

Assessment of Skeletal Muscle Oxygen Kinetics Using Quantitative BOLD (qBOLD)

Xiang He¹, Serter Gumus¹, Jung-Hwan Kim¹, Ted Huppert¹, Bret Goodpaster², Dmitry Yablonskiy³, and Kyong Tae Bae¹

¹Department of Radiology, University of Pittsburgh, Pittsburgh, PA, United States, ²Department of Endocrinology and Metabolism, University of Pittsburgh, Pittsburgh, PA, United States, ³Mallinckrodt Institute of Radiology, Washington University in St Louis, St Louis, MO, United States

Introduction: Abnormal skeletal muscle energetics and oxygen kinetics in vascular and metabolic disorders are often associated with exercise intolerance (1) and other musculoskeletal (MSK) diseases (2, 3). Existing techniques such as muscle BOLD (blood oxygen level dependent) functional MRI (mfMRI) (4) and near infrared spectroscopy (NIRS) lacks either the specificity or the spatial/temporal resolution. Previously proposed MR-based MSK quantitative BOLD (qBOLD) technique (5) provided a physiologically relevant assessment of the skeletal muscle oxygenation in the baseline state. However, the measurement during isometric or dynamic muscle contraction is still inconclusive due to limited temporal resolution (~20 sec). To resolve rapid changes on intracellular muscle water content and acidity, as well as separate changes on intra- and extra-vascular signal contribution during mfMRI (6), single-voxel qBOLD technique will be used to investigate muscle hemodynamics during muscle exercise.

Methods: All experiments were performed on a 3T Siemens Trio scanner using standard 8-channel knee coil. Three healthy volunteers were scanned in multiple sessions. Subjects were asked to perform isometric or dynamic dorsiflexion muscle contraction, followed by muscle relaxation during recovery. For dynamic muscle exercise, subjects were instructed to synchronize the muscle movement with MR acquisition. Two exercise protocols were used. The first was a 3 minutes maximal intensity exercise. The second was 45 second exercise followed by 75 second relaxation. MR parameters for single voxel qBOLD acquisition were: fat saturation; TR of 3 or 2.5 sec; bandwidth of 2000 Hz; spin echo at 70 ms (FID acquisition starts at 20 ms before SE); voxel size of 10x12x20 mm³. In addition to standard R2, R2', muscle frequency shift Δf , we measured changes in oxygen extraction fraction (OEF) and deoxygenated blood volume (DBV) during and after isometric or dynamic knee dorsiflexion.

Results & Discussions: Fig. 1 shows the hemodynamic response of the anterior tibias muscle estimated during a 3 min isometric contraction. While an increase in extravascular tissue R2' (also reflected in Δf map as Fig 1d (7)) dominated BOLD response during contraction, post-exercise BOLD hyper-intensity was mostly originated from the decreased muscle intrinsic R2 (Fig 1b). OEF increased slightly during contraction and decreased below the baseline at the initial period of recovery (Fig 1e), consistent with post-exercise hyperemia. Several-folds increase in deoxygenated blood volume during isometric contraction is consistent with the process of capillary recruitment and increased resistance in large vessels (8).

Fig. 2 displays the BOLD hemodynamic response by a 3-min dynamic dorsiflexion. After an initial OEF hike at the start of exercise, OEF decreased gradually and bottomed at the initial period of post-exercise recovery (~10% below baseline). Similarly to the isometric exercise, sustained increase of DBV was present in the dorsiflexion. The time course of OEF and DBV was consistent with that of tissue R2' (Fig 2b). Some of our studies showed variable time courses in DBV and OEF (data not shown), suggesting that initial muscle status, especially possible restrictions on muscle blood flow by compression may be the origin of variations in muscle hemodynamic response.

Fig. 3 demonstrates a typical response during a repetitive isometric dorsiflexion exercise (TR of 2.5s). Muscle OEF increased (2 - 4%), followed by a post-exercise hyperemia (4 - 8%). During a short isometric exercise (45 s), DBV increased two to three fold.

Conclusion: This study demonstrated that the single voxel qBOLD technique facilitates the assessment of skeletal muscle oxygen kinetics during static or dynamic muscle exercises. While the BOLD response is mainly dominated by the deoxygenated blood volume and deoxy-hemoglobin concentration, changes on muscle OEF by exercise as well as post-exercise hyperemia can be detected.

References: (1) Green, et al., *Diabetologia* 2007; 50:859. (2) Jenson, et al., *Neurology* 2002; 58:1533. (3) Langham, et al., *JAmCollCardio* 2010; 55:598. (4) Damon, et al, *JApplPhysiol* 2005; 98:264. (5) He, et al, *Proc. 20th ISMRM 2012*. (6) Damon, et al, *MRM* 2007; 58:335. (7) He & Yablonskiy, *PNAS* 2009; 106:13558. (8) Gray, et al, *AJPhysiol* 1967; 213:683.

