**Title:** Assessing Acute Cardiac Inflammation after Left-sided Breast Cancer Radiotherapy with Hybrid PET/MRI

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## Structured Abstract:

INTRODUCTION: Breast cancer accounts for 25% of total yearly female cancer mortalities. Adjuvant radiation therapy of the breast plays a vital role to breast cancer treatment and has shown to improve both local control and overall survival. The five-year survival rate for breast cancer is now 89%. However, patients with left-sided breast cancer are at an increased risk of coronary artery disease and myocardial infarction due to the proximity of the heart to the high radiation dose. Using hybrid PET/MR imaging, cardiac abnormalities, changes in myocardial viability, and coronary artery disease can be assessed noninvasively. A previous canine study done in our lab demonstrated that hybrid PET/MRI detected an increase in myocardial perfusion and was associated with a global inflammatory response after a low radiation dose exposure. These responses were as early as one week and confirmed with histology one year after radiotherapy. These findings suggest that radiation induced cardiac effects are occurring at much lower radiation doses than previously believed.

HYPOTHESIS: We believe that hybrid PET/MR imaging acquired serially will: 1) Detect an inflammatory response, changes in myocardial perfusion, and the development of scar/fibrosis in breast cancer patients that were treated with chemo-radiation; 2) Aid in correlating these responses to regional radiation dose deposition.

SPECIFIC AIMS: Identify the presence of acute low-dose radiation induced cardiac toxicity, including in left-sided breast cancer patients undergoing radiotherapy using hybrid PET/MRI.

STUDY DESIGN: A longitudinal cardiac imaging study composed of 15 left-sided breast cancer patients before and after standard radiotherapy is proposed. Patients will be imaged at baseline, within the first month and the first-year post radiotherapy using a hybrid 3T-PET/MRI system. The PET imaging protocol is designed to assess changes in 13N-ammonia myocardial perfusion under rest and adenosine stress condition; followed by a 18F-FDG PET scan to image macrophage-related inflammation during the same imaging session. Cardiac perfusion will be quantified using a 1-compartment tracer kinetic model, FlowQuant software. Cardiac inflammation will be calculated respect to the change in the mean standard uptake value. Both perfusion and inflammation results will be grouped as per the standardized 17-segment model for tomographic imaging of the left ventricle. The MR imaging protocol, acquired simultaneously will be used to identify mature fibrosis or scar which consist of standard cine imaging and slice-matched T1-weighted imaging followed by cardiac-gated 3D-coronary MR angiography and standard 2D late gadolinium enhancement imaging. Mature fibrosis or scar will be quantified by fusing and volume-rendering each MR dataset to simultaneously display coronary artery, vein and myocardial scar. Measures obtained from the radiation dose distributions will be correlated to all measures described above.