Combined measurement of perfusion and venous oxygen saturation during reactive hyperemia in the leg

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INTRODUCTION. Recent studies suggest that detection of peripheral arterial disease (PAD) may be achieved through MRI measurement of parameters of vascular physiology in the lower extremity during reactive hyperemia [1-2]. Current MRI techniques are limited to the measurement of either macrovascular parameters, such as venous oxygen saturation (S_vO_2) using MR susceptometry [3-5], or microvascular parameters, such as perfusion using arterial spin labeling (ASL) [6]. MR susceptometry is capable of determining oxygen saturation based on differences in phase accumulation between blood and surrounding tissue [3]. Pulsed arterial spin labeling (PASL) has been shown to produce accurate perfusion in skeletal muscle during reactive hyperemia post cuff occlusion [6]. In all ASL sequences, a long post-labeling delay (PLD) is required for tagged spins to enter the imaging slice. To make use of this dead time, we propose to insert a susceptometry sequence into the PLD, and to investigate the sequence during reactive hyperemia in the leg. We aim to demonstrate the capability of a combined PASL and MR susceptometry sequence (PASL/S_vO_2) to measure perfusion and venous oxygen saturation simultaneously.

METHODS. Perfusion imaging was performed using a PASL variant, saturation inversion recovery (SATIR) [6]. Similar to FAIR, control and tag conditions were achieved using a non-selective and slice-selective adiabatic inversion pulse, respectively. ASL image acquisition followed a 930 ms PLD during which susceptometry data were acquired at a slice 3 cm distal to the ASL imaging slice. Because the non-selective inversion pulse disrupts magnetization in the entire coil sensitivity region, only susceptometric images acquired after slice-selective inversion could be used to calculate S_vO_2, though the susceptometry sequence was run every PLD to control for magnetization transfer effects. Reactive hyperemia was induced with a cuff (Aspen Labs A.T.S. 1500 Tourniquet System, Littleton, CO) secured around the superior thigh inflated to 200 mmHg for 3 mins. Perfusion and S_vO_2 were calculated as:

$$f = -\frac{\lambda}{T}\cdot\ln\left[\frac{M_{SS}-M_{NS}}{M_{SS}+M_{NS}}\cdot\left(1-e^{-T/T_1}\right)+1\right]$$ [6], and $$\%HbO_2 = \left[1-\frac{2\cdot\frac{\Delta\varphi}{\Delta TE}}{\gamma\,\Delta\chi_{do}\,Hct\cdot B_0\left(\cos^2\theta-1/3\right)}\right]\times 100$$ [5].

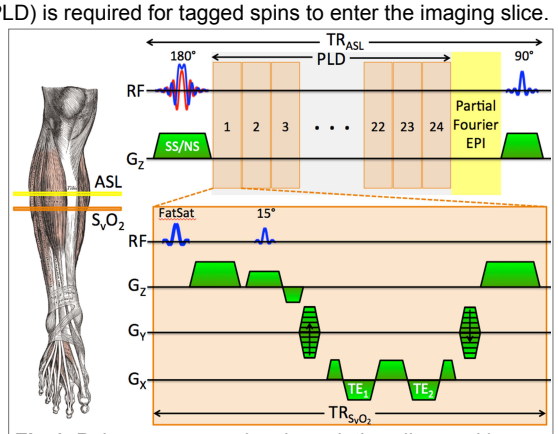

Fig 1. Pulse sequence showing relative slice positions and timing of susceptometry interleaved with PASL.

An 8-ch Tx/Rx knee coil (Invivo Inc., Pewaukee, WI) was used for image acquisition at 3T with the following parameters: PASL – partial Fourier GRE-EPI with TR/TE=1000/9 ms, FOV=20×20 cm, ST=1 cm, matrix=64×40 (reconstructed to 64×64), BW=1562.5 Hz/pixel; Susceptometry – multi-echo spoiled GRE, with TR/TE/ΔTE= 38.75/7.6/3.68 ms, FOV=96×96 mm, ST=1 cm, matrix=96×24 (keyhole, reconstructed with reference scan to 96×96), BW=694 Hz/pixel (**Fig 1**).

Experimental Protocol. In one healthy subject (F, 24 years) twelve consecutive acquisitions alternating between PASL alone, PASL/S_vO_2 combined, and S_vO_2 alone were obtained, each with 1 min baseline, 3 mins occlusion, 4 mins recovery, and 1 min rest between scans. On a different day, the protocol was repeated with only PASL alone and PASL/S_vO_2 combined. Therefore for PASL experiments there were 8 datasets for PASL alone and 8 PASL/S_vO_2 combined, and for S_vO_2 experiments there were 4 for S_vO_2 alone and 8 for PASL/S_vO_2 combined. S_vO_2 was quantified in the peroneal vein, and washout time and upslope were calculated for each S_vO_2 dataset. Perfusion was calculated in a region of interest in the gastrocnemius (gastroc) muscle for each PASL dataset. A paired Student's t-test was used to test for differences between measurement methods.

RESULTS. **Fig 2a** compares average perfusion in the gastroc measured using PASL and PASL/S_vO_2. **Table 1** shows mean and standard deviation (SD) of average peak perfusion and time to peak in the gastroc, and upslope and washout time in the peroneal vein. No significant differences were detected. **Fig 2b** compares S_vO_2 measurements made with susceptometry alone and with PASL/S_vO_2. In **Fig 2a** and **2b**, error bars indicate SD. Perfusion and oxygen saturation time courses are similar for the singular and combined measurement techniques. **Fig 2c** shows simultaneous perfusion and S_vO_2 from a single acquisition.

Table 1. Mean (SD) peak perfusion and time to peak in the gastroc using PASL & PASL/S_vO_2, and upslope and washout time in the peroneal vein using PASL/S_vO_2 & S_vO_2.

	PASL	PASL/S_vO_2	S_vO_2
Peak Perfusion $\left(\frac{mL}{min\cdot 100g}\right)$	48 (7)	43 (4)	
Time to Peak (s)	24 (4)	24 (3)	
Upslope $\left(\frac{\%HbO_2}{s}\right)$		1.4 (0.2)	1.5 (0.2)
Washout Time(s)		16 (3)	16 (1)

DISCUSSION. Measured peak perfusion and time to peak match literature reported values [6]. Calculated upslope and washout time agree with measurements made in young healthy subjects in the femoral vein [5]. One potential concern with our method is interference between the PASL and S_vO_2 measurements. We chose to measure S_vO_2 downstream from perfusion to prevent spins affected by S_vO_2 measurement from flowing into the perfusion slice. This work suggests that simultaneous measurement of S_vO_2 and perfusion is feasible using the hybrid PASL/S_vO_2 sequence. This method quantifies parameters of macrovascular and microvascular physiology in a single study, which may help to better understand the pathophysiology of PAD and aid in the diagnosis and treatment of this disease.

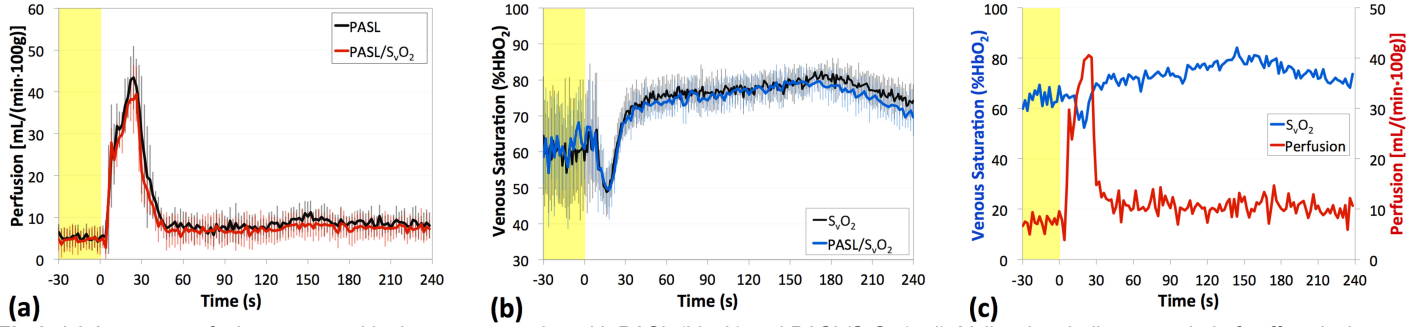

Fig 2. **(a)** Average perfusion measured in the gastrocnemius with PASL (black) and PASL/S_vO_2 (red). Yellow box indicates period of cuff occlusion, with release at 0 s. **(b)** S_vO_2 measured with susceptometry alone (black), and PASL/S_vO_2 (blue) in the peroneal vein. In **(a)** and **(b)** vertical bars indicate standard deviation. **(c)**. Simultaneous measurement of oxygen saturation and perfusion using PASL/S_vO_2 sequence in a single scan.

REFERENCES. [1] Wu et al, JACC 2009; [2] Langham et al, ISMRM 2011; [3] Haacke et al, Human Brain Mapping 1997; [4] Fernández-Seara et al, MRM 2006; [5] Langham et al, JACC 2011; [6] Raynaud et al, MRM 2001. **Acknowledgements**. NIH Grants R01HL075649 and 5T32EB009384.