Assessment of calf perfusion kinetics in response to exercise and ischaemia using Q2TIPS-Arterial Spin Labelling method

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Introduction

Assessment of skeletal muscle perfusion during recovery from physiological stimuli such as ischaemia and exercise provides valuable information reflecting the functional integrity of the microvascular system, thus oxygen delivery to the muscle. Arterial spin labelling (ASL) allows for non-invasive measurement of tissue perfusion using labelled (inverted) blood water spins as endogenous tracer. Since its first introduction in brain[1], this has been increasingly adapted for skeletal muscle. Q2TIPS is a variant of pulsed ASL which offers the technical advantages of minimising errors related to variable transit delay from the labelled to the imaging region, reducing signal contamination from large vessels, and improving the saturation profiles and labelling efficiency of the QUIPSS II sequence, all of which contribute to improved accuracy of perfusion measurement[2]. Although this technique has been used for quantitative perfusion imaging in the brain, it has not been applied to skeletal muscle. This study therefore aims to characterise the temporal pattern of perfusion in response to physiological stimuli (exercise & ischaemia) using ASL-Q2TIPS, and to establish its reproducibility.

Methods

6 healthy volunteers (2M/4F, mean age 38±7 years) participated in the post ischaemia perfusion study. Subjects underwent 4 sets of ASL measurements in 2 separate days. Arterial occlusion was achieved by inflating the thigh cuff for 5 minutes to 200mmHg. Experiments were conducted on a 3T Siemens Trio scanner. Scanning started 30 seconds prior to cuff deflation and continued for 5 minutes. 4 subjects underwent another 4 sets of ASL measurements in response to exercise in a single session (2 scans done after complete leg re-positioning). Subjects were instructed to sustain contraction (plantar flexion) for 30 seconds at 80% of maximal effort. To avoid motion interference, the scan was started immediately (within 3s) after release of contraction. ASL data was collected in a single slice with 6s temporal resolution. Throughout, scanning parameters used were: TR 3s; TE 21ms; FOV 20cm; 6mm slice thickness; TI_1 700ms; TI_{stop} 1300ms; TI_2 1400ms; 10mm gap between labelling and imaging plane. A calibration scan without labelling and with TR 10s was included in order to quantify perfusion. Resting data were also obtained in a separate run prior to stimulus application.

Data Analysis

A locally written Matlab program was utilised to calculate perfusion within a trapezoid-shaped mask in 4 areas of calf muscle (Gastroc-m, Soleus, Gastroc-l and Tibialis Anterior) using a single blood compartment model[3]. Equilibrium magnetization of arterial blood was estimated from the muscle tissue, incorporating a correction to muscle:blood partition coefficient (λ=0.9) according to relative $T2^*$ of water in muscle and blood[4]. Other assumed parameters include $T2_b$=0.1s, $T2_t$ = 0.03, $T1_b$ =1.66s, $T1_t$ =1.42s. A biexponential function was fitted to the time-course data to calculate the $t_{1/2}$ of perfusion recovery. Reproducibility was determined as the relevant coefficient of variation (CV).

Results

Mean resting perfusion in all 4 muscle groups was 2.7 ± 1.8 and 0.8 ± 0.1 ml/min/100g tissue before ischaemia and exercise, respectively. Perfusion recovery kinetics and CV are summarized in Fig1 & Table 1. There is heterogeneity in the temporal pattern of perfusion recovery across different muscle groups following exercise, but the response is more rapid and homogeneous after ischaemia.
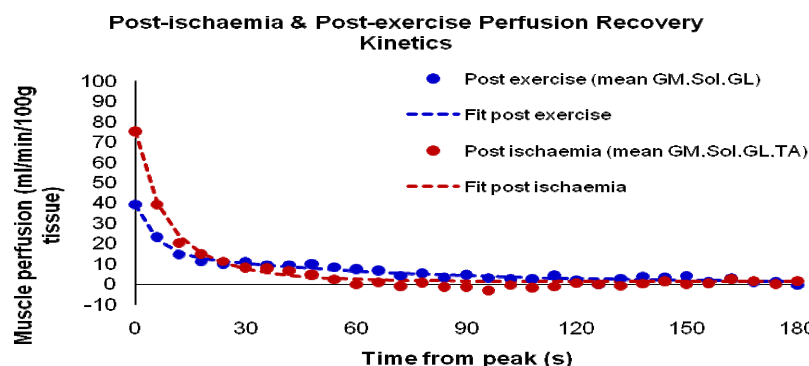

Figure 1

Parameter	Mean ± SEM	CV
Post ischaemia peak perfusion (ml/min/100g)	**75.3 ± 7.8**	**10%**
Post ischaemia true $t_{1/2}$ perfusion recovery (s)	**6 ± 1**	**17%**
Post exercise peak perfusion (ml/min/100g)	**38.7 ± 1.7**	**10%**
Post exercise true $t_{1/2}$ perfusion recovery (s)	**7 ± 2**	**22%**

Table1

Discussion

This study demonstrates successful application of Q2TIPS-ASL to determine the kinetics of calf perfusion in response to two physiological stimuli, exercise and ischaemia. This technique is reproducible as reflected by reasonably low CV values for both peak perfusion and $t_{1/2}$. The post-ischaemia peak perfusion value obtained in our experiment is somewhat lower than previously reported[5,6]. This may be due to less intense ischaemic stimulus in our study and our use of a $T2^*$correction factor to λ (which reduces calculated perfusion by 37%).There appears to be a very fast initial recovery phase indicating rapid vascular reactivity in response to both stimuli. Our exercise protocol gives results which resemble the ischaemic response but with a lower peak perfusion. This protocol may be suitable for investigation of vascular reserve in patients who have difficulty tolerating ischaemia. There are differences in the kinetics of perfusion decay across different areas of muscle following exercise, probably reflecting anatomical differences in activation during exercise, and in fibre-type distribution.

References: 1. Detre et al, Magn Reson Med, 21, 1992. 2. Luh et al, Magn Reson Med, 41, 1999. 3. Parkes & Tofts, Magn Reson Med, 48, 2002. 4. Buxton et al, MRM, 40, 1998. 5. Raynaud et al Magn Reson Med, 46, 2001. 6. Wu et al, J Magn Reson Imaging, 28, 2008.