Title: Changes in global longitudinal strain according to *BRCA1/2* mutation status in patients with history of breast cancer treated with anthracyclines

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Background: Recent studies have suggested an association between *BRCA1/2* mutations and cardiovascular disease related to the potential deleterious effects of early surgical menopause and the cardiac toxicity of breast cancer treatment. Furthermore, laboratory investigations have demonstrated increased susceptibility of *BRCA1/2* mice to anthracycline-related cardiac toxicity. However, at the present time there is no human data that confirms these findings.

Methods: Our study tested the hypothesis that *BRCA1/2* mutation carriers have increased susceptibility to anthracycline-related cardiac toxicity compared to women with sporadic breast cancer. 116 women with a history of breast cancer treated with anthracycline therapy within the prior six months underwent assessment of baseline clinical and echocardiographic variables. From the original cohort, 32 patients with follow-up echocardiograms were analyzed to determine changes in myocardial function over time. Speckle tracking strain imaging analysis was performed using Epsilon Imaging® software.

Results: Mean age of the study participants was 50.5 years. *BRCA1/2* mutations were present in 21.9%. Co-morbidities included hypertension in 25%, diabetes in 9.4%, and hyperlipidemia in 18.8%. Average doxorubicin dose was 245.2 mg/m^2. Follow-up echocardiograms occurred on average 2.7 years after the baseline study. Baseline global longitudinal strain (GLS) was 11% greater in the BRCA+ versus BRCA- patients (-18 vs. -16). At follow-up, *BRCA+* patients had a greater proportional decline (16%) in GLS compared with *BRCA*- patients (10%). After excluding patients with hypertension who were limited to the *BRCA*- group, the the larger proportional decline in strain persisted (16% vs. 11%) for *BRCA+* patients.

Conclusions: In patients with a history of breast cancer treated with anthracyclines, those with a *BRCA* mutation had a greater proportional decline in GLS compared with control subjects over an average of 2.7 years post-treatment. Additional studies are necessary to further explore the potential interaction between *BRCA* status and cardiac toxicity related to anthracycline therapy.