Cerebral Perfusion Imaging with Hyperpolarized ^{13}C-Tert-Butanol at 9.4 Tesla: Long Relaxation at High Fields

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Purpose: Hyperpolarized ^{13}C-labeled tert-butanol (IUPAC name 2-methylpropan-2-ol) is freely diffusible in tissue, allowing perfusion imaging with high SNR[1]. Studies on renal cell carcinoma mouse models have demonstrated the high sensitivity of this method in characterizing early response and resistance to anti-angiogenic therapy. *In vivo* T_2 relaxation of ^{13}C-tert-butanol is 2-4 s in the rat brain at 4.7 T, but measurements at 9.4 T in blood have suggested a shorter T_2 on the order of 500ms. T_2 is a key determinant of the sensitivity of hyperpolarized perfusion imaging. Here we report *in-vivo* measurements of T_1 and T_2 at 9.4 T.

Methods: Mouse imaging was performed on a 9.4 T horizontal-bore animal system (Bruker Biospec, Billerica MA) using methods approved by our Institutional Animal Care and Use Committee. Tert-butanol was polarized to ~5% by DNP as described previously[1]. Anatomical ^{1}H images of the brain were obtained with a turbo spin echo sequence (TR/TE 1000/40 ms, echotrain of 8, 4 NEX, 4.8 x 4.8 cm FOV, 2.3 mm slice, 125^2 μm resolution). Approximately 10 s after injection of 200 μL of 230 mM ^{13}C-tert-butanol solution via a tail vein, 256 successive images were acquired at the level of the diencephalon via a balanced steady-state free precession (bSSFP) sequence (180° refocusing flip angle α, TR/TE 2.4/1.2 ms, 2.3 mm slice, 4.5 x 4.5 cm FOV, 750^2 μm resolution, 182 ms/frame). With these parameters, static spins in tissue decay at a rate set by T_2, while venous blood flowing through the imaging slice shows persistent high signal owing to a time-of-flight effect. Regions of interest were drawn over the brain parenchyma and an adjacent large vein, and average intensity values were graphed against time and fitted to exponential decay curves. The overall signal decay rate T reflects a combination of T_1 and T_2 relaxation and tracer flow in brain tissue, demonstrated by the following relationship:

$$\frac{1}{T} = \frac{\cos^2(\alpha/2)}{T_1} + \frac{\sin^2(\alpha/2)}{T_2} + \frac{f}{\lambda},$$

where α is the refocusing angle, f is the vascular flow rate, and λ is the blood/tissue partition coefficient of tert-butanol. A reported value of f = 209 ± 11 mL/100g/min was used[2] and f/λ = 0.045± 0.014 s^{-1} was estimated using the partition coefficient of n-butanol[1]. T_1 was calculated from the signal decay within a large vein, whose signal is maintained by fresh inflowing ^{13}C-tert-butanol (effective α = 0). T_2 was calculated using the above equation with a 180° refocusing flip angle.

Results: Figure 1 shows a T2-weighed image of the brain where the measurement was performed. Figures 2 and 3 demonstrate early and late bSSFP frames showing ^{13}C-tert-butanol within both the brain parenchyma and veins initially, followed by brain washout and persistent venous signal. The decay curves fits are show in in Figure 3. Exponential fits to the above equation yield T_2 = 0.71 ± 0.03 s and T_1 = 78 ± 26 s. The extracted T_1 in brain tissue is sensitive to uncertainties in the partition coefficient. However, a value in this range is supported by low tip-angle whole-body measurements showing T_1 = 34 ± 5 s, with expected variability between brain versus whole-body spectra.

Discussion: Quantitative MR-based perfusion imaging is valuable for *in-vivo* assessment tumor dynamics and response to treatment. ^{13}C-tert-butanol is an attractive agent because it is freely diffusible, penetrates the blood brain barrier, and possesses a low toxicity profile. The relatively long *in-vivo* T_1 of 78 s and T_2 of 0.71 s of ^{13}C-tert-butanol at 9.4 T allows for robust perfusion imaging in combination with more detailed anatomical imaging and greater spectroscopic sensitivity.

Conclusion: *In-vivo* ^{13}C-tert-butanol perfusion imaging 9.4 T is feasible given relatively high T_1 and T_2 relaxation times.

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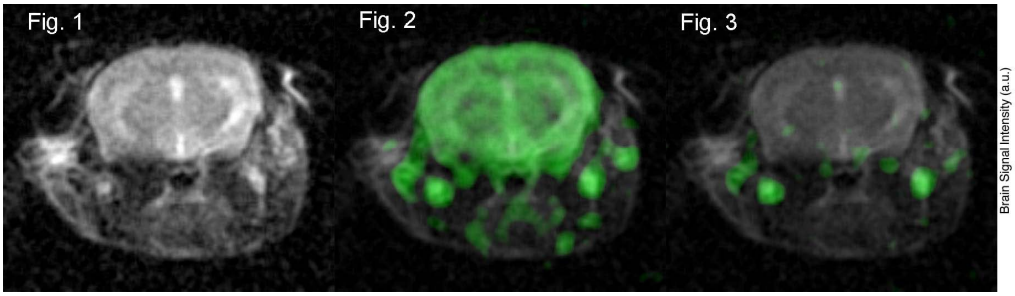

Fig. 4

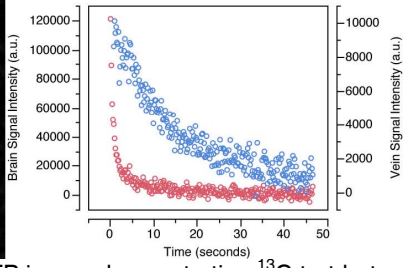

Figure 1: T_2-weighed anatomical image at the level of the diencephalon. Figure 2: Early bSSFP image demonstrating ^{13}C-tert-butanol perfusion (superimposed in green) diffusely throughout the brain parenchyma and large veins. Figure 3: Later bSSFP image demonstrates brain washout with signal remaining within the veins. Figures 2 and 3 were reconstructed from data averaged over ~1s. Figure 4: Plots of average signal intensities within ROIs centered about the brain parenchyma (red) and large veins (blue).

References:1. Grant AK, Vinogradov E, Wang X, Lenkinski RE, Alsop DC. Perfusion Imaging with a Freely Diffusible Hyperpolarized Contrast Agent. Man Reson Med 2011;66:746-755. 2. Sun Y, Schmidt NO, Schmidt K, et al. Perfusion MRI of U87 brain tumors in a mouse model. Magn Reson Med 2004;51:893-899.