

Assessing Lower-Extremity Hemodynamics in Individuals with Diabetes

Jie Zheng¹, Mary K Hasting¹, Xiaodong Zhang², Andrew Coggan³, Hongyu An⁴, David Muccigrosso³, Darrah Snozek³, Adil Bashir³, Robert J Gropler³, and Michael Mueller⁵

¹Washington University in St. Louis, Saint Louis, Missouri, United States, ²Peking University First Hospital, Beijing, Beijing, China, ³Washington University in St. Louis, Saint Louis, MO, United States, ⁴University of North Carolina, Chapel Hill, NC, United States, ⁵Physical Therapy, Washington University in St. Louis, Saint Louis, MO, United States

Target Audience Radiologist, vascular surgeon, physical therapist, and the professionals involved with diabetic patient care.

Purpose Foot ulcers are a significant complication of diabetes mellitus and often precede lower-extremity amputation. The arterial insufficiency of the local tissue, including both periphery vascular disease and micro-vascular dysfunction, is considered to be the most important limiting factor for healing ischemic or neuroischemic diabetic foot ulcers [1]. Determination of muscle perfusion in the lower legs as a biomarker for early vascular intervention is important so that future amputation can be avoided. Last year, we reported a technique to assess skeletal muscle perfusion and oxygenation in healthy volunteers. In this project, the feasibility of this technique to detect differences in perfusion and oxygenation was investigated in the calf muscles of diabetic patients.

Methods **Imaging Methods:** Skeletal muscle oxygenation is specifically referred to as oxygen extraction fraction (SMOEF) and oxygen consumption rate (SMVO₂). The MRI method for SMOEF measurement is based on a method developed for the brain [2], which relies on the susceptibility effect of intravascular deoxyhemoglobin. In this skeletal muscle study, the susceptibility effect of deoxyhemoglobin is not considered in the model due to its 10-fold lower concentration, in comparison with deoxyhemoglobin, and much slower response to muscle exercise [3]. A multi-slice 2D triple-echo asymmetric spin-echo sequence was employed to acquire source images for SMOEF measurements [4]. Other imaging parameters are: TR = 4 sec; TE₁/ TE₂/ TE₃ = 44/62/80 ms; Field of View (FOV) = 160 x 140 mm²; matrix size = 64 x 56 and interpolated to 128 x 112; single slice, slice thickness = 8 mm; total acquisition = 3 min 48 sec. SMVO₂ is calculated using Fick's law: SMVO₂ = SMOEF x SMBF.

To measure skeletal muscle blood flow (SMBF), a FAIR type of arterial spin labeling (ASL) method was adapted for skeletal muscle imaging [5]. Two sets of inversion recovery images were acquired with TI of 190 ms: a slice-selective inversion (SS) and nonselective inversion (NS). SMBF was calculated using the equation:

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

where λ is the constant blood-tissue coefficient of water; $T_{1,NS}$ 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; 10 T₁-weighted images for each T₁ measurement; flip angle = 5°; FOV = 160 x 112 mm²; matrix = 128 x 90; average = 3; acquisition = 50 sec.

Experiments: In this ongoing study, 4 healthy volunteers (69±1y) and 4 diabetic patients (60±11y, HbA1c = 9.2±1.9) were scanned for the measurement of perfusion and oxygenation in skeletal muscle of the calf. The volunteers lay supine on MRI table with their dominant foot firmly strapped to a custom-built isometric exercise device. The SMOEF and SMBF measurements were performed at rest and during contraction of the calf achieved by statically pushing the pedal against a resistance of 10 psi (~30% maximal voluntary contraction), all starting 2 min after the start of the contraction.

Data Analysis: SMOEF map was calculated in a similar fashion as reported in the brain study [2]. SMBF map was obtained using a T₁ algorithm reported previously [4] and Eq. (1). ROI measurements were then performed in soleus muscle regions of SMBF and SMOEF maps.

Results SMBF and SMOEF were successfully measured in all 8 subjects. The table shows 10-fold increase in SMBF, 17% elevation in SMOEF, and 10-fold increase in SMVO₂ during the sustained muscle contraction in healthy subjects compared to resting values. In diabetes, the increases in SMBF and SMVO₂ were all attenuated with exercise compared to healthy subjects. Moreover, resting SMBF was significantly reduced while SMOEF was elevated, perhaps to compensate the loss of oxygen supply. **Figure** shows sample images from one healthy and one diabetes subject.

Conclusion This is the first study for the absolute quantification of regional skeletal muscle oxygenation in diabetic patients using non-contrast MRI. Attenuation of perfusion and oxygenation during exercise may have implications for early detection of compromised hemodynamics in the lower extremities of diabetic patients. This may help therapeutic strategy to target local angiogenic factors so that future amputation can be avoided.

References [1] Wagner FW Jr, et al, Foot Ankle 1981;2:64-122. [2] An H, et al, J Cereb Blood Flow Metab. 2000; 20: 1225 - 1236. [3] Lebon V, et al, MRM, 1998; 40: 551 - 558. [4] An H, et al. MRM, 2003; 50: 708 - 716. [5] Zhang H, et al, MRM, 2005; 53: 1135 - 1142.

Table Perfusion and oxygenation in soleus muscle (n = 4)

Perfusion & Oxygenation	Rest		Isometric exercise	
	Healthy	Diabetes	Healthy	Diabetes
SMBF(ml/100g/min)	7.2 ± 0.9	5.8 ± 0.6†	56.7 ± 20.8 *	31.3 ± 7*†
SMOEF	0.36 ± 0.02	0.40 ± 0.01†	0.43 ± 0.07	0.44 ± 0.07
SMVO ₂ (ml/100g/min)	0.50 ± 0.06	0.43 ± 0.05	5.28 ± 1.43*	2.56 ± 0.82*

* P < 0.05 (rest vs. exercise); † P < 0.05 (Healthy vs. Diabetes)

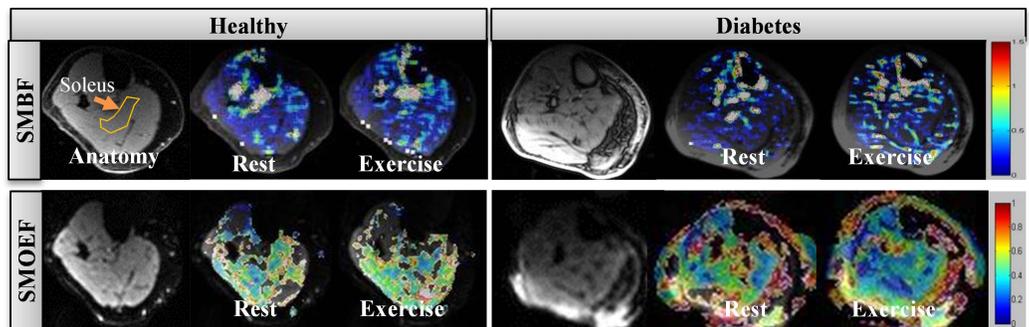


Figure SMBF and SMOEF maps of two subjects at rest and during sustained muscle contraction exercise: healthy vs. diabetes. ROI and arrow in the first anatomy image indicate soleus muscle region. Reduced SMBF (both resting and exercise) and elevation of resting SMOEF are seen in diabetes. The color bar for SMBF: 0 – 150 ml/100g/min; for SMOEF: 0 – 1.