Intravoxel Incoherent Motion (IVIM) in healthy skeletal muscle pre- and post-exercise

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Background: Skeletal muscle pathologies manifest abnormalities both macroscopically (compartment size, engorgement) and microscopically (myofiber dilation, degradation, edema, microvascular changes), and thus diffusion-weighted imaging (DWI) has a powerful role in both diagnosing and monitoring disorders like such as ischemia [1], inflammation, injury [2], and compartment syndrome [3-5]. Conventional DWI is sensitive to random water motion and thereby to tissue microstructure, and several variants beyond the isotropic apparent diffusion coefficient (ADC) model exist. Diffusion tensor imaging (DTI) is commonly used to capture muscle anisotropy [6-8]. Intravoxel incoherent motion (IVIM) microcirculation effects have been probed in skeletal [9-11] and cardiac [12] muscle, but their sensitivity to exercise or disease remains to be fully explored. We compared IVIM metrics in skeletal muscle pre- and post- exercise to probe the biophysical sources of muscle diffusion contrast.

Materials and Methods: Five healthy volunteers underwent MR imaging of the leg along with an IVIM imaging protocol approved by the local institutional review board (IRB). IVIM results were obtained both at rest and after 10 minutes of treadmill exertion. Images were collected in a wide-bore Siemens Verio 3 T scanner and a unilateral 8-channel knee coil. Axial IVIM used a twice-refocused spin echo sequence with bipolar diffusion gradients with echo-planar imaging (EPI) readout (TR / TE = 5700 / 44, 64x64x10 matrix, 3x3x5 mm resolution), b-values 0,10,30,50,80,150,250,400,600,800 s/mm^2 and 3 orthogonal directions stored separately. Data were processed offline with software written in Igor Pro (Wavemetrics). Regions of interest (ROI) were drawn on all IVIM slices to segment anterior tibialis (AT), extensor digitorum longus (EDL), posterior tibialis (PT), peroneus longus (PL), soleus (SOL), gastrocnemius lateralis (GL) and gastrocnemius medialis (GM). IVIM signal decays were extracted from ROI-integrated signal intensities for each muscle group and fitted with a segmented biexponential model to extract perfusion fraction f_p, pseudodiffusivity D_p, and tissue diffusivity D_t. Apparent diffusion coefficient (ADC) was derived from a monoexponential fit to all b-values. Parameter averages and exercise response factors were calculated for all muscle groups.

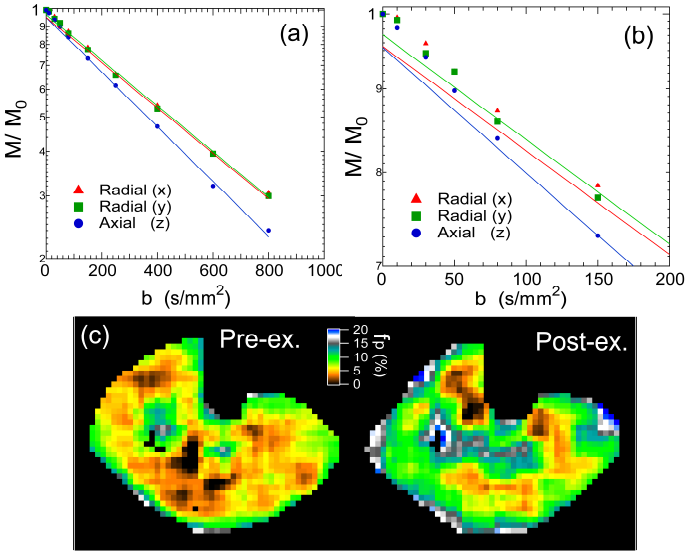

Figure 1: (a) IVIM signal decays for soleus compartment of a healthy volunteer post-exercise. (b) Enlargement of low b-value region of (a) showing IVIM effect. (c) Parametric f_p maps pre- and post-exercise.

Results: Figure 1a shows example IVIM ROI decay curves along 3 orthogonal axes in the soleus group of a healthy volunteer pre-exercise. Figure 1b shows an enlargement of the region near b=0 where the signal departure from the extrapolated trend from high b-values indicates the microcirculation fraction. Figure 1c shows parametric maps of the perfusion fraction in a volunteer pre- and post-exercise, obtained from voxelwise fits of smoothed trace-weighted images, showing a diffuse increase in f_p across the leg. Figure 2 shows the distribution of average f_p values over all subjects pre- and post-exercise as a function of muscle compartment. Increases occur for all muscle groups, most strongly for the posterior SOL, GM and GL compartments. Table 1 summarizes the average values and response factors (ratios of post/pre exercise) of IVIM metrics for all subjects and muscle groups in this study. Axial values are those for diffusion sensitizing gradient along the superior-inferior axis (z) , while radial values are the mean of the two orthogonal axes (x,y). f_p and ADC show significant axial and radial exercise changes. Quantitatively, the response factors for f_p are the largest (~50%), followed by D_p (~20%) and finally D_t, which showed very little change (2%).

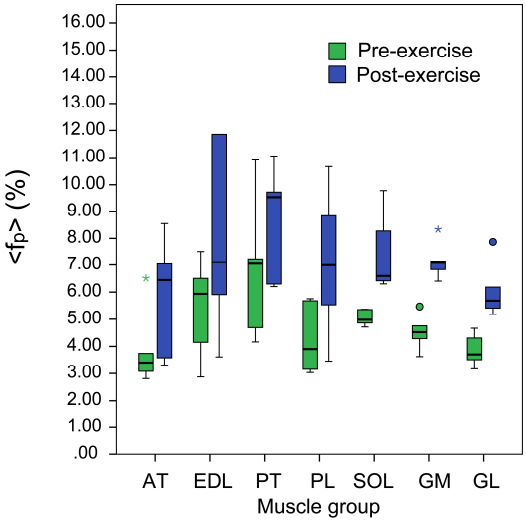

Figure 2: Average perfusion fraction f_p distribution over the subjects in this study as a function of muscle compartment pre- and post-exercise.

Discussion: IVIM analysis highlights the role of microvascular flow in diffusion-weighted contrast. The small blood volume in skeletal muscle leads to low perfusion fractions [9], but sufficiently large that the IVIM analysis allows quantification of both their baseline values and their response to exercise. Within the regime of this IVIM protocol, the exercise responses observed here are consistent with an isotropic increase in blood volume and perhaps a directional increase in longitudinal blood velocity. Structural effects such as edema, fiber dilation, or membrane degradation which might affect D_t may be minimal here due to the short diffusion time (22 ms). The results of the present study indicate IVIM to be a potent measure of vascular changes in the kinematic process and potentially a useful marker of ischemia when such microvascularity is disrupted. Future work will explore the overlap of IVIM and DTI biomarkers of microvascularity and microstructure and their respective alteration in the exertion process, accumulate further subject data for improved statistical power, and apply the IVIM technique to muscle pathology.

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	D_t (μm^2/ms)	f_p(%)	D_p(μm^2/ms)	ADC(μm^2/ms)
Pre-Radial	1.36 ± 0.10	4.47 ± 1.46	13.3± 5.3	1.44 ± 0.10
Post-Radial	1.37 ± 0.11	**7.54 ± 4.94***	12.9± 3.6	**1.50 ± 0.11***
Response–Radial	1.02 ± 0.03	1.54 ± 0.48	1.11± 0.31	1.04 ± 0.03
Pre–Axial	1.84 ± 0.12	5.56 ± 2.45	27.4± 12.9	1.94 ± 0.13
Post–Axial	1.89 ± 0.12	**7.55 ± 3.27***	33.1± 15.7	**2.02 ± 0.12***
Response–Axial	1.02 ± 0.03	1.46 ± 0.42	1.36± 0.85	1.04 ± 0.02

Table 1 : Mean IVIM values and exercise response factors in the radial and axial directions over all muscle groups and volunteers in this study. * in this Table indicates significant (p<0.05) change from pre-exercise condition.