Assessment of Background Parenchymal Enhancement in Breast MRI of BRCA 1/2 Mutation Carriers Compared to Matched Controls

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PURPOSE

Lifetime breast cancer risk in female BRCA mutation carriers is approximately 85% in BRCA 1 mutation carriers and about 45% in BRCA 2 mutation carriers. Recent studies have shown that the background parenchymal enhancement (BPE) from dynamic contrast-enhanced MRI correlates with breast cancer risk. BPE reflects the vascularity of the breast parenchymal tissue and is sensitive to hormonal changes. Assessment of BPE kinetic properties of BRCA mutation carriers in comparison with non-mutation carriers may help better understand the role of the BRCA gene in breast physiology and improve diagnostic accuracy of MRI in this population with an increased risk of familial breast cancer. Hence, the purpose of this study is to investigate whether quantitative kinetic analysis of benign lesions and background parenchyma (BP) in breast MRI can elucidate differences between BRCA carriers and sporadic controls with high risk for breast cancer.

METHODS

After IRB approval, a retrospective review of 360 women who underwent a breast MRI using a whole body 3T MRI system (Siemens, Erlangen) and subsequent MRI-guided biopsy between March 2008 and June 2012 was performed. DCE-MRI data were acquired using a sagittal 3D VIBE sequence with TR/TE=4.01 ms/1.52 ms, resolution 1.4 x 0.9x1.5mm, and fat suppression for five frames (40 sec each). After the first frame, a single dose of Gd-DTPA (Magnevist, Bayer, Germany) contrast agent with a dose of 0.1 mM/kg was injected at 2 mL/sec. We identified 49 BRCA 1/2 mutation carriers and 49 control cases with benign lesions. Indications for MRI in the control cohort included strong family history (n = 22), personal history of breast cancer (n = 11), personal history of high-risk lesion (n = 13) and newly diagnosed breast cancer (n = 2) and nipple discharge (n = 1). Controls were matched with BRCA patients for age, lesion type, similar pathology results and year of MRI-guided biopsy. Principal component analysis was applied to extract the characteristic signal enhancement pattern of background parenchyma from DCE-MRI data [1]. The principal eigenvector of BPE was used for quantitative analysis of dynamic signal in background parenchyma (B) in terms of initial enhancement ratio (IER) and delayed enhancement ratio (DER) that correspond to % enhancement at 80s and 160s post-contrast injection, respectively. IER and DER were chosen to quantify wash-in and delayed contrast enhancement characteristics, respectively. Statistical analysis was performed using the Chi-square and Student's t-tests.

RESULTS

Control B-IER and B-DER were significantly higher than BRCA cases in all women with benign lesions (p = 0.005, p = 0.005, respectively). In the BRCA+ group, there was no significant difference between pre and post-menopausal women (Fig.1a). In contrast, control premenopausal women had significantly higher B-IER (p=0.05) and B-DER (p=0.02) than the control postmenopausal women (Fig.1b). Among the premenopausal women, the BRCA group had significantly lower B-IER (p=0.006) and B-DER (p=0.003) than the control group (Fig.1c). However, such difference between BRCA and control groups was not seen in the post-menopausal women (Fig.1d).

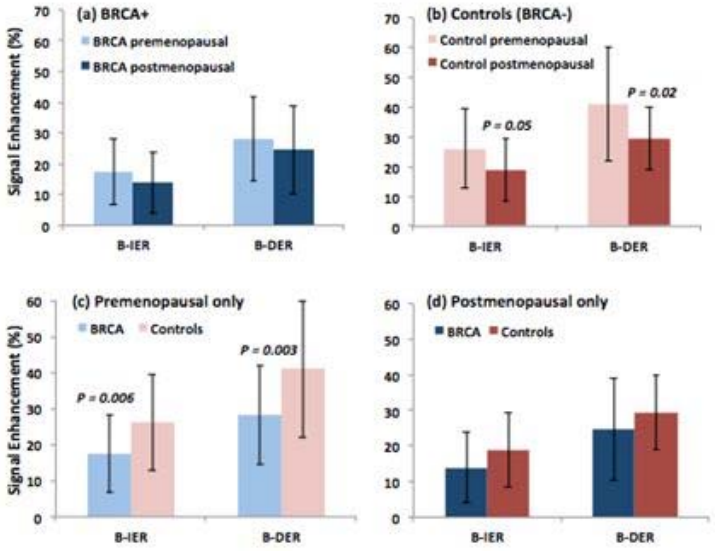

Figure 1. (a) Mean B-IER and B-DER for premenopausal and postmenopausal BRCA patients. (b) Mean B-IER and B-DER for premenopausal and postmenopausal control patients. (c) Mean B-IER and B-DER for premenopausal BRCA patients and controls. (d) Mean B-IER and B-DER for postmenopausal BRCA patients and controls.

DISCUSSION

Recent studies have suggested the need for a better understanding of BPE and the observed effects of hormonal fluctuations on BPE [2]. In the literature, there is scant information on the effect of the BRCA gene mutation on breast physiology and enhancement kinetics. In our study, the response of BP kinetic enhancement to hormonal fluctuations in BRCA mutation carriers occurred to a lesser extent than to controls; these findings suggest that there are biologic differences between BRCA carriers and sporadic high-risk controls. Our results also indicate that the BRCA gene mutation has multifactorial and complex clinical and biologic implications. The decreased responsiveness to physiologic hormonal changes in the BRCA carriers compared to high-risk controls suggests that the BRCA gene may alter the local environment and surrounding BPE, accounting for these findings.

CONCLUSION

The varying responsiveness of BPE to menopausal status change in the two populations suggests that its etiology is multifactorial. BPE may serve as an imaging biomarker in BRCA carriers who undergo annual screening MRI and should be further explored. In addition, high levels of BPE may be an indicator that high-risk women, including BRCA gene mutation carriers, may benefit from chemoprevention [3].

REFERENCES

1. Amarosa AR et al. Radiology 2013;268(2):356-365. 2. Price ER et al. Eur Radiol 2014;24(1):162-168. 3. Weinstein S. Radiographics 2014;34(1):247-249.

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