Can dynamic contrast-enhanced MRI (DCE-MRI) predict tumor recurrence and lymph node status in patients with breast cancer?

The lymph node status is regarded as one of the most important prognostic factors for the overall and disease-free survival of patients with breast cancer. While morphological features and contrast enhancement kinetics of breast cancer shown on dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) have been correlated with tumor histological type, grade, and biomarkers [1–4], there were only few studies reporting the association of lesion features such as rim enhancement and kinetic feature (early maximal enhancement and washout) with node status and showed controversial results [5–7]. In this study, we investigated the MRI features of the primary tumor between patients who had early recurrence versus those who remained cancer free and also between node-positive and -negative patients.

We analyzed 62 patients (30–83 years old, median 58) with histologically confirmed breast cancer who were enrolled into a breast MRI study during years 2000–2003. A telephone survey was conducted in 2006 to follow-up all patients regarding their disease status. Of the 62 patients, six had confirmed cancer recurrence in the previously treated breast. The MRI features of these 62 patients were retrospectively reviewed and compared between the six with early recurrence versus those who were cancer free. Of these six patients with early recurrence, three had positive nodes (sentinel and/or axillary) at the time of first cancer diagnosis and three had negative nodes. Of the 56 patients who were cancer free, 28 had positive node and the other 28 had negative nodes.

Breast MRI was carried out on a 1.5T MR scanner. The protocol included precontrast images and dynamic contrast-enhanced imaging. The characteristics of primary tumor were analyzed. The longest and perpendicular dimension of the tumor size was measured on contrast-enhanced MRI and then converted to one-dimensional size. The morphological appearances were characterized using features described in BI-RADS MRI lexicon [8], separated into mass lesions and nonmass-like enhancements. The following enhancement kinetic parameters were analyzed: the % enhancement at 1 min (E1), 2 min (E2), 7 min (E3), and the washout slope between 7 and 2 min. Furthermore, pharmacokinetic parameters, including transfer constant ($K_{trans}$) and exchange rate constant ($k_{ep}$), were also analyzed with the Toft’s two-compartmental model [9].

The comparison of lesion morphology, size, and enhancement kinetic parameters in three groups was summarized in Table 1. LN(+) group had more irregular mass lesion (19/28, 68%) compared with LN(−) group (12/28, 43%), fewer round mass (4/28, 14% versus 10/28, 36%), and more nonmass-like lesions (3/28 versus 0/28). The tumor size in the LN(+) group (0.7–4.0 cm, mean 1.8 cm) was bigger...
Similar as the washout slope, the found that LN( ) group had a stronger washout and faster recurrence. We hypothesized that a tumor with higher angiogenesis may show lymph node metastasis and earlier recurrence. Thus, the recurrence group, none of the parameters showed significant differences compared with the other two groups. Since only six cases were found in the recurrence group, none of the parameters listed in the table. Since only six cases were found in the recurrence group, none of the parameters showed significant difference compared with the other two groups. Therefore, the MRI morphology or enhancement kinetics could not predict recurrence.

Noninvasive MRI may evaluate the tumor angiogenic activity. On the basis of the fact that angiogenesis is required to support cancer growth and metastasis, it may be hypothesized that a tumor with higher angiogenesis may facilitate the spread of cancer cells, and thus is more likely to show lymph node metastasis and earlier recurrence. We found that LN(+) group had a stronger washout and faster $k_{wp}$ than the LN(−) cohort, suggesting that invasive breast cancers with higher angiogenesis are more likely to have positive nodes. Our results were consistent with that of Tuncbilek et al. [6], which showed correlation of lymph node metastasis and washout slope of the primary tumor.

In six recurrent patients, three showed positive and three showed negative nodes. Three patients with negative lymph nodes developed early recurrence within 4 years. The uncommon clinical presentation was more likely due to substandard treatment, or the primary tumor expressing highly aggressive biomarkers or genetic markers. The development in oncogene profiling in the last decade has slowly been established as clinical tools. For example, Oncotype DX® on the basis of 21 genes has been shown to predict 10-year distant recurrence in patients with estrogen receptor-positive, axillary lymph node-negative breast cancer [10, 11]. The wide spread use of these tools is expected to provide additional prognostic predictors other than the traditional tumor staging and node status to determine the optimal management for each patient. In addition to help deciding which node-negative patients should receive chemotherapy and who can be spared, these genomic assays may predict the response to chemotherapy and endocrine therapy and help to select the optimal treatment [12, 13].

In summary, although the angiogenic activity of breast cancer evaluated by DCE-MRI was significantly higher in node-positive compared with node-negative patients, it is not sensitive to accurately predict the node status. In our cohort of 62 subjects, the angiogenic activity could not predict which patient would have early recurrence. Further development of genetic profile, biomarkers, and imaging markers may be combined to evaluate each specific cancer from different aspects and to develop the most accurate prognostic predictors [14]. Such predictors will further impact on selection of optimal management plan, contributing to ‘personalized medicine’ for each individual patient.

### Table 1. Comparison of tumor morphology, size, and enhancement kinetic parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LN(−), N=28</th>
<th>LN(+), N=28</th>
<th>P value</th>
<th>Recurrence, N=6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass—round</td>
<td>10/28 (36%)</td>
<td>4/28 (14%)</td>
<td>NS</td>
<td>3/6 (50%)</td>
</tr>
<tr>
<td>Mass—irregular</td>
<td>12/28 (43%)</td>
<td>19/28 (68%)</td>
<td>NS</td>
<td>3/6 (50%)</td>
</tr>
<tr>
<td>Mass—oval</td>
<td>1/28</td>
<td>2/28</td>
<td>NS</td>
<td>0</td>
</tr>
<tr>
<td>Mass—lobulated</td>
<td>4/28</td>
<td>0</td>
<td>NS</td>
<td>0</td>
</tr>
<tr>
<td>Focus (&lt;5 mm)</td>
<td>1/28</td>
<td>0</td>
<td>NS</td>
<td>0</td>
</tr>
<tr>
<td>Nonmass</td>
<td>0</td>
<td>3/28</td>
<td>NS</td>
<td>0</td>
</tr>
<tr>
<td>Size (cm)</td>
<td>1.5 ± 0.8</td>
<td>1.8 ± 0.9</td>
<td>0.12</td>
<td>2.1 ± 0.7</td>
</tr>
<tr>
<td>E1</td>
<td>126 ± 37</td>
<td>125 ± 29</td>
<td>0.9</td>
<td>156 ± 77</td>
</tr>
<tr>
<td>E2</td>
<td>151 ± 34</td>
<td>146 ± 37</td>
<td>0.6</td>
<td>185 ± 83</td>
</tr>
<tr>
<td>Washout slope</td>
<td>0.6 ± 3.3</td>
<td>3.7 ± 5.1</td>
<td>0.02</td>
<td>4 ± 1</td>
</tr>
<tr>
<td>$k_{trans}$</td>
<td>273 ± 101</td>
<td>338 ± 154</td>
<td>0.07</td>
<td>327 ± 173</td>
</tr>
<tr>
<td>$k_{ep}$</td>
<td>0.38 ± 0.11</td>
<td>0.48 ± 0.16</td>
<td>0.01</td>
<td>0.44 ± 0.1</td>
</tr>
</tbody>
</table>

NS, nonsignificant. P values (<0.05) in bold are statistically significant.

Compared with that in the LN(−) group (0.5–3.0 cm, mean 1.5 cm), but not significant (P=0.12). The % enhancements at 1 min (E1) and 2 min (E2) were about the same, but the washout slope was significantly faster in the LN(+) group (P=0.02). After analyzing the enhancement kinetics with the pharmacokinetic model, the parameter $k_{trans}$ was higher in the LN(+) group, with borderline significance (P=0.07). Similar as the washout slope, the $k_{ep}$ was faster in the LN(+) group (0.48 versus 0.38 1/min, P=0.011), indicating significant differences between the two groups. The mean values of these parameters in the recurrence group are also listed in the table. Since only six cases were found in the recurrence group, none of the parameters showed significant difference compared with the other two groups. Thus, the MRI morphology or enhancement kinetics could not predict recurrence.

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