Evaluation of unexpected enhancing lesions on preoperative MRI of breast cancer patients

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Purpose

MRI is the most accurate technique for diagnosis and delineating of breast cancer. MRI has been shown to high sensitivity (83-100%) and relatively low specificity (40-80%), additional enhancing lesions with limited specificity except index cancer are frequently detected on preoperative MRI. MRI-guided biopsy is a reasonable next step, but it is expensive and time consuming procedure and furthermore, it has not yet prevailed all over the world. Ultrasound guided biopsy, when possible, is preferable because it is less expensive and more convenient for the patients. So, second look US (SLUS) is become important more and more about unexpected enhancing lesion on MRI, especially breast cancer patients.

We evaluated the characteristics and long term follow-up results of unexpected enhancing lesions on preoperative MRI of breast cancer patients and suggested the management of these lesions without MRI-guided biopsy.
Methods and Materials

- Patients

From August 2007 through February 2010, 312 patients underwent breast MRI for a preoperative evaluation of breast cancer. Indications for an MRI examination included preoperative evaluation before planned breast conserving operation to exclude multicentricity and bilaterality and to assess axillary lymph node status.

We defined unexpected enhancing lesions as another enhancing lesion except biopsy proven cancer and not detected initial US. In these 312 patients, we excluded patients who had single cancer, multiple enhancing lesions but correlated with initial ultrasound, multiple enhancing lesions but showed typical benign nature and who didn’t have initial ultrasound at our hospital. In these 312 patients, 84 patients were recommended second look ultrasound for unexpected enhancing lesions.

In these 84 patients, 12 patients were also excluded due to be transferred to other hospital, to be scheduled for neoadjuvant chemotherapy and not to be performed second look US, although we recommended second look US.

So we performed second look US on 85 unexpected MRI detected enhancing lesions in 72 patients.

- MRI technique and interpretation

Examinations were performed by using a 1.5-T (Gyroscan Intera, Philips Healthcare) and a 3-T (Achieva 3 T X-series, Philips Healthcare) MRI unit.

1. 1.5-T

- Dedicated four-element sensitivity encoding-compatible breast surface coils
- Dynamic contrast-enhancing bilateral axial breast imaging for high spartial and temporal resolution with active fat suppression
- Bilateral SPAIR images (TR/TE, 4317.80/90) and T1-weighted turbo field echo 3D gradient-echo sequence with active fat suppression after infection of contrast material
- The imaging parameters : TR/TE, 5.4/2.1; flip angle, 10°, FOV, 32cm;matrix, 328x328; section thickness, 1.5mm interpolated to 1mm; and acquisition time, 70seconds
- Temporal resolution per dynamic acquisition : 60 seconds
• Dynamic study: 60, 120, 360 seconds after IV injection of 0.1 mmol/kg of Gadobutrol (Gadovist, Bayer Scherring Pharma) at a rate 2mL/s, followed by a 20-ml saline flush after the rate of 2ml/s

2. 3T

• Seven-phase dynamic contrast enhanced bilateral axial breast imaging studies for high spatial and temporal resolution and contrast-enhanced affected and contralateral unilateral sagittal breast imaging studies for in-plane and through-plane high spatial resolution with active fat suppression protocol
• Bilateral fat-saturated T2-weighted image(TR/TE, 7202/71)
• T1-weighted high-resolution isotropic volume examination 3D gradient-echo sequence with active fat suppression was performed before and 43 seconds after the injection of contrast material
• Imaging parameters were as follows: TR/TE, 6.2/3.1; flip angle, 12°; FOV, 34 cm; matrix, 424x 368; section thickness, 1.5 mm interpolated to 0.9 mm; and acquisition time, 82 seconds
• Temporal resolution per dynamic acquisition: 60 seconds per
• Dynamic study: before and 60, 120, and 360 seconds after the initiation of an IV injection of 0.1mmol/kg of Gadobutrol (Gadovist, Bayer Schering Pharma) at a rate of 2 mL/s, followed by a 20-mL saline flush at the rate of 2 mL/s

Two experienced radiologists for 4-20 years in breast imaging performed retrospective review to determine size, type (mass vs non-mass or foci), enhancement pattern of kinetic curve and location for relation with index cancer by quadrant of each lesion.

• **US and US-guided intervention**

We performed whole-breast sonography on all patients using 5-12-MHz transducers on an HDI-5000, or IU-22 unit (Philips Medical systems).

Second look US was performed an average of 7 days after MRI by radiologists who had interpreted the MRI images.

On Second look US, 72 (85.0%) of the 85 unexpected lesions were detected. Of the 72 detected lesions, 39 (54.2%) lesions were confirmed with US-guided core needle biopsy
and 33 (45.8%) lesions with US-guided or mammography guided hook-wire localization and excision.

- **MRI and ultrasound correlation**

Radiologists performed careful scanning with high-quality ultrasound unit.

Considering knowledge of enhancing lesions as follows:

# Knowledge of lesion location, size, type and shape

# Knowledge of relationship between the lesion and other breast landmark such as nipple, subcutaneous fat, glandular tissue and subglandular fat

# Consider positional change between ultrasound and MRI

# Using another landmark such as dominant cyst, known fibroadenoma, post surgical scars, intramammary lymph nodes and implant

# Using 3D MRI reconstruction, multiplanar view

# Knowledge of size discrepancy between ultrasound and MRI

- **Follow up protocol**

MR-guided biopsy was not available at our hospital, so in case of negative finding on second look US, we performed image follow-up with mammography, ultrasound and MRI at least more than 2 years.

The period of follow-up interval with mammography was one-year, with ultrasound was 6-month.

In case of follow-up with MRI, we checked once and then we confirmed that a lesion was no longer visible or typical benign feature, no further follow-up was performed.

- **Data analysis**

We used a software (SPSS 14.0, Illinois, US).
Fisher's exact test was used to assess relation with cancer rate and mass type, size, kinetic curve and location for relation with index cancer.

Significance was assumed at a level of $p<0.05$. 
Results

- Preoperative MRI

We performed second look US on 85 unexpected enhancing lesions which were detected on preoperative MRI.

Of the 85 lesions, 76 (89%) lesions were mass and 9 (11%) lesions were non-mass like enhancement or foci.

Of the 85 detected lesions, 24 (28%) lesions were located at contralateral breast of index cancer and 61 (72%) lesions were located at ipsilateral breast of index cancer. And 47 (77%) lesions of ipsilateral breast were located same quadrant of index cancer and 14 (23%) lesions were located other quadrant of index cancer.

Kinetic curve types are divided by 3, delayed enhancement pattern

A type (persistent) : enhancement continues to increase over time
B type (plateau) : signal intensity does not change after initial rise
C type (washout) : signal intensity decreases after peaking

<table>
<thead>
<tr>
<th>Kinetic curve type</th>
<th>Numbers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A persistent</td>
<td>22 (26%)</td>
</tr>
<tr>
<td>B plateau</td>
<td>17 (20%)</td>
</tr>
<tr>
<td>C washout</td>
<td>46 (54%)</td>
</tr>
</tbody>
</table>

Table: number of lesions according to kinetic curve type

- Second look US

On Second look US, 72 (85.0%) of the 85 unexpected enhancing lesions were detected. Of the 72 lesions that US correlate, 41 (56.9%) lesions were confirmed as malignant, 27 (37.5%) lesions as benign and 4 (5.5%) lesions as no tumor present.
• **Pathology**

41 Malignant lesions

: Invasive ductal carcinoma (n=28), ductal carcinoma in situ (n=12), microinvasive ductal carcinoma (n=1)

27 Benign lesions

: Fibroadenoma (n=5), fibroadenomatous mastopathy (n=1), intraductal papilloma (n=1), adenosis (n=1), atypical ductal hyperplasia (n=2), sclerosing adenosis (n=2), fibrocystic change (n=10), papillary neoplasm (n=1), fat necrosis (n=2), usual ductal hyperplasia (n=1)

• **Data analysis**

The cancer rate was statistically higher in lesions with early enhancement and delayed washout pattern (type C) on kinetic curve and located same quadrant of breast cancer.

There is no statistical significance of cancer rate with mass size and type.

In 13 cases of negative finding on second look US, there is no detected abnormal finding on follow-up mammography, US and MRI at least more than 2 years.

• **case 1 (fig. 1-6)**

53-year-old woman revealed metastatic lymph nodes from ductal carcinoma origin in left axilla.

• **case 2 (fig. 7-12)**

68-year-old woman with IDC in right breast

• **case 3 (fig. 13-19)**
39-year-old woman with known right IDC who underwent breast MRI for preoperative staging
Fig. 1: Initial ultrasound showed malignant looking lymph nodes in left axilla and no abnormal finding in both breasts.

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**Fig. 2:** Dynamic enhanced and subtracted T1WI axial MR image shows non-mass like enhancing lesion in left UOQ.

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Fig. 3: On second look US, radiologist detected suspicious low echoic lesion with architectural distortion in left breast (1-o’clock direction).

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**Fig. 4:** Preoperative PET-CT shows suspicious parenchymal thickening in left UOQ without FDG uptake.

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**Fig. 5:** The patient was performed left axilla dissection and radiation therapy of left breast. This image was taken at initial preoperative state.

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Fig. 6: After 6 month of operation, follow-up MRI was performed and we couldn't detect abnormal enhancing lesion in left UOQ any more, detected on initial preoperative MRI.

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Fig. 9: Preoperative MRI shows biopsy proven IDC in right UQO with early rapid enhancement and delayed washout pattern on kinetic curve (blue arrow).

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Fig. 11: We could detect another enhancing mass with similar kinetic curve in left inner central breast on preoperative MRI (yellow arrowhead).

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Fig. 10: We could detect another enhancing mass with similar kinetic curve in left inner central breast on preoperative MRI (yellow arrowhead).
**Fig. 8:** Preoperative MRI shows biopsy proven IDC in right UQO with early rapid enhancement and delayed washout pattern on kinetic curve (blue arrow).

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**Fig. 7:** Initial breast US shows single IDC in right breast, 10:30-o’clock direction.

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Fig. 12: On second look US, partially ill defined isoechoic mass that was not detected on initial US is noted in left breast, 9-o’clock direction (red arrow). The pathology result of core needle biopsy of this lesion revealed DCIS.

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Fig. 18: Second look US correlates another malignant looking masses in right breast and pathology result was IDC. Subsequently, surgical plan changed from BCS to mastectomy.

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Fig. 17: Dynamic enhanced and subtracted TI-weighted axial MR image shows another non-mass like enhancing lesion in lower portion of index cancer with persistent enhancing pattern on kinetic curve (red arrows).

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Fig. 19: Second look US correlates another malignant looking masses in right breast and pathology result was IDC. Subsequently, surgical plan changed from BCS to mastectomy.

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**Fig. 16**: Dynamic enhanced and subtracted TI-weighted axial MR image shows another non-mass like enhancing lesion in lower portion of index cancer with persistent enhancing pattern on kinetic curve (red arrows).

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**Fig. 15**: Dynamic enhanced and subtracted TI-weighted axial MR image shows biopsy proven IDC in right upper central breast with persistent enhancing pattern on kinetic curve (yellow arrowhead).

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Fig. 14: Dynamic enhanced and subtracted T1-weighted axial MR image shows biopsy proven IDC in right upper central breast with persistent enhancing pattern on kinetic curve (yellow arrowhead).

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Fig. 13: Breast US shows biopsy proven IDC in right breast, 11:30-o'clock direction (red arrow).

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Conclusion

There are several reports which have attempted to demonstrate the usefulness of second look US.

1. MR-directed ("second-Look") ultrasound examination for breast lesions detected initially on MRI: MR and sonographic findings. AJR 2010;194:370-377

2. Targeted ultrasound for MR-directed lesions in breast cancer patients. KJR 2007;8:475-483


In these reports, second look US has been shown to be useful for the identification of lesions detected on MRI.

In our study, 72 (85.0%) of the 85 unexpected enhancing lesions were detected on second look US and detectability rate is higher than other reports and because there was no cancer in negative cases which were performed follow-up for 2 years, we consider that we could detect all cancers in US-MRI-second look US series.

---> Probably it is due to perform initial ultrasound in all case (Initial US-preoperative MRI-second look US) and due to relatively smaller-sized breasts of Asian people in our study.

---> It is main difference between previous reports and our study.

The cancer rate was statistically higher in lesions with early enhancement and delayed washout pattern (type C) on kinetic curve and located same quadrant of breast cancer.

So in case of negative on second look US with type C kinetic curve or located same quadrant of index cancer, we should consider MRI-guided biopsy than follow-up.
Surgical plan was altered in 3 patients of 72 (4%) and in other patients, we performed US-guided core needle biopsy in advance or performed excision with US- or mammography-guided localization at the same time of operation.

In case of benign results from excision, preoperative MRI may lead to unnecessary surgical excision. Performing core needle biopsy in advance or second look US with elastography will help to avoid unnecessary loss of normal tissue.

- **Limitation of this study**

  1. We did not perform MRI-guided biopsy in negative case of second look US.
  2. It was not always possible to be confident of exact MRI-ultrasound correlation.
  3. In cases without pathologic confirm, we performed image follow-up just for 2 years.
  4. We performed follow-up with MRI in only small group of patients.

- **Conclusion**

  In case of unexpected enhancing lesion on preoperative MRI of breast cancer patients, second look US can be useful to find out matched lesion which was not detected initial breast US.

  We should consider possibility of the lesion with early enhancement and delayed washout pattern or located at same quadrant of breast cancer on MRI as another breast cancer (daughter nodule or multifocal cancer).

  If experienced radiologist couldn’t detect any suspicious finding on second look US (initial US-preoperative MR- second look US setting) about enhancing lesion on preoperative MRI and if enhancing lesion didn’t show early enhancement and delayed washout pattern on kinetic curve and didn’t locate same quadrant with index cancer, we might perform follow-up with image within short interval, preferentially.
References


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