Voxel-based Analysis of early DCE-MRI Changes May Predict the Response to Neoadjuvant Chemotherapy in Breast Cancer Patients

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INTRODUCTION To monitor tumor response to neoadjuvant chemotherapy, investigators have begun to employ the quantitative physiological parameters available from dynamic contrast enhanced MRI (DCE-MRI). However, most studies track the changes in parameters obtained from the tumor ROI or histograms, thereby discarding all spatial information on tumor heterogeneity. We have presented and validated a method for the registration of breast MR images obtained at different time points throughout the course of neoadjuvant chemotherapy [1-2]. In this study, we applied this method to longitudinal DCE-MRI data and performed a voxel-by-voxel analysis to examine the ability of early changes in parameters at the voxel level to separate pathologic complete responders (pCR) from non-responders (NR).

METHODS 22 patients with Stage II/III breast cancer were enrolled in an IRB-approved clinical trial where serial breast MRI scans were acquired pre-therapy (t_1) and after one cycle of neoadjuvant chemotherapy (t_2). Imaging was performed on a 3.0 T Achieva MR scanner (Philips Healthcare, Best, The Netherlands). The DCE-MRI acquisition employed a 3D spoiled gradient echo sequence with TR\TE\α =7.9ms\1.3ms\20°. The acquisition matrix was 192×192×20 over a sagittal (22 cm)^2 FOV with a slice thickness of 5 mm. Each 20-slice set was collected in 16.5 seconds at 25 time points and 0.1 mmol/kg of Magnevist was injected at 2 ml s^{-1} after the third dynamic scan. Responders (n=11) were defined as those patients who had a pathologic complete response at time of surgery. Non responders (n=11) were defined as patients with residual invasive cancer at the primary tumor site.

The fast exchange regime model (FXR) was applied to the original DCE-MRI data to estimate tumor perfusion and permeability (K^{trans}), extravascular extracellular volume fraction (v_e), and the average intracellular water lifetime of a water molecule (τ_i). ROI analysis was performed on the segmented tumor regions in the original DCE-MRI data to obtain three variables: the change of mean, median, and mean of the top 15% parameters. The serial parametric maps were then registered *via* a constrained non-rigid registration [1-2]. For each parameter, the voxel-based analysis was performed on the registered parametric maps by computing the change of mean, median, and mean of the top 15% parameters on voxels showing an increase in the parameter from t_1 to t_2. A Wilcoxon rank sum test was then used to determine if there was a significant difference between the pCR and NR groups.

RESULTS Figure 1 shows the registered DCE-MRI data at three time points with the corresponding K^{trans} maps superimposed; the top row is a NR, while the bottom row is a pCR. The table lists the p values of three variables of K^{trans} obtained by both the ROI and voxel analyses. It shows that the voxel-based analysis yielded significant results ($p < 0.05$) in all three ways of summarizing K^{trans}. Most results for v_e and τ_i, by both the ROI and voxel analyses, were not significant.

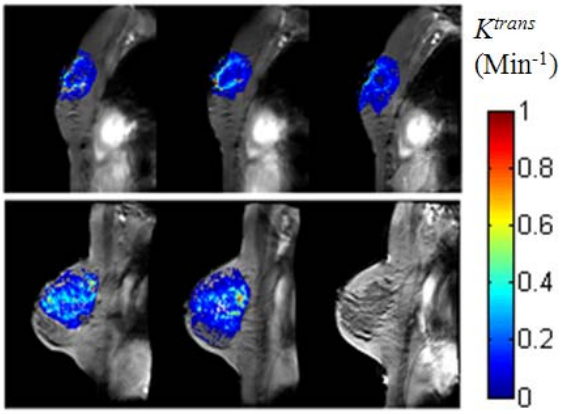

Figure 1: The registered DCE-MRI data at three time points (columns) with the corresponding K^{trans} superimposed; the top row is for a NR, while the bottom row is for a pCR.

Analysis	K^{trans} ROI	K^{trans} Voxel
Δmean	0.12	**0.02**
Δmedian	**0.02**	**0.03**
Δmean of top15%	0.15	**0.02**

The Table lists the p values for three ways of summarizing K^{trans} by the ROI and voxel-based analyses. The changes of mean, median, and mean of the top 15% K^{trans} all lead to significant results, indicating the voxel-based analysis after longitudinal registration may improve the ability of DCE-MRI to separate pCR from NR patients.

CONCLUSION The results indicate that the voxel-based analysis after longitudinal registration may improve the ability of DCE-MRI to separate pCR from NR after one cycle of therapy when using the FXR model.

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