

**Title:** Preliminary analysis of DCE-MRI images obtained prior to and 1 week following neoadjuvant SBRT in early stage breast cancer patients

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**Structured Abstract:**

**Introduction:** The SIGNAL trial is an ongoing phase I/II clinical trial aiming to assess the utility high dose radiotherapy (21 Gy in a single fraction) in early stage breast cancer patients [Guidolin et al. J Radiat Oncol., 2015]. This is a unique opportunity to use dynamic contrast enhanced (DCE) MRI to non-invasively assess early functional changes related to angiogenesis and perfusion due to the high dose radiotherapy one week later. Our objective was to explore changes that occur following radiotherapy using semi-quantitative and quantitative metrics in DCE-MRI.

**Methods:** DCE-MRI breast images were acquired on a 3T-PET/MRI system (Siemens Biograph mMR) in five patients before and seven days following high dose radiotherapy. 3-D fat suppressed fast low angle shot (FLASH) images were acquired (spatial resolution of 1.0x2.1x1.2mm, time resolution of 18s) which included one pre-contrast and 28 post-contrast images. Intra-session motion was corrected using deformable registration [Mouawad et al. 2016 - ISMRM Annual Scientific Meeting 2017]. Tumours were segmented using a signal to noise criteria of 7 (empirically chosen) followed by Otsu's method. Following segmentation, three empirical metrics were calculated 1) the number of voxels, 2) the signal enhancement at 3 minutes (SE3min), and 3) the area under the concentration curve at six minutes (AUC6min). Quantitative analysis was performed using Toft's kinetic model, which was fit, voxel-by-voxel, to the concentration vs time curve to extract the transfer rate of (Ktrans) and the fractional tissue volume of extravascular-extracellular space (ve). The percent change in the mean of the distribution of voxels before and after radiotherapy was calculated for each parameter for each patient and the mean  $\pm$  standard deviation of these values across patients was used to assess changes following radiotherapy.

**Results:** Concerning the semi-quantitative metrics, there was an average percent increase in the number of voxels of  $(52 \pm 26)\%$ . The SE3min and AUC6min increased by  $(18 \pm 11)\%$  and  $(36 \pm 23)\%$ , respectively. There was a percent increase in Ktrans and ve of  $(37 \pm 23)\%$  and  $(30 \pm 22)\%$ , respectively.

**Discussion:** A previous study [Wang C., et al. Technol Cancer Res Treat., 2015] also found an increase to the AUC6min and ve, but not for Ktrans though they used a much lower time resolution, a different model, and regional analysis. They interpreted this as reflective of radiotherapy treatment response. In contrast, we found that both the level of enhancement and the volume of enhancing tissue increased, suggesting inflammatory changes beyond the tumor boundaries. Future work will look to use PET tracers to try and further elucidate the inflammatory vs tumour response differences.