Purpose

The purpose of this study was to evaluate the usefulness of 2\textsuperscript{nd} -look US for suspicious lesions initially detected with breast MRI and compare the US and MRI findings of the index and synchronous contralateral cancers.
Methods and Materials

Patients

Between January 1, 2006, and December 31, 2009, 1,066 women underwent MRI examinations at our institution. Among them, 213 examinations were performed for the cancer screening in patients with breast augmentation, assessment of response to neoadjuvant chemotherapy or evaluation of breast cancer recurrence. 853 MRI examinations were performed for the preoperative staging of histologically confirmed breast cancer patients. Of 853 patients, 111 had suspicious contralateral enhancing lesions on MRI. We excluded 13 patients who had suspicious contralateral enhancing lesions on MRI, however did not receive 2nd-look US. Finally, we included 126 contralateral enhancing lesions noted in 98 patients. The patients’ ages ranged from 26 to 75 years (mean age, 45 years) at the time of examinations.

MRI Technique and image interpretation

MR images were acquired on a 1.5-T scanner (Signa, GE Healthcare) or 3-T system (Achieva; Philips Healthcare, Best, the Netherlands) with the use of a dedicated breast coil. Patients underwent imaging in the prone position with the breasts immobilized. Contrast material was injected (0.1mmol/kg gadopentetate dimeglumine [Magnevist; Schering, Berlin, Germany]) and followed by a 20mL saline flush at a rate of 2mL/s.

The imaging protocol of a 1.5-T scanner consisted of fat suppressed axial fast spin-echo T2-weighted images (TR/TE, 4,000/74; slice thickness, 3 mm) and dynamic unenhanced and contrast-enhanced axial T1-weighted images obtained using a spoiled gradient-recalled acquisition in the steady state (SPGR) (19.6/3.3; flip angle, 60°; slice thickness, 3 mm).

The imaging protocol of a 3-T scanner consisted of fat suppressed axial fast spin-echo T2-weighted images (TR/TE, 7,562/70; slice thickness, 3 mm) and dynamic unenhanced and contrast-enhanced fat saturated 3D gradient-echo T1-weighted imaging (7.6/3.9; flip angle, 10°; slice thickness, 3 mm). Sagittal and coronal reformatted images were obtained using raw data. Standard subtraction images were obtained by subtracting the precontrast images from the early peak postcontrast image on a pixel-by-pixel basis. Reverse subtraction images were obtained by subtracting the last postcontrast image from the early peak postcontrast image.

Two breast imaging radiologists (D.K.K. and T.H.K) who had 12 and 3 year-experiences performed a consensus review of the breast MRI examinations. If MRI revealed additional contralateral enhancing lesion which was not detected on previous mammography and US, we recommended 2nd-look US to look for US correlates amenable to further biopsy or localization. These abnormalities included any enhancing masses or non-mass-like...
lesions in the contralateral breasts. We excluded tiny enhancing foci smaller than 5mm. Lesions visible sonographically were biopsied using sonographic guidance, and those without a definite sonographic correlation were deemed sonographically occult and were biopsied using CT guidance [14] or followed up with mammography, US, MRI and PET-CT.

**Ultrasound Imaging Technique**

Before patients underwent MRI, mammography and US examinations had been performed in all patients by one of two radiologists (D.K.K. and T.H.K). Each patient was evaluated with real-time sonography an average of 5 days after MRI, using an Acuson Sequoia 512 system (Siemens Medical Solutions, Mountain View, CA), with an 8-13MHz linear array transducer.

After MR examinations, all 2nd-look US examinations were performed by same radiologists (D.K.K. and T.H.K) who interpreted the MR images. Sonographic findings were analyzed according to the US ACR-BIRADS lexicon classification. US was performed with special attention to the area of the detected enhancing lesion using MR images as a guide. Only lesions detected on US showing exact correlation with regard to position, approximate match in size and similarity in shape to the MR findings were recorded as sonographic correlations.

**Statistical Analysis**

SPSS version 15.0 (SPSS Inc, Chicago, IL) software packages was used for the statistical analyses. The Pearson #2 statistic was used for the statistical comparison of the MRI findings between sonographically correlated and noncorrelated groups with the significance level set at 0.05. The Fisher's exact test was used for the comparison of the MRI and US findings between detected on initial US and detected on 2nd-look US groups.
Results

98 patients (12%) had 126 suspicious lesions in contralateral breast on MRI. 17 lesions (13%, 17/126) of 13 patients (1.5%, 13/853) were confirmed contralateral breast malignancy. All lesions were detected as enhancing lesions on dynamic contrast MR study. The MRI enhancement types were mass in 100 of 126 (79%) and non-mass-like enhancement in 26 (21%). The mean size was 9.4 ± 2.7mm in mass lesions and 32.6 ±7.4mm in non-mass-like lesions.

81 lesions (64%) were correlated on US and 45 lesions (36%) were not. Of correlated 81 lesions, 16 (20%) were pathologically proven malignant lesions and 65 (80%) were benign lesions (39 with pathologic confirmation and 26 clinically benign lesions based on imaging follow-up). Of 16 cancers with US correlation, 10 lesions were confirmed as invasive ductal carcinoma and six as ductal carcinoma in situ. Forty-five lesions (36% [45/126]) were not correlated on both initial and 2nd-look US, including 1 (2%) malignant lesion and 44 (98%) benign lesions (2 with pathologic confirmation and 42 lesions judged benign on the basis of imaging follow-up). This noncorrelated malignant lesion was presented as regional distributed heterogeneous nonmasslike lesion on MRI and confirmed as ductal carcinoma in situ. Most malignant lesions (16/17, 94%) had sonographic correlation and only one lesion didn't have. Malignant lesions had more frequently sonographic correlation than benign lesions (94% and 60%, respectively) and it was statistically significant (p=0.006).

A significant difference was seen in the sonographic correlation of lesions on the basis of MRI morphology type. Sonographic correlation was most frequent for masses (69% [68/100]) compared with nonmasslike enhancement (46% [12/26]) (p=0.03). On the basis of lesion size, lesions < 10mm were more frequently correlated on US (72% [46/64]) than lesions # 10mm (56% [35/62]), however there was no statistical significance (p=0.071).

Of 81 correlated lesions, 51 lesions were found on initial US and 30 lesions on 2nd-look US. DCIS was more frequently seen in contralateral cancers than index cancers (41% for contralateral cancers and 8% for the index cancers). Axillary lymph node metastasis was more frequently found in the index cancer (69% for the index cancers and 15% for contralateral cancers).

There were no significant differences in the shape (p=1.0), margin (p=0.199), internal enhancement pattern (p=0.143) and initial enhancement pattern of kinetic curve (p=0.783) between two groups. Delayed enhancement pattern was significantly different (p=0.042) and the index cancer showed washout pattern and the contralateral lesion showed persistent pattern, more frequently.

The index and contralateral cancers showed statistically significant differences in the sonographic boundary (p=0.003) and posterior echogenicity (p=0.013), but no
significant differences in other sonographic findings, including shape (p=0.41), margin (p=0.488), orientation (p=0.143), echo pattern (p=0.174), and calcifications (p=0.466).

The contralateral cancers detected on initial US or 2\textsuperscript{nd}-look US showed statistically significant differences in the echo pattern (p=0.001). However, they show no significant differences in shape (p=1.0), margin (p=0.083), orientation (p=1.0), boundary (p=1.0), calcifications (p=1.0) and posterior echogenicity (p=0.245). Example images are demonstrated in figures 1-5.
• (c) and (d) Kinetic curve showed initial rapid and delayed persistent pattern suggesting benign pattern. However, sonographic findings suggested relatively high suspicion for malignancy. Subsequent US-guided core needle biopsy was performed, and pathology result was ductal carcinoma in situ.
**Fig. 2**-62-year-old woman with known left breast cancer.

(a) Axial subtraction MR image showed oval smooth enhancing nodule at 4-o'clock position in right breast, which was not detected on initial US.
(b) and (c) Kinetic curve image of additional enhancing nodule in right breast showed initial rapid and delayed persistent pattern.
(d) 2nd-look US correlated lesion at 4-o’clock position in right breast. Lesion was oval, circumscribed, and isoechoic; was parallel to skin; and had increased internal blood flow (not shown). Subsequent US-guided core needle biopsy was performed and pathology result was DCIS.

Fig. 0

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Fig. 3-63-year-old woman with newly diagnosed left breast cancer.
(a) Whole-breast US showed another irregular indistinct hypoecholic nodule at 7-o’clock position in right breast.
(b) Axial subtraction image showed irregular enhancing nodule at 7-o’clock position in right breast and additional oval smooth enhancing nodule at 6-o’clock position which was not detected on initial US.
(c) and (d) Kinetic curve images of both lesions at 7-o’clock and 6-o’clock position showed early rapid and delayed persistent.
(e) 2\textsuperscript{nd}-look US was performed and oval circumscribed isoechoic nodule was observed. Subsequent US-guided core needle biopsy was performed and pathology results were invasive ductal carcinomas in both lesions.
Fig. 4-38-year-old woman with newly diagnosed right breast cancer.

(a) Whole-breast US showed another irregular hypoechoic nodule at 12-o’clock position in left breast.

(b) Preoperative axial MR image showed contralateral irregular enhancing lesion at the same location in left breast (arrow). And we found additional regional distributed heterogeneous non-mass-like enhancement at 2-o’clock position which was not detected on initial US (large arrow).
(c) 2nd-look US did not correlate non-mass-like enhancement at left upper outer quadrant. Excision was performed and pathologic results of both correlated and not correlated lesions were ductal carcinoma in situ.

Fig. 0

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**Fig. 1**- 46-year-old woman with newly diagnosed right breast cancer.
(a) Whole-breast US showed another irregular indistinct hypoechoic nodule at 11-o’clock position in left breast. This nodule had echogenic boundary to surrounding tissue and was parallel to the skin.
(b) MRI was performed for preoperative staging and subtraction image showed irregular enhancing nodule at 11-o’clock position in left breast.

**Fig. 5**- 39-year-old woman with bilateral silicone bag implants and newly diagnosed right breast cancer.
(a) Whole-breast US showed an enhancing mass with irregular shape, microlobulated margin and low echogenicity in right breast.
(b) Preoperative MRI showed additional enhancing nodule at 4-o’clock position in left breast which was not detected on initial US. Kinetic curve showed initial rapid and delayed persistent pattern (not shown). 2nd-look US was performed but we couldn’t find any suspicious lesion.
(c) Follow-up MRI after 6 months showed disappearance of this irregular enhancing nodule. During follow-up period of 20 months, mammography, US and PET-CT have showed no newly developed lesion in left breast.
Conclusion

In conclusion, 2\textsuperscript{nd}-look US provides additional information for further characterization and categorization of additional enhancing lesion on MRI. With 2\textsuperscript{nd}-look US, we can search additional bilateral synchronous cancer. When enhancing lesions on MRI are not correlated on US, MRI-guided biopsy is recommended. However, because of the low malignancy rate of noncorrelated lesion on 2\textsuperscript{nd}-look US and some disadvantages of MRI-guided biopsy, short-term MRI follow-up or CT-guided biopsy can replace MRI-guided procedure.
References


26. Demartini WB, Eby PR, Peacock S, Lehman CD. Utility of targeted sonography for breast lesions that were suspicious on MRI. *AJR Am J Roentgenol* 2009;192:1128-1134


