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Diagnostic Magnetic Resonance Imaging of the Breast

Tanısal Meme Manyetik Rezonans İnceleme

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Abstract

Contrast enhanced breast magnetic resonance imaging is a modality that is frequently used into the breast radiologist's daily clinical practice. MRI examination should have optimal technical proficiency in order to attain diagnostic quality avoiding false positive and negative diagnoses. Furthermore, due to increasing usage fields of the examinations uniting with high sensitivity phenomenon, excessive usage and excision/interventional procedures are inevitable. Therefore, we hope to highlight the appropriate usage of the MRI technique and it's clinical applications.

Key Words: Breast, Breast cancer, Diagnosis, Indications, Magnetic resonance, Technique

Özet

Kontrast madde kullanılarak uygulanan meme manyetik rezonans görüntüleme, meme radyologlarının günlük klinik kullanımlarına artan sıklıkla giren bir yöntemdir. Manyetik rezonans görüntüleme (MRG), yanlış pozitif ve negatif teşhislerden kaçınacak tanısal kaliteye ulaşabilmesi için optimal teknik yeterliliğe sahip olmalıdır. Ayrıca artan kullanım alanları ile birleşen yüksek hassasiyet fenomeni nedeniyle, yöntemin ve eksizyonel/girişimsel prosedürlerin lüzumsuz kullanımı kaçınılmazdır. Bu nedenle, MRG tekniğinin uygun kullanım yöntemlerini ve klinik uygulama alanlarını vurgulamak istedik.

Anahtar Kelimeler: Meme, Meme kanseri, Tanı, Endikasyonlar, Manyetik rezonans, Teknik

Introduction

Breast magnetic resonance imaging (MRI) is an integral component of breast imaging protocols, and its importance has increased in recent years. The overall sensitivity of MRI for breast cancer is relatively high, with estimates ranging from 85% to 100% [1]. In cases of invasive ductal carcinoma, its sensitivity approaches 100%. The MRI sensitivities for invasive lobular carcinoma and ductal carcinoma in-situ are lower and not yet well defined [2].

The emerging role of MRI in breast imaging has been appreciated by many authors. It is important and vital for MRI to be used for the right indications because of economic outcomes and over-estimations. However, the unknown specificity of breast MRI indicates that continuing clinical trials are required. Through the evaluation of a combination of morphological features and contrast patterns, the rate of false-positive diagnoses will be reduced and the specificity will be increased. No well-defined standard of practice has been achieved for the usage of MRI in the diagnosis of breast cancer, staging or surveillance. The commonly accepted techniques and indications will be outlined below.

Imaging Technique

Sufficient data on contrast-enhanced breast MRI are only available for devices with field strengths of 1-7 tesla. It is currently unknown if the results obtained with these field strengths can be reproduced with lower field strengths, which cannot accurately delineate lesion morphology [2-4]. Fast and high-performance gradients, which are important for high-resolution imaging, can be obtained. Breast MRI is performed with patients in a prone position using a dedicated biopsy breast array coil equipped with mediolateral compression plates. The compression plates immobilize the breast and reduce motion artifacts. They also allow interventional procedures. Plate over-compression should be avoided to prevent reduced contrast uptake in the breast [5].

It is advised to scan both breasts simultaneously to compare the affected breast with the contralateral breast. Axial and sagittal planes are preferred for correlations with mammographic images [2]. According to the European Society of Mastology (EUSOMA) criteria [6], the slice thickness should be less than or equal to 3 mm and the temporal resolution should be lower than 120 sec. MR scanning starts with fast T2-weighted (T2W) images, such as Fast Spin Echo (FSE),

Turbo Spin Echo (TSE), Rapid Acquisition with Refocusing Echoes (RARE) sequences without contrast administration. Fat saturation (Spectral Attenuated Inversion Recovery (SPAIR), Short TI Inversion Recovery (STIR)) is not essential, but it is advised. The detection and characterization of the lesions are both crucial and are performed via contrast-enhanced dynamic and volumetric (such as FLASH, SPGR, T1-FFE) T1W sequences. Most modern MRI devices use rapid image acquisition with a FLASH 3D sequence. Volumetric series have favorable multiplanar reconstructed and high-resolution thin slices [2, 3] (Table 1).

Contrast material (0.1 to 0.2 mmol/kg Gd-DTPA, via an automated injector in 2-3 cc/s followed by a saline flush) is applied, and multiple postcontrast scans are obtained at equally spaced time intervals, typically 1 to 1.5 minutes apart [6]. Typically, 5-7 post-contrast scans are recorded. There is a linear relationship between the signal increase and the tissue concentration of the contrast medium, which leads to better differentiation between carcinomas and benign entities in the dynamic enhancement profile. To better visualize the enhanced areas, the unenhanced images should be subtracted from the first to last enhanced images (Figure 1) [3, 6, 7].

Imaging techniques such as DWI, perfusion and spectroscopy must be considered as additional data support and should not be used to replace dynamic or T2W-TSE studies [6].

Breast contrast enhancement is affected by hormonal changes. Contrast-enhanced MRI is performed between days 7 and 17 of the menstrual cycle in premenopausal women to avoid false-positive contrast enhancement (Figure 2). For post-

menopausal women, it is advised to perform breast MRI after 6 weeks of hormone replacement therapy interruption. It should be mentioned that post-surgical changes may result in false-positive enhancement for up to 6 months after surgery [2, 9].

Contrindications

Cardiac pace-makers, metallic ocular fragments, ferromagnetic vascular clips and metallic implants are contrain-
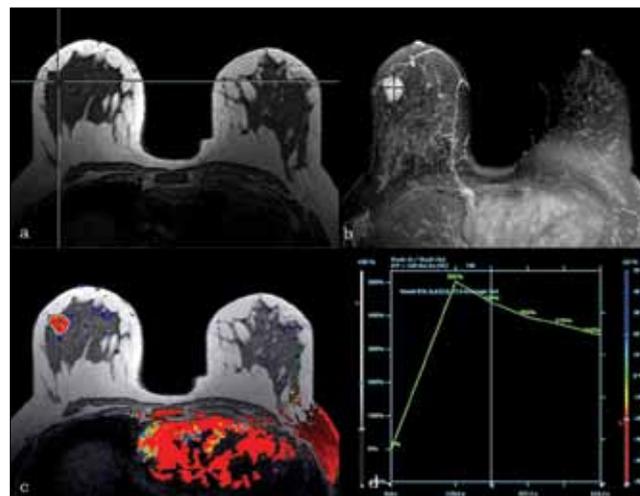

Figure 1. *MRI images of a malignant tumor mass. (a) T1 weighted image; note the undistinguishable lesion without contrast administration; (b) axial subtraction maximum-intensity-projection (MIP) image demonstrates tumour more prominent; (c) T1-weighted, contrast enhanced section with color coding which represents enhancement characteristics; and (d) Time intensity curve represents early intensive contrast uptake and washout characteristics of the mass.*

Table 1. Example Breast MRI sequences (Istanbul University Cerrahpasa Medical Faculty Radiology Department, Siemens Magnetom Smyphony 1.5T MRI Device)

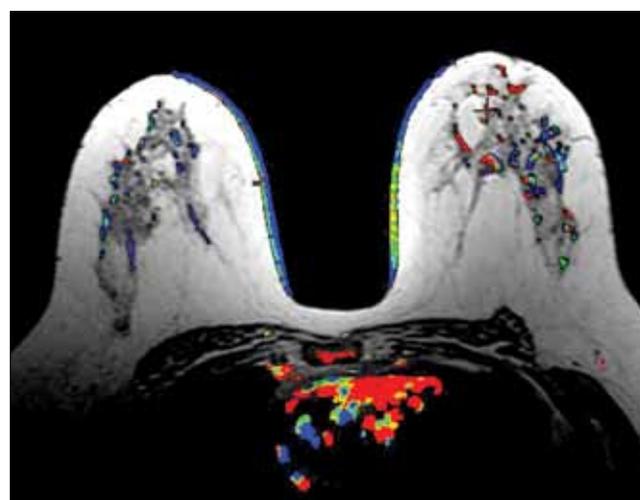| Sequences	T2 TSE	T1 Dynamic 3D Flash (enhanced/ nonenhanced)
Parallel Imaging	-	GRAPPA (Factor 2)
Fat Saturation	No	No
Respiratory State	Free	Free
TR (ms)	4500	11
TE (ms)	97	4.76
FA (degree)	150	25
FOV (mm)	350	450
Phase FOV	100	68.8
Matrix (pixels)	384x512	269x384
Slice Thickness (mm)	3	1.5
Slice Gap (mm)	0	0
Bandwith (Hz/pixel)	160	150
Acquisition Time (min:sec)	3:10	8:39

Figure 2. *Color coding T1 weighted image demonstrates various types of focuses due to unattended MRI scheduling in 24th day of menstural cycle of 42 years old pre-menstural woman. Appropriate scheduled MRI shows no suspicious contrast enhancement (not shown).*
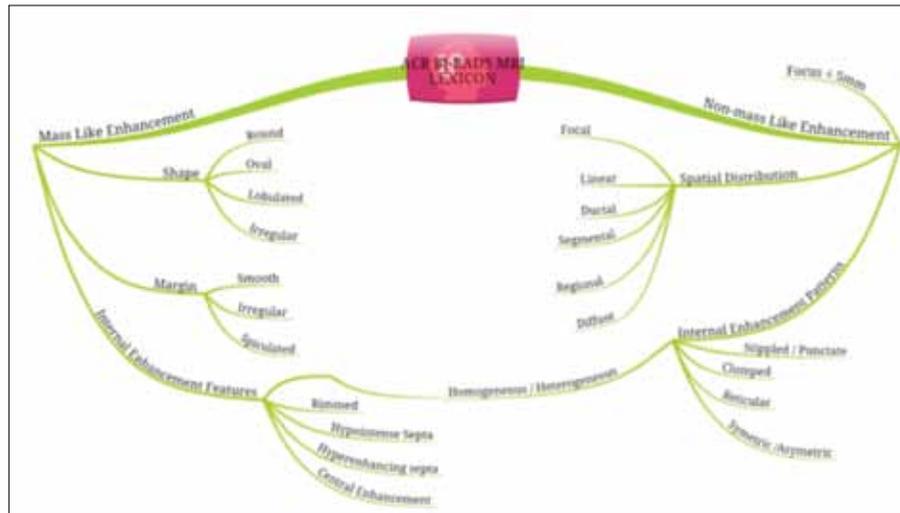
Figure 3. *ACR BI-RADS MRI Lexicon.*

dicated for breast MRI. People who are not suitable for prone positioning, obese and claustrophobic patients should not be evaluated with MR imaging [2]. Metallic clips implanted during breast surgery are not contraindicated, but they can produce metallic artifacts as signal voids.

Image Display and Interpretation

The morphologic and kinetic features of breast lesions should be considered in contrast-enhanced MR images and reported with the BI-RADS MR classification [2, 8] (Figure 3, breast MRI evaluation criterias). The evaluation of MR images starts with T2W sequences; hyperintense lesions, such as cysts, edema, intramammarian lymph nodes and some fibroadenomas, can be discriminated from normal breast parenchyma. It is essential to observe how the contrast enhancement resolves over time, and a series of consecutive scans must therefore be obtained. In routine dynamic MR imaging, very small areas of contrast uptake can be observed normally and are termed as "foci". These areas cannot be evaluated for either morphological or functional descriptors and typically appear and disappear due to hormonal alterations; there is no need for follow up if there is no other evidence of disease [7].

Masses with contours observed on T1W and T2W images should be discriminated. The first step of the investigation starts with the assessment of the morphologic characteristics of the lesion. A differential diagnosis is made by defining the shape, contour and contrast uptake of the lesion. Benign lesions tend to be round, oval or smoothly lobulated with a sharp demarcation between the mass and surrounding tissues (Figure 4), while malignant lesions tend to have spiculated or ill-defined margins and an irregular shape (Figure 5) [2, 6, 8].

Many benign entities, such as scars and cysts, do not enhance, while others, such as fibroadenomas, sclerosing adenosis and fibrocystic changes, do enhance. Additionally, many malignant lesions have characteristic enhancement patterns due to A-V shunts. Dynamic contrast enhancement is used to further distinguish between benign-enhancing lesions and malignant lesions. In this scheme, cancers were found to enhance quickly following contrast injection, while benign entities, such as fibroadenomas, exhibited delayed enhancement. Dynamic imaging cannot reliably distinguish between benign and malignant breast tumors alone. Lesions should be evaluated by morphological and dynamic characteristics simultaneously.

Homogenous enhancement is more common in benign lesions, while heterogeneous enhancement is more common in malignant lesions, although not all irregularly shaped, heterogeneously enhancing masses are malignant. The rim enhancement pattern is more common in malignant lesions (Figure 6) and is rare for benign lesions; inflammatory cysts and oil necrosis can also demonstrate the rim enhancement pattern. As a helpful diagnostic clue, cancers have low signal intensity and cysts have high signal intensity on T2W images. Central nidus and septal enhancement are observed in malignant lesions (figure 7), while non-enhancing septation is observed in benign lesions (Figure 4) [2, 10].

Non-mass contrast enhancement is used to define lesions that have no space-occupying effect on the adjacent breast parenchyma. These lesions cannot be distinguished from glandular breast tissue in non-contrast scans but only in contrast-enhanced scans. Special characteristics for the differential diagnosis of such lesions include symmetry, bilaterality and contrast uptake characteristics. A 'non-mass-like' contrast enhancement is characterized by the distribution pattern of the enhancements; linear, focal, segmental (Figure 8), regional, diffuse or ductal (Figure 9). An asymmetric ductal and segmental clumped enhancement is suspected to be ductal carcinoma in situ [2, 7].
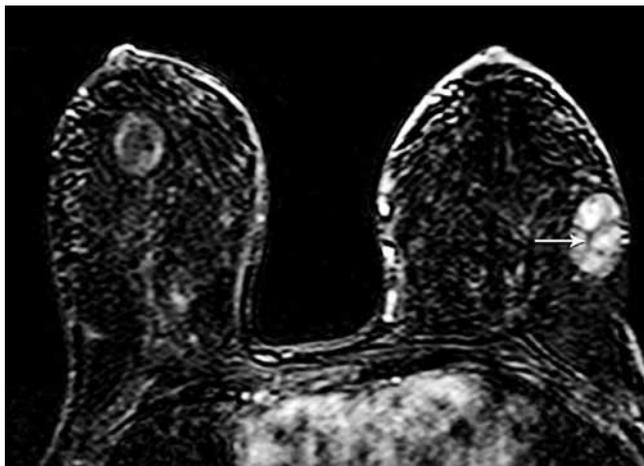
Figure 4. A 40-year-old female with high risk family history. Mammogram and ultrasound show enlarging mass correlate with MRI (not shown). Substraction image show well defined prominent masses. Note absence of nonenhancing septations of fibroadenoma in the left breast (arrow).
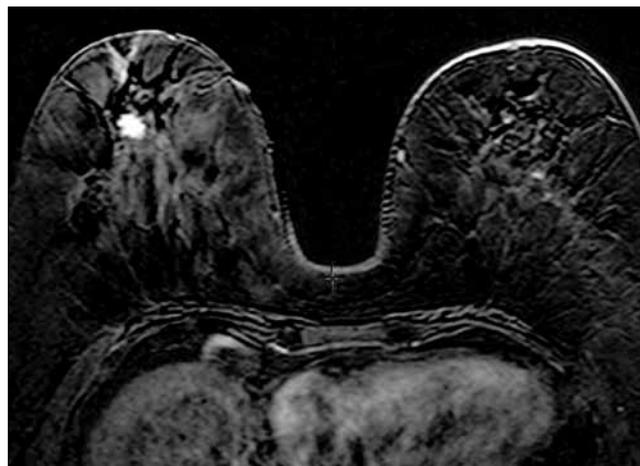

Figure 5. A 48-year-old woman had invasive ductal carcinoma. Axial contrast enhanced substraction image shows mass with spiculated margins in the right breast.
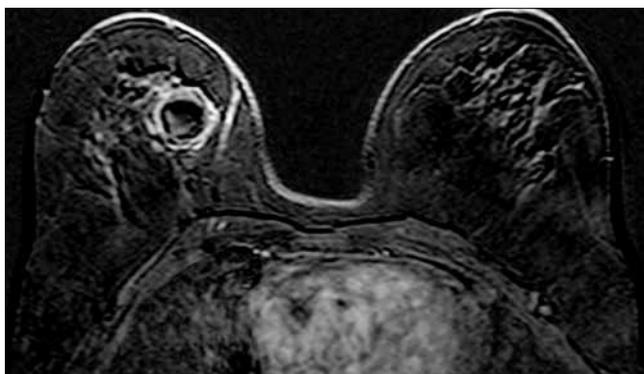

Figure 6. A 49-year-old woman with invasive ductal carcinoma. Axial contrast enhanced substraction image shows prominent enhancement of the peripheral zone of this thick rim enhancing mass with lobulated margins in the right breast.
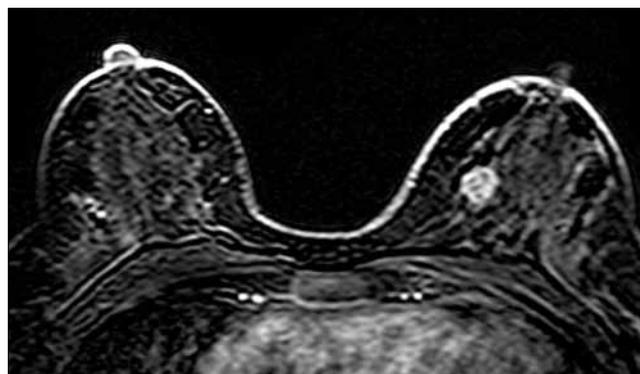

Figure 7. A 66-year-old woman had grade 3 invasive ductal carcinoma. Axial contrast enhanced substraction image shows a thin rim and septation enhancing mass with an irregular margin in the left breast.

Time intensity [kinetic] curves demonstrate area signal intensity changes over a selected time interval and provide the opportunity to determine the contrast uptake characteristics. They are obtained by selecting and placing a region of interest (ROI) over a suspected enhancement and are quantified by the change in signal intensity before and after contrast administration. The ROI should be selected from the region of the most rapid and strongest contrast uptake in all dynamic series and should not be larger than 3-4 pixels. If this procedure is not performed carefully, incorrect kinetic contrast curves can be obtained.

The shape of the time-signal intensity curve of suspicious lesions over a time period is obtained and is described as three different curve types: the type I (persistent/steady) curve corresponds to a straight or slightly curved enhancement pattern

with progressive increased enhancement over time; the type II (plateau) curve remains steady after an initial sharp increase in the enhancement level; and a type III (washout) curve has a drop in signal intensity after the initial upstroke, indicating contrast washout (Figure 10) [5, 7, 9]. These types are described as follows: type 1 as benign, type III as malignant and type II as a borderline pattern [3, 5, 10]. Furthermore, over a 100% increase in signal intensity in the early phase (first 1-2 minutes) is a significant sign of malignancy [2, 3].

Clinical Applications of Breast MRI

Carcinoma Unknown Primary

Occult cancer is an uncommon type of breast carcinoma and represents less than 1% of all breast carcinomas [9]. When axillary adenopathy with histologically confirmed metastasis
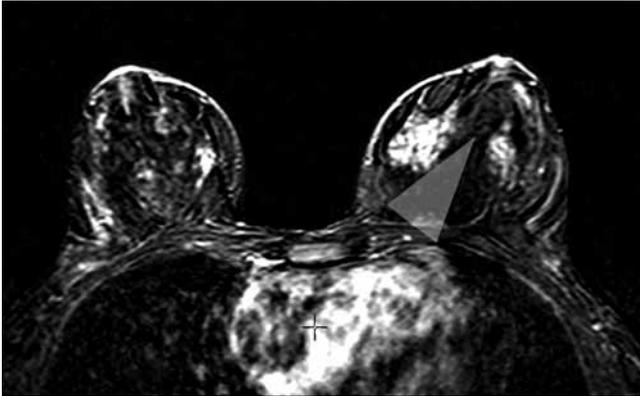
Figure 8. *A 40-year-old woman with DCIS in the left breast. Triangular region of enhancement with the apex pointing to the nipple (symbolized by triangle), suggesting a duct or its branches.*

Figure 9. *Enhancement in a branching line that points toward the nipple conforming to a duct in the left breast.*
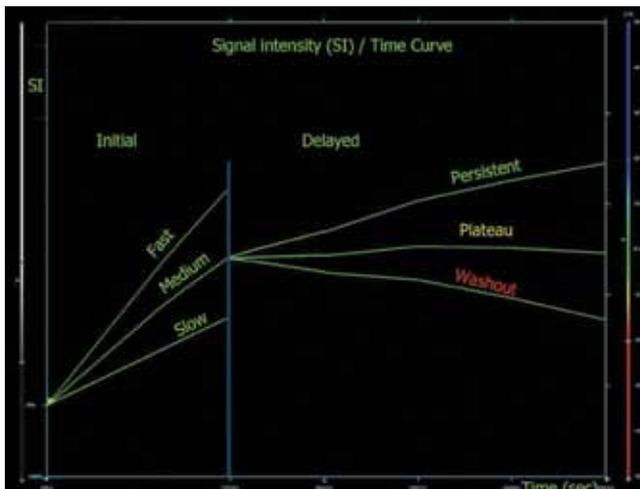

Figure 10. *Types of signal intensity/time curves in the kinetic study of breast MR.*

is present but the findings of a physical examination, mammography and US are negative for primary malignancy, breast MR imaging is indicated to locate the site of primary malignancy in the breast due to its higher sensitivity. Because of its low specificity for malignant lesion detection, any identified lesions should be histologically confirmed. When the MRI is negative, breast surgery is not indicated [7, 9, 11].

Monitoring Neoadjuvant Chemotherapy

In patients with locally advanced breast cancer, the determination of a standard imaging protocol for neoadjuvant chemotherapy is difficult. MRI has been shown to be better than a physical examination, mammography and sonography for assessing residual disease after neoadjuvant chemotherapy [13, 14]. MR imaging may be performed before, during and after the course of chemotherapy to evaluate the tumor

response and the extent of residual disease before surgical intervention (Figure 11). It has been shown that MRI can indicate the response to chemotherapy as early as 6 weeks after its initiation in areas where contrast enhancement is reduced before any change in tumor size can be detected [14].

The clinical, sonographic and mammographic detection of the tumor response to chemotherapy can be impaired by chemotherapy-induced fibrosis [14]. The fibrous tissue may simulate residual tumor tissue on clinical examination, sonography and mammography. Thus, MRI is essential for detecting and discriminating active malignant tissue with contrast uptake (Figure 12).

Dynamic MRI is performed to evaluate the response of the first two chemotherapy cycles. After treatment, the tumor can be reduced in size or even disappear. The signal intensity curves convert to the benign type. Therefore, calculating and comparing tumor volumes with contrast-enhanced dynamic breast MRI are advised to determine the response to therapy before and after treatment [15].

However, there are limitations to the contrast MRI evaluation of residual disease after neoadjuvant chemotherapy. MRI tends to overestimate the size of residual disease because of the angiogenic effects of certain chemotherapeutic agents on the tumor, and the ability of contrast MRI to evaluate lesion enhancement can be significantly decreased [11, 12].

Preoperative Tumor Staging

Women with newly diagnosed breast cancer should be treated with breast-conserving surgery and radiation therapy with consideration of the tumor size, multifocality or multicentricity, local extent vs distant spread, nodal status and patient preference. The potential use of MRI is the staging of breast cancer to determine if breast conservation surgery is appropriate and to avoid re-excision for inadequate margins.

Figure 11. Contrast enhanced MR images showing breast cancer responding to neoadjuvant chemo-
therapy. The images were acquired before chemotherapy (a), after two cycles (b) and after the end of che-
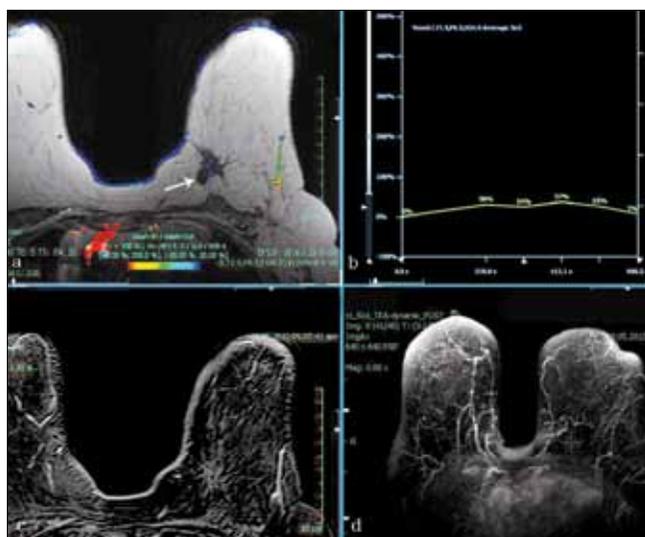motherapy regimen (c).

Figure 12. A 51 years old post-operative follow up patient. After first
year of surgery, MRI performed for suspicious clinical examination
with dense post-operative region on mammography. Post-contrast MRI
examination (a; T1 weighted contrast enhancement w/o fat saturation,
b; signal intensity/time curve, c; substraction image, d; MIP image) did
not show contrast uptake in the suspected area just next to the surgical
clip (arrow). The suspected area is followed up as post-operative fibrosis.

When breast cancer surgery is performed with a curative
purpose, the accurate determination of the disease extent is
essential to avoid recurrent disease. Confirmation of the exact
tumor size and spread in the breast, identifying contraindica-
tions for breast conservation, such as infiltration of the chest
wall (Figure 13) or areola, and identifying breast cancer in the
opposite breast are the key factors guiding the therapeutic
options of surgery or neoadjuvant chemotherapy.

Studies have shown that MRI is more accurate than mam-
mography and ultrasonography in defining the extent of
tumor burden as characterized by tumor size and multifocal-
ity or multicentricity (Figure 14) [7, 11, 12]. Staging-oriented
bilateral breast MRI showed that 3-5% of the patients had a
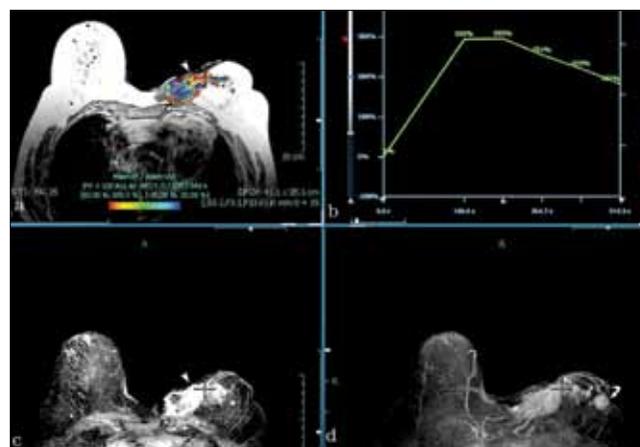synchronous tumor site in the contralateral breast [16]. MRI

Figure 13. A 63 years old patient with invasive ductal carcinoma. Post-
contrast MRI examination shows pectoralis muscle (white arrow) and
skin invasion (arrowhead) (a; T1 weighted contrast enhancement w/o
fat saturation, c; substraction image d; MIP image) with washout char-
acteristics (b; signal intensity/time curve) and multicentric (d) lesions
(curved arrow).

should be performed for breast cancer patients if dense breast
tissue, a silicone implant, a strong family history or a suspicion
of pectoralis muscle involvement, chest wall invasion or an
invasive lobular carcinoma diagnosis is present [2, 11].

Problem Solving

Mammographic and sonographic findings may be unclear
as to whether a suspected lesion is truly present because of
the radiographic density of fibroglandular breast tissue. Most
lesions are detected on single projections as parenchymal
distortions and asymmetrical densities in some cases, the
lesion morphology is indeterminate for malignancy. These
findings can typically be solved with the combined use of an
additive mammographic (such as magnification or compres-
sion) and second-look sonographic workup. If the findings
are still inconclusive after this additional workup, MRI may be
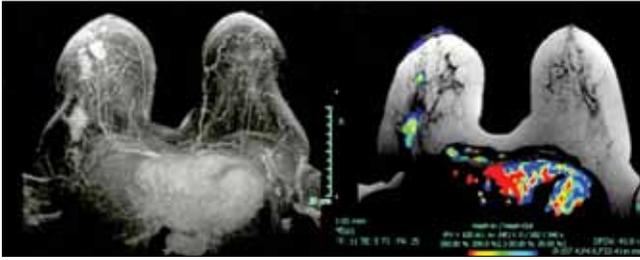useful (Figure 15). Contrast-enhanced temporal imaging mor-

Figure 14. A 45 years old patient with invasive lobular carcinoma. Mamographic and sonographic evaluation showed multifocal tumor areas in anterior segment of right breast (not shown). Additional MRI examination revealed non-mass enhancement in axillary tail conforming multicentricity (crosshair).
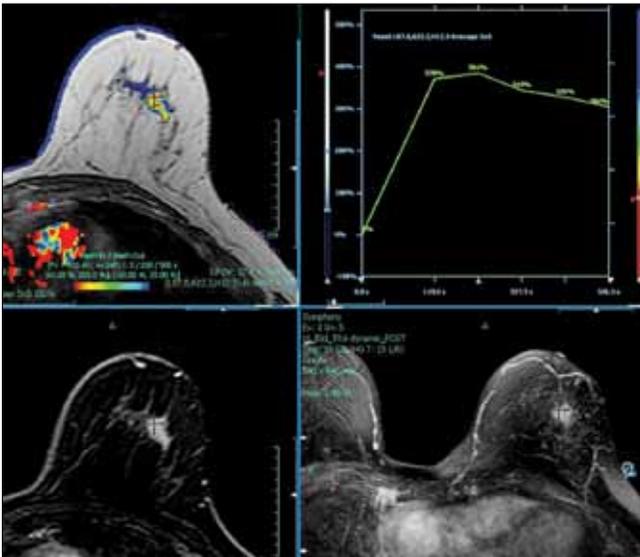

Figure 15. A 52 years old patient with invasive lobular carcinoma. Mamographic screening revealed asymmetrical parenchymal density with no ultrasound equivalent. MRI showed irregular marginated lesion, intense contrast enhancement with washout kinetics.

Figure 16. A 47 years old post-operative follow up patient with invasive ductal carcinoma recurrence. After first year of surgery, MRI performed for suspicious clinical examination with dense post-operative region on mammography similar with patient presented in the 12th figure. Post-contrast MRI examination (a; T1 weighted contrast enhancement w/o fat saturation, b; signal intensity/time curve, c; substraction image, d; MIP image) shows non-mass contrast uptake in the suspected area with washout contrast kinetics. Note the pectoralis muscle retraction.

phology and spatial dynamic enhancement characteristics may offer clues as to whether a lesion is benign or malignant. Although MRI is expensive compared to mammography, the MRI cost is much lower than that of interventional biopsy, which is excluded by negative MRI results. However, the false-positive rates of MRI should be determined carefully.

Moreover, a lesion identified in a physical examination or hemorrhagic nipple discharge with conventionally negative radiologic findings is a candidate for advanced MRI examination [2].

MRI may be used to distinguish benign and malignant lesions even in cases that are inconclusive on conventional imaging; the most established indication being the differentiation of tumor recurrence versus scar tissue during the follow up of patients who underwent breast conservation therapy [17]. F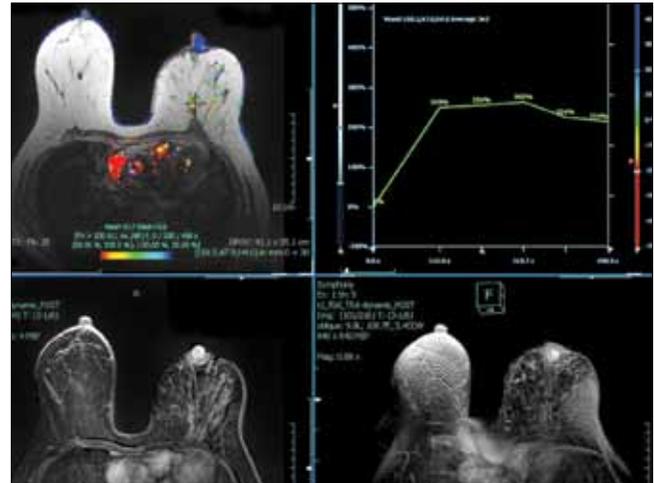or these patients, post-treatment follow up can some-times be difficult because post treatment changes can mimic and obscure recurrent disease. For these patients, MRI can differentiate between recurrence and scar tissue by using contrast enhancement of recurrent tumor tissue (Figure 16) [18].

Postoperative Reconstruction and Breast Augmentation

Breasts with silicone augmentation pose problems for mammographic examination due to the high X-ray density of the implant. The implant may obscure an estimated 22-83% of the breast tissue from mammographic examination [19]. The detection of breast cancer using mammography can be challenging in patients with silicone or other implants as free silicone injections, and contrast-enhanced breast MR imaging may be used as a supplement to routine conventional imaging for those patients. MRI can visualize lesions behind the implant, and it is advocated as the study of choice for the evaluation of breast cancer in patients with implants. In patients who have undergone complete or partial breast reconstruction with autologous myocutaneous flaps or implants, MR imaging may be helpful for detecting tumor recurrence when the findings of conventional imaging are inconclusive [12].

Suspected Invasion Deep in the Pectoral Fascia

Both mammography and sonography have limitations in the evaluation of the chest wall. MR imaging is most useful in the preoperative evaluation of patients in whom breast

cancer is suspected to have invaded the pectoralis major, serratus anterior, or intercostal muscle. Enhancement of the muscle of the chest wall is indicative of chest wall invasion in patients with a posterior breast tumor (Figure 13) [20].

Possible Contralateral Breast Lesions

Women with a history of breast cancer are at increased risk for additional breast cancer. In patients in whom cancer has been found in one breast using mammography or US, contrast-enhanced MR imaging has been able to identify occult malignancy in the contralateral breast [21].

Previous Lumpectomy

In patients who underwent lumpectomy without preoperative MR imaging and those with close or positive surgical margins after lumpectomy, the extent of residual disease and possible multifocality or multicentricity demonstrated on MR images may help determine whether repeat excision or mastectomy is appropriate. The visualization of residual disease may be more difficult with mammography because of scar tissue related to a lumpectomy [12].

High Individual Cancer Risk

High-risk patients with BRCA1 or BRCA2 mutation or untested first-degree relatives of a known carrier (breast or ovary), chest irradiation between the age of 10-30 years for Hodgkin's lymphoma and other genetic mutations, including p53 and Cowden, have a lifetime risk of 20-25% as determined by statistical risk assessment models, such as BRCAPRO and Gail. Screening mammography or ultrasound evaluation may not have adequate sensitivity because these women have a higher risk of developing breast cancer at earlier ages with denser breast parenchyma [7]. The addition of an annual MRI of the breast to mammography demonstrated more than 90% sensitivity, which is more than twice that of mammography alone. Breast MRI has a significantly higher sensitivity than mammography, breast ultrasound, or a combination of mammography and breast ultrasound [22-24].

Suspicion of Cancer Recurrence

The rate of local recurrence at the chest wall following mastectomy ranges between 5% and 27%. Approximately 80% of local recurrences occur within the first 5 years and 25%-35% cause significant morbidity. Although it had been thought that the early diagnosis of local recurrence did not affect prognosis, it is currently known that early diagnosis is important for prognosis because only 30% of recurrences have distant metastases at the time of diagnosis [25]. Postoperative mammography is able to detect residual calcifications, although it is limited in the evaluation of residual

uncalcified DCIS or residual masses. MR imaging is able to detect bulky residual disease at the lumpectomy site and residual disease in the same quadrant [multifocal] or a different quadrant (multicentric). MR imaging can be helpful in the determination of whether the patient would best be served with directed re-excision [residual disease at the lumpectomy site or multifocal disease] or whether the patient warrants a mastectomy (multicentric disease) [26].

Conflict of interest statement: The authors declare that they have no conflict of interest to the publication of this article.

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