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

C. P. Elder[1], M. A. Chance[1], R. N. Cook[2], and B. M. Damon[1,2]

[1]Radiology and Radiological Sciences and Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States, [2]Biomedical 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. R_2' 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 R_2' 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°. Maximal voluntary contraction was assessed. The submaximal contraction protocol began with 60s resting baseline followed by a 6s force ramp up to 30% of maximal force held for 114 s. The protocol was performed for R_2*, R_2, perfusion, and NIRS measurements.

NIRS: 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: Data were obtained with a Philips 3T scanner using an 8-channel SENSE knee coil centered on the largest cross section of the TA. For anatomical reference a single slice T_1w scan was obtained: TR/TE=500/20 ms, FOV=180x180 mm^2, matrix size=256x128 reconstructed 512x512, slice thickness 10mm. Single slice functional images of both R_2* and R_2 were obtained with a dual echo EPI sequence. TR/TE=2500/6, 46 ms for R_2* and TR/TE=2500/42.5, 85 ms for R_2, FOV=180x180 mm^2, matrix size=64x64 reconstructed 128x128, slice thickness=10 mm. Perfusion was assessed using a flow-sensitive alternating inversion recovery sequence (FAIR) TR/TE=5000/26.79 ms, inversion time 1000 ms, FOV=180x180 mm^2, 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 R_2*, R_2 and perfusion were calculated from a region of interest traced around the borders of the TA excluding resolved vessels. R_2' was calculated as R_2* - R_2. For R_2' 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 R_2' 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. R_2' 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. R_2' 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 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 R_2'. Future studies will address the reproducibility of these results under similar conditions and at other contraction intensities as well as investigating the biophysical basis of limited perfusion effects on R_2' during contraction.

Conclusion

This study suggests that R_2' and [Hb] have similar time courses in response to submaximal muscle contraction under conditions of free perfusion. Time courses are not similar when perfusion is limited.

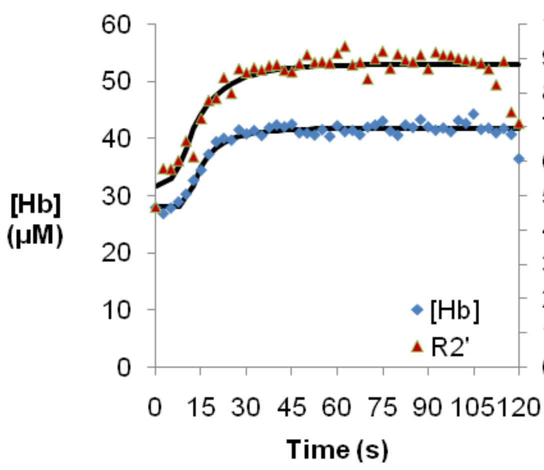

Figure 1: Time course data and best fit lines for [Hb] (blue) and R_2' (red) Time zero represents the start of contraction.

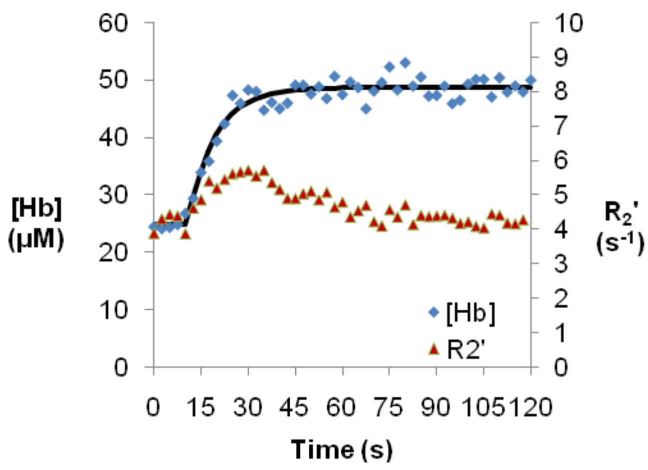

Figure 2: Time course data and best fit line for [Hb] (blue) and R_2' (red). R_2' data could not be fit to an exponential recovery. Time zero represents the start of contraction.

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