



Research article

Background parenchymal enhancement assessment: Inter- and intra-rater reliability across breast MRI sequences



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ABSTRACT

Objective: To evaluate inter- and intra-rater reliability of background parenchymal enhancement (BPE) assessment across breast MRI sequences.

Materials and methods: Institutional review board approval was obtained and the requirement for consent was waived. Three radiologists qualitatively categorized BPE on 150 breast MRI using a four-point scale (minimal, mild, moderate or marked) according to BI-RADS category system. According to MR-sequence used for the assessment of BPE, inter-rater and intra-rater reliability across a simulated reading strategy with four options was performed: (1) initial contrast-enhanced (CE) fat-suppressed T1-weighted images (2) initial CE subtracted images (3) maximum-intensity-projection (MIP) of the first CE subtracted images (4) combination of initial CE fat-suppressed T1-weighted, initial CE subtracted and MIP images. Raters repeated BPE assessment of 45 breast MRI four weeks after the initial assessment. Gwet's AC1 index with ordinal weights was used to assess reliabilities.

Results: Gwet's index for the reliability among the three raters was 0.68 (0.63–0.74) using initial contrast-enhanced fat-suppressed T1 weighted images, 0.74 (0.69–0.80) using subtracted images, 0.80 (0.76–0.83) using MIP, 0.80 (0.77–0.84) using a combination of the initial contrast-enhanced fat-suppressed T1 weighted, initial contrast-enhanced subtracted and MIP images. Test-retest reliability was 0.81 (0.60–1.00) for rater 1, 0.77 (0.55–0.98) for rater 2, 0.79 (0.59–0.99) for rater 3 using the combination of initial contrast-enhanced fat-suppressed T1 weighted, initial contrast-enhanced subtracted and MIP images.

Conclusions: Overall, the combination of all CE MRI images showed the highest reliability of BPE assessment. However, MIP showed a high reliability with lower reading time compared to the combination of all CE MRI images.

1. Introduction

In breast magnetic resonance imaging (MRI), background parenchymal enhancement (BPE) is the amount of fibroglandular tissue that enhances after intravenous contrast administration [1–3]. Specifically, according to the Breast Imaging-Reporting and Data System (BI-RADS), BPE refers to the volume and the intensity of enhancement of normal breast tissue [4]. The possible association between BPE and breast cancer risk is one of reasons explaining the growing interest in BPE over the last few years [1,2,5,6]. In addition, the effect of BPE on

breast MRI reading and interpretation has been investigated [7–9]; indeed, a high amount of BPE may reduce breast MRI accuracy obscuring enhancing lesions or enhancing normal breast parenchyma mimicking cancers, as well as affecting the accuracy of tumor extent evaluation [7–10].

Considering the ongoing knowledge on BPE impact, the reliability of BPE assessment among readers could be crucial. Currently, BPE can be visually categorized on a four-point scale as minimal, mild, moderate or marked [4]. However, a large variability on visual estimation of BPE exists, although the interreader agreement could be improved with

Abbreviations: BPE, background parenchymal enhancement; BI-RADS, Breast Imaging-Reporting and Data System; CE, contrast-enhanced; MIP, Maximum intensity projections; CI, confidence interval

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training [11,12]. In addition, a wide heterogeneity in the breast MR-sequence used for BPE assessment has been found in literature [11]. Post-contrast MRI sequences may enhance the variability on visual estimation of BPE. It is not known if a sequence or a combination of sequences could reduce the variability of BPE assessment. In this perspective, we postulated that there could be one MRI sequence that could show a higher reliability of BPE assessment compared to the others. Therefore, the aim of our study was to assess the inter- and intra-rater reliability of qualitative BPE assessment across breast MRI sequences.

2. Materials and methods

Institutional review board approval was obtained and the requirement for consent was waived. A dataset of 150 consecutive breast MRI of 150 patients with unilateral breast cancer were retrospectively included. Breast MRI were performed between 2010 and 2014 in one Centre for preoperative staging of newly diagnosed breast cancer. Patients' age and cancer histotype were recorded.

2.1. MR imaging technique

All MRI examinations were performed on a clinical 1.5 T MRI scanner (Philips, Achieva, Best, The Netherlands). Patients were placed in a prone position and a dedicated seven-channel breast coil was used (Philips Sense breast 7). MRI acquisition standard protocol included the following standard sequences: localizing sequence; T1-weighted and fat-saturated T2-weighted sequences; three-dimensional fat-suppressed gradient-echo T1-weighted sequences (Dyn-EThrive, 5.18 ms repetition time/2.52 ms echo time; 352 × 352 matrix; 340 × 340 mm field of view; 1 mm section thickness; 1 × 1 × 0.9 mm voxel size; acquisition time < 70 s), before and after bolus injection of gadolinium-based contrast medium (gadobenate dimeglumine, MultiHance, Bracco Imaging, Milano, Italia; 0.1 mmol/L per kilogram of body weight; injection rate of 2.0 mL/sec followed by 20 ml saline flush). Subtraction images were then reconstructed in axial plane from the contrast-enhanced images to unenhanced images. The first subtracted contrast-enhanced (CE) dynamic sequence was used to perform the maximum-intensity-projection technique.

2.2. BPE assessment

We decided to divide each MRI examination into four image-sets to simulate a four-reading strategy. Therefore, all the images of each MRI examination were fully anonymized and stored in a dedicated study hard disk by a person not involved in BPE assessment to avoid bias. The same person divided four image-sets of sequences into separate folders, by assigning a code, for each examination:

- 1) initial CE three-dimensional fat-suppressed gradient-echo T1-weighted images (initial CE fat-suppressed T1-weighted images);
- 2) initial CE three-dimensional fat-suppressed gradient-echo T1-weighted subtraction images (initial CE subtracted images);
- 3) maximum-intensity-projection (MIP) of the first CE subtracted images;
- 4) the initial CE fat-suppressed T1-weighted images, initial CE subtracted images and MIP.

The four anonymous image-sets of each examination were then randomized in reading sequence to the raters using a randomization table made by Excel (Microsoft, version 14.3.9 for Mac) by the same person not involved in BPE assessment, as previously performed in literature to avoid bias of interpreting images consecutively [13]. Three raters, radiologists with different breast imaging experience, (BLIND four years of experience, BLIND ten years of experience; BLIND more than twenty years of experience) evaluated independently each image

set for BPE assessment in distinct sessions. All BPE assessment were performed after training, that consisted of a single hour presentation of examples of minimal, mild, moderate, and marked background parenchymal enhancement using each CE images, both from the literature [3–5,8,9,12,14–17], and our collection (not included in this study), similarly to that suggested in literature [12]. We were not able to find examples in literature related to BPE assessment using the initial CE fat-suppressed T1-weighted and only examples from our collection were used for training in this case.

High-resolution PACS monitors were used for the evaluation. For each image-set, BPE was assessed on the unaffected breast. BPE was visually categorized on a four-point scale as minimal, mild, moderate or marked in accordance with BI-RADS categories [4].

Raters repeated BPE assessment of 45 breast MRI four weeks after the initial assessment to assess intra-rater reliability.

Following BPE assessment of BPE intra-rater reliability, raters jointly revised the 150 breast MRI examinations to assess the amount of BPE in consensus.

The reading time of each image-set was recorded by a person not involved in BPE assessment with a commercially available swatch.

2.3. Statistical analysis

Inter-rater reliability and intra-rater reliability among the three raters according to the four reading strategy/image set were assessed using the absolute agreement and the Gwet's AC1 index with ordinal weights (with 95%CI) [18]. Gwet's index, instead of Cohen's Kappa, was used since has been demonstrated to be more stable and less affected by prevalence and marginal probability [19]. Stata (v.14; StataCorp) was used for the computation.

3. Results

Among the 150 patients included in the study, the median age was 58 (range, 31–77 years). The final post-surgical histopathology was invasive ductal carcinoma in 24% of patients (36 of 150), invasive lobular carcinoma in 13% patients (19 of 150), invasive ductal carcinoma and in situ components in 31% patients (47 of 150), invasive lobular carcinoma and lobular intraepithelial neoplasia in 11% patients (16 of 150), and others hystopatologies in 21% patients (32 of 150). After consensus of the three raters, the amount of BPE was minimal in 18% patients (27 of 150), mild in 55% patients (81 of 150), moderate in 25% patients (38 of 150) and marked in 2% patients (4 of 150).

Gwet's AC1 values of 0.68 (0.63-0.74) for BPE assessment with an absolute agreement of 87% among the three raters reading the initial CE fat-suppressed T1-weighted images.

Gwet's AC1 values of 0.74 (0.69-0.80) for BPE assessment with an absolute agreement of 90% among the three raters reading the initial CE subtracted images.

Gwet's AC1 values of 0.80 (0.76-0.83) for BPE assessment with an absolute agreement of 92.4% among the three raters reading the MIP.

Gwet's AC1 values of 0.80 (0.77-0.84) for BPE assessment with an absolute agreement of 91.8% among the three raters reading the combination of the initial CE fat-suppressed T1-weighted images, the initial CE subtracted images and the MIP.

Test re-test reliability is summarized in Table 1. Table 2 summarize the inter-rater agreement for the different classes of BPE.

Mean reading time was 21 s reading the initial CE fat-suppressed T1-weighted images, 18 s reading the initial CE subtracted images, 4 s reading the MIP and 38 s reading the combination of the initial CE fat-suppressed T1-weighted images, the initial CE subtracted images and the MIP.

Figs. 1–3 show examples of BPE assessment.

Table 1
Test-retest reliability of BPE assessment of the three raters (95%CI).

CE sequences	Rater 1	Rater 2	Rater 3
Initial CE fat-suppressed T1-weighted images	0.76 (0.56-0.96)	0.61 (0.41-0.80)	0.39 (0.13-0.64)
Initial CE subtracted images	0.77 (0.56-0.98)	0.53 (0.35-0.72)	0.76 (0.56-0.96)
MIP	0.83 (0.61-1.00)	0.66 (0.46-0.86)	0.78 (0.56-0.99)
Combination of all CE MRI images	0.81 (0.60-1.00)	0.77 (0.55-0.98)	0.79 (0.59-0.99)

Table 2
Interrater agreement (weighted analysis) of the three raters according to breast density. Data express as Percent Agreement (95%CI).

Breast Density (number of patient)	Initial CE fat-suppressed T1-weighted images	Initial CE subtracted images	MIP	Combination of all CE MRI images
Minimal (27)	0.84 (0.78-0.90)	0.92 (0.86-0.98)	0.78 (0.65-0.90)	0.83 (0.78-0.89)
Mild (81)	0.88 (0.85-0.90)	0.90 (0.88-0.93)	0.83 (0.80-0.86)	0.84 (0.80-0.88)
Moderate (38)	0.75 (0.69-0.81)	0.84 (0.81-0.88)	0.90 (0.88-0.92)	0.81 (0.77-0.85)
Marked (4)	0.67 (0.05-1.00)	0.67 (0.05-1.00)	1	1

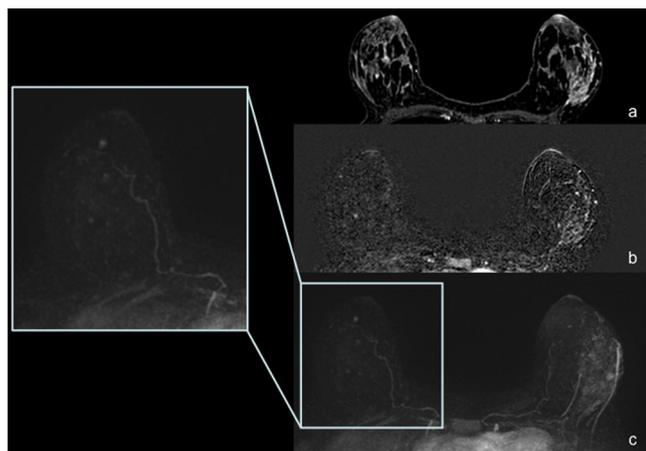


Fig. 1. Example of BPE assessment using the four reading strategies. BPE assessment by reading: (a) the initial CE fat-suppressed T1-weighted images was mild for all three raters, (b) the initial CE subtracted images was mild for rater 2 and rater 3, and BPE was minimal for rater 1, (c) the MIP was mild (left-sided box) for both rater 1 and rater 2, and BPE was minimal for rater 3. BPE assessment by reading the combination of all the CE sequences was mild for all the three raters. BPE assessment after consensus was mild.

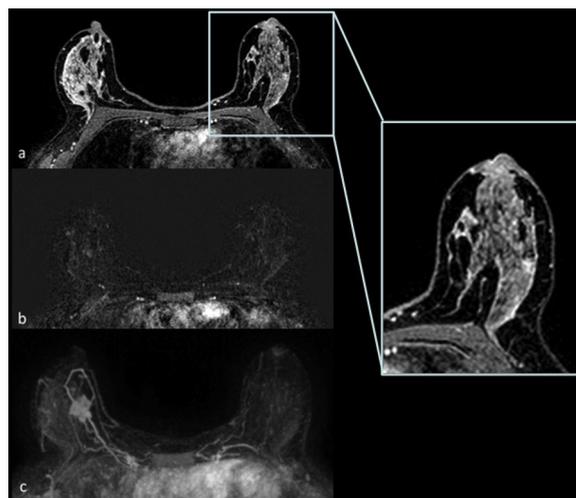


Fig. 2. Example of BPE assessment using the four reading strategies. BPE assessment by reading: (a) the initial CE fat-suppressed T1-weighted images was moderate (right-sided box) for rater 2 and rater 3, and BPE was mild for rater 1, (b) the initial CE subtracted images and (c) the MIP was moderate for all the three raters. BPE assessment by reading the combination of all the CE sequences was moderate for all the three raters. BPE assessment after consensus was moderate.

4. Discussion

Over the last few years, the use of breast MRI has increased for both diagnostic and screening indications [20,21]. Breast MRI report should include an overall description of the breast composition, including the amount of BPE [4]. BPE refers to the volume and the intensity of enhancement of fibroglandular breast tissue [4].

Quantitative method to assess BPE is an emerging topic [11]. However, no standardized method to assess BPE quantitatively has been found [11]. Indeed, assessment based on percentage is not recommended yet and the amount of BPE is currently performed by visual estimation and categorized on a four-point scale as minimal, mild, moderate and marked [4]. Considering that breast MRI examination includes several post-contrast images, we performed a study to evaluate the reliability of BPE assessment among three raters across contrast-enhanced MRI sequences of patients with unilateral breast cancer.

BPE assessment was performed in the contralateral healthy breast to avoid the influence of the presence of the tumor in BPE assessment reliability, according to the literature [11].

Regarding inter-rater reliability, we found that the combination of the initial CE fat-suppressed T1-weighted images, the initial CE subtracted images and the MIP and the use of only the MIP showed the highest reliability, with the first of the two reading strategies with the

highest 95%CI. However, we found that MIP showed the highest absolute agreement; this result could be related to the unique image evaluation that is needed for BPE assessment using only MIP, resulting in a more intuitive assessment. This data is particularly relevant in clinical practice; indeed it could be possible to have a reliable, quick and reproducible BPE assessment directly on a single image.

The use of only the initial CE subtracted images showed a higher reliability in comparison to the use of only the initial CE fat-suppressed T1-weighted images. The relative low reliability on the visual estimation of BPE using only the initial CE fat-suppressed T1-weighted images could be partially explained by the simultaneous visualization of the normal fibroglandular tissue that is enhanced (amount of BPE) and the normal fibroglandular tissue that is not; indeed, in this context, the assessment of the extent of small foci of enhancement of the normal fibroglandular tissue could be challenging. In addition, we were not able to find in literature images related to BPE assessment using only the initial CE fat-suppressed T1-weighted to use for training; therefore the reliability of BPE assessment using only this sequence could have been reduced.

Similarly to inter-rater reliability, the combination of all CE MRI images and the use of only the MIP showed the highest intra-rater

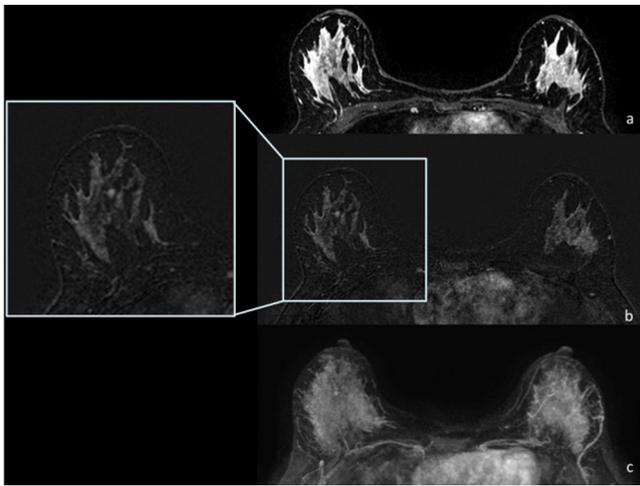


Fig. 3. Example of BPE assessment using the four reading strategies. BPE assessment by reading: (a) the initial CE fat-suppressed T1-weighted images and (c) the MIP was marked for all the three raters, (b) the initial CE subtracted images was marked (left-sided box) for both rater 1 and rater 3, and BPE was moderate for rater 2. BPE assessment by reading the combination of all the CE sequences was marked for all the three raters. BPE assessment after consensus was marked.

reliability. In addition, rater 1 showed a higher test-retest reliability using only the MIP than using the combination of all CE MRI images, probably due to the more intuitive assessment of MIP.

We performed a time record of BPE assessment using each reading strategy. Reading time in BPE assessment could be of interest in the perspective of breast MRI as a screening modality. Not surprisingly, the use of only the MIP for BPE assessment showed the lower reading time. On the contrary, the initial CE fat-suppressed T1-weighted images and the combination of all CE MRI images showed the highest reading time. The number of images seems to influence this result, but the reading time may have been affected by the characteristic of our patient sample, too. Our patient sample included patients with unilateral breast cancer that underwent breast MRI for presurgical staging, and in this clinical context, the optimal timing for breast MRI according to menstrual cycle may not have always been followed increasing BPE of some patients [22]. Indeed, our patient sample had a wide range of amount of BPE, from minimal to marked, possibly influencing our results of the reliability. Therefore, in ideal conditions, when MRI is performed also for other clinical indications, it is likely that the results will be even better than those of the present paper. However, it was not possible to estimate menstrual cycle influence on BPE assessment reliability due to the retrospective nature of the study. When BPE was divided according to different classes, no clinically significant differences are identifiable. Our study has several limitations. First, we did not perform any evaluation of the quality of the breast MRI examinations; among all the combinations, MIP could have been the most affected considering that MIP is a reconstructed image; however, we found high reliability among raters using only MIP, suggesting that the eventual artefacts did not affect the total amount of our results. Second, we did not support the visually assessment of BPE with a quantitative assessment. However, the aim of our study was to focus on high reliability of a visual estimation of BPE. The correlation with quantitative assessment as a surrogate of reference standard could be the scope of future research. In addition, we did not perform a correlation between BPE assessment and breast density on MRI because it was not the aim of our study. Finally, we performed reliability of BPE assessment only among three raters. However, the three raters had different years of experience, consequently it is highly likely that our findings could be similar to real daily clinical practice.

5. Conclusions

In conclusion, the combination of the initial CE fat-suppressed T1-weighted images, the initial CE subtracted images and the MIP showed the highest inter and intra-rater reliability. The use of only the MIP showed a high reliability with lower reading time compared to the combination of all CE MRI images, with potential for routine clinical usage.

Conflict of interest

All authors have no conflicts of interest and no disclosures of financial interest to report.

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