Can DW-MRI replace DCE-MRI in local staging in patients with operable breast cancer?

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Purpose

Breast cancer is one of the most frequent tumour in female population, and one of the most frequent cause of death. In women with biopsy-proven breast neoplasia, Dynamic Contrast Enhanced MRI (DCE-MRI) is used for local staging [1-6]. In patients with operable breast cancer, MRI is helpful in planning the surgery, that is to decide to perform breast conservative surgery (BCS) or mastectomy. In fact MRI is used to define the lesion dimension, the presence of multifocal or bilateral neoplasia and abnormal axillar node [1-6]. Diffusion-Weighted MRI (DW-MRI) is an unenhanced MRI sequence that measured the mobility of water molecules in vivo. DW-MRI is sensitive to biophysical characteristic of tissues, such as cellular density, membrane integrity and microstructure. Normally water molecules move in all space directions, that is their movement is unrestricted. In presence of a lesion, a condition called anisotropy is found, that leads to a variation of the Apparent Diffusion Coefficients (ADC) [7]. The purpose of our study is to compare DW-MRI and Dynamic DCE-MRI in planning the surgical treatment in patients with operable breast cancer.
Methods and Materials

PATIENTS

This prospective multicentre study was performed in two different hospital: Universital Hospital of Udine and IRCC of Candiolo. Inclusion criteria were asymptomatic women with previously mammographic examination and histological-proven breast cancer, that were candidates to surgical treatment. In the period from February to July 2011, 45 patients (22 from Universital Hospital of Udine and 23 from IRCC of Candiolo) with all the characteristics written before, were enrolled. All patients underwent both DW-MRI and DCE-MRI for local staging before surgical treatment. Patients' age varied from 27 to 74 years, with a mean of 51 years.

IMAGING PROTOCOL

Before MR evaluation patients performed a mammography (MX) using a dedicated mammographic digital system with 2 projections (CC MLO) and in addition supplemental mammographic views, spot compression or magnification to better characterized the findings.

In the University Hospital of Udine Magnetic resonance imaging was performed using a 1.5 T MR-scanner (Avanto, Simens, Erlangen, Germany). All patients were imaged lying prone with both breast positioned in a dedicated 4-channel breast coil. After a survey scan, DW-MRI was performed with an axial EPI sequence (FOV 330x165 mm, matrix 164x84, in-plane resolution 2x2 mm, slice thickness 4 mm, distance factor 2 mm, 24 slices, TR 7100 ms, TE 84 ms, NEX=5, b-value 0 and 1000 s/mm², acquisition time: 2 minutes and 29 seconds) with suppression of the fat signal using spectral selection attenuated inversion recovery (SPAIR). Afterwards all patients were studied with DCE-MRI. The protocol used was: T1-weighted 3D-FLASH (fast low-angle shot pulse) on axial plane (FOV 340x340 mm, matrix 512x512, in-plane resolution 0.7x0.7 mm, slice thickness 2 mm, number of slices 72, TR 9 ms, TE 4.7 ms, Flip Angle 25°, NEX=1, phase oversampling 17, acquisition time: 1 minute and 20 seconds) repeated six times. Gadobenate Dimeglumine (Gd-BOPTA; Multihance, Bracco, Milan, Italy) was automatically administered as a bolus injection at a dose of 0.1 mL/Kg body weight at a flow of 2 mL/s, followed by flushing of 20 mL of saline. Serial dynamic images were acquired before injection of contrast agent and five times after the start of injection. After the examination, images underwent post-processing: subtraction of the pre-contrast images from the post-contrast images, multi-planar reconstruction (MPR) and maximum intensity projection (MIP). Curves of the variations in time/signal intensity were constructed placing a region of interest (ROI) on detected lesion. T2-weight images were acquired on the axial plane using a STIR (fat-saturated fast spin-echo short-time inversion recovery) sequence (FOV 320x320 mm, matrix 384x230, in-plane resolution...
In the IRCC of Candiolo MR Imaging was acquired at 1.5T using a dedicated eight-channel coil (GE Healthcare, Milwaukee) with the patient in the prone position. After a localizer on the three orthogonal planes and coil calibration, DWI was performed using a single-shot echo-planar image (EPI) sequence on the axial plane with the following parameters: TR/TE 10000/85ms, matrix 128x128, NEX 2, FOV 34, Slice thickness 4mm and Acquisition Time 80sec. Sensitizing diffusion gradients were applied along x, y and z axis with b-value= 0 and 900s/mm².

DCE-MRI studies were acquired by a 3D Vibrant sequence on the axial plane with the following parameters: TR 5,4msec, TE 2,6msec, flip angle 10°, slice thickness 2.6mm, matrix 416x416, FOV according to the volume of the breasts and temporal resolution ranging of 90 sec. Acquisition was performed before and 5 times after IV administration of 0.1 mmol/Kg of Gadolinium chelates at a rate of 2ml/sec (Gadobenate Dimeglumine-Gd-BOPTA; Multihance, Bracco, Milan, Italy) followed by 20 ml of saline flush. Post-processing of dynamic images consisted of MIP, MPR and time/signal intensity curve construction.

**IMAGES EVALUATION**

For each patient, two experienced radiologists evaluated independently and separately MX and DW-MRI and later on, after few weeks MX and DCE-MRI, blinded to the histopathological results of the lesions. For both examination, each suspicious lesion of malignancy found, was classified in Target Lesion (TL) and Non Target Lesion (NTL) and measured in accordance to RECIST 1.1 criteria [8].

In planning the surgical treatment, tumour size greater than 3 cm or the presence of large tumour in small breast were considered as contraindications to BCS.

The kind of surgical treatment(i.e. BCS v.s. mastectomy), planned on the basis of the data found with MX+DW-MRI was finally compared with that planned with MX+DCE-MRI.

**DATA ANALYSIS**

It was evaluated the number of lesions, classified as TL and NTL, found with both MX+DW-MRI and MX+DCE-MRI and their relative sensitivity. It was also evaluated the concordance in planning the surgical treatment using the two-systems.
Results

We found 55 TL with MX+DCE-MRI, while MX+DWI recognized 48 TL, with a sensitivity of 87% (48/55) (Fig. 1 on page 6 and Fig. 2 on page 6). For what concerns NTL, MX+DCE-MRI identified 23, and MX+DW-MRI only 13, with a sensitivity of 56% (13/23) (Fig. 3 on page 7). The results were showed in Table 1 on page 8.

The surgical treatments planned with MX+DCE-MRI and MX+DW-MRI respectively were described in Table 2 on page 9.

The concordance in planning surgical treatment (BCS vs mastectomy) between MX+DCE-MRI and MX+DW-MRI was obtained in 42 cases, respectively 29 BCS and 13 mastectomy (Fig. 4 on page 10 - Fig. 5 on page 11 - Fig. 6 on page 12). In remaining 3 cases, on the basis of the lesions found with MX+DCE-MRI, was planned mastectomy, while MX+DW-MRI under staged the disease, planning BSC (Fig. 7 on page 13).
Fig. 2: (A) CC projection of the left breast shows an architectural distortion of parenchyma in the internal-inferior quadrant, that is defined as target lesion. Diagnosis of breast invasive carcinoma was confirmed at biopsy. Mammography finding corresponds at DCE-MRI to an inhomogeneous enhancing round mass with irregular margins (B). In the anterior region, but in the same quadrant, an additional suspicious mass enhancing area is identifiable and it is considered non target lesion (C), suggesting a multifocal disease at MIP reconstruction (D). At DWI both the lesions are correctly identified (E,F). By combining mammography and DWI data, breast conserving surgery (BCS) was properly planned, confirming surgical treatment suggested by mammography and DCE-MRI. After BCS at final pathological evaluation both the lesions were defined as ductal invasive carcinoma. Surgical margins were negative.
**Fig. 1:** The two mammographic projection (A-B) show a mass (TL) in the superior-external quadrant of the right breast. DCE-MRI (C) and DW-MRI (D) recognized the lesion as a single TL. For this reason, both with DCW-MRI and DW-MRI, BCS was correctly planned. At the pathological examination of the specimen was found a ductal invasive carcinoma, with negative margins.

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**Fig. 3:** MX examination (A) shows asymmetry of density in the central region of the left breast. DCE-MRI (B) identified an inhomogeneous enhancing mass-like lesion with irregular shape and margins (TL), about 35 mm of size, in the central region of the breast. In addition it was also visualized a pathologic axillar node. These findings were recognized with DW-MRI (C) too. DCE-MRI identified also an enhancing focus in the inferior quadrant, that was classified as NTL (D). This NTL was not found with DW-MRI. Due to the large TL diameter, the surgical treatment planned with both MX+DCE-MRI and MX+DW-MRI was the same (mastectomy).

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Table 1: Lesions found whit MX+DCE-MRI and MX+DW-MRI.

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**Table 2:** Surgical treatments planned on the base of MX+DCE-MRI and MX+DW-MRI.

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<td>MX+DCE-MRI</td>
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<td>MX+DW-MRI</td>
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Fig. 4: MX shows in CC (A) and MLO (B) projections two suspected masses round in shape, with spiculated margins, that were confirmed to be ductal invasive carcinoma at the histopathological examination. DCE-MRI (C) recognized the two lesions as characterized by rim enhancement (TL). The diameter of each lesion was respectively 30 mm and 21 mm, and for these reasons a mastectomy was planned. DW-MRI (D and E) confirmed the findings and the surgical treatment planned was the same of DCE-MRI.

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Fig. 5: The MX examination in 2 projections, CC (A) and MLO (B), of the left breast, shows a mass with irregular shape and margins in inferior region. At the histopathological evaluation it was proved to be an invasive ductal carcinoma. DCE-MRI recognized the lesion as a TL with rim enhancement (C). For this reason BCS was planned as surgical treatment. With DW-MRI (D) and the ADC map (E) the lesion wasn't recognized. Thanks to MX, also with MX+DW-MRI a BCS was planned.

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**Fig. 6:** Mammography projections (A-B) show an architectural distortion of parenchyma between the superior quadrants of left breast. Diagnosis of invasive breast carcinoma was biopsy proven and it was defined as target lesion. At DCE-MRI an inhomogeneous enhancing mass with irregular shape and margins was confirmed (C, D). An additional suspicious smaller mass enhancing area is identifiable in the external quadrants of the same breast. It was considered as target lesion too (E), suggesting a multicentric disease at MIP reconstruction (F). At DWI only the lesion between the superior quadrants was identified (G-H), while the other one was not visible (I). Even if only one lesion was correctly detected, mastectomy was planned because of the large size of the cancer. Omolaterally a large axillary node is visible both at DCE-MRI (L) and DWI (M).

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Fig. 7: At mammographic examination, (A) craniocaudal and (B) MLO projections, no lesion was found. The patient had a suspicious lesion at sonographic evaluation, resulted to be an invasive ductal carcinoma at the histological analysis. DCE-MRI (C) shows a large inhomogeneous enhancing area (diameter of 5 cm), corresponding to the TL. For this reason was planned mastectomy. With DW-MRI (D-E) no lesion was found and BCS was planned. This is one of the three cases, where MX+DW-MRI under staged the disease.

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Conclusion

Different studies showed a difference in the means of the ADC values between breast cancer and the normal glandular tissue. In particular Sinha et al. first demonstrated that the mean ADC value of the cancer is inferior compared to that of normal tissue [9]. Guo et al. also proved a difference between different ADC, even if they found a overlapping between the two different mean ADC [10]. The presence of a difference statistically significant was confirmed by a recent review [11].

Yabuuchi et al. evaluated the role of the DW-MRI associated with T2-weighted images in confront of DCE-MRI and found a low sensitivity [12]. Other studies demonstrated an important role of the unenhanced MRI, thanks to DW-MRI. In particular Kuroki-Suzuki showed high sensitivity [13] and Balzer et al. demonstrated a sensitivity value more elevated than DCE-MRI, with a similar specificity between them [14].

Unenhanced-MRI can be useful particularly in patient with hypersensibility to contrast media and renal failure. Also, injection of a contrast medium is an invasive procedure and so if is possible to obtain the same information without it, unenhanced-MRI represents an effectively altering choice.

At our knowledge there are not studies that evaluate the role of DW-MRI in association with MX in planning surgical treatment in patient with proven breast cancer. For these reasons we begin this study, comparing the sensitivity of DCE-MRI+MX and DW-MRI+MX and their concordance in planning surgical treatment.

We didn't found high sensitivity with MX+DW-MRI in detection of lesions, in particular concerning NTL. But we found a good concordance in planning the surgical treatment (42/45), so the association of MX and DW-MRI may represent an alternative approach to DCE-MRI in local staging in operable breast cancer.

One of the most limitation of this study is the small patients' number and for this reason further evaluation is required and the study is still ongoing.
References


