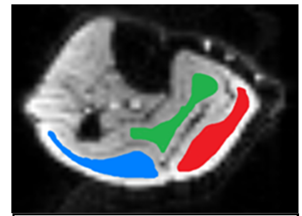

Fig. 1. The locations of ROIs: GL (blue); GM (red) and Soleus (green).

fMRI study of the hemodynamics of calf muscle during exercise in peripheral arterial disease

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Introduction: Since the most typical symptom of peripheral arterial disease (PAD) is leg pain during walking [1], blood flow regulation during exercise in PAD is of a great interest. PAD not only involves the great vessels, but also the microcirculation and muscle pysiological changes [2]. As the blood flow and oxygenation level change greatly during exercise, BOLD fMRI was applied to assess such changes during dynamic plantar flexion exercise in healthy control (HC) and PAD subjects. Our goal was to characterize the BOLD time course in response to low intensity exercise.

Methods: The subjects included 3 PAD patients (mean age= 65.0 years, 0 females) and 6 age-matched HC (mean age= 66.3 years, 2 females). MRI data were acquired on a 3T scanner (Siemens Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany). The subjects were supine with their lower leg fitted into an 8-channel knee coil. Gradient-echo EPI was used to acquire time-course images of the calf muscle with voxel size = 2.5x2.5 mm, 10 slices, slice thickness = 5.0 mm, FoV = 160 mm^2, flip angle = 70 deg, TE = 25 ms and TR = 3 s with a delay of 2 s. The paradigm consisted of a one-minute baseline at rest followed by dynamic plantar-flexion exercise with 2 kg load at a pace of 20 contractions/min (about14 min.) and a 5-minute recovery. To reduce the motion artifact, plantar-flexion was performed only during the 2 s delay time of each TR. Blood pressure and heart rate were recorded during the paradigm. The time-course MRI images were realigned with SPM8 software (The Welcome Trust Centre for Neuroimaging, UCL, UK).

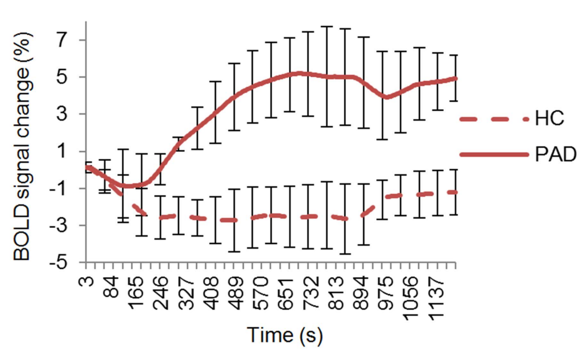

Fig. 2. BOLD signal time course for GM during plantar flexion exercise at 2 kg in HC and PAD. Error bars: standard deviation.

The regions of interest (ROI) of gastrocnemius lateral head, gastrocnemius medial head and soleus were manually segmented (Fig. 1) with MRIcron (Neuropsychology Lab, Columbia, SC, USA). The average signal intensity (SI) of each ROI was calculated and normalized as percent change. To remove motion artifact, the time-course data were filtered with wavelet (Wavelet toolbox in Matlab, Math Works, Natick, MA, USA).

Results: Dynamic plantar-flexion exercises produced the most reproducible data in the GM among the 3 muscle groups studied. Exercise was rated as “low intensity” for HC and “moderately painful” for PAD subjects. Fig. 2 shows the time-course of BOLD signal change in GM of the two groups. For the HC subjects, the BOLD signal decreased (2-3%) during exercise and recovered within 2 minutes. In contrast, in the PAD patients the BOLD signal was significantly increased by 3-7% and stayed elevated during the entire 5-min recovery period.

Discussion: The BOLD time-course data in our paradigm clearly differentiated the two groups. Most interestingly, the increased BOLD signal intensity in PAD is counterintuitive, as PAD is clinically characterized by compromised blood flow and oxygenation in the exercising muscle. The main contributing factors of BOLD signal change include blood perfusion, blood volume and oxygenation. It has been reported that peak exercise calf perfusion of healthy controls was higher than PAD [3] and that muscle postcontractile BOLD signal changes depend critically on the balance between O_2 delivery and O_2 consumption [4], thus, the observed increase in BOLD is likely due to the dominant contribution of hyper oxygenation in PAD. The leg pain experienced in PAD is thought to be secondary to the ischemic insult as a result of poor blood supply. Conversely, our data suggest a new hypothesis that O_2 extraction/utilization in the PAD muscle is compromised such that muscle tissue is in an ischemic state even though arterial blood pressure and bulk flow are higher in PAD during low intensity exercise. Testing this hypothesis will further advance the understanding PAD pathophysiology, which is important for development of its treatments.

Conclusion: The time-course of BOLD signal during exercise was evaluated in both PADs and HCs. The BOLD MRI is promising in evaluating exercise capability of PAD patients, which along with other traditional measurements can provide a comprehensive assessment of the severity of the illness and may aid the evaluation of therapies.

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