Quantitative Effects of Inclusion of Fat on Diffusion Tensor MRI of Human Thigh Muscles

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Introduction

Diffusion tensor MRI (DT-MRI) is quickly becoming a useful tool for *in vivo* studies of muscle architecture, damage, and inflammation (1-6). Cellular structures such as membranes and myofibrils allow water to more freely parallel to the long axis of the fibers than transverse to the long axis of the fibers (1-3). Clinically, DT-MRI allows for assessment of skeletal muscle integrity on a microscopic level (3). The diffusion of water in all directions may increase due to injury or disease as the muscle microstructure loses integrity and is no longer capable of hindering the motion of the water molecules (4). This sensitivity may make DT-MRI useful in the monitoring of several muscular dystrophies and inflammatory myopathies. One problem arising in these conditions is the infiltration of adipose tissue into muscle. For muscles with greater fat infiltration, diffusivities are typically lower than values recorded in normal muscle (3). Therefore, the presence of adipose tissue due to conditions such as myositis, aging, obesity, or injury may complicate the use of muscle diffusion measurements to represent muscle damage (6). The purpose of this study was to determine the minimum level of water signal percentage that must be present in a normal skeletal muscle region of interest (ROI) to accurately represent the diffusion properties of the muscle tissue *per se*.

Methods

Experimental Protocol Five healthy subjects provided written, informed consent to participate. MRI was performed on a 3T Philips Achieva Intera MR imager. The subjects lay supine on the patient bed with an 8 channel SENSE torso coil positioned around the thighs. T_2-weighted images were acquired with TR=3500 ms, TE=18.3 ms, field of view=200x200 mm, and acquired matrix=128x128 (reconstructed at 256x256). T_2-weighted images with fat saturation (FS) were acquired using the same parameters and a spectrally-selective adiabatic inversion recovery (SPAIR) FS pulse with inversion time=190 ms and a 225 Hz bandwidth as well as an 18.3 ms sinc-gauss pulse 100 Hz downfield of water to saturate the lipid vinyl proton resonance. The diffusion weighted images had identical slice geometry, an acquired matrix size of 96x96 (reconstructed at 128x128), TR = 4000 ms, TE = 50 ms, and diffusion weighting in 15 directions with *b*-value=400 s/mm^2.

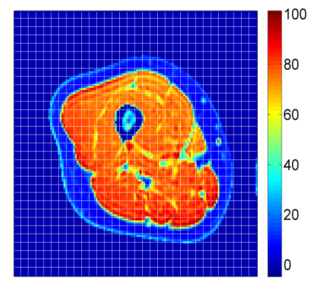

Figure 1. The water signal percentage image, with an overlay of the 4×4 grid system. The colorbar indicates the water signal percentage.

Image Analysis All calculations were made using MATLAB 7.6.0. A water signal percentage image was created by dividing the T_2-weighted image with FS by the non-FS T_2-weighted image and multiplying by 100%. The water percentage image was resized to 128x128. All images were gridded into 4×4 squares (Figure 1). For each grid square in the DT-MRI data, a signal vector **S** containing the mean signal in the non-diffusion weighted image and each of the diffusion weighted images was formed. The diffusion tensor, **D**, was formed using a weighted least squares fit of **S** on the diffusion encoding matrix as described in (6). **D** was diagonalized, the eigenvalues (L1, L2, L3) were magnitude-sorted, and fractional anisotropy (FA) was calculated.

Data Analysis In each grid square, the mean water signal percentage was calculated and the eigenvalues and FA were obtained from the analysis described above. The water signal percentages, eigenvalues, and FA in all grid squares containing between 0 and 10% water were averaged. This was repeated for water signal percentages ranging from 10 to 90%, in bin sizes of 10%. For each water signal percentage bin, the values were averaged across the five subjects and the standard error (SE) was calculated. The 90-100% water signal bin was not consistently observed in all subjects, so the diffusion properties of water in the 80-90% signal bin were considered to represent best the diffusion properties of muscle water. For each of the eigenvalues and FA, a one-way ANOVA was performed with multiple comparisons using Tukey's HSD test to determine the water signal percentage bin at which the mean values first differed from the values in the 80-90% water signal bin. In cases of missing subject data from a particular water signal percentage bin, mean substitution was performed.

Results and Discussion

Figure 2a shows L1, L2, and L3 plotted as functions of the water signal percentage. The ANOVA with multiple comparisons showed that the mean values of L1 in the water signal percentage bins of 0-10%, 10-20%, and 20-30% all differed significantly ($p<0.05$) from the mean value for the 80 to 90% water signal percentage bin. L2 and L3 behaved similarly: the mean values of both of these parameters in the 0-10%, 10-20%, 20-30%, and 30-40% water signal bins differed significantly ($p<0.05$) from the respective mean values calculated for the 80-90% water signal bin.

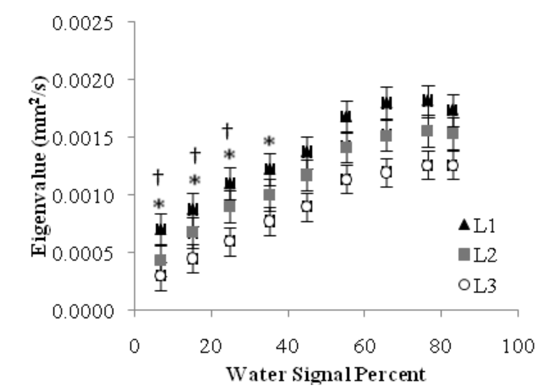

Figure 2a. The eigenvalues of the diffusion tensor are plotted as a function of the water signal percentage. Error bars represent the SE. †p<0.05 for L1 *vs*.L1 at 80-90%. *p<0.05 for L2 *vs*. L2 at 80-90% and L3 *vs*. L3 at 80-90%.

The FA is plotted as a function of the percent of water signal present in a region in Figure 2b. As the percentage of water and therefore the percentage of muscle in a region increases, the fractional anisotropy decreases. The ANOVA revealed the mean FA values differ significantly from the mean value calculated for the 80-90% water signal bin at a threshold value of 40% water signal. The paradoxical behavior is probably because at very low water signal percentages, the signals from these fat-suppressed images are dominated by noise; the random nature of the noise erroneously causes the diffusion to appear very anisotropic (6).

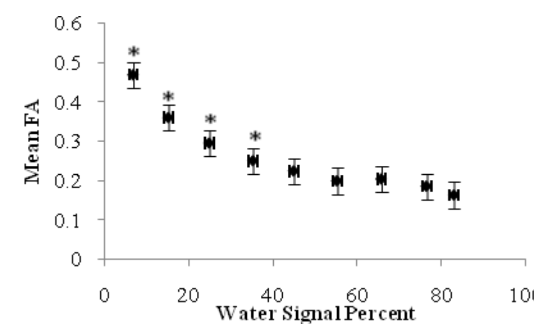

Figure 2b. The FA is plotted as a function of the water signal percentage. Error bars represent the SE. *p<0.05 for FA *vs*. FA at 80-90%.

Conclusions

The inclusion of fat into regions of interest purported to represent skeletal muscle causes the apparent water diffusion properties to differ from those of muscle only. The effect is statistically significant for regions containing water signal percentages of <40%; below this level, the diffusion properties no longer represent those of normal muscle. This threshold should be used when using water diffusion to represent microstructural damage in muscle.

References

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