Diffusion tensor MRI for the in vivo determination of skeletal muscle architecture in two ankle angles

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Introduction:

Mechanisms of force loss that occur during progressive muscular diseases are more and more studied using mouse models. Such diseases generally cause both a decrease in maximal tension and progressive muscle wasting, which may result in profound changes in muscle architecture. Muscle architecture is a main determinant of the mechanical behavior of skeletal muscle [1], and is characterized by various parameters, including muscle length, fiber length, pennation angle, and physiological cross-sectional area (PCSA). The pennation angle is the angle between the muscle fibers and the tendon plate, while the PCSA is the sum of the cross-sectional areas of all fibers.

Recently it has been established that Diffusion Tensor Imaging (DTI) with MRI offers the opportunity to quantitatively determine the muscle architecture of rodents [2,3]. Until then this architecture was determined by ultrasonography or anatomical reconstruction methods [1], which both have severe limitations. DTI is a non-invasive technique and enables the reconstruction of whole muscles in longitudinal studies.

The aim of this study was to detect changes in skeletal muscle architecture using DTI-based fiber tracking. Therefore, the architecture of the tibialis anterior (TA) was determined in two ankle angles. It was hypothesized that an increased ankle angle would result in increased fiber length and a decreased PCSA and pennation angle.

Materials and methods:

Specimen: Male C57BL/6 mice (n=3) were anaesthetized with isoflurane (1.0-1.5% in air). The body temperature was maintained at 36-39 °C and the animal's respiration was continuously monitored. Two ankle angles were used, i.e. plantar and dorsal flexion (difference ~ 70 degrees).

MRI: MR was performed with a horizontal 9.5 cm bore, 6.3 Tesla MRI scanner using a 1.5 cm solenoidal RF coil. A 3D diffusion-weighted fast spin echo sequence with fat suppression was used. The diffusion gradients were applied along 6 non-collinear directions and one reference image was recorded without diffusion weighting. Scan parameters were: FOV=15x15x30 mm^3, matrix size=60x60x128 (zero filled to 64x64x128), TE=10 ms, ETL=6, NSA=2 and TR=1 s and Δ=20 ms, δ=10 ms and b-value=0 or 584 s/mm^2. The scan time for one DTI measurement was 2:20 hours and the total protocol took approximately 6 hours. Initial analysis was done using Mathematica (Wolfram Research). The pixel intensities of the 3D DTI dataset were fitted to obtain the six elements of the diffusion tensor. For every dataset, we have drawn three ROIs in the TA and gastrocnemius from which the means of the eigenvalues, ADC (Trace(D)/3) and fractional anisotropy (FA) were calculated.

Fiber tracking: Fiber tracking was performed using a visualization tool for DTI data as described by Vilanova et al. [4]. The fiber paths were calculated starting from a user defined seed point. A minimal fractional anisotropy (FA) of 0.2 and a maximal angle change of 10 degrees per integration step were used as stop criteria. The muscle structural parameters were determined as described before [2].

Results and Discussion:

No differences in DTI indices were observed between the two ankle angles (Table 1) and values are comparable with literature (2,3).

The possibilities of 3D DTI and fiber tracking are depicted in Figure 1. Figures 1a-1c illustrate the procedure for estimating pennation angle, fiber length and PCSA, respectively. Fiber tracking in the whole leg was possible and the fiber orientation corresponded with known fiber architecture.

Table II summarizes the structural parameters for the two ankle settings. The values were comparable with invasive anatomical reconstruction methods (1). The pennation angle and PCSA changed as expected with variations in ankle angle. The fiber length did not show a difference.

Conclusion:

Fiber tracking enables reproducible and reliable determination of muscle architecture. This was demonstrated by the ability to detect significant changes in the muscle architectural parameters, i.e. pennation angle and physiological cross-sectional area, with a change in ankle angle. These findings were in accordance with expectations. The developed DTI tools make it possible to perform longitudinal studies on wild-type and transgenic mice to assess possible alterations in muscle architecture.

References:

[1] Burkholder TJ et al., *J Morphol* 221:177-90, 1994

[2] Heemskerk AM et al., MRM 53:1333-40, 2005

[3] Damon BM et al. MRM 48:97-104, 2002

[4] Vilanova A et al., *VisSym '04 Joint Eurographics –IEEE TCVG Symposium on Visualization*: 173-82, 2004

Table 1) values (mean ± SD) for the DTI indices of the TA and G in two ankle angles.

	TA dorsal	TA plantar	Gastrocnemius dorsal	Gastrocnemius plantar
λ_1 ($x10^{-3}$ $mm^2 \cdot s^{-1}$)	1.85 ± 0.06	1.83 ± 0.03	1.79 ± 0.06	1.76 ± 0.04
λ_2 ($x10^{-3}$ $mm^2 \cdot s^{-1}$)	1.20 ± 0.03	1.27 ± 0.03	1.23 ± 0.03	1.27 ± 0.07
λ_3 ($x10^{-3}$ $mm^2 \cdot s^{-1}$)	0.79 ± 0.07	0.81 ± 0.08	0.96 ± 0.10	0.92 ± 0.03
ADC ($x10^{-3}$ $mm^2 \cdot s^{-1}$)	1.28 ± 0.01	1.28 ± 0.02	1.32 ± 0.05	1.32 ± 0.02
FA	0.40 ± 0.05	0.40 ± 0.02	0.31 ± 0.03	0.31 ± 0.01

Table II) Muscle architectural parameters (mean ± SD) of the TA in two ankle angles obtained by fiber tracking. Significance between dorsal and plantar is indicated; 1-tailed paired t-test is performed.

	TA dorsal	TA plantar	p-value
fiber length (mm)	8.5 ± 1.0	8.4 ± 1.5	0.472
pennation angle (deg.)	24 ± 2.2	14 ± 2.1	0.02 *
PCSA (mm^2)	7.1 ± 0.9	6.4 ± 0.9	0.013 *

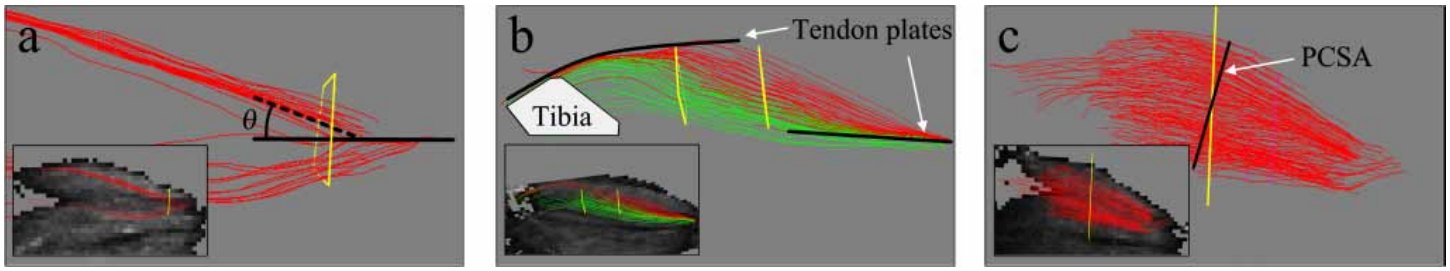

*Fig. 1) Representative examples of fiber tracking in the mouse hind limb. Fiber tracking was started from the ROIs indicated with the yellow lines. The insets show the fibers projected on a 2D MRI slice for anatomical reference. (**a**) Determination of the pennation angle (**θ**). (**b**) Tracking of fibers in the TA muscle, from which the fiber length between the two tendon plates was determined. (**c**) Determination of the PCSA (the black solid line).*