Change in water diffusion properties with altered muscle architecture

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Introduction

Diffusion tensor imaging provides information on the underlying tissue structure, by means of three eigenvalues (λ_1 , λ_2 , and λ_3) and corresponding eigenvectors. Studies have shown that the principal eigenvector is aligned along the skeletal muscle fiber direction [1,2]. The three eigenvectors are orthogonal to each other; therefore λ_2 and λ_3 represent diffusion perpendicular to the fiber direction. Several studies support the hypothesis that the differences between λ_2 and λ_3 are real and not due to the sorting bias. It has been reported that λ_2 and λ_3 differ between human calf muscles; however these differences are not consistent between research groups [3, 4]. The distinct structural origin is further supported by the finding that upon muscle damage induced by ischemia the greatest relative difference in eigenvalue amplitude occurred in λ_3 [5]. All together, there is evidence of diffusion anisotropy perpendicular to the muscle fiber, but the structural basis for this remains unknown. To verify this evidence, we investigated whether and how the DTI indices changes upon muscle lengthening and consequential small structural changes.

Methods

<u>Subjects:</u> DTI datasets were obtained from 10 healthy subjects (5 male), with their foot in 0° of plantar flexion (anatomical position), +15° of plantar flexion, and twice at 0° on a different day.

<u>MRI</u>: Data were obtained with a Philips 3T scanner using a double flexible surface coil covering the length of the Tibialis Anterior (TA) muscle. For anatomical reference a proton density weighted scan was obtained: FOV=196x196 mm², matrix size=256x256, slices thickness=6 cm, 55 slices, TR=4152 s, TE=11 ms. DTI images were acquired in 5 continuous stacks with a total of 55 slices, using an EPI sequence with FOV=192x192 mm², matrix size=96x64 with 128x128 reconstructed matrix, 4 excitations, TR=3300 ms, TE=48 ms and SENSE factor=1.2, b=500 s/mm², and 10 directions specified according to Jones et al. [6].

Image processing: Image registration was performed of 1) diffusion weighted images to the b=0 image, 2) DTI stack to the adjacent

stack, and 3) DTI set to the anatomical image set. From the anatomical images, an ROI for each slice was traced covering the cross sectional area (CSA) of the TA. This CSA was eroded to exclude partial volume effects. For each ROI the mean values for λ_1 , λ_2 , λ_3 , ADC, and FA were calculated. Statistics: The values of 20 slices were used for the statistical analysis. A one-way ANOVA was used with foot position as between subject factor. p<0.05 was considered significant.

Results

The mean difference between measurements is depicted in figure 1. As expected, the diffusion indices did not differ for the measurements with the foot in the same anatomical position (grey line). The values were also constant for λ_1 , λ_3 , ADC and FA between the two foot positions (black line). However, λ_2 decreased with the foot in 15° (p = 0.008). The mean λ_2 were 1.530 and 1.476 mm²·s⁻¹ for 0° and 15° respectively. All subjects showed this decrease, although the extent varied between an average difference along all slices of 0.019 to 0.0956 mm²·s⁻¹. Table 1 summarizes the statistical analysis.

Discussion

The results verify that λ_2 and λ_3 have different structural origins. However, a convincing explanation is still to be found. A decrease in diffusivity can be expected the fibers lengthen and consequently the fiber diameter decreases. However, this decrease in diameter is small (± 3%), and is unlikely to be solely responsible for the change in λ_2 . Another possibility might be a decrease in sarcomere overlap and spacing with fiber lengthening, although these differences are on μ m scale.

The current available data on changes in eigenvalues and a thorough investigation on muscle (micro)-structure need to be combined with computational models to explore the connection between fiber structure and diffusion values.

Conclusion

The second eigenvalue is significantly decreased with increased foot rotation, whereas the other indices remain constant. This confirms that the λ_2 and λ_3 have different structural origins.

		Table) p-values for $\Delta(0^{\circ}-15^{\circ})$ and $\Delta(0^{\circ}-0^{\circ})$		
References 1) Doorn et al Eur J Morphol 1996 34(1):5-10 2) Donkelaar et al J Anat 1999 194:79-88 3) Galban et al EJAP 2004 93:253-62 4) Sinha S et al MRI 2006 24(1):182-90 5) Heemskerk AM et al MRM 2006 56(2):272-81 6) Jones DK et al MRM 1999, 42(3), 515-25			0°-15°	0°-0°
		λ_1	.879	.980
	Acknowledgements NIH/NINDS R01 NS034834 NIH/NIAMS AR050101 NIH/NCRR M01 RR 00095	λ_2	.008*	.625
		λ_3	.520	.945
		ADC	.147	.931
		FA	.424	.946



⁰ ¹⁰ ²⁰ Figure 1) plots of the difference (mean \pm SD) between the foot at 0° and 15° (black) or the foot twice at 0° (grey). For each subject 0°-15° was determined for each slice that corresponds anatomically. Diffusivities in mm²·s⁻¹ and FA dimensionless.