An Exercise-Recovery Protocol Depicts Muscle Perfusion and Capillary Recruitment Heterogeneity in Peripheral Arterial Disease

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Target Audience: Clinicians/Researchers evaluating peripheral arterial disease and vascular function through exercise induced hyperemia.

Purpose: Like cardiac stress tests for coronary artery disease, exercise-recovery muscle perfusion has the potential to improve the diagnosis and management of peripheral arterial disease (PAD). When a healthy skeletal muscle performs work during dynamic exercise, initial capillary recruitment (associated with muscle fiber recruitment) is limited and heterogeneously spaced (1,2). As workload increases, muscle fiber and capillary recruitment also increases with the total capillary recruitment becoming more homogeneously spaced (3). Perfusion to a healthy skeletal muscle is proportional to both capillary recruitment as well as bulk flow through the feeding arteries (related to cardiac output and flow redirection). In contrast to healthy skeletal muscle, chronic ischemia in patients with PAD results in near maximal capillary recruitment even at small workloads. Since capillary recruitment is near maximal, increases in perfusion occur primarily by increasing bulk flow through feeding arteries and the peak perfusion, measured as vascular reserve (4), is limited. However, since changes in capillary recruitment occur before reductions in peak perfusion, measuring capillary recruitment and visualizing its spatial homogeneity are proposed as an earlier predictor of PAD than vascular reserve. To date, no method to visualize or quantify spatial homogeneity of capillary recruitment has been reported. Using a validated exercise regimen in the MR scanner, in healthy and PAD subjects, we demonstrate for the first time the varying spatial distribution of capillary recruitment in muscle corresponding to disease and exercise induced hyperemia.

Method: The pattern of capillary recruitment generated by exercise cannot be duplicated with a pressure cuff (5), adenosine (6), or even electrical stimulation (7). We therefore make use of a MRI compatible plantar flexion device (Fig. 1a) to exercise inside the magnet where perfusion measurements can be begin rapidly following cessation of exercise using a validated protocol. After three minutes of plantar flexion exercise at 1Hz, perfusion was measured every 10 sec with an EPI pulsed ASL sequence with a 2.5mmx2.5mmx10mm resolution and a local flex coil.

Results: To date we have imaged 3 PAD patients and 3 healthy subjects with ongoing recruitment. The distribution of peak perfusion values for a representative healthy volunteer (5.4 Watts exercise) and PAD patient (2.7W exercise) are shown in Fig. 1b and 1c. Figure 2 shows capillary recruitment patterns with increasing workload. The spatial and temporal characteristics of functionally similar muscle bundle groups across the lateral gastrocnemius in a healthy volunteer are shown in Figure 3.

Discussion: The 60 yo M PAD patient in Fig. 1c shows a greater and more homogeneous increase in muscle perfusion at rest compared to the 38 yo M healthy volunteer (Fig. 1b). During exercise, unlike the healthy subject who demonstrated substantial changes in perfusion distribution and higher perfusion values with exercise, the PAD subject exhibited only minor alterations in the distribution of tissue perfusion despite the greater metabolic demand from the exercising muscle. This finding is indicative of an important perfusion-metabolism mismatch in this patient. The 55 yo MPAD patient in Fig. 2 shows little change in capillary recruitment pattern, reflecting a more progressed disease state. In Fig. 3, we see that not only is there a distribution of peak perfusion values but that the recovery curve also varies depending on spatial location. Overall, these results suggest that perfusion distribution can be assessed by ASL and this technique may provide a valuable tool for diagnostic as well as assessing disease progression in PAD patients

Conclusion: Perfusion heterogeneity and distribution of peak perfusion values provide new and important information about stress-rest muscle physiology in PAD.

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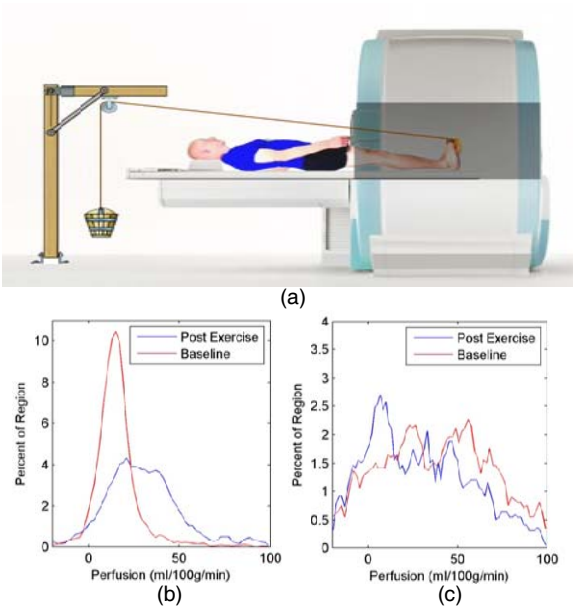

Figure 1: An MRI compatible ergometer was used to exercise inside the magnet (a). Distribution of peak perfusion values found in the lateral gastrocnemius muscle in a healthy (b) and PAD patient (c).

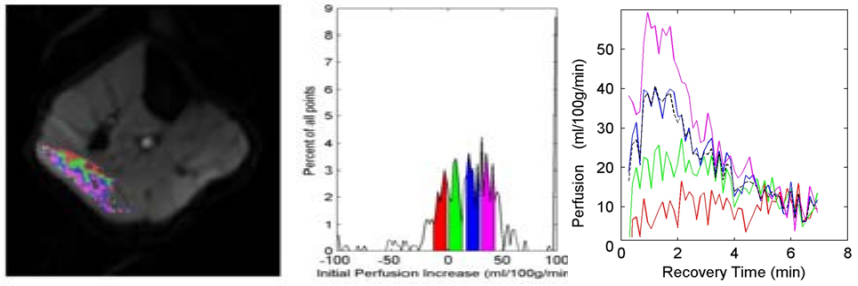

Figure 3: Spatial distribution of peak perfusion values. Four clusters of pixels are color coded with their spatial location shown in (a), their range of peak perfusion values shown in (b) with their temporal recovery curves following 5.4W plantar flexion shown in (c).

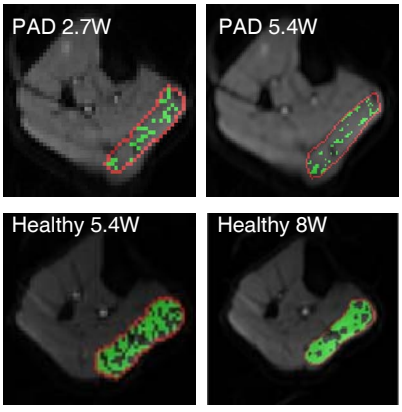

Figure 2: Homogeneity of pixels with greater than a 5ml/100g/min perfusion increase with exercise.