Multi-parameter Characterization of a Rat Cerebral Tumor Model using 2D GRE: Measurements of Blood Volume, Water Exchange, and Inflow Velocity

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ABSTRACT A novel technique to simultaneously quantify blood volume (V_b), intra/extra-vascular water exchange rate, and infow velocity of local blood volume (i.e., perfusion) was proposed for the *in vivo* assessment of hemodynamic parameters. Using a multi-parameter fit strategy and long-circulating intravascular T1 contrast agent, the tissue MRI signal dependence on pulse sequence parameters was used to characterize the tumor vascular physiology. In particular, the relationship between the measured blood volume fraction and various physiologic parameters was established utilizing a two-compartment tissue model. An absolute blood volume quantification method using a single slice 2D GRE (Gradient Recalled Echo) pulse sequence and the assumption of no intra/extra-vascular water exchange were considered to generate a theoretical fit data as previously described(1). Using animal tumor models (9L gliosarcoma), highly non-linear dependence of measured local fractional blood volume on the 2D MRI pulse sequence parameters(1) was obtained and used for calculating the vascular parameters. As the result of multi-parametric fit, tumor tissue was characterized with significantly high blood volume, high water exchange rate, and low inflow velocity in comparison to normal brain tissue.

METHODS All experiments were performed using a 1.5T GE Signa scanner with a body gradient coil and a solenoid extremity RF coil. Four male Fisher rats, approximately 2 weeks after tumor inoculation (9L gliosarcoma) in the right hemisphere, were studied with catheters at both femoral vein and artery for the injection of contrast agent and the withdrawal of blood. Previous simulations indicated that TRs between 20 and 60ms yield measurement results that are highly affected by both inflow and water exchange. Therefore, MR images were acquired with TR=[35, 60ms], matrix=256x128, slice thickness=3mm, FOV=8cm, and TE=6.1ms as the flip angle was varied from 20 to 90^o (20, 30, 60, and 90^o). The number of average was varied to take each image within 2 minutes. In addition, one proton weighted image was taken to normalize the acquired signal to proton density. Local T2* was measured by varying TE (15 and 25ms) for the post data T2* corrections. The V_b was calculated assuming no intra-/extra-vascular exchange (2) (i.e., using MRI signal intensity (SI)) as the following:

$$V_b=(SI_{post\_tissue}-SI_{pre\_tissue})/(SI_{post\_blood}-SI_{pre\_blood}),$$

where pre_ and post_ indicate prior to and following a contrast agent administration, respectively. The number of voxels in a single ROI was between 16 and 64. The local signal intensity was determined by averaging the signal intensities of collected voxels. The acquired signal intensity of each ROI was locally corrected for the measured T2* values; therefore, there was no T2* weighting in the corrected signal intensity. For each region (tumor periphery and corresponding contralateral normal tissue), same number (2-4) of ROIs were selected in each animal for analysis. Multi-parametric fit was performed using the simplex search method (Matlab©). In order to avoid local minima, physiologically–relevant multidimensional initial values were chosen for each variable (i.e., blood volume, exchange rate, and inflow) and used for the fit, the error of which was compared to identify the global minimum for each ROI data.

RESULTS AND DISCUSSION For all the selected ROIs, strong dependences of the measured V_b on pulse sequence parameters were observed. The fit values of water exchange rate and inflow velocity widely varied in both normal and tumor tissues. For the contralateral normal tissue, the exchange rate and inflow velocity maximally varied from 0.3 to 1.7Hz and 0.2 to 1.3cm/s, respectively. Since regional analysis by differentiating the tissue type (e.g., gray and white matter) was not performed here, it is probable that the variations within the normal tissue data were due to the intrinsic physiological inhomogeniety in brain. Nevertheless, the variability became more significant when tumor tissue was considered. In general, the fitting error and variances for each ROI were smaller for normal tissue than tumor. For the normal tissue, the mean V_b ($1.84 \pm 0.31\%$) is highly consistent with the independently-obtained histological value of $1.89 \pm 0.39\%$(3). Other physiological parameters, mainly water exchange rate and blood inflow velocity, derived from V_b fit data revealed that tumor and normal tissue have a qualitative distinction. In conclusion, the tumor tissues were characterized as having higher blood volume, higher intra-/extra-vascular water exchange rate and lower blood inflow velocity than normal brain tissue. With an appropriate histological validation, this method may provide an efficient means to monitor the local and long-term progression of tumor tissue.

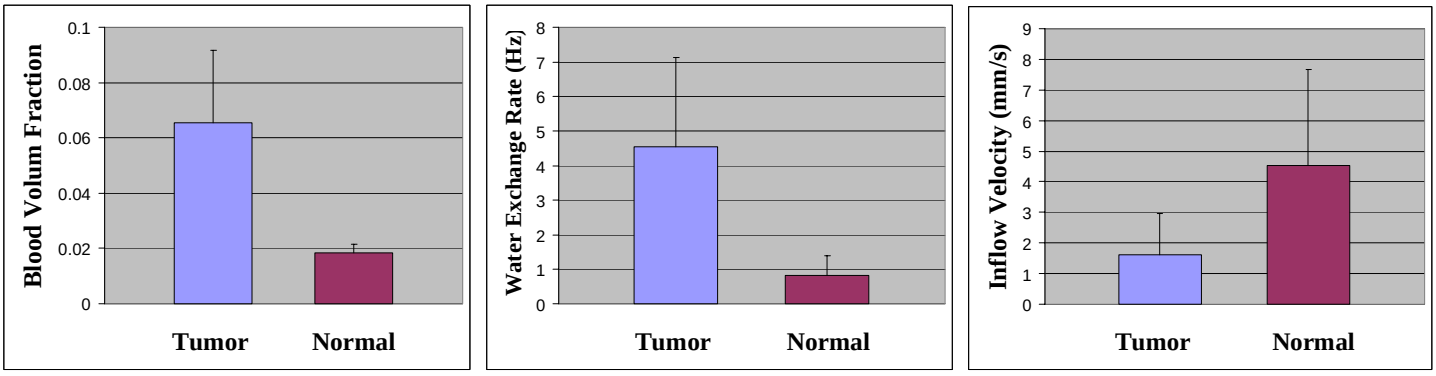

Figure 1. Comparison of tumor blood volume, intra/extra-vascular water exchange rate, and inflow velocity to corresponding contralateral normal tissue.

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