Optimization of Quantitative MRI Background Parenchymal Enhancement Metrics to Predict Breast Cancer Risk

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Purpose: Breast cancer is extremely common, accounting for 40,000 deaths annually in the U.S. alone. Early detection with imaging remains essential for minimizing mortality, particularly among those women at highest risk of developing breast cancer. With the exception of genetic tests (e.g. BRCA 1, 2 mutations), determining breast cancer risk primarily relies on family history and hormonal risk factors, and these markers perform poorly at the individual level. Physiologic enhancement of normal breast tissue on MRI, known as background parenchymal enhancement (BPE), has been proposed to be a biomarker of breast cancer risk that could enable individualized screening and chemoprevention strategies. Two prior studies have demonstrated that increasing qualitative BPE assessments are associated with breast cancer risk [1, 2]. However, qualitative BPE assessments are limited by inter-observer variability, and an accurate quantitative BPE approach could provide substantial clinical value. The purpose of this study was to develop a quantitative BPE measurement tool and to identify the optimal quantitative BPE metrics for determining breast cancer risk.

Methods: In this IRB approved, HIPAA compliant study, we used a case-control matched cohort comprised of women ≥ 18 years of age with no history of breast cancer who underwent high-risk screening breast MRIs from Jan 2006 through Dec 2011 at our institution. MRIs were performed at either 1.5 tesla (T) or 3T field strength with dynamic contrast enhanced (DCE) technique (pre- and post-contrast T1-weighted, fat-suppressed images acquired axially) using a dedicated breast coil. The cancer cohort included women who developed breast cancer at any time-point after the screening breast MRI but not identified on the MRI (n= 18 women; mean age, 47 ± 8.7 years; six patients with BRCA mutations). The control cohort was comprised of women matched 1:1 for age and BRCA status while maximizing follow-up time (mean = 47 ± 8.5 years). For each MRI, fibroglandular tissue (FGT) and BPE maps were calculated from the pre-contrast and first post-contrast (k0 at 90-120 sec) DCE MR images using an in-house developed semiautomatic quantitative method using customized software (Matlab, Mathworks, Natick, MA). BPE maps were calculated at varying enhancement thresholds ranging from 5% to 100%, with enhancement calculated as $(SI_1\text{-}SI_0)/SI_0 \times 100\%$, where SI_0 and SI_1 are the signal intensities for the pre-contrast and first post contrast images, respectively (Figure 1a). BPE metrics of BPE area (mm^2), ratio of BPE area to FGT area (BPE/FGT, %), and BPE intensity (median, max, mean, standard deviation [SD], skew, and kurtosis, %) were measured at each threshold. Differences in BPE metrics between the cancer and control cohorts were evaluated by Wilcoxon rank sum test, and optimal enhancement thresholds for significant BPE metrics were identified by comparing areas under the receiver operator characteristic curve (AUCs).

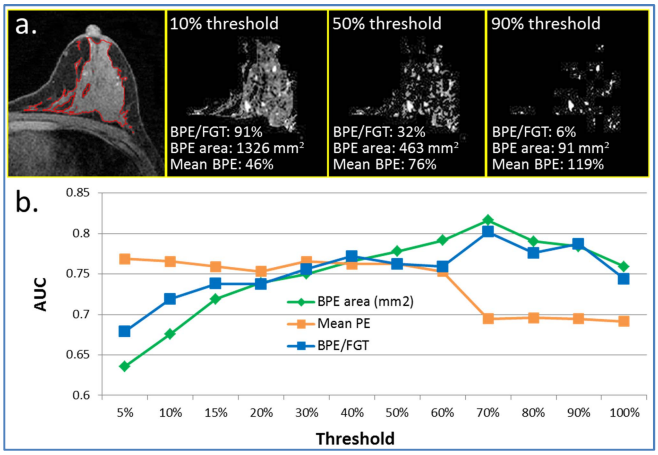

Figure 1. Optimization of quantitative BPE metrics. Example BPE maps (a) and performance (based on AUC) across thresholds (b).

Results: Quantitative BPE area, BPE/FGT ratio, and BPE intensity (median, max, mean, SD, and skew) all demonstrated significantly higher values in the cancer cohort than the no-cancer cohort, while BPE kurtosis did not (Table 1). Optimal enhancement thresholds varied across BPE metrics. The greatest AUCs for discriminating between the cancer and control cohorts were achieved using BPE area and BPE/FGT ratio at an enhancement threshold of 70% (AUC: 0.82 and 0.80, respectively; Figure 1b). The quantitative BPE metrics using optimized enhancement thresholds provided higher AUCs than previously reported qualitative BI-RADS BPE assessments[2, 3] (Figure 2).

Table 1. BPE measures for cancer vs. control cohorts.

Metric	Cancer (Mean ± SD)	Control (Mean ± SD)	Wilcoxon (P-value)	Max AUC	Optimal Threshold
BPE area	125 ± 306 mm²	18 ± 33 mm²	0.006	0.82	70%
BPE/FGT	8 ± 11 %	2 ± 3 %	0.008	0.80	70%
BPE intensity					
Median	78 ± 9 %	60 ± 29 %	0.027	0.78	60%
Max	185 ± 57 %	108 ± 73 %	0.001	0.79	70%
Mean	32 ± 14 %	21 ± 7 %	0.0008	0.77	5%
SD	23 ± 8 %	15 ± 7 %	0.004	0.78	15%
Skew	1.5 ± 0.92	0.99 ± 0.99	0.014	0.76	80%
Kurtosis	3.06 ± 3.31	2.89 ± 3.62	0.095	0.66	100%

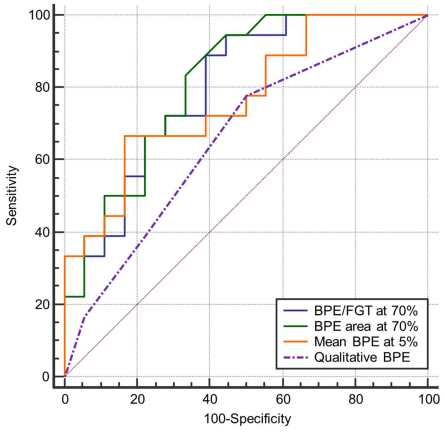

Figure 2. ROC curves of quantitative vs. qualitative BPE assessments for predicting cancer development.

Discussion: Quantitative BPE measurements are significantly higher in patients who develop breast cancer than in patients who do not and provide greater predictive power when compared to qualitative assessments. For BPE and BPE/FGT area, 70% enhancement threshold provided the best performance for predicting development of breast cancer. Future studies are warranted to confirm the value of quantitative BPE measurements to determine breast cancer risk in larger patient cohorts.

References: 1. King V, et al. Radiology 2011. Jul; 260(1):50-60. 2. Dontchos BN, et al. RSNA 2014. 3. D'Orsi CJ, et al. ACR BI-RADS® Atlas, American College of Radiology 2013.

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