In Vivo Characterization of Skeletal Muscle Fiber Ellipticity with Diffusion-Weighted MRI

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Introduction:

Diffusion-Weighted (DW) proton-MRI has been extensively used to represent the three-dimensional architecture [1, 2] and to quantify the microstructural properties of skeletal muscles [3]. The Diffusion Tensor Imaging (DTI) technique constitutes the most frequent approach in characterizing the anisotropic muscle organization. The results of all the previous DTI studies in the skeletal muscle [1-3] have consistently shown a difference between the secondary and tertiary eigenvalues that characterize diffusion on the plane perpendicular to the myofiber orientation. Galban et al [3] suggested that the secondary eigenvalue is related to the diffusion process within the endomysium and the tertiary eigenvalue corresponds to the diffusion process within the individual fibers. In the present study, we are proposing a two-compartment diffusion model in order to explain the asymmetry of the diffusion on the transverse plane by accounting for the elliptical shape of skeletal muscle fibers, which is a microstructural feature well documented in prior histological studies [4, 5]. We also explore the effect of this asymmetry on the strain of the muscles upon contraction.

Materials and Methods:

Model formulation: We assume that there are two main compartments contributing to the diffusion properties of the tissue: the intracellular space (within the myocytes) and the extracellular space (collageneous intramuscular connective tissues consisting of endomysium and perimysium). Given a short diffusion time, the DW-MRI acquisition can only probe structures of size of a few microns, so the extracellular features responsible for the anisotropy of the signal are limited to the endomysium only. We then model the muscle fibers as infinite cylinders with an elliptical cross section of geometric ratio α (=short axis length/long axis length), a representation consistent with histology. Diffusion is then described independently along the three principal axes (parallel to the fiber direction, along the long axis of the elliptical cross section and along the short axis of the elliptical cross section) by adopting a unified approach accounting for both T_2 relaxation and exchange effects based on Kärger's model [6]. Due to the random arrangement of collagen fibrils in the endomysium, we assume that endomysium microstructure does not induce any anisotropy in diffusion. However, water diffusion in extracellular space is hindered partially by the membranes of myocytes, which are asymmetric. Therefore, the idea of an apparent extracellular diffusion coefficient depending on the direction of the applied diffusion gradient is introduced in the spirit of Stanisz [7]. This modulation of the extracellular diffusion coefficient by the diffusion direction relative to the orientation of the ellipses expresses the dependence of the model on the muscle fiber shape, which is parameterized by the fiber ellipticity. The basic input parameters of the model are taken from other skeletal muscle studies: $T_{2,in}$=30 ms, $T_{2,ex}$=140 ms, average residence time within a myocyte=1100 ms, intracellular volume fraction=0.9 and extracellular diffusion coefficient=2.0×10^{-9} m^2 s^{-1}. Given the above assumptions, an analytical model is formulated with unknowns the diffusion coefficients within the myocytes parallel and perpendicular to the fiber direction ($D_{in}^{\parallel}$ and $D_{in}^{\perp}$) and the degree of fiber ellipticity α.

Data acquisition: A single-channel lower extremity coil was used to scan the calf region of one male subject's right leg on a 3T full-body GE scanner. Diffusion-weighted images were acquired using a single-shot diffusion-weighted stimulated-echo EPI sequence with the following parameters: TR/TE=2000/52 ms, FOV=20x20 cm^2, slice thickness=9 mm, acquisition matrix=64x40 (5/8 partial phase encoding), and N_{ex}=6. Diffusion-weighted gradients were applied along 30 non-collinear directions with an average b-value of 541 s mm^{-2}. The diffusion-encoding parameters were: δ=15 ms, Δ=40 ms,: g_{max}=30 mT/m. One axial slice was acquired centered on the widest cross section of the calf muscle and fat suppression was performed using a spatial-spectral RF pulse.

Results and Discussion:

Fiber ellipticity: Diffusion tensor analysis is implemented on a voxel-by-voxel basis and the extracted diffusion parameters are averaged over the corresponding ROIs. The results for the main DTI parameters for ROIs in different muscle regions are summarized in Table 1 (Medial Gastrocnemius-MG, Lateral Gastrocnemius-LG, Anterior Tibialis-AT, Soleus-SOL). The intracellular diffusion coefficient perpendicular to the myofiber direction is approximately equal to the 80-90 % of intracellular diffusion coefficient parallel to the myofiber direction. We suggest that this small difference is related to the fact that for a short Δ=40 ms, the mean diffusion length on the transverse plane is around 15 μm and this is comparable to the near-micron length scale of the subcellular barriers that induce the intracellular anisotropy. The CP planar index of the diffusion tensor constitutes a good measure of the ellipticity, as it increases for more elliptical shapes and decreases for more circular shapes. The predicted values for the fiber ellipticity are within the range 0.53-0.73, in accordance with previous histological measurements in humans (values in the range 0.4-0.8 [4]).

	ADC	λ_1	λ_2	λ_3	*FA*	*CP*	θ_1	$D_{in}^{\parallel}$	$D_{in}^{\perp}$	α
MG	1.46±0.02	1.92±0.06	1.33±0.05	1.13±0.08	0.28 ±0.04	0.09	24 ±2	1.89	1.81	0.62
LG	1.47±0.09	1.93±0.10	1.37±0.08	1.11±0.12	0.28 ±0.04	0.11	23 ±3	1.91	1.79	0.53
AT	1.60±0.05	2.11±0.10	1.41±0.05	1.27±0.03	0.27 ±0.03	0.06	33 ±3	2.16	2.05	0.73
SOL	1.49±0.08	2.06±0.10	1.30±0.09	1.13±0.11	0.32 ±0.04	0.08	45 ±3	2.09	1.79	0.67

Table 1. Mean values and standard deviations for the mean diffusion coefficient and the eigenvalues of the diffusion tensor ($\times10^{-9}$ m^2 s^{-1}), the fractional anisotropy (FA), the planar index (CP) and the azimuthal angle of the primary eigenvector (°) and the model results for the intracellular diffusion coefficient parallel and perpendicular to the fiber direction ($\times10^{-9}$ m^2 s^{-1}), and the geometric ratio of the elliptical fiber (α).

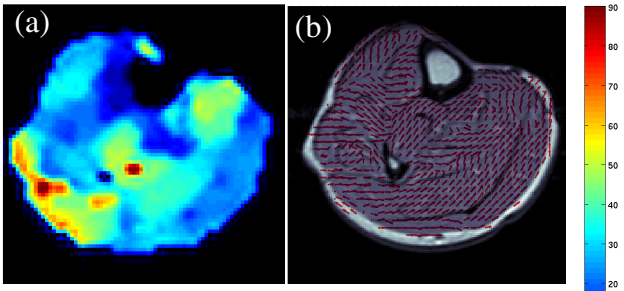

Figure 1. (a) Colormap of the azimuthal angle of the primary DTI eigenvector and (b) field map consisting of line segments representing the intersection of the plane formed by the primary and secondary eigenvector with the slice plane overlaid by a T_2-weighted high resolution image..

Fiber ellipse orientation: Fig. 1a shows the azimuthal angle of the primary eigenvector with the B_o field axis, which can be considered as a rough estimate of the pennation angle for the different muscle regions. Fig. 1b shows the intersection of the plane formed by the primary and secondary eigenvector with the slice plane. For tissues with small pennation angles (MG and LG), we suggest that this field map gives the orientation of the long axis of the elliptical fiber cross section and the corresponding maximum strain along the slice plane when the muscles contract. For instance, our model implies that in the medial gastrocnemius (MG), the long axis and the maximum strain remain parallel to the exterior muscle surface, and the latter is consistent with strain measurements in animal models [8]. We thus advance the hypothesis that the observed ellipticity [5] is also consistent with the fact that muscles adapt to mechanical strain with age.

Conclusion: On the basis of a two-compartment model we propose an explanation for the eigenvalue asymmetry ($\lambda_2>\lambda_3$) found in all DTI measurements in skeletal muscle. The model accounts for this asymmetry by introducing myofibers with elliptical cross section and this is consistent with the kinematics of muscle deformation.

References: [1] Damon B. M. et al, *Magn Res. Med.* 48: 97-104 (2002), [2] Sinha S. et al *J. Magn. Res. Imag.* 24: 182-190 (2006), [3] Galban C. J et al. *Eur. J. Appl. Physiol.* 93: 253-262 (2004), [4] Venema et al, *Med. Biol. Engin.* 12:681-692 (1974), [5] Andersen et al, *Scand. J. Med. Sc. Sports* 13: 42-47 (2003), [6] Kärger et al, *Adv. Magn Res.* 12:1-89 (1988), [7] Stanisz G. J. et al, *Magn. Res. Med.* 37: 103-111 (1997), [8] Van Donkelaar C. C. et al, *J. Biomechanics* 32: 755-762 (1999).