The Background Parenchymal Enhancement in Preoperative Breast MRI: The Effect on Tumor Extent Evaluation

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ABSTRACT

Objective: To evaluate whether the level of background parenchymal enhancement (BPE) on MRI has an effect on the accurate assessment of tumor extent of breast cancer.

Methods: This retrospective study included the preoperative MR images from 62 patients, who had been diagnosed with breast cancer and imaged between 2005 and 2014. The BPE was classified into minimal-mild and moderate-marked groups by visual evaluation. The tumor extent was classified into three types (unifocal, multifocal and multicentric). The concordance and discordance of the tumor extent at low and high BPE were evaluated, and compared with the pathological results.

Results: Minimal-mild BPE was more common in post-menopausal or older women, while pre-menopausal or younger women had more moderate-marked BPE with statistical significance ($p = 0.01$). 84% of tumors with minimal-mild level of BPE and 73% of tumors with moderate-marked level of BPE, were accurately evaluated for the tumor extension. There was no significant difference in accuracy of tumor extent between minimal-mild and moderate-marked groups ($p = 0.35$).

Conclusion: The preoperative MRI can evaluate the tumor extent of breast cancer with high accuracy and moderate-marked background enhancement does not affect to the tumor extent assessment.

Keywords: Breast; MRI; background enhancement; breast cancer (Siriraj Med J 2017;69: 290-296)

INTRODUCTION

The magnetic resonance imaging (MRI) is considered to be the most accurate imaging tool for the preoperative evaluation of breast cancer, compared with mammography and ultrasound.[1,2] The accurate evaluation of tumor extent could help surgeons to decide appropriate surgical plans. The prior meta-analysis study with 2,610 patients demonstrated that a preoperative MR imaging increased the detection of multifoci and multicentric disease more than 16 percent.[3] In addition, the MRI could estimate the tumor size accurately and reduce the rate of re-surgery in patients who have undergone breast conservative surgery (BCT).[4,5] On the other hand, the high sensitivity of MRI may generate false-positive findings, by detecting nonspecific lesions or biologically indolent cancers in the setting of preoperative evaluation. Consequently, the patients may undergo an unnecessary mastectomy and the clinical benefits of MRI on rate of recurrence and disease-free survival are still controversial.[3,4]

Background parenchymal enhancement (BPE) is an enhancement of normal breast tissues after a Gadolinium injection, which is affected by many factors, especially the age and hormonal levels. The degree of BPE in the same woman can vary during the menstrual cycle.[6,7] BPE normally demonstrates bilateral, diffuse and symmetric appearance with persistent delayed enhancement, or sometimes as a nodular form with less than 1 cm in size. While a breast tumor will have unilateral, focal and asymmetrical appearance compared to the rest of the remaining breast tissue.

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Received 14 November 2016 Revised 21 March 2017 Accepted 22 March 2017
doi:10.14456/smj.2017.56

To our knowledge, BPE may create a false-positive lesion, by appearing as a cluster or mass-like enhancement and may result in a false-negative interpretation on MR images, by masking true lesions in the marked BPE.[8,9] DeMartini et al.,[8] found that BPE caused the radiologist confusion and misinterpretation, but the misinterpretation had no effect on the sensitivity and specificity in the diagnosis of breast cancer. This was in contrast to the study of Uematsu et al.,[9] which found the moderate and marked degree of BPE affected the detection and staging of breast cancer. In conclusion, the high degree or atypical BPE can affect the interpretation of MR images.

Therefore, we aimed to evaluate whether the level of BPE has an effect on the accurate assessment of tumor extent.

MATERIALS AND METHODS

Patient selection

This retrospective study was approved by The Institutional Review Board (Si 606/2014). This study collected the MR images from 84 patients, who had been diagnosed with breast cancer and imaged between 2005 and 2014. The medical records, operative notes and pathological reports were checked. We excluded 22 patients, who had prior treatment effecting menopausal status (prior hormonal treatment within 6 months or hysterectomy), underwent neo-adjuvant chemotherapy, and did not have surgical or pathological reports at our hospital. Sixty-two patients were included in this study. Data were collected including age, menstrual status, tumor characteristics (e.g., tumor size, histologic features, lymph nodes and hormone receptor status).

MR Imaging Technique

The breast MR imaging protocol included bilateral prone imaging using a 1.5-T (Achieva, Philips Medical Systems, Best, The Netherlands) or a 3.0T (Ingenia, Philips Medical Systems, Best, The Netherlands) with a dedicated breast surface coil. MR pulse sequences included an axial T2-weighted turbo spin-echo, an axial T2-weighted SPAIR (Spectral Attenuated Inversion Recovery), an axial T1-weighted turbo spin-echo, axial diffusion weighted images (b= 50,400,800 s/mm^2), and axial dynamic T1-weighted fat-suppressed three-dimensional fast spoiled gradient-echo sequences over a period of 1.23 minutes after injection of gadolinium at 0.1 mmol/kg. Post processing included subtraction and maximum intensity projection (MIP) images. The image parameters were as follows: TR/TE/FA, 4.24/2.12/12; FOV, 28x34 cm; matrix, 280x280; section thickness, 1 mm and acquisition time, 123 seconds (centered at 60 seconds).

Image analysis

Two radiologists with 3 and 5 years of reading MRI breasts experience, were not blinded to history of patients' breast cancers, but were blinded to menopausal status, tumor extensions, pathological and surgical results. The radiologists evaluated the level of BPE by visual assessment based on first dynamic phase and the corresponding MIP image. The BPE were classified into 4 levels based on the Breast Imaging Reporting and Data System (BIRADS) lexicon, which is as follows: minimal (less than 25% enhancement of glandular tissue), mild (25-50% enhancement of glandular tissue), moderate (50-75% enhancement of glandular tissue), and marked (more than 75% enhancement of glandular tissue). The imaging findings of BPE were recorded as location, symmetry, distribution, size, and overall pattern. A kinetic curve would evaluate in a focus with a size more than 5 mm. If a focus showed slow early and persistent delayed kinetic features (kinetic curve type 1), a diagnosis of BPE was determined. The radiologists also evaluated the tumor extent of breast cancer, classified as unifocal, multifocal and multicentric disease. In our study, the definition of tumor extension evaluated on MRI were carefully established which were as follows[2,8]: A unifocal type was when only one malignant lesion was seen. A multifocal type was when other malignant lesions were found in the same quadrant of the index cancer. A multicentric type was, when other malignant lesions were found in the different quadrant from the index tumor, or were contiguous in the same quadrant but extended at least 4 cm beyond the index tumor. The results of tumor extension from MR images were compared with pathological results. In the discordant assessment, specific assessment of underestimation or overestimation was collected.

Statistical analysis

Descriptive statistics were used for reporting MR findings of BPE in pre and post- menopausal groups, with mean and SD for age, and number and percentage for qualitative data. The accurate assessment of tumor extension from the MRI and pathological results was categorized into concordant and discordant groups and the clinicopathologic data were compared between these groups using the Chi-squared test and Fisher's exact test. Student t test was used to assess the age between the levels of BPE. p value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA).

RESULTS

Of the 62 bilateral breast MRI examinations which were evaluated, 44 patients were treated with mastectomy and 18 patients were treated with BCT, who underwent follow-up lasting more than 24 months without evidence of local recurrence. The histopathological types were invasive ductal carcinoma (IDC, n=16), IDC with DCIS (n=41), invasive lobular cancer (n=1), and DCIS (n=4). The tumor extensions were unifocal (n=38), multifocal (n=13), and multicentric (n=11). Minimal-mild BPE was more common in post-menopausal or older women, while pre-menopausal or younger women had more moderate-marked BPE with statistical significance (p = 0.01) (Table 1). The typical and atypical MR findings of BPE were reported in Table 2. The findings were mainly bilateral (97%), symmetrical (90%), diffuse (91%), and small foci less than 0.5 cm (95%) in both pre-menopausal and post-menopausal groups. No BPE lesion appeared as a large foci, measuring more than 20 mm.

TABLE 1. Level of background parenchymal enhancement according to age and menstrual status.

	Minimal	Mild	Moderate	Marked	p^1	p^2
Age					0.011	0.015
<50	3 (14.3)	3 (14.3)	8 (38.1)	7 (33.3)		
>50	13 (31.7)	13 (31.7)	13 (31.7)	2 (4.9)		
Menopause status					0.117	0.050
Premenopausal	4 (21.1)	2 (10.5)	8 (42.1)	5 (26.3)		
Postmenopausal	12 (27.9)	14 (32.6)	13 (30.2)	4 (9.3)		
Total	16	16	21	9		

Note: Values are numbers of patients with percentages in parentheses
p^1 of significant difference between minimal, mild, moderate and marked background parenchymal enhancement, by Chi-square
p^2 of significant difference between minimal-mild and moderate-marked background parenchymal enhancement, by Chi-square

TABLE 2. Frequency of background parenchymal enhancement patterns between pre-and post-menopausal women.

	Premenopausal (n=19)	Postmenopausal (n=43)	All patients (n=62)
Age	43.79 +/- 5.473	58.72 +/- 6.223	54.14 +/- 9.072
Level of BPE			
Minimal-mild	6 (31.6)	26 (60.5)	32 (51.6)
Moderate-marked	13 (68.4)	17 (39.5)	30 (48.4)
Location			
Bilateral	19 (100)	41 (95.3)	60 (96.8)
Unilateral	0 (0)	2 (4.6)	2 (3.2)
Symmetry			
Symmetry	19 (100)	37 (86)	56 (90.3)
Asymmetry	0 (0)	6 (14)	6 (9.7)
Distribution			
Diffuse	18 (94.7)	39 (90.7)	57 (91.9)
Regional	1 (5.3)	3 (7)	4 (6.5)
Focal	0 (0)	1 (2.3)	1 (1.6)
Foci			
<5 mm	17 (89.5)	42 (97.7)	59 (95.2)
5-20 mm	2 (10.5)	1 (2.3)	3 (4.8)

Note: Values are numbers of patients with percentages in parentheses
Abbreviation: BPE: background parenchymal enhancement

The tumor extension was accurately evaluated in twenty-seven of the 32 tumors (84%) with minimal-mild BPE and 22 of 30 tumors with moderate-marked BPE (73%). There was no significant difference in accuracy between these two groups (Table 3, $p = 0.35$). The underestimation was found in 1 case (3%) of minimal-mild BPE and 3 cases (10%) in moderate-marked BPE. The overestimation was found in 4 cases (12%) of minimal-mild BPE and 5 cases (16%) of moderate-marked BPE. There was no significant difference of accuracy, underestimation and overestimation between levels of BPE (Table 4, $p = 0.45$).

TABLE 3. Accuracy of tumor extent evaluation using MRI in correlation with tumor- and patient- related parameters.

	Total (n=62)	Concordance (n=49)	Discordance (n=13)	*P*
Age				0.514
<50	21	18 (85.7)	3 (14.3)	
>50	41	31 (75.6)	10 (24.4)	
Menopause status				0.310
Premenopausal	19	17 (89.5)	2 (10.5)	
Postmenopausal	43	32 (74.4)	11 (25.6)	
Morphologic type				0.176
Mass	51	42 (82.4)	9 (17.6)	
Non-mass	11	7 (63.6)	4 (36.4)	
BPE				0.357
Minimal-mild	32	27 (84.4)	5 (15.6)	
Moderate-marked	30	22 (73.3)	8 (26.7)	
DCIS				0.319
No	17	12 (70.6)	5 (29.4)	
Yes	45	37 (82.2)	8 (17.8)	
ER				0.312
Negative	18	16 (88.9)	2 (11.1)	
Positive	44	33 (75)	11 (25)	
PR				0.485
Negative	17	15 (88.2)	2 (11.8)	
Positive	45	34 (75.6)	11 (24.4)	
HER2				0.717
Negative	49	38(77.6)	11(22.4)	
Positive	13	11(84.6)	2(15.4)	

Note: Values are numbers of patients with percentages in parentheses.
Abbreviations: BPE: background parenchymal enhancement; DCIS: ductal carcinoma in situ, ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor.

TABLE 4. Accuracy, underestimation and overestimation of tumor extent evaluation using MRI.

Total	Concordance	Underestimation	Overestimation	p^1	p^2
Level BPE				0.357	0.459
Minimal-mild	27 (84.4)	1(3.1)	4 (12.5)		
Moderate-marked	22 (73.3)	3 (10)	5 (16.7)		

p^1 of significant difference between concordance and discordance, by Chi-square
p^2 of significant difference between concordance, underestimation and overestimation, by Chi-square

All the four false negative cases were interpreted as unifocal type in MR images but presented as multifocal type from pathology, being small foci of intermediate grade DCIS. There were four false positive cases in minimal-mild BPE group. Two of these were unifocal cases interpreted as multifocal types, being an IDC with DCIS and a triple-negative breast cancer. One of them was multifocal type interpreted as multicentric disease, showing extensive segmental non-mass like enhancement (NME), but pathology found to be fibrocystic change with sclerosing adenosis. The last case showed two irregular shaped masses in different quadrants of breast with kinetic curve type 3. However, the patient underwent BCT and whole breast radiation without recurrence after 2 years of follow-up periods. In moderate-marked BPE, all five unifocal cases were overestimated as multifocal types. Two of five cases were fibrocystic change and the remaining three cases revealed small mass like enhancement.

The accuracy of tumor extent evaluation at MRI was not significantly impacted by the age of patients, menopausal status, histologic features, lymph nodes and hormone receptor status.

DISCUSSION

MRI is a superior modality for an accurate estimation of tumor size, disease extension, and additional or contralateral cancers, compared with mammography and ultrasound.[2,3,5,10-11] Preoperative MRI would help surgeons to achieve clear tumor margins especially in cases of BCT, which may reduce the chance of local recurrence. As reported by Bae et al,[12] who found benefits to use preoperative MRI in the triple negative breast cancer patients with dense breast or family history of breast cancer. Sung et al, also found a reduction of re-excision rate in the patients undergoing BCT, although there was no benefit on rates of local recurrence or disease free survival.[4] However, the presence of local recurrence or improved disease free survival, does not solely depend on preoperative MRI or adequate surgery, but also depends on tumor aggressiveness, types of adjuvant therapy e.g. chemotherapeutic regimens, etcetera. The previous studies, which evaluated the use of preoperative MRI, commented on a moderate-marked degree of BPE as a cause of inaccurate estimation.[5,10] Because high BPE could either mimic or obscure true lesions, thus, an underdiagnosis or overdiagnosis of MRI may occur.

However, our study showed that the levels of BPE did not affect to the accuracy of tumor extent evaluation (p= 0.357). Moreover, we also demonstrated the high accuracy of the MRI in both minimal-mild and moderate-marked BPE groups (72-84%) (Table 4). These results agreed with the prior studies showing the accuracy as high as 78-85%.1,12 Because BPE appearance is typical, this may not cause radiologists' confusion when the bilateral symmetrical diffuse enhancement is recognized, even in high degree (Fig 1). Uematsu et al,[10] found that the higher degree of BPE in late dynamic phase of MRI led to inaccurate tumor extent assessment with statistical significance. Since we used the first dynamic phase to evaluate BPE levels, we found less impact of the high BPE by demonstrating no significant difference between the low and high groups.

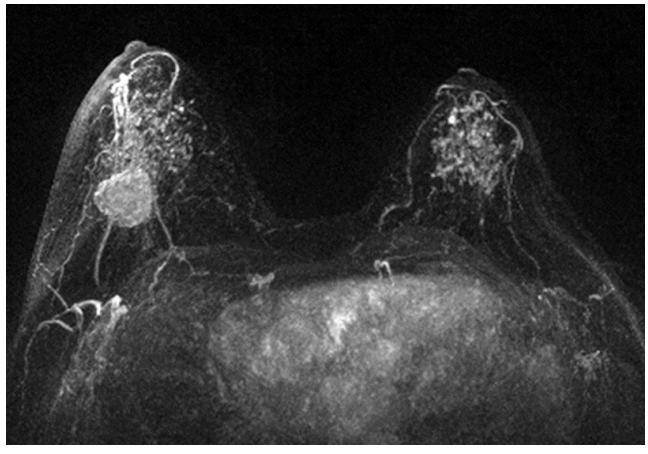


Fig 1. Axial T1-weighted fat-suppressed contrast-enhanced MIP image showed marked BPE but the unifocal extension of invasive ductal carcinoma was accurately determined.

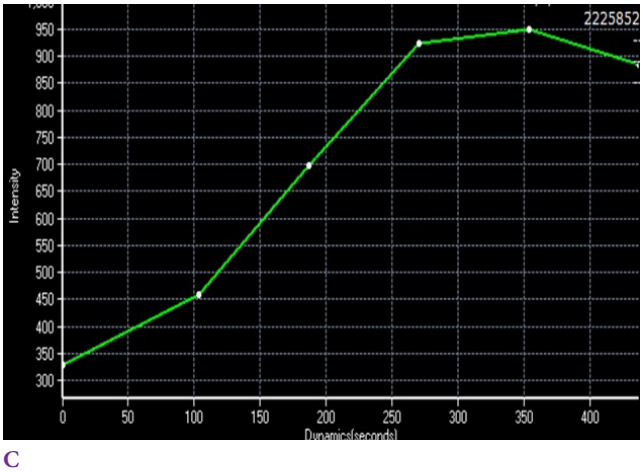
In the present study, the cases of MRI underestimation were intermediate DCIS which were similar to the previous reports.[1,8] It is possible for a small enhancing DCIS to be obscured by the high BPE or, to be misinterpreted as a BPE focus in the low background. The DCIS often appears as NME with linear or segmental pattern, but variable kinetic curves.[13] When DCIS demonstrated diffuse pattern, it was difficult to differentiate from BPE. Uematsu et al,[10] suggested using a late dynamic phase for better evaluation of DCIS, since this usually appears as slow and persistent enhancement. However, this underestimation may not affect to the patient's survival. The study of Boyages et al,[14] supported that multifocal and multicentric cancers would have a worse 10-year breast cancer specific survival when tumors were larger than 2 cms.

In terms of overestimation, some of our cases were fibrocystic change mimicking malignant lesions, which appeared diffuse segmental NME. To be aware of misinterpretation, evaluation of the high signal intensity on T2-weighted images would be helpful to represent benign conditions. Alternatively, MR-guided biopsy is recommended when an indeterminate lesion exists.

There was another unifocal case that overestimated as multicentric type, showing two masses situated in the upper outer and inferior quadrants of breast, with suspicious morphology and kinetic curves for malignancy.

A

B



C

Fig 2. A case of unifocal type that overestimated as multicentric type in mild BPE. A, Axial contrast-enhanced T1-weighted MR image showed a spiculated mass in the upper outer of left breast. The breast conservative surgery revealed invasive ductal carcinoma with ductal carcinoma in situ (DCIS). B and C, There was another irregular mass in inferior quadrant with kinetic curve type III. But this lesion was not proved at pathology. The patient underwent whole breast radiation and no recurrence within 2 years was occurred.

The mass at inferior region was mammographically occult. The patient underwent BCT at upper outer region, whole breast radiation, and had no recurrence within 2 years. Then, the final diagnosis was a unifocal disease (Fig 2). A previous meta-analysis study reported that MRI could detect the additional cancers in 16% of patients[3] and caused more patients to be over-treated with mastectomy. To our knowledge, it is not necessary to remove all the additional cancers detected by MRI as being likely to be biologically indolent cancers which can be sufficiently treated with radiation therapy.

The factors that correlated with levels of BPE in our study, were menopausal status and age (Table 1). These results were similar to other published studies.[6,8,15] In postmenopausal women, the degree of BPE is usually less than that seen in premenopausal women. Presence of high BPE may represent active breast tissues correlated with high hormonal levels in the body.

There were several limitations in this study. First, this was a retrospective study and contained small sample size. Second, we did not strictly perform MRI during 1st and 2nd weeks of menstrual cycle of premenopausal women, a recommended timing with a minimum effect by endogenous hormone. However, the BPE in our study was not confounded by other factors of exogenous hormones, since the patients with those factors had been excluded. Third, one-third of our patients underwent BCT in which the whole breast tissues were not evaluated on pathology, so there was the possibility to be underdiagnosed of multifocal or multicentric type. However, we followed those patients for more than 2 years and no recurrence was detected.

CONCLUSION

The preoperative MRI can evaluate the tumor extent of breast cancer with high accuracy and moderate-marked background enhancement does not affect to the tumor extent assessment.

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