Simultaneous quantification of intravascular blood T_1 and T_2 with multiple-readout TRUST (mTRUST)

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INTRODUCTION: Quantification of intravascular blood T_1 and T_2 has several important applications in quantitative MRI. Blood T_1 values are needed in order to accurately measure perfusion in arterial spin labeling (ASL)[1], to determine the blood inversion recovery null point in vascular-space occupancy (VASO)[2] MRI and black blood imaging techniques[3], and can also be used for estimation of hematocrit (Hct)[4,5,6], the main protein constituent in blood. Quantification of blood T_2 can be used to estimate venous blood oxygen saturation (Y_v)[7], for instance, using the T_2-relaxation-under-spin-tagging (TRUST) technique[8]. TRUST and other T_2-based Y_v quantification techniques require estimation of Hct in order to convert T_2 to Y_v. While Hct can be obtained from a venous blood draw, this is not always practical, and can vary substantially from day to day in certain diseases such as anemia, making a current value essential. Thus, simultaneous T_1 and T_2 measurement is an attractive approach for quantification of Y_v. This was recently demonstrated using the T_2-TRIR technique[6], where intravascular venous blood signal is measured during inversion recovery following various degrees of CPMG T_2-preparation. Unlike TRUST, T_2-TRIR does not use a tag-control approach to eliminate partial voluming, relying instead of saturation of the repeatedly excited tissue signal. Partial voluming errors represent a major concern in blood T_1 and T_2 quantification techniques due to the small size of the vessels of interest relative to the limited spatial resolution required for fast EPI readouts. We propose a modification of the TRUST sequence using multiple EPI readouts (mTRUST), allowing rapid determination of whole-brain venous blood T_1, T_2, and, therefore, Y_v, with optimal control of partial volume errors.

METHODS: ***Pulse Sequence*** **–** Like TRUST, mTRUST (**Figure 1**) uses non-selective MLEV-16 CPMG T_2 preparation pulses of varying effective echo time (eTE) following either blood inversion with an adiabatic hyperbolic secant pulse (tag) or application of an equivalent off-resonance pulse without gradient (control). An inversion time allows complete replacement of venous blood in the SSS of the imaging slice with inverted spins, after which a series of 90° excitation pulses with EPI readouts are applied every 200 ms to allow complete replacement of blood spins in each readout. The TR (6 s) and number of EPI readouts (8) were chosen based on signal equation calculations suggesting this combination would produce maximum T_2 measurement precision, assuming perfect inversion and T_2-preparation and no noise correlation between EPI readouts. ***T_1/T_2 Determination*** - Control–tag subtraction of each eTE image pair isolates venous blood signal with various degrees of T_1 and T_2 relaxation: $S = S_0 e^{-eTE\cdot(1/T_2 - 1/T_1)} e^{-t/T_1}$ where t is time relative to the end of the CPMG. An ROI containing only the four brightest pixels is selected, and T_1 determined from the 0 eTE data only, as these signals will have the highest SNR for fitting. This T_1 value is plugged back into the signal equation to calculate T_2, although it is worth noting that because $T_1 >> T_2$, the fitted T_2 is negligibly dependent on T_1 values within the physiologic range. Y_v is then determined from T_2 using a published calibration curve[9]. ***In-Vivo Study*** **–** 4 young healthy subjects (ages 32 ± 7, 3 males) were scanned with 10 repeats of the mTRUST sequence (8 mins total acquisition time). Mean and standard deviation (s.d.) T_1, T_2, and Y_v values were determined across the 10 repeats for each subject.

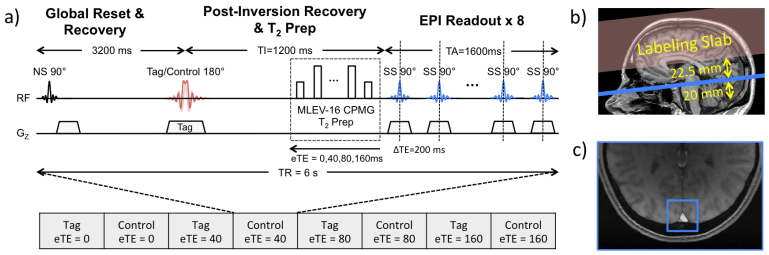

Figure 1: a) mTRUST pulse sequence diagram. Each 6 s module is repeated at 4 eTEs for both tag and control conditions, producing data for T_1 and T_2 fitting every 48 s. Additional sequence parameters: τ_{CPMG}=10ms, TE_{EPI}=7ms (5/8th partial Fourier), matrix=64×40, resolution=3.4×3.4×5.0mm. b) Sagittal image indicating locations of the labeling slab and imaging slice and c) axial image highlighting the SSS in the imaging slice.

RESULTS: **Figure 2a** shows mean ± s.d. raw difference signal intensities as well as corresponding Y_v values for Subject 2. In **Figure 2b**, 0 eTE log difference signal intensities are plotted to determine T_1. **Figure 2c** displays mean ± s.d. Y_v values across the four subjects vs. EPI readout number, demonstrating a consistent trend of Y_v over-estimation and reduced precision at later EPI readouts. Y_v values (derived from the first EPI readout only) and T_1 values for each subject are summarized in **Table 1**. Group Y_v values are similar to previous studies using TRUST[8], whereas the quantified T_1 values are lower compared to recent reports using a similar fast T_1 approach[9], especially for subjects 3 and 4.

Table 1: Subject Y_v and T_1 values.

Subject	Y_v	T_1
1	61.3 ± 2.8	1643 ± 137
2	65.5 ± 1.6	1676 ± 105
3	67.7 ± 3.1	1466 ± 96
4	66.4 ± 2.3	1449 ± 57
Mean	65.2 ± 2.5	1559 ± 99

DISCUSSION: ***T_1 estimation*** **–** The main motivation for a combined blood T_1 and T_2 quantification approach is the ability to calibrate the T_2 estimation of Y_v based on T_1-derived Hct. Although the data suggest relatively precise T_1 fitting with a subject-averaged s.d. across repeats of 99 ms, the reported values are somewhat low. This would be expected were tissue partial voluming a concern, though this is unlikely given that the described sequence is optimally designed to reduce partial volume effects. A more likely explanation is that later arriving blood has a reduced degree of initial adiabatic inversion, causing a reduction in the difference signal measured at later EPI readouts unrelated to T_1 decay, and thus causing underestimation of T_1. This potential confound could be mitigated by using a larger inversion slab covering the entire head and measuring blood signal in the internal jugular vein, which would result in a longer bolus of fully inverted blood and also allow for a longer train of EPI readouts.

T_2 estimation **–** Another theoretical advantage of mTRUST as well as the previously described T_2-TRIR technique is the potential for improved T_2 estimation precision via the additional data acquired over multiple EPI readouts. In the T_2-TRIR study, all data was fitted to a single model, and it was not investigated whether the later EPI readouts improved T_2 estimation or not. However, it is clear from Figure 2a and 2c that Y_v is not only less precise at later EPI readouts, but also overestimated, suggesting that only the first EPI readout should be used for T_2/Y_v quantification. This reduced precision and bias is likely a function of the lower SNR of the later EPI readout signals, which would tend to result in T_2 overestimation.

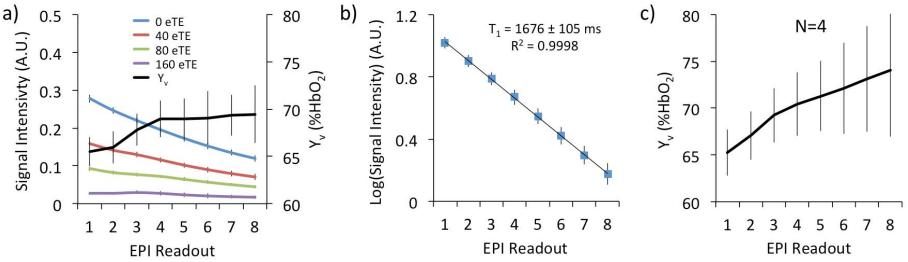

Figure 2: a) Difference signal values and and corresponding Y_v values for Subject 2, with error bars indicating s.d. across repeats; b) T_1 fitting from data in Subject 2 demonstrates exponential behavior of the 0 eTE signal data; c) T_2-derived Y_v versus EPI readout across subjects with error bars indicating intersubject s.d.

CONCLUSIONS: mTRUST provides a fast approach to simultaneous T_1 and T_2 mapping of intravascular blood, but fitting should be preformed only with the 0 eTE data for T_1 and the first EPI readout data for T_2. Our results suggest that the T_2-TRIR approach of fitting all data to a single model may cause overestimation of T_2 and Y_v; however, determining the cause of this bias requires further investigation. While the proposed mTRUST approach is attractive in terms of control for partial volume effects, more work is needed to determine the validity of the approach for T_1 quantification, as the quantified values in the initial subjects studied were on the low end of normal. Future studies will directly compare mTRUST derived T_1 values to a similar sequence without T_2-preparation[9], and also compare T_1 values to venipuncture-derived Hct to establish the feasibility of T_1-based Hct quantification for improved Y_v quantification.

REFERENCES: [1] Buxton et al., *MRM* (1998); [2] Lu et al., *MRM* (2003); [3] Chien et al., *JMRI* (1992); [4] Lu et al., *MRM* (2004); [5] Varela et al., *NMR Biomed* (2011); [6] De Vis et al., *Neuroimage* (2014); [7] Wright et al., *MRM* (1991); [8] Lu et al., *MRM* (2008); [9] Qin et al., *MRM* (2011). Grant Support: **NIH R21-HD069390 / T32-EB000814.**