Breast magnetic resonance imaging in detection and characterization of multifocality and multicentricity: usefulness of DWI in the pre-operative setting

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Purpose

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women worldwide (1). Breast cancer often involves several areas within a quadrant (multifocal disease), within different quadrants (multicentric disease) or even both breasts (bilateral disease). An accurate pre-operative examination is necessary to evaluate the extent of the disease because multicentric disease is a main contraindication to breast conserving surgery due to the higher recurrence rate (2).

Contrast-enhanced magnetic resonance imaging (CE-MRI) has been introduced in the preoperative setting in women with newly diagnosed breast cancer because it frequently detects additional foci of cancer occult on triple assessment (clinical examination, mammography and ultrasound) (3, 4). However, the role of CE-MRI in the preoperative setting needs to be further investigated because, despite its high sensitivity (89-100%), its specificity is extremely variable (50-90%) (5). There is indeed an important overlap between the morphologic and the dynamic features of CE-MRI benign and malignant findings (6).

Diffusion-weighted imaging provides qualitative and quantitative information about tissue cellularity and micro-architecture and it has been reported to be a useful technique for characterizing MRI breast tumour. Since tumour cellularity is inversely related to the ADC value, malignant tumours usually have a higher cellularity and a lower ADC than benign lesions (5). As previously reported, use of DWI can increase the specificity of breast CE-MRI and reduce the number of false positives results, without significantly increasing examination time (5, 7). Moreover, the ADC value of malignant lesions seems to be related to the cancer histotype and histological grade (8).

The purposes of our study were to evaluate the performance of pre-operative breast MRI in detecting additional lesions missed by conventional imaging and to assess the role of ADC provided by DWI in predicting malignancy of the additional MRI findings.
Methods and Materials

Study population

After permission was acquired from our Institution review board, a retrospective study was conducted on all patients identified in a prospectively collected database as having performed a bilateral breast MRI at our Institute for loco-regional staging from September 2010 to May 2011.

We included only women with enhancing MRI findings of at least 5 mm and who later underwent breast surgery at our Institution. Exclusion criteria were primary chemotherapy and unenhancing lesions.

Breast Magnetic Resonance Imaging

After written informed consent was obtained, each patient performed a bilateral contrast-enhanced breast MRI at our Institute on a 1.5 T magnet equipped with magnetic field gradients of 30 mT/m and a dedicated phased-array coil.

Examinations were acquired in the prone position, on the 7th to 14th day of menstrual cycle in premenopausal women or for women receiving hormone replacement therapy (HRT) after a 3 months HRT withdrawal.

After localizing scout views, an axial T2-weighted Turbo Spin Echo (TSE) (TR 4,000 ms, TE 120 ms, 436 x 323 matrix, 2.2 mm slice thickness, GAP 0.5, time of acquisition = 2' 50''), an axial Echo Planar diffusion-weighted spin-echo sequence (TR/TE 10,000/66 ms, FA 90°, Spectral Presaturation Inversion Recovery fat suppression technique, matrix 224, field of view (FOV) 310x310, slice thickness 3 mm acquisition time 70 s, b-value 0 and 900 s/mm², time of acquisition = 70'') and a contrast-enhanced dynamic three-dimensional T1-weighted gradient echo sequence were performed (TR: 499, TE: 4.6, FOV 375 x 321 x 162, matrix 528, 2.5 mm slice thickness, FA 90°, GAP = 0, time of acquisition = 8' 30''). The dynamic study was acquired after intravenous injection of 0.1 mmol/kg of gadolinium chelate at a rate of 2 ml/s, followed by 20 ml of saline and 10 s after the contrast medium injection the T1 weighted fat suppressed sequence was repeated 5 times with the same parameters. See our full MRI protocol in Figure 1.

Post processing evaluation

Image analysis was performed using a dedicated software and comprised subtracted images and time-intensity curves of a region of interest (ROI) of 3 x 3 pixels placed in the most enhancing region of the lesion. The post-processing for DWI included both a qualitative and quantitative analysis of diffusion properties. We evaluated the difference
of signal intensity between the b=900 and b=0 images of the lesion previously depicted on the dynamic study. If possible, a ROI was placed on the lesion in the b=900 image and then transferred to the ADC map to calculate the mean ADC of the lesion, sparing the necrotic and cystic components. In case of lesions larger than 1 cm or dishomogeneous, the ADC value was calculated as the mean of 3 measurements. See the post processing evaluation in Figure 2.

Management of additional MRI findings

When a lesion was identified on breast MRI, the previous mammography and US were reviewed according to the additional information given by contrast-enhanced MRI. Then, a targeted US was performed and, if a lesion was identified, a US-guided fine-needle aspiration biopsy or a core biopsy was performed. If a mammographic-only finding was depicted in the areas corresponding to the suspicious enhancements at MRI, a mammography-guided biopsy was recommended. If the lesion was not identifiable in the previous examinations or by targeted US, a MRI-guided biopsy was executed.

Breast specimens were analysed by an experienced breast pathologist; the histological type of breast cancer was defined according to the WHO classification.

Reports of the MRI, histo-pathological and clinical data of all patients were reviewed.

Statistical analysis

A MRI finding was considered a false positive if the biopsy of the enhancing lesion revealed a benign histology. On the other hand, MRI was regarded as a false negative examination if it could not detect any suspicious finding but malignancy was found at the histological examination on surgical specimen in women submitted to surgery or at follow up.

The difference between the mean ADC value of malignant and benign additional lesions was evaluated by Mann-Whitney U test.

Study endpoints

- The ADC value for additional enhancing lesion
- The difference between the mean ADC of malignant and benign additional lesions
- Sensitivity, specificity, PPV and NPV of ADC
- Conversion rate to multifocal, multicentric or bilateral disease
Fig. 1: Breast MRI protocol

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Fig. 2: Breast MRI post-processing

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Results

A total of 90 enhancing lesions were detected by both dynamic study and DWI and were confirmed by the histological analysis on surgical specimen. Fifty-six of these findings had already been reported by conventional breast imaging, while 34 lesions were MRI-only detectable. At least one additional lesion was detected in the 53% of patients (21/40) (range of additional lesions: 1 - 5).

At the pathological examination on the surgical specimen of all the enhancing MRI-findings, 79 findings were found to be malignant, while 11 benign lesions. Among the cancer detected, 48 lesions were invasive ductal carcinomas, 18 were invasive lobular carcinomas, 8 tubular carcinomas, 1 mucinous carcinoma and 4 in situ ductal carcinomas (Figure 3).

The mean size of the additional lesions was 14 mm (range 3 - 70 mm). Twenty-nine of the additional lesions were regarded as suspicious for malignancy at the morphological and dynamic MRI. The histological analysis on the surgical specimen revealed that 25 of the additional lesions were malignant (9 lesions were invasive ductal carcinomas, 12 were invasive lobular carcinomas, 1 tubular carcinomas, 5 in situ ductal carcinomas), while 9 were benign findings (fibroadenomas and parenchyma).

The mean ADC value of additional malignant findings was significantly lower than benign lesions (0,99 x 10-3mm2/s versus 1,38 x 10-3mm2/s, p<0,001) (Figure 4 and 5).

Setting the ADC cut-off at 1,29 mm2/s, as we previously established in a larger series of patients (9), 53 known lesions and 24 additional findings (overall 77 enhancing lesions) showed an ADC value below this threshold, suspicious for malignancy. Thirteen enhancing findings showed a higher ADC.

Seventy-six histologically proven cancers presented an ADC value lower than this threshold as well as one benign finding (DWI - false positive result). Three histologically proven cancers presented an ADC value higher than this threshold (DWI - false negative result) as well as 10 benign findings.

The sensitivity and specificity of ADC in the differential diagnosis between malignant and benign lesions were 96% and 91%, respectively; while the PPV and NPV were 99% and 77%.

See figures 6 and 7 for two clinical cases.
Twenty-five additional findings changed the definition of the disease extent (Figure 8). The detection of additional lesions led to:

- 32% conversion rate to multifocal disease (11/34)
- 38% conversion rate to multicentric disease (13/34)
- 3% conversion rate to bilateral disease (1/34)
Fig. 3: Breast cancer histology

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Woman with recent diagnosis of tubular carcinoma of the left breast. CE-MRI showed in the outer upper quadrant of the left breast three mass-like enhancements with irregular margins of respectively 9mm, 7 mm and 5 mm. She underwent a quadrantectomy and a trifocal tubular carcinoma was confirmed on the surgical specimen.

**Fig. 6: Clinical Case 1**

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Woman with recent diagnosis of ductal carcinoma of the left breast. CE-MRI showed in the outer upper quadrant of the left breast a mass enhancement of 1.5 cm with irregular margins and another mass enhancement of 1.3 cm between the upper quadrants of the same breast. She underwent a quadrantectomy and a bifocal IDC was confirmed on the surgical specimen.

**Fig. 7: Clinical Case 2**

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**Fig. 4:** ADC value of malignant and benign MRI findings

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Fig. 5: ADC value of the different MRI findings

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Fig. 8: Additional MRI lesions
Conclusion

In the pre-operative setting, breast MRI identified a significant number of additional malignant lesions missed by mammography and ultrasound, modifying the surgical planning. Furthermore, quantitative DWI showed a very high PPV in the characterization of additional findings. As previously demonstrated, DWI shows potential for improving the PPV of breast MRI for lesion of different type and size (10).

Therefore, ADC evaluation can provide additional diagnostic information to improve the differential diagnosis and it could potentially avoid supplemental biopsies before surgery.

However, our study has some limits. In our population there were few carcinomas in situ, which can be difficult to recognize at DWI due to small size and non-mass-like enhancements.

Our results need therefore to be confirmed in a larger series of patients with different type and size of enhancements.
References

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