Experimental assessment of pCASL labeling efficiency in the peripheral vasculature

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Target audience. Researchers and clinicians interested in quantify skeletal muscle perfusion with ASL.

Introduction. Recent studies have shown that the dynamics of skeletal muscle perfusion during reactive hyperemia can provide insight into endothelial function and impaired vascular reactivity in disease states [1]. While several different ASL labeling schemes exist, they each work by taking the pair-wise difference of two images – one with magnetically-labeled blood (tag) and one without (control). The resultant signal difference removes static tissue signal, yielding a signal that is proportional to micro-vascular perfusion. Skeletal muscle perfusion has been quantified with pulsed ASL (PASL) [2], which achieves inversion using a single adiabatic inversion pulse [3], and continuous ASL (CASL) [1], which relies upon flow-driven adiabatic inversion to label arterial blood [4]. More recently, pseudo-continuous ASL (pCASL) has been used to measure perfusion [5] as current transmit coils are not optimized to drive long RF pulses. Similar to CASL, labeling for pCASL relies on flow-driven adiabatic inversion, which requires blood flow velocity (v) to satisfy the adiabatic condition: $\frac{1}{T_2} \ll \frac{Gv}{|B_1|} \ll \gamma|B_1|$, where G is the average gradient amplitude [6].

In contrast to the vessels supplying the brain, the peripheral circulation has higher impedance resulting in a different flow waveform. Specifically, blood flow in the popliteal artery is triphasic at baseline (Figure 1a), with antegrade flow during systole, followed by retrograde and antegrade flow during diastole. During reactive hyperemia, the flow waveform becomes entirely antegrade (Figure 1b). Average blood flow velocity differs substantially between baseline, ischemia, and reactive hyperemia, which may result in variable tagging efficiency for techniques that rely upon flow-driven adiabatic inversion. Theoretical explorations of the dependence of blood flow velocity on tagging efficiency suggest that with decreasing peak flow, there is a decrease in tagging efficiency [5,6]. These simulations have been corroborated by experimental investigations of tagging efficiency performed in the brain [7]. However, those results may not apply to muscle perfusion, due to the different blood flow waveform in the peripheral vasculature. The purpose of this work was to experimentally investigate pCASL label efficiency as a function of arterial velocity in the peripheral vasculature, and to compare muscle perfusion measured using pCASL and PASL.

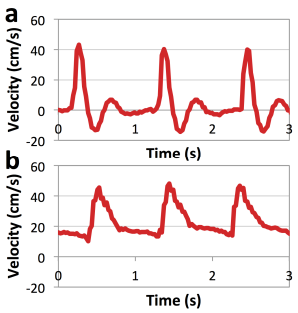

Figure 1. Popliteal artery waveform during baseline (a) and hyperemia (b).

Methods. *pCASL pulse sequence.* A pCASL sequence was implemented at 3T with the following sequence parameters: Single-slice GRE-EPI with acquired matrix=80×50 (reconstructed to 80×80), FOV=25×25 cm, slice thickness=10 mm, TR/TE_1=4000/8.1ms. Labeling duration=1.45-2s, post-labeling delay (PLD)=1.5-1.9 s, Hanning window-shaped pulses with average B_1=1.7 μT, pulse interval = 1 ms, G_{max}/G_{avg}=9/1 mT/m. Control condition utilized average gradient = 0 mT/m and 180° phase increment between adjacent RF pulses.

PASL pulse sequence. An established PASL sequence [2] was used for comparison of perfusion results. Sequence parameters were as follows: Slice-selective or non-selective adiabatic inversion, PLD=942 ms, GRE-EPI readout.

pCASL labeling efficiency during reactive hyperemia. To experimentally assess inversion efficiency, the pCASL sequence was modified such that the readout immediately followed labeling (PLD = 1.6 ms, additional time for signal recovery following readout = 1.9 s). Data were acquired in two young healthy subjects. Spatial resolution was increased to 2.5× 2.5 mm in order to better resolve signal intensity in the femoral artery. Temporal sampling of the time course was maximized by conducting three separate experiments with EPI data acquired following label only, following control only, without label or control preparations. Additionally, projection phase-contrast [8] data (VENC = 80-120 cm/s, temporal resolution = 48 ms) were acquired in the tagging plane to characterize the baseline and hyperemic velocity waveforms. For each scan, data were acquired during 1 min baseline, 3 min ischemia, and 2 min recovery. Additional time was allotted between scans to ensure the subjects recovered back to their relative baseline state. For all EPI datasets, signal intensity in the artery was averaged for each time point, and control and label signals were normalized to images acquired without pCASL preparation (M_0).

pCASL vs. PASL. Perfusion was quantified with PASL and pCASL during a series of ischemia-reperfusion paradigms in two subjects. After masking out the large arteries, signal intensity was averaged in the soleus, and perfusion was computed according to the appropriate models for each labeling method (pCASL – as described by Alsop, et al. [9], and PASL – as described by Raynaud, et al [2]).

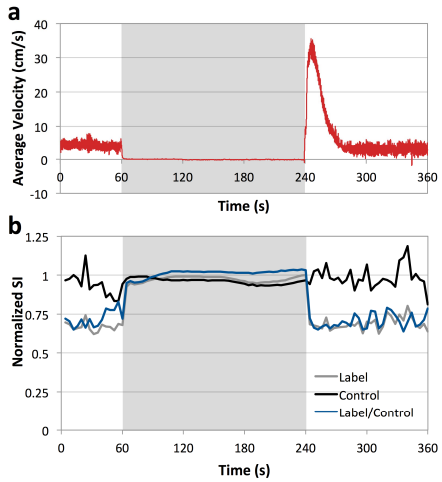

Figure 2. Results averaged over two subjects for mean blood flow velocity (a) and relative signal intensity (normalized with respect to M_0) in the vessel following label and control conditions (b) through-out an ischemia reperfusion paradigm (grey box indicates ischemia). There is no apparent impact of the variable average blood flow velocity on inversion efficiency, measured as ≈ 65% during baseline and recovery.

Results. *pCASL labeling efficiency during reactive hyperemia.* Figure 2a shows sliding-window averaged (over one second, approximately one cardiac cycle) blood flow velocity during an ischemia-reperfusion paradigm for a single subject. Although peak velocity does not substantially change during hyperemia (as seen in Figure 1), there is a large increase in average blood flow velocity during hyperemia. This variability in blood flow does not impact labeling efficiency, as is shown in Figure 2b (data are averaged over both subjects). During ischemia (grey box) there is no flow, thus no inversion is achieved, and label and control conditions have the same signal intensity as M_0. However, both during baseline and hyperemia, there is no change in relative label or control signal with respect to the M_0 signal. Experimentally derived average labeling efficiency was 65% – lower than the estimated 85% labeling efficiency achieved in the brain [5].

pCASL vs. PASL. Averaged over both subjects, temporal dynamics of perfusion measured with PASL and pCASL are in good agreement (Figure 3). However peak perfusion measured with pCASL is larger than PASL, even before correcting for the tagging efficiency of approximately 65%.

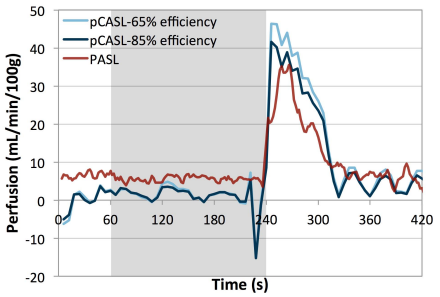

Figure 3. Average perfusion during an ischemia reperfusion paradigm (grey box = ischemia) quantified with PASL and pCASL (using literature reported (dark blue) and experimentally measured (light blue) inversion efficiencies). Temporal dynamics agree, although peak perfusion measured PASL is lower than pCASL.

Discussion and Conclusions. In the peripheral vasculature, blood flow velocity varies substantially throughout the cardiac cycle (including periods of retrograde flow) and even more so over the course of an ischemia reperfusion paradigm. This variability does not appear to impact the labeling efficiency of pCASL. As expected, the control condition does not impact signal in the feeding artery. The labeling condition achieves consistent inversion efficiency for blood flow velocities at baseline and during hyperemia. Partial-volume effects due to the low resolution of the EPI readout may have caused underestimation of the calculated tagging efficiency, however this would likely not affect the observed consistency of tagging efficiency throughout baseline and hyperemia. Although PASL provides much higher temporal resolution sampling of the perfusion time course, it has consistently yielded lower peak perfusion values [2,10], potentially due to finite inversion slab thickness. Future studies investigating skeletal muscle perfusion will need to weigh the tradeoffs between PASL and pCASL when deciding which method to pursue.

References. [1] Wu, et al. JACC 2009; [2] Raynaud, et al. MRM 2001; [3] Kim, et al. MRM 1995; [4] Detre, et al. MRM 1992; [5] Dai, et al. MRM 2008; [6] Williams, et al. PNAS 1992; [7] Aslan, et al. MRM 2010; [8] Langham, et al. MRM 2010; [9] Alsop, et al. MRM 2014; [10] Englund, et al. JCMR 2013. **Grant Support.** AHA award, NIH R01 HL075649 and HL109545.