Multi-parametric MRI Assessment of Breast Cancer Treatment Response in a Clinical Setting

T. E. Yankeelov[1,2], M. Lepage[3], K. J. Niermann[2,4], A. Chakravarthy[5], C. R. Herman[2], M. C. Kelley[6], C. I. Truica[7], R. R. Price[1,2], J. C. Gore[1,2]

[1]Institute of Imaging Science, Vanderbilt University, Nashville, Tennessee, United States, [2]Radiology, Vanderbilt University, Nashville, Tennessee, United States, [3]University of Sherbrooke, Sherbrook, QC, Canada, [4]Institute of Imaging Science, Vanderbilt University, Nasvhille, Tennessee, United States, [5]Radiation Oncology, Vanderbilt University, Nashville, Tennessee, United States, [6]Surgical Oncology, Vanderbilt University, Nashville, Tennessee, United States, [7]Medical Oncology, Vanderbilt University, Nashville, Tennessee, United States

INTRODUCTION Breast cancer is the second leading cause of cancer death among American women; approximately one in eight women will develop breast cancer in her lifetime (1). Although X-ray mammography and ultrasound imaging play a critical role in the detection and diagnosis of breast cancer, there are currently no adequate imaging methods for assessing the state of tumors or their response to treatments. We are exploring whether combining quantitative analysis of dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) and diffusion weighted MRI (DW-MRI) data can non-invasively provide accurate and quantitative measurements of tumor response to treatment.

METHODS MRI data were obtained (before and after neoadjuvant chemotherapy) with consent as part of an IRB-approved breast MR research study at Vanderbilt University. A 1.5T GE Signa LX scanner body RF transmit coil and a four-channel phased-array breast receive coil were used for imaging. For the T_{10} map, a gradient echo multi-flip angle approach used these parameters: TR\TE of 200\1.8 ms, flip angles of 10, 20, 25, 35, and 50 degrees, a 256x128x28 imaging matrix over a FOV of $(20\ cm)^2$ with slice thickness of 5 mm and 2 averages. The dynamic scan used identical parameters with 30^o flip angle. Each 28 slice set was collected in 52 seconds at 12 time points. A catheter within the antecubital vein delivered 0.1 mmol/kg Magnevist after the second acquisition, followed by a saline flush. A dual spin echo diffusion weighted single shot echo planar imaging sequence was employed for ADC mapping with the following parameters: TR = 5000 ms, TE = 84 ms, b-values of 0 and 300 s/mm^2, nex=16, and a 64^2 matrix over the same FOV and slice thickness as above. The total imaging time was just under 21 minutes; the total exam time was 30-35 minutes.

T_{10} values were computed from the mutli-flip angle data. An arterial input function was estimated by the signal intensity time course obtained from the axillary artery (present within the FOV) and converted to a T_1 time course by the fast exchange limit relation (8) assuming a a blood T_{10} of 1.2 ms (appropriate for 1.5T). The T_1 time courses for each voxel were analyzed by the fast exchange regime formalism (9,10) yielding estimates of K^{trans} (vessel perfusion permeability product), v_e (extravascular extracellular volume fraction, and τ_i (average intracellular H_2O lifetime). ADC values were computed for each voxel via ADC = -ln[S(b)/S$_0$)]/b, where b reflects the strength and duration of a diffusion-sensitizing gradient.

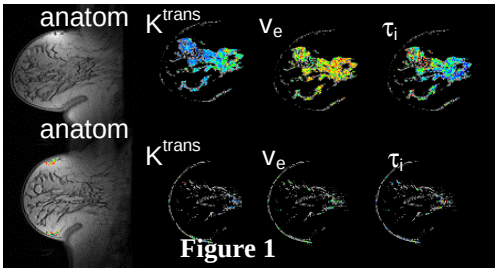

Figure 1

RESULTS We summarize the initial results of one of the 13 patients scanned at the time of submission.

Pathology Patient 1 was diagnosed with invasive mammary carcinoma of intermediate histologic grade and low proliferative rate. Hormone status was both ER and PR positive and HER2/neu negative. Notably, the pre-surgical high-resolution ultrasound exam revealed a tumor of 1.6 cm in greatest extent. Following four cycles of dose dense taxotere every two weeks at 100 mg/m^2, histological analysis of a biopsy obtained at surgery again reported an invasive mammary carcinoma of intermediate histologic grade and low proliferative rate. At surgery, the tumor was 4.0 cm in greatest extent; 2.5 times larger than estimated on pre-treatment ultrasound.

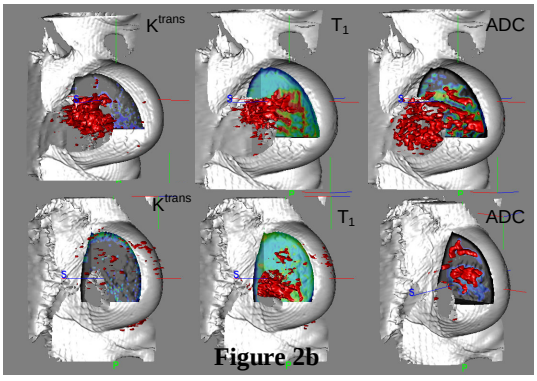

Figure 2b

Quantitative analysis Fig. 1 presents the pre- (top row) and post-treatment (bottom) results for the central slice. Both the pre- and post-treatment scans indicate the tumor is considerably larger than the 1.6 cm indicated by clinical sonography. The top row presents the pre-treatment K^{trans}, v_e, and τ_i parametric maps; the bottom row presents the post-treatment maps. The red voxels indicate higher values, blue voxels lower, and black voxels indicate data which the models could not fit. The maps depict a large area of increased perfusion and/or permeability (K^{trans}~0.2-0.3 min^{-1}) and an associated increase in extravascular extracellular volume fraction (v_e~0.4-0.5) before treatment. There is a marked decrease in these values following treatment: K^{trans}~0.1 min^{-1}, v_e~0.2). The 3-D representations of Fig. 2 are surface renderings of each parameter leveled at 50% of its maximum value (13). The K^{trans} rendering indicates that the tumor vasculauture has been markedly reduced, while the T_1 and ADC renderings indicate the persistence of pathologic tissue.

DISCUSSION We have implemented quantitative, multi-parametric MRI measures of breast cancer response to treatment. Preliminary analysis of the first 13 patients show that this is feasible and may be more reliable than currently available breast imaging techniques in monitoring therapeutic response.

REFERENCES 1. Harms. *JMRI*1999;10:979-1015. 8. Landis, Li, Telang, Coderre, Micca, Rooney, Latour, Vétek, Pályka, Springer. *MRM* 2000;44:563-574. 9.Yankeelov, Rooney, Li, Springer.*MRM* 2003;50:1151-1169. 10. Li, Huang, Yankeelov, Tudorica, Li, Rooney, Springer. *2004 ISMRM Annual Meeting*. 11. Guo, Cai, Cai, Gao, An, Ma, Mahankali, Gao. *JMRI* 2002;16:172-178. 12.Sinha, Lucas-Quesada, Sinha, DeBruhl, Bassett.*JMRI* 2002;16:693-704. 13. Li. MSEE Thesis. 2001; Vanderbilt University.

ACKNOWLEDGEMENTS NCI 1R25 CA92043 and NCI 1P50 098131-01