Multifocal, multicentric, and contralateral breast cancers: MR imaging in preoperative assessment of local extent disease

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Purpose

Magnetic resonance imaging (MRI) of the breast is a diagnostic examination that can identify breast lesions that appear occult on other imaging techniques [1,2]. Due to its high sensitivity in the diagnosis of invasive breast tumours [3,4], several works have evaluated the preoperative use of supplemental MR imaging to assess the extent of disease [5,6].

However, the main limitations to the technique are the high number of false positive findings and the difficult management of incidental findings at MRI. In a recent meta-analysis on the role of breast MRI in the preoperative evaluation of malignant disease, MRI proved to be superior to mammography and ultrasound in identifying additional neoplastic foci in 6-34% of women affected by breast tumours, but only 66% of the suspicious MRI findings turned out to be malignant at histology [7]. The problem of false positive results therefore appears to be numerically important, and in addition to being a source of anxiety for the patient, it generates additional costs and delays in definitive treatment as well as unnecessarily extensive surgical procedures.

To reduce the costs, it would be best to select patients for whom there is evidence of benefit after use of preoperative breast MRI [6].

This study was conducted with the aim of identifying parameters for selecting, among newly diagnosed breast cancer patients, the patients to be referred for preoperative MR because in such cases the detection of additional malignant lesions is significantly higher.
Methods and Materials

Population

This series consists of 291 patients (range age 33-87 years, mean age 54 years) with histological diagnosis of infiltrating breast carcinoma consecutively undergoing to mammography, ultrasound and MRI before surgery (period: January 2006-November 2009).

As regard histological type, the pathological examination of surgical specimen demonstrated invasive ductal carcinoma in 218 (75%) patients, lobular in 61 cases (21%) and other histologies in the remaining cases (1 case in tubular, mucinous in 2 cases, bone marrow in 3 cases, papillary in 6 cases). The average size of the lesion (± SD) was 21.5 ± 11 mm in cases of ductal histology and 44.6 ± 24 mm in cases with lobular histology. The axillary lymph nodes were metastatic in 101 (35%) patients.

MR imaging and lesion management

The study was performed with a 1.5-T system (Symphony, Siemens Medical System, Erlangen, Germany) and 3D-GRE sequence acquired in the coronal plane until October 2007 (TR/TE 12/5.65 ms; flip angle 25°; matrix 254×320 pixels; FOV 380×75; thickness 1.24 mm; acquisition time 60 s) and in axial plane thereafter (TR/TE: 10/4.76 ms; flip angle 25°; matrix 384x90 pixel; FOV 385×91.7; thickness 1.10 mm; acquisition time 74 second). Sequences were performed before and after contrast agent intravenous injection with a dose of 0.1 mmol/kg and flow rate of 2.5 ml/second followed by 20 ml of saline solution.

Images were post-processed with subtraction tools and analysed according to the parameters of enhancement (mass-like; non-mass-like) and time-intensity curves.

When interpreting MR images, previous mammograms and sonograms were available for comparison. MRI lesions with no definite correlate at first-look mammography and US were recommended for second-look US.

In cases of MRI lesion with US correlate, the diagnostic workup proceeded according to the degree of US suspicion and, if necessary, with US-guided biopsy. The cancer cases found at second-look US were excluded from evaluation of benefits of MRI, as their depiction was attributed to ultrasound. In the cases in which the MRI finding had no US correlate, the finding was monitored with MRI after 6 months for BI-RADS 3 lesions or underwent pathological examination for BI-RADS 4 and 5 lesions. The reference standard was 12-month follow-up and histopathology examination, respectively.

Analysis
Results of the association of pre-operative MR in patients with breast cancer diagnosed at conventional imaging were evaluated in following terms.

- MRI detection rate of additional malignant lesions occult to mammography and ultrasound (in the same quadrant, in another quadrant, in the contralateral breast);
- distribution of additional malignant lesions identified by MRI according to histology (ductal vs lobular) and primary tumor size (less than 20 mm), mammographic density (BI-RADS classification into categories dense vs fatty dichotomised in D1-2 vs D3-4).

The data were analyzed using the Fisher's statistical test (significance: p value <0.05)
Results

MRI detection rate

Supplemental MR imaging after mammography and ultrasound depicted additional tumor in 27/291 newly diagnosed breast cancer patients (9%). A total of 40 synchronous malignant lesions were identified by MRI (Table 1).

They were ipsilateral to the main lesion in 25 cases: in the same quadrant in 13/291 (Figure 1); in another quadrant in 12/291 (Figure 2). In the remaining 2 cases (1%), were in the controlateral breast compared to the primary tumor.

The histological diagnosis of ipsilateral malignant lesions was invasive disease in 17/25 cases (68%) and in situ lesions in 8/25 cases (32%). The histological diagnosis of contralateral malignant lesions was invasive disease in both cases.

With regard to the pathological outcome in relation to the size of the lesion, 5/40 (12.5%) malignant lesions were # 5 mm, 26/40 (65%) were between 6 and 10 mm, 8/40 (20%) were extended from 10 to 20 mm and only 1/40 (2.5%) case was higher than 20 mm.

Table 1. Location, histology and size in 40 MRI otherwise occult additional cancer found in 27 newly diagnosed breast cancer patients.

<table>
<thead>
<tr>
<th>STUDY VARIABLE</th>
<th>VARIABLE CATEGORIES</th>
<th>N° CASES (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location from the index cancer</td>
<td>In same quadrant</td>
<td>22 (55)</td>
</tr>
<tr>
<td></td>
<td>In different quadrant</td>
<td>16 (40)</td>
</tr>
<tr>
<td></td>
<td>Controlateral breast</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Histology of MR additional cancer</td>
<td>Infiltrating carcinoma</td>
<td>32 (40)</td>
</tr>
<tr>
<td></td>
<td>In situ carcinoma</td>
<td>8 (20)</td>
</tr>
<tr>
<td>Size</td>
<td># 5 mm</td>
<td>5 (12.5)</td>
</tr>
<tr>
<td></td>
<td>6-10 mm</td>
<td>26 (65)</td>
</tr>
<tr>
<td></td>
<td>&gt;10 mm</td>
<td>9 (22.5)</td>
</tr>
</tbody>
</table>

MRI performance as a function of histological type and tumor size
Breast MRI was more sensitive in the depiction of lobular carcinoma and tumor greater than 2 cm (Table 2).

Specifically, MRI showed synchronous neoplastic foci in 25/218 (11%) cases of invasive ductal carcinoma versus 15/61 (25%) cases of lobular carcinoma (p value: 0.03). MRI depicted synchronous tumors in 14/176 (8%) cases where the primary tumor was smaller than 2 cm versus 26/115 (27%) cases with primary tumor larger than 2 cm (p value: 0.001).

Breast density did not affect the sensitivity of MR imaging as a malignant lesion was found in 9/67 (14%) cases with dense breasts and in 31/224 (14%) cases with breast adipose tissue (p value: 0.48).

Table 2. The MRI detection rate of otherwise occult additional cancer according to histological type and tumor size of the established index tumor and mammographic density (BI-RADS classification into categories from D1-fat to 4 - dense).

<table>
<thead>
<tr>
<th>STUDY VARIABLE</th>
<th>N°ADDITIONAL MALIGNANT MRI LESION (%)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology of index cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infiltrating ductal carcinoma</td>
<td>25/218 (11)</td>
<td>0.03</td>
</tr>
<tr>
<td>Infiltrating lobular carcinoma</td>
<td>15/61 (25)</td>
<td></td>
</tr>
<tr>
<td>Size of index cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td># 2 cm</td>
<td>14/176 (8)</td>
<td>0.001</td>
</tr>
<tr>
<td>&gt; 2 cm</td>
<td>26/115 (27)</td>
<td></td>
</tr>
<tr>
<td>Breast density pattern</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat (BI-RADS D1-2)</td>
<td>9/67 (14)</td>
<td>0.48</td>
</tr>
<tr>
<td>Dense (BI-RADS D3-4)</td>
<td>31/224 (14)</td>
<td></td>
</tr>
</tbody>
</table>

Additional biopsies

Findings at MRI study prompted a total of 102 breast biopsies, of which 38 findings were malignant (37%: true positives) and 64 were benign (63%: false positives).
As regard technique, biopsies were performed with ultrasound guidance in 50 cases, with MRI guidance in 33 cases and with surgical method in 19 cases.

Second-look US guided biopsy allowed identification of 11/38 synchronous malignant lesions (Figura 3) and 39/64 benign lesions. Findings at MRI also identified 58 breast lesions with MRI appearance probably benign (RM BIRADS 3), without second-look correlate, that underwent MRI follow-up (range time:12- 36 months).
Fig. 0: Figure 1. Women 54 years presented with palpable node on the right. Infiltrating lobular carcinoma. Right breast mammography examination (A, B) show heterogeneously dense breast density pattern (BI-RADS D2). In the pre-pectoral region, there is irregular spiculated mass. Transverse sonogram (C) obtained in the palpable node position, confirm the finding. US-guided 14-g core biopsy revealed infiltrating lobular carcinoma. The MIP of subtracted contrast enhanced three-dimensional gradient echo MRI (D,E) shows the known mass of cancer and two other small foci of satellites enhancement. Additional lesions found by MRI are located in front of the main mass and 1 cm distant. Histological examination of the surgical specimen confirmed the presence of multifocal cancer in upper outer right breast quadrant.

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Fig. 0: Figure 2. 40-year-old woman with infiltrating ductal carcinoma of the right breast. Mammography examination (A,B), extremely dense breast density pattern (BI-RADS D4). Mammograms show 3 cm cluster of pleomorphic calcifications in central area of right breast (arrows in A). Stereotactic guided biopsy yielded infiltrating ductal carcinoma. In C, some core samples with granular calcifications (arrows). Preoperative breast MRI (D-G: axial plane, subtracted T1-weighted contrast-enhanced images) shows clumped linear and ductal enhancement (arrow in D) adjacent to biopsy camera (arrowhead) corresponding to residual disease of known index cancer. MR image of right breast shows three other similar mass enhancement. There are additional irregularly shaped, irregularly marginated, heterogeneously enhancing masses in parasternal position (E), in right lower outer (F) and upper inner quadrant (G). Mastectomy revealed infiltrating ductal carcinoma, solid and cribriform type, with multicentric extension in right breast.

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**Fig. 0:** Figure 3. 45-year-old asymptomatic woman with infiltrating lobular carcinoma of right breast. Mammography examination (A-D) shows irregular spiculated mass (arrow in A, C) in right upper outer quadrant. US-guided core biopsy yielded infiltrating lobular carcinoma and lobular carcinoma in situ. Preoperative breast MRI (E,F: axial plane, subtracted T1-weighted contrast-enhanced images) shows irregular spiculated heterogeneously enhancing mass (arrow in E) corresponding to index cancer, with additional irregular spiculated mass in the controlateral breast (arrow in F). The second look transverse US obtained in left right upper outer quadrant after MRI, shows irregular hypoechoic shadowing mass (G) corresponding to the abnormality detected by MRI. The lesions was sampled for biopsy with US guidance, which yielded infiltrating lobular carcinoma in the left (controlateral) breast.

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Conclusion

MRI depicts lesions synchronous to the primary tumor, occult to mammography and ultrasound, in 9% of patients with invasive cancer. The use of pre-operative MR as an adjunct to conventional breast imaging in women with infiltrating lobular index cancer and index cancer larger than 2 cm is especially beneficial. In those groups of patient the MRI cancer detection rate is 25% and 27%, respectively.

On the other hand, addition of MR imaging carried a substantial risk of false positive findings and generate a large number of further investigation.

For this reason, preoperative breast MRI examination should be recommended for selected patients with newly diagnosed breast cancer that are more likely to multifocality and multicentricity.
References


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