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Prediction of background parenchymal enhancement on breast MRI using mammography, ultrasonography, and diffusion-weighted imaging

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ABSTRACT

This retrospective study assessed the effects of menopausal status and menstrual cycle on background parenchymal enhancement (BPE) of breast magnetic resonance imaging (MRI), and investigated whether the degree of BPE can be predicted by findings of mammography, ultrasonography (US), and diffusion-weighted MR imaging (DWI). There were 160 study patients (80 premenopausal, 80 postmenopausal). Degree of BPE was classified into minimal, mild, moderate, or marked. Mammographic density was classified into fatty, scattered, heterogeneously dense, and extremely dense. BP echotexture on US and BP intensity on DWI were visually classified as homogeneous or heterogeneous. Apparent diffusion coefficient (ADC) values of normal breast tissue were measured. Associations of the degree of BPE with menopausal status, menstrual cycle, or imaging features were evaluated by univariate and multivariate analyses. No significant correlation was found between mammographic density and BPE (p=0.085), whereas menopausal status (p=0.000), BP echotexture (p=0.000), and BP intensity on DWI (p= 0.000), and ADC values (p=0.000) showed significant correlations with BPE. Multivariate analysis showed that postmenopausal status was an independent predictor of minimal BPE (p=0.002, OR=3.743). In premenopausal women, there was no significant correlation between menstrual cycle and BPE, whereas BP echotexture was an independent predictor of whether BPE was less than mild or greater than moderate (p=0.001, OR=26.575). BPE on breast MRI is associated with menopausal status and the findings of US and DWI. Because premenopausal women with heterogeneous BP echotexture may be predicted to show moderate or marked BPE, scheduling of breast MRI should preferentially be adjusted to the menstrual cycle.

Key Words: background parenchymal enhancement, menopausal status, mammography, ultrasonography(US), diffusion-weighted imaging(DWI)

INTRODUCTION

Background parenchymal enhancement (BPE) on breast magnetic resonance imaging (MRI) is normal enhancement of the patient's fibroglandular tissue after contrast material administration. Increased BPE can mask malignant lesions and decrease the sensitivity of MRI.[1)] On the other

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hand, when BPE manifests with a focal, asymmetric, or regional distribution, it may be hard to distinguish from non mass enhancement and may lead to a false-positive imaging interpretation.[2)] Several studies have reported the impact of BPE on MRI diagnostic performance for high-risk screening and staging of breast cancer.[3-6)]

It is well known that BPE is dependent on the hormonal milieu and varies according to menopausal status and the menstrual cycle.[7-12)] To minimize the effect of BPE, it has been recommended that breast MRI in premenopausal women be performed during the 2nd week of the patient's menstrual cycle.[11)] However, previous studies did not show good agreement, and some controversy remains.[13-15)] In our practice, the effects of BPE often cannot be removed even by adjusting the date of MRI to the appropriate phase of the menstrual cycle. Conversely, even in the inappropriate phase, we have found that BPE is sometimes absent or minimal and does not affect breast cancer diagnosis. This may be due to greater variability in the individual level of BPE. It is actually difficult to schedule MRI considering the menstrual cycle of each patient. If patients who have a strong level of BPE can be predicted and selected in advance, it might be reasonable to schedule contrast-enhanced breast MRI for these patients with appropriate adjustment of the menstrual cycle.

The purpose of this study was to assess the effects of menopausal status and menstrual cycle on BPE of breast MRI and to investigate whether the degree of BPE can be predicted using mammography, ultrasonography (US), and diffusion-weighted MR imaging (DWI).

MATERIALS AND METHODS

Study Patients

For this research, the institutional review board approved the retrospective data collection and analysis, with informed consent from patients being waived. Using our breast imaging report database, study patients who underwent mammography, US, and MRI of bilateral breasts from January 2009 to June 2010 at our hospital were identified and recruited. During this period, 359 consecutive women underwent mammography, US, and MRI of bilateral breasts. Women who did not undergo mammography and ultrasonography within the previous 6 months of MRI (n=71), who had received chemotherapy or hormonal therapy (n=61), or who had bilateral breast cancers (n=23) were excluded. An additional 44 women whose apparent diffusion coefficient (ADC) values of the background could not be measured because of various artifacts on DWI-MRI, such as susceptibility, or extremely fatty breast with poor glandular tissue were also excluded. The remaining 160 patients (age range, 16–78 years; mean age, 51 years) were enrolled in this study. Eighty patients were premenopausal (age range, 16–53 years; mean age, 42 years), and 80 patients were postmenopausal or had surgical menopause (age range, 43–78 years; mean age, 60 years). The clinical indications for breast MRI included evaluation of newly diagnosed cancer (diagnosis for extent of disease) (73% [117 of 160]) and problem-solving (26% [43 of 160]) after mammography or ultrasound.

Mammography

Mammography (MMG) was performed using a full-field digital mammography unit equipped with 24 cm × 29 cm amorphous selenium detectors of 70-μm pixel size (Lorad Selenia, Hologic, Danbury, CT). Two standard views, medio-lateral oblique and cranio-caudal, were acquired for each breast. All mammograms were evaluated on a set of two monochrome 5-megapixel liquid crystal displays (MFGD5621HD, 2,048×2,560 pixels, 21.3 inch; BARCO, Torhout, Belgium) with image viewer software (Mammoread; TOYO Corporation, Tokyo, Japan).

Ultrasound

Whole breast US examinations for all 160 patients were performed independently by four radiologists (HS, SI, RK, and KS) who specialized in breast imaging. All radiologists were required to obtain representative images of the normal breast and capture several static images for each quadrant area of the breast. All US examinations were performed using a digital electronic ultrasound scanner (EUB-8500; Hitachi Medical, Tokyo, JAPAN) equipped with a 6 to14-MHz linear array probe (EUP-L65, Hitachi Medical).

MRI

Patients were examined in the prone position using a 3-T MRI scanner (MAGNETOM Trio; Siemens Medical Solutions, Erlangen, Germany) with a dedicated 4-channel phased-array bilateral breast coil. Before administration of contrast media, axial bilateral images of fat-suppressed T2-weighted fast spin echo series and DWI were acquired. DWI was performed using spin-echo single-shot echo-planar imaging (EPI) with the following parameters: repetition time (TR)/echo time (TE) 7800/71 msec, field of view (FOV) 385 mm × 289 mm, matrix 128 × 128, thickness 3.0 mm, gap 0.6 mm, acquisitions 2, and acquisition time 136 seconds. Spectral attenuated with inversion recovery (SPAIR) was used for fat suppression. An acceleration factor of two was applied using the generalized autocalibrating partially parallel acquisition (GRAPPA) of parallel imaging technique. Motion-probing gradients (MPGs) in three orthogonal orientations were applied with b values of 50, 800, and 1500 s/mm^2. Isotropic diffusion-weighted (trace) images were reconstructed for each b-factor. For quantitative analysis of the data acquired from DWI, ADC maps were automatically created using software provided by the MRI system manufacturer (Syngo, Siemens Healthcare) using three b values (50, 800, and 1500 s/mm^2).

Finally, dynamic axial bilateral breast images of fat-suppressed high-resolution T1-weighted three-dimensional fast gradient echo images (VIEWS) were sequentially acquired before and 75, 185, and 295 seconds after the administration of contrast medium. For the dynamic study, gadopentetate dimeglumine (Magnevist; Bayer Schering, Osaka, Japan) was administered intravenously using a power injector at a dose of 0.1 mmol/kg per body weight at a flow rate of 2 mL/s, followed by flushing of 20-mL saline. The parameters of the VIEWS sequence were as follows: TR/TE 4.2/1.8 msec, flip angle 15°, FOV 340 mm × 340 mm, matrix 512 × 410, thickness 0.9 mm, acquisitions 1, and acquisition time 110 sec. SPAIR for fat suppression and a GRAPPA acceleration factor of two for parallel imaging technique were also applied. With this parameter setting, the spatial voxel size was 0.7 mm × 0.8 mm × 0.9 mm. After image acquisition, the unenhanced images were subtracted from the contrast-enhanced images on a pixel-by-pixel basis.

Image interpretation

The background parenchyma of dynamic contrast-enhanced (DCE)-MRI, DWI-MRI, mammography, and ultrasound of the contralateral breast to the lesions were reviewed retrospectively by consensus of the two radiologists (SI, HS, with 10 years and 16 years of experience in breast imaging, respectively.). Evaluation of each image was individually scheduled with intervals of more than one week apart without knowledge of age and menstrual status.

Initially, the BPE of DCE-MRI was reviewed. The BPE of the entire breast parenchyma was assessed visually using a combination of post-contrast fat-suppressed T1-weighted and subtraction images of the first phase (75 sec after contrast injection). The BPE was graded based on proposed Breast Imaging Reporting and Data System (BI-RADS) criteria as follows: minimal enhancement (≤ 25% enhancement of glandular tissue); mild enhancement (26–50% enhancement of glandular tissue); moderate enhancement (51–75% enhancement of glandular tissue); and marked enhancement (>75% enhancement of glandular tissue) (Fig.1).[1,16,17]

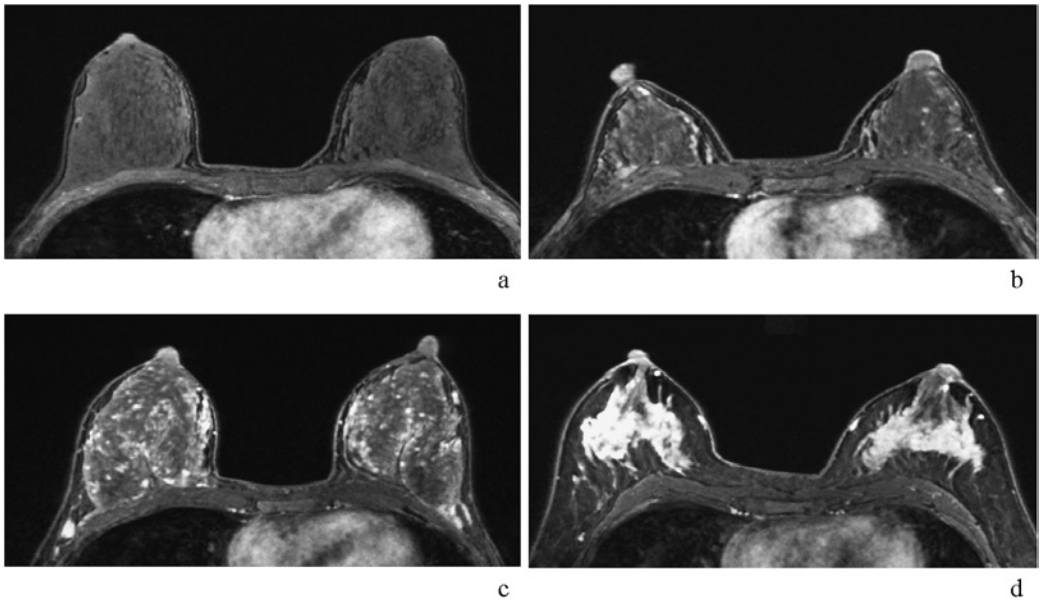

Fig. 1
Axial T1-weighted fat-suppressed contrast-enhanced MR images showing different degrees of BPE: (a) minimal (≤ 25% enhancement of glandular tissue); (b) mild (26–50% enhancement of glandular tissue); (c) moderate (51–75% enhancement of glandular tissue); and (d) marked (>75% enhancement of glandular tissue).

For DWI-MRI, background parenchymal intensity (BP intensity) of normal breast tissue was visually classified as homogeneous or heterogeneous (Fig.2). Homogeneous BP intensity was defined as normal breast tissue with a visually homogeneous decrease of signal intensity according to the increase of b values. Heterogeneous BP intensity was defined as normal breast tissue with a visually heterogeneous decrease of signal intensity according to the increase of b values. For quantitative assessment of DWI, ADC values were measured by placing regions of interest (ROIs) on the axial images of the ADC maps at the level of the nipple. Three ROIs were drawn as large as possible in the breast gland to avoid the fat. One ROI was placed in the anterior (near the nipple) of the breast, and the other two ROIs were placed in lateral and medial posterior regions, as shown in Fig.3. If there was not sufficient breast tissue visible in a region of the breast, that case was omitted from the analysis. The average ADC values of the three regions were calculated.

MMG breast composition was classified visually according to the BI-RADS scale: entirely fat, scattered fibroglandular densities, heterogeneously dense, and extremely dense.[17)]

For ultrasound, background parenchymal echotexture (BP echotexture) of the normal breast was classified as homogeneous BP echotexture and heterogeneous BP echotexture according to the BI-RADS US lexicon.[17)] Homogeneous BP echotexture was considered a uniformly echogenic layer of glandular tissue. Even if tiny or linear echo-poor areas were mixed in the gland, when these echo-poor areas were scattered regularly throughout the gland,[18)] they were judged as homogeneous BP echotexture. Heterogeneous BPE was characterized as a gland with multiple small island-like echo-poor areas including posterior shadowing, which were mixed locally and diffusely (Fig.4).

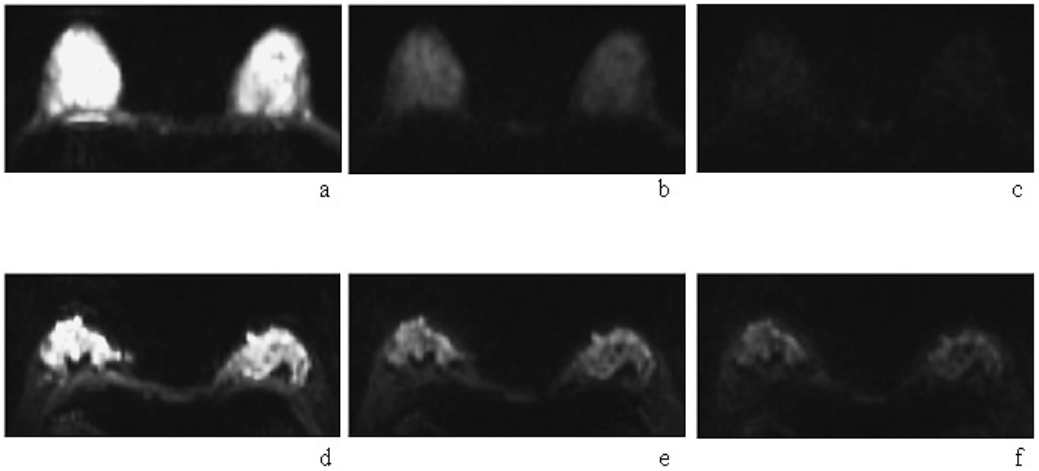

Fig. 2
Classification of BP intensity on DWI. Based on the increase of b values (50, 800, and 1500 s/mm^2), normal breast tissue with a visually homogeneous decrease of signal intensity was defined as homogeneous BP intensity ((a) b value of 50s/mm^2 ; (b) b value of 800s/mm^2 ; (c) b value of 1500s/mm^2), and normal breast tissue with a visually heterogeneous decrease of signal intensity was defined as homogeneous BP intensity ((d) b value of 50s/mm^2 ; (e) b value of 800s/mm^2 ; (f) b value of 1500s/mm^2).

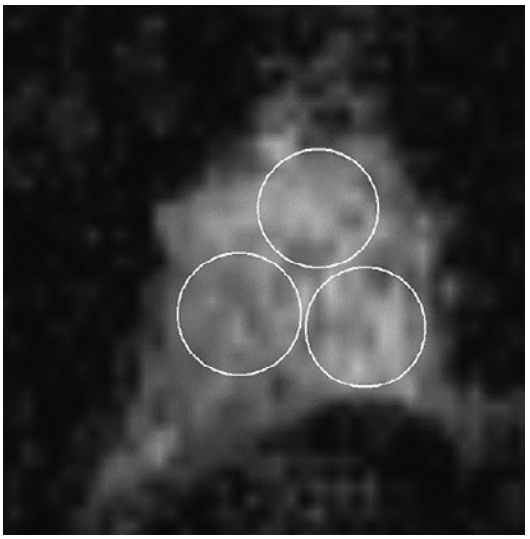

Fig. 3
Measurement of ADC values of the breast tissue. In the axial slice of ADC maps at the level of the nipple, one ROI is placed in the anterior (near the nipple) of the breast, and the other two ROIs are placed in the lateral and medial posterior regions.

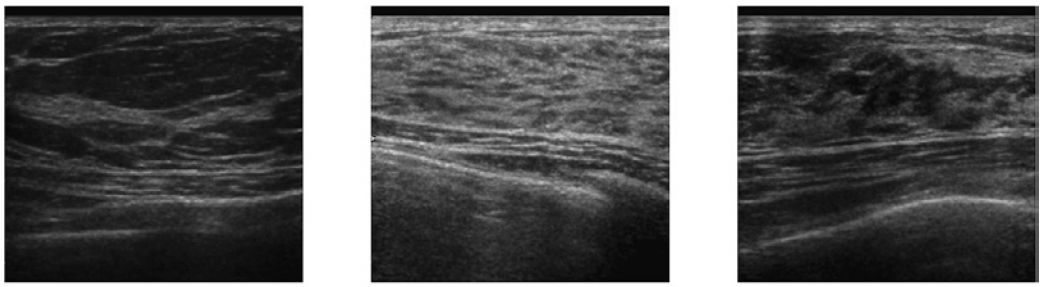

Fig. 4
Classification of BP echotexture on US. Homogeneous BP echotexture is considered a uniformly echogenic layer of glandular tissue (a, b). Even if tiny echo-poor areas are mixed in the gland, when these echo-poor areas are scattered regularly throughout the gland, it is judged to be homogeneous BP echotexture (b). Heterogeneous BPE is characterized as a gland with multiple small island-like echo-poor areas, including posterior shadowing (c).

Menopausal status and menstrual cycle

A questionnaire survey of patients was conducted on the first day in hospital. Patients were asked whether they were premenopausal or postmenopausal; whether they had regular or irregular menstrual cycles if they were premenopausal; and the first day of the last menstrual period (LMP). These records of the patients were reviewed, and the date from the LMP at the time of the breast MRI examination was estimated for the premenopausal women with regular cycles. The premenopausal women with regular cycles were further subdivided into the following categories: women who were considered to be in the appropriate phase of the cycle if the MR examination was performed during the 2nd week after the LMP, and women who were considered to be in the inappropriate phase of the cycle if the MR examination was performed during the 1st, 3rd, or 4th week after the LMP. The premenopausal women with irregular menstrual cycles and without menstrual cycle information were excluded from the analysis of BPE and menstrual cycle.

Statistical Analyses

Statistical analysis was performed with SPSS software (version 19, IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA). Chi-square analysis was used to compare BPE grade with menopausal status, menstrual cycle, mammographic density, and visual background status of US and DWI. Analysis of variance (ANOVA) was used to analyze the relationship between BPE grade and ADC values of background breast tissue.

To find the best predictor for differentiation of BPE grade, univariate and multivariate logistic regression analyses were performed with the following variables: menopausal status, mammographic density, visual background status of US and DWI, and ADC values of background breast tissue. For these analyses, BI-RADS scales of mammographic density were dichotomized to entirely fat or scattered fibroglandular densities versus heterogeneously dense or extremely dense. Four-point scales of BPE were dichotomized into the following three models: minimal vs mild-marked, minimal-mild vs moderate-marked, and minimal-moderate vs marked. $P<0.05$ was accepted as significant.

RESULTS

Of the 160 patients included in this study, 64 (40.0%) showed minimal BPE, 63 (39.4%) showed mild BPE, 14 (8.8%) showed moderate BPE, and 19 (11.9%) showed marked BPE. The distribution of menopausal status and the visual classification of mammographic density, BP echotexture, and BP intensity on DWI are given in each Fig.5. There was no significant correlation between mammographic density and BPE (p = 0.085), whereas menopausal status (p = 0.000), BP echotexture (p = 0.000), and BP intensity on DWI (p = 0.000) showed significant correlations with BPE.

The average ADC values of breast parenchyma were $1.73\times10^{-3}\pm0.17$ mm^2/sec with minimal BPE, $1.63\times10^{-3}\pm0.24$ mm^2/sec with mild BPE, $1.46\times10^{-3}\pm0.17$ mm^2/sec with moderate BPE, and $1.34\times10^{-3}\pm0.14$ mm^2/sec with marked BPE. ADC values were significantly lower according to the increase of the degree of BPE (p = 0.000).

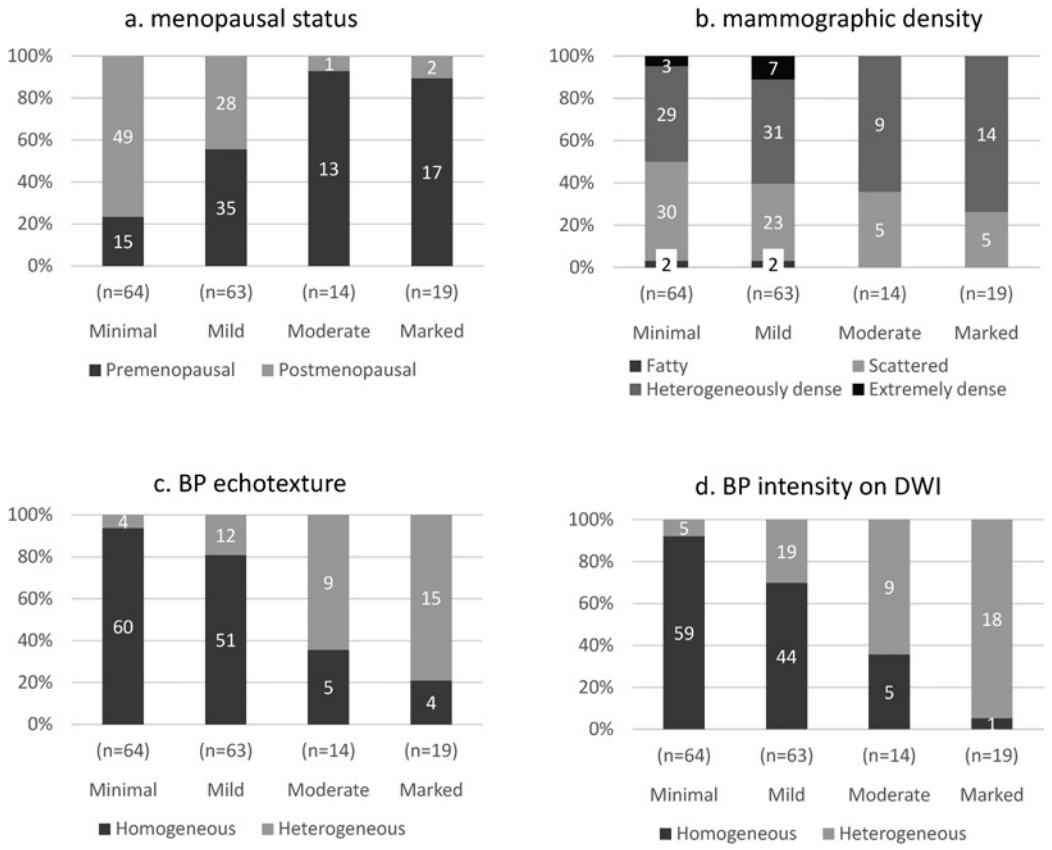

Fig. 5

Correlation of BPE with menopausal status, mammographic density, BP echotecture, and BP intensity on DWI. (a) menopausal status; (b)mammographic density; (c) BP echotecture; (d) BP intensity on DWI. There was no significant correlation between mammographic density and BPE (p = 0.085), whereas menopausal status (p = 0.000), BP echotexture (p = 0.000), and BP intensity on DWI (p = 0.000) showed significant correlations with BPE.

Number in the graph is number of the patients.

BPE: background parenchymal enhancement

Table 1 Multivariate analysis of BPE by menopausal status, BP echotexture, BP intensity on DWI, and ADC values

	BPE					
	Minimal vs mild-marked		Minimal-mild vs moderate-marked		Minimal-moderate vs marked	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Menopausal status						
Premenopausal	1		1		1	
Postmenopausal	3.743 (1.643–8.828)	0.002	4.103 (0.898–18.739)	0.069	1.417 (0.202–9.98–54)	0.726
BP echotexture						
Homogeneous	1		1		1	
Heterogeneous	3.077 (0.825–11.481)	0.094	6.713 (1.965–22.935)	0.002	5.063 (1.106–23.177)	0.037
BP intensity on DWI						
Homogeneous	1		1		1	
Heterogeneous	3.548 (1.144–11.000)	0.028	4.903 (1.400–17.171)	0.013	19.317 (2.048–182.19)	0.010
ADC values	0.997 (0.995–0.999)	0.005	0.994 (0.991–0.997)	0.001	0.993 (0.989–0.998)	0.002

Multivariate analysis was performed for the variables that showed significant differences on univariate analysis.

On univariate analysis, mammographic density was not significantly associated with any differentiation of BPE grade (minimal vs mild-marked, minimal-mild vs moderate-marked, and minimal-moderate vs marked), whereas all other variables were significantly associated. Table 1 shows the results of the multivariate analysis for BPE. For the distinction between minimal vs mild-marked BPE, menopausal status (p = 0.002), BP intensity on DWI (p = 0.028), and ADC values (p = 0.005) were significant. For the distinction between minimal-mild vs moderate-marked BPE and between minimal-moderate vs marked BPE, BP echotexture, BE intensity on DWI, and ADC values were significant, whereas menopausal status was not significant. Excluding ADC values, which are a continuous quantitative scale, postmenopausal status was the most predictive variable of minimal BPE (OR = 3.743), heterogeneous BP echotexture was the most predictive variable of moderate or marked BPE (OR = 6.713), and heterogeneous BP intensity on DWI was the most predictive variable of marked BPE (OR =19.317).

Premenopausal women

Among 80 premenopausal women, 49 appeared to have regular menstrual cycles. Of these 49 premenopausal women, 10 underwent breast MRI in the 2nd week of the menstrual cycle, whereas 39 underwent MRI without consideration of the menstrual cycle (Fig.6). Marked BPE was present in 40% (4/10), even when MRI scheduling was adjusted to the appropriate phase of the menstrual cycle. There was no significant relationship between BPE and menstrual cycle

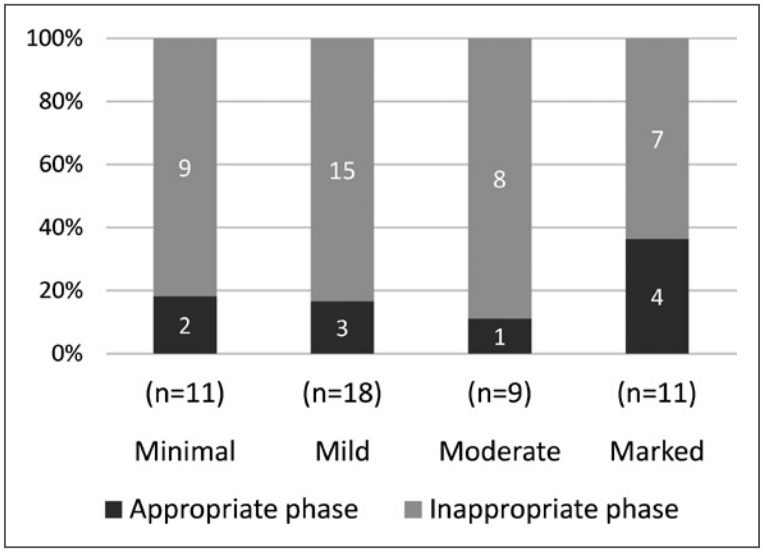

Fig. 6
Correlation between BPE and the menstrual cycle.
The appropriate phase is the 2nd week of the menstrual cycle when the MR examination was performed, while inappropriate phase is 1st, 3rd, or 4th week of the menstrual cycle when the MR examination was performed. There was no significant relationship between BPE and menstrual cycle (p = 0.214).
Number in the graph is number of the patients.
BPE: background parenchymal enhancement.

(p = 0.214).

On univariate analysis, mammographic density and menstrual cycle were not significant predictors for any differentiations of BPE: minimal vs mild-marked, minimal-mild vs moderate-marked, and minimal-moderate vs marked. Table 2 shows the results of the multivariate analysis for BPE. ADC values (p = 0.023) were the only significant variable for the distinction between minimal vs mild-marked BPE and between minimal-moderate vs marked BPE. For the distinction between minimal-mild vs moderate-marked BPE, BP echotexture (p = 0.001) and ADC values (p = 0.010) were significant. The odds ratio of moderate or marked BPE for women with heterogeneous BP echotexture versus for those with homogeneous BP echotexture was 26.575.

DISCUSSION

The results of the present study demonstrated that premenopausal women had significantly higher degrees of BPE than postmenopausal women, and this result is consistent with some previously published studies.[7-10] Furthermore, on multivariate analysis, whether women were pre- or postmenopausal was significantly predictive of distinguishing minimal BPE from BPE of a higher degree. Consequently, since postmenopausal status was significantly associated with minimal BPE, risk of interference by BPE is considered to be relatively less in the breast MR examinations of postmenopausal women.

Women showing heterogeneous BP echotexture on ultrasound had higher degrees of BPE, and this result is in agreement with a study by Ko *et al.*[19] BP echotexture of premenopausal women was an independent predictor of whether BPE was lower than mild or higher than moderate.

Table 2 Multivariate analysis of BPE of premenopausal women: BPE by mammary gland echo pattern, diffusion weighted images, and the ADC values

	BPE					
	Minimal vs mild-marked		Minimal-mild vs moderate-marked		Minimal-moderate vs marked	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
BP echotexture		–		0.001		0.097
Homogeneous	–		1		1	
Heterogeneous	–		26.575		5.670	
	–		(3.680–191.0905)		(0.730–44.063)	
BP intensity on DWI		0.350		–		0.141
Homogeneous	1		–		1	
Heterogeneous	2.513		–		7.755	
	(0.365–17.319)		–		(0.508–118.447)	
ADC values	0.995	0.023	0.994	0.001	0.992	0.023
	(0.991–0.999)		(0.991–0.997)		(0.986–0.999)	

Multivariate analysis was performed for the variables that there were significant on univariate analysis.

Since breast ultrasound is a noninvasive examination conducted frequently prior to MRI, observing whether BP echotexture is heterogeneous or homogeneous can be a useful clinical step to predict the degree of BPE prior to MRI examination. There have been few reported studies that address the histological correlation with BP echotexture. Izumori *et al.*[20] compared the echotexture of the normal breast gland with histological specimens in detail, and they reported that lobules and ducts together with the surrounding stroma of densely packed fibrous connective tissues were visualized as echo-poor structures. On the other hand, stroma that are rich in substrates, edematous, and contain loosely packed fibrous connective tissues were visualized as hyperechoic areas that fill in the space between the echo-poor structures. Furthermore, they reported that the thickness of the stroma surrounding lobules and ducts was not always uniform, and we consider that this non-uniformity may make the BP echotexture heterogeneous. Ko *et al.*[19] also emphasized the importance of the histological difference between loose and dense stroma in the breast gland, and they suggested that ducts and lobules with surrounding stroma tissues make the BP echotexture heterogeneous. Since BP echotexture showed a significant correlation with BPE in the present study, it is expected that there is some histophysiological link between BP echotexture and BPE. Ko *et al.*[19] suggested that heterogeneous BP echotexture means that there is abundant gland-associated tissue including lobules, ducts, and surrounding stroma that is conjectured to be more hypervascular, which might explain the higher grade of BPE. Considering that the degree of MRI enhancement is correlated with not only vascular perfusion but also permeability, it is suggested that the volume and proportion of stroma surrounding lobules and ducts may also be significant factors for increased BPE.

The present study showed that a higher degree of BPE was associated with a lower ADC value of the breast tissue. Multivariate analysis showed a significant correlation between BPE and ADC values of the breast parenchyma. If applying the histological association of BP echotexture on ultrasound as mentioned, the area of abundant gland-associated tissue of lobules and ducts

together with the surrounding stroma with densely packed fibrous connective tissue may correlate with the area of lower water diffusion, and the area of intervening stroma with edematous and loosely packed fibrous connective tissue may correlate with the area of higher water diffusion. Our ADC values of $1.34\times10^{-3} \pm 0.14$ mm^2/sec for marked BPE overlapped with the values of benign and malignant lesions reported in a previous study in our institution.[21] In women with marked BPE, there is a risk that signal contrast between lesions and parenchyma decreases not only on contrast-enhanced MRI, but also on DWI. Visual assessment of BP intensity on DWI showed an independent association with BPE in the overall study but not in premenopausal women. Although the small number of premenopausal women in the present study is one reason for these results, visual assessment of DWI has some problems, such as obscurity and reproducibility of the classification.

Several studies have assessed the correlation between BPE and the menstrual cycle of premenopausal women. In intra-individual comparison studies,[11] BPE was significantly less in the 2nd week of the menopausal cycle, so currently MR examinations are recommended during this week. Physiologically, this intra-individual increase of BPE can be explained by the histamine-like effect of estrogen that induces an increase in microvascular permeability and vasodilation, and by the mitogenic effect of progesterone, which may promote metabolic activity and result in an increase in perfusion.[22] In cohort comparison studies, Kajihara *et al.*[23] reported that BPE was significantly stronger in the 4th week than in the 2nd week of the menstrual cycle. In contrast, Baltzer *et al.*[13] reported that the degree of BPE was independent of menstrual cycle, which agrees with the results of the present study. Amarosa *et al.*[14] reported that BPE appeared to be affected by the menstrual cycle in patients with benign lesions, but not in patients with malignant lesions. Kang *et al.*[15] reported that the influence of the menstrual cycle on the BPE differs according to breast composition. The variance in these results may have been due to individual-related differences, such as hormone levels, hormonal tissue activity, and so on, which produce a large variability in BPE. Based on these, when scheduling MRI for a premenopausal patient, women who are predicted to have a strong baseline level of BPE should be considered individually and scheduled according to their menstrual cycle. From the results of this present study, BP echotexture can be a candidate predictor of BPE in premenopausal women for scheduling of breast MRI. On a practical level, patients with heterogeneous BP echotexture are predicted to have moderate or marked BPE; therefore, scheduling should be adjusted to the phase of the menstrual cycle. While ADC values are also useful indicators for prediction of the degree of BPE, it is not realistic to examine DWI studies in advance for scheduling contrast-enhanced MRI. There is another problem, in that ADC values of normal breast tissue can themselves vary according to the physiological changes in the menstrual cycle, although a previous study reported that differences in ADC values throughout the menstrual cycle did not reach statistical significance.[24]

There are some limitations to the present study. First, this retrospective investigation was limited by the small size of the patient population, especially in the number of premenopausal women with information about their menstrual cycle. Further studies with more patients are needed. Second, the imaging analysis of this study was qualitative. Appropriate quantitative analysis needs to be developed and applied for the accurate evaluation of BPE. Third, inter-observer variability for the assessment of BPE was not addressed. Moreover, since the data were obtained in Japanese women with relatively fibroglandular dense breasts, the study results may not be directly relevant to the Western population. Despite these limitations, this study is the first to have examined BPE by menopausal status, menstrual cycle, and multimodality imaging using multivariate analysis to identify the best predictors for differentiation of BPE grade. We believe that the results may be useful clinically for scheduling and interpreting breast MRI.

In conclusion, BPE on breast contrast-enhanced MRI can be predicted by patients' menopausal

status and background parenchymal findings of US and DWI, but not by menstrual cycle and mammographic density. Since postmenopausal status significantly correlated with minimal BPE, breast MRI examination in postmenopausal women can be anticipated to have less risk of interference by BPE. In premenopausal women, heterogeneous BP echotexture was an independent predictor of moderate or marked BPE. Premenopausal women showing heterogeneous BP echotexture need to be preferentially considered for scheduling of breast MRI according to the menstrual cycle.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interests.

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