# Age Dependence of Water Diffusivity in Human Skeletal Muscle

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**Introduction:** Skeletal muscle is a highly dynamic system that undergoes morphological changes as a result of environment, lifestyle, or disease. Some of these alterations include a change in muscle mass or even muscle fiber phenotype. Aging in healthy adults has also been shown to contribute to alterations in muscle fibers[1]. Recent work by our group has shown that diffusive properties of water measured by diffusion tensor imaging (DTI) differ between adjacent muscles, and that these differences may be attributed to the overall function of the muscle[2]. We have also shown that there are gender-related differences[3]. The following study expands on the previous work by determining if water diffusivity in skeletal muscle measured by DTI is related to age or the physical characteristics (height, weight, and body mass index) of the subjects.

**Methods and Materials:** *Subjects:* Thirty-eight untrained subjects were separated into three age groups: 27-39 (young, n=17), 42-59 (middle, n=10), and 60-67 (aged, n=11) years of age. Prior to the MRI examination, subjects provided their height and weight. Body mass index (BMI) was determined from the expression height/weight$^2$ (m/kg$^2$).

*MRI Experiment:* All MRI scans were performed with the subjects lying supine, feet first in a 1.5 T full-body scanner (Siemens Sonata, Erlangen, Germany). A standard extremity coil was used to scan the calf region of each subject's left leg. $T_2$-weighted images were acquired using a single-shot spin-echo EPI sequence with the following parameters: repetition time/echo time = 2000/95 ms, field of view (FOV) = 18x13.5 cm, matrix size = 128x96, slice thickness = 6 mm, and number of averages = 16. Diffusion gradients were applied along six directions with a b value of 400 s-mm$^{-2}$. In addition, a $T_2$-weighted image, used for calculating the diffusion tensor, was acquired with a b value of 0 s-mm$^{-2}$. A single slice was acquired approximately at the thickest cross-sectional area of the calf. To specify the regions of interest (ROI) for the individual muscles, a high contrast $T_1$-weighted FLASH sequence was used with the following parameters: repetition time/echo time = 165/4.5 ms, number of averages = 2, and the same FOV and matrix size as the DTI sequence.

*Data Analysis:* The images were processed and the diffusion tensor was calculated as described in Basser and Pierpaoli, [4] for each pixel. Using the FLASH image, ROI's were specified for four different muscle groups: the soleus (SOL), lateral gastrocnemius (LG), medial gastrocnemius (MG), and anterior tibialis (AT). For each ROI, six calculations were made: three eigenvalues of the diffusion tensor ($\lambda_1 \geq \lambda_2 \geq \lambda_3$), the trace of the diffusion tensor Tr(**D**), the ellipsoid eccentricity *e*, and the fractional anisotropy FA. Statistical differences between groups for acquired parameters were assessed using an ANOVA. Pearson correlations were performed to determine the relationship between the DTI parameters with age, height, weight, and BMI. P<0.05 denoted statistical significance. Data are shown as mean ± standard error of the mean.

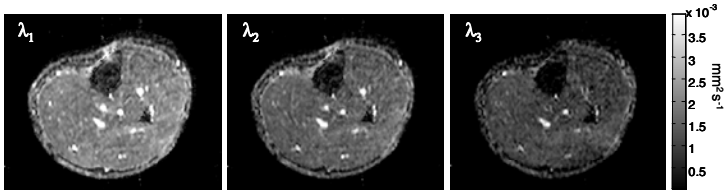


Figure 1: Principal ($\lambda_1$), second ($\lambda_2$), and third ($\lambda_3$) eigenvalue maps of the calf of a young subject.

**Results:** As presented in Figure 1, there are three discrete eigenvalues in skeletal muscle. These eigenvalues were found to be sensitive to the age of the subjects (Figure 2). Age-related differences extended to the trace of the diffusion tensor and the anisotropic parameters. Significant variation between the young and the two older groups were observed for all muscles, except AT which was only significantly different in the third eigenvalue. AT was also the only muscle group whose eigenvalues were smaller in the young group than in the older groups. Significant linear relationships were observed between some of the DTI parameters and age, but not with height, weight, or BMI. Figure 3 illustrates the strong dependence of the principal eigenvalue on age in MG. The fit generated an $R^2$=0.448 (P<0.01), and only one individual was beyond a confidence interval of 95%.

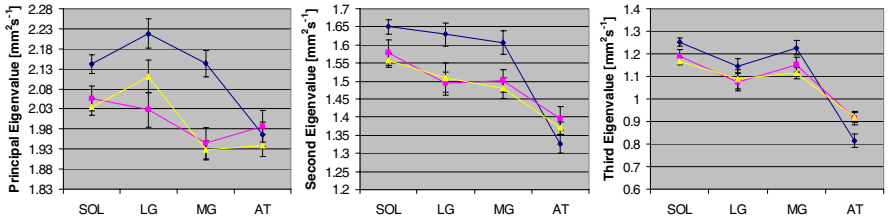


Figure 2: Principal, second, and third eigenvalues of the SOL, LG, MG, and AT in young (blue), middle (pink), and aged (yellow) subjects.

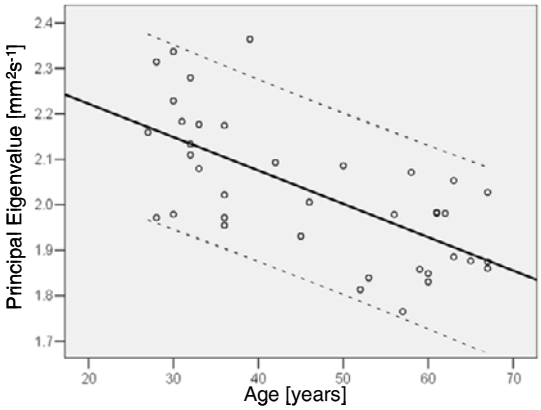


Figure 3: Linear regression of the principal eigenvalue of MG with age. Solid line represents best fit and dashed lines signify the 95% confidence interval.

**Discussion:** The present study clearly demonstrates that water diffusivity, measured by DTI, within skeletal muscle is sensitive to age. In general, results from AT were similar between young and older subjects, whereas the large plantar flexor muscles (SOL, LG, and MG) in young subjects were different from older subjects. Correlation analysis of the data suggested a strong relationship between the DTI acquired parameters and age. These observations may be a result of physical inactivity of the older subjects or the natural aging process in skeletal muscle. Nevertheless, we postulate that DTI may be capable of monitoring muscle health and patient wellness by measuring structural alterations in skeletal muscle as it adapts to changing patient condition.

**References:**

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