Title: Neoadjuvant Stereotactic Ablative Body Radiotherapy to Treat Early Stage Breast Cancer Patients: The role of DCE-MRI

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Structured Abstract:

The current standard of breast conserving treatment for early stage breast cancer patients is a lumpectomy followed by adjuvant whole breast radiotherapy (RT) over 4-6 weeks. This is prohibitively long for many patients. The London Regional Cancer Program (LRCP) is enrolling early stage breast cancer patients in a prospective phase I/II clinical trial called SIGNAL with the aim of assessing the safety/efficacy of neoadjuvant stereotactic ablative radiotherapy (SABR) to reduce treatment time. Treating before surgery provides a unique opportunity to assess tumour response to ablative radiotherapy using non-invasive imaging biomarkers. Parameters extracted from dynamic contrast enhanced (DCE) MRI have been shown to be useful for this. Patients enrolled in the research arm received a pre- and post-RT DCE-MRI scan using the hybrid PET/MRI. The pre-RT DCE-MRI was used for target volume delineation for RT planning and the change in parameters pre- to post-RT was used to assess biological response to SABR.

Enrollment into the research arm was temporarily suspended due to concerns of gadolinium contrast agent safety. We decided to use half a clinical dose of contrast agent for the DCE-MRI in the research arm, but the impact of this on target volume delineation for RT planning had to be carefully considered. One thesis chapter focused on investigating the impact of a reduced dose of contrast on the inter- and intra-observer variability for target volume delineation. Five radiation oncologists defined the tumour and we found that observers did not perform worse using a half-dose of contrast and so all patients enrolled in the research arm began receiving a half dose to minimize their potential risk due to the contrast.

Another thesis chapter focused on using DCE-MRI for biological response assessment to SABR which has been studied very little - especially at early timepoints post-RT. Particularly, it is unclear what imaging time delay to use post-SABR to minimize the influence of known acute inflammation. In addition, the effect of radiation dose per treatment (or fractionation) is not well studied. In this study, patients were treated and imaged with: 21 Gy/1 fraction imaged 6 days post-RT, 21 Gy/1 fraction imaged 17 days post-RT, and 30 Gy/3 fractions imaged 16 days post-RT. The results indicate that one-week post-RT is too early due to acute inflammation. Parameter changes at three weeks corresponded to indicators of response from previous studies. We also observed increased vascular permeability in the surrounding tissue for patients who received 21 Gy/1 fx but not 30 Gy/3 fx which has not been previously reported.

The work presented is the underpinning of a change in the way we treat breast cancer patients. We hope in the future, that if the response metrics evaluated here are sufficiently predictive of response, it may be possible to eliminate surgery altogether, greatly decreasing the physical and emotional burden for breast cancer patients.