MAGNETIZATION "RESET" IN T2-RELAXATION-UNDER-SPIN-TAGGING (TRUST) MRI

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INTRODUCTION: Recently, a T2-Relaxation-Under-Spin-Tagging (TRUST) MRI technique was developed to quantitatively estimate blood oxygenation (Y) via the measurement of pure blood R2 (=1/T2) (1). Spin labeling was used in TRUST to separate pure venous blood signals from surrounding static tissue, and additional T2 weighting was applied using non-slice-selective preparation pulses. This technique has shown great promises in the normalization of fMRI signals (2) and in the measurement of cerebral metabolic rate of oxygen ($CMRO_2$) (3). A limitation of the current TRUST protocol is that an excessively long TR (e.g. 8 sec) needs to be used, as a shorter TR results in an over-estimation of R2 due to spin history effect that causes additional signal decay at longer T2-prep time (denoted as effective TE, eTE) (1). In this work, a non-selective 90° RF pulse was added immediately following the EPI acquisition to "reset" the magnetization of all spins, and we showed that unbiased R2 estimation can now be achieved independent of TR. Shorter TR does reduce signal intensity and the precision of R2 fitting, and was more so for TRUST with post-sat. We found that a TR of 3 s for TRUST with post-sat provides a reasonable tradeoff between scan duration and precision. In addition to TR dependence, we have also tested the impact of TE (the interval between excitation and center k-line, not the T2-prep eTE). Although previous TRUST studies have already used a relatively short TE of 7 ms in a single-shot EPI, we used more aggressive parallel imaging and half-scan factors to reduce the TE to 4.9 and 3.6 ms. Although these changes do not seem to be a huge difference, they were found to reduce R2 estimation uncertainty by 50%. Thus TE of 3.6 ms is recommended for future studies.

METHODS: The TRUST sequence diagram is shown in Fig. 1, as described previously (1). Note that there is a difference between effective TE (eTE) and TE. The following imaging parameters were fixed in this study: TI=1200ms, matrix 64x64, voxel size 3.4x3.4x5mm^3, eTE=0ms, 40ms, 80ms and 160ms with an inter-pulse interval τ_{CPMG}=10ms, single-shot gradient-echo EPI. TR and TE were varied. The data processing of TRUST involves mono-exponential fitting of the control-label signal as a function of eTE, which yields the blood R2 value. Two aspects of the TR/TE-dependence were assessed. Accuracy was evaluated by investigating whether the estimated R2 values are different across TR or TE. Precision was studied by assessing whether the standard error of R2, ε_{R2}, (from the goodness-of-fit measure in Matlab's nlinfit routine) are different. TR and TE dependence of TRUST MRI were studied in separate cohorts.

TR study (27±7 yrd, 5 F, 5 M): Both the original TRUST sequence and the TRUST with post-sat sequence (red symbol in Fig. 1) were tested. For each sequence, nine TR values ranging from 1500ms to 7500ms with an interval of 750ms were used. The order of TR was pseudo-randomized.

TE study (27±3 yrd, 5 F, 3 M): It is well known that in ASL and TRUST a shortest possible TE should be used. However, due to the length of EPI echo train, TE cannot practically approach 0. The previous TRUST protocol used parallel imaging techniques to reduce the TE to 7.0ms, which is already shorter than most ASL studies. TE can be further reduced by using a higher SENSE factor and a smaller half scan factor, which, however, may result in greater image artifact. The effect on SNR is also not clear as shorter TE increases the SNR but few k-lines decreases the SNR. Therefore, the benefit of further reducing TE is really not clear especially given that the change is only 3-4 ms. Here we tested TE values of 7.0, 4.9 and 3.6 ms, corresponding to k-line number of 31 (SENSE 2, half scan 0.9), 20 (SENSE 3, half scan 0.9), 17 (SENSE 3, half scan 0.7), respectively. TR was 8 s.

RESULTS and DISCUSSION: *TR study* Fig. 2 shows the estimated R2 as a function of TR. For the original TRUST sequence (blue symbols), a TR dependence was observed (P<0.001 with ANOVA), confirming the previous report (1). For TRUST with post-sat (red symbols), no such dependence was observed (P=0.98 with ANOVA), suggesting that the addition of the post-saturation RF pulse indeed helped to remove the estimation bias. Fig. 3 shows the estimation error index, ε_{R2}, as a function of TR. There seems to be a trend of increased ε_{R2} with shorter TR for both sequences, especially for TR less than 3 s (P=0.005 ANOVA). This can be attributed to a TR-dependent decrease in the blood signal (i.e. control-label), as shown in Fig. 4. Fig. 4 also revealed that, at shorter TR, the TRUST with post-sat yields lower signal compared to the original TRUST sequence, which may explain the greater ε_{R2} in Fig. 3. Based on these results, a TR of 3 s using TRUST with post-sat is recommended.

TE study The SNR of the blood signal was 33±6, 40±6 and 62±7 for TE of 7.0ms, 4.9ms and 3.6ms, respectively, with an increase at shorter TE (mix-effect model analysis, P=0.004). This SNR increase is considerable given the relatively smaller change in TE perhaps because the outflow effect of the blood has been dramatically reduced at shorter TE. Accordingly, ε_{R2} showed a significant reduction with shorter TE (Fig. 5a, P=0.03) and the ε_{R2} value at TE=3.6 ms was only 51% of that at TE=7.0ms. A smaller dependence of R2 on TE was observed (Fig. 5b, P=0.02) which was due to an over-estimation of R2 under low SNR conditions (confirmed by Monte Carlo simulation).

In summary, we recommend the use of TRUST with post-sat sequence at TR=3 s and TE=3.6 ms for future TRUST studies, which is expected to reduce the scan duration by 60% while reduce the estimation error by 50%.

REFERENCES: 1) Lu and Ge. MRM, 60:357, 2008; 2) Lu et al. MRM, 60:364, 2008; 3) Xu et al. MRM, 62:141, 2009.

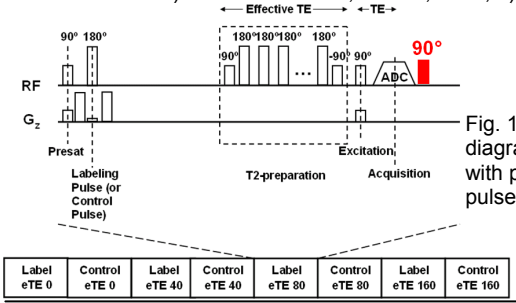


Fig. 1: Sequence diagram of TRUST with post- saturation pulse.

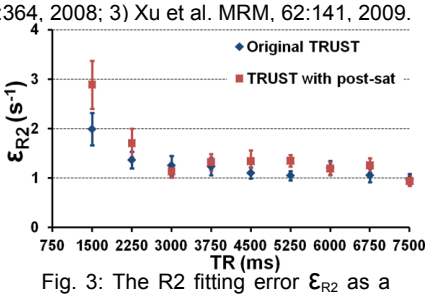


Fig. 3: The R2 fitting error ε_{R2} as a function of TR.

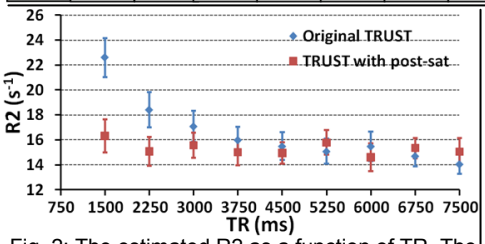
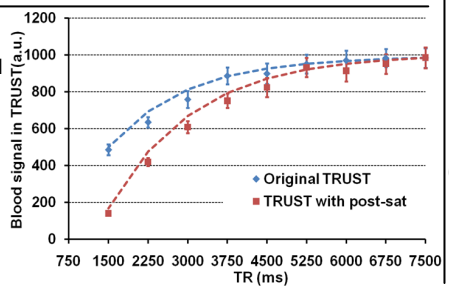


Fig. 2: The estimated R2 as a function of TR. The error bars indicate SE across subjects (N=10).

Fig. 4: The blood signal in TRUST MRI as a function of TR. The dashed lines represent simulation results.



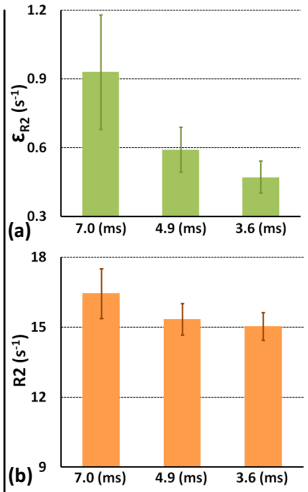


Fig. 5: Estimation error, ε_{R2} and R2 as a function of TE.