3 mm with no gap, and field of view (FOV): ranged from 280 to 340 mm depending on the breast size, matrix = 256 × 160 or 256 × 192.
- Five continuous dynamic contrast-enhanced THRIVE 3D acquisitions were performed (TR/TE: 4.4/1.6, flip angle: 12°, and slice thickness: 1 mm). The time taken for each acquisition was around 1 min.
- Axial DWI with single-shot echo-planar imaging (EPI) was performed at *b* values = 0, 400, and 800 s/mm^2, TR/TE: ⩾1036/80, FOV: 350 mm, and slice thickness: 3 mm with no gaps, NEX = 2, matrix = 256 × 256.

2.2. ADC value measurement

The mean ADC value of the lesion was calculated by positioning multiple regions of interest (ROI) over the lesion in consecutive image sections. The ROIs may be placed directly onto the ADC map or copied onto the map from those drawn on morphological or *b*-value DW-MR images. Necrotic areas were avoided.

2.3. Statistical analysis

Receiver operating characteristic (ROC) curve analyses were performed to assess the diagnostic performance of the ADC values in characterization of breast lesions and to determine suitable ADC cut-off points to separate benign and malignant lesions. Mann–Whitney *U*-test was used to compare ADC values of benign versus malignant lesions. A *p*-value of less than 0.05 was considered statistically significant. All analyses were performed using IBM SPSS statistical software version 20.0.

3. Results

All the 40 patients enrolled in this study successfully underwent both DCE-MRI and DWI for their suspicious breast findings and had a histopathology reference standard test for their index lesion.

Histopathology analyses revealed malignant tumors in 18 patients (45%), 16 of which were invasive ductal carcinomas (IDCs) (Fig. 1) and two were invasive lobular carcinomas (ILCs) (Fig. 2).

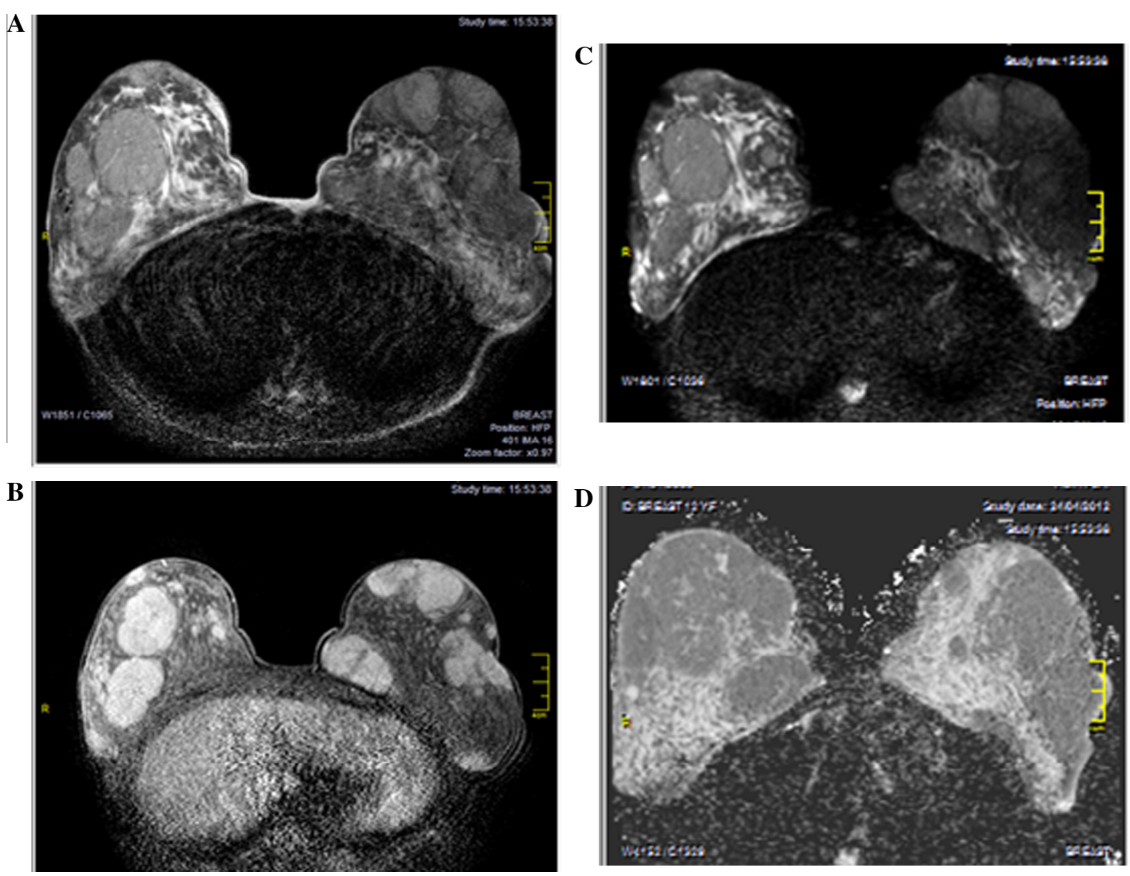

Fig. 3 A – T2W axial images show multiple bilateral variable sized well defined oval and globular lesions ranging in size between a few mms to a maximum of 7.5 cm in diameter exhibiting intermediate signal intensity. B – DCE-MRI shows moderate homogenous enhancement with intrasubstance nonenhancing septations. C – On DWI's lesions show facilitated diffusion. D – Corresponding ADC map. The mean ADC value was 1.3×10^{-3} mm^2/s.

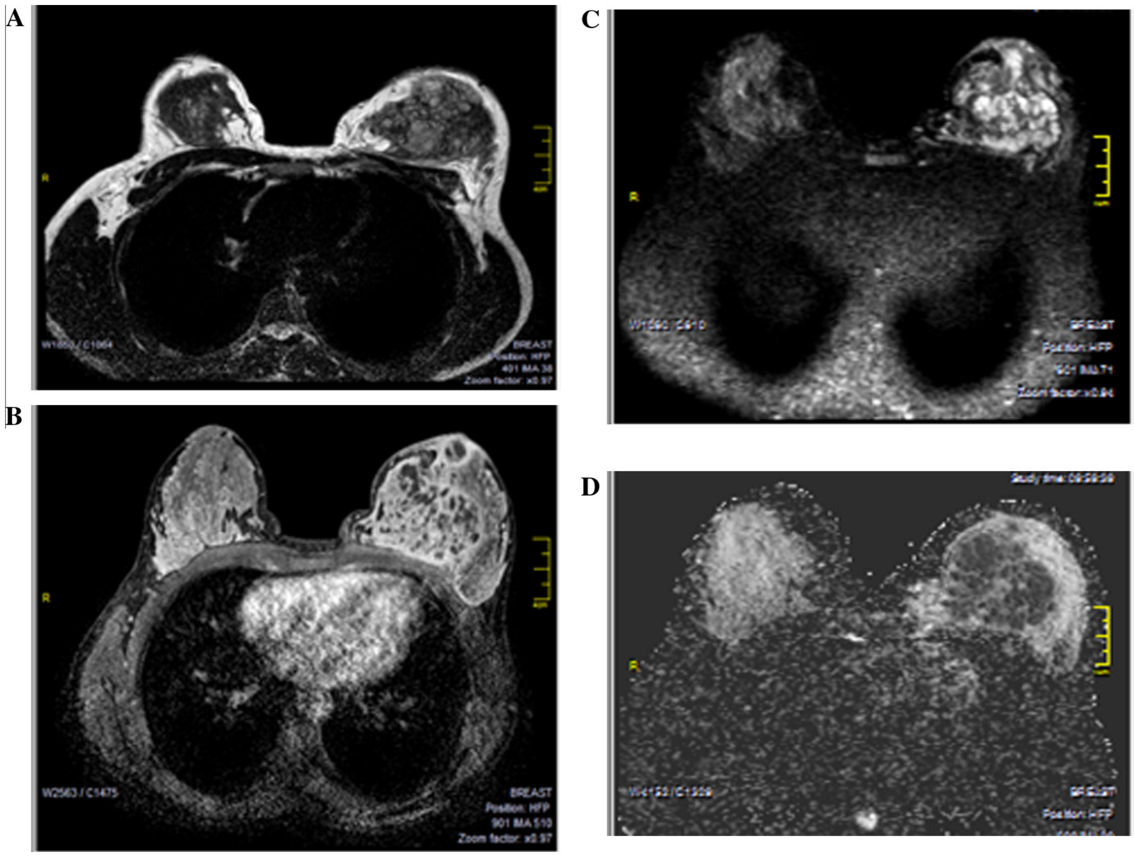

Fig. 4 A – Axial T2WI shows a $7.6 \times 7.6 \times 6.3$ cm well defined lobulated heterogenous large mass occupying most of the left breast with compression of adjacent breast parenchyma and displays multiple small hyperintense locules separated by hypo intense septa. B – DCE-MRI: The lesion shows heterogeneous enhancement. C – DWI-MR revealed restricted diffusion. D – Corresponding ADC map. The mean ADC = 0.83×10^{-3} mm^2/s.

A benign lesion was found in 22 (55%) of the 40 patients: Six patients had fibroadenomas, one of them had multiple bilateral lesions and biopsy was taken from the largest one (Fig. 3), two papillomas, four fat necrosis, six abscesses (Fig. 4) and two phylloid tumors.

In all the 40 patients, we measured the ADC value of the index lesion. The median ADC of malignant lesions was 0.81×10^{-3} mm^2/s and that of benign lesions was 1.2×10^{-3} mm^2/s.

ADC values were significantly lower in malignant lesions compared to benign lesions ($p < 0.001$). ROC curves of the ADC values are represented in (Fig. 5). The best cutoff level for ADC derived from the ROC analysis was 1.25×10^{-3} mm^2/s, giving 100% sensitivity and 77.3% specificity.

4. Discussion

DWI provides important biological information about the composition of tissues and their physical properties (11). The information is obtained noninvasively and without the need for contrast administration (12). DWI reflects some tissue characteristics, such as perfusion and diffusion. Diffusion is mainly affected by cellularity, presence of edema, fibrosis, and necrosis of the tissue (9). The perfusion effect is seen when a b value less than 400 s/mm^2 is used (10). Hence this study was done with b values = 400 and 800 s to eliminate perfusion related diffusion.

DWI is quantified by ADC values, which calculates the amount of water diffusion through the tissues. ADC values vary between malignant and benign breast masses, whereby the ADC values of malignant breast lesions are usually lower than those of benign lesions, indicating restricted water diffusion and increased cellularity. The ADC values of benign lesions are higher, reflecting normal cellularity with no restriction of water movement. However, there is overlap between both entities as benign breast changes can give low ADC values and mimic malignancies (13–15).

Abscess has low ADC values similar to malignant tumors. The area of low ADC value within an abscess usually gives high signal intensity on T2-weighted images, which indicates the high water content and high viscosity of the abscess. In clinical practice, physical examination findings should be considered when assessing these entities, thereby simplifying the radiologic diagnosis (16).

In our study there were 6 cases of abscess, all showed restricted diffusion with the mean ADC value 0.85×10^{-3} mm^2/s. This diffusion restriction can lead to false positive results by DWI.

Both benign and malignant papillary lesions show high cellularity and vascularization, and commonly presented with restricted diffusion which may create problems in the

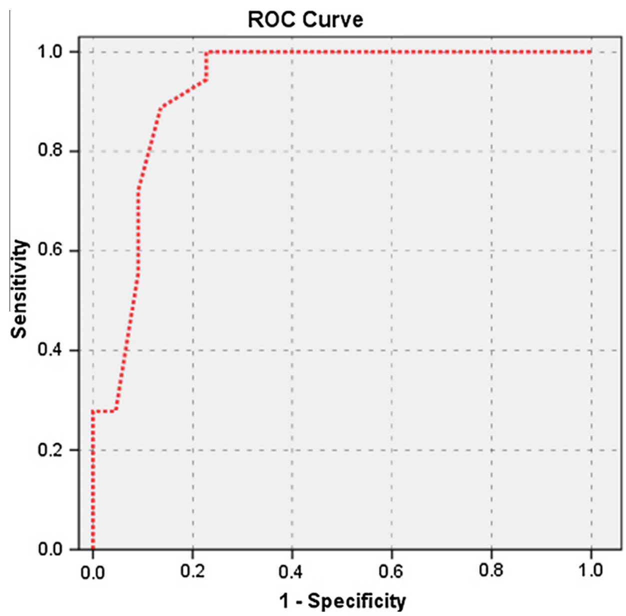

Fig. 5 ROC curve demonstrating area under the curve for ADC in detecting breast malignancy.

characterization of the papillary lesions both at DCE-MRI and DWI (13).

In our study, there were two cases of benign intraductal papilloma that showed diffusion restriction with mean ADC value of 0.91×10^{-3} mm^2/s.

Small breast lesions measuring less than 5 mm and necrotic lesions are difficult to delineate on DWI and as such can give inaccurate ADC value calculations. Liberman et al. (17) stated that there is a low likelihood for lesions < 5 mm to be cancerous. In the present study, the selected lesions were set above 1 cm in size. The smallest lesion was a 1.2 cm fibroadenoma.

The role of DWI, with the calculation of the ADC values on the 1.5T MR scanner, in differentiation between benign and malignant breast lesions has been evaluated in the previous studies (7,17,18). The current study obtained statistically significant differences between benign and malignant lesions ($p < 0.001$) and our results are comparable to other studies performed at 1.5T scanners (7,13,17–20).

The cut-off ADC value for benign and malignant lesions was determined in our study as 1.25×10^{-3} mm^2/s, giving 100% sensitivity and 77.3% specificity with an overall accuracy of 92.45%. Using different ADC cut values, different studies showed variation in DWI sensitivity and specificity. Tozaki and Maruyamain (21) used a cutoff ADC value of 1.13×10^{-3} mm^2/s and achieved a specificity of 67% and a sensitivity of 97%. Orguc et al. (22) used a cut-off value of 1.46×10^{-3} mm^2/s for ADC in receiver operating characteristic analysis and 95% sensitivity and 85% specificity were achieved for differentiating between benign and malignant lesions. Spick et al. (23) demonstrated that an ADC cut-off level of 1.258×10^{-3} mm^2/s would produce a sensitivity and specificity for the ADC measurements of 80% and 79.8% respectively.

Yoshikawa et al. (24) demonstrated a correlation between ADC and histological type. The present study did not establish a significant correlation when comparing tumor grades, tumor size to ADC values. The poor correlation of ADC values with the prognostic factors of the malignant tumors in this study may be due to the small sample size.

In conclusion, the present study supports the usefulness of quantitative DWI assessment in the characterization of breast lesions using 1.5T MRI. The results from the present study and previous studies provide consistent evidence that DWI is a good diagnostic tool for breast lesion characterization and when added to the standard breast MRI protocols, it aids the diagnosis of breast cancer.

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