Response Evaluation of Breast Cancer after Neoadjuvant Chemotherapy: Dynamic MRI vs. FDG-PET

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Purpose

Neoadjuvant chemotherapy (NAC) increases the possibility of breast conserving surgery, and provides the information of in vivo tumor sensitivity.

Pathological complete response (pCR) is associated with long-term survival, and used as the primary end point for neoadjuvant therapy.

The conventional diagnostic tools to evaluate the response are clinical breast examination, ultrasonography and mammography. Recently, we began to use dynamic Magnetic Resonance Imaging (MRI) and Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) in addition. However, it is sometimes problematic when the discrepancy between those diagnosis results comes up, so it is important to know ability of each characteristic tool in order to make a correct clinical decision.

The objective of this study is to assess the diagnostic accuracy of dynamic MRI and FDG-PET after neoadjuvant chemotherapy to predict pathological results.
Methods and Materials

Fourteen lesions in 13 patients who underwent neoadjuvant chemotherapy with histopathological diagnoses of invasive breast cancer were examined by dynamic MRI and FDG-PET before surgery in Kyoto University.

All patients received anthracycline and/or taxane based regimens. 7 patients received trastuzumab containing regimen. After every 2 cycles, clinical assessment of response was conducted according to clinical breast examination, the Response Evaluation Criteria in Solid Tumors (RECIST) and patients' tolerance at meeting with oncologists, radiologists and surgeons.

MRI protocol:
Using the same protocol, MRI evaluation was conducted after neoadjuvant therapies. MRI was acquired with a 3T scanner (Magnetom Trio Tim; Siemens Medical Solutions, Erlangen, Germany) with a breast-dedicated 4-channel coil (Invivo, FL, USA) at the end of NAC. After getting pre-contrast axial T2-weighted, T1-weighted and diffusion-weighted images, fat-suppressed T1-weighted dynamic images were acquired once before and three times after Gadolinium infusion.

At 0 - 1, 1 - 2 and 5 - 6 minutes after injection. The whole breasts were scanned in high temporal resolution of 1 minute (3D-VIBE: TR/TE 3.8/1.48 ms, FA 15, FOV 330\times330 mm, matrix 448\times461, 2.5 mm thickness, 60 slices) in axial orientation. At 2 - 5 minutes, a scan was conducted with high spatial resolution (3D-VIBE: TR/TE 4.2/1.5 ms, FA 15, FOV 330\times330 mm, matrix 448\times412, 0.8 mm thick, 176 slices) in coronal orientation. Infused Gadolinium contrast materials were either Gadoteridol (ProHance, Eisai Inc., Tokyo, Japan) or Gadodiamide (Omniscan, Daiichi-Sankyo Inc., Tokyo, Japan) for 0.2 ml/kg power injected at the speed of 2.0 ml/sec and flashed with 20 ml of saline at the same rate.

PET protocol:
PET/CT scanning was performed using a combined PET/CT scanner (Discovery ST Elite-Performance, GE Healthcare). Patients fasted for at least 4 hour before administration of FDG. The data acquisition started approximately 60 min after the injection of a standard dose of 200-250 MBq of 18F-FDG.

Image analysis:
All the image data was transferred to Aquarius NET Server (TeraRecon Inc., Tokyo, Japan) and analyzed.

Residual tumor in dynamic MRI was defined by their degree, pattern and distribution of dynamic enhancement. Enhancements at the area where a tumor existed before therapy were considered to indicate a residual tumor. Enhancements in other area were considered non-specific except when they had definite malignant morphology or dynamic enhancement pattern. Evaluation was conducted by an experienced radiologist (S.K.) with 10-year experience in breast MRI examination. The largest diameter was measured using contrast-enhanced 3D-volume images reconstructed in multiple planes.

PET images were visually interpreted by at least 2 experienced nuclear medicine physicians (K.K.M. and Y.N.) No visualized FDG uptake was regarded as clinical complete response (cCR).

Pathological analysis

The specimen were dissected and evaluated by pathologists. They were sectioned at 5-mm intervals perpendicular to the longest axis of the specimen. Partial resection specimens were completely embedded (and in cases of mastectomy grossly visible tumor beds were also thoroughly sampled) for optimal evaluation of tumor response. Pathological complete response (pCR) was defined as no residual invasive tumor on the specimen. The pathological size was defined as longest diameter of invasive tumor.

Analysis:

For all lesions, the sensitivity, specificity and accuracy of prediction for pCR by dynamic MRI or FDG-PET after neoadjuvant chemotherapy were calculated.
Results

Diagnostic accuracy:

The clinical response and the size of residual tumor as assessed by MRI, clinical response as assessed by FDG-PET and pathological findings (size, therapeutic grade, Ki67 index and phenotype) are shown in Table 1.

Five lesions achieved pathological complete response and 9 lesions had measurable pathological residual disease (size range; 2-35mm). The diagnosis of MRI showed 1 lesion of CR and 13 lesions of PR, the diagnosis of FDG-PET was 8 lesions were CR and 6 lesions were PR. The diagnostic accuracy of MRI and FDG-PET are shown in Table 2. The MR prediction accuracy of pCR: sensitivity is 20% (1/5 lesions), specificity is 100% (9/9 lesions) and predictive rate is 71% (10/14 lesions). The FDG-PET prediction accuracy of pCR: sensitivity is 60% (3/5 lesions), specificity is 44% (4/9 lesions) and predictive rate is 50% (7/14 lesions). MRI tends to overestimate the presence of residual carcinoma after NAC and FDG-PET tends to underestimate.

Assessment of residual tumor size:

To look at this result the other way around, MRI can detect residual invasive cancer more accurately than FDG-PET as 4 small lesions 2-5.5mm. Figure 1 shows pre and post-therapy MRI and FDG-PET and pathological findings N0.7 lesion. Post-therapy MRI predicted residual lesion but FDG-PET didn't. The size of the lesion predicted by MRI was almost the same as that by pathological examination. Generally the size of residual lesion by MRI is comparable but a little larger than that by pathological size.

False positive case:

In No.14 lesion (Figure2), both MRI and FDG-PET couldn't predict CR. Although both post-therapy MRI and FDG-PET showed abnormal enhancement and FDG uptake definitely, only scar existed in the excised specimen. Inflammation may be the reason.

Complementary effect:

Table 3 shows the correlation of both modalities and pathological response. This analysis demonstrates that even if we use both MRI and FDG-PET after NAC, the predictive accuracy for pCR is still not satisfactory.

Table# Imaging findings and pathological diagnoses of each patients.
<table>
<thead>
<tr>
<th>No</th>
<th>MRI size(mm)</th>
<th>MRI Tx grade</th>
<th>PET size(mm)</th>
<th>PET Tx grade</th>
<th>Pathology size(mm)</th>
<th>Ki67(%)</th>
<th>phenotype</th>
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<td>42</td>
<td>SD</td>
<td>SD</td>
<td>PR</td>
<td>32</td>
<td>30</td>
<td>HER2</td>
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<tr>
<td>2</td>
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<td>PR</td>
<td>CR</td>
<td>PR</td>
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<td>L-HER2</td>
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<tr>
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<td>PR</td>
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<td>9</td>
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</tr>
<tr>
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<td>12</td>
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<td>CR</td>
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<td>5.5</td>
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<tr>
<td>7</td>
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<td>PR</td>
<td>3</td>
<td>PR</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>15</td>
<td>PR</td>
<td>CR</td>
<td>PR</td>
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<td>N.E.</td>
</tr>
<tr>
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<td>11</td>
<td>PR</td>
<td>PR</td>
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<td>PR</td>
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<td>Basal</td>
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<tr>
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<td>CR</td>
<td>CR</td>
<td>N.E.</td>
<td>CR</td>
<td>N.E.</td>
<td>HER2</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>PR</td>
<td>CR</td>
<td>N.E.</td>
<td>CR</td>
<td>N.E.</td>
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</tr>
<tr>
<td>12</td>
<td>8</td>
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<td>PR</td>
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<tr>
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<tr>
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<td>PR</td>
<td>N.E.</td>
<td>CR</td>
<td>N.E.</td>
<td>Basal</td>
</tr>
</tbody>
</table>

Abbreviations, Tx grade; therapeutic grade, SD: stable disease, PR: partial response, CR: complete response, N.E.: Not evaluable,

Table 2. Overall diagnosis performance of MRI and FDG-PET

<table>
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<tr>
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<th>non-pCR</th>
<th>pCR</th>
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<td>MRI-nCR</td>
<td>9(100%)</td>
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<td>MRI-CR</td>
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<td>1(20%)</td>
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<tr>
<td></td>
<td>9</td>
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<td>PET-nCR</td>
<td>4(44%)</td>
<td>2</td>
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<td>PET-CR</td>
<td>5</td>
<td>3(60%)</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>non-pCR</td>
<td>pCR</td>
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<tr>
<td>--------</td>
<td>---------</td>
<td>-----</td>
</tr>
<tr>
<td>MRI nCR</td>
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<td></td>
</tr>
<tr>
<td>PET nCR</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>PET CR</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>MRI CR</td>
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<tr>
<td>PET nCR</td>
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</tr>
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<td>1</td>
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<tr>
<td></td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>
Fig. 0: Figure 1. Fifty-five-year-old female with invasive ductal carcinoma of the right breast. Figure 1a. Axial T1-weighted MR image of pre-systemic therapy showed round mass with rim enhancement.

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**Fig. 0:** Figure 1b FDG-PET image of pre-systemic therapy showed tumor uptake FDG (SUV=5.5).

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**Fig. 0:** Figure 1c. Axial T1-weighted MR image after neoadjuvant chemotherapy showed focus about 4 mm in diameter. MRI predicted clinical partial response.

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**Fig. 0:** Figure 1d. FDG-PET image after neoadjuvant chemotherapy showed no abnormal uptake.

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**Fig. 0:** Figure 1e. Continuous 5mm slices of surgical specimen. There was residual lesion at slice #20.

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Fig. 0: Figure 2. Fifty-five-year-old female with invasive ductal carcinoma of the left breast. Figure 2a. Axial Axial T1-weighted MR image after neoadjuvant chemotherapy showed mass lesion with heterogeneous enhancement. MRI predicted residual tumor.

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**Fig. 0:** Figure2b. FDG-PET image after neoadjuvant chemotherapy showed focal abnormal uptake (SUV=1.3), predicted residual active tumor.

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Fig. 0: Figure 2c. There was only fibrosis with granulation. No residual tumor identified.

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Fig. 0: Figure 1f. Pathological slide showed residual invasive ductal carcinoma about 3 mm in diameter.

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Conclusion

Our data suggested that MRI tends to overestimate residual carcinoma after NAC and FDG-PET tends to underestimate. It is warranted to study more about for predicting pCR correctly.
References


Personal Information

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