Fast Exchange Regime Analysis of the Response to Treatment in Human Breast Cancer

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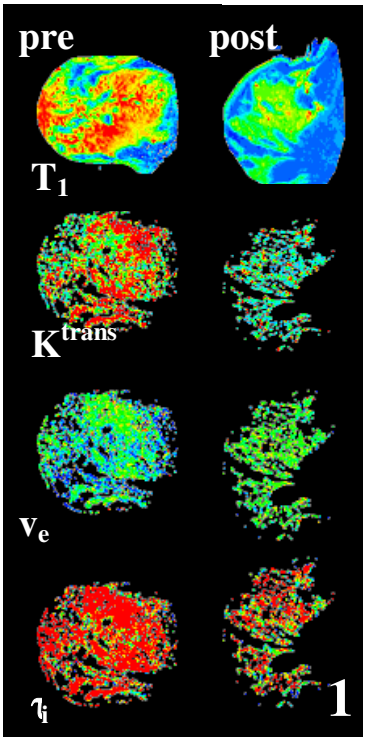
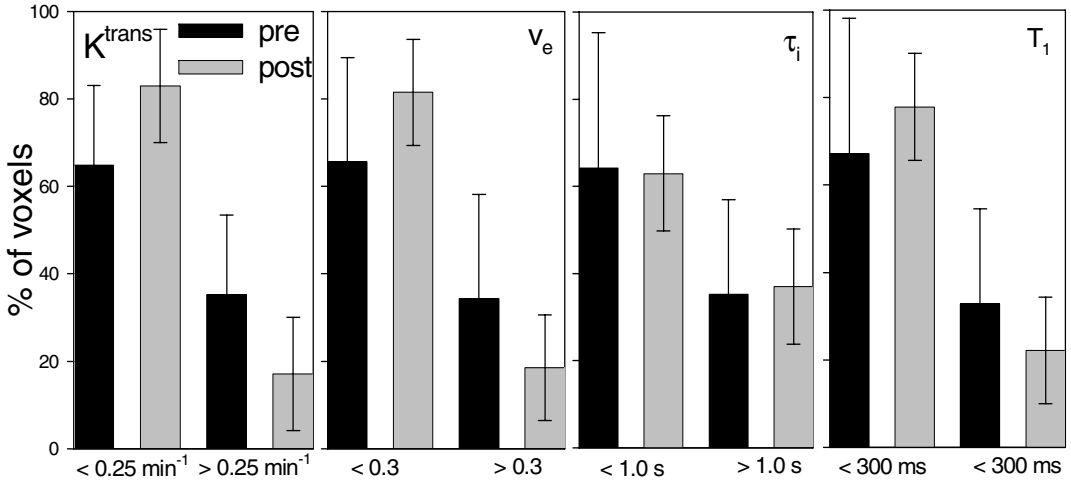


INTRODUCTION Models have been developed for analysis of dynamic contrast enhanced MRI (DCE-MRI) data that include the effects of transendothelial and transcytolemmal water exchange (1,2). Models that do no include such effects are known as fast exchange limit models, whereas those that, for example, include the effects of transcytolemmal water exchange are known as fast exchange regime (FXR) models. It has recently been shown that FXR models yield significantly different results than the FXL method in the study of human disease in general and, in particular, in breast cancer (3,4). It has been hypothesized that the FXR models are more sensitive. Here we present the first data on FXR analysis of the response to treatment in human breast cancer.

METHODS Ten Patients with high-risk, operable breast cancer were treated with four cycles of docetaxel 100-mg/m^2 every 2 weeks followed by definitive surgery. MRI scans were obtained prior to treatment and just prior to surgery. A 1.5T GE Signa LX scanner was used for imaging. A pre-contrast T_1 map and anatomic images were obtained. Following the delivery of 0.1 mmol/kg Magnevist DCE-MRI data was acquired for 8.5 minutes. T_1, K^{trans} (vessel perfusion permeability index), v_e (extravascular extracellular volume fraction), and τ_i (average intracellular H_2O lifetime) were all computed for all slices. These maps were used to build histograms to study the changes in the distributions of parameter values before and after treatment. For simplicity, each histogram was separated into two bins (elevated and low) and cut-offs are labeled below.

RESULTS Figure 1 displays parametric maps on sagittal sections of patient 5 for each parameter measured in the study. From the maps, histograms are constructed to yield quantitative information on parameter changes pre- and post-treatment. In all figures, red pixels indicate the highest values and blue the lowest. There is a move toward lower values, and fewer enhancing pixels, for all maps with the exception of the τ_i parameter. Figure two shows the pre- and post-treatment distributions averaged over all 10 patients. The number of highly permeable and/or perfused voxels (K^{trans}>0.25min^{-1}) decreased from 35% to 17%; the number of voxels with v_e > 0.3 decreased from 34% to 19%; and elevated T_1 values (>300 ms; T_1 of adipose tissue at 1.5T is 250 ms) decreased from 33% to 22%. All of these changes were statistically significant ($p<0.05$). The one parameter that did change significantly was τ_i. While there were several individual patients that showed marked changes in τ_i before and after treatment; these changes are lost when averaged with the group.



DISCUSSION Preliminary analysis of the first 10 patients show that FXR-analysis of DCE-MRI data is sensitive to breast cancer response to treatment. The changes in K^{trans} and v_e are reasonable and consistent with other efforts (5). Though τ_i does not significantly change in response to treatment (over the whole group), there were individual patients in which it did change significantly. In those patients, it will be interesting to see if those changes correlate with disease state as assessed by pathology obtained at the time of surgery. In addition to working to increase our sample set we are also working to correlate the parametric maps with whole breast mounts of mastectomy specimens. The long term goal is to use these methods as quantitative, surrogate biomarkers to predict treatment response to neoadjuvant therapy.

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