

# Feasibility and Reproducibility of Measurement of Skeletal Muscle Blood Flow, Oxygen Extraction and VO<sub>2</sub> with Dynamic Exercise Using MRI

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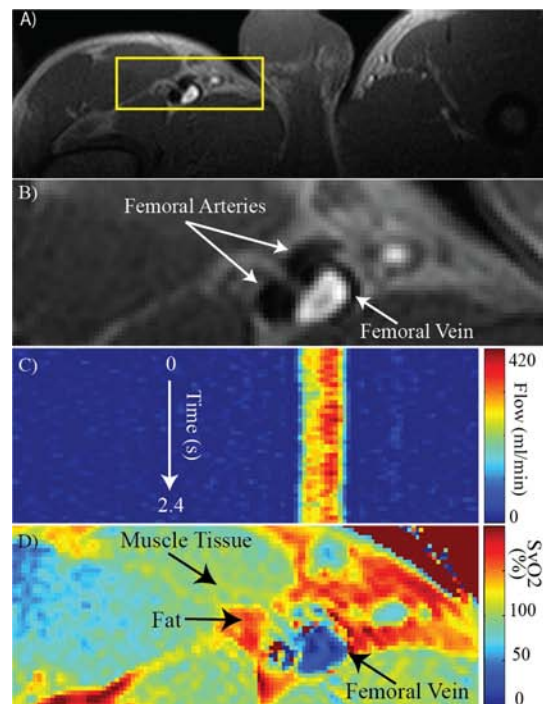
**Purpose:** We propose a new imaging approach which interleaves complex-difference (CD)<sup>1</sup> and susceptibility<sup>2</sup> MRI pulse sequences for real-time imaging of skeletal muscle blood flow (SMBF) and venous oxygen saturation (SvO<sub>2</sub>), respectively, for the calculation of skeletal muscle oxygen consumption (VO<sub>2</sub>). The goal of this study was to determine the reproducibility of this approach during sub-maximal knee extensor (KE) exercise. There is currently no non-invasive method for measuring skeletal muscle VO<sub>2</sub> and its determinants during dynamic exercise, which is necessary to expose mechanisms of dysfunction along the oxygen cascade in health and disease.

**Methods:** 9 healthy young (mean 31±6 yrs.) male subjects performed two 2-minute, 5-Watt, knee-extension exercise bouts, separated by a 10 minute recovery period, on an MRI-compatible KE ergometer that isolates the quadriceps muscle, within the bore of a 1.5T MRI scanner (Sonata, Siemens Healthcare, Erlangen, Germany). Measurements of femoral vein SMBF, using CD-MRI, and SvO<sub>2</sub>, using susceptibility MRI, were made at rest and continuously immediately (<1 second delay) post-exercise. CD-MRI is a subtractive flow imaging method, using flow encoding gradient pairs similar to phase contrast MRI, designed to remove static tissue signal and yield a projection whose intensity is proportion to flow.<sup>1</sup> Susceptometry estimates SvO<sub>2</sub> based on the deoxyhemoglobin-induced magnetic field shift within a cylindrical vessel, relative to surrounding reference tissue.<sup>2</sup> Our custom pulse sequence interleaves CD flow and susceptibility acquisitions by including through-plane flow encoding gradients in a multi-echo gradient echo sequence (for quantification of magnetic field shift), with in-flow saturation of arterial blood signal. Typical acquisition parameters: 5mm slice thickness, 2mm in-plane resolution, TR/TE<sub>1</sub>/TE<sub>2</sub> = 30ms/5ms/10ms, flip angle = 25°, FOV: 384x160mm, V<sub>enc</sub> = 170cm/s, temporal resolution = 60ms (CD flow) and 2.4s (susceptometry). VO<sub>2</sub> was calculated, using Fick's principle, as the product of SMBF and the arteriovenous oxygen difference (AVO<sub>2</sub>diff) calculated from arterial oxygen saturation (pulse oximetry), susceptibility measured SvO<sub>2</sub>, the oxygen carrying capacity of hemoglobin, and an assumed hemoglobin level and hematocrit (Hgb = 146 g/L, Hct = 0.43).<sup>3</sup> Mass of the quadriceps muscle was measured from volumetric anatomical images (assumed density = 1.06 g/mL) to index VO<sub>2</sub> to exercising KE muscle mass. Test-retest reliability was measured by correlation, coefficient of variation (CV), and interclass correlation (ICC) of peak post-exercise SMBF, SvO<sub>2</sub> and VO<sub>2</sub>, between the two trials.

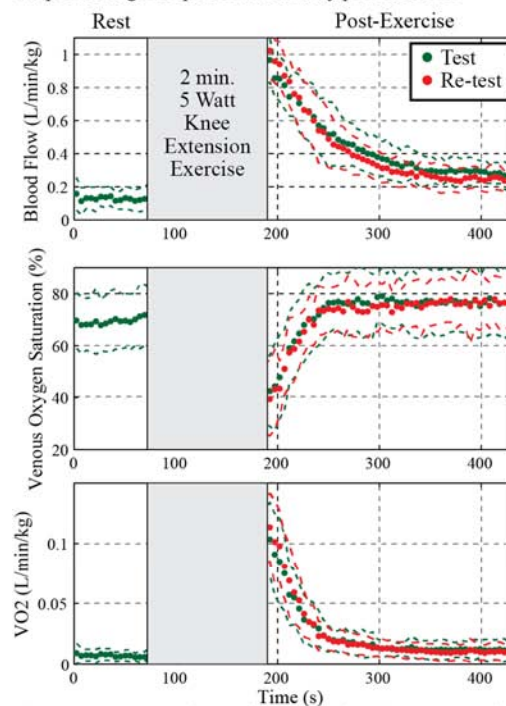
**Results:** Fig. 1 shows a magnitude image of the femoral vein from a susceptibility acquisition, showing the saturated arteries (1A, B), a CD-MRI velocity projection image, with arterial signal saturated (1C), and the corresponding oxygen saturation map acquired immediately post-exercise (1D). Our interleaved CD/susceptometry protocol measured peak SMBF, SvO<sub>2</sub> and VO<sub>2</sub> in close agreement between the two trials (SMBF: 0.9±0.1 vs. 1.0±0.2 L/min/kg; SvO<sub>2</sub>: 43.2±13.5 vs. 40.9±13.1 %; VO<sub>2</sub>: 95.7±18.0 vs. 108.9±17.3 mL/min/kg). The CV for SMBF, SvO<sub>2</sub> and VO<sub>2</sub> was 7.6%, 15.6% and 12.3% respectively, the Pearson correlation was 0.828, 0.878, and 0.881 respectively and the ICC was 0.678, 0.878, and 0.800 respectively. Fig. 2 shows the group average normalized SMBF, SvO<sub>2</sub> and VO<sub>2</sub> time course data (test-retest). Mean quadriceps muscle mass was 2.43±0.31 kg.

**Discussion:** Simultaneous femoral vein blood flow, oxygen saturation and skeletal muscle VO<sub>2</sub> measurements are feasible and reproducible immediately post-exercise (thus capturing peak exercise values). Peak values and time course data during recovery are in general agreement with previous reported values from invasive hemodynamic KE studies.<sup>3</sup> Simultaneous measurement of SMBF and SvO<sub>2</sub> enables the independent consideration of these physiologic factors as mechanisms of impaired VO<sub>2</sub> in subjects with reduced exercise capacity. When combined with cardiac and vascular studies, these methods can investigate the relative importance of the mechanisms that contribute to reduced exercise capacity in common conditions including those at risk for or with heart failure.

**References:** 1. Thompson et al. Magn Reson in Med. 2003 50(6). 2. Jain et al. J. of Cer Blood Flow & Met. 2010 30(5). 3. Andersen & Saltin. J. Physiol. 1985 (366).



**Figure 1** – A,B) Magnitude image of femoral vein, C) complex-difference flow and D) susceptibility saturation map. All images acquired immediately post-exercise.



**Figure 2** – Mean and SD of normalized SMBF, SvO<sub>2</sub> and VO<sub>2</sub> time course data (test and retest) in all subjects.