**Longitudinal Registration of Quantitative PET and MRI Data Acquired During Neoadjuvant Chemotherapy**

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**Target Audience** Scientists studying breast cancer and image registration

**Introduction** DCE-MRI, DW-MRI, and FDG-PET can provide information about the tumor microenvironment such as tumor perfusion, microvascular vessel wall permeability, blood volume fractions, cellularity and glucose consumption. Longitudinal analysis of changes in these parameters as measured by these different image modalities can provide information about the efficacy of chemotherapy and can also enable early predictions of therapy response. Here, we propose a method whereby serially acquired FDG-PET, DW- and DCE-MRI breast data are spatially co-registered to enable the comparison of parameter maps at the voxel level.

**Methods** MRI Acquisition Six patients with locally advanced breast cancer were given neoadjuvant chemotheraphy (NAC). FDG-PET, CT, 3D T1-weighted high-resolution isotropic volume examination (THRIVE) MRI, DCE- and DW-MRI data was obtained prior to (t1) and after one cycle of therapy (t2). Details of the DCE-MRI and DW-MRI data acquisition and analysis are provided elsewhere1,2 and resulted in ADC, $K_{trans}$, $v_r$ and $v_p$ maps. Following the DCE-MRI, a 3D THRIVE scan was acquired for inter-modality registration purposes with a fat-nulling inversion pulse, TR/TE= 6.98/3.6ms/10°, FOV =170×170×129mm$^3$ and a SENSE factor of 2. PET/CT data were acquired with a GE Discovery STE (GE Healthcare, Waukesha, WI). The activity of FDG administered was approximately 370 MBq (10 mCi), the tube current was 80 mAs for a 70 kg patient and both were scaled according to weight. FDG was administered intravenously via an antecubital vein contra-lateral to the affected breast. Emission data was collected 60 minutes after injection in 3D mode for two minutes per bed position. The Standard Uptake Value (SUV) was calculated from the FDG-PET data. Tumor ROIs were manually selected for all the time points on the enhanced DCE-MRI data.

**Image Registration** The CT image at each time point was rigidly registered to the THRIVE image using a rigid body registration (RBR) algorithm3 based on normalized mutual information. A non rigid body registration (NRBR) algorithm4 that relies on the adaptive basis function (ABA) was then applied to the resultant images to register the CT image to the THRIVE image. Since the CT and PET images are inherently coregistered to each other, the rotation, translation and deformation fields from the RBR and NRBR algorithms were applied to the FDG-PET image to register it to the THRIVE image. The DCE- and DW-MRI’s at each time point were also registered to the THRIVE image using the RBR algorithm. The longitudinal THRIVE images were then registered to each other using RBR and the NRBR algorithm extended to incorporate a tumor volume-preserving constraint5. Since the THRIVE, PET/CT, DW- and DCE-MRI images were registered to each other at each time point, the rotation, translation and the deformation field obtained from the longitudinal registration of the THRIVE images were then applied to those images, thus placing all imaging data, across both modality and time, in the same image space.

**Results** The Figure shows the longitudinal registration of the $K_{trans}$, $v_r$, $v_p$, ADC and SUV of the FDG-PET data for a patient who achieved pathologic complete response (pCR) at the conclusion of NAC. Changes in the mean values of these tumor parameters from t1 to t2 normalized to t1 are shown in the Table. In particular, the sum of $v_r$ and $v_p$ from t1 to t2 decreased for patients achieving non-response (NR) and increased for the patient achieving pCR.

**Discussion** The ability to register multi-parametric, multi-modality data enables the search for a method to integrate voxel level information to establish a robust, predictive algorithm to predict the response of breast tumors to neoadjuvant chemotherapy.

**Conclusion** Sequential FDG-PET, DW- and DCE-MRIs, obtained on different scanners and at different time points, of patients with breast cancer undergoing NAC were successfully aligned to a common image space while keeping the tumor size and shape from being substantially altered. The ability to integrate such data may provide unique insights into tumor status and therapy monitoring.


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**Table:** Change in tumor quantitative parameters. pCR is pathological complete response and NR is non-response.