Quantitative Measurement of Blood Flow in Contracting Rat Muscle Using MR Angiography

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Targeted audience: cardiovascular and skeletal muscle physiologists

Introduction: Non-contrast enhanced Phase Contrast Magnetic Resonance Angiography (PC-MRA) is now commonly used to measure regional blood flow in humans in response to skeletal muscle activity in physiological [1-2] and pathological conditions [3]. However, with a diameter lower than 1 mm for large peripheral vessels such as femoral vein in adult rat, the corresponding application in small animal model is more challenging despite an extensive use of such models to investigate pathologies known to affect peripheral blood circulation in human such as diabetes [4].

The purpose of this study was to investigate 1) the effect of skeletal muscle workload on the local muscle blood flow and 2) the corresponding time-course of flow recovery in the rat hindlimb from 2D_ PC-MRA measurements at the femoral vein level.

Methods:

• MR angiography experiments were performed under anesthesia (isoflurane gas inhalation) at 7T (Bruker BioSpec 70/30, Ettlingen, Germany) using a commercial ^{1}H surface 2*2 array coil (transmit: quadrature volume resonator ^{1}H 112/086, Bruker) positioned over the femoral region prior any branching to the lower leg.

• Contractions were electrically-induced via direct sciatic nerve stimulation (such as the lower leg entire muscle compartment was activated) at 0.5Hz, 1Hz, 2Hz, 3Hz, 4Hz and 5Hz for 3min separated by 20 min of recovery in 6 wistar rat (312 ± 14 g). Twitch torque was measured via a Force transducer attached to the achilles tendon.

• Post-contraction blood velocity (cm/s) was measured continuously for 20 min in the femoral vein from Phase Contrast images recorded with the following parameters: 1 slice (0.8mm slice thickness), slice direction encoded, TE/TR=3.9/15ms, Flip angle= 20°, , matrix size = 256*256, FOV 35*35, 2 averages, total acquisition time 15.6s. The slice geometry was determined from (maximal intensity) projections of a standard 2D Time-Of-Flight (2D_TOF, TE/TR =2/12 ms, flip angle =80°, 3 averages, matrix size=320*320, FOV 30*30, total acquisition time 7min40, Figure 1) such as the measurement plane was perpendicular to the femoral vein blood flow. The velocity threshold was ranged from 10 to 40 cm/s according to the measurement period to avoid any aliasing artifact with increasing flow (Figure 2).

•The femoral vein was manually delineated from the velocity map using image display and processing software (Bruker). Blood flow (ml/min) was calculated as vessel area (cm^2) *velocity (cm/s)*60 and expressed per 100g lower leg muscle.

• The effect of contraction intensity to blood flow was tested using One way repeated measured ANOVA with significance level at P<0.05. Values are presented as mean ± standard error.

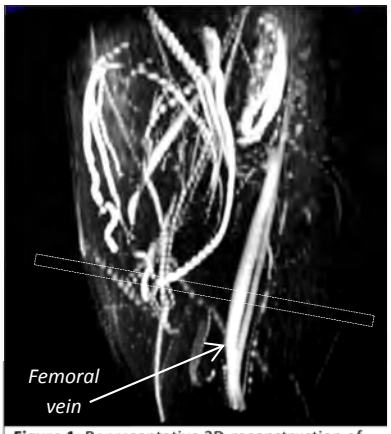

Figure 1: Representative 3D-reconstruction of Maximal Intensity projection of 2D_TOF. The dashed rectangle represents slice geometry the subsequent velocity mapping.

Results:

• Prior to the stimulation protocol, flow was 47.1 ± 7.9 ml/min/100g muscle given a total muscle weight of the lower leg of 3.56 ± 0.15g.

• The torque produced at the beginning of the protocol was 332 ± 39 g. No significant change in initial torque production was observed with stimulation intensity.

• As illustrated in Figure 3, stimulation resulted in a significant increase in Flow regardless of the intensity (Figure 3) which was significantly higher for fatiguing contraction (i.e. 2Hz and above) compared to non-fatiguing stimulation (i.e. 0.5 and 1Hz). At the end of the 2Hz stimulation the magnitude of change quantified, was twice the one observed post 0.5Hz stimulation (63.6 ± 10.4 vs 29.3 ± 8.9 ml/min/100g muscle respectively).

• A post-contraction reactive hyperemia was observed at intensity higher than 1Hz delaying flow recovery at these intensities compared to non-fatiguing contractions.

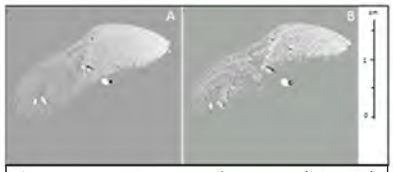

Figure 2: Representative velocity map (2D_PCA), recorded A) at rest (10 cm/s threshold) and B) after 3min 2 Hz stimulation (20 cm/s threshold).

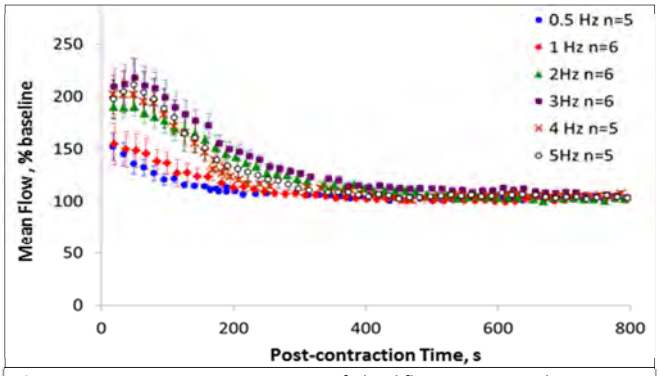

Figure 3: Post-contraction time course of Blood flow recovery with respect to stimulation intensity expressed as a percent of baseline flow (i.e. flow at the end of 20 min recovery).

Discussion: These results disagreed with a single exponential model of flow recovery after contraction for stimulation intensity above the aerobic threshold, i.e. 1Hz [5]. Further investigations are required to determine the exact physiological implications of the present findings.

Conclusion: This study clearly showed that MRI-based regional blood flow measurement can be used to investigate the time-course of post-contraction flow recovery.

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