Similarity between deoxyhemoglobin concentration and R2’ time course during isometric dorsiflexion

C. P. Elder1, M. A. Chance1, R. N. Cook2, and B. M. Damon1,2

1Radiology and Radiological Sciences and Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States, 2Biomedical Engineering, Vanderbilt University, Nashville, TN, United States

Introduction
An increase in muscle oxygen extraction leads to an increase in deoxyhemoglobin concentration ([Hb]). Standard near-infrared spectroscopy (NIRS) measurements of [Hb] are limited to small areas of superficial muscles and signal is highly dependent on the thickness of the subcutaneous fat layer (1). Positron Emission Tomography has been used to measure oxygen extraction in superficial and deep muscles (2), but requires ionizing radiation. Developing MR methods to measure [Hb] would allow measurement in superficial and deep muscles without radiation and eliminate the limitation of fat layer thickness. R2’ represents the relaxation rate due to reversible dephasing of proton magnetization and may be heavily influenced by the presence of susceptibility gradients due to paramagnetic Hb in capillaries. Therefore, the purpose of this study was to determine if R2’ and [Hb] demonstrate similar time courses during submaximal muscle contraction.

Methods

Subjects: Anatomical, muscle functional, muscle perfusion, and NIRS measurements were obtained from the right leg of 6 healthy subjects (4 male). Testing occurred on three non-consecutive days.

Muscle Contractions: Isometric dorsiflexion was performed with the subject supine, the leg at the level of the heart, and the foot secured at 90°. Isometric dorsiflexion was performed with the subject supine, the leg at the level of the heart, and the foot secured at 90°.

MRI: Analysis of the [Hb] and MRI were performed using Matlab version 7.5.0. A 7 point (1.09s) moving average was applied to the NIFS data. Deoxyhemoglobin data were collected using a frequency domain, multidistance NIRS oximeter. A rigid emitter–detector head was placed over the maximum cross-sectional area of the tibialis anterior (TA) muscle, as identified by visual inspection and palpation. MRI: For MRI, rigid image registration was performed for motion correction registering the anatomical image to the first dynamic scan. R2 data were obtained with a dual echo EPI sequence. TR/TE=2500/42.5, 85 ms for R2’ and TR/TE=2500/6, 46 ms for R2. For anatomical reference a single slice T1w scan was obtained: TR/TE=5000/20 ms, FOV=180x180 mm2, matrix size=256x128 reconstructed 512x512, slice thickness 10mm. Single slice functional images of both R2’ and R2 were obtained with a dual echo EPI sequence. TR/TE=2500/6, 46 ms for R2’ and TR/TE=2500/42.5, 85 ms for R2. FOV=180x180 mm2, matrix size=64x64 reconstructed 128x128, slice thickness 10mm. Perfusion was assessed using a flow-sensitive alternating inversion recovery sequence (FAIR) TR/TE=5000/26.79 ms, inversion time 1000 ms, FOV=180x180 mm2, matrix size=64x64 reconstructed 128x128, slice thickness 10 mm.

Data analysis: Analysis of the [Hb] and MRI were performed using Matlab version 7.5.0. A 7 point (1.09s) moving average was applied to the NIRS measurements. For MRI, rigid image registration was performed for motion correction registering the anatomical image to the first dynamic scan and each dynamic scan in the series to the first dynamic. Mean signal intensity time courses for R2’, R2 and perfusion were calculated from a region of interest traced around the borders of the TA excluding resolved vessels. R2’ was calculated as R2’ - R2. For R2’ and [Hb], time course analysis began at the start of the force ramp and continued for 120s. Data were fit to an exponential recovery equation, and then scaled from 0 to 1. Mean Euclidean distance was calculated to assess time course similarity. For perfusion data, means of the perfusion sensitive signal intensity difference were calculated for baseline and contraction periods. All results are presented as mean (SD).

Results and Discussion

Subjects showed one of two general patterns in R2’ time course and were thus divided into two groups. In the group with the expected time course (n=3, Figure 1), [Hb] ranged from 27.8 (6.4) µM at the beginning of contraction to 36.3 (10.7) µM after 120s. R2’ ranged from 4.7 (2.5) s⁻¹ at the beginning of contraction to 7.1 (3.3) s⁻¹ after 120s. The mean Euclidian distance between scaled time courses was 0.04 (0.01), suggesting a high degree of similarity. The result of a one sample t-test indicates that this value is not significantly different from zero. In the group with an unexpected time course (n=3, Figure 2), [Hb] ranged from 24.5 (12.0) µM at the beginning of contraction to 49.9 (40.1) µM after 120s. R2’ ranged from 3.9 (1.9) s⁻¹ at the beginning of contraction to 4.3 (1.2) s⁻¹ after 120s. Data could not be fit to an exponential recovery equation and similarity analysis was not performed. Perfusion increased by 44.8 (19.9) % from baseline to contraction in the expected time course group, but only increased 10.0 (4.6) % with the unexpected time course. This might indicate that perfusion limitations have an additional effect on R2’ during contraction.

Conclusion

This study suggests that R2’ and [Hb] have similar time course responses to submaximal muscle contraction under conditions of free perfusion. Time courses are not similar when perfusion is limited.

Figure 1: Time course data and best fit lines for [Hb] (blue) and R2’ (red) Time zero represents the start of contraction.

Figure 2: Time course data and best fit line for [Hb] (blue) and R2’ (red). R2’ data could not be fit to an exponential recovery. Time zero represents the start of contraction.

References
1. Ferrari et al. CJAP 2004 29:463-87
2. Mizuno et al. JAP 2003 95:2204-10

Acknowledgments
NIH/NIAMS AR050101
1 UL1 RR024975