# Differentiation of Benign from Malignant Non-Mass-Like-Enhancement in BRCA 1 Mutation Carriers Using Quantitative Kinetic Analysis

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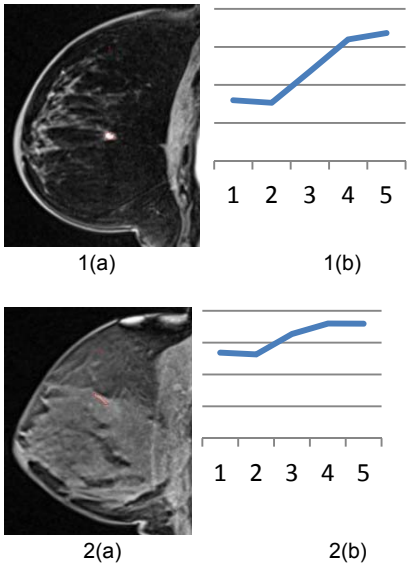
**Introduction:** Annual screening breast MRI is recommended in BRCA1 and BRCA2 mutation carriers given their high-risk for developing mammographically occult breast cancers [1]. Studies show the breast carcinomas in BRCA1 carriers often have benign morphological features presenting as round masses with smooth margins [2]. However, these young women often have indeterminate enhancing non-mass–like enhancement (NMLE) detected on breast MRI. A MR biopsy is often recommended to exclude ductal carcinoma-in-situ (DCIS). However, this malignancy is rare in BRCA1 carriers. Therefore, another imaging tool that may help distinguish between benign physiologic NMLE and DCIS would be clinically significant in this high-risk population who undergo close radiologic surveillance. Our hypothesis is that the ability to quantify the kinetic analysis of enhancing lesions may help reduce the number of MR biopsies and MR follow-up that are recommended in BRCA1 patients.

**Materials and Methods:** Bilateral dynamic contrast enhanced breast MRI was performed on a Siemens 3T magnet (Tim Trio) using a dedicated 7 channel breast coil (Invivo). MR biopsies were performed using the Suros ATEC device. For these patients, DCE-MRI using a 3D VIBE sequence (resolution 1.4 x 0.9 x 1.5 mm) with fat suppression was acquired for at least five consecutive frames; administration of Gd-DTPA (Magnevist, Bayer) contrast agent was administered after the first frame. Between July 2008 and September 2011, 27 consecutive asymptomatic BRCA1 mutation carriers underwent a MRI guided biopsy for a NMLE lesion that was occult on mammography and ultrasound at our institution. The pathology and radiology medical records of these patients were retrospectively reviewed. Data collected included patient age, last menstrual period (LMP), mammographic breast density, background parenchymal enhancement (BPE), BIRADS lesion features (size, distribution, internal enhancement pattern, and kinetic curve analysis of the NMLE lesions). Post-image processing was performed using IDL software. After careful review of the MRI images and associated report, a single reader manually drew regions of interest (ROI) around the suspicious lesion. A second ROI was drawn around the entire breast on a separate single sagittal image that did not contain the suspicious lesion and was used to measure BPE quantitatively using a linear principal component analysis (PCA). PCA transformation was applied to the second ROI to decompose the datasets into eigenvalues, eigenvectors, and projection coefficient maps [3]. The primary principal component was assumed to reflect BPE. The PCA method was then applied to two additional slices for each patient for confirmation. Signal percent enhancement (PE) was calculated as $(SI_{post} - SI_{pre})x100/SI_{pre}$, where $SI_{pre}$ and $SI_{post}$ are the signal intensities before administration of contrast (i.e. 1st time point) and at the last time point, respectively. The lesion signal curve was normalized to between 0 and 1 and the difference between the 2nd and 3rd time points (S23) was measured as the early enhancement rate. For BPE, the primary eigenvector was used for the measurement of PE and S23.




**Figures 1 and 2** (a) ROIs drawn around malignant and benign lesions, respectively. (b) Signal enhancement curves corresponding to the lesions.

**Results and Discussion:** Twenty-seven MR guided core biopsies were performed on twenty-seven BRCA1 carriers yielding 4 (14.8%) malignancies. Two malignancies were DCIS, one malignancy was invasive ductal carcinoma, and the fourth lesion was an invasive lobular carcinoma. All 27 NMLE lesions were linear and/or segmental in distribution, 15 (55.6%) had clumped and 12 (44.4%) had heterogeneous internal enhancement. Thirteen (48.1%) had Type 1, 10 (37%) Type 2, and 4 (14.8%) had Type 3 kinetic curve. Of the 27 lesions, there was no correlation between the LMP, mammographic density, and BPE. There was no statistically significant difference in the internal enhancement pattern, distribution and kinetic curve assessment of the NMLE lesions that were benign vs. malignant. Using our quantitative analysis, we found the percent enhancement (PE) measurement to be helpful in distinguishing between benign and malignant lesions. However, neither PE nor S23 reached statistical significance with p=0.19 and p=0.72, respectively. Table 1 displays the results of PE and S23 for both malignant and benign lesions as well as associated BPE; these results are summarized graphically in Figure 3. Conventional assessment of the morphologic and kinetic features of NMLE could not predict the likelihood of NMLE in BRCA1 women. Although we were limited by the small number of malignancies, our retrospective review found that a quantitative analysis of contrast uptake may help to identify those NMLE lesions that should be biopsied.

| | Lesion PE | BPE PE | Lesion S23 | BPE S23 |
|---|---|---|---|---|
| Benign | 79.04±40.19 | 29.37±12.28 | 0.48±0.16 | 0.44±0.16 |
| Malignant | 107.38±25.96 | 32.32±24.08 | 0.50±0.09 | 0.58±0.08 |

**Table 1** Results of percent enhancement (PE) and slope between 2nd and 3rd time points (S23) for malignant/benign lesions and BPE.

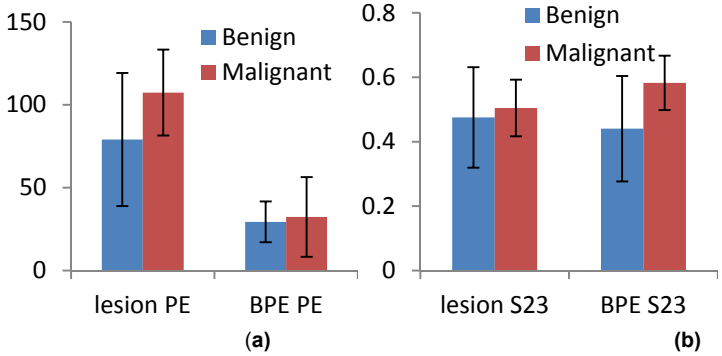



**Figure 3** (a) Mean PE for benign and malignant lesions compared to PE of BPE in BRCA1 patients. (b) Mean S23 for benign and malignant lesions compared to S23 of BPE in BRCA1 patients.

**References**: 1. Saslow D, et al. CA Cancer J Clin 2003; 53(3):141-69. 2. Shah P et al, Breast Cancer Res Treat 2009; 118(3):539-46. 3. Eyal E, J Magn Reson Imaging 2009; 30:989-998.