Regional Measurement of Skeletal Muscle Blood Flow During Post-Ischemic Reactive Hyperemia

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Introduction: Obstructive peripheral artery disease affects 15% of adults over age 55, of whom over one-third are symptomatic. Typical manifestations are pain during walking or threat of limb loss. Lower extremity perfusion measures would be useful in the diagnosis of peripheral vascular disease and for the evaluation of treatment with mechanical intervention or biological agents. We adapted first-pass contrast-enhanced (Gd-DTPA) perfusion methods for the measurement of skeletal muscle blood flow. Because resting perfusion in skeletal muscle is low, highly variable and insensitive for pathology, first-pass studies were carried out during a period of post-ischemic reactive hyperemia (RH) following transient cuff occlusion of the inflow artery. We used a novel contrast delivery method to provide a step-input of tracer concentration that is coincident with the onset of hyperemic flow (Thompson RB *et. al., Proceeding of the 11th ISMRM 2003:* 499). This method allowed for simple evaluation of the unidirectional influx constant, K_i, and the tracer distribution volume in the tissue, v_e, with 2 mm in-plane resolution (K_i = flow (F) * extraction fraction (E)). Regional studies in normal volunteers were used to characterize flow in different calf muscle groups. Patients with documented peripheral artery disease (PAD) were studied in order to illustrate complex spatial distributions of blood flow with obstructive disease.

Methods: Eleven normal volunteers and three patients with PAD were studied with the step-input perfusion method. Post-ischemic RH was induced in both calfs with 5 minutes of thigh-cuff inflation to supersystolic pressures (180 – 220mmHg) to occlude arterial inflow. The occlusion both induced calf muscle ischemia and excluded Gd-DTPA from the leg until the time of cuff release. This method was designed to produce a step-input of contrast concentration coincident with the high flow period during early post-ischemic RH. The step-input conditions allow for direct calculation of the rate constant, K_i, and the tracer distribution volume in the tissue, v_e, by fitting tissue time intensity curves with a simplified single-exponential equation without the need for deconvolution (Tofts PS *et. al., J Magn Reson Imaging*. 1999;10:223-32). Saturation recovery experiments with either steady state free precession or spoiled gradient echo acquisitions were used for contrast-enhanced perfusion imaging (2x2x8 mm spatial resolution, .9-1.3 second temporal resolution, 2-6 slices). The whole blood concentration of Gd-DTPA was measured in the femoropopliteal arteries of all subjects using a saturation recovery experiment. All MR imaging was performed on a Siemens 1.5 T Sonata scanner (Siemens Medical Sytems, Erlangen, Germany) using a peripheral coil array.

Results: Table 1 displays the means and standard errors of the mean transit times (MTT), Gd-DTPA fractional distribution volumes (v_e) and unidirectional influx constants (K_i) for three muscle groups in both legs (RL and LL) from eleven normal volunteers. Figure 1 displays a sample perfusion image and time intensity curves from a patient with PAD. Note the considerable flow impairment ($K_i \leq$ 40ml/100g/min) in the medial gastrocnemius group (region 2).

Table 1 – Tracer Kinetic Parameters and Distribution Volumes from 11 Normal Volunteers

	Gastrocnemius		Soleus		Tibialis Anterior	
	RL	LL	RL	LL	RL	LL
MTT (sec)	7.86±0.56	8.21±0.58	5.44±0.41	5.06±0.32	6.98±0.50	7.28±1.04
v_e (%)	8.32±0.65	8.25±0.62	9.46±0.54	9.00±0.59	7.96±0.51	7.89±0.67
K_i (ml/100g/min)	110.6±6.6	106.7±8.7	183.9±12.6	185.0±14.8	120.4±11.5	124.1±9.9

K_i = flow (F) * extraction fraction (E), v_e = fractional distribution volume of Gd-DTPA in tissue

Conclusions: An arterial step-input of Gd-DTPA concentration that is coincident with the onset of RH generates a simple tissue time intensity response. Gd-DTPA fractional distribution volumes (v_e) and unidirectional rate constants ($K_i = EF$) were estimated by fitting the tissue response with standard kinetic equations. We measured up to six slices every 1.3 seconds with 2 mm in-plane resolution. Significant regional differences in skeletal muscle blood flow (K_i) were measured in normal volunteers with the highest flow in the soleus group and the lowest in the gastrocnemius group. Gd-DTPA distribution volumes measured the simple kinetic model agree with those measured with T_1 methods (results not shown), and with those previously reported in the literature (Donahue KM *et. al., Magn. Reson. Med.* 1995;34:423-32). Very large regional variations in flow were observed in patients with peripheral artery disease, which demonstrates the utility of high spatial resolution imaging in order to asses the impact of disease or therapy.

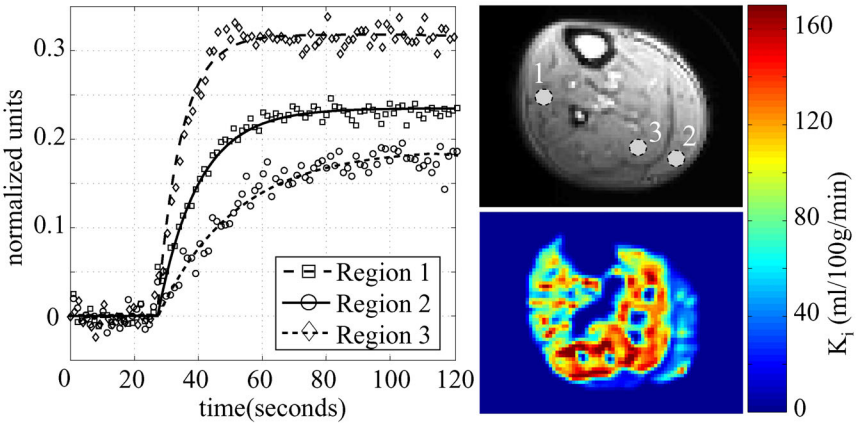

Figure 1: A perfusion map from a patient with PAD highlights flow impairment in the medial gastrocnemius muscle (blue region on the right (Region 2)). Tissue time intensity curves show the variation in contrast arrival in three muscle groups.