EFFECT OF RISK-REDUCING SALPINGO-OOPHORECTOMY ON BREAST MRI FIBROGLANDULAR TISSUE AND BACKGROUND PARENCHYMAL ENHANCEMENT IN *BRCA1/2* MUTATION CARRIERS: A QUANTITATIVE ASSESSMENT

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TARGET AUDIENCE: Radiologists, oncologists, and quantitative scientists interested in imaging biomarkers of breast cancer risk reducing interventions in high-risk women.

PURPOSE: Women with *BRCA 1/2* mutations are at high risk for developing breast cancer. Several risk-reducing interventions exist such as risk-reducing salpingo-oophorectomy (RRSO), prophylactic mastectomy, and chemoprevention with raloxifene or tamoxifen.[1] The purpose of this study is to perform an accurate and robust quantitative assessment to measure the effect of RRSO on breast MRI fibroglandular tissue volume (FGT) and background parenchymal enhancement (BPE) in *BRCA1/2* mutation carriers.

METHODS: This study was conducted using a fully automated breast MRI image segmentation method for quantitative FGT and BPE estimation. Beginning with bilateral clinical MRI scans, we first separated each breast in the T1-weighted non-fat-suppressed sagittal images using a previously validated chest wall line extraction algorithm.[2] Within each segmented breast, we applied a previously validated FGT segmentation algorithm to estimate the FGT content.[3] The absolute volume of FGT (|FGT|) and the percentage of the FGT volume relative to the volume of the entire breast (FGT%) were computed. BPE was estimated on a voxel-wise basis, by identifying enhanced voxels in the subtraction (SUB) images (SUB=post-contrast – pre-contrast); where a voxel is considered enhanced if the intensity value (*Is*) in the SUB image increases at least 30% above that (*Ip*) of the corresponding pre-contrast image (i.e., *Is*/*Ip* ≥30%). This minimum cutoff ratio of 30% was determined from the manual BPE segmentation (performed by a 15-year experienced breast imaging radiologist) using a separate training sample dataset. The whole-breast segmentation masks obtained from the T1 series were translated to the corresponding pre-contrast and first time-point subtraction (SUB 1) series after a prior inter-series alignment by rigid registration. Following this, the enhanced voxels in the SUB 1 images were identified within the whole-breast area and the absolute volume of the total background enhancement (|BPE-b|) was computed. Likewise, the FGT segmentation masks obtained from the T1 series were also translated after alignment to the pre-contrast and SUB 1 series and within the FGT area, the absolute volume of the enhancement (|BPE-f|) was computed. Three relative (i.e., percentage-based) measures were also computed for BPE: percentage of |BPE-b| relative to the absolute volume of the whole-breast (BPE-b/b); percentage of |BPE-f| relative to the absolute volume of the FGT (BPE-f/f), and percentage of |BPE-f| relative to the absolute number of the whole-breast (BPE-f/b). Therefore, 7 measures (2 for FGT and 5 for BPE; Table 1) in total were computed for both the pre-RRSO and post-RRSO MRI scans for each woman. The mean (±SD) across scans for each measure in both the pre-RRSO and post-RRSO groups were computed and the 7 measures were compared using a paired *t*-test for significance between the pre-RRSO group and post-RRSO group.

RESULTS: We analyzed a cohort of 52 *BRCA1/2* mutation carriers with who underwent bilateral breast MRI before and after RRSO at our institution (a total of 104 MRI scans, Fig. 1 and Table 1). Two of these women were excluded for BPE estimation as their pre-contrast series were not available; but were included for FGT estimation. Five women were diagnosed with breast cancer at a median of 3.4 years after RRSO.

Table 1. Quantitative comparison of the 7 measures on quantifying FGT and BPE before and after RRSO. The p-values refer to the comparison between pre- and post-RRSO for the entire dataset. P-values were not shown for the comparison within only the cancer cases, due to small sample size.

		|FGT| [cm^3]	FGT% [%]	|BPE-b| [cm^3]	|BPE-f| [cm^3]	BPE-b/b [%]	BPE-f/f [%]	BPE-f/b [%]
All cases	pre-RRSO	206.80±100.10	31.09±9.94	0.27±0.24	0.084±0.087	35.98±19.66	36.96±21.41	11.67±8.56
	post-RRSO	205.64±87.54	30.57±8.56	0.16±0.14	0.048±0.045	27.90±16.84	28.34±18.52	8.43±5.37
	P-value	*0.773*	*0.950*	*0.007*	*0.010*	*0.030*	*0.034*	*0.026*
5 cancer cases	pre-RRSO	164.62±59.22	33.30±8.22	0.20±0.15	0.067±0.038	55.97±12.00	62.48±12.13	21.50±8.56
	post-RRSO	160.03±79.26	32.89±8.35	0.22±0.19	0.071±0.078	36.21±16.33	35.38±22.21	11.94±7.74

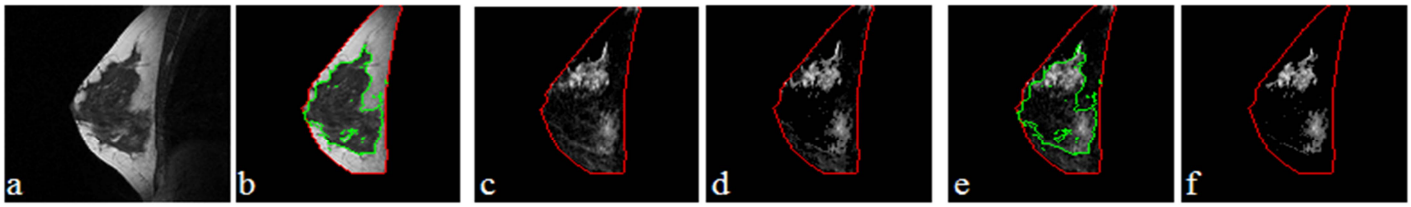

Fig. 1: FGT and BPE estimation. a. T1 image. b. Whole-breast segmentation (red) and FGT estimation (green). c. SUB 1 image. d. BPE estimation on the whole-breast (BPE-b). e. Translated FGT estimation (green) on the SUB 1 image. f. BPE estimation over the FGT area on SUB 1 image (BPE-f).

DISCUSSION: After RRSO, a significant reduction ($p<0.05$) is observed in all of the 5 BPE-related measures, while no significant difference is seen in any of the FGT measures for the full cohort. The absolute measures of BPE appear to be more significant, potentially due to directly measuring the actual amount of enhancing tissue, rather than a relative percentage over the entire breast. Comparing the 5 cancer cases against the full cohort, higher measures in |BPE-b| and |BPE-f| were observed after RRSO, and higher measures in BPE-b/b, BPE-f/f and BPE-f/b were observed both before and after RRSO, suggesting that these measures may be used to indicate women associated with higher risk of developing breast cancer after RRSO, who may be potential candidates for additional risk-reducing interventions. Further work is underway to validate these findings in larger prospective high-risk populations.

CONCLUSION: Quantitative rates of BPE-related measures are different before and after RRSO in *BRCA 1/2* carriers, while FGT-related measures are not. Such BPE-related measures could potentially be used as imaging biomarkers to assess response to RRSO as a risk reduction intervention, and may help to further sub-stratify breast cancer risk after RRSO for these high-risk women.

REFERENCES:

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