Determination of axillary lymph node metastasis in breast cancer: differentiation with dynamic MRI by signal intensity-time curve graphics

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Authors: D. yildirim, B. Gurses, B. Ekci, A. Kaur; Istanbul/TR
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Purpose

Determination of the axillary lymph node metastasis has key role in the treatment strategy of breast cancer. We aimed to evaluate the role of dynamic MRI based on the signal intensity-time curves, in the detection of axillary lymph node metastasis.

Methods and Materials

Patients

Screening archive images of patients evaluated in our center between January 2008 and December 2009, those patients with medical records regarding US/mammography findings and clinical characteristics were evaluated and 120 patients who had breast and axilla (for malignant lesions) surgery as well as preoperative dynamic breast MRI evaluations (91 patients with primary benign lesions and 29 patients with malignant lesions) were included in the study. Mean age was 43 years (range: 24-61). This retrospective study was approved by the institutional ethical board.

MRI protocol and related axillary node dynamic data processing

MR imaging was performed with a 1.5-T system (Siemens Symphony, Erlangen, Germany) with the patient in the prone position and the breast suspended in a dedicated large breast coil. Another inclusion criterion of the study was the inclusion of axilla in the image plane. After an axial localizer sequence, axial T1W (TSE, TR:613 msec, TE: 9.1 msec, ST: 3.5 mm), axial STIR sequence (TE: 9370 msec, TE: 70 msec, ST: 3.5 mm) images were acquired (FOV:400x350 mm). On dynamic evaluation, immediately following the acquisition of precontrast series, a standard dose (0.1 mmol/kg) of gadodiamide based contrast agent was injected from antecubital vein in each patient. Following the injection of contrast agent, bolus injection of 15 ml physiological saline was also performed. After the contrast enhancement, by the same parameters dynamic contrast-enhanced gradient-recalled sequences were administered (repetition time, 4.4 msec; echo time, 1.6 msec; flip angle, 12, FOV 350x350 mm, 256 x 128; section thickness 1.5 mm with no section gap). Including those acquired in the precontrast period, a total of 7 series each consisting of 80 consecutive images were acquired in every 51 seconds. Six subtraction images (image series achieved by subtracting the precontrast image from each series) were transferred to the mean curve analyses (Siemens medical solutions) program in the work station. Contrast dynamic curves were generated from the cortices of axillary lymph nodes (separately from upper-middle-lower poles) exhibiting corticomedullary contrast enhancement by placing a 1.0 mm diameter round ROI. After the dynamic study, sagittal late postcontrast fat-saturated T1-weighted TSE images (TR:
532 msec, TE: 4.01 msec, ST: 3.0 mm, FOV: 400x400 mm) were acquired in order to
double check and correlate the lesions and axillary lymph nodes.

A total of 41 patients with contradictory archive data, those cases without
histopathological diagnoses or those without preoperative dynamic breast MRI
evaluations were excluded.

Biopsy was performed in dominant lymph node or nodes visualized in axillary
section images in all cases. Dominance criteria of the lymph node or lymph nodes
were: asymmetric cortical thickening, cortical irregularity, abnormal growth, cortical
heterogeneity, hilar deformation and loss of fatty sinus, loss of ovality (rounding).
Contrast enhanced components in upper-middle-lower poles of each lymph node were
marked by 1.0 mm diameter ROIs and dynamic curves were drawn in a special
work station (Leonardo running workspace-mean curve). In order to determine the
most probable metastatic lymph node, dynamic curve measurement was performed
in the lymph node with most abnormal contrast morphology (asymmetric cortical
thickening, asymmetric contrast enhancement, nodular corticomedullary foci, hilar fat
loss, rounding). Dominant pattern was defined as the pattern that was prominent in more
than 2/3 of the measurements (upper-middle and lower poles of each lymph node).

In the end, even if evaluation was performed in more than one lymph node, MRI
dynamic characteristics representing the axilla have been evaluated by means of average
technique as axilla has been evaluated as a whole during surgery. Main curve types
representing graphic data samples were schematized (Figure 1).

**Benign cases:**

Patients with no lesions were classified as BIRADS category I (n=21)

BIRADS category II consisted of patients with fibrocystic changes [adenosis (n=7), focal
hyperplastic nondemarked hypoechogenic changes (n=9)], ductal ectasy (n=11), simple
cyst (n=29), complicated cyst (n=7), fibroadenoma (n=24) and mastitis [granulomatous
mastitis (n=1), puerperal mastitis (n=3)].

Among benign cases, axillary lymph nodes were noted unilaterally in 6 patients and
bilaterally in the remaining 85 patients. Thus, bilateral markings were performed in
dominant lymph nodes of 85 patients and unilateral markings were performed in 6
patients and graphics were generated.

**Malignant cases:**

A total of 29 malignant breast lesions (7 diagnosed as lobular carcinoma, 22 as ductal
carcinoma) were present. Measurements were made from the axillary dominant lymph
node both at the affected and at the unaffected side in all cases. On histopathological
evaluation of the affected side in 29 malignant cases, metastatic involvement was
reported as positive in 21 patients and negative in 8 patients.
In this study, 176 (85 bilateral, 6 unilateral) dominant lymph nodes were evaluated in 85 benign cases and 58 lymph nodes consisting of 21 metastatic and 8 reactive lymph nodes on the ipsilateral side with breast ca and 29 benign-reactive lymph nodes on the contralateral side with breast ca were evaluated in 29 malignant cases. Measurements were performed in a total of 234 lymph nodes. Benignity criteria were based on 3-year follow-up results and requirement of no further histopathological evaluation (except in one patient with rounded lymph nodes). One of these patients was evaluated by FNAB and the other two were further evaluated by surgical exploration.

In all cases diagnosed as primary breast malignancy, evaluation involved ipsilateral axillary dissection. Lymph nodes on the intact side of cases with malignancy were evaluated based on 3-year follow-up and then were diagnosed as benign.

**Statistical analyses**

All study data are reflected in Table I. Comparison of age between the groups was performed by independent samples t-test, comparison of demographic characteristics was performed by Chi-square test. The relationship between the groups in terms of pattern distribution was also assessed by Chi-square test.

**Table I**: Various signal intensity-time curves of the whole study population

<table>
<thead>
<tr>
<th>Benign Cases</th>
<th>Distribution rates of curve types *</th>
</tr>
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<tbody>
<tr>
<td><strong>Bilateral (n=170)</strong></td>
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</tr>
<tr>
<td>Fibrocystic changes (n=13)</td>
<td>Type Ia: 1</td>
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<tr>
<td>Ductal ectasy (n=10)</td>
<td>Type Ib: 5</td>
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<tr>
<td>Simple cyst (n=27)</td>
<td>Type II: 11</td>
</tr>
<tr>
<td>Complicated cyst (n=7)</td>
<td>Type III: 121</td>
</tr>
<tr>
<td>Fibroadenoma (n=24)</td>
<td>Type IV: 32</td>
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<tr>
<td>Mastitis (n=4)</td>
<td></td>
</tr>
<tr>
<td><strong>Unilateral (n=6)</strong></td>
<td></td>
</tr>
<tr>
<td>Fibrocystic changes (n=3)</td>
<td>Type Ia: 0</td>
</tr>
<tr>
<td>Ductal ectasy (n=1)</td>
<td>Type Ib: 1</td>
</tr>
<tr>
<td>Simple cyst (n=2)</td>
<td>Type II: 0</td>
</tr>
<tr>
<td></td>
<td>Type III: 3</td>
</tr>
<tr>
<td></td>
<td>Type IV: 2</td>
</tr>
</tbody>
</table>
Malignant Cases (n=29)

Tumor side, metastasis positive FNAB/surgery (n=21)

<table>
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<tr>
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<tbody>
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<td>Ia</td>
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<td>12</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
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Tumor side, metastasis negative FNAB/surgery (n=8)

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<tr>
<td>II</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
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</table>

Nontumor side (n=29)

<table>
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<th>Count</th>
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</thead>
<tbody>
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<tr>
<td>Ib</td>
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<tr>
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<td>III</td>
<td>14</td>
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<tr>
<td>IV</td>
<td>8</td>
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</tbody>
</table>

*: Types of curves

Type Ia: Progressive straight contrast enhancement

Type Ib: Progressive curved contrast enhancement

Type II: Plateau type contrast enhancement

Type III: Washout type contrast enhancement

Type IV: Nonclassified or atypical graphical contrast enhancement

Images for this section:
Fig. 1
Results

There were no new lesions suspected of malignancy in any of the benign cases (in whom 3-year follow-up data were available) included in the study.

In 21 out of 29 malignant breast lesions, axillary metastatic lymph nodes were reported as positive. No new lesions or other data suggesting malign transformation were noted in the reports of normal axilla side in malignant cases in 2 or 3 year follow-up data.

Statistically significant difference was noted in age distribution of malignant and benign patients and malignant cases were significantly older (P<0.05; independent samples t-test). No statistically significant difference was found between other demographic characteristics of the patients (p>0.05; Chi-square test).

When signal intensity time curves were evaluated;

Pattern distribution in reactive-nonmetastatic lymph nodes was Type Ia (1.4%), Type Ib (5.6%), Type II (6.2%), Type III (66.2%) and Type IV (20.6%).

Pattern distribution in metastatic lymph nodes was Type Ia (9.5%), Type Ib (14.3%), Type II (57.2%), Type III (9.5%) and Type IV (9.5%).

Some forms among benign lymph nodes (n=7, 3.2%) that were observed as type III and continued as atypical were categorized as type IV. Not to complicaterd things any further, a separate category was not formed for this group. Results of each group according to graphic type are presented in Table II.

There was no statistically significant difference between malignant and benign cases in terms of Type Ia, Type Ib, Type IV distribution (p=0.12). However, significant difference was noted between the two groups in terms of Type II and Type III signal-intensity curve distributions (p<0.01). Type II pattern was significantly more frequent in malignant cases and Type III pattern was significantly more frequent in benign cases. Type II was observed OR= 20.5 times more in malignant cases (95% CI: 7.31-57.49). Type III was observed OR= 0.05 times more in benign cases (95 CI: 0.01-0.23). Thus, while Type II pattern is a strong indicator of malignancy, Type III reflects a protective character for benign lesions.

Conclusion

The method we have used in this study is a functional assessment that measures the contrast dynamics formed within the microenvironment of the lymph node. In cases with known primary breast mass, kinematic characteristics of axillary lymph nodes can be generated from signal intensity-time curves by using dynamic CE breast MRI examination
images obtained by expansion of FOV towards the axillary fossa. Contrast enhancement kinetics Type Ia, Ib, II are more common in malignant axillary lymph nodes; Type III and Type IV signal intensity curves are more common in benign lymph nodes; dominant contrast enhancement pattern is Type III (66.2%) in non-metastatic axillary lymph nodes and Type II (57.2%) in metastatic lymph nodes. The mechanism underlying these contrast kinetics may be associated with metastasis related increased vascularity in the lymph node due to prolongation of the distance traveled by the contrast agent and the time the contrast agent remained within the lymph node without being rapidly washed-out. We believe that the sensitivity of routine dynamic CE-breast MRI examination to determine axillary status will improve by this method.

References


Personal Information