Age Related Changes in Diffusion Tensor Indices in the Medial and Lateral Gastrocnemius.

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Target Audience: MSK Radiologists (focus on aging, sarcopenia), Physicists, Graduate Students (focus on image analysis/ Diffusion tensor analysis)

Purpose: Age related changes in muscle alter both fiber architecture (fiber lengths and pennation angles) as well the microstructure (fiber type, diameter, fibrosis). Diffusion tensor imaging allows the mapping of fiber architecture as well as the microstructure through the DT indices. To investigate age related changes in diffusion tensor indices (eigenvalues and FA) of the medial and lateral gastrocnemius (MG and LG).

Methods: Five young (32 ± 7 yrs) and five senior (83 ± 3 yrs) Japanese women were recruited with informed consent; participants were free of internal or orthopedic disease. DWI were acquired on a 3 T GE scanner using a fat suppressed single shot EPI sequence without dual 180º pulses. Thirty-two non-collinear gradient directions with a b-factor of 400s/mm^2 were used; imaging parameters were (TE)/ (TR): 49 ms/4000 ms, 4averages. The FOV, slice thickness/gap, and matrix were 240 × 240 mm2, 5 mm/0 mm, and 80 × 80 respectively. A custom built coil with a large field of view was used to image approximately 22 cm of the lower leg without moving the subject or coil; the intent was to cover the medial and lateral gastrocnemius muscles from their origin to insertion in a single acquisition. Diffusion weighted image volumes were registered to the baseline image to correct for eddy current and motion related artifacts. The baseline and diffusion weighted images were then denoised using a Rician linear minimum mean square error (LMMSE) estimator (3DSlicer, //wiki.slicer.org). The tensor was calculated from the denoised data followed by correction for susceptibility based distortion artifacts present in the EPI-based diffusion dataset (3D Slicer). We compared three methods of evaluating DTI indices: ROI based (regional and global), histogram based, and tract based. The regional and global analysis of the eigenvalues and fractional anisotropy was performed in two ways: (i) the entire muscle (MG or LG) was chosen for analysis with manual contours of the muscles generated from the matched reference images. (ii) ROIs in the muscle compartments (manual contour of the whole muscle cross section) were defined in slices located at specified distances from the insertion (25%, 50% and 75% of total muscle length). The ROIs were not corrected for non-muscle voxels. The second method is similar to whole muscle ROI analysis but was based on editing the histogram of the ADC values for each muscle (whole volume) using the information of subject specific % connective tissue and % fat calculated from customized image sequences. This editing utilizes the fact that the ADC of voxels containing fat and connective tissue is close to zero (as the signal in these voxels at baseline is close to the noise level). Voxels corresponding to the lowest ADC values (cutoff determined by the subject's % fat and % connective tissue voxels) were flagged and excluded from the DTI indices analysis. The last method calculated the DTI indices for select fibers that originated from the distal and middle regions. Values of the DTI indices were reported as the average of all voxels in the selected fiber tracts. No voxels were excluded from the average as it was presumed that all voxels on a track belonged to muscle (based on the tracking criteria).

Results : The three methods (ROI, Histogram, and Tract Based) provided internally consistent measures of the DTI indices (Table 1). Significant difference ($p<0.05$) between the young and old cohort are highlighted in yellow. Table 1 shows that, for both the MG and LG, the three eigenvalues increased with age while FA showed a small but not significant increase. The changes in the LG were smaller than those in the MG. The largest % increase with age was in λ1 (MG and LG). The histogram method proved most stable as it leveraged the statistics of a large number of voxels while enabling flagging and deletion of connective tissue and fat voxels.

MG	Young		Old		**LG**	Young		Old	
ROI	Mean	SD	Mean	SD	*ROI*	Mean	SD	Mean	SD
FA	0.2340	0.0207	0.2380	0.0444	FA	0.2520	0.0311	0.2840	0.0783
L1	0.0018	0.0001	0.0020	0.0001	L1	0.0018	0.0001	0.0020	0.0001
L2	0.0013	0.0001	0.0014	0.0001	L2	0.0013	0.0001	0.0014	0.0001
L3	0.0011	0.0001	0.0013	0.0001	L3	0.0011	0.0001	0.0012	0.0002
Histogram					*Histogram*				
FA	0.2527	0.0785	0.2813	0.1004	FA	0.2378	0.0617	0.2419	0.0707
L1	0.0017	0.0004	0.0022	0.0005	L1	0.0018	0.0003	0.0021	0.0003
L2	0.0013	0.0003	0.0015	0.0003	L2	0.0014	0.0002	0.0015	0.0003
L3	0.0011	0.0002	0.0012	0.0003	L3	0.0012	0.0002	0.0013	0.0003
Tract Based					*Tract Based*				
FA	0.2065	0.0432	0.2096	0.0448	FA	0.2902	0.0523	0.3125	0.0621
L1	0.0017	0.0002	0.0020	0.0003	L1	0.0019	0.0002	0.0020	0.0003
L2	0.0013	0.0002	0.0016	0.0003	L2	0.0013	0.0003	0.0013	0.0003
L3	0.0011	0.0002	0.0014	0.0002	L3	0.0010	0.0003	0.0011	0.0003

Table 1: The DTI indices FA: Fractional anisotropy, L1: lead eigenvalue, L2: secondary eigenvalue and L3: tertiary eigenvalue. Eigenvalues are in mm^2/sec. DTI indices are listed for the three proposed methods, two muscles (MG and LG) and two cohorts (young/old)

Discussion and Conclusions: Tract based analysis of diffusion indices provides anatomically relevant measures as opposed to ROI or whole muscle analysis. However, as tracking is challenging and very sensitive to image quality alternate methods may be more viable for routine acquisitions. The limitation of the ROI method was that it was difficult to exclude non-muscle voxels due to the lower resolution of the DTI data and residual (even though small after corrections) mismatch between the structural high res imaging and DTI. The histogram method allows exclusion of non-muscle voxels based on knowledge of DTI values for the different tissues and is a robust alternate method to the tract based analysis.

Histological studies on humans and rodent models enables one to infer that the following changes occur at the microstructural level with aging: loss of fiber, selective atrophy of type II fibers which have larger diameters, hypertrophy of all fibers, increase in the asymmetry of muscle fiber cross-section along with an increase in fibrosis (connective tissue) [1]. The DTI model proposed here to explain the observed age related changes is an extension of earlier muscle model of diffusion [2] and has the following factors that affect the DTI indices: decreasing fiber diameters and muscle fiber fraction (increasing extracellular tissue). λ1 is not affected by changes in fiber length or diameter. However, the increasing contribution of the more freely diffusing extracellular tissue contributes to an overall increase in λ1. Decreasing fiber diameters will cause reductions in λ3 and possibly, λ2. Further, this reduction is mitigated by the increasing contribution from the extracellular tissue. This also explains why the effect of aging is higher in λ1 while reduced in the other two eigenvalues. Further, the fact that λ1 has the largest increase results in a greater asymmetry of diffusion and is reflected in the small increase in FA values. DTI combined with modeling can thus lead to a better understanding of the microstructural/compositional muscle changes with age.

References

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