Investigation of Diffusion Tensor Imaging Indices, Mean BOLD Signal and Calf Muscle Cross Sectional Area Following Bed Rest

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Introduction: Many imaging studies that assess muscle cross sectional area (CSA) are usually conducted after the subject had been resting for an hour in the supine position **[1]**. This is because changes in posture from erect to supine are known to influence the measured muscle CSA **[2,3]** due to shifts in regional fluid **[4]**. Two noninvasive tools that have been used to investigate water diffusivity and muscle microvasculature are diffusion tensor imaging (DTI) and blood oxygen level dependent (BOLD) imaging, respectively. In this study, we sought to evaluate any changes in DTI indices, BOLD signal and muscle CSA due to brief bed rest. Specifically, DTI metrics ($\lambda 1$, $\lambda 2$, $\lambda 3$, apparent diffusion coefficient (ADC) and fractional anisotropy (FA)) and BOLD signal were investigated in five compartments of the calf muscle (the triceps surae and the anterior and posterior tibialis) at baseline and following thirty and sixty minutes of supine rest. The calf muscle CSA was also measured at these three time points.

Methods: Scanning was performed using a GE Signa HD 3T short-bore MR scanner and an 8-channel phased array knee coil (GE Healthcare, Milwaukee, WI). Images of the dominant leg of healthy subjects (n=6, 29±5 years) were acquired from the region with the largest calf diameter (approximately at 66% of the tibia length from the distal end). To ensure that all subjects had their feet in the same position and angle, a footrest was used which kept the calf muscles suspended. Following baseline image acquisitions, data was collected at thirty and sixty minutes following supine rest. Subjects remained on the MR imaging table during the resting periods. In each of the three imaging sessions, T1-weighted axial images were collected (FSE, TE/TR= 14.9/707 ms, 5mm thickness, 20 slices). This was followed by DTI scans (spin-echo EPI, 15 gradient directions, b-value of 400s/mm^2, TE/TR=68.8/6000ms, 4 NEX, ASSET factor=2, 20 slices) and T2*-weighted BOLD slices (GRE-EPI, TE/TR=35/250ms, 10mm thickness, α=33°, 64x64 matrix, 3 slices, 2400 time points). A single slice (at the thickest calf diameter) was used for all the analyses. Calf muscle CSA analysis was carried out using Osirix (http://www.osirix-viewer.com/). Regions of interest (ROIs) encompassing all the calf muscles were selected using the high contrast T1 image. Care was taken to avoid including blood vessels and fascia. DTI indices and BOLD signal were investigated in five compartments of the calf muscle: the two heads of the gastrocnemius (lateral and medial), the soleus, and the anterior and posterior tibialis. ROIs in each muscle were selected using AFNI **[5]**. DTI analysis was performed using a BASH script that calls FSL **[6]** tools. Each NEX was eddy current and motion corrected prior to addition and subsequent tensor analysis. The BOLD timecourse was analyzed using an in-house program written in Matlab (The MathWorks, Natick MA). One-way analysis of variance with repeated measures over time used was to determine significance (level set at $p < 0.05$).

Results and Discussion: Significant decreases in calf muscle CSA were observed due to bed rest (3.5±0.6 % at 30 minutes and 5.1±1.1% at 60 minutes) (**Fig.1**). However, no significant changes were found in the mean BOLD signal intensity in any of the muscles in response to the postural change (**Table 1**). With regards to DTI, some indices were significant in some muscles, but not others (see the highlights in **Table 1**). These results were also inconsistent. DTI metrics that showed significant differences also had calculated F-values that were very close to the critical F at p=0.05.

DTI has been recently used to assess changes in the calf due to the application of external pressure **[7]**. That study found that an approximate decrease of 30% in CSA was accompanied by an increase of 12% in FA and a decrease of 8% in $\lambda 3$ (from the graphs). This would suggest that a decrease of 5% in CSA (the change observed in this study) should correspond to changes of 2% in FA and 1.3% in $\lambda 3$. The fact that our study did not produce similar results to those anticipated may be because the false positive rate was high due to the low power of the study.

Conclusion: Although changes in calf CSA were observed with time of supine rest, no changes in mean BOLD signal intensity were measureable up to an hour post postural change. In terms of DTI measurements, the inconsistent results that were obtained in the various muscles suggest the false positive rate may have been high and thus a larger study is warranted. For the metrics that didn't change, it is postulated that muscle cross sectional changes of the magnitude observed are either too small to be reflected in these diffusion and BOLD metrics, or any diffusion changes occurred too fast with respect to the minimum TE used.

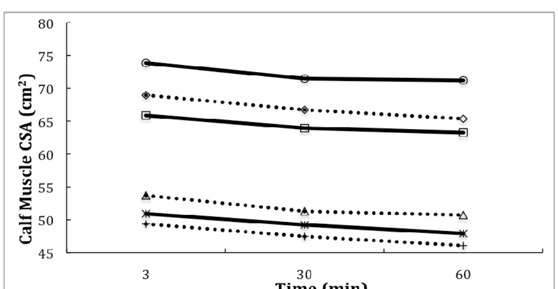

Fig.1: Calf muscle CSA for the 6 subjects

	Baseline	30 minutes of bed rest	60 minutes bed of rest
ANT	992.2 ± 100.1	967.3 ± 76.2	983.2 ± 131.9
	2.14 ± 0.06	2.08 ± 0.08	2.06 ± 0.08
	1.63 ± 0.07	1.58 ± 0.06	1.58 ± 0.04
	1.43 ± 0.04	1.40 ± 0.05	1.37 ± 0.04
	1.73 ± 0.05	1.69 ± 0.06	1.67 ± 0.04
	0.17 ± 0.09	0.21 ± 0.01	0.17 ± 0.09
POST	782.2 ± 51.0	776.5 ± 57.8	749.1 ± 78.9
	2.18 ± 0.20	2.12 ± 0.20	2.11 ± 0.14
	1.68 ± 0.15	1.65 ± 0.16	1.60 ± 0.11
	1.42 ± 0.15	1.36 ± 0.13	1.35 ± 0.14
	1.76 ± 0.16	1.71 ± 0.16	1.68 ± 0.12
	0.22 ± 0.02	0.22 ± 0.02	0.23 ± 0.02
MED	989.8 ± 270.0	991.6 ± 257.4	981.1 ± 275.9
	2.19 ± 0.15	2.10 ± 0.05	2.06 ± 0.07
	1.49 ± 0.07	1.41 ± 0.07	1.40 ± 0.04
	1.39 ± 0.08	1.32 ± 0.04	1.26 ± 0.09
	1.69 ± 0.10	1.61 ± 0.04	1.57 ± 0.05
	0.26 ± 0.02	0.26 ± 0.02	0.27 ± 0.04
LAT	936.8 ± 101.4	1063.9 ± 224.8	965.7 ± 103.3
	2.13 ± 0.17	2.04 ± 0.15	2.00 ± 0.13
	1.55 ± 0.10	1.48 ± 0.10	1.47 ± 0.06
	1.29 ± 0.07	1.24 ± 0.07	1.25 ± 0.02
	1.66 ± 0.10	1.59 ± 0.10	1.57 ± 0.07
	0.25 ± 0.02	0.25 ± 0.02	0.24 ± 0.02
SOL	810.6 ± 79.9	832.4 ± 83.6	832.5 ± 98.9
	2.07 ± 0.07	1.98 ± 0.08	1.99 ± 0.07
	1.57 ± 0.07	1.54 ± 0.07	1.54 ± 0.04
	1.37 ± 0.07	1.32 ± 0.06	1.32 ± 0.05
	1.67 ± 0.06	1.62 ± 0.06	1.61 ± 0.04
	0.21 ± 0.02	0.21 ± 0.02	0.21 ± 0.02

Table 1: Mean BOLD signal intensity (black), $\lambda 1$(red), $\lambda 2$ (blue), $\lambda 3$(brown), ADC (green) and FA (orange) for the various muscles. Lambdas and ADC are in units of 10^{-3} mm^2/s Highlighted are the indices that showed significance (P<0.05)

References: **[1]**Trappe *et al.*(2001)*Int J Sports Med* 22:186-191 **[2]**Berg *et al*(1993)*Acta Physiol Scand* 148:379-385 **[3]**Conley *et al*(1996)*J Appl Physiol* 81:1572-1577 **[4]**MAW *et al*(1995)*Acta Physiol Scand* 155:157-163 **[5]**Cox.(1996)*Comput Biomed Res* 29(3):162-73 **[6]**Jenkinson *et al*(2012) *NeuroImage* 62:782-790 **[7]**Hata *et al*(2010) *Magn Reson Med Sci* 11(3):179-18