Early Detection of Cardiotoxicity by Advanced Cardiac Imaging and a Novel Biomarker in Breast Cancer Patients Undergoing Chemotherapy

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Background

Survival from breast cancer has significantly improved due to advances in detection, chemotherapy and radiation therapy.

However, the incidence of cardiovascular events related to cancer therapy has also risen considerably and account for substantial morbidity and mortality in breast cancer survivors.

Current methods of assessment cardiac function in response to cancer treatment include two-dimensional echocardiography and MUGA scans that measure the left ventricular ejection fraction (LVEF).

Serial assessment of LVEF alone by these techniques is inadequate for the monitoring of chemotherapy related cardiotoxicity as reductions in LVEF are observed only after significant and irreversible myocardial damage has occurred.

Detection of early cardiotoxic changes with subclinical dysfunction would allow interventions such as alteration in chemotherapy and/or addition of cardiac medications to prevent subsequent cardiovascular morbidity and mortality.

Hypothesis

Non-invasive modalities such as cardiac magnetic resonance imaging (CMR), 3D echocardiography, strain imaging and novel biomarkers allow accurate detection of early cardiac dysfunction in breast cancer patients undergoing chemotherapy.

Specific Aims

- To detect early myocardial injury.
- To evaluate early predictors of left ventricular dysfunction.
- To evaluate timing of monitoring during or post treatment.

Design

Trial design: Prospective, cohort study with internal control conducted as a single center pilot study at the University of Connecticut Health Center Breast Cancer Clinic.

Inclusion: Women between ages of 18-75 years with a new diagnosis of stage I-III breast cancer that are to undergo treatment with trastuzumab or anthracycline based chemotherapy.

Exclusion: Patients with a history of cardiovascular disease and/or an LVEF < 55%, hypertension (BP >140/90 mmHg) and presence of a pacemaker. Additionally, patients with past mediastinal radiotherapy, renal/hepatic dysfunction (GFR < 30 ml/min; AST/ALT > 100 IU/L), and history of claustrophobia.

Eligible patients that are consented and enrolled undergo blood investigations, cardiac MRI, two and three-dimensional echocardiography at described time points.

Primary imaging and biomarker end-points:

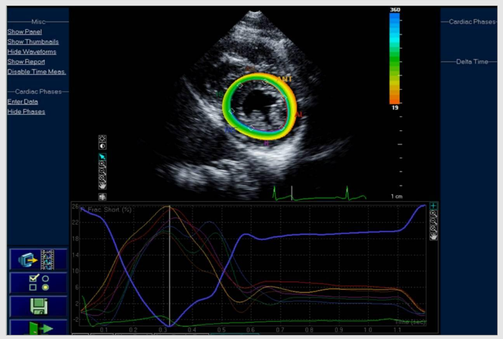
1. Decline in LVEF by CMR and 3D-echo undetected by conventional methods 2. Presence of either myocardial fibrosis or edema by CMR. 3. Changes in myocardial deformation detected by echo or CMR strain 4. Increase in cardiac biomarkers

Secondary clinical end-points:

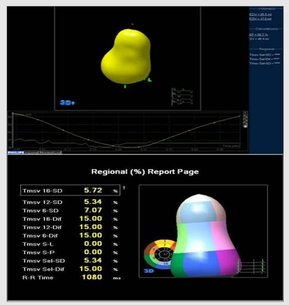
1. Development NYHA class I-IV heart failure 2. Decrease in LVEF to ≤ 50%

Test/Procedure	Baseline	After 2nd Cycle of Chemotherapy	2 Weeks After Last Cycle of Chemotherapy	6 Months After last Cycle of Chemotherapy
Cardiology visit			X	
Routine blood work	X	X	X	X
Lipid profile	X	X	X	X
B-type Natriuretic Peptide (BNP)	X	X	X	X
C-Reactive Protein	X	X	X	X
Troponin I	X	X	X	X
EKG	X	X	X	X
Echocardiogram	X	X	X	X
Cardiac MRI	X	X	X	X
Serum p17	X	X	X	X

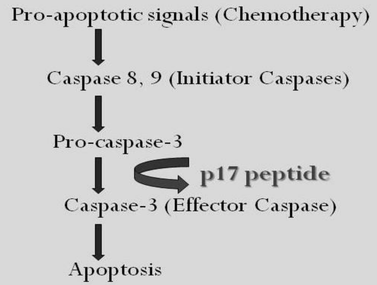
Strain Analysis by Tissue Doppler Imaging: Quantify Regional Myocardial Deformation



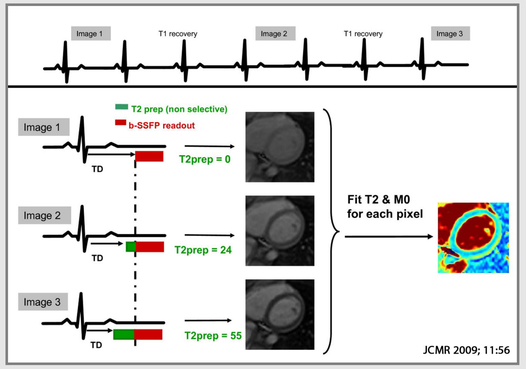
3-Dimensional Echocardiography: LV Function and Morphology



Serum p17 Peptide Levels: Assessed by Biochemical Assay

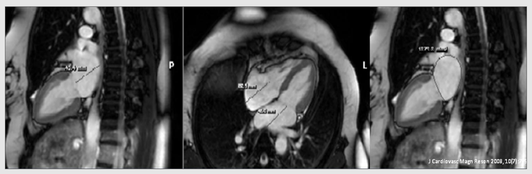


T2 Mapping by CMR: A Quantitative Assessment of Myocardial Edema



Cardiac MRI: Assessment of Left Ventricular Function and Volumes

Left Atrial Volume by CMR: Assessment of Diastolic Function



Present Accrual/Contact Information

- Target enrollment: 20 patients
- Current enrollment: 15 patients
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