# Association of the Amount of Fibroglandular Tissue on MRI and background parenchymal enhancement on DCE-MRI with Breast Cancer Risk

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**Introduction**: Increased mammographic breast density is associated with an increased risk for breast cancer [1]. Recent studies have shown that the background parenchymal enhancement (BPE) from DCE-MRI has been correlated with breast cancer risk; a higher grade of BPE correlates with an increased risk for breast cancer [2, 3]. The amount of fibroglandular tissue (FGT) and the grade of BPE are assessed using standard categorical scales. Furthermore, BPE can be measured quantitatively and may provide additional information regarding breast cancer risk. The purpose of our study is to investigate whether the amount of fibroglandular tissue (FGT) on MRI, the grade of BPE or a quantitative analysis of BPE correlates with breast cancer risk.

**Materials and Methods**: Bilateral DCE-MRI of the breast was performed on a Siemens 3T magnet (Tim Trio) using a dedicated 7 channel breast coil (Invivo). Our standard DCE-MRI protocol uses a 3D VIBE sequence (resolution 1.1 x 0.9 x 1.0 mm) with fat suppression was acquired for four consecutive frames; administration of Gd-DTPA contrast agent was administered after the first frame. Between March 2008 and September 2011, 44 consecutive asymptomatic BRCA1/2 mutation carriers underwent a MRI guided biopsy for an enhancing lesion that was occult on mammography and ultrasound. This group of patients was matched for age and year of MRI-guided biopsy (within 0-3 yrs of age and 0-1 yr of biopsy) in patients without known BRCA gene mutation who underwent MR biopsy. Two independent blinded readers assessed amount of FGT and the grade of BPE using a categorical scale: FGT – Fatty, Scattered, Heterogeneously Dense, Dense; BPE – Minimal, Mild, Moderate, Marked (based on ACR criteria for FGT and based on proposed BIRADS criteria for BPE). Afterwards, a third independent reader performed a quantitative kinetic assessment of the enhancing foci in normal appearing FGT that were presumed to be BPE. In addition, we used the principal component analysis (PCA) method [4] to extract the BPE information from the whole breast, rather than manually selected small areas. The PCA processing was performed using IDL software. A single reader manually drew a ROI around the entire breast on a single sagittal image that did not contain the suspicious lesion and was used to measure BPE. PCA transformation was then applied in accordance with a recently published study [4] which effectively decomposed datasets into eigenvalues, eigenvectors, and projection coefficient maps. The first principal component captured the major source of variance, which was the signal change between pre- and post-contrast images and was presumed to reflect BPE. The PCA method was then applied to two additional slices for each patient for confirmation. For BPE, the primary eigenvector was used for the measurement of delayed enhancement and early enhancement rate. Signal percent enhancement (PE) was calculated as $(SI_{post} - SI_{pre})x100/SI_{pre}$, where $SI_{pre}$ and $SI_{post}$ are the signal intensity before administration of contrast (i.e. 1st time point) and at the last time point, respectively. For kinetic analysis, eigenvectors were normalized between 0 and 1. The difference between the 2nd and 3rd time points (S23) was measured as the early enhancement rate. After the above analyses, the pathology and radiology medical records of both groups of patients were retrospectively reviewed. Data collected included the patient age, menopausal status, lesion size, lesion type, morphologic and kinetic features of the lesions, and the histopathologic results.

**Results and Discussion**: Forty-four MR guided core biopsies were performed on 40 BRCA1/2 carriers yielding 4 (9.1%) malignancies. Forty-four MR guided core biopsies were performed on 42 women in our control group yielding 3 (7.1%) malignancies. Given the few number of malignancies in both groups of women, we excluded the patients with a malignant biopsy result from our analysis. Our patient cohort consisted of 36 BRCA1/2 mutation carriers of whom 12 (33.3%) women were post-menopausal. The control group consisted of 40 women, of whom 11/40 (27.5%) women were post-menopausal. Table 1 reveals FGT, BPE, and BPE PCA results for pre-menopausal and post-menopausal BRCA carriers and respective controls. There was a statistically significance difference between percent enhancement (PE) of pre-menopausal and post-menopausal BRCA carriers, as demonstrated in Figure 1. It was also found that the menopausal BRCA group had higher S23 (early enhancement rate) than the pre-menopausal BRCA group. Such differences between pre- and post-menopausal were not observed in the age-matched control groups. These findings substantiate our hypothesis that the breast cancer risk is associated with breast density. In the future, this hypothesis will be further evaluated with a larger cohort.

**Table 1** MRI and PCA analysis results for BRCA carriers and controls

| | BRCA1/2 mutation carriers | | Control | |
|---|---|---|---|---|
| Parameters | Pre-menopausal (n = 24) | Post-menopausal (n= 12) | Pre-menopausal (n=29) | Post menopausal (n =11) |
| FGT on MRI | | | | |
| Predominantly fatty | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Scattered FGT | 1 (4.2%) | 4 (33%) | 6 (20.7%) | 3 (27.3%) |
| Heterogenously dense | 17 (70.8%) | 5 (41.7%) | 15 (51.8%) | 6 (54.5%) |
| Dense | 6 (25%) | 3 (25%) | 8 (27.6%) | 2 (18.2%) |
| BPE | | | | |
| Minimal | 2 (8.3%) | 3 (25%) | 2 (6.9%) | 4 (36.4%) |
| Mild | 9 (37.5%) | 3 (25%) | 13 (44.8%) | 5 (45.5%) |
| Moderate | 11 (45.8%) | 4 (33.3%) | 11 (37.9%) | 2 (18.2%) |
| Marked | 2 (8.3%) | 2 (16.7) | 3 (10.3%) | 0 (0%) |
| BPE PCA | | | | |
| PE | 28.45 ± 15.93 | 19.45±5.10 | 32.47 ± 16.03 | 33.13±5.61 |
| S23 | 0.43 ± 0.14 | 0.52±0.07 | 0.44±0.14 | 0.43±0.14 |

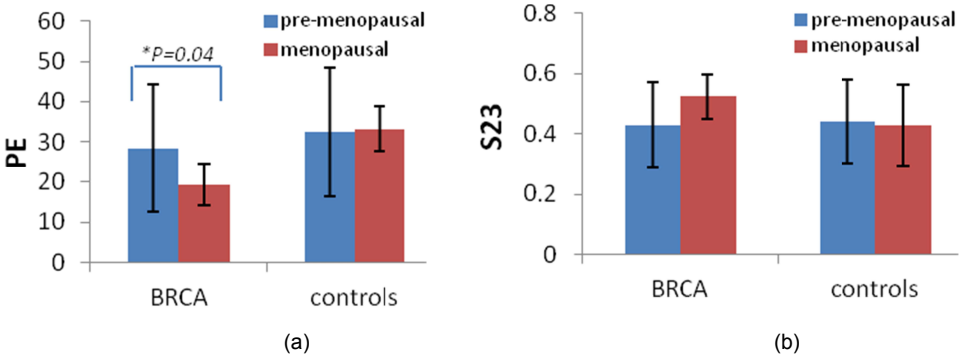


**Figure 1** (a) Mean PE for pre-menopausal and menopausal BRCA patients and controls. (b) Mean S23 for pre-menopausal and menopausal BRCA patients and controls.

**References**: 1. Harvey, J.A. Radiology, 2004. 2. Jansen, S.A. Eur Radiol, 2011. 3. King, V. Radiology, 2011. 4. Eyal et al, J Magn Reson Imaging 2009; 30:989-998