Muscle perfusion reserve (MPR) measured from exercise-recovery MRI: a new functional index for diagnosing PAD

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Introduction: Peripheral arterial disease (PAD) affects nearly 8 million Americans. Without a reliable way of assessing calf muscle function, therapeutic management of PAD is highly controversial (1). Normal muscle function mostly depends on its ability of recruiting more capillary upon exercise, which enables enhanced tissue perfusion delivering more oxygenated blood. None existing functional imaging is capable of quantifying exercise-induced capillary recruitment, while muscle biopsy provides only structural information that does not reflect dynamic state. We have applied a validated plantar-flexion exercise protocol within MRI scanner (2) together with ASL perfusion measurements at exercise recovery to measure exercise-induced capillary recruitment, which we term Muscle Perfusion Reserve (MPR). In the following, we first describe the exercise protocol and the MPR concept, and then examine MPR in healthy volunteers subject to different workloads.

Methods: In our *exercise-recovery MRI protocol*, human subject is in supine position in MR scanner and with a MR compatible apparatus does plantar flexion with one leg. Exercise workload can be changed by changing the weight attached to the apparatus. In this experiment, plantar flexion was performed at frequency of 1Hz for 1 min, and repeated with different loads: 2 lbs, 4 lbs, and 6 lbs. Immediately after exercise with each load, we started ASL scan using a FAIR EPI sequence: matrix 64×64, TE 13 ms, TR 6 sec, number of averages 1, FOV 16×16 cm, slice thickness 10 mm. Each acquisition collected two images: one with slice-selective inversion and one with non-selective inversion, from which we generated a perfusion map (2). On a separate day, the same subjects performed the same exercise and ultrasound was used to measure artery flow velocity (v_a) during muscle recovery. Two healthy subjects were included in this study. *The MPR model* is based on mass conservation principle, which relates change rate of vascular volume (V) with arterial inflow (v_a) and capillary perfusion (f),

$$\frac{dV}{dt} = v_a \cdot S_a - f \qquad [1]$$

where S_a is the effective cross-sectional area of the upstream artery that feeds the tissue of interest. Integrating Eq [1] from a fully recovered time point back to recovery start point, we can get vascular volume change stimulated by exercise, or MPR,

$$MPR = V_{exercise} - V_{rest} = \int_{\infty}^{0}(v_a \cdot S_a - f)dt. \qquad [2]$$

MPR actually equals to the area between ASL-measured perfusion curve and PC-measured velocity curve calibrated by S_a (Fig 1). S_a can be estimated at a time point where V does not change.

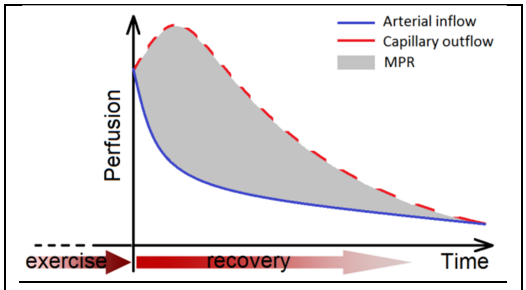
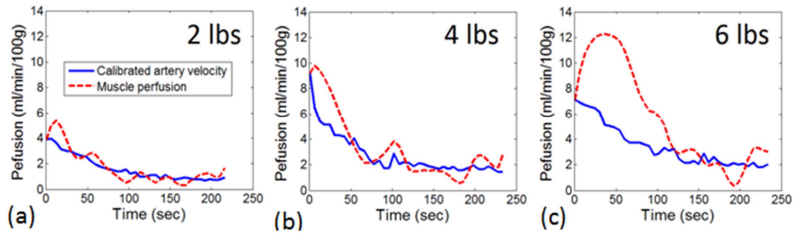


Fig. 1 MPR estimation from exercise recovery protocol

Results: Fig. 2 shows an example of perfusion changes in medial gastroc after exercise of different weights. MPR values quantified by the model are shown in Table 1.



←Fig 2. Medial gastroc (MG) perfusion after plantar flexion with loads of 2, 4 and 6 lbs.

Table 1. MG MPR of healthy subjects.

MPR (ml/100g)	2 lbs	4 lbs	6 lbs
Subject 1 (**BMI 29.6**)	0.4	2.2	**9.1**
Subject 2 (**BMI 20.5**)	-0.2	8.7	**27.4**

Discussion: The proposed model is the first one in the literature to quantify exercise-induced capillary recruitment in calf muscle. In healthy subjects, MPR was detected with plantar flexion of load heavier than 2 lbs. The MPR difference between the two healthy subjects was presumably due to possible wide range of physical fitness among healthy population. The proposed MPR estimated with the exercise-recovery ASL data has great potential of evaluating calf muscle function of PAD patients and improving their therapeutic management.

References: 1. Murphy et al. Circulation. 2012;125(1):130. 2. Raynaud et al. MRM. 2001;46(2):305.