The role of breast MRI in planning the surgical treatment of breast cancer

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CONCLUSION
Contrast-enhanced magnetic resonance imaging (MRI) is a complementary imaging technique that is increasingly used in the surgical treatment planning of breast cancer. Contrast-enhanced MRI has a sensitivity of 40%–100% in detecting ductal carcinoma in situ (DCIS) and up to 100% sensitivity in detecting invasive breast cancer (1, 2). In many studies, MRI had a higher accuracy than mammography (MMG) and ultrasonography (US) in detecting multiple malignant foci, in defining the actual size and spread of a solitary tumor, and in diagnosing contralateral synchronous breast cancer (3–5).

Many studies have indicated various detection rates of MRI (16%–37%) for occult multiple lesions. The detection rate for a larger spread of the cancer is as high as 34% (1, 5, 6).

Larger extension of local disease affects not only the surgical and systemic treatment but also the axillary lymph node approach for staging leading to a direct full axillary dissection instead of sentinel node excision (5, 7).

Our objective in this prospective study was to investigate 1) the rate at which additional evidence is obtained with a pre-operative MRI and 2) how often the MRI findings change the surgical plan in patients for whom physical examination, MMG, and US findings make them candidates for breast-conserving surgery.

Materials and methods
The study was approved by the Ethics Committee of the Ege University School of Medicine. Retrospective analyses were performed on the prospectively obtained information. All of the patients were asked to read and sign informed consent prior to the MRI examination.

Contrast-enhanced breast MRIs were performed on 69 female patients undergoing physical examination, MMG, and US between August 2006 and December 2008. These patients exhibited evidence of breast cancer based on clinical and radiologic findings and were candidates for breast-conserving surgery.

Inclusion criteria were as follows:
1) Cytologically or histopathologically (fine-needle aspiration biopsy, Tru-cut excisional or incisional biopsy) proven breast cancer,
2) In accordance with the TNM classification used for malignant tumors (8), a clinical stage of T1, or 2 (T2) according to the physical examination, MMG, and US findings (usual imaging protocol),
3) Evaluation of the local spread of the disease via a pre-operative MRI examination prior to or following the biopsy,
4) Histopathological confirmation of additional findings with the MRI,
5) Revised treatment planning based on the true-positive findings with the MRI.
Cases in which multifocality or multicentricity were observed in multiple quadrants according to the MMG and US findings were excluded from the study. One case was excluded from the study as the breast volume was small and the mass exhibited a retroareolar location, although the clinical stage was T2,N0,M0.

Breast MRI technique

All of the cases underwent a breast MRI in a 1.5 Tesla MRI (Magnetom Vision Siemens, Erlangen, Germany) in our department. The conventional breast MRI protocol was performed using a standard breast coil in the prone position. The field of view was 300 mm, and pre-contrast and dynamic post-contrast images were obtained in the axial plane with turbo inversion recovery magnitude (9400/70 ms; slice thickness, 3 mm; number of slices, 32; NEX, 1; fat-suppression sequence). A T1-weighted fast low-angle shot (FLASH) three-dimensional (3D) sequence (TR/TE, 5.6/1.6 ms; slice thickness, 2 mm; number of slices, 64; NEX, 1) was performed. Vascular access was obtained with a 21 G antecubital needle for the administration of the contrast material prior to the MRI. In the dynamic study, a T1-weighted 3D FLASH sequence was performed following the contrast injection. The image sequence was repeated six times with 60 s intervals, and the images were obtained in the axial plane. The contrast material, such as the gadolinium, was manually administered via intravenous administration at a dose of 0.1 mmol/kg.

The evaluation of the images

All of the MRI examinations were interpreted by an experienced radiologist (A.O.). For the dynamic images, a standard subtraction program was performed using a Siemens MRI console. This was performed by subtracting the pre-contrast images from the post-contrast images on a pixel basis. Subtracted series aided in the visualization of the contrast-enhanced images. The images were transferred to a Leonardo (Siemens) workstation, and the time/signal curves of the lesions were drawn from the dynamic contrast-enhanced images.

After the images were processed, the MRI examinations were evaluated with respect to the patients’ histories and prior studies, i.e., MMG and US, using the system recommended by the American College of Radiology (9).

According to the MRI findings, the primary tumor size, the presence of additional suspicious lesions (multifocal, multicentric, or bilateral), muscle invasion, and the presence of a suspicious axillary and/or medial thoracic lymph node were noted.

The evaluation criteria

Following findings were not accepted as additional evidence:
1) An absence of a significant change in the size of the lesion as defined by the imaging methods. That is, the absence of a variation in size that would alter the treatment plan defined prior to the MRI (e.g., the presence of single mass measuring 1.5 cm on the MMG/US and 2.8 cm on the MRI or 3.2 cm mass on the MMG/US and 4 cm on the MRI),
2) If the examination was made following the excisional biopsy, the observation of a minimal residual signal change on the cavity wall (without mass),
3) The absence of a change with the MRI in the axillary lymph node status determined by the physical examination and conventional imaging methods.

Following findings were accepted as additional evidence:
1) The size of the primary tumor was sufficiently large to change the surgical plan according to breast cancer treatment protocol (10, 11),
2) Multifocality defined as additional suspicious lesion(s) nearer than 5 cm from the primary tumor in the same or the adjacent quadrant,
3) Multicentricity defined as additional suspicious lesion(s) 5 cm or further away from the primary tumor,
4) Contralateral lesion which is additional suspicious lesion in the contralateral breast,
5) Lymph node involvement which is suspicious axillary node that was not defined with the physical examination, US, or MMG, or mediastinal thoracic chain lymph node(s),
6) Involvement of the pectoral fascia/muscle.

In the following situations, the additional findings were accepted as being suspicious of a malignancy (9):
1) A suspicious morphology (e.g., irregular or spiculated mass, irregular edge, central internal septation enhancement or heterogeneous enhancement, enhancement that was not linear-ductal that was irregular or was in the form of a cluster and exhibited the morphology of the segmental mass, and being not in the form of a mass),
2) A suspicious enhancement pattern or a dynamic pattern of enhancement that was evaluated as type 3,
3) The existence of an ipsilateral lesion that exhibited a type 2 dynamic enhancement pattern, if compatible with the kinetic pattern of the primary tumor.

The histopathological verification of the additional MRI findings

Following findings were evaluated as true positive:
1) All of the additional intra-mammary findings that were histopathologically proven to be DCIS or invasive carcinoma (i.e., ductal, lobular, or mixed type),
2) Histopathologically proven fascia or muscle invasion,
3) The existence of a histopathologically proven metastatic lymph node that was only observed with the MRI.

Results

The age of the 68 cases included in the study ranged from 26 to 60 years (mean, 40.2 years).

The breast parenchymal pattern was identified as type 4 (extremely dense) in 14 cases, type 3 (heterogeneous dense) in 36 cases, and type 2 (scattered fibroglandular elements and fat-containing) in 18 cases based on the MMG findings and according to the BI-RADS classification method. In the conventional sequences, the mean dimensions of the detected lesions were between 0.4 and 4.5 cm (mean, 1.69 cm). An MRI examination was performed for 23 patients following the biopsy and pre-operatively for 45 patients. The time between the MRI examination and the operation date ranged from 1 to 20 days (mean, 9.5 days).

In nine cases, although the physical examination findings were negative, a mass was detected with the MMG or the US. In two of these cases, the MMG findings were negative, and the mass...
was detected only with US. In three cases, the US findings were negative, and the mass was detected only with MMG.

In eight of the 68 cases, positive surgical margins were histopathologically detected. An MRI was performed following the excisional biopsy in six of these cases and pre-operatively in two. In four of the six cases that received an MRI following the excisional biopsy, residual tumor was detected with MRI. Whereas the existence of residual tumor was histopathologically proven in two cases, the residual lesion could not be shown in the MRI that was obtained following the excisional biopsy. The histopathological diagnosis was DCIS in one of these cases and was invasive lobular carcinoma in the other. The dimensions of the lesions that were not observed in the MRI were 0.3 and 0.5 mm, respectively.

An MRI examination was performed pre-operatively in 45 cases and following the excisional biopsy in 23 cases. Residual tumor was histopathologically detected in two (4.4%) of the cases that were examined pre-operatively and in six (26%) of the cases that were examined following the excisional biopsy.

Sixteen additional findings were obtained with the MRI among the 68 cases included in the study (Table 1). Of these, the dynamic enhancement pattern was identified as type 2 in 11 cases and type 3 in five cases. Two of the six multifocal lesions in the MRI were determined to be false positives. A positive surgical margin was noted following the excisional biopsy in one of these cases, and a total mastectomy was performed. In the other case, the tumor that was predicted to be multifocal was located in the same quadrant with the primary lesion, so breast-conserving surgery was performed. In both of these cases, the MRI did not influence the surgical treatment plan despite the false positivity. The histopathological diagnoses of the lesions that led to the false positivity in these two cases were fibrocystic disease and fibroadenoma.

A false positive result was obtained in only one of the cases in which the breast MRI influenced the surgical plan. In the MRI examination performed prior to the surgery, the lesion that was predicted to be multicentric was histopathologically diagnosed as atypical ductal hyperplasia, so the case was treated with total mastectomy (Fig. 1).

False negative results were obtained by MRI in two of the 68 cases. In one case, multiple foci went undetected; in the other case, multifocal/multicentric foci went undetected. In both cases, the multifocal/multicentric foci were observed upon histopathological examination to be smaller than 0.5 cm. The histopathological diagnoses of these cases were DCIS.

One of the two contralateral masses that were observed by MRI was histopathologically proven to be malignant; this case was treated with bilateral partial mastectomy. In the other case, in whom a contralateral suspicious mass was observed, the excisional biopsy revealed fibrocystic disease and further treatment was not required.

Of the four lesions that were evaluated as false positives by the MRI, three exhibited a type 2 enhancement pattern, and one exhibited a type 3 enhancement pattern. In these two lesions, the dynamic enhancement pattern was the same as that of the primary tumor.

Pectoral muscle infiltration was observed in one patient, who was treated with total mastectomy. In three cases, skin invasion was observed. In three cases, an axillary lymph node was palpated during the physical examination. In these cases, axillary lymph node dissections were performed and the cases were treated with partial mastectomies.

In one of the cases, an axillary lymphadenectomy was observed by US and MRI but not by physical examination or MMG. An axillary lymph node dissection was performed during the operation.

Four (10%) of the 40 cases were candidates for a sentinel lymph node biopsy based on the pre-surgical physical examination, US, and MMG findings. Given that the spread of the tumor was relatively larger (multifocal and/or multicentric disease), an axillary lymph node dissection was performed. The histopathological examination revealed axillary involvement in three (75%) of these four cases.

Sixteen (23.5%) of the 68 cases had their surgical plan changed to mastectomy. This was due to multifocality in four cases, multicentricity in four cases (Figs. 2 and 3), the observation of a larger primary lesion in three cases, and surgical margin positivity following the excisional biopsy in three cases.

Of the three cases for which the surgical plan changed due to surgical margin positivity, MRI examinations were pre-operatively performed in two cases and following the excisional biopsy in one case. In the latter case, multiple foci were suspected, but no additional focus was observed on the histopathological analysis.

The number of cases for which the surgical plan changed due to the MRI findings alone was 13 (19.1%). The histopathological results of these 13 cases are summarized in Table 2; the distribution of the cases with respect to the pattern of breast parenchyma and tumor histopathology is given in Tables 3 and 4. With respect to the histopathology of the lesions, no statistically significant difference was detected between the groups in the frequency of changes to the surgical plan after the MRI (P = 0.403). When considering the breast parenchymal pattern groups, the surgical plan in the type 4 group changed by 53.8% after the MRI. This rate was statistically significant when

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Table 1. Additional findings observed in MRI

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<tr>
<th>Findings</th>
<th>Total (n)</th>
<th>Dynamic enhancement pattern (n)</th>
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<tr>
<td></td>
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<td>Type 2</td>
</tr>
<tr>
<td>Multifocality</td>
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<td>5</td>
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<tr>
<td>Multicentricity</td>
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<td>3</td>
</tr>
<tr>
<td>Primary tumor in larger size</td>
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<td>2</td>
</tr>
<tr>
<td>Pectoral muscle invasion</td>
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<td>0</td>
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<tr>
<td>Contralateral mass</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Total</td>
<td>16</td>
<td>11</td>
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</table>
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- Compared to other groups (Chi-square test, \( P = 0.006 \)).

When considering its effects on the surgical plan, the sensitivity of the breast MRI was 85%, the specificity was 98%, and the positive predictive value in terms of detecting additional positive findings was 92% (Table 5). When the additional positive MRI findings were compared with the histopathological findings, a compatibility rate of 86% (very good) was defined with Kappa test.

**Discussion**

If the MRI findings meet the criteria for breast-conserving surgery, the surgical plan does not change if pre-surgical tests reveal that 1) the solitary primary tumor is larger than was believed or that 2) additional foci are present in the same quadrant. In these cases, the tumor foci can be resected with a single surgical intervention (12, 13).

In the present study, when considering only additional true positive MRI findings, 12 (17.6%) of the 68 cases had changes made to their surgical plans (sensitivity, 80%; specificity, 98%; positive predictive value, 92%; negative predictive value, 94%). A compatibility rate of 81% between the additional MRI findings and the histopathological examination was obtained based on the Kappa test.

The increase in the mastectomy rate in the present study is similar to that reported in other studies (Table 6). The results obtained from both the present and similar studies demonstrate that MRI findings change the surgical plan in between 10% and 48% of cases (1, 5, 12, 14–24). However, the question arises whether the mastectomies will positively affect the survival of the patients. In other prospective studies, it was reported that when cases of early stage breast cancer are treated with arbitrary breast-conserving surgery or total mastectomy, no significant difference is observed in terms of survival. Nevertheless, recurrence rates were between 8% and 39% in the cases treated with breast-conserving surgery, whereas they were between 2% and 10% in the total mastectomy cases (7). Kuhl et al. (25) claimed that the additional foci detected by the MRI were successfully treated with adjuvant radiotherapy, even without mastectomy. When considering candidates for breast-conserving surgery, there is a need for randomized clinical studies that examine the clinical value of the detection of additional foci that change the surgical plan.

Figure 1. a–c. Negative conventional MMG (a) of the left breast. Axial T1-weighted contrast-enhanced MRI (b) shows an irregularly shaped mass that exhibits a type 2 dynamic enhancement pattern and is extremely suspicious of malignancy (BI-RADS 5). Axial T1-weighted contrast-enhanced MRI (c) shows another lesion with a linear shape. The histopathological diagnosis of the primary mass on total mastectomy was tubulolobular carcinoma. Another mass lesion that appeared suspicious for a second focus was diagnosed as atypical hyperplasia.
Breast MRI examinations performed prior to the surgery reduce the rate of positive surgical margin because this imaging technique demonstrates the true margins of the tumor. The MRI is also successful in selecting appropriate candidates for breast-conserving surgery by excluding those with multifocal or multicentric disease. The breast MRI reduces the need for repeated surgical interventions and minimizes the risk of residual disease due to recurrence.

In the present study, suspicious surgical margin positivity observed by MRI was also detected in the histopathological examination. However, as this finding did not affect the surgical plan, it was not treated as a positive additional finding. However, the observation of a residual lesion in only two (4.4%) of the patients who received a pre-surgical MRI examination demonstrates the success of MRI in determining the actual tumor margins. In the two cases in which the residual disease was not observed by MRI, the histopathological diagnosis was DCIS. The reason for the false negativity appears to be that the dimensions of the lesions were smaller than 1 mm in both cases. The 4.4% surgical margin positivity rate that we observed in the patients who received a pre-surgical MRI is lower than the rate reported in similar studies (17, 26).

The breast MRI provides more accurate results than the MMG in determining the size of primary tumor. Consequently, evaluating the size of primary central tumor (Figure 2). a, b. MRI of a 48-year-old female patient. Axial and sagittal T1-weighted contrast-enhanced MRI (a) shows an irregularly shaped mass with a type 3 dynamic enhancement pattern. This mass was extremely suspicious of malignancy (BI-RADS 5). Axial and sagittal T1-weighted contrast-enhanced MRI (b) shows another lesion with a similar morphology and enhancement pattern, with a suspicious additional focus on the same breast. The histopathological diagnosis was multicentric invasive ductal carcinoma and invasive lobular carcinoma.

Figure 3. a, b. Mediolateral oblique and craniocaudal MMG (a) of the right breast. Highly dense tissue on the MMG obscures the limits of a palpable mass, measuring 2 cm in the upper outer quadrant of the right breast. Axial and sagittal T1-weighted contrast-enhanced MRI (b) shows wide multifocality and multicentricity, which was confirmed on histopathological examination. The mastectomy specimen was confirmed to be invasive ductal carcinoma, invasive lobular carcinoma, and DCIS.
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The detection rates of multifocality (5.8%) and multicentricity (4.4%) in the present study are near to those of similar studies (Table 7).

In three of the cases (4.4%), the size of the primary tumor was observed to be large enough to change the surgical plan, with a specificity rate of 100%. The specificity of the MRI, alternatively, was found to be relatively lower in detecting multifocality (66%) and multicentricity (75%). The observed specificity of MRI in evaluating the size of primary tumor, multifocality, and multicentricity was similar to that of previous studies (1, 5, 16–22, 28, 29).

A contralateral synchronous malignancy that was not observed with physical examination, US, and MMG was detected by MRI in only one case. This number is low when compared to similar studies. MRI findings exhibit good correlation with histopathological results for lesions with a suspicion of malignancy that was not observed with physical examination, US, and MMG was detected by MRI in only one case. This number is low when compared to similar studies. MRI findings exhibit good correlation with histopathological results for lesions with a suspicion of malignancy.
of malignancy. The incidence rate of contralateral malignancy was reported to be 1.3%–29% in similar studies (5, 14, 16–22, 27–30) (Table 8).

The rates of multifocality, multicentricity, and the incidence of contralateral malignancy in the present study differ from those reported in previous studies, which may be due to the patient selection criteria in the present study. Only candidates for breast-conserving surgery based on physical examination, US, and MMG findings were included in the present study. If additional suspected lesions were detected by these methods in terms of malignancy, the MRI findings were not considered to be additional evidence according to our criteria. For instance, contralateral malignancy was suspected in one case in the present study. However, as the lesion was detected by both MRI and US, the MRI finding was not considered to be additional evidence. Similarly, in cases with a suspicion of multifocality based on MMG and/or US findings, and in those undergoing breast-conserving surgery, the MRI findings were not considered to be additional evidence.

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<tr>
<th>Table 7. Rates of detecting multifocal-multicentric tumor with MRI in literature and in the present study</th>
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<td><strong>Multifocality</strong></td>
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<td>Orel et al. (1)</td>
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<td>Mameri et al. (5)</td>
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<td>Wiener et al. (16)</td>
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<td>Pediconi et al. (18)</td>
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<td>Berg et al. (19)</td>
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<td>Lee et al. (20)</td>
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<td>Braun et al. (21)</td>
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<td>Bagley (22)</td>
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<td>Liberman et al. (28)</td>
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<td>Sardanelli et al. (29)</td>
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<td>Results of our study</td>
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<th>Table 8. Rates of detecting contralateral tumor with MRI in literature and in the present study</th>
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<td><strong>Contralateral tumor</strong></td>
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<td>Mameri et al. (5)</td>
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<td>Bilimoria et al. (14)</td>
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<td>Schelfout et al. (27)</td>
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<td>Turnbull et al. (30)</td>
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<td>Results of our study</td>
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In two cases, there was false negativity in the detection of multifocality/multicentricity related to DCIS foci with the MRI. The 80% sensitivity rate that we obtained in the detection of malignant foci by MRI is comparable with previous results. The frequency of false negative results, especially in the detection of DCIS, is mentioned in many studies (2, 3, 12, 31, 32). Orel et al. (31) stated that the sensitivity of MRI was 77% in DCIS diagnosis, and Fischer et al. (12) indicated that the histopathological diagnosis was DCIS in 29 of 30 false negative lesions. Furthermore, Boetes et al. (32) reported that among 204 cases, analysis of the malignant tumors that were not detected in the MRI revealed that the false negative rate for the existence of DCIS was 23%; the majority of these occult lesions were DCIS. The sensitivity of MRI in DCIS diagnosis is reported to vary between 40% and 100% (3, 31, 32). The reasons that have been noted for false negativity include the lesion size, the variable histological characteristics of DCIS, and the degree of tumor angiogenesis (31). Gilles et al. (2), when correlating the histopathological features of DCIS and MRI findings, indicated that DCIS cases with increased angiogenesis in the tumor stroma were detectable with MRI. In contrast, weak tumor angiogenesis resulted in false negative MRI findings. In the present study, tumor angiogenesis was not histopathologically evaluated; however, in both cases where MRI gave false negative results, it appears reasonable to associate the absence of contrast enhancement with poor vascularity of the lesions. Furthermore, in these two cases, the lesion being less than 0.5 cm in size may have been another reason for the false negativity.

Among the 40 patients who had previously been selected to receive sentinel node detection and excision as the primary approach for the staging the axillary chain, four (10%) were converted directly to full axillary dissection. All of these cases were converted because a larger extension of the disease was observed with the MRI (i.e., a larger single tumor, multifocal or multicentric disease). In three (75%) of these four cases, histopathologic examination revealed axillary involvement. This rate is higher than that reported in previous publications (33). It must be noted that these four axillary dissections did
not depend on an observation of a suspicious lymph node by MRI.

In conclusion, the pre-operative MRI evaluates the local tumor extent in breast-conserving surgery candidates and changes the surgical plan significantly by increasing the mastectomy rate. The surgical plan changes in approximately 20% of cases where breast-conserving surgery was planned. The MRI findings with respect to primary lesion dimension, multifocality, multicentricity, and contralateral spreading can be evaluated with nearly perfect correlation to the histopathological examination. We believe that MRI verification would be useful, especially when breast-conserving surgery is planned in cases with heterogeneously dense or extremely dense breast parenchyma, both of which are tissue types for which MMG and US exhibit low sensitivity. Prospective, randomized, and blinded imaging studies are necessary to evaluate the impact of MRI on the therapeutic planning in breast cancer, thus on overall and disease-free survival.

Conflict of interest disclosure
The authors declared no conflicts of interest.

References