

Analysis of background parenchymal echogenicity on breast ultrasound

Correlation with mammographic breast density and background parenchymal enhancement on magnetic resonance imaging

Kyung Hee Ko, MD*, Hae Kyoung Jung, MD, Inwha Kim, MD

Abstract

The purpose of this study was to analyze the background parenchymal echotexture (BP echo) on breast ultrasound in detail and to evaluate the relation BP echo with menopausal status. In addition, we correlated BP echo with mammographic breast density (MGD) and background parenchymal enhancement (BPE) on magnetic resonance imaging (MRI).

The institutional review board of our hospital approved this retrospective study, and the requirement of informed consent was waived. We studied 138 women (mean age 51.6 years, range from 26 to 79 years) with newly diagnosed invasive breast cancer, who had performed preoperative mammography, ultrasound, and MR from June 2013 to June 2015. BP echo was classified as homogeneous and heterogeneous according to the BI-RADS US lexicon. MGD was described into fatty, scattered, heterogeneously dense, and extremely dense. BPE was categorized as minimal, mild, moderate, and marked. The relationship between the BP echo and menopausal status was investigated. Associations between the degree of BP echo with MGD grades and BPE grades were also evaluated.

Of the 138 women, 74 (54%) were premenopausal and 64 (46%) were postmenopausal. Premenopausal women were more likely to have heterogeneous BP echo (60/74, 81%) compared with postmenopausal women (10/64, 16%) ($P=.000$). BP echo showed significant correlation with BPE in both premenopausal and postmenopausal women ($P=.000$). However, MGD showed no significant correlation with BP echo or BPE, regardless of menopausal states. In the postmenopausal group, 70% women (21/30) with dense MGD showed homogeneous BP echo and 77% women (23/30) with dense MGD showed nondense BPE.

In conclusion, we demonstrated that the BP echo was influenced by menopausal status. Our data support the concept that BP echo is influenced by breast hormonal changes. Because there was a significant association between BP echo and BPE in pre- and post-menopausal women, the BP echo might be a good predictor for BPE.

Abbreviations: ACR = American College of Radiology, BI-RADS = Breast Imaging Reporting and Data System, BP echo = background parenchymal echotexture, BPE = background parenchymal enhancement, MGD = mammographic breast density, MRI = magnetic resonance imaging.

Keywords: background parenchymal echogenicity, background parenchymal enhancement (BPE), breast MRI, breast ultrasound, mammographic density

1. Introduction

With recent significant advances of ultrasound technology, clinical indications of breast ultrasound (US) include evaluation of palpable abnormalities and characterization of masses detected at mammography and magnetic resonance (MR)

imaging. US has been performed as an adjunct breast cancer screening modality in women with dense breast tissue and a negative mammogram.^[1]

According to the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) lexicon, the background parenchymal echotexture (BP echo) in breast ultrasound is classified into the following 3 categories: homogeneous background echotexture-fat, homogeneous background echotexture-fibroglandular, and heterogeneous background echotexture.^[2] Just as increasing breast density diminishes the sensitivity of mammography in the detection of small breast masses, heterogeneous background echotexture of the breast may affect the sensitivity of breast ultrasound for lesion detection. Therefore, it would be imperative to include the assessment of BP echo in ultrasound report, as with other imaging modalities. It is described that heterogeneous background echotexture occur in younger patients and those with heterogeneously dense parenchyma depicted mammographically, but we have observed in daily practice the patients with same mammographic densities may demonstrate different BP echo.

Similar to breast density at mammography, the level of background parenchymal enhancement (BPE) in breast MR after contrast injection, is a feature of normal breast tissue.^[3] BPE is

Editor: Kavindra Nath.

The authors report no conflicts of interest.

Department of Radiology, CHA Bundang Medical Center, CHA University, School of Medicine, Gyeonggi-do, South Korea.

* Correspondence: Kyung Hee Ko, Department of Radiology, CHA Bundang Medical Center, CHA University, School of Medicine, 351 Yatapdong, Bundang-gu, Seongnam-si, Gyeonggi-do, South Korea (e-mail: yourheeya@gmail.com).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Medicine (2017) 96:33(e7850)

Received: 31 October 2016 / Received in final form: 30 May 2017 / Accepted: 31 July 2017

<http://dx.doi.org/10.1097/MD.0000000000007850>

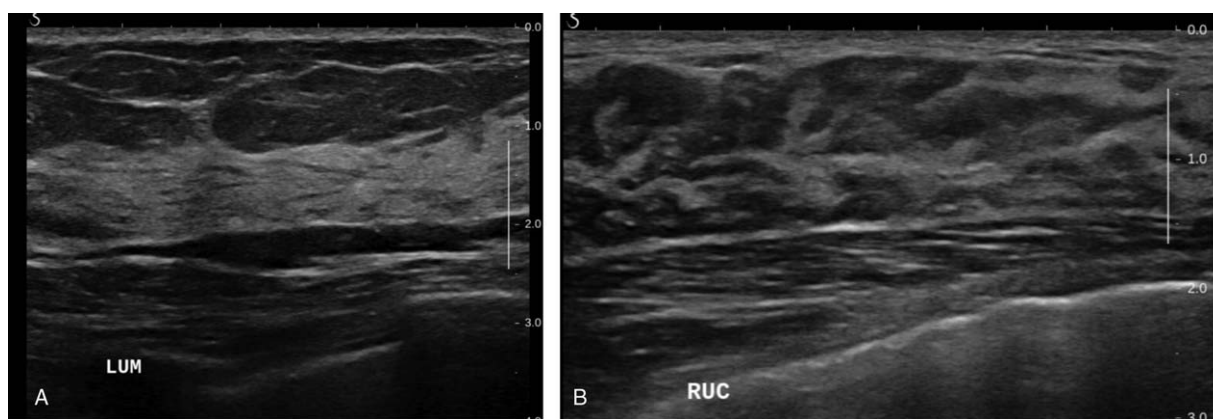


Figure 1. Examples for BP echo on breast US. (A) Homogeneous BP echo is considered a uniformly echogenic layer of glandular tissue. (B) Heterogeneous BP echo is considered if the gland had multiple island-like isoechoic areas including posterior acoustic shadowing. BP echo = background parenchymal echogenicity, US = ultrasound.

dependent on hormonal status and varies according to the menstrual cycle.^[4,5] Initial studies indicate that increased BPE could lead to higher rates of misinterpreting benign tissues as suspicious, though the precise reasons are not clear.^[6–8] Besides the negative aspect of BPE which represents noise on imaging, recent studies reported that BPE could be a strong predictor for breast cancer risk and potentially serve as an imaging biomarker of estrogen responsive malignant transformation.^[9–11] Even if BPE can occur only in the breast glandular tissue which has associated vessels, not in the fat tissue, it has been reported that the degree of BPE does not correlate with mammographic density (MGD).^[12,13]

We can assume that BP echo could be influenced by hormonal status because there is histological association between BP echo and the area with abundant gland-associated tissue.^[14] So far there have been few studies which analyzed the relation of BP echo and MGD or BPE.^[15,16] We also hypothesized that BP echo in US could also be a marker for physiologically active tissue more prone to tumorigenesis such as BPE in MR, if they had significant correlation.

Therefore, the purpose of our study was to classify the BP echo in detail and to evaluate the relation BP echo with menopausal status. In addition, we correlated BP echo with MGD and background BPE.

2. Materials and methods

2.1. Study populations

Using our breast imaging data base, from June 2013 to June 2015, patients with newly diagnosed breast cancer who had performed preoperative mammography, ultrasound, and MRI at our hospital were identified. All women with a prior history of breast radiation ($n=11$), mastectomy ($n=15$), or interstitial mammoplasty ($n=5$) were excluded. Postmenopausal women who had received hormonal therapy within the last 6 months before the imaging studies ($n=12$) were also excluded. A total of 138 women (mean age 51.6 years, range from 26 to 79 years) were included in this study. Seventy-four patients (54%) were premenopausal (mean age 43.3 years, range from 26 to 53 years) and 64 patients (44%) were postmenopausal (mean age 60 years, range from 45 to 79 years). The institutional review board of our hospital approved this retrospective study, and the requirement of informed consent was waived.

2.2. Ultrasound

Bilateral whole breast ultrasound was performed using a 5–12 MHz transducer with IU-22 unit (Philips Medical Systems, Best, The Netherlands) or 4–15 MHz transducer with Aixplorer System (Supersonic Imagine, Aix en Provence, France) by 1 of 4 board-certified radiologists. At our institution, all patients with newly diagnosed breast cancer undergo whole breast US as loco-regional staging. Breast US is performed to evaluate for multifocal and multicentric disease. Even though there is no pathologic lesion in breast, radiologists in our institution usually obtain more than 6 images for each breast including representative images for 4 quadrants, subareolar area, and axilla.

The background parenchymal echotexture (BP echo) were classified as homogeneous and heterogeneous according to the BI-RADS lexicon. Homogeneous BP echo were divided into 2 groups including homogeneous BP echo-fat and homogeneous BP echo-fibroglanular. However, there was no patient showing homogeneous BP echo-fat in this study group. Therefore, we used the “homogeneous” BP echo as a meaning of homogeneous BP echo-fibroglanular. Homogeneous BP echo was considered when a uniformly echogenic layer of glandular tissue is present beneath the thin hypoechoic layer of fat lobules. In cases of mixture of multiple tiny hypoechoic areas, if scattered regularly throughout the gland, they were also considered as homogeneous BP echo. Heterogeneous BP echo was considered if the gland had multiple islands such as areas of increased and decreased echogenicity including posterior acoustic shadowing (Fig. 1). Two radiologists, 1 with 12 years’ and 1 with 13 years’ clinical experience (KHK and HKJ) retrospectively reviewed ultrasound images in consensus for the classification of BP echo without knowledge of clinical or other radiological information. BP echo was evaluated on the contralateral normal breast for avoiding the subtle change of echogenicity by breast cancer or ductal carcinoma in situ.

2.3. Mammography

Mammography in 2 standard imaging planes (MLO and CC) was performed using Senographe 2000D or Senographe DS (GE Healthcare, Milwaukee, WI) full-field digital mammography unit. Two radiologists (KHK and HKJ) reviewed retrospectively in consensus the mammography for the overall mammographic breast density (MGD) according to the BI-RADS classification. MGD was scored as grade 1: almost entirely fatty (<25%

glandular), grade 2: scattered fibroglandular densities (25–50% glandular), grade 3: heterogeneously dense (50–75% glandular), and grade 4: extremely dense (>75% glandular).

2.4. MRI

We recommend all patients with breast cancer to perform breast MR to find additional malignant lesions. If we find additional suspicious lesions other than proven malignancy on breast MR, we perform second look US. Because our institution does not have MR-guided biopsy, we usually perform US-guided biopsy for suspicious lesion or suspicious axillary lymph node. All breast MRI examinations were performed as standard dynamic axial contrast-enhanced subtracted images of both entire breasts using the 3.0-T MR system (Signa HDxt; General Electric Medical Systems, Milwaukee, WI) with a dedicated breast coil. T1 3D FSPGR images were obtained with 1 precontrast and 4 postcontrast dynamic series at 1 minutes, 2 minutes, 3 minutes, and 6 minutes after contrast injection. The following imaging parameters were used: TR/TE, 4.9/2.3; flip angle, 10°; matrix, 320 × 288; field of view, 320 × 320 mm; section thickness, 1.8 mm. Gadoterate meglumine (Prohance; Guerbet, Auulnay-Sous-Bois, France) was injected into an antecubital vein with an automated injector (Spectris MR; Medrad Europe, Maastricht, The Netherlands) at a dose of 0.1 mmol/kg of body weight and a rate of 3 mL/s followed by a 20 mL saline flush.

Two radiologists (KHK and HKJ) blinded to the patient's clinical and radiologic findings, retrospectively evaluated all subtracted MR enhanced images for classifying background parenchymal enhancement (BPE). BPE was evaluated on the contralateral normal breast in order to avoid any increased vascularization caused by breast cancer. In order to standardize the image interpretation, the subtracted images of the second dynamic sequence (acquired 2 minutes after contrast injection) were used. It was scored according to the 4-point scale of the BI-RADS lexicon as 4 grades. BPE was scored as grade 1: minimal (<25% of the glandular tissue showing enhancement), grade 2: mild (25–50% enhancement), grade 3: moderate (50–75% enhancement), and grade 4: marked (>75% enhancement).

2.5. Statistical analysis

MGD, BP echo, and BPE were dichotomized for statistical analyses. MGD was divided as nondense (grade 1, 2) and dense (grade 3, 4). BP echo was divided as homogeneous and heterogeneous. BPE on MR was also divided as nondense (grade 1, 2) and dense (grade 3, 4). Fisher's exact test was used to compare BP echo with MGD grades and BPE grades separately according to the menopausal status. Statistical analysis was performed by SPSS software (version 21.0; Chicago, IL). Statistical significant was assigned if the *P*-value was <.05.

3. Results

The patients' characteristics are shown in Table 1. Among the 138 patients, 68 (49%) showed homogeneous BP echo and 70 (51%) showed heterogeneous BP echo. Table 2 summarizes the histologic subtypes of 138 breast cancers according to BP echo. There was no significant correlation between histologic subtype and BP echo (*P* = .279). Premenopausal women were more likely to have heterogeneous BP echo (60/74, 81%) compared

Table 1

Demographics and distribution of 138 breast cancer patients.

Variables		N = 138
Age, years	≤50	70 (51%)
	>50	68 (49%)
Menopausal status	Premenopause	74 (54%)
	Postmenopause	64 (46%)
MGD on MMG	Grade1	2 (1%)
	Grade2	33 (24%)
	Grade3	92 (67%)
	Grade4	11 (8%)
BP echo on US	Homogeneous	68 (49%)
	Heterogeneous	70 (51%)
BPE on breast MR	Grade1	31 (23%)
	Grade2	43 (31%)
	Grade3	42 (30%)
	Grade4	22 (16%)

BPE = background parenchymal enhancement, BP echo = background parenchymal echogenicity, MGD = mammographic density, MMG = mammography, US = ultrasound.

with postmenopausal women (10/64, 16%) (*P* = .000). The distribution of MGD grades was skewed toward a higher than normal prevalence of heterogeneously dense or extremely dense with 2 women (1%) classified as grade 1, 33 (24%) as grade 2, 92 (67%) as grade 3, and 11 (8%) as grade 4. At MR, 31 (23%) had minimal BPE, 43 (31%) had mild BPE, 42 (30%) had moderate BPE, and 22 (16%) had severe BPE.

3.1. The relationship between each modality

3.1.1. BP echo and BPE. After dichotomizing of BPE grades into nondense (grade 1 or 2) and dense (grade 3 or 4), 76% (56/74) women showed dense BPE in the premenopausal group and 13% (8/64) women showed dense BPE in the postmenopausal group. The difference in proportions between the 2 groups was statistically significant (*P* = .000).

The relationship between BP echo and BPE is displayed at Table 3. There was a significant correlation between BP echo and BPE in both premenopausal and postmenopausal women (*P* = .000). In the premenopausal group, 87% (52/60) women with heterogeneous BP echo showed dense BPE and in the postmenopausal group, 98% (53/54) women with homogeneous BP echo showed non-dense BPE.

3.1.2. BP echo and MGD. There was no significant correlation between BP echo and MGD regardless of menopausal state. In the premenopausal group, 83% women (60/72) with dense MGD showed heterogeneous BP echo. In the postmenopausal group,

Table 2

Distribution of histologic subtypes according to BP echo.

Histologic subtype	BP echo on US		
	Homogeneous	Heterogeneous	
Invasive ductal carcinoma	56	62	118 (85.5%)
Invasive lobular carcinoma	4	4	8 (5.8%)
Mucinous carcinoma	2	3	5 (3.6%)
Medullary carcinoma	3	0	3 (2.2%)
Tubular carcinoma	2	0	2 (1.4%)
Other invasive carcinoma	1	1	2 (1.4%)
Total	68	70	138

BP echo = background parenchymal echogenicity, US = ultrasound.

Table 3

Distribution of classified background parenchymal echotexture (BP echo) and background parenchymal enhancement (BPE) in pre- versus postmenopausal women.

	Background parenchymal echotexture	Background parenchymal enhancement				Statistical analysis
		Grade 1	Grade 2	Grade 3	Grade 4	
Premenopausal (n=74)	Homogeneous (n=14)	0 (0%)	10 (71%)	4 (29%)	0 (0%)	P=.000
	Heterogeneous (n=60)	1 (2%)	7 (21%)	31 (52%)	21 (35%)	
Postmenopausal (n=64)	Homogeneous (n=54)	28 (52%)	25 (46%)	1 (2%)	0 (0%)	P=.000
	Heterogeneous (n=10)	2 (20%)	1 (10%)	6 (60%)	1 (10%)	

BPE=background parenchymal enhancement, BP echo=background parenchymal echogenicity.

70% women (21/30) with dense MGD showed homogeneous BP echo. All women with grade 4 MGD (n=11) showed heterogeneous BP echo. There was only 1 patient (3%, 1/35) who showed heterogeneous BP echo with nondense MGD.

3.1.3. MGD and BPE. There was no significant correlation between MGD and BPE in either pre- or postmenopausal women. In the premenopausal group, 87% women (56/72) with dense MGD showed dense BPE. In the postmenopausal group, 77% women (23/30) with dense MGD showed nondense BPE.

3.2. Distribution of dichotomized MGD, BP echo, and BPE in premenopausal and postmenopausal women

Changes of distribution of dichotomized grades in each modality according to menopausal state are detailed in Fig. 2. After dichotomizing of MGD grades of mammography into dense and nondense, the distribution of premenopausal versus postmenopausal women was as follows: 99% (74/73) dense in the premenopausal group versus 47% (30/64) dense in the postmenopausal group. As for BP echo in breast US, the distribution of pre- versus postmenopausal group was as follows: 81% (60/74) heterogeneous in the premenopausal group versus 16% (10/64) heterogeneous in the postmenopausal group. Dichotomization of BPE in breast MR into dense and nondense BPE in pre- versus postmenopausal group was as follows: 76% (56/74) dense in the premenopausal group versus 13% (8/64) dense in the postmenopausal group.

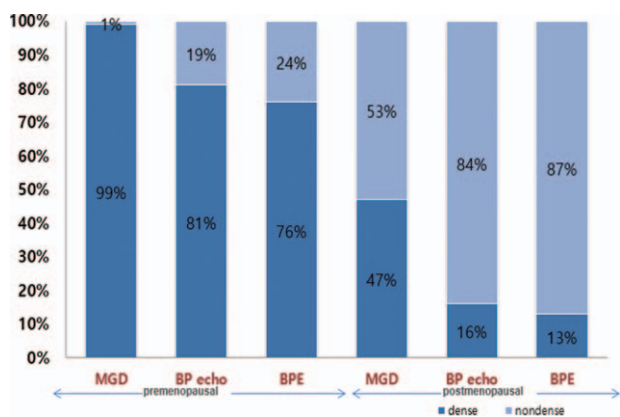


Figure 2. Distribution of dichotomized MGD, BP echo, and BPE in premenopausal and postmenopausal women. BPE=background parenchymal enhancement, BP echo=background parenchymal echogenicity, MGD=mammographic density.

4. Discussion

In accordance with previous published studies, we found that BP echo on breast US correlates significantly with menopausal status.^[15,16] For premenopausal women, the vast majority showed heterogeneous BP echo (60/74, 81%). On the other hand, postmenopausal women were likely to have homogeneous BP echo significantly (54/64, 84%). This means that BP echo is influenced by breast hormonal changes. Ramakrishnan et al^[17] analyzed the morphologic changes in breasts tissue with menstrual cycle. They reported that there were distinct morphologic alterations of the lobule and the intralobular stroma but interlobular stroma was relatively unaltered according to the menstrual cycle. One recent study by Izumori et al^[14] described the histologic correlation with BP echo using mastectomy specimens in detail. They found that stroma with densely packed connective tissue surrounding ducts are visualized as isoechoic structures. On the contrary, stroma with loosely packed fibrous connective tissues was hyperechoic. The differences of echogenicity between the loose and dense stroma might cause heterogeneous background echogenicity. Taken together with the results from previous studies, we suggest that premenopausal women can show heterogeneous BP echo because of abundant lobules and intralobular stroma. However, postmenopausal women can show homogeneous echogenic BP echo from relatively small percentage of lobules and intralobular stroma.

Surprisingly, we found no relationship between MGD and BP echo in either pre- or postmenopausal group. In the postmenopausal group, 70% women (21/30) with dense MGD showed homogeneous BP echo. On a mammography, fibroglandular tissue and connective tissue appear white (dense), whereas fat appears dark (non-dense). But, on breast US, as mentioned before, there is a difference in echogenicity between gland-associated tissue including lobules, ducts with surrounding connective tissue, and loose connective tissue which appear equally white on mammography. Following the menopause, the circulating level of estrogen and progesterone decline and the breast begins to involute. Even though the total amount of fibroglandular tissue and connective tissue is same, the parenchymal echogenicity would be changed according to the proportion of loosely packed connective tissue. Therefore, the meaning of “heterogeneous” in background echogenicity should be distinguished from that of “heterogeneous” dense parenchyma in mammography. The “heterogeneous” dense in mammography is related to the difference of density between the fibroglandular tissue and fat. Of course, sometimes, the “heterogeneous” BP echo may be caused by the mixture of echogenic fibroglandular tissue and fat lobules. However, in majority, we usually conclude that background echotexture is “heterogeneous” when the fibroglandular tissue shows a

confusing pattern intermingled with isoechoic and echogenic portion. In such a case, radiologists have some difficulties to detect small subtle lesions, which might affect the sensitivity of breast ultrasound.

The present study showed that a BP echo showed significant correlation with BPE regardless of menopausal state. Although the precise mechanism of BPE is unclear, it has been reported about relation with hormonal status, particularly the estrogen level.^[5,18] King et al^[19] reported that there is a significant association between the treatment of tamoxifen and decrease in BPE in breast MRI. From the results of our study, we can suggest that there would be difference in vascular permeability and perfusion between isoechoic gland-associated tissue and echogenic loose connective tissue which are affected by hormonal influence. In addition, as Ko et al^[16] suggested, we also think that abundant gland-associated tissue which cause heterogeneous echogenicity is supposed to be more hypervascular, which might explain the higher degree of BPE on breast MR.

Recently, several studies have shown that the moderate and marked BPE significantly correlated with an increased risk of breast cancer.^[9,10,20] Furthermore, the relationship between molecular subtype of breast cancer and BPE has been suggested.^[21,22] They described the possibility that BPE is a marker of physiologically active tissue more prone to tumorigenesis. Pike and Pearce^[23] reported that changes in mammographic density and BPE may be useful in predicting response to chemo-preventive agents aimed at blocking breast cell proliferation. As our study showed the strong association between BP echo and BPE regardless menopausal status, we suggest that BP echo might be another useful predictor for BPE.

Our study has several limitations. First, the study included a small number of patients with breast cancer, and the study was a retrospective design. In addition, the data were obtained in Korean patients, with relatively dense breasts. There would be some difficulties for generalization of these results. Second, the effect of patient's menstrual cycle could not be eliminated. Although we recommended the patients to perform breast MR in their 2nd week of the menstrual cycle, some women had no choice to take breast MR regardless of menstrual cycle for urgent surgery or chemotherapy. Third, the imaging analysis was subjective using visual assessment by the radiologist. However, there was no significant discrepancy between reviewers for categorization of MGD, BP echo, and BPE, as we usually assess them in daily practice. In the future, further studies with more objective and clinically feasible technique to quantify them would be necessary for more valuable results.

In conclusion, we demonstrated that the BP echo was influenced by menopausal status. Our data support the concept that BP echo is influenced by breast hormonal changes. Because there was a significant association between BP echo and BPE in pre- and post-menopausal women, the BP echo might be a good predictor for BPE as a physiologically active tissue.

References

- [1] Hooley RJ, Scoutt LM, Philpotts LE. Breast ultrasonography: state of the art. *Radiology* 2013;268:642–59.
- [2] D'Orsi C, Sickles EA, Mendelson EB, et al. Breast Imaging Reporting and Data System: ACR BI-RADS Breast Imaging Atlas. 5th ed. Reston, Va: American College of Radiology; 2013.
- [3] Giess CS, Yeh ED, Raza S, et al. Background parenchymal enhancement at breast MR imaging: normal patterns, diagnostic challenges, and potential for false-positive and false-negative interpretation. *Radiographics* 2014;34:234–47.
- [4] Scaranelo AM, Carrillo MC, Fleming R, et al. Pilot study of quantitative analysis of background enhancement on breast MR images: association with menstrual cycle and mammographic breast density. *Radiology* 2013;267:692–700.
- [5] Kuhl CK, Bieling HB, Gieseke J, et al. Healthy premenopausal breast parenchyma in dynamic contrast-enhanced MR imaging of the breast: normal contrast medium enhancement and cyclical-phase dependency. *Radiology* 1997;203:137–44.
- [6] Morris EA. Diagnostic breast MR imaging: current status and future directions. *Radiol Clin North Am* 2007;45:863–80. vii.
- [7] Kuhl C. The current status of breast MR imaging. Part I. Choice of technique, image interpretation, diagnostic accuracy, and transfer to clinical practice. *Radiology* 2007;244:356–78.
- [8] DeMartini WB, Liu F, Peacock S, et al. Background parenchymal enhancement on breast MRI: impact on diagnostic performance. *AJR Am J Roentgenol* 2012;198:W373–380.
- [9] Telegrafo M, Rella L, Stabile Ianora AA, et al. Breast MRI background parenchymal enhancement (BPE) correlates with the risk of breast cancer. *J Magn Reson Imaging* 2016;34:173–6.
- [10] King V, Brooks JD, Bernstein JL, et al. Background parenchymal enhancement at breast MR imaging and breast cancer risk. *Radiology* 2011;260:50–60.
- [11] Delille JP, Slanetz PJ, Yeh ED, et al. Physiologic changes in breast magnetic resonance imaging during the menstrual cycle: perfusion imaging, signal enhancement, and influence of the T1 relaxation time of breast tissue. *Breast J* 2005;11:236–41.
- [12] Cubuk R, Tasali N, Narin B, et al. Correlation between breast density in mammography and background enhancement in MR mammography. *La Radiol Med* 2010;115:434–41.
- [13] Klifa C, Suzuki S, Aliu S, et al. Quantification of background enhancement in breast magnetic resonance imaging. *J Magn Reson Imaging* 2011;33:1229–34.
- [14] Izumori A, Horii R, Akiyama F, et al. Proposal of a novel method for observing the breast by high-resolution ultrasound imaging: understanding the normal breast structure and its application in an observational method for detecting deviations. *Breast Cancer* 2013; 20:83–91.
- [15] Kawamura A, Satake H, Ishigaki S, et al. Prediction of background parenchymal enhancement on breast MRI using mammography, ultrasonography, and diffusion-weighted imaging. *Nagoya J Med Sci* 2015;77:425–37.
- [16] Ko ES, Lee BH, Choi HY, et al. Background enhancement in breast MR: correlation with breast density in mammography and background echotexture in ultrasound. *Eur J Radiol* 2011;80:719–23.
- [17] Ramakrishnan R, Khan SA, Badve S. Morphological changes in breast tissue with menstrual cycle. *Mod Pathol* 2002;15:1348–56.
- [18] Kajihara M, Goto M, Hirayama Y, et al. Effect of the menstrual cycle on background parenchymal enhancement in breast MR imaging. *Magn Reson Med* 2013;12:39–45.
- [19] King V, Kaplan J, Pike MC, et al. Impact of tamoxifen on amount of fibroglandular tissue, background parenchymal enhancement, and cysts on breast magnetic resonance imaging. *Breast J* 2012;18: 527–34.
- [20] Dontchos BN, Rahbar H, Partridge SC, et al. Are qualitative assessments of background parenchymal enhancement, amount of fibroglandular tissue on MR images, and mammographic density associated with breast cancer risk? *Radiology* 2015;276:371–80.
- [21] Mazurowski MA, Zhang J, Grimm LJ, et al. Radiogenomic analysis of breast cancer: luminal B molecular subtype is associated with enhancement dynamics at MR imaging. *Radiology* 2014;273: 365–72.
- [22] Wang J, Kato F, Oyama-Manabe N, et al. Identifying triple-negative breast cancer using background parenchymal enhancement heterogeneity on dynamic contrast-enhanced MRI: a pilot radiomics study. *PLoS One* 2015;10:e0143308.
- [23] Pike MC, Pearce CL. Mammographic density, MRI background parenchymal enhancement and breast cancer risk. *Ann Oncol* 2013;24(suppl 8):viii37–41.