Using Diffusion-Tensor (DT-) MRI Calculated Fiber Orientation To Improve the Quantification of EMCLs and IMCLs.

Theodore F Towse[1,2], Amanda KW Buck[1], Jared A Godar[3], and Bruce M Damon[1,4]

[1]Radiology, Vanderbilt University, Nashville, TN, United States, [2]Institute of Imaging Science, Nashville, TN, United States, [3]Molecular Physiology and Biophysics, Vanderbilt University, Nashville, TN, United States, [4]Institute of Imaging Science

Introduction: Lipid in skeletal muscle occurs in two distinct pools. Extramyocellular lipids (EMCL) are lipid strands that are oriented along the long axis of the muscle fibers, whereas intramyocellular lipids (IMCL) form spherical lipid droplets and are located in close proximity to the mitochondria, suggesting a pivotal role of these lipids in skeletal muscle metabolism. Interest in quantifying myocelluar lipid content and turnover has increased recently due to the finding of increased IMCL in insulin resistant subjects (1), suggesting a possible role in the pathogenesis of diabetes. However quantification of these lipid moieties is not trivial due to the overlap between the IMCL and EMCL peaks in the ^{1}H spectrum.

Recently, Khuu, *et al* (2) proposed modeling of the EMCL peak's chemical shift based on a fitted distribution of fiber orientations within the muscle of interest. However, fiber orientations may vary with aging (3) and following periods of muscle disuse (4). Also, if the distribution of fiber orientations with respect to B_0 could be measured by diffusion-tensor (DT-) MRI, this information could potentially be incorporated as subject-specific prior knowledge into the EMCL/IMCL peak fitting routines. The purpose of this study was to test the necessary pre-condition that the fiber orientation as represented by the first eigenvector of the DT (ε_1) is correlated with the orientation as represented by the EMCL chemical shift.

Methods: Three apparently healthy, untrained subjects (1 female) gave informed consent and participated in the study. MR images and ^{1}H spectroscopic data were acquired using an Intera Achieva 3T MR scanner (Philips Medical Systems, Best, The Netherlands). High-resolution anatomical images, using T_1-weighted, turbo-spin echo images [TR/TE 500/16 ms; 192 x 192 mm^2 field of view; 512 x 512 reconstructed matrix] were acquired mid-shank. These images were acquired for planning the spectroscopy acquisition voxels and included regions of the tibialis anterior (TA) and medial gastrocnemius (MGAS) muscles.

^{1}H-MRS spectra were acquired using an 8-channel SENSE knee coil and point-resolved spectroscopy (PRESS). The PRESS spectra [TR/TE of 2000/50 ms, 2048 points, 256 acquisitions, 16 step phase cycle] were acquired with CHESS water suppression and voxel size=[12 x 12 x 6 mm^3] were positioned over a region from either the TA, or the MGAS. Saturation bands were used to suppress signals from the marrow of the fibula and tibia and from subcutaneous fat. For quantification, 16 non-water suppressed spectra were acquired from the same voxel immediately prior to each data acquisition. Data were acquired from multiple muscle groups in two of the subjects. The PRESS voxels were placed to avoid regions containing visible blood vessels, connective tissue or subcutaneous fat. Spectroscopy data were analyzed in jMRUI v4. Data were filtered with a 5 Hz Gaussian filter and phase-corrected. Prior knowledge for chemical shift resonances was used to constrain shift assignments for creatine and IMCL. Data were normalized to the unsuppressed water signal.

DT-MRI was performed using a single-shot EPI sequence [TR/TE=4000/46 ms; b=485 s/mm^2; 192×192 mm^2 field of view; 128×128 reconstructed matrix; 15 diffusion encoding directions (6 in one subject, due to a data entry error)]. The mean signal was calculated in an 8×8 voxel region of interest (ROI) corresponding to the PRESS voxel and was used to solve the diffusion tensor, **D**. **D** was diagonalized, and ε_1 was used to represent the mean fiber orientation with respect to B_0 (θ). Also, **D** was calculated in each voxel of the ROI, and the standard deviation (SD) of all of the 64 individual voxels' θ was used to represent heterogeneity in fiber orientation. ε_1 was used to calculate the theoretical chemical shift of the EMCL peak from the IMCL peak by assuming that the chemical shift ranges from +.26 ppm (for fibers aligned parallel to B_0) to -.13 ppm (for fibers aligned perpendicular to B_0), according to a $(3\cos^2(\theta) - 1)$ dependence.

Statistical analysis included a comparison of the mean values for θ determined from DT-MRI and the EMCL peak (θ_{DTMRI} and θ_{EMCL}, respectively) and linear regression/correlation analysis of θ_{DTMRI} vs. θ_{EMCL} and of the line-width of the EMCL peak at half-maximum amplitude ($FWHM_{EMCL}$) vs. the SD of θ_{DTMRI}.

Results

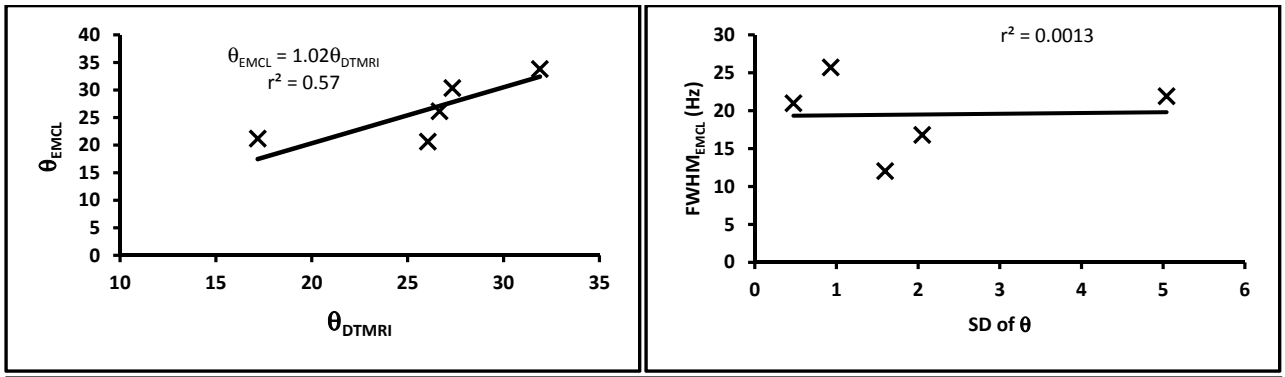

Figure 1: Panel A shows the strong, positive association between the mean fiber orientation with respect to B_0 calculated from the DT-MRI and the mean fiber orientation calculated from the chemical shift of the EMCL relative to the IMCL peak. Panel B shows the lack of association between the FWHM of the EMCL peak and the SD of the 64 individual voxels' θ as a marker of the heterogeneity in fiber orientation.

Discussion and Conclusion: As expected the mean fiber orientation calculated from the DT-MR images was correlated ($r^2 = 0.57$) with the fiber orientation calculated from the chemical shift of EMCL relative to IMCL. Furthermore the mean values for θ determined from DT-MRI and the EMCL peak were not significantly different, p=0.38 paired t-test. Somewhat surprisingly however the FWHM of the EMCL peak was not related to the dispersion of θ calculated from the DT-MRI. This may have been due to significant B_0 inhomogeneities and can potentially be resolved using more sophisticated shimming techniques. Information regarding fiber orientation and (with improved shimming algorithms) the dispersion of the fiber orientation may be useful prior information for quantifying EMCL and IMCL content in different muscle groups in a subject-specific manner.

References: 1. Machann *et al* Diabetes 48:1113,1999. 2. Khuu *et al* Mag Reson Med 61:16,2009. 3. Narici *et al* J Appl Physiol 95:2229, 2003. 4. Seynnes *et al* Acta Phys Scand 193:265, 2008.