Repeatability of a dual gradient-recalled echo MRI method to measure post-isometric contraction blood volume and oxygenation changes

O. A. Sanchez[1], E. A. Louie[1], and B. M. Damon[1]
[1]Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States

Introduction

Measuring the hemodynamic and metabolic responses of the microvasculature to muscle contraction can provide insight into the functional state of the vascular endothelium and oxygen supply-demand coupling of muscles (1). A clinical tool to assess these physiological parameters is urgently needed due to the high prevalence of conditions that negatively affect the microvasculature (2). To accurately and consistently differentiate between healthy and dysfunctional microvasculature, a clinical tool must be validated and have a low within subject day to day variation. In this study, we present the repeatability of a previously validated (3) dual gradient-recalled echo (GRE) MRI sequence that can simultaneously measures change in blood volume and oxygenation in the skeletal muscle microvasculature at high temporal resolution.

Methods

Protocol: Nine apparently healthy subjects (8 males), 32.7 ± 5.7 years of age, reported to the lab for one orientation testing and two testing sessions. To control for factors that affect microvascular function, subjects were instructed to refrain from moderate to vigorous physical activities and alcohol for 24 hours before testing session and not to use caffeine or tobacco products for 6 hours before the testing sessions. One each testing day, the subjects performed 3 types of isometric dorsiflexion contractions: 1) maximal voluntary contraction (MVC), 2) 50% MVC (50MVC) or 3) 50% MVC with arterial cuff occlusion ($50MVC_{cuff}$), all in random order. Each type of contraction was performed twice on the same day. For 20 s before, during, and for 150 s after each contraction, functional MRI data were obtained as described below. *MRI data acquisition and analysis*: MRI data were obtained on a 3T Philips Intera Achieva MR Imager/Spectrometer. A pair of 15x10 cm (length x width) surface coils were placed along the anterior surface of the leg. After acquiring 3-plane scout images, the sagittal slices were used to identify the maximal width of the tibialis anterior (TA) muscle. Subsequent imaging was performed at this location. A T_1-weighted anatomical image was obtained with TR/TE=500/16 ms, slice thickness=5 mm, one slice, FOV=18x18 cm, matrix size=256x256, N_{EX}=2. Dual GRE EPI dynamic scans were acquired with TR/TE= 1000/6, 46 ms, slice thickness=7.5 mm, FOV= 18x18, matrix size=128x128, N_{EX}=1. Image analysis was performed in Matlab v. 7.0.1. Regions of interest (ROI) were drawn around the TA and the extensor digitorum longus (EDL) muscles. The TE=6 ms and TE=46 ms signal intensities (SI_6 and SI_{46}, respectively) were expressed as percentage of pre-contraction intensity and plotted as a function of time. Each SI_6 and SI_{46} time course was characterized by its minimum and maximum post-contraction signal intensities, the difference between them (ΔSI), the time to half peak (THP) and time to peak (TTP). SI_6 and SI_{46} have been correlated to near infrared spectroscopic data and reflect changes in blood volume and oxygenation, respectively (3). *Statistical analysis*: The average ΔSI_{avg}, THP_{avg} and TTP_{avg} of the two procedures within the same day were determined for each muscle and TE, for each of the three different experimental conditions (50MVC, $50MVC_{cuff}$ and MVC). A general linear model (GLM) repeated measures analysis was performed to test for differences in ΔSI_{avg}, THP_{avg} and TTP_{avg} between 50MVC, $50MVC_{cuff}$ and MVC. The intraclass correlation coefficient and the repeatability coefficient (4) was determined to compare the between-day variations in ΔSI_{avg}, THP_{avg} and TTP_{avg} in the different conditions.

Results

ΔSI_{avg}, for TE_6 showed a trend towards a main effect by condition, p = 0.07 and for TE_{46} demonstrated a main effect for condition, p = 0.04. THP_{avg} showed no significant differences by experimental conditions, but TTP_{avg} was lower in $50MVC_{cuff}$ than for MVC, p = 0.05.

Table 1. Mean ± SD of ΔSI_{avg} and TTP_{avg} by muscle and condition and the mean difference between the two testing days and their respective repeatability coefficients and intraclass correlations.

Muscle	Condition	Parameter (average of 2 days)	Mean ± SD	Mean (day1 – day2)	RC	ICC (p value)
EDL	MVC	ΔSI_6_	2.58 ± 0.6	0.32 ± 0.67	1.39	0.94 (p = 0.04)
EDL	MVC	ΔSI_{46}	7.11 ± 1.4	-0.23 ± 1.89	3.41	0.91 (p = 0.02)
TA	MVC	TTP_6	15.6 ± 2.9	1.17 ± 5.81	10.9	0.83 (p = 0.04)
TA	50MVC	TTP_6	12.6 ± 2.8	-0.02 ± 5.82	4.2	0.93 (p = 0.005)

RC= repeatability coefficient, ICC= intraclass coefficient correlation.

Conclusions

The repeatability of the method depends on the parameter evaluated, the muscle, and the TE. The parameters that have the lowest day to day variability are ΔSI_6 for the EDL and TTP_6 for the TA at TE_6, for MVC and 50MVC, respectively. For most variables tested, this method meets the requirement of repeatability to consistently determine hemodynamic and metabolic responses in the microvasculature of skeletal muscle.

References

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