Flow Heterogeneity within Muscle of Calf, Forearm, and Foot using Continuous Arterial Spin Labeling,

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Introduction: Measurement of muscle(calf) tissue perfusion has been achieved utilizing Continuous Arterial Spin Labeling MRI(CASL)(1, 2). This approach may offer new and important insight for researchers examining microvascular flow in normal physiology and in disease states. Heterogeneity in muscle flow with exercise and hyperemia has been noted in non-diseased muscle and may be secondary to differences in muscle fiber population, metabolic rate, nitric oxide synthetase concentration, water exchange rates, and time course of flow and oxygenation(3-5). Pathologic variability in flow within individual muscle groups may exist in states of small vessel disease(diabetes mellitus), peripheral vascular disease, and other muscle diseases.

Methods: With IRB approval and appropriate consent obtained, 29 healthy subjects with no evidence of vascular disease, assessed by the San Diego Claudication Questionnaire and noninvasive vascular systolic pressure indices, underwent a total of 39 imaging sessions, where flow in the mid-calf, mid foot, and mid-forearm was assessed. Studies were conducted on a 3.0 Tesla Siemens Trio whole-body MR system. A custom designed dual-tuned proton/phosphorous transmit-receive knee coil (Nova Medical, Inc., Wakefield, MA) was utilized. A single-slice version the CASL sequence(6), optimized for 3.0T(7) was utilized. The labeling plane was 6 cm proximal to the imaged 1cm slice(axial), FOV -22cm, matrix-64 x 64 for calf and 128 x 128 for the foot/forearm. TE was 13ms and the duration of the tag was 2 sec. During the control state, the inversion plane was placed 6cm distal to the imaging slice. Post labeling delay was 1900 msec and TR = 4 seconds. A tourniquet system with nonmagnetic cuff placed on the thigh or upper arm was utilized at 250 mm-Hg to create a 5 minute period of ischemia followed by a period of hyperemic flow. Post-processing, implementing VOXBO(http://www.voxbo.org/) and IDL(RSI, Boulder, CO), utilized the matching slice from a high resolution MPRAGE or 2D Spoiled GRE anatomic image to hand draw regions of interest(ROI) for 6 muscle groups in the calf, and for the flexor and extensor muscle groups of the forearm and foot. Calculation of flow followed the model in reference (1), assuming blood T1=1.5s, blood T2*=80ms and tissue T1=1.2s, tissue T2*=20ms at 3.0T.

Results: Peak flow in the soleus and deep flexors of the calf were higher than in other calf muscle groups, (Tukey-Kramer). Peak flow in the extensors of the forearm was significantly elevated over that in the flexor group. Within subject coefficient of variation averaged 0.35 when examining 6 ROI's, from 8 subjects, and when measurements were repeated 1 hour apart.

Extremity	Muscle Group	Peak Flow(ml/100g/min)
Calf(n=24)	Gastrocnemius Lateral Head	82 ± 30
	Gastrocnemius Medial Head	79 ± 37
	Soleus	111 ± 56, p<.05
	Deep Flexors	107 ± 41
	Anterior Extensors	78 ± 32
	Lateral Extensors	76 ± 35
Foot(n=26)	Dorsal Flexors	92 ± 41
	Plantar Flexors	88 ± 41
Forearm(n=27)	Extensors	88 ± 43, p=.007
	Flexors	60 ± 28

Conclusions: Following a 5 minute ischemic period, flow in predominantly slow-twitch soleus muscle is markedly elevated over that in predominantly fast-twitch muscle groups such as gastrocnemius or anterior extensors. Muscles with predominantly slow-twitch fibers are known to maintain lower lactate levels during exercise versus those with predominantly fast-twitch fibers and thus the relatively larger increase in flow in the soleus in response to a period of ischemia is counter intuitive. CASL-MRI may prove an especially effective tool for the investigation of muscle physiology and pathophysiology through its ability to allow repeated measurements in large populations, noninvasively.

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