Myofiber and Microvasculature Architecture of Human Calf Muscle Alteration in Passive Dorsiflexion

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Introduction:

Changes in the architecture of human skeletal muscles after contraction, which are of importance in sports medicine and rehabilitation, have been quantified *in vivo* via mostly ultrasound techniques [1]. However, such techniques have low spatial resolution and cannot track the alterations in muscle blood perfusion. Diffusion-Weighted (DW) MRI has been used to represent the three-dimensional architecture [2, 3] and to quantify the microstructural properties of skeletal muscles [4], while fMRI has been used to probe muscle perfusion during contraction [5]. With the exception of [6], most MRI studies have focused on the increase of blood perfusion in leg muscles during isometric (active) contractions, or after vigorous exercise or vascular occlusion. In the present study, we are focusing on the effects of passive muscle stretch on fiber orientation and perfusion, which has been shown to produce sarcomere lengthening and decrease in muscle perfusion [7, 8]. We employ the direction-sensitive IntraVoxel Incoherent Motion (IVIM) technique in conjunction with Diffusion Tensor Imaging (DTI) in order to quantify the alteration of muscle fiber orientation and of directional perfusion for the human calf muscles following passive dorsiflexion of the foot, which causes stretching of the gastrocnemius muscle [1].

Materials and Methods:

Experimental Set-up: In order to maintain good spatial registration of the leg during foot dorsiflection, we designed and fabricated a cylindrical cradle which immobilizes the lower leg (below the knee) of a human volunteer, allows the foot to pivot so that the ankle joint position can be adjusted, and fits inside a lower extremity RF coil. The cradle is MRI compatible since it is fabricated from acrylic material, and uses elastic cords to push the pedal against the sole of the foot, see Fig. 1. The volunteer lies supine on the MRI scanner table so the leg to be imaged is at full extension, and the acquisition is performed at two ankle joint positions, one with the foot at rest (no tension on the elastic cords) and the other at maximum dorsiflexion without causing discomfort to the subject.

Fig. 1. MRI-compatible cradle for leg immobilization with adjustable ankle joint positions.

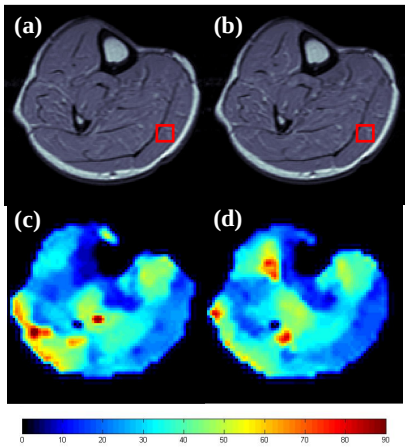

Fig. 2. T_2-weighted spin echo images of the calf cross-section with foot (a) at rest and (b) at dorsiflexion. Colormaps of the azimuthal angle of the primary eigenvector (c) at rest and (d) during dorsiflexion. Scale: 0 º (blue)-90º (red)

Data acquisition: A single-channel lower extremity coil was used to scan on a 3T full-body GE scanner the calf region of one male subject's right leg fixed in the cradle, as depicted in Fig. 1. For each flexion state, one axial slice with 9 mm thickness was acquired centered on the widest cross section of the calf muscle, and fat suppression was performed using a spatial-spectral RF pulse. For all the diffusion measurements a single-shot diffusion-weighted stimulated-echo EPI sequence was used. The parameters for the IVIM measurement were: FOV= 20 cm, 64×64 acquisition matrix, 5/8 partial phase encoding, N_{ex}=10, TR/TE=1500/52 ms, δ=15 ms, Δ=40 ms and 3 directions with 15 values of diffusion gradient strength with g ≤3.0 G/cm. The parameters for the DTI measurement were FOV= 20 cm, 64×64 acquisition matrix, 5/8 partial phase encoding, N_{ex}=6, TR/TE=2000/52 ms, δ=15 ms, Δ=40 ms and 30 directions with single values of diffusion gradient strength g_{max}=3 G/cm. The T_2 estimation was performed with a multi-echo spin-echo sequence with TR/TE=2000/14 ms and a 256x128 acquisition matrix using 4 echo times to fit the exponential T_2 decay.

Results and Discussion:

The diffusion tensor analysis was implemented on a voxel-by-voxel basis and the extracted diffusion parameters were averaged over a 5×4 ROI located in the medial gastrocnemius, cf. Fig. 2(a-b). Table 1 summarizes the results for the main DTI parameters for the above representative ROI inside the medial gastrocnemius muscle at rest and at dorsiflexion. A notable difference between the two flexion states is the value the azimuthal angle θ_1 of the primary eigenvector. The azimuthal angle of the primary eigenvector corresponds approximately to the pennation angle of the gastrocnemius. Our results indicate that this angle reduces by 5º during passive dorsiflexion, and this is corroborated by ultrasound measurements [1]. The IVIM fit at high b-values gives also estimates of the apparent vascular volume fraction *f* and the extravascular diffusion coefficient along the applied diffusion direction. Table 2 shows the IVIM fitting parameters for the 3 applied directions. When the diffusion gradient is applied along the S/I direction (essentially along the gastrocnemius fibers), there is a significant decrease on the apparent vascular volume fraction as the foot position changes from rest to dorsiflexion. This nearly 50% decrease in *f* is consistent with the previously reported reduction in capillary perfusion during muscle stretching obtained via intravital microscopy [7]. The decrease in *f* cannot be accounted by geometric considerations such as the decrease in pennation angle with stretching, since the latter means that the muscle fibers, and consequently the majority of the capillaries, align more with the S/I direction [7], which would then tend to increase *f* along that direction. The observed decrease of the mean T_2 relaxation time by 1.7 ms is also corroborated by measurements in passively stretched skeletal muscle [6]. Similarly, the decrease in T_2 would tend to increase, rather than decrease, the apparent vascular volume fraction *f*. We are therefore confident that the measured decrease in *f* reveals a decrease in gastrocnemius blood perfusion.

	λ_1	λ_2	λ_3	ADC	FA	θ_1
Rest	1.93	1.33	1.13	1.47	0.28	23
Dorsiflexion	1.84	1.31	1.12	1.43	0.26	18

Table 1. Mean values for the eigenvalues of the diffusion tensor, the mean diffusion coefficient ($\times 10^{-9}$ m^2/s), the fractional anisotropy (-), and the azimuthal angle of the primary eigenvector (º) averaged over the 5×4 ROI in medial gastrocnemius at the two flexion states.

	f			*D*			T_2
	L/R	A/P	S/I	L/R	A/P	S/I	
Rest	2.95	2.79	7.47	1.21	1.24	1.68	28.6
Dorsiflexion	1.53	1.76	3.85	1.17	1.18	1.68	26.9

Table 2. Mean values for the fitted IVIM parameters (*f* in % and *D* in 10^{-9} m^2/s) along the 3 applied diffusion directions and T_2 relaxation times (ms) over a 5x4 ROI in medial gastrocnemius at the two flexion states.

Conclusion:

This project aims to consolidate and evaluate Diffusion-Weighted MRI techniques for the *in vivo* quantification of local muscle fiber architecture and perfusion. By combining IVIM and DTI measurements and employing a MRI-compatible cradle for leg immobilization, we demonstrate that there is significant decrease of capillary perfusion in the gastrocnemius muscle during passive dorsiflexion of the foot.

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