Role of diffusion-weighted imaging in differential diagnosis of R3 breast lesions.

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Purpose

Borderline breast lesions, which are classified as Breast Imaging Reporting and Data System (BI-RADS) 3 (B3), have been increasing in recent years as a consequence of the widespread diffusion of mammographic screening programmes and continuing improvements in diagnostic ultrasound [1]. B3 palpable and non palpable lesions are commonly detected with mammography or ultrasound and their probability being cancer is considered to be less than 2% [2].

Currently, the diagnostic work-up of B3 lesion should be a follow-up with mammography and ultrasound every 6 months for 2 years: if the lesion is stable in size and its ultrasound and mammographic pattern doesn't change its benign nature is confirmed. Conversely, a core-needle or surgical excisional biopsy is necessary. Therefore most patients undergo biopsy of the lesion detected at first imaging evidence. Despite its high sensitivity (85-97%) and low false negative rate (2-7%), core-needle biopsy is associated with significant underestimation of malignancy in the context of B3 lesions [1].

Although the negative predictive value of magnetic resonance imaging (MRI) is highest of all imaging techniques, it is not yet common practice to use breast MRI as a problem-solving modality to exclude patients for further diagnostic work-up [2]. Therefore, the European Society of Breast Cancer Specialists (EUSOMA) has recently outlined current indications for breast MRI: one of these is the characterisation of equivocal findings at conventional imaging, in particular when it is not possible to perform or define a site for needle biopsy [3].

In this study we aimed to analyse the role of breast MRI as a problem-solving modality to characterize suspicious lesions in order to highlight the features which could suggest benign nature of the lesions to exclude patients for further diagnostic work-up.
Methods and Materials

Study population

We retrospectively reviewed our institutional electronic database in order to identify all patients with B3 lesions that underwent breast surgery from January 2008 to December 2010. We identified 50 patients. All these patients underwent mammography, ultrasound and MRI before biopsy. Later however the patients underwent breast surgery on clinical indication.

MRI protocol

Following patients' informed consent and exclusion of contraindications, MRI was performed with a 1.5 T unit with 23 mT/m gradient intensity (Signa Excite; GE Medical System, Milwaukee, WI, USA) with women in the prone position using a dedicated breast coil.

The following sequences were acquired:

- Short Tau Inversion Recovery (STIR) axial sequence;
- Diffusion-Weighted Imaging (DWI) axial sequence. DWI was acquired before dynamic sequences with a spin echo EPI (echo-planar imaging) sequence in the axial plane. Sensitising diffusion gradients were applied sequentially in the x-, y-, and z- directions with b values of 0 and 1000 s/mm2;
- Three-dimensional Fast Spoiled Gradient Echo (3DFSPGR) fat-suppressed coronal before and five times after intravenous administration of 0.1 mmol/kg of Gd-DTPA (Gadopentetate dimeglumine). Contrast medium was injected with a 10-s timing delay into the antecubital vein with an 18-20 G needle at a flow rate of 2 ml/s followed by a flush of 20 ml of saline solution;
- 3D FSPGR sagittal enhanced fat-suppressed sequence;
- 3D FSPGR axial enhanced fat-suppressed sequence.

Acquisition time was 18-20 min. Dynamic and DWI sequences were evaluated using a dedicated workstation.

Interpretation of MRI

All MRI images were analyzed by a radiologist experienced in breast MR imaging.

We analyzed lesion size, morphological features, time-signal intensity curve pattern on dynamic contrast-enhanced images, and the ADC (apparent diffusion coefficient) value derived from the ADC map obtained from DWI sequence.
Morphological features

Interpretation of breast MRI was based on the following three characteristics according to the American College of Radiology BI-RADS MRI criteria [4]:

- **shape** (round, oval, lobular or irregular);
- **margin** (smooth, irregular, or spiculated);
- **internal enhancement** (homogeneous, heterogeneous, rim enhancement, dark internal septa, enhancing internal septa, or central enhancement).

Kinetic pattern

For the signal-intensity measurements, the radiologist placed regions of interest (ROIs) to evaluate the enhancement pattern. Thereafter, time-signal-intensity curves were constructed. Kinetic analysis was performed according to the BI-RADS MRI guidelines [4]. Time-signal-intensity curve patterns were categorized into three types on the images obtained during the last four phases of contrast-enhanced dynamic imaging (Fig. 1 on page 5):

- the **persistent pattern**, in which the signal intensity continues to increase over time (type 1);
- the **plateau pattern**, in which the signal intensity does not change over time after its initial increase during the delayed phase of the enhancement (type 2);
- the **washout pattern**, in which the signal intensity decreases after reaching the highest point of its initial increase during the delayed phase (type 3).

DWI sequence

For the ADC measurements, the radiologist also manually placed a single ROI within the lesion. To place the ROI for both time-signal-intensity curve construction and ADC measurement in the same area, we used reference lines on an image viewer to compare coronal contrast-enhanced-MRI and axial DWI. DWI sequence was considered positive when ADC <0.0014mm$^2$/s, negative when ADC >0.0014mm$^2$/s or in absence of hyperintensity areas [5].
Fig. 1: Time-signal-intensity curve patterns

- **Type 1: persistent pattern** (signal intensity continues to increase over time)
- **Type 2: plateau pattern** (signal intensity does not change over time after its initial increase)
- **Type 3: washout pattern** (signal intensity decreases after reaching the highest point)
Results

In 20 patients (40%) there was no evidence of enhancement abnormalities at MRI examination. The 30 positive findings (60%) were divided into mass (22/30, 73%) and nonmass-like (8/30, 27%) breast lesions.

Among mass lesions, the size ranged between 5 and 50 mm with an average of 15.4 mm.

*Table 1 on page 8* summarizes mass-like lesions MRI morphological and internal enhancement findings, according to BI-RADS MRI lexicon [6].

*Table 2 on page 8* summarizes nonmass-like lesions MRI distribution pattern and internal characteristics, according to BI-RADS MRI lexicon [6].

Time-signal-intensity curve patterns among 30 mass and non mass lesions were:

- persistent pattern 12/30 (40%);
- plateau pattern 16/30 (54%)
- wash-out pattern 1/30 (3%)

In one nonmass lesion time-signal-intensity curve was not detectable, because of very little size of enhancement foci which made difficult to place a single ROI within the lesion.

DWI sequence didn't show hyperintensity areas in 12/30 patients (40%). In 3 cases (10%) DWI was illegible because of artifacts. In 15 cases (50%) in which measuring ADC was possible, the ADC value was <0.0014mm$^2$/s in 12/15 (80%), ADC >0.0014mm$^2$/s in 3/15 (20%).

In 20/50 B3 lesions MRI was negative. Suspicious morphological characteristics or internal enhancement was found in 16/50 (32%) B3 lesions (11 mass-like, 5 nonmass-like). Among these lesions 9 (6 mass-like, 3 nonmass-like) showed a type 2 or 3 enhancement kinetic curve and in only 5 of these (4 mass-like, 1 nonmass-like) the ADC value was <0.0014mm$^2$/s.

However on clinical indication all these 50 Patients underwent core-needle biopsy and later conservative breast surgery (lumpectomy). All core-needle biopsies were negative for cancer.
Final histological examination showed 16 intraductal papillomas, 27 sclerosing adenosis and 7 radial scar.

Some cases are reported and described in Fig. 2 on page 8, Fig. 3 on page 9, Fig. 4 on page 10, Fig. 5 on page 11, Fig. 6 on page 12.
### Table 1: Mass-like lesions MRI features

<table>
<thead>
<tr>
<th>SHAPE</th>
<th>MARGINS</th>
<th>INTERNAL ENHANCEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>round 8/22, 36%</td>
<td>smooth 7/22, 32%</td>
<td>homogeneous 12/22, 54%</td>
</tr>
<tr>
<td>oval 3/22, 14%</td>
<td>irregular 12/22, 54%</td>
<td>heterogeneous 6/22, 28%</td>
</tr>
<tr>
<td>lobular 6/22, 28%</td>
<td>spiculated 3/22, 14%</td>
<td>rim enhancement 4/22, 18%</td>
</tr>
<tr>
<td>irregular 5/22, 22%</td>
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</tbody>
</table>

### Table 2: Nonmass-like lesions MRI features

<table>
<thead>
<tr>
<th>DISTRIBUTION PATTERN</th>
<th>INTERNAL CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>focal 6/8, 75%</td>
<td>homogeneous 3/8, 37,5%</td>
</tr>
<tr>
<td>segmental 1/8 12,5%</td>
<td>stippled/punctate 2/8, 25%</td>
</tr>
<tr>
<td>regional 1/8 12,5%</td>
<td>clumped 2/8, 25%</td>
</tr>
<tr>
<td></td>
<td>reticular/dendritic 1/8, 12,5%</td>
</tr>
</tbody>
</table>

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Fig. 2. Papilloma

STIR view (a) shows dilated duct (arrow) interrupted by a slightly hyperintense lesion which appears lobular in shape with irregular margins and rim enhancement in axial 3D-FSPGR enhanced sequence (b). DWI (c) shows an hyperintense area with ADC value <0.0014mm²/s. The lesion has type I kinetic curve (d).

Fig. 2: Papilloma

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**Fig. 3: Sclerosing Adenosis**

Sagittal (a), coronal (b) and axial 3D-FSPGR enhanced sequence (c) show irregular lesion with irregular margins and heterogeneous enhancement with type 2 kinetic curve (d). DWI sequence doesn’t show any hyperintensity areas.

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**Fig. 3: Sclerosing adenosis**

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**Fig. 4: Radial scar**

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**Fig 4. Radial Scar**

Sagittal 3D-FSPGR enhanced sequence of two different patients (a, d) shows irregular lesion with irregular margins and heterogeneous enhancement, but both with type 1 kinetic curve (b, e). DWI sequence shows in the first case an hyperintensity area with an ADC value <0.0014mm²/s (c), while in the second case it was illegible because of artifacts.
Fig. 5. Papilloma

STIR axial and sagittal view (a, b) shows dilated duct (arrow). In coronal 3D-FSPGR enhanced sequence we can see a lesion oval in shape with irregular margins and heterogeneous enhancement (c), with a type 3 kinetic curve (d). DWI sequence doesn't show any hyperintensity areas.
Fig. 6: Sclerosing adenosis (non mass)

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Fig 6. Sclerosing Adenosis (non mass-like pattern)
Sagittal (a) and coronal (b) 3D-FSPGR enhanced sequence show a non mass-like lesion with homogeneous enhancement and segmental distribution pattern. DWI sequence shows in the first case an hyperintensity area with an ADC value <0.0014 mm²/s (c). The lesion has type 1 kinetic curve (d).
Conclusion

Currently, the diagnostic work-up of B3 lesion should be a biopsy or a follow-up imaging modality after 6 months. According EUSOMA guidelines [3] there is no evidence in favour of breast MRI as a diagnostic tool to characterise equivocal findings at conventional imaging when needle-biopsy procedures can be performed, but our results showed that MRI could be useful to distinguish lesions with different risk to be malignant if we consider only mammographic and ultrasound findings.

Regarding morphological characteristics, kinetic pattern and DWI sequence not associated each other, we had a number of false positives results, respectively, of 16/50 (32%), 19/50 (38%) and 15/50 (30%).

Instead, even considering the small number of patients, our results showed that despite 32% of B3 lesions were suspicious for their morphological and internal enhancement characteristics, evaluating also kinetic pattern only 9 of these were considered suspicious. Moreover, evaluating also DWI sequence and measuring ADC value if possible, only 5 lesions showed suspicious characteristics, considering both morphological, kinetic and DWI pattern.

Thus, by integrating the three different breast MRI parameters (morphological, kinetic and DWI), we could have avoided 90% unnecessary surgical procedures, because it is not currently possible, on the basis of these data, to avoid biopsies for these patients.

Therefore we can conclude that although MRI is not currently considered an alternative to biopsy, its use as a diagnostic technique might be a useful tool to avoid surgery in patients with B3 lesions detected on mammography and/or ultrasound with negative histological result on biopsy. In fact, these patients, on the basis of our results, may be more confidently sent to follow-up.

However, our preliminary data require validation on larger samples.
References


