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Is Breast Background Parenchymal Enhancement on MRI Related to BI-RADS Score and Follow-Up Rate?

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Abstract

Objective: We investigated the correlations between background parenchymal enhancement (BPE) and MRI interpretations with respect to short-interval follow-ups and biopsy rates. **Methods:** All accessible MRI examinations from 128 women during a limited time period in 2016 were evaluated. A blinded radiologist visually categorized BPE as minimal, mild, moderate, or marked. A BI-RADS category was also assigned. We used descriptive statistics to report the findings and chi-square and Fisher's exact tests to compare categories. **Results:** Prevalence of minimal, mild, moderate, and marked BPE was 14.1%, 43.0%, 32.0%, and 10.9%, respectively. The short-interval follow-up rates were 22.2%, 27.3%, 26.8%, and 7.1% in women with minimal, mild, moderate, and marked BPE, respectively. BPE was not associated with the short-interval follow-up rate (p-value = 0.477). Biopsy rates were 22.2%, 27.3%, 22.0%, and 57.1% in women with minimal, mild, moderate, and marked BPE, respectively. Although there was no significant relationship between biopsy rates and BPE levels (p-value = 0.095) in the total population, these two factors were significantly associated in premenopausal women (p-value = 0.023) and in women of 30 - 39 years (p-value = 0.001). **Conclusion:** Higher BPE does not correlate with short-interval follow-up rates, but appears to be related to biopsy rate, thus causing false-positives and unnecessary biopsy recommendations, particularly in younger, premenopausal women.

Keywords

Breast MRI, Background Parenchymal Enhancement, BI-RADS,
Short-Interval Follow-Up, Biopsy

1. Introduction

Background parenchymal enhancement (BPE), representing normal fibro-glandular tissue enhancement in dynamic contrast-enhanced magnetic resonance imaging (MRI), corresponds to hormonally responsive glandular tissue [1]. BPE may represent blood flow and hormonal activity of dense tissue [2]. Histamine-like effects of estrogen cause vasodilation and increase breast tissue vascular permeability, and the proliferative effects of progesterone increase metabolic activity resulting in increased perfusion of breast [3] [4]. BPE is higher in younger women with hormonally active breasts [5] [6]. BPE varies between patients and is currently reported using the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) [7].

MRI is the most sensitive imaging method for detection of breast cancer (BC), yet it has limited specificity [8] [9]. Some authors have suggested that an increased BPE has the possibility to obscure breast lesions and decrease MRI sensitivity for detection of BC or may even be misinterpreted as a suspicious finding itself, thus leading to an increased false-positive biopsy rate and short-interval follow-up rate [4] [10] [11] [12], but some others believe BPE does not significantly affect the diagnostic accuracy of breast MRIs [13]. Imaging material and hormonal status also affect BPE and can limit breast MRI interpretation [14] [15]. We aimed to investigate the correlations between BPE and the interpretation of MRI examinations with respect to BI-RADS scores, short-interval follow-up rates, and biopsy rates.

2. Materials and Methods

Design: From January 2016 to January 2017 and after taking written informed consents, we randomly included 128 women who had breast MRI in a tertiary referral hospital to investigate the correlation between BPE and BI-RADS score. All MRI images retrospectively were observed by a specialized breast radiologist. Indications for breast MRI were questionable mammographic or ultra-sonographic findings, unexplainable clinical findings, BIRADS 3 lesions' follow-ups, and planning for 12 new cases of biopsy-proven malignancies. The exclusion criteria consisted of a history of conservative breast surgery, chemotherapy, radiotherapy, and/or hormone replacement therapy.

In a dedicated surface breast coil, the same techniques for all patients were performed in a 1.5 Tesla MRI scanner, and a blinded expert breast radiologist reviewed all of the images. Localization, T1-weighted non-fat-suppressed sequences, and T2-weighted fat-suppressed sequences were conducted following standard protocols, and six sequences after injection of 0.1 mmol/L gadopentetate dimeglumine (Magnevist, Bayer and Germany) were then obtained and subtracted pixel-by-pixel from the first non-contrast images. The radiologist visually assessed BPE in post-contrast fat-suppressed T1-weighted subtracted images and categorized BPE on the basis of fifth edition of BI-RADS criteria as minimal, mild, moderate, or marked [7].

BI-RADS categories consisted of 6 groups: 0 (incomplete assessment, recall); 1 (normal findings, routine screening); 2 (benign findings, routine screening); 3 (probably benign findings, short-interval follow-up); 4 (suspicious findings, biopsy); 5 (highly-suspicious findings, biopsy); and 6 (biopsy-proven malignancy, excision). Biopsies were taken with a Tru-cut needle from patients who had been recommended for a biopsy based on BI-RADS 4 or 5 which was given by another radiologist who was blind to the study. Following standard protocols, an expert pathologist examined breast specimens' biopsies from patients who had been classified as BI-RADS 4 or 5 (Figures 1-3).

Data analysis: We used descriptive statistics (count, frequency distributions) to report BI-RADS categories, short-interval follow-up and biopsy rates, and positive predictive biopsy value (PPV). Comparing categories, we used chi-square and Fisher's exact tests. Type I error was considered 0.05. The data was collected on MS Office Excel datasheets (Microsoft, Redmond, USA). All analyses were conducted using SPSS v.22 (IBM Corp., Armonk, USA).

Ethical considerations: The study protocol was evaluated and approved by the Atieh hospital institutional ethics committee considering the retrospective setting of the study and taking written informed consents from patients for using their data.

Confidentiality of information was followed. Researchers caused no adverse or harmful events to patients. Authors were committed to the principles of the Declaration of Helsinki and declared no conflicts of interests.

3. Results

We studied 89 (69.5%) pre-menopausal and 39 (30.5%) postmenopausal women aged 18 to 74 years old. Approximately a third of the women (count = 44) were aged 30 - 39 years. Minimal, mild, moderate, and marked BPE were observed in 18 (14.1%), 55 (43.0%), 41 (32.0%), and 14 (10.9%) women, respectively.
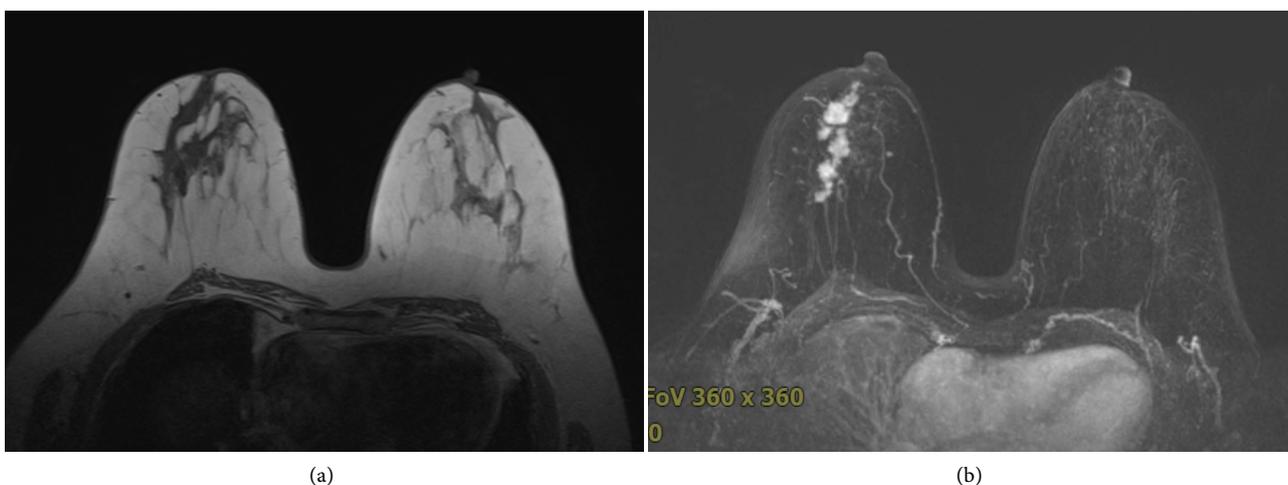

(a)　　　　　　　　　　　　　　　　　(b)

Figure 1. Breast MRI in a 40 years old woman with right breast mass sensation which was proved to be a cancer regarding biopsy under ultrasound guide. In T1 sequence, scattered fibroglandular tissue is seen (a). After contrast injection in a mild background parenchymal enhancement, multiple irregular masses with segmental distribution are seen in right breast lateral part (b).
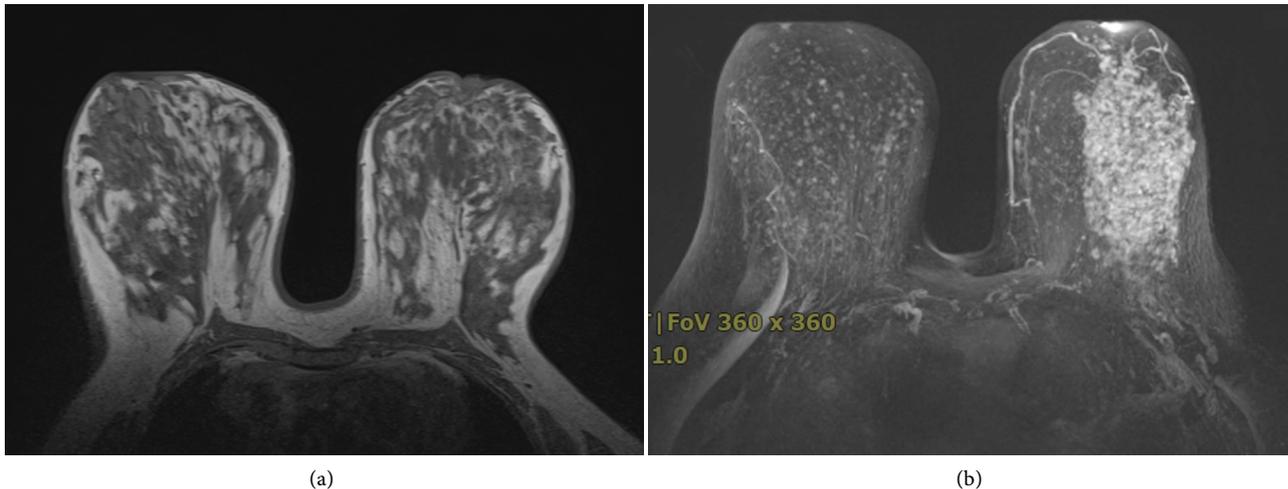
(a)

(b)

Figure 2. This is MRI of a 45 years old woman with an extremely dense mammography. In T1 sequence before contrast, extremely compact fibroglandular tissue is seen in breasts (a). Maximum intensity projection images (MIP) shows a large area with non-mass like clumped nodular enhancement in a moderate nodular background parenchymal enhancement context which was proved to be extensive ductal carcinoma in situ with some foci of invasive ductal carcinoma (b).
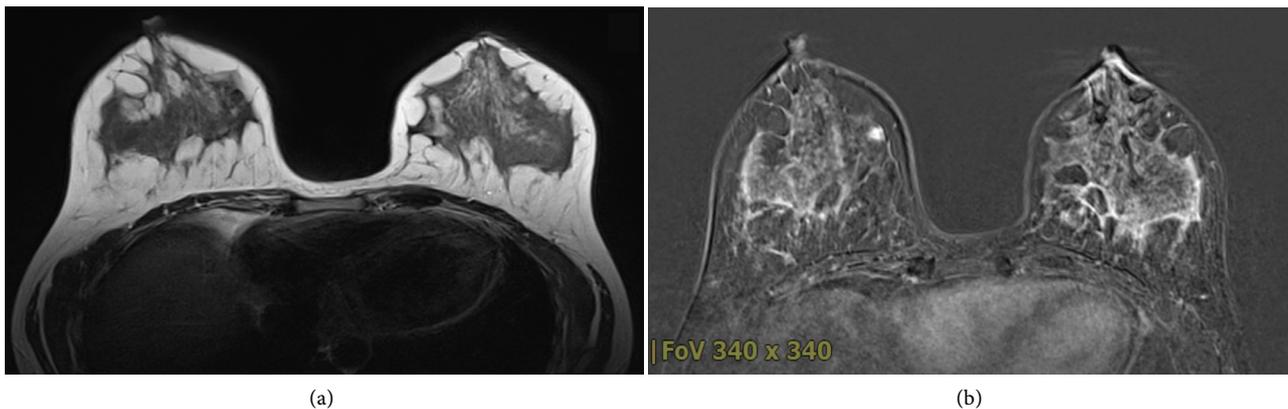

(a)

(b)

Figure 3. Breast MRI in a middle age woman with heterogenous type of fibroglandular tissue in T1 sequences without contrast (a) and moderate background parenchymal enhancement after contrast (b), a small mildly irregular shape early enhancing mass is seen in right breast central inner part which was given BIRADS 4 and then after with benign pathology's result in biopsy.

BPE and BI-RADS score level, Table 1 represents a significant association between BI-RADS score and BPE level (Fisher's exact p-value = 0.023). According to a sub-analysis, the association remained significant in premenopausal women (Fisher's exact p-value = 0.031) and in women 30 - 39 years (Fisher's exact p-value = 0.024).

BPE and short term follow up, overall, 49 women (38.3%) presented with normal or benign examinations (such as BI-RADS 1 or 2) and continued routine screening. About 55% of women with minimal BPE were assigned a BI-RADS category of 1 or 2 versus 36.4%, 39.0%, and 21.4% of women with mild, moderate, and marked BPE, respectively (Table 2).

As shown in Table 2, 31 women (24.2%) were assigned to BI-RADS category 3 (probably benign) and underwent short-interval follow-ups. The short-interval follow-up rate was 22.2%, 27.3%, 26.8%, and 7.1% in women with minimal,

Table 1. Cross-tabulation of "background parenchymal enhancement" level and BI-RADS score in breast magnetic resonance imaging of 128 women. No one was assigned to a BI-RADS category of 0 (incomplete assessment).

BI-RADS category	Total[a]	Background Parenchymal Enhancement[a]			
		Minimal (n = 18)	Mild (n = 55)	Moderate (n = 41)	Marked (n = 14)
1) Normal findings	5 (3.9)	3 (16.7)	1 (1.8)	0 (0.0)	1 (7.1)
2) Benign findings	44 (34.4)	7 (38.9)	19 (34.5)	16 (39.0)	2 (14.3)
3) Probably benign findings	31 (24.2)	4 (22.2)	15 (27.3)	11 (26.8)	1 (7.1)
4) Suspicious findings	32 (25.0)	2 (11.1)	13 (23.6)	9 (22.0)	8 (57.1)
5) Highly-suspicious findings	4 (3.1)	2 (11.1)	2 (3.6)	0 (0.0)	0 (0.0)
6) Biopsy-proven malignancy	12 (9.4)	0 (0.0)	5 (9.1)	5 (12.2)	2 (14.3)

BI-RADS: breast imaging-reporting and data system, n: count. [a]numbers represent "count (percentage within each column)".

Table 2. Associations of routine screening rate, short-interval follow-up rate, biopsy rate, and positive predictive value of biopsy with "background parenchymal enhancement" level in breast magnetic resonance imaging of 128 women.

MRI interpretation	Total[e]	Background Parenchymal Enhancement[e]				p-value*
		Minimal, n = 18	Mild, n = 55	Moderate, n = 41	Marked, n = 14	
Recommended routine screening[a]	38.3 (49)	55.6 (10)	36.4 (20)	39.0 (16)	21.4 (3)	0.274
Recommended short-interval follow-up[b]	24.2 (31)	22.2 (4)	27.3 (15)	26.8 (11)	7.1 (1)	0.477
Recommended biopsy[c]	28.1 (36)	22.2 (4)	27.3 (15)	22.0 (9)	57.1 (8)	0.095
PPV for biopsy[d]	16.7 (6)	50.0 (2)	20.0 (3)	0.0 (0)	12.5 (1)	0.107

n: count, PPV: positive predictive value; [a]BI-RADS 1 or 2; [b]BI-RADS 3; [c]BI-RADS 4 or 5; [d]percentage of malignant lesions detected in women who underwent biopsy; [e]numbers represent "percentage within each column (count)"; *Fisher's exact test.

mild, moderate, and marked BPE, respectively. BPE was not associated with short-interval follow-up rates (p-value = 0.477).

BPE and biopsy, biopsies were recommended for 36 women (28.1%) with BI-RADS category of 4 or 5. Table 2 shows the rate and PPV (positive predictive value) of biopsy according to BPE levels. The biopsy rates were 22.2%, 27.3%, 22.0%, and 57.1% for women with minimal, mild, moderate, and marked BPE, respectively. Although there were no significant relationships between the biopsy rates and BPE levels (p-value = 0.095) in the total population, a sub-analysis showed significant associations between BPE and biopsy rates in premenopausal women (Fisher's exact p-value = 0.023) and in women 30 - 39 years (Fisher's exact p-value = 0.001).

Biopsies proved the presence of malignancies (invasive ductal carcinoma) in six patients, giving a PPV of 16.7%. PPV for biopsy did not associate with BPE in the total population (p-value = 0.107).

According to sub-analyses, PPV for biopsy was 16.7% in both premenopausal (4/24) and postmenopausal (2/12) women and 8.3% (1/12) in women aged 30 - 39 years. PPV for biopsy and age decade were not associated (Fisher's exact p-value = 0.318).

4. Discussion

Few studies have evaluated the impact of BPE on MRI diagnostic performance. In our study, BPE associated with BI-RADS scores in all women, including premenopausal ones and women aged 30 - 39 years. De Martini *et al.* reported that abnormal interpretation rates for women with moderate or marked BPE were significantly higher than that for women with minimal or mild BPE, but positive biopsy rates were not affected by different BPE [13]. However, in a study by Hambly in women with minimal BPE, no significant difference in BI-RADS category for women with mild, moderate, or marked BPE was found [4].

In contrast to the De Martini *et al.* study [13], we considered the relationships between BPE and the menopausal status variable.

Almost quarter of our subjects underwent short-interval follow-ups and rates of short-interval follow-ups did not associate with BPE; these results are in contrast to the previous Hambly study [4]. They showed an association of short-interval follow-ups with BPE levels but the rate of BIRADS 3 in their study was greater than usual (43.6%).

In agreement with Hambly *et al.* [4], biopsy rates did not correlate with BPE in our study. Yet, it was associated with BPE in sub-groups of premenopausal women and in women living their third decade although the PPV for biopsy was limited.

Only one out of six biopsies revealed a malignancy in our study. In agreement with Hambly *et al.* and De Martini *et al.* [4] [13], our study showed that PPV was not affected by BPE regardless of menopausal status or age decade.

According to low predictive values of biopsy in premenopausal women and women aged 30 - 39 years in our study, and the point that BPE is higher in younger breasts [16] [17], it can be implied that increased BPE, misinterpreted as malignancy, may lead to false-positive diagnosis.

Our study like Hambly and colleagues [4] included only patients who underwent biopsy, so sensitivity and specificity were not measured.

There were some limitations to this study as: small sample size and visual qualitative BPE assessment. In addition, being a single-centered study is a challenge for making generalizations about the results. One other limitation was assigning a single BI-RADS assessment to both breasts because the breast with the lower BI-RADS category data was lost. It is especially important when women with BI-RADS category 4 or 5 in one breast had BI-RADS category 3 in the contralateral breast.

5. Conclusion

Higher BPE on breast MRIs does not correlate with short-interval follow-up

rates but can increase false-positive interpretations, leading to unnecessary biopsies, particularly in younger, premenopausal women.

Authors' Contributions

AA designed the concept. All authors collaborated in data acquisition. FR provided statistical advice on study design and data analyses. AA and FR analyzed and interpreted the data. SAK drafted the manuscript. All authors critically reviewed the manuscript. All authors read and approved the final manuscript. AA takes responsibility for the paper as a whole.

Conflict of Interest

The authors declare that there is no conflict of interest.

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