Early DCE-MRI Changes Predict Residual Enhancing Volume in Breast Cancer Patients Undergoing Neoadjuvant Chemotherapy

X. Li[1], L. R. Arlinghaus[1], E. Welch[1], A. Chakravarthy[1], L. Xu[1], J. Farley[1], I. Mayer[1], M. Kelley[1], I. Meszoely[1], J. Means-Powell[1], V. Abramson[1], A. Grau[1], M. Levy[1], J. C. Gore[1], and T. E. Yankeelov[1]
[1]Vanderbilt University Institute of Imaging Science, Nashville, TN, United States

INTRODUCTION Tumor response to neoadjuvant chemotherapy is currently monitored by gross changes in tumor size as measured by physical exam, mammography and/or ultrasound. Unfortunately, these methods are difficult to quantify and often do not correlate with each other or with pathologic findings at time of definitive surgery. Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) can offer information related to tumor perfusion and permeability (K^{trans}), vascular volume (v_p), and extravascular extracellular volume fraction (v_e). In this study, we use the extended Tofts model to return estimates on these parameters during neoadjuvant chemotherapy. The changes observed in these parameters early in the course of therapy were used to predict changes in tumor size at time of surgery.

METHODS *Data Acquisition* Nineteen patients with Stage II/III breast cancer were enrolled in an IRB-approved study. 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 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 over 20 seconds after the third scan. Sixteen patients were scanned at three time points: pre treatment (t_1), 7-14 days following initiation of chemotherapy (t_2) and pre surgery (t_3). Three patients were scanned only at the first two time points. Pathologic determination of tumor sizes was performed by dedicated breast pathologists and compared to the enhancing volume at MRI at t_3.

Data Processing The extended Tofts model was used to extract K^{trans}, v_p, and v_e. The volume of enhancing tumor was calculated by detecting the voxels in which the signal increased 50% post-contrast. The change of mean K^{trans} from t_1 to t_2 was compared with the change of volume of enhancing voxels from t_1 to t_3 and the measured pathologic tumor sizes.

RESULTS Figure 1 shows a boxplot for the nineteen patients. Six of the patients show an increase of K^{trans} from t_1 to t_2 (denoted as $\uparrow K^{trans}@t_{12}$) and all six had residual tumor burden at time of surgery. Thirteen patients show a decrease of K^{trans} from t_1 to t_2 and only two of them have residual tumors. The red bars show that the group with $\uparrow K^{trans}@t_{12}$ has a much higher median tumor burden at the time of surgery. The Wilcoxon rank sum test also indicates the tumor size of these groups are significantly different (p=0.0002). Furthermore, for all five patients displaying $\uparrow K^{trans}@t_{12}$ and decreased volume of enhancing tumor from t_1 to t_3, $\uparrow K^{trans}@t_{12}$ is strongly correlated with the change of the volume of enhancing tumor from t_1 to t_3 (Figure 2). Changes in tumor volume from t_1 to t_2 were not able to predict residual invasive tumor or the final volume of enhancing tumor. Thus, in this small patient set, quantitative DCE-MRI was more specific than morphology changes. Also, in this limited patient set, there is no strong correlation found in v_e or v_p.

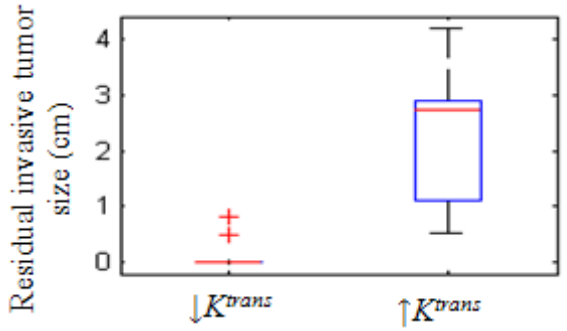

Figure 1: K^{trans} increased in six patients from t_1 to t_2 and all of them have residual tumor burden at time of surgery. Thirteen patients show a decrease of K^{trans} from t_1 to t_2 and only two of them have residual tumor at time of surgery. (p=0.0002).

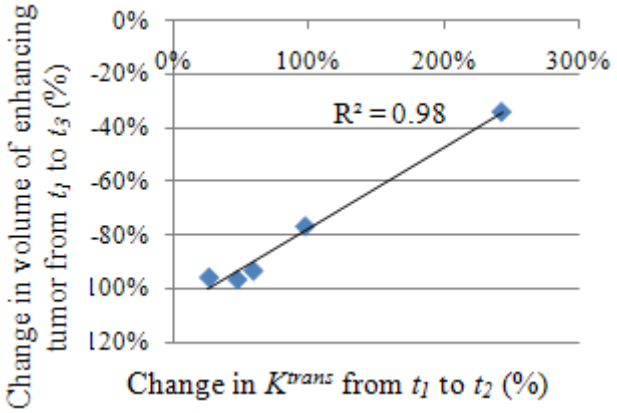

Figure 2: Change in K^{trans} from t_1 to t_2 is strongly correlated with the change of volume of enhancing tumor from t_1 to t_3.

CONCLUSION We found a strong correlation between the early change in K^{trans} and residual tumor burden, as well as the change in the enhancing volume of tumor tissue at conclusion of therapy. Future work includes expanding the data set to explore if MRI performed 7-14 days following initiation of chemotherapy can predict pathologic response.

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