Invasive ductal carcinoma: role of MRI in predicting histopathological grading and prognosis assessment

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Aims and objectives

The aim of this study is to investigate the relationship between diffusion-weighted imaging and the dynamic contrast enhanced MRI findings with the histopathological grade of invasive breast carcinoma.
Methods and materials

Patients

From October 2013 to April 2014, 30 patients with a mean age of 49.4 years (range 33 - 75 years) were enrolled in this retrospective study.

Included masses are those with BI-RADS 5 category on imaging (fig. 1, 4, 7, 10, 13 and 16) with no previous biopsy or treatment. There was no knowledge about the histopathological diagnosis at the time of initial evaluation.

Exclusion criteria were breast masses with diagnosed or proved benign features.

All patients were scheduled for dynamic MRI with diffusion weighted imaging in addition to the conventional MR imaging.

The final tumor diagnosis and grading were established by mean of surgery or core needle biopsy considered as the gold standard reference. Only patients with invasive duct carcinoma were included in the study.

MRI examination

Conventional MRI, diffusion MR imaging and post Gd- DTPA dynamic MRI was performed. First detection and characterization of breast lesions was performed, and then the diffusion images with ADC values were reviewed.

MR imaging was performed on high field system (1.5 Tesla) magnet units (Philips Achieva XR) using a 8 channel breast coil with the patient in the prone position.

MR protocol used

a) Pre-contrast imaging included

- T1 weighted images (turbo spin echo): TR = 540 ms, TE= 10 ms, FOV:300 , matrix : 340 x 271 , slice thickness 3.5 mm and no slice gap.

- T2 weighted images (turbo spin echo): TR #4861ms, TE=120 msec, matrix 424 x 384 with a FOV:300, slice thickness 3.5mm, no slice gap.

- T2 STIR sequence with TR = 6806 ms, TE =165 ms, TI = 70 ms, matrix: 272x 223 with FOV: 300, slice thickness 3.5 mm and no slice gap

b) Diffusion study
Diffusion-weighted MRI was carried out using a single shot spin-echo echo-planar imaging sequence with fat saturated spectral pre attenuation inversion recovery (SPAIR) in the transverse plane with tri-directional diffusion gradients by using b values 0, 50 & 850 sec/mm$^2$ to increase the sensitivity to cellular packing.

The other parameters were as follows: TR= 8923 m sec, TE= 81 m sec, number of excitations (NEX) = 2, matrix= 188x 186 with a FOV: 400, slice thickness= 3 mm, no gap, scan time 2 minutes.

c) Dynamic study

Dynamic study was performed after manual bolus injection of 0.1mmol/kg body weight of Gd-DTPA , flushed with 20ml of sterile 0.9% saline solution from the antecubital vein.

Dynamic imaging using T1 THRIVE (High Resolution Isotropic Volume Examination) technique was performed at the following time points: 80 seconds after injection and then every 80 seconds for 9 minutes.

Post processing image subtraction was obtained between the post-contrast imaging showing maximum enhancement and pre-contrast images (in the same axial plane), using the software subtraction function available on the work station.

Quantitative analysis was done by placing the region of interest (ROI) at the most enhanced part within the lesion resulting in automatically created time / signal intensity curve and maximum relative enhancement percentage (MRE%) values.

Imaging evaluation

The morphological features, the dynamic MRI parameters and the diffusion weighted imaging findings of each lesion values were recorded. The criteria of malignancy of the lesions in the study included some or all of the following:

*Morphological: irregular or spiculated margins, low or intermediate signal on T2 weighted image, bright signal on STIR image, breast edema, skin thickening, nipple retraction and pathological axillary lymph nodes.

*Dynamic MRI: avid enhancement, with rapid initial rise followed by plateau or washout pattern in the delayed phase on the time/signal intensity curve.

*Diffusion weighted imaging: persistent high signal at b 850 and low to intermediate signal in the ADC map denoting true restricted diffusion. ADC value of $< 1.25 \times 10^{-3}$ mm$^2$/s. The aforementioned value is the cutoff value between benign and malignant lesions as described by Bogner et al (2009).

ADC calculation
ADC was generated for each pixel of the diffusion-weighted image in the form of parametric maps on the operating console or on the workstation. The mean ADC of each lesion detected is measured by drawing a region of interest (ROI) over the lesion in the ADC maps. ROI ranged from 60 to 150 mm$^2$ and was traced within the boundaries of the lesion using an electronic cursor. It was manually placed such that it is smaller in size than the actual lesion, does not contain any necrotic parts, fat or adjacent normal tissue. T2 weighted image and dynamic post contrast sequence were used as source images for placement of ROI and measurement of the ADC value. On masses with massive cystic changes and no considerable solid component; multiple values were taken and then their mean was the considered the ADC value.

**Statistical analysis**

Data was analyzed using SPSSwin statistical package version 21 (SPSS Inc., Chicago, IL).

Comparison of Median between more than 2 groups was done by Kruskall Wallis ANOVA, and then pairwise comparison was done with Bonforoni adjustment.

Spearman's rho correlation was done to test the correlation between grade & ADC value.

ROC analysis (Receiver Operator Characteristic) was done to select the best cutoff point for ADC value to discriminate high grade from low grade.
Fig. 1: Case 1: Mammogram; CC and MLO views showed left breast upper central (12 clock) spiculated dense mass (arrow)

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Fig. 4: Case 2: Mammogram MLO and CC views showed right breast spiculated mass (arrow) in the upper outer quadrant with underlying clustered microcalcifications

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Fig. 7: Case 3: Mammogram CC and MLO views showed left breast upper central mass (arrow) of indistinct margins

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Fig. 10: Case 4: Mammogram of the left breast CC and MLO views; upper outer quadrant multifocal indistinct mass (pink arrow) with adjacent pathologically enlarged intramammary lymph node (blue arrow) likely sentinel node.

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Fig. 13: Case 5: Right breast spiculated dense mass (pink arrow) in the upper central portion with two nearby foci representing satellite lesions (blue arrows) and pathologically enlarged axillary node with asymmetrical cortical thickening (white arrow)

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Fig. 16: Case 6: Mammogram MLO and CC views of right breast retroareolar indistinct mass (arrow) associate with nipple retraction and skin thickening.

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Results

The study included four malignant lesions of grade I differentiation, 21 lesions of grade II and 5 lesions of grade III (fig. 19).

Points of analysis included:

- Morphological criteria such as the size, the margins of the lesion, the presence of edematous changes, the presence of pathological axillary lymph nodes and the T2 weighted-image signal intensity of the lesion.
- Diffusion-weighted imaging analysis
- Dynamic MRI parameters.

Diffusion-weighted imaging:

All 30 lesions (100%) showed persistent high signal on DWI (b850) with low to intermediate signal on ADC map denoting restricted diffusion.

ADC values ranged from 0.67 to 1.15 × 10^{-3} mm^2/s (mean 0.88 ± 0.11 × 10^{-3} mm^2/s) (fig. 20 and table 1).

Tumors with higher grade showed lower ADC value compared with those of lower grade \( p=0.001 \) (fig. 3,6,9,12,15,18). There was significant difference between the mean ADC value of tumors of grade I and III \( p=0.005 \); and between grade II and III \( p=0.021 \). However, there was less significant difference between grade I and II \( p=0.053 \).

According to our statistical analysis, the ADC value of 0.804 × 10^{-3} mm^2/s present an acceptable cutoff value between high grade tumours (grade III) and low grade tumours (grades I and II), with a sensitivity, specificity and accuracy of 80%, 92% and 90% respectively.

Dynamic MRI results:

Both qualitative (morphological) and quantitative (kinetic) assessment were performed.

Twenty-five lesions (83.3%) showed type 2 (plateau) curve (fig.2,5,14,17), while 5 lesions (16.6%) showed type 3 (washout) curve.

Figure 21 present the frequency of time/signal intensity curves among the different tumor grades in the study.
High grade tumors (grade III) were more associated with washout curve (fig. 8,11) compared to those with lower grades (grades I and II) ($p= 0.04$).

However, there was no statistically significant relation between the grade of the tumour and the pattern of enhancement or the maximum relative enhancement of the tumour (table 2).

The size, the margins of the lesion, the presence of edematous changes, the presence of pathological axillary lymph nodes, and the signal of the lesion on T2WI were evaluated.

The relation between each of the morphological characteristics and the histological grade of the tumor did not show any statistical significance.
Fig. 19: The distribution of different histological grades in the study.

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Fig. 20: The range and the mean ADC values of different histological grades.

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Table 1: Mean ADC values of different histological grades

<table>
<thead>
<tr>
<th>Grade</th>
<th>Mean ADC value</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>$0.96 \pm 0.09 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>II</td>
<td>$0.89 \pm 0.11 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>III</td>
<td>$0.76 \pm 0.07 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
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Fig. 2: Case 1: right image; early post contrast THRIVE sequence where the mass (arrow) displayed homogeneous enhancement and left image; dynamic curve showed initial peak of contrast uptake at 2 minutes with Max relative enhancement of 22% and plateau (borderline) pattern

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**Fig. 3:** Case 1: right image; DWI at b 850 the mass (arrow) showed persistent high SI and left image; ADC map, the mass showed intermediate-low SI (restricted diffusion) and ADC value of 0.861 x 10^-3 mm2/s. Pathology revealed IDC; grade II

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**Fig. 5:** Case 2: right image; Early phase post contrast THRIVE image, the mass (arrow) showed homogeneous enhancement. Left image; dynamic curve of plateau pattern with initial peak of contrast uptake at 1.8 minutes and corresponding MRE% of 51%

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**Fig. 6:** Case 2: The right breast mass showed restricted diffusion at b 850 (right image) and intermediate-low SI on the ADC map (left image) with an ADC value of $0.957 \times 10^{-3}$ mm$^2$/s. Pathology revealed IDC grade II.

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**Fig. 8:** Case 3: Right image presented early phase post contrast THRIVE image that showed heterogeneous enhancement of the left breast mass (arrow) with eccentric areas of breaking down. Left image showed mass kinetics of early initial contrast uptake at 70 sec. with MRE% of 71% and early wash out curve pattern.

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**Fig. 9:** Case 3: DWI (right) and ADC map (left) showed restricted diffusion of the left breast mass (arrow) seen framed with patchy perifocal edema of bright SI on both images. Estimated ADC value is 0.761 x 10^-3 mm^2/s and pathology reported IDC grade III

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**Fig. 11:** Case 4: Left breast upper outer mass (arrow) of heterogeneous enhancement with areas of liquefaction in the early post contrast series (right image). Kinetic behavior of the left breast mass presented early contrast uptake at 2 minutes with MRE% of 103% and early wash out curve pattern.

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Fig. 12: Case 4: DWI at b 850 (right) and ADC map (left); left breast upper outer quadrant multifocal mass (pink arrow) that showed restricted diffusion surrounded by perifocal edema. ADC value was 0.725 x 10^-3 mm²/s. Note ipsilateral upper outer enlarged intramammary lymph node (blue arrow). Pathology revealed IDC grade III

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Fig. 14: Case 5: Right breast mass (arrow) of heterogeneous enhancement on the early post contrast phase (right image) and plateau curve pattern (left image) with estimated MRE% of 46%

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Fig. 15: Case 5: DWI; b 850 (right image) and ADC map (left image) showed restricted diffusion of right breast mass (arrow) and ADC value of $1.096 \times 10^{-3}$ mm$^2$/s. Pathology revealed IDC grade I.

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Fig. 17: Case 6: right breast retroaerolar mass (arrow) of early homogeneous enhancement in the post contrast THRIVE series (right image) of initial peak of contrast uptake at 3 minutes with MRE% of 90% and plateau curve pattern (left image).

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**Fig. 18:** Case 6: DWI (right image and ADC map (left image): Restricted diffusion of the right breast mass (arrow) with evident areas of breaking down presented in the form of bright SI foci in the ADC map. Estimated ADC value was 0.914 x 10^-3 mm^2/s and pathology revealed IDC grade I

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**Enhancement curve**

- Plateau: 17%
- Wash out: 83%
**Fig. 21:** The distribution of time/enhancement curves in the study

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<table>
<thead>
<tr>
<th>Grade</th>
<th>Max Relative Enhancement (mean)</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>54.50%</td>
</tr>
<tr>
<td>II</td>
<td>63.00%</td>
</tr>
<tr>
<td>III</td>
<td>68.40%</td>
</tr>
</tbody>
</table>

**Table 2:** The mean max. relative enhancement of different histological grades

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Conclusion

There was no consensus across different studies regarding the role of dynamic MRI in predicting the histological grade of breast carcinoma.

On the contrary, DWI and ADC mapping seemed more reliable and more consistent across different studies.

Our study found a significant inverse correlation between the ADC value and the histological grade of the tumor.


This makes ADC value the best non-invasive tool currently available to identify highly aggressive breast carcinomas.
**Personal information**

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