Quantitative Assessment of Microstructure Properties of Human Corpus Callosum using Parametric T1 and Myelin imaging

Byeong-Yeul Lee[1], Xiao-Hong Zhu[1], Xiufeng Li[1], and Wei Chen[1]

[1]*Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, Minnesota, United States*

Introduction The corpus callosum (CC) facilitates the largest and intense neural pathways connecting two cerebral hemispheres in mammals, and it contains numerous intra- and inter-hemispheric myelinated axonal projections. The major function of the CC is to transfer perceptual, motor, cognitive, learned, and voluntary information and cooperate them between the two hemispheres of the brain. Thus, accurate information of callosal microstructures such as fiber composition (density and diameter) is of upmost importance to understand its functional and anatomical connectivity to cortical areas. To date, diffusion tensor MRI (DTI) has provided information regarding major orientation of fiber tracks of CC, and their structural connections with processing areas in the cortex. However, there are no characteristic *in vivo* biomarkers by which callosal microstructures and functional callosal-subdivisions can be quantitatively identified due to extremely complicated white matter structures; this impedes understanding on microstructure and tissue properties of CC. We hypothesized that the parametric T_1 measure could be sensitive to the CC microstructure and its change associated with the fiber diameter size; and it should be logically correlated to the CC myelin content mapped by T_1/T_2 ratio image. To test this hypothesis, we incorporated three imaging techniques in this study: T_1 mapping, myelin content mapping and collosal parcellation mapping for differentiating and correlating the fiber size and myelin content in the healthy human CC.

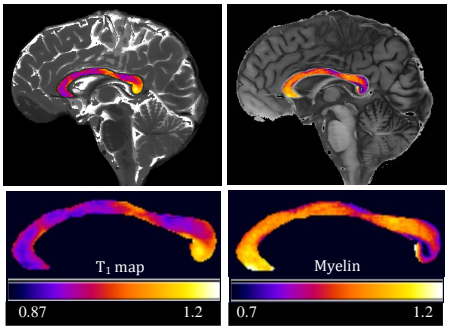

Figure 1. T_1 maps (left panels) and myelin (T_1w/T_2w) maps (right panels) acquired from a representative subject brain at 7T.

Methods: Eight subjects (6 male and 2 female, 30±10 years old) participated in this study and provided written informed consent approved by the University of Minnesota IRB committee. All MR studies were performed at 7.0T/90cm whole body MRI scanner (Siemens) with an 32-channel transmit-receive head coil (Nova Medical). High-resolution 3D-MPRAGE T_1 images were acquired (TR/TE/TI= 3000ms/2.4ms/1500ms, FA= 5°, pixel size = 0.5x0.5x1 mm^3) for guiding the selection of a single mid-sagittal CC image slice for acquiring T_1 image. ***T_1 mapping:*** The parametric T_1 image (1 mm slice thickness) across the selected mid-sagittal CC slice was measured using the single-shot fast spin-echo image sequence[1] with seven varied inversion recovery times (0.1, 0.15, 0.3, 0.5, 0.8, 1.2 and 1.6 s) plus one dummy scan for obtaining a T_2-weighted image. A high in-plane resolution (500x500μm^2) was applied to reduce the partial volume effect from surrounding ventricles. To minimize B_1^+ inhomogeneity in the corpus callosum regions, the RF pulse reference voltage was adjusted using 2D single slice actual flip angle method [2]. To correct the head movement of subjects, all echo images (2^{nd} to 7^{th}) were co-registered to the 1^{st} echo image using FSL's FLIRT with 6 parameters (rigid body) and the mutual information cost function. All images were acquired within 30 minutes (TR/TE = 6s/16ms, parallel imaging acceleration factor = 2). ***Myelin mapping***: The ratio of T_1-weighted and T_2-weighted MRI signal intensity (T_1w/T_2w) was used for mapping myelin contents in CC [3,4]. The ratio image was generated by using T_2w (dummy scan) and T_1w (6^{th} echo) images, and this ratio method is able to remove the B_1 inhomogeneity effect on image intensity. ***Parcellation of Corpus Callosum***: Callosal parcellation mapping technique was described in detail[5]. Briefly, after manual segmentation of mid-sagittal region of CC using MRIcro software, the extracted CC was divided into a superior (top), inferior (bottom) and medial line using Euclidean transform. Subsequently 150 equidistant surface points making up the callosal surface boundaries were calculated and callosal region was parcellated into 7 regions according to Witelson's model[6].

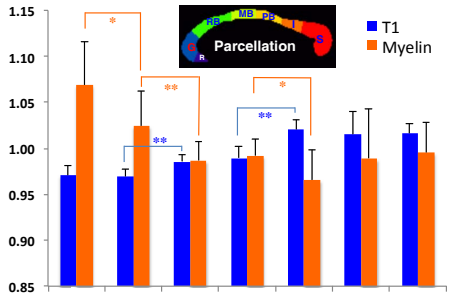

Figure 2. Normalized mean values of T_1 and myelin in the seven parcellated regions of CC from 8 subjects. R: rostrum; G: genu; RB: rostral body; AB: anterior mid-body; PB: posterior mid-body; I: isthums; S: splenium. * p <0.05, ** p < 0.005.

Normalization and Statistics: To account for the variations of individual subjects, the T_1 and myelin values were normalized based on their mean value of CC in each subject, thus, resulting in the T_1 or myelin content ratio images. A Student's t-test was applied for the statistical comparisons of the normalized T_1 and myelin ratios between adjacent regions and a p value <0.05 was considered statistically significant.

Results: Figure 1 represents a typical maps of normalized T_1 and myelin ratio within the CC from a representative subject, showing highest T_1 values at posterior mid-body (PB) and lowest T_1 values at genu (G). In contrast, the myelin content ratios were highest at genu and rostrum and lowest at PB as summarized in Fig. 2. Moreover, Fig. 2 shows that there were statistically significant changes of the normalized T_1 and myelin ratios between G and rostral body (RB), anterior mid-body (AB) and posterior mid-body (PB). Figure 3 shows a negative correlation between normalized T_1 and myelin ratios.

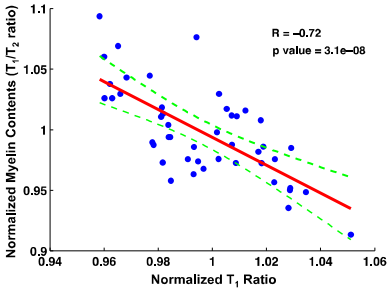

Figure 3. A linear regression curve between normalized mean T_1 myelin values of 8 subjects. R is correlation coefficient (red line) and green line indicates the 95% confidence region.

Discussion: Previous *ex vivo* post-mortem histology study[7] had identified the distinctive fiber composition (highest dense in the anterior corpus callosum and lowest dense in posterior mid-body) and fiber diameter distribution (smallest in R and G, and largest in splenium) in human CC (see Fig. 4). The CC microstructures characters and spatial patterns are strikingly consistent with the spatial T_1 and myelin distributions as imaged in the living human CC in this study. The high similarities between the MRI and histology results suggest that T_1 values of CC have a positive correlation with fiber (or axon) diameter and myelin values of CC possibly reflect the myelin densities, thus, leading to an approximately inverse relationship between fiber size and myelin density. Furthermore, we also observed that T_1 and myelin distribution within the same subdivision of CC are highly inhomogeneous, for instance, the inferior splenium region has lower T_1 values than posterior splenium as demonstrated in Fig. 1. These findings are supported by a previous diffusion tensor MRI study[9], which indicate distinctive corpus callosal projections to different cortical regions, and also suggest the need for fine parcellation.

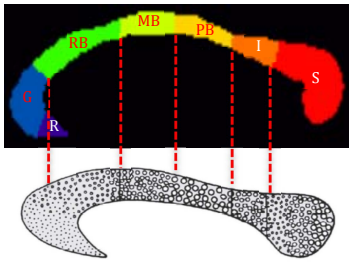

Figure 4. Callosal parcellation map (top panel) from the same subject shown in Fig. 1, and the fiber composition of the human corpus callosum[8] (low panel) for comparison.

Conclusion: In this study, we demonstrated the utility of complementary parametric T_1 and myelin imaging approaches to quantitatively assess the fiber microstructure of human corpus callosum. This hybrid imaging approach should provide a robust and useful imaging tool for detection of fiber abnormality in the human white matter.

Acknowledgement: NIH R01: NS057560, NS041262, NS070839, S10RR026783, P41 EB015894, and P30 NS057091.

References: [1] de Bazelaire *et al*., *Radiology* 2004;230:625-659; [2] Yarhykh *et al*., *MRM* 2007;57:192-200; [3] Sigalovsky *et al*., *NueroImage* 2006;32:1524-1537; [4] Glasser *et al*., *J of Neuroscience* 2011;31:11597-11616; [5] Luders *et al*., *NeuroImage* 2007; 37:1457-1464; [6] Witelson *et al*., *Brain* 1989;112:799-835; [7] Aboititz *et al*., Brain Research, 1992;598:143-153; [8] Aboitiz and Montiel, *Braz J Med Biol Res*, 2003;36:409- 420; [9] Park *et al*., HBM, 2008;29:503-516.