CONSISTENCY OF POST-EXERCISE SKELETAL MUSCLE BOLD RESPONSE

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Target audience: Musculoskeletal researchers interested in functional imaging of muscle.

Purpose: Blood oxygenation level dependent (BOLD) imaging is increasingly being applied to skeletal muscle in order to examine physiological parameters related to muscle perfusion and oxygenation [1,2]. Whether employing exercise or ischemic methods, studies involve time series data acquisition to chronicle the effects. Analysis is usually done on regions of interest (ROIs) to increase the signal to noise ratio (SNR) of temporal changes. Although an entire muscle's cross section is sometimes used as the ROI, many studies involve rectangular ROI selection from within a muscle [3]. As far as the present authors know, no studies have been performed to justify choosing a small ROI. In fact, evidence has been presented that suggests the BOLD signal varies widely voxel-by-voxel following single short contractions [4]. Therefore, we examined the variation in BOLD signal across muscles to determine whether small ROI selections are reasonable.

Although no standardized procedure exists to fit curves to post-exercise BOLD data, a promising function involving a gamma variate has been shown to fit well with ischemic re-perfusion BOLD data [5]. This study also examined the adaptability of gamma variate fitting to post-exercise data.

Muscle Group	1GV R^2	1GV BIC	2GV R^2	2GV BIC
Med. Gastroc. (MG)	0.997	-10.82	0.998	-11.05
Lat. Gastroc. (LG)	0.995	-10.35	0.999	-11.74
Soleus (SOL)	0.818	-8.02	0.967	-9.73
Peroneii (PER)	0.990	-9.62	0.993	-9.95

Table 1. R^2 and BIC values of fits.

Methods: The exercise protocol was 2.5 minutes of dynamic (0.5 Hz) plantar flexion at 50% of a subject's 1-repetition maximum (1RM). Post-exercise BOLD data from the calf was acquired using a GE 3T MRI with a single receive channel flex coil. The axial images used a single shot EPI (TE/TR/flip=35/250ms/33°, 3 10mm thick slices, FOV/matrix = 16cm/64×64). ROIs which excluded major vessels were drawn manually for each muscle group in Table 1. A mean time-signal for each muscle was calculated, followed by the correlation coefficient of each voxel to the muscle mean signal. Next, a curve-fitting scheme was undertaken, fitting a gamma variate + linear (1GV) curve to the mean BOLD signal of each muscle [6]. If the fit was found to be poor, a fit with 2 gamma variate (2GV) curves was attempted.

Figure 1: Correlation value of each voxel to its muscle mean signal.

Results: The correlation coefficients for each voxel to the muscle mean signals are shown in **Figure 1**. The R^2 and bayesian information criterion (BIC) values for the fits of 1 and 2 gamma variates to the muscles involved in plantar flexion are shown in **Table 1**. Selected fits for the MG and SOL are shown in **Figure 2**.

Discussion: The signal within each muscle involved in plantar flexion exercise was found to be very uniform, with a correlation coefficient approaching 1.0 in most voxels. The shape of the mean time-signal differed widely between the gastrocnemius and soleus, however.

Although the 1GV fits produced R^2 values of 0.997 and 0.995 in MG and LG, respectively, the SOL value was relatively low at 0.818. When the 2GV fit was applied to SOL, R^2 increased to 0.967. The BIC also decreased from -8.02 to -9.73, indicating a significantly improved fit despite the extra coefficients.

Using these fits, it was found that the SOL BOLD response peaked much earlier (56 s) than MG and LG (188 s and 148 s). SOL also had a higher overall change (0.27) than MG and LG (0.22 and 0.18). When the components of the 2GV fit to SOL data are taken separately, however, the peaks were 0.13 at 60 s, and 0.17 at 151 s. It is tempting to infer that the SOL signal has a component similar to MG and LG, overlain with a fast component.

Conclusion: The high intra-muscular correlation of the time signals validated the method of choosing small ROIs for analysis. This result likely only applies to the type of intense exercise performed in this study, rather than the single contraction or ischemic protocols sometimes performed. Despite having fewer coefficients than the function of [5], it was found that an excellent fit to this type of data could be achieved in most muscle groups using only a 1GV curve. This trend did not hold for the soleus, which needed 2GV to improve the fit quality.

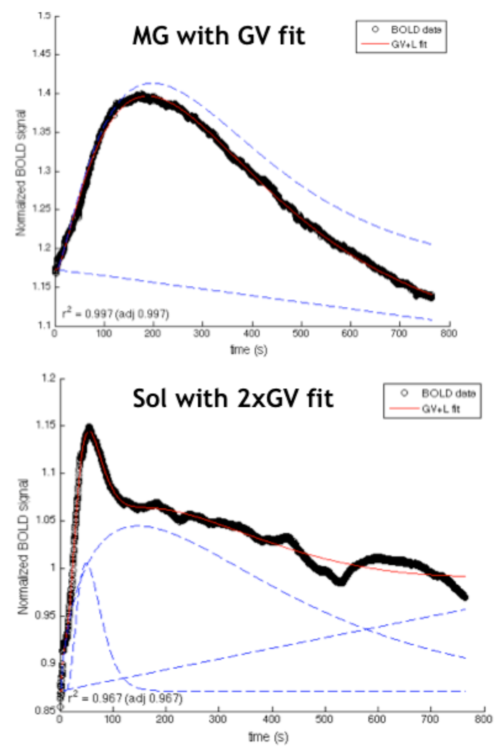

Figure 2: BOLD data from MG and Sol (black) with fit curve (red) and component curves (blue)

References: **[1]** Carlier PG, *et al.* (2006) *NMR Biomed* 19:954–967. **[2]** Noseworthy MD, *et al.* (2010) *Semin Musculoskel Radiol* 14:257–268. **[3]** Partovi S, *et al.* (2012) *J Magn Reson Imaging* 35:1227–1232. **[4]** Wigmore DM, *et al.* (2004) *J Appl Physiol* 97:2385–2394. **[5]** Schewzow K, *et al.* (2011) *Proc Intl Soc Mag Reson Med* 19:1162. **[6]** Madsen MT, (1992) *Phys Med Biol* 37:1597–1600.