Title: Cardiac high energy phosphates in breast cancer patients during anthracyclines: relationship with ejection fraction and high sensitivity cardiac troponin

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BACKGROUND
Early identification of anthracycline-induced cardiotoxicity during breast cancer treatment may guide strategies and treatments to modify both short and long term cardiac events. We assessed and compared the utility of $^{31}$P Magnetic Resonance Spectroscopy ($^{31}$P MRS), cardiac magnetic resonance imaging (CMR) and high sensitivity cardiac troponin-I (cTnI) in this clinical setting.

METHODS
20 female patients with primary breast cancer, scheduled to receive anthracycline-based chemotherapy either adjuvantly or neoadjuvantly, had CMR scans to assess left ventricular ejection fraction and $^{31}$P MRS to assess high energy phosphates (phosphocreatine to adenosine triphosphate (PCr/ATP) ratio) performed at 3 time-points: baseline (pre-chemo), mid-chemo and end of chemo. Plasma high sensitivity cardiac troponin-I and electrocardiograms (ECG) were also performed at these same time points.

RESULTS
Plasma cardiac TnI increased progressively during chemotherapy from baseline to mid-chemo ($1.35\pm0.81$ to $4.40\pm2.64$ng/l; $p=0.0001$) and from mid- to end-chemo ($4.40\pm2.64$ to $18.33\pm13.23$ng/l; $p=0.0001$). LVEF remained unchanged between pre-chemo and mid-chemo ($61.6\pm4.4$ to $60.5\pm5.2\%$, $p=0.21$) and fell between mid- and end-chemo ($60.5\pm6.2$ to $56.3\pm8.1\%$, $p=0.02$). Cardiac high energy phosphates (PCr/ATP ratio) showed a non-significant fall between pre- and mid chemo ($2.16\pm0.46$ vs $2.00\pm0.56$, $p=0.19$) and was unchanged between pre- and end-chemo time-points ($2.16\pm0.46$ vs $2.17\pm0.86$, $p=0.75$). Change in LVEF correlated inversely with changes in high energy phosphates ($r=-0.77$, $p=0.002$). The ECG-QT interval prolonged significantly between baseline and mid-chemo for all patients ($421.6\pm12.8$ vs $434.1\pm18.1$ msec, $p=0.023$).

CONCLUSIONS
Anthracycline-based chemotherapy for breast cancer is associated with clinically significant increases in high sensitivity cardiac TnI, reductions in LVEF and increases in myocardial high energy phosphates. These findings provide novel insights into the mechanisms of anthracycline-induced cardiac toxicity.