The Ratio of T2* and T1 Relaxivities in Experimental Cerebral Tumor and Normal Brain

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Introduction: In dynamic contrast enhancement (DCE) studies, T2* contrast is a common mechanism for following and estimating the concentration-time curve. In leaky vascular beds, such as those of aggressive tumors, it is known that T1 contrast competes with T2* contrast when the contrast agent (CA) extravasates. Less well understood is that the T2* relaxivity also changes. We demonstrate and quantitate that change at 7 Tesla in a rat model of cerebral tumor.

Materials and Methods: Male Fischer 344 rats (N=5) weighing 250 to 300 g were implanted with 10,000 9L cells using methods previously described[1] and studied about 14 days post-implantation (14.2±0.8 days) in a 7 Tesla, 12 cm (clear bore) magnet with actively shielded gradients of 25 gauss/cm, 100 µs rise times, interfaced to a Bruker Avance console running Paravision V2.6 (Bruker Inc., Billerica MA). RF coils were a Bruker volume resonator for transmission and 2 cm surface coil for reception. Following established procedures[2], a TOMROP[3] sequence was employed to produce maps of T1 at baseline, and at 145 s intervals following injection of the experimental CA, Gadomer (Schering Corp, Montville NJ). Matrix size was 128X64, FOV 32 mm, three 2 mm slices.

Prior to the administration of CA, two baseline TOMROP studies were obtained. Gadomer, a synthetic dendrimer of 17 kD, was then administered (250 µmol/kg in a 1 ml dose over 1 minute). After Gadomer administration, 10 iterations of TOMROP were run to produce T1 maps across a 25 min period. Changes in R1 (R1=1/T1) were used to estimate changes in tissue concentration. In an analysis previously described[4] the transfer constant (K_1) was computed pixel-by-pixel, using R1 estimates generated from the TOMROP data.

TOMROP is an imaging variant of the Look-Locker sequence. As such, its signal depends on both T1 and T2* in a manner that is calculable[5]. If, after the administration of CA, we assume that both R1 and R2* change proportional to the voxel concentration of CA, i.e., $\Delta R1 = \Re_1[Gd]$, and $\Delta R2^* = \Re_2^*[Gd]$ where $\Re_1$ and $\Re_2^*$ are the R1 and R2* relaxivities, respectively, and [Gd] is the concentration of contrast agent, then a straightforward but tedious calculation demonstrates that the ratio of $\Re_2^*$ to $\Re_1$ can be determined pixel-by-pixel after CA administration. Let us call this ratio Γ_2.

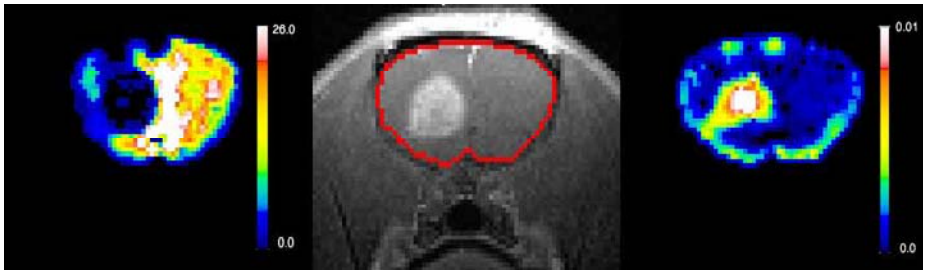

Figure: Map of Γ_2 (left), post-contrast T1-weighted image (center), map of vascular transfer constant [min^{-1}] (right)

For the purpose of calculating Γ_2, the second through fifth TOMROP image after administration of CA were selected and the ratio Γ_2 calculated pixel-by-pixel. These image sets were selected in order to have experimental conditions in which neither T2* or T1 were changing quickly across the imaging time. ROI's in the tumor and normal tissue were selected using the post-contrast T1-weighted image and the mean Γ_2 measured and compared for each region.

Results: See figure for a map of Γ_2 (left) and K_1 (right) in a rat with a 9L tumor 13 days after implantation. In the tumor, with its high permeability to CA, the profound decrease in Γ_2 is evident. For the 4 studies in 5 animals (mean ± S.D.) Γ_2 in the tumor ROI (0.745 ± 0.092) was much lower ($p < 0.005$) than that of normal tissue (4.24± 1.63). The ratio of Γ_2, normal/tumor was 5.6 ± 2.1. In no case was the ratio of relaxivities in tumor higher than in normal tissue.

Discussion: To our knowledge, this is the first determination of the ratio of T2* to T1 relaxivities in normal brain and tumor. Since T1 relaxivity measured under the conditions of the TOMROP experiment is known to be relatively constant, the findings reflect on the difficulty of establishing a direct estimate of CA concentration from T2*-weighted images. An increasing interest in using T2*-weighted sequences for the evaluation of tumor permeabilities after therapy (e.g. Cao et al [6]) speaks to the significance of this finding, particularly at higher field strengths.

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References: 1. Kim, J.H., et al., International Journal of Radiation Oncology, Biology, Physics, 1995. 33: p. 861. **2.** Ewing, J.R., et al., Magn Reson Med, 2003. 50(2): p. 283. **3.** Brix, G., et al., Magnetic Resonance Imaging, 1990. 8: p. 351. **4.** Ewing, J.R., et al., J Cereb Blood Flow Metab, 2005. 00: p. 00. **5.** Gelman, N., et al., Magn Reson Med, 2001. 45(1): p. 71. **6.** Cao, Y., et al., J Clin Oncol, 2005. 23(18): p. 4127.