Quantification of skeletal muscle perfusion using Velocity Selective Arterial Spin Labeling at 3T

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Introduction: Peripheral arterial disease (PAD) affects 10% of the population over the age of 60 [1]. Arterial stenosis can restrict local perfusion, causing a clinical spectrum from intermittent claudication to gangrene. There is a need for accurate assessment of the perfusion of lower limb skeletal muscle in patients with PAD to aid diagnosis and management. One method that showed promise was Continuous Arterial Spin Labeling (CASL), which uses magnetically labeled blood protons as an endogenous contrast agent to directly quantify perfusion [2]. However, prolonged transit delay between the labeling and imaging planes underestimates skeletal perfusion [3]. To overcome this, we present a Velocity Selective ASL (VSASL) sequence, which tags spins based on their velocity rather than spatial location [4]. Through careful selection of the cut-off velocity (V_C), the leading edge of the labeled bolus is generated at the arteriole-capillary bed interface, eliminating the transit delay associated with traditional ASL methods [4]. VSASL has previously been performed in skeletal muscle but the authors were unable to quantify resting perfusion due to low contrast-to-noise [5]. In this study the VSASL acquisition and V_C are optimized for calf skeletal muscle. Secondly, we aimed to demonstrate the feasibility of VSASL in measuring perfusion at rest in the calf skeletal muscles of five healthy volunteers.

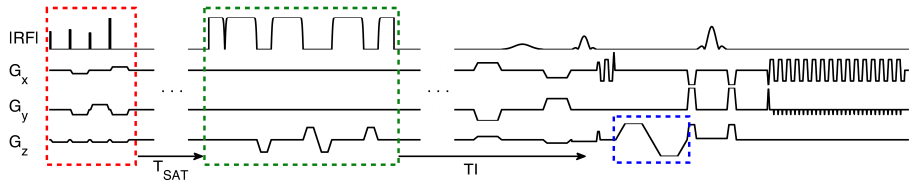

Figure 1: Pulse diagram showing the global presaturation (red box), the BIR-8 tagging module (green box) and fat sat SE-EPI with flow crushing gradients (blue box), for a tagging along the z axis.

Methods: **Pulse Sequence (Figure 1)**: A global pre-saturation [6] is used to remove spin history effects, and is followed by recovery time T_{SAT}. A B_1 and eddy current insensitive BIR-8 tagging module then saturates spins with velocity $V > V_C$. Flow crushing gradients are added to the readout to only acquire spins with $V < V_C$ after inflow time (TI). To remove static tissue, a second acquisition is made with the BIR-8 gradients off, and the subtraction of the two images (ΔM) gives the perfusion signal. **V_C Calibration**: V_C was varied from 1-8 cm/s with the tagging gradient applied serially on three orthogonal axes in one volunteer [4]. Sensitivity to the vascular orientation was removed by calculating the point at which the measurement of perfusion at a single V_C is independent of tagging gradient direction. **Data Acquisition**: Five healthy subjects (4 males, 1 female, age 26-32, mean 29) were scanned on a 3T scanner (Siemens Healthcare, Erlangen, Germany) with a 32-channel body array coil. A spin echo T1W image was acquired for anatomical reference as the subjects rested in the scanner bore prior to perfusion measurements. The TR, T_{SAT} and number of slices were optimized to give the maximum contrast to noise on the central slice, by solving a modified single compartment model [7]. Acquisition parameters were TR = 4.9 s, TE = 32 ms, readout FOV = 290-320 mm, 64x32 matrix, 50% phase FOV, 10 mm slice thickness, 40 tag-control pairs, TI = 0.9 s, T_{SAT} = 3.1 s, V_C = 2, velocity selection on the x axis. A spin echo EPI readout was used to acquire 15 axial slices per TR to give whole calf coverage. Data were corrected for coil sensitivity using a separate volume coil acquisition. Total scan time was 18 minutes. **Post Processing**: Perfusion, *f*, was quantified on a voxelwise basis by modifying the general kinetic model [7] to account for the VSASL parameters. Data were fitted to

$$\Delta M(TI) = M_{0,b} \cdot \alpha \cdot f \cdot TI \cdot q_p(TI,f) \cdot (1-\exp[-T_{SAT}/T_{1,b}]) \cdot \exp(-TI/T_{1,b})$$

where q_p accounts for differences in relaxation between muscle and blood [7]. The saturation efficiency of the BIR-8 preparation (α = 0.89) was found through Bloch equation simulations. The equilibrium magnetization of blood ($M_{0,b}$) was found by taking the mean of the muscle signal M_0 sequence and correcting for the muscle-blood partition coefficient (λ) and relative T_2 decay [8]. We assumed λ = 0.9 [9], $T_{2,muscle}$ = 32 ms [10], $T_{2,blood}$ = 150 ms [11] and a $T_{1,muscle}$ of 1.4 s [10]. Perfusion values are reported in a muscle mask excluding large arteries that was defined on the anatomical T1W data.

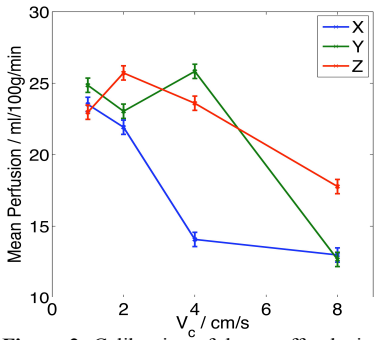

Figure 2: Calibration of the cutoff velocity in the calf of subject A, showing the apparent perfusion reaches a plateau for $V_C \leq 2$ cm/s.

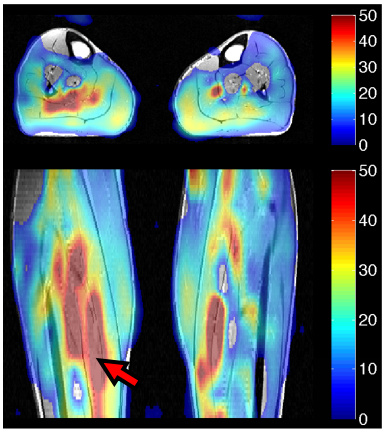

Figure 3: Perfusion map from subject B overlaid onto the T1W anatomical, with colour scale in ml/100g/min. Voxels of $f <$ 5 ml/100g/min are excluded. Red arrow indicates arterial artefact (see discussion).

Results: Perfusion reached a plateau for all three axes at $V_C \leq 2$ cm/s (fig. 2). The mean perfusion for the five subjects was 19.25 ± 1.46 ml/100g/min (table 1). Representative perfusion maps are shown in fig. 3 for subject B, depicting muscle group specific perfusion.

Subject	Age/Sex	Perfusion / ml/100g/min
A	26 M	23.52 ± 0.47
B	29 M	18.53 ± 0.43
C	32 F	21.56 ± 0.45
D	30 M	15.49 ± 0.51
E	26 M	17.15 ± 0.48
	Mean	19.25 ± 1.46

Table 1: Resting calf perfusion in five healthy volunteers (mean ± SEM).

Discussion and Conclusions: We have demonstrated that VSASL is able to provide quantitative measures of resting perfusion in calf skeletal muscle of healthy volunteers, without the transit delay errors associated with CASL. To quantify resting skeletal perfusion we improved contrast-to-noise compared to a previous VSASL study [5] by scanning at 3T, implementing a BIR-8 preparation to overcome B_1 inhomogeneity and using a spin-echo readout to overcome intra-slice dephasing across the 10 mm slice. Although we exclude large arteries in the muscle mask, hyper-perfused voxels appear in the perfusion maps close to these arteries, which may bias our results due to partial volume effects. We attribute this to the inflow of blood in the arteries during systole, so the sequence may benefit from a travelling saturation superior to each slice or physiological gating. The potential clinical applications of this work are numerous, including the assessment of regional perfusion in patients with PAD before and after percutaneous transluminal angioplasty; and in the assessment of compartment syndrome.

Acknowledgements: Funding from Cancer Research UK, National Institute for Health Research (NIHR) and EPSRC.

References: [1] Criqui, Vascular Medicine 6:3-7 (2001) [2] Frank et al. MRM 42:258-67 (1999) [3] Wu et al. JMRI 28:445-52 (2008) [4] Wong et al. MRM 55:1334-41 (2006) [5] Frank & Wong proc. ISMRM p2401 (2004) [6] Golay et al. MRM 53:15-21 (2005) [7] Buxton et al. MRM 40:383-96 (1998) [8] Chen et al. proc. ISMRM p.300 (2011) [9] Raynaud MRM 46:305-311 (2001) [10] Gold et al. AJR 183:343-351 (2004) [11] Zhao et al. MRM 58:592-97 (2007)