A Comparison of DCE-MRI Pharmacokinetic Models in Human Breast Cancer

X. Li\textsuperscript{1}, L. R. Arlinghaus\textsuperscript{1}, E. Welch\textsuperscript{1}, A. Chakravarthy\textsuperscript{1}, L. Xu\textsuperscript{1}, J. Farley\textsuperscript{1}, I. Mayer\textsuperscript{1}, M. Kelley\textsuperscript{1}, I. Meszoely\textsuperscript{1}, J. Means-Powell\textsuperscript{1}, V. Abramson\textsuperscript{1}, A. Grau\textsuperscript{1}, M. Levy\textsuperscript{1}, J. C. Gore\textsuperscript{1}, and T. E. Yankeelov\textsuperscript{1}

\textsuperscript{1}Vanderbilt University Institute of Imaging Science, Nashville, TN, United States

Introduction Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) involves the serial acquisition of $T_1$-weighted images before, during, and after the injection of a contrast agent. By fitting the resulting signal intensity time course to a proper pharmacokinetic model, physiological parameters related to vessel perfusion and permeability, or extravascular extracellular volume fraction can be extracted. There is currently controversy regarding the predictive value of quantitative DCE-MRI in monitoring treatment response in patients with breast cancer [1-2]. A possible reason for this is that the fast exchange limit model (FXL) used to analyze such data may not adequately describe the relevant physiology. Here we report the results of statistical tests on the analyses provided by the FXL with and without (FXL\textsubscript{vp}) the plasma component [3], and the fast exchange regime model (FXR) [4] to assess which model is provides better fits and is more robust in the presence of noise. We perform a rigorous comparison between these models by applying four statistical measures to assess model accuracy.

Method Fifteen patients with Stage II/III breast cancer were enrolled in an IRB-approved clinical trial where serial breast MRI scans were acquired before chemotherapy, 7-14 days following chemotherapy, and just prior to surgery, resulting in 28 usable data sets. Imaging was performed on a 3.0 T Achieva MR scanner (Philips Healthcare, Best, The Netherlands) equipped with a 4-channel receive double-breast coil (Invivo Inc., Gainesville, FL). The DCE-MRI acquisition employed a 3D spoiled gradient echo (SPGRE) sequence with TR/TE/\alpha = 7.9 ms/1.3 ms/20°. The acquisition matrix was 192\times192\times20 over a sagittal (22 cm)$^3$ FOV with a slice thickness of 5 mm. Each 20- second slice set was collected in 16.5 seconds at 25 time points and 0.1 mmol/kg of Magnevist was injected over 20 seconds after the third set. All available tumor voxels (manually segmented) for each data set were analyzed by the three models described above to extract pharmacokinetic parameters. The standard chi-square test ($\chi^2$) was used to assess the goodness of fit. The Durbin-Watson statistic (DW) was computed to detect serial correlation of residuals. Both the Akaike Information Criteria (AIC) and the Bayesian Information Criterion (BIC) are used to detect the balance between the goodness of fit and the model complexity, with the BIC applying a heavier penalty on model complexity.

Results The results show that the FXL\textsubscript{vp} and FXR models yielded the smallest $\chi^2$ in 42.42% and 43.15% of the voxels, respectively. They also had the smallest number of voxels showing serial correlation with 0.77% and 2.16%, respectively. The AIC indicated that the FXL\textsubscript{vp} and FXR models were preferred in 38.06% and 41.51% of the voxels, respectively. The BIC also indicated the FXL\textsubscript{vp} and FXR models were preferred in 33.38% and 39.31% of the voxels, respectively. Figure 1 and Table 1 summarize the statistical results. For all cases, the differences between the FXL and FXL\textsubscript{vp} models were statistically significant, as were the differences between the FXL and FXR models. This led to statistically significantly differences in the parameter values estimated by each model.

Conclusion In order to accurately assess changes in physiological parameters during therapy, it is important to choose the proper model. The statistical metrics indicate that the FXL\textsubscript{vp} and the FXR models provide the best fit of DCE-MRI time courses to practical data. This has practical implications for analysis of the breast DCE-MRI data.

Acknowledgments NCI 1R01CA129961, NCI 1P50 098131, NCI 1U01CA142565, and NCI P30 CA68485.