Functional Diffusion Mapping (fDM) for Quantitative DW-MRI to Predict Breast Cancer Response to Neoadjuvant Chemotherapy

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PURPOSE Diffusion weighted MRI (DW-MRI) reports on tissue cellular characteristics and has been used to predict treatment response in breast cancer[1]. The functional diffusion mapping (fDM) method has been used to correlate changes in the apparent diffusion coefficient (ADC) with the response of various brain tumors to therapy,[2,3] but there is only one study applying the fDM method to breast cancer.[4] The goal of this study is to determine if the fDM analysis applied to ADC changes from pre- to post-one cycle of chemotherapy can be used to improve predictive accuracy over a region-of-interest based analysis.

METHODS Thirty-three patients with Stage II/III breast cancer were enrolled in an IRB-approved clinical trial in which DW-MRI data were acquired before (t_1) and after one cycle of chemotherapy (t_2). At surgery, 12 patients achieved a pathological complete response (pCR) while 21 patients were non-responders (i.e., non-pCR). Imaging was performed on a 3.0T MR scanner (Philips Healthcare, The Netherlands). DW-MRI was acquired with a single-shot spin echo (SE) echo planar imaging (EPI) sequence, with two *b*-values (0 and 500 s/mm^2 for 13 patients, and 0 and 600 s/mm^2 for 20 patients), *TR*/*TE* = 3080 ms/43 ms and NSA =10 for a total scan time of 4 m and 40 s.

A longitudinal registration algorithm[5,6] with a tumor volume-preserving constraint was employed to register the ADC maps from t_1 to t_2. A set of thresholds, from 0.1×10^{-3} mm^2/s to 0.8×10^{-3} mm^2/s with a 0.1×10^{-3} mm^2/s increment, were evaluated to detect the voxels with a significant increase in ADC. The percentage of tumor voxels with ADC changes above the threshold was calculated (V_i) for each patient and receiver operating characteristic (ROC) analysis was performed to test the ability of V_i to predict pCR. The Wilcoxon rank sum test was also employed to evaluate whether V_i between responders and non-responders was significantly different. A region-of-interest (ROI) analysis, in which the ROC was directly applied to the change in mean ADC from t_1 to t_2, instead of V_i, was also performed to evaluate whether the fDM approach improved the ability to predict treatment response.

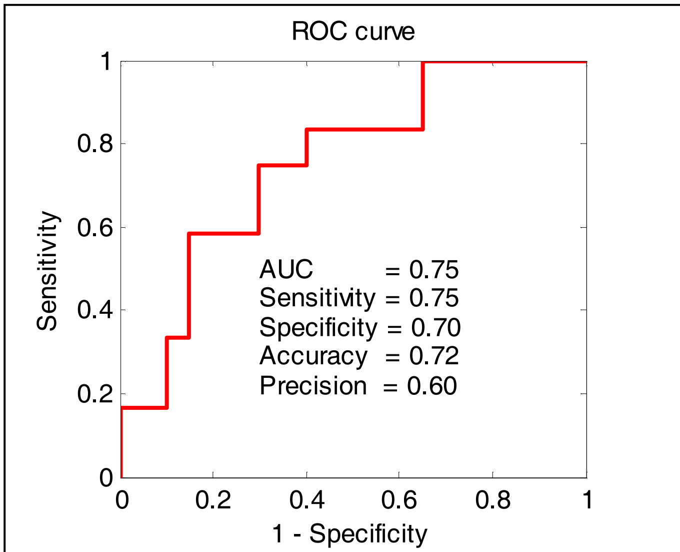

Figure 1. The ROC curve using the fDM on the ADC data.

RESULTS The optimal threshold to detect the voxels with a significant ADC increase was 0.4×10^{-3} mm^2/s , resulting in the best area under ROC curve (AUC) of 0.75. Figure 1 shows the ROC curve for V_i estimated from the ADC values. The AUC, sensitivity, specificity, accuracy, and precision were 0.75, 0.75, 0.70, 0.72, and 0.60, respectively. The p value was 0.02, indicating that the percentages of voxels with increased ADC between responders and non-responders were significantly different. For comparison, the ROI analysis conducted on the change in mean ADC yielded an AUC of 0.62, with sensitivity, specificity, accuracy, and precision of 0.50, 0.76, 0.67, and 0.55, respectively.

DISCUSSION We applied the fDM approach on DW-MRI data obtained in 33 breast cancer patients. When compared to the ROI analysis with an AUC of 0.62, the fDM analysis improved the predictive ability by achieving an AUC of 0.75. The optimal threshold of significant ADC changes was 0.4×10^{-3} mm^2/s, similar with the threshold 0.5×10^{-3} mm^2/s derived from short interval exams in the study of Ma et al[4].

CONCLUSION The study indicates that the spatial analysis of the DW-MRI data after registration retains the information of tumor heterogeneity, therefore allowing for an improved ability to predict treatment response. Future work includes investigating a multi-parameter predictive model based on a larger cohort of patients.

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ACKNOWLEDGMENTS NCI 1R01CA129961, NCI 1U01CA142565, NCI 1P50 098131, NCI P30 CA68485, NCRR/NIH UL1 RR024975-01.