MR Skeletal Muscle Oximetry

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Purpose

Skeletal muscle is unique among tissues in that its demand for energy can rapidly increases during contractile activity. The coupling of skeletal muscle O_2 uptake to mitochondrial ATP synthesis and ultimately to the production of useful work (e.g., force generation at the myofibrillar level) is therefore a very important determinant of both the overall energy needs of the body as well as the capacity to perform physical exercise. Historically, this has required either performing arterio-venous balance measurements to directly quantify limb O_2 uptake, or inferring changes in skeletal muscle O_2 uptake from changes in whole-body O_2 uptake during exercise. The purpose of this project was to develop a new non-contrast MRI method to directly quantify skeletal muscle oxygenation non-invasively.

Methods

Imaging Methods: Skeletal muscle oxygenation is specifically referred to as oxygen extraction fraction (SM_OEF) and oxygen consumption rate ($SMVO_2$). They are related in the following equation:

$$SMVO_2 = [O_2] \times Y_a \times SM\_OEF \times LBF \quad (1)$$

Where the constant $[O2]_a$ is defined as the total oxygen content of arterial blood (=7.99 μmol • mL^{-1}); Ya is the oxygen saturation in arterial blood. LBF is the leg blood flow (mL/100g/min).

The MRI method for SM_OEF measurement is based on the susceptibility effect of intravascular deoxyhemoglobin within a magnetic field [1]. It was used to calculate brain tissue OEF [2]. For skeletal muscle imaging, a multi-slice 2D triple-echo asymmetric spin-echo sequence was employed to acquire source images with three TE1/ TE2/ TE3 = 44/62/80 ms [3]. Other imaging parameters are: TR = 4 sec; Field of View (FOV) = 160 x 140 mm^2; matrix size = 64 x 56 and interpolated to 128 x 112; slice thickness = 8 mm; total acquisition = 3 min 48 sec. Although only one slice was acquired in our study, the sequence is capable of acquiring up to 18 slices.

Table Skeletal muscle perfusion and oxygenation in soleus muscle (n = 5), * $P < 0.05$ vs Rest

	Rest		Isometric exercise	
	Mean ± STD	Repeat-ability	Mean ± STD	Repeat-ability
LBF(mL/100g/min)	34 ± 11	17 ± 7 (%)	75 ± 24 *	13 ± 6 (%)
SM_OEF	0.37 ± 0.09	3 ± 3 (%)	0.27 ± 0.03 *	2 ± 1 (%)
$SMVO_2$(mL/100g/min)	3.2 ± 1.8	17 ± 7 (%)	3.8 ± 1.3	12 ± 8 (%)

To measure LBF, a new arterial spin labeling (ASL) method validated in cardiac perfusion imaging was adapted for skeletal muscle imaging [4]. Two sets of inversion recovery images were acquired with TI of 190 ms and 230 ms: a slice-selective inversion (SS) and nonselective inversion (NS). LBF can be calculated using the following equation:

$$LBF = \lambda \frac{T_{1,NS}}{T_{1,Blood}} \left(\frac{1}{T_{1,SS}} - \frac{1}{T_{1,NS}} \right) \quad (2)$$

where λ is the constant blood-tissue coefficient of water (λ = 0.92 mL/g); $T_{1,NS}$ and $T_{1,SS}$ are T_1 values of the tissue after nonselective and slice-selective inversion recovery pulse is applied. The 2D ASL sequence parameters included: gradient-echo acquisition TR/TE = 2.8 msec/1.2 msec; flip angle = 5°; FOV = 160 x 112 mm^2; matrix = 128 x 90; bandwidth = 650 Hz/pixel; acquisition = 26 sec.

Experiments: In this ongoing study, seven healthy volunteers (25 – 68 y, 3F) were so far recruited and scanned for the measurement of O_2 uptake and perfusion in skeletal muscle of the calf. The volunteers lay supine on MRI table with their right foot firmly strapped to a home-built isometric exercise device. The SM_OEF and LBF measurements were performed at rest and during the contraction of the calf by statically pushing the pedal against a resistance of 10 psi. The same protocol was repeated again after a 3-min rest to assess repeatability of the measurements.

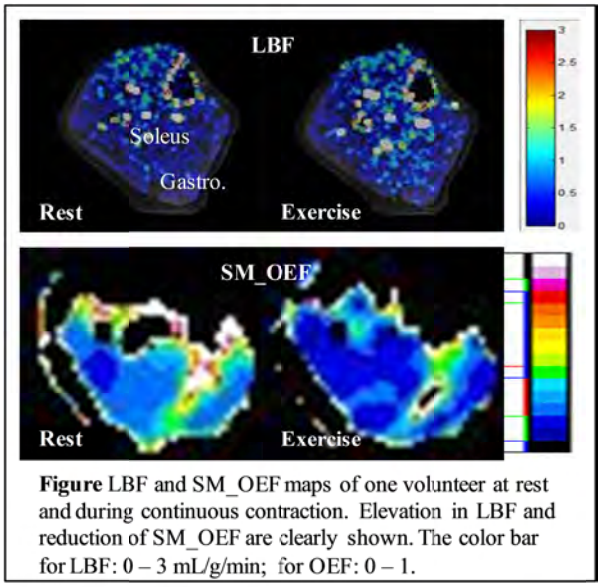

Figure LBF and SM_OEF maps of one volunteer at rest and during continuous contraction. Elevation in LBF and reduction of SM_OEF are clearly shown. The color bar for LBF: 0 – 3 mL/g/min; for OEF: 0 – 1.

Data Analysis: SM_OEF map was calculated in a similar fashion as reported in the brain study [2], but with consideration of different capillary structure in muscle. LBF map was obtained using a T_1 algorithm reported previously [4] and Eq. (2). ROI measurements were then performed in soleus and gastrocnemius muscle regions. $SMVO_2$ data was subsequently calculated based on Eq. (1).

Results

LBF and SM_OEF were successfully measured in 5 volunteers. The table shows 2-fold increase in LBF and significant drop in oxygen extraction during the continuous muscle contraction. However, the oxygen consumption was not significantly changed, perhaps due to the moderate exercise and limited subject number. While LBF values were higher than those reported using PET, they are comparable to reports using other ASL methods [5]. **Figure** shows sample images from one subject, demonstrating the regional distribution of LBF and OEF.

Conclusion

This is the first MRI oximetry developed for absolute quantification of skeletal muscle O_2 uptake. The technique would have broad applicability to many medical fields, including gerontology, cardiac patients, physical therapy, and neuromuscular disease (e.g., Barth syndrome).

References [1] Yablonskiy DA, etal, MRM, 1994; 32:749 - 763. [2] An H, et al, J Cereb Blood Flow Metab. 2000; 20: 1225 - 1236. [3] An H, et al. MRM, 2003; 50: 708 - 716. [4] Zhang H, et al, MRM, 2005; 53: 1135 - 1142. [5] Carlier PG, et al, NMR Biomed, 2006; 19: 954 – 963.