Quantitative Multi-Parametric MRI for Evaluating Early Treatment Response in Recurrent Glioma

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TARGET AUDIENCE: The focus of this study is relevant to those in both the clinical and research community who are interested in the information gleaned from quantitative MR methods as it pertains to treatment response in brain tumors.

PURPOSE: Current clinical approaches for monitoring treatment response in brain tumors often rely on imaging tumor size using CT or MRI (1). This approach can be insufficient, however, because changes in tumor size often occur later in time (months) relative to changes in a tumor's physiological features (days to weeks). Interpretation of the effectiveness of therapies, such as the anti-angiogenic drug bevacizumab, can also be confounded by changes in BBB integrity as observed on post-Gd T_1-weighted images. Quantitative MRI methods assessing blood flow, blood volume, cellularity and permeability may help determine response to these treatments earlier than conventional standard of care (SOC) imaging. In this study we employed diffusion weighted (DW) MRI, chemical exchange saturation transfer (CEST), and a multiple-echo perfusion protocol for simultaneous acquisition of dynamic susceptibility contrast (DSC) and dynamic contrast enhanced (DCE) data in glioma patients receiving bevacizumab.

METHODS: In this newly initiated study, with a target recruitment of 25 patients, we have completed scanning on the first patient with a confirmed recurrent glioma (post-resection) undergoing bevacizumab therapy. Images were acquired at 3T (Philips Achieva) prior to and two weeks after the first treatment. CEST data, DW-MR images (b = 0, 25, 50, 75, 100, 200, 500, 1000 s/mm^2), and a T_1 map (FA = 2°-20°) were acquired prior to contrast injection. A single dose of Gd-DTPA (0.1 mmol/kg, 4 mL/s) was administered, followed by a DSC-MRI scan (multiple gradient-echo single-shot EPI, TR=1.5s, TE= 7ms/31ms, NEX=1, voxel size: 2.5 x 2.5 x 5 mm^3, flip=70°). DCE T_1-weighted data was extracted from the multi-echo acquisition via interpolation of image signal intensity to $S_{TE=0}$ (2). Automated extraction of the arterial input function (AIF) was performed based on bolus arrival time, peak height, and AUC (3). Measures of cerebral blood flow (*CBF*), blood volume (*CBV*), and mean transit time (*MTT*) were estimated from the DSC data via a SVD method with block-circulant deconvolution (4, 5). DCE-MRI data was analyzed using the extended Tofts model (6).

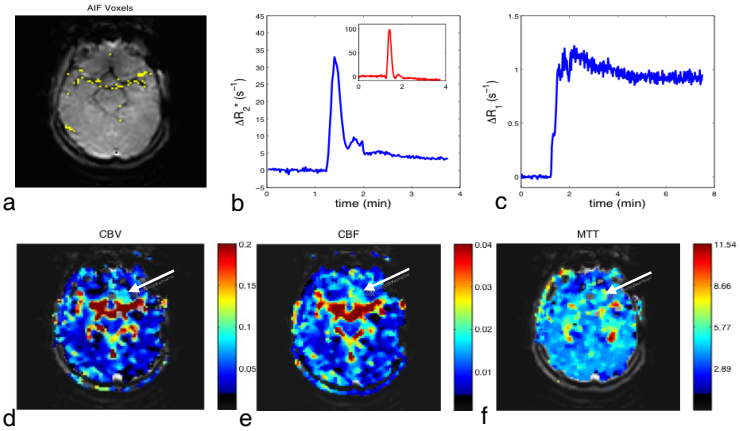

Figure 1. a) Voxels selected from automated AIF selection and corresponding ΔR_2^* curve (1b, inset). ΔR_2^* (b) and ΔR_1 (c) tumor tissue curves. Pre-treatment parametric DSC maps d) CBV, e) CBF, f) MTT.

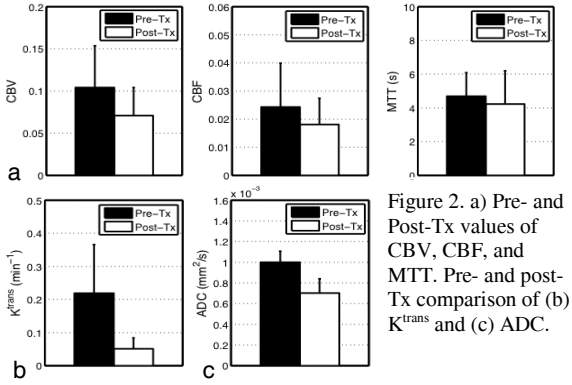

Figure 2. a) Pre- and Post-Tx values of CBV, CBF, and MTT. Pre- and post-Tx comparison of (b) K^{trans} and (c) ADC.

RESULTS AND DISCUSSION: Automated AIF selection, based on the first echo, resulted in voxels found in and around the MCA (Fig. 1a). After treatment, the tumor *CBF* and *CBV* slightly decreased (Fig 2a), while K^{trans} and *ADC* were more substantially reduced (Fig. 2b,c). These latter changes likely reflect altered BBB integrity and reduced edema, emphasizing the potential importance of using CEST data (analysis ongoing) to assess changes in tumor cellularity. With continued patient recruitment, it is postulated that correlation between these changes and tumor size, as well as overall survival time, may ultimately help determine the efficacy of these biomarkers in predicting early treatment response**.**

CONCLUSION: Quantitative MRI measurements made at the onset and throughout the duration of tumor treatment may provide crucial information about tumor physiology that is not readily available from SOC imaging. This information may be important in establishing detailed disease prognoses and treatment regimens in the context of recurrent glioma treated with bevacizumab.

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