Twisting Motion as a Confound to Skeletal Muscle BOLD

A. D. Davis[1,2], G. D. Wells[3,4], B. Falk[5], and M. D. Noseworthy[6,7]

[1]Medical Physics and Applied Radiation Sciences, McMaster University, Hamilton, Ontario, Canada, [2]Medical Physics and Applied Radiation Sciences, St. Joseph's Healthcare, Hamilton, Ontario, Canada, [3]Department of Anesthesia, University of Toronto, Toronto, Ontario, Canada, [4]Physiology and Experimental Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada, [5]Department of Physical Education and Kinesiology, Brock University, St. Catharines, Ontario, Canada, [6]Electrical and Computer Engineering, School of Biomedical Engineering, McMaster University, Hamilton, Ontario, Canada, [7]Brain-Body Institute, St. Joseph's Healthcare, Hamilton, Ontario, Canada

Introduction: Blood oxygen level dependent (BOLD) imaging in skeletal muscle shows promise in examining physiological parameters related to perfusion and oxygenation, due to its high sensitivity and excellent time resolution [1]. Although many studies use an ischemia/reactive hyperemia paradigm [2], and some use hyperoxia [3], exercise as the perturbation method of muscle perfusion and oxygenation is perhaps the most natural and thus physiologically relevant. Although BOLD data has been collected immediately after single flexion exercise [4,5], during exercise data would be most useful. Unfortunately, the motion associated with imaging during exercise can be problematic for image registration, which is required to do a general linear model (GLM) BOLD time series analysis, as is done in brain imaging studies. A twisting motion can be particularly problematic, since it gives a signal change that exactly follows the model, but has nothing to do with perfusion or oxygenation.

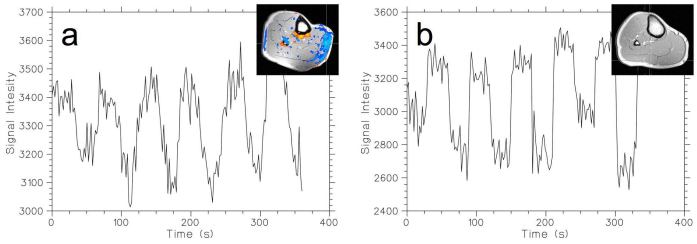

Figure 1: (a) BOLD signal time-series of an activated pixel in the gastrocnemius during repeated exercise/rest. **(b)** BOLD signal time-series of an activated pixel in the gastrocnemius during twist, without exercise.

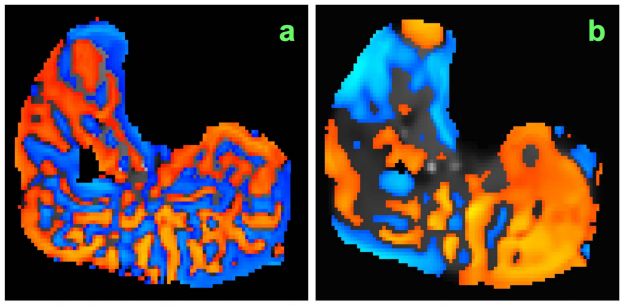

Figure 2: (a) Twist. Warm colours indicate correlation to the square wave-based on/off type model. Cool colours are anti-correlated. **(b) Motion corrected.** Correlated with a square-wave model; FSL MCFLIRT motion correction applied.

Materials and Methods: MR imaging data was collected using a GE 3T HD Signa MRI and a single channel, general purpose flex coil (GE Healthcare, Milwaukee, WI). A gradient echo EPI pulse sequence (TE=35ms, TR=2s, α=90˚) was used to acquire 10, 5mm thick, axial slices of BOLD data in the lower leg with a 64x64 (interpolated to 128x128) pixel resolution and a 16cm FOV. 180 time points were acquired, for a total scan time of 360s. Two paradigms were employed: exercise and twisting. The exercise paradigm was 30s rest, followed by 30s of isometric plantar flexion exercise, repeated 6 times. An elastic band was used for resistance. The twist paradigm was a small rotation of the lower leg from the original position at t=30s, then returning at t=60s, twisted again at 90s, and so on. The magnitude of the twist was approximately 4˚, and no exercise was performed during this motion. The data was analysed with FEAT in the FSL package [6], using a square wave based model with the temporal derivative of the model added.

Results and Discussion: The BOLD data results from the exercise paradigm are summarized in **fig.1a**. Following statistical analysis with FEAT, correlation in the medial gastrocnemius was found with a high/low square wave based model (i.e. signal intensity is initially high). The correlated pixels (P<0.05) are shown in blue in the inset of **fig.1a**. The time series of a correlated pixel is also shown in **fig.1a**. The signal is reduced during exercise, since there is an increase in the ratio of deoxy- to oxy-hemoglobin. The signal intensity of the rest phases also show a slight increase over time due likely to increased perfusion.

The BOLD data results from the twist paradigm are summarized in **figs.1b** and **2**. **Fig.1b** shows the time series of a voxel in the gastrocnemius, which has the same characteristic square wave shape as the exercise data from **fig.1a**. The data may actually be a better fit to a square wave type model, since the transitions are sharper. This occurs because bright voxels are simply shifted into the location of darker ones, and then shifted back. After statistical analysis with FEAT, there was a strong correlation in these pixels with the square wave based model. An example with 2.5 mm FWHM smoothing, and uncorrected thresholding to P<0.05 is shown in **fig.2a**. The red-yellow colour-scheme indicates correlation to a low/high type model, and the dark-light blue scale is anti-correlation, or correlation to a high/low type model. Correlation gets more pronounced when increased smoothing is applied to the image before applying the model, as is commonly practised. Thresholding (voxel, cluster) did not eliminate the large areas of correlation.

After performing analysis including MCFLIRT motion correction, the twisting motion appeared to be eliminated from the data set, leaving only small warp artifacts. When FEAT analysis was performed on the motion corrected data, however, the correlation still existed, but was confined to certain areas of the leg, mimicking single muscle activation data. An example with 5.0 mm FWHM smoothing, voxel corrected thresholding to P<0.05 is shown in **fig.2b**.

Conclusions: It is not hard to imagine an in-plane twisting motion of 4˚ being introduced during plantar- or dorsi-flexion of the foot. This motion must be eliminated during MR experiments where image data is acquired during exercise. Even with linear in-plane motion correction complete removal of artefacts was not possible. Compared to the exercise data in the inset of **fig.1a**, the twisting data of **fig.2** shows strong anti-correlative behaviour. Because of this, BOLD data obtained during exercise should be examined for anti-correlative behaviour. Data sets that show such behaviour should be closely examined for motion, to be sure that the BOLD signal intensity changes have a physiological basis. Motion based signal intensity changes may mask or mimic the true BOLD signal, causing incorrect conclusions on the oxygenation or perfusion of muscles during exercise.

References: **[1]** Carlier *et al.* (2006) NMR Biomed. 19:954-967. **[2]** Schulte *et al.* (2008) Radiology 247:482-489. **[3]** Bulte *et al.* (2006) JMRI 24: 886-890. **[4]** Damon *et al.* (2007) MRM 57:670-679. **[5]** Damon *et al.* (2007) MRM 58:335-345. **[6]** Smith *et al.* (2004) Neuroimage 23:S208-S219.