Balanced tissue magnetization reduces confounding BOLD effect in post-ischemic muscle perfusion quantification

Michael C LANGHAM[1], Erin K Englund[1], Cheng Li[2], Thomas F Floyd[3], Emile R Mohler III[4], and Felix W Wehrli[1]

[1]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Radiology, University of Pennsylvania, Philadelphia, PA - Pennsylvania, United States, [3]Anesthesiology, SUNY Stondy Brook, Stony Brook, New York, United States, [4]Vascular Medicine Section, University of Pennsylvania, Philadelphia, PA, United States

Introduction: Microvascular dysfunction, associated with peripheral arterial disease, has previously been assessed by quantifying post-ischemic perfusion in calf muscle with continuous arterial spin labeling (CASL) [1]. The most common application of CASL has been brain perfusion quantification [2] and it is preferable to pulsed ASL (PASL) because greater SNR can be achieved. In this work we demonstrate that the saturation inversion-recovery (SATIR) PASL [3] outweighs the SNR gain of CASL significantly by reducing the confounding blood oxygenation level dependent (BOLD) effect in temporally resolved quantification of post-ischemic muscle perfusion.

Methods: All experiments were performed on a 3T system (Siemens Tim Trio) using an 8-channel phased array Tx/Rx extremity coil (Invivo Inc., Pewaukee, WI). An automatic tourniquet was placed on the thigh and inflated to 200 mmHg to induce ischemia. The paradigm consisted of 1 min baseline, 5 min occlusion and 3 min recovery. Implementation of single-slice CASL [4]: TR = 4s with 2s tag (consisting of 20 rectangular 2.5 µT RF pulses of 100 ms duration with 120 µs gap played out with gradient amplitude of 2.5 mT/m), post-label delay 1.9s. The gradient polarity was reversed between labeling and control planes which were located 6 cm proximal and distal to the imaging plane (calf) placed at isocenter. Imaging parameters for SATIR PASL (see [3] for details) were: TR =1s, adiabatic inversion was applied for label (slice-selective) and control (non-selective), post-label delay 0.93s. The spatial-encoding portion of the sequence consisted of a single-shot GRE-EPI (slice thickness 10 mm, FOV 200x200 mm^2, matrix 64x64 , BW 3125 Hz/pix, echo spacing 0.78 ms, effective TE 9 ms with partial Fourier fraction of 0.625). Prior to next cycle slice-selective saturation pulse is applied to eliminate residual magnetization. In a healthy male subject (age 39 years) the following protocols were performed with cuff occlusion: (1) CASL control only, (2) SATIR PASL control only, (3) CASL and (4) SATIR PASL (repeated in a different scan session). The data from the protocols 1 and 2 serve as reference to the protocols 3 and 4, for assessing the residual confounding signal caused by the rapid nonlinear change in the BOLD effect. For the control-only acquisitions, the images were separated into "odd" and "even" datasets with the latter being treated as control data. In order to temporally match the control and label images, the control images were linearly interpolated [4] prior to subtraction.

Results: **Fig 1** shows the time-course of the signal intensity after cuff deflation (t = 360s). For both CASL and PASL there is a steep rise in the signal resulting from the rapid change in the BOLD signal. Comparison of **Figs 1a** and **b** suggests that for CASL there is only a small difference between control and label signal (**Fig 1b**) suggesting that any imbalance in tissue magnetization between control and label due to the BOLD effect can cause significant errors in the derived perfusion. The signal difference between successive images in the control-only PASL data is much smaller (**Fig 1c**), and the isolation of the perfusion signal is significantly improved (**Fig 1d**) with SATIR PASL. In **Fig 3** post-ischemic muscle perfusion quantified in two different scan sessions is plotted jointly and was found in good agreement with results reported in [3].
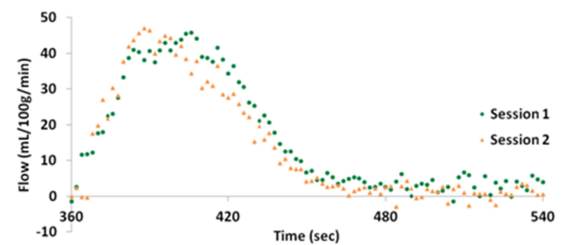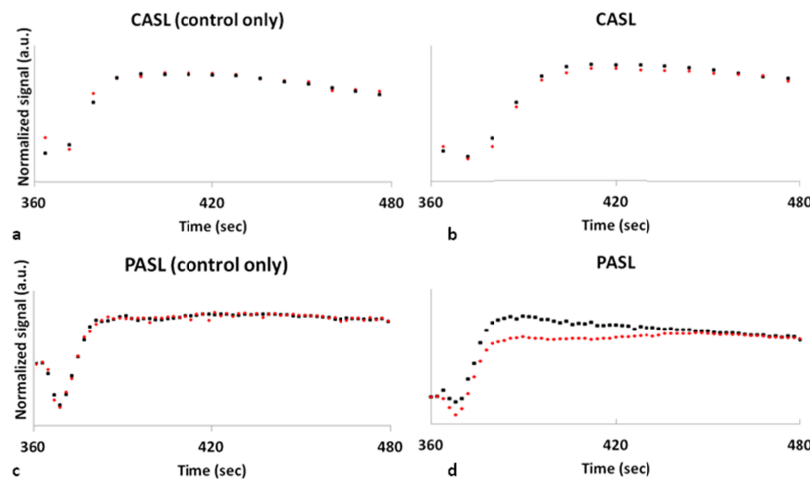

Fig 2 Quantification of post-ischemic perfusion in gastrocnemius muscle of a healthy 39 yr-old subject with SATIR PASL. The measurements were performed on separate scan sessions.

Fig 1 Post-ischemic label and linearly interpolated control signal acquired with **a**) CASL (control only), **b**) CASL, **c**) SATIR PASL (control only) **d**) SATIR PASL. The effective temporal resolution is 8s for **a** and **b** and 2s for **c** and **d**, i.e. TR=4s and 1s, respectively. The black and red markers correspond to alternate data points in the control only images (**a** and **c**), and control and label (**b** and **d**),

Conclusions: The two main features of SATIR PASL, higher temporal resolution (1 s vs 4s) and the slice-selective saturation pulse played out at the end of each pulse sequence cycle, result in post-ischemic muscle perfusion quantification less susceptible to confounding residual BOLD effect. The saturation pulse and the greater temporal resolution significantly reduce the imbalance in the tissue magnetization caused by the BOLD effect between successive images. A TR of 4s (minimum for CASL) limits its application because the rate of change in the tissue oxygenation between successive TR cycles is not constant, thus linear interpolation is not adequate to minimize errors from the time-varying BOLD effect.

References: [1] Wu et al, JACC 2009, [2] Williams et al, PNAS 1992, [3] Raynaud et al, MRM 2001, [4] Wu et al, JMRI 2008.