Comparison of Optimized Single-PLD, Sequential and Time-Encoded Multi-PLD PCASL Methods for CBF Accuracy and Reproducibility

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Introduction: There are many experimental designs which use a pseudo-continuous Arterial Spin Labelling[1] (PCASL) preparation for measuring cerebral blood flow (CBF), the main distinction being whether images are acquired at one or multiple post-labelling delays (PLDs). Using one PLD is recommended for clinical applications[2] because it is simple and many averages can be acquired at this single time point. However, arterial transit time (ATT) variation cannot be accounted for and so CBF may be mis-estimated. Multi-PLD ASL can estimate both CBF and ATT, reducing this potentially large source of bias. Furthermore, multi-PLD acquisitions can be time-encoded (TE), where the tag and control conditions are varied within the PCASL labelling period using a Hadamard scheme. Decoding results in signal averaging, but the label durations are limited, reducing the available ASL signal. It is not yet clear which method is capable of producing the most accurate CBF estimates, since previous comparison studies have not fully optimised each protocol. In this work, we compare optimised protocols for common variants of these methods, and compare them using Monte Carlo (MC) simulations and in vivo experiments.

Methods: The protocols shown in Figure 1 were optimised for CBF accuracy using the Cramér-Rao lower bound across an ATT range of 0.5-2 s.[3] Scan time was fixed at 5 minutes and the maximum label duration was 1.8 s. MC simulations and in vivo experiments (10 healthy volunteers, single-shot 3D GRASE readout) were performed. Data was fit for CBF and ATT using a single-compartment model[4]. An ATT of 1.3 s was assumed for single-PLD data. Ground truth CBF and ATT values were generated by fitting the combined data from all protocols. Test-retest comparisons were performed by splitting data from each protocol in two and fitting separately.

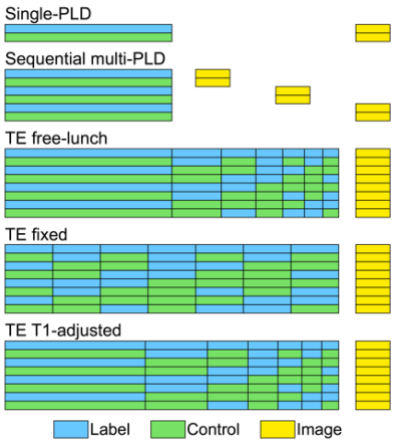

Figure 1: *Examples of the protocols included in this comparison.*

Results: Figure 2 shows the in vivo root-mean-squared-errors (RMSE) relative to the ground truth values, across subjects, for each protocol, which agree well with Monte Carlo simulation results (not shown). Single-PLD and TE-fixed have significantly larger CBF errors than the other protocols, while the TE protocols all have significantly lower ATT errors than the sequential protocol. The test-retest correlation coefficients are shown in Table 1. All protocols had high within-scan CBF reproducibility, though sequential, $TE_{free\text{-}lunch}$, and $TE_{T1\text{-}adj}$ were the most reproducible. The ATT estimates were less reproducible, but still show good agreement.

Discussion and conclusions: We have demonstrated that well optimised multi-PLD PCASL protocols can not only be more accurate than a single-PLD protocol, by taking ATT into account, but can also be more reproducible. In agreement with previous work[5], we found that TE_{fixed} produced worse CBF estimates, but better ATT estimates, than a sequential multi-PLD protocol. By increasing the SNR of earlier TE blocks, as in $TE_{free\text{-}lunch}$ and $TE_{T1\text{-}adj}$, CBF estimates were comparable to the sequential method, while maintaining more accurate ATT estimates. However, TE methods are more sensitive to motion than sequential acquisitions, so the latter may be preferred for studies of less compliant subjects.

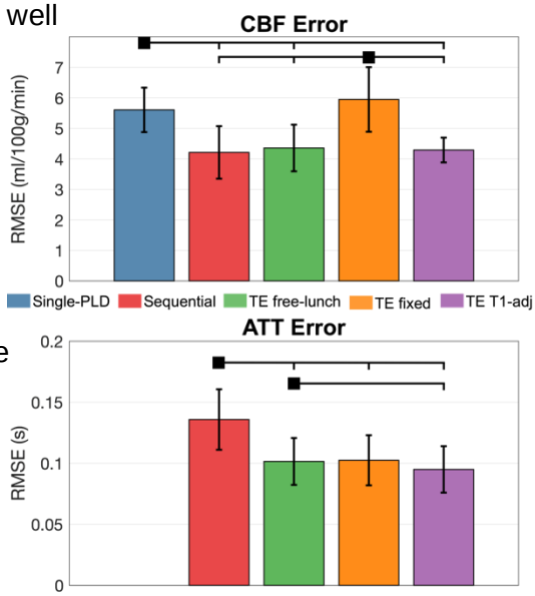

Figure 2: *In vivo CBF and ATT RMSE. Bar heights and error bars are the mean and SD across subjects. Significant improvements are shown by horizontal bars (one tailed Wilcoxon signed rank test, $p < 0.05$).*

Protocol name	*CBF corr coefficient*	*ATT corr coefficient*
Single-PLD	0.919	–
Sequential	0.938	0.838
$TE_{free\text{-}lunch}$	0.931	0.853
TE_{fixed}	0.902	0.866
$TE_{T1\text{-}adj}$	0.935	0.869

Table 1: *Voxel-wise test-retest correlation coefficients for in vivo data, combined across all subjects. All differences were significant.*

References: [1]Dai et al. MRM 2008; [2]Alsop et al. MRM 2015; [3]Woods et al. ESMRMB 2017; [4]Buxton et al. MRM 1998; [5]Guo et al. JMRI 2017.