Independent effect of extravascular BOLD effects on muscle relaxation parameters

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Introduction

Transverse relaxation in skeletal muscle is affected by changes in the intracellular T_2 of water and by intravascular and extravascular BOLD effects; during brief exercises, BOLD effects predominate. The extravascular BOLD effect depends on blood oxygenation, blood volume, the diffusion coefficient of water and blood vessel orientation with respect to B_0. The first three factors are modified during and following exercise and the last depends on the muscle's orientation with respect to B_0. The independent contribution of these factors and their interactions are not yet completely understood. Therefore, the purpose of this study was to evaluate the effects of blood oxygenation and capillary orientation with respect to B_0 on the R_2 and R_2* of skeletal muscle.

Methods

Protocol: Water diffusion properties, R_2, and R_2* were measured in the lateral gastrocnemius (LG) muscle of eight healthy subjects (4 males). The subjects were studied with the leg fully extended and partially flexed. In each position, subjects were studied with and without proximal arterial occlusion. For the occlusion procedure, the cuff was placed in the mid-thigh and rapidly inflated to 240 mm/Hg using a rapid cuff inflator. R_2 and R_2^* were measured after oxygen saturation (%HbO_2) decreased to a steady level. In each position, the ankle was maintained at an angle of 90°.

Data acquisition: MRI data were obtained on a 3T Philips Intera/Achieva MR Imager/Spectrometer using a pair of surface coils placed over the posterior compartment. T_1-weighted anatomical images were obtained at the maximum girth of the leg with TR/TE=500/16 ms, slice thickness (ST)=10 mm, one slice, FOV=18x18 cm, matrix size= 256x256, N_{EX}=2. Since capillaries run parallel to the longitudinal length of the muscle fibers, muscle fiber orientation also reflects capillary orientation (α). Therefore, diffusion weighted images were acquired in ten diffusion directions using: TR/TE= 4000/49 ms, ST=6 mm, b=500 sec/mm^2, FOV 18x18 cm, matrix size=128x128, N_{EX}=4. For R_2 calculations, multiple spin-echo images were obtained with the same geometric parameters as the diffusion images and TR/TE=5000/26, 52, 78 and 102 ms; for R_2^* calculations gradient-echo EPI images were obtained with TR/TE 5000/15 and 40 ms. During all MRI procedures, near infrared spectroscopy measurements of %HbO_2, oxy and deoxyhemoglobin (HbO_2 and HHb, respectively) and total hemoglobin (THb) were obtained from the LG muscle.

Data analysis: The diffusion weighted images were registered to the b=0 image using an affine transformation. The tensor's eigenvalues (λ_1, λ_2 λ_3), first eigenvector (ε_1), and the ADC were estimated. The mean orientation of ε_1 with respect to B_0 and the mean values for ADC, λ_1, λ_2, λ_3, R_2 and R_2^* were calculated in a region of interest drawn around the LG muscle.

Statistics: Data are presented as mean ± SE. General linear model repeated measure analysis was performed to test for main effects of occlusion, leg position and the Occlusion × Leg Position interaction. Significance was set at $p \leq 0.05$.

Results

During cuff occlusion, %HbO_2 decreased by 20% and R_2^* and R_2' increased by 4% and 6%, respectively (Table 1). Flexing the leg increased α by 46%; but contrary to what was expected, R_2^* and R_2' decreased 4% and 16%, respectively. A significant increase, of no practical significance was observed for λ_3 when the leg was placed in the flex position. No Occlusion × Leg Position interaction was observed for any of the relaxation parameters.

Conclusions

The absence of a significant Occlusion × Leg Position interaction indicates that the effect of %HbO_2 on R_2 and R_2* is the same at all measured values for α. Therefore, the extravascular BOLD effect does not contribute to signal intensity changes in T_2 and T_2*-weighted images of exercising muscle at 3T.

Acknowledgments

NIH/NIAMS AR050101, NIH/NCRR M01 RR 00095 and Vanderbilt CTSA grant UL1 RR024975 from the National Center for Research Resources, National Institutes of Health

Table 1. Oxygenation, diffusion, and relaxation parameters. Mean ± SE is given.

Leg Position	Occlusion	%HbO_2 (%)	THb (μM)	λ_3 (10^{-3} mm^2 ·s^{-1})	α (°)	R_2 (s^{-1})	R_2^* (s^{-1})	R_2' (s^{-1})
Ext	No	67.1 ± 1.5	71.4 ± 8.2	1.12 ± 0.5	21.9 ± 3.0	27.2 ± 0.4	45.8 ± 1.2	18.6 ± 1.0
	Yes	53.1 ± 3.6*	67.8 ± 7.8*	1.28 ± 0.3	20.4 ± 1.5	26.0 ± 1.0	48.0 ± 1.1*	22.7 ± 1.7*
Flex	No	65.6 ± 2.7	73.6 ± 8.8	1.10 ± 0.3	38.9 ± 3.8#	27.8 ± 0.3	45.0 ± 0.9#	17.2 ± 0.7#
	Yes	53.3 ± 3.1*	68.4 ± 8.0*	1.27 ± 0.3#	39.7 ± 4.0#	28.1 ± 0.3	45.5 ± 1.1*#	17.4 ± 1.1*#

* Between occlusion and non-occlusion and # between extended and flexed positions, $p \leq 0.05$.