The many advantages of arterial spin labeling with long label duration

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Introduction: Pseudo-continuous arterial spin labeling (PCASL) is a method for non-contrast perfusion imaging that tags blood flowing across a labeling plane. The labeling plane in the neck is active for a finite period of time (the label duration, τ) followed by a delay time for blood to reach the brain tissue (the post label delay, PLD), then image data is acquired. Generally, τ is about 1.5 s; a recent consensus paper recommends 1.8 s [1]. However, image SNR is expected to scale with $\left(1-\exp(-\tau/T_{1b})\right)$ where T_{1b} is the longitudinal relaxation time of arterial blood (~1.6 s at 3 T) [1], which suggests τ should be long. It has been demonstrated that SNR-efficiency is near optimal with τ between 3 s and 4 s, assuming typical transit delays (δ) [2]; longer τ are predicted to provide benefit if δ is abnormally long [3]. Here we report benefits, beyond the recognized SNR advantages, observed with long label durations. Specifically, we characterize improved temporal signal stability and reduced sensitivity to long transit delays.

Methods: All data were acquired on a GE MR750 3T scanner; subjects provided informed consent. Temporal signal stability was assessed via serial perfusion-weighted imaging. Thirty consecutive label/control pairs were acquired with a single-shot 3D stack-of-spiral readout and τ = 1.5 s, then repeated with τ = 3.0 s. Temporal resolution was 8.2 s and 10.2 s for short and long τ, respectively. The PLD was 0.7 s; vessel suppression was applied. Five regions (between 1.6 ml and 3.7 ml) were placed in territories fed by the middle, anterior, and posterior cerebral arteries. Sensitivity to δ was quantified theoretically for $\tau \geq 0.5$ s by calculating the signal with knowledge of δ (using Eq. 1 in [3]), then modeling this signal with the common assumption that $\delta \leq$ PLD. Empirical evidence supporting long τ is shown in a subject with mild cognitive impairment. PLD was 2 s and vessel suppression was not applied.

Results: Improved temporal stability was observed with long label ASL relative to τ = 1.5 s, **Fig. 1**. A standard deviation of 0.57 was measured with τ = 1.5 s; 0.33 with τ = 3.0 s. This change in variance is not explained by SNR differences: image SNR was between 20 and 50 in most cases and large regions further reduced random noise. The high correlation between regions suggests a global signal fluctuation between shots that is reduced in amplitude with long τ. The source(s) of these fluctuations are unknown but may be related to physiological effects such as cardiac pulsations, respiratory motion, and/or changes in functional activity.

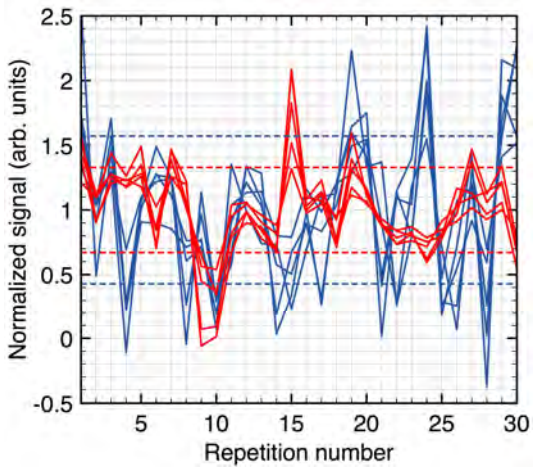

Figure 1: Perfusion-weighted signal in 5 regions during repeat scans with τ = 1.5 s (blue) and 3.0 s (red). Standard deviations (dashed lines) of 0.57 and 0.33 were measured for τ = 1.5 s and 3.0 s respectively. The increased SNR with τ = 3.0 s does not account for reduced variance.

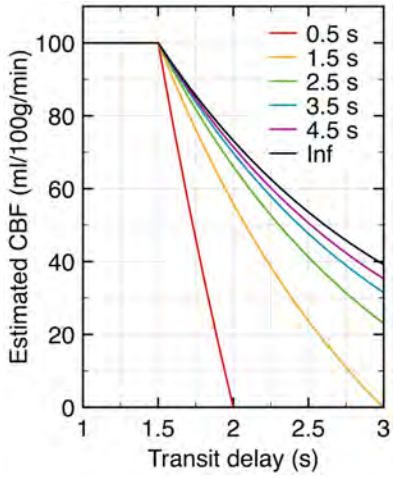

Figure 2: Predicted flow versus δ for several values of τ. PLD = 1.5 s and 100 ml/100g/min flow were assumed. Flow is underestimated when δ > PLD, but long τ is less severely impacted by long δ than short τ.

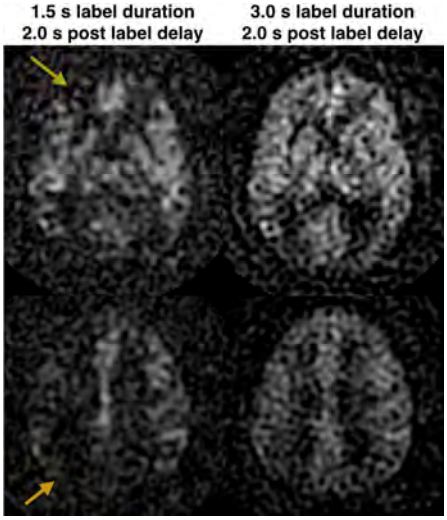

Figure 3: Perfusion-weighted images of a 77 year old subject with mild cognitive impairment acquired with τ = 1.5 s (left) and 3.0 s (right). The PLD was 2 s. Apparent hypo-perfusion is widespread in regions of suspected long δ's (arrows) with τ = 1.5 s. Increased SNR and reduced sensitivity to potentially long δ's are hallmarks of long labeling times.

Sensitivity to long δ was predicted to be less severe with long labeling than with short labeling, **Fig. 2**. In the case of long transit delays—consider a δ = 3 s, for example—a 1.5 s label duration will report no flow while long labeling will report up to 40% of the true flow. While still highly vulnerable to long δ, sensitivity to δ is reduced with longer labeling. Furthermore, the longest δ that can be observed is given by τ + PLD, which favours long τ in cases of delayed arrival, such as stroke and aging.

Discussion and conclusions: Long labeling is known to improve SNR in PCASL measurements, but additional benefits exist. We observe reduced temporal fluctuation with long τ than with standard τ. This may be due to increased averaging over the cardiac and respiratory cycles. Regardless of the explanation, multi-shot acquisitions may benefit from improved stability. Sensitivity to transit delays is a major limitation of ASL. While long τ does not solve this problem, it does somewhat mitigate the effect. Our experience with long label PCASL in a variety of subjects, including those with cognitive impairment, **Fig. 3**, suggests that overall image quality is significantly improved for reasons beyond increased SNR.

References: [1] Alsop DC, *et al.* MRM. 2014. [2] Zun Z, *et al.* ISMRM 2014. [3] Dai W, *et al.* MRM. 2012.