NON-RIGID REGISTRATION OF SEQUENTIAL DCE-MRI IN THE ASSESSMENT OF RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Target Audience: Physicists and radiologists with an interest in measuring DCE-MRI treatment response in oncology trials.

Purpose: Tumor heterogeneity is well recognized in breast cancer and is associated with differential responses to chemotherapy. DCE-MRI is an established biomarker for predicting treatment response and has previously been exploited to measure tumor vasculature following anti-angiogenic therapies1. Quantitative and semi-quantitative perfusion metrics are well established in breast radiology2,3. Typically, perfusion parameters are summarized and reported over a region of interest (ROI), a highly data reductive process. ROI-based definitions are subjective, fail to capture tissue heterogeneity and discard spatial information. Methods that retain spatial information typically require that sequential images are co-registered into a common image space. Registration algorithms have previously been reported for breast DCE-MRI1,4. Li et al. validated registration of 3D breast MR images acquired at different time points to allow for analysis of corresponding low-resolution parameter maps1. The purpose of this work is to improve the quality of diagnostic information obtained over sequential DCE-MRI examinations, retaining its inherent high-dimensional data characteristics, by performing intra- and inter-visit non-rigid registration on DCE-MRI data and extracting semi-quantitative perfusion metrics to monitor voxel-wise heterogeneity and tumor response to neoadjuvant chemotherapy (NACT).

Methods: Breast cancer patients were imaged on a 3T whole body MRI scanner (MR750 GE Healthcare, Waukesha, WI) over a course of NACT, as part of an ongoing randomized double-blinded oncology trial (www.clinicaltrials.gov/NCT01093235). Patients received six cycles of taxane and anthracycline-based NACT with randomization to additional bevacizumab (a monoclonal antibody which inhibits vascular endothelial growth factor). Patients were scanned at four time points (Visits A-D): at baseline and after completion of chemotherapy cycles one, three and six. To date, two patients have been analyzed following the completion of their treatment regime; upon study completion both patients underwent biopsy and were characterized as partial responders.

3D Registration. Image registration code was developed in C++ by extending functionality within the Insight Toolkit (www.itk.org). (Visit A) Mattes’ mutual information-based B-spline non-rigid registration was used to register each temporal phase to the pre-contrast image to correct for intra-visit motion occurring due to respiratory, cardiac and involuntary patient movement. (Visits B-D) A 3D rigid translation was used to initialize a non-rigid B-spline transform to align the inter-visit pre-contrast images. This initial ‘bulk transform’ accounted for global motion due to patient repositioning on the scanner table. Subsequent temporal phases were registered to the transformed pre-contrast phase using known transform parameters established from the initial inter-visit registration step to correct any motion artifacts. In all cases a low-resolution B-spline mesh (35 mm spacing) was used to account for gross local distortion while reducing the potential to distort treatment effects.

Image Analysis. In-house software was developed in Matlab (version 7.14) to allow the user to import and navigate through unaligned and aligned 5-dimensional datasets (x, y, slice, phase, visit), render the selected image, plot voxel-wise and ROI based pharmacokinetic response to Gadolinium and compute semi-quantitative perfusion metrics.

Results: Spatially registered parameter maps showing area under the SI-time curve (AUC) were generated for both patients (Fig 1). Our approach demonstrates following the completion of their treatment regime; upon study completion both patients underwent biopsy and were characterized as partial responders. At the conclusion of this study, following unblinding of the anti-angiogenic randomization, our techniques will be repositioning and large deformations of the breast tissue between sessions. We have introduced the ability to perform voxel-wise comparisons of physiological parameters obtained from sequential DCE-MRI examinations, which provides an insight into tumor microstructure and physiology in response to therapy.

Discussions: Dynamic and sequential DCE-MRI data were registered into a common image space to account for intra-session motion artifacts as well as patient repositioning and large deformations of the breast tissue between sessions. We have introduced the ability to perform voxel-wise comparisons of physiological parameters obtained from sequential DCE-MRI examinations, which provides an insight into tumor microstructure and physiology in response to therapy.

Conclusions: Dynamic and sequential DCE-MRI data were registered into a common image space to account for intra-session motion artifacts as well as patient repositioning and large deformations of the breast tissue between sessions. We have introduced the ability to perform voxel-wise comparisons of physiological parameters obtained from sequential DCE-MRI examinations, which provides an insight into tumor microstructure and physiology in response to therapy.

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