Functional Correlates of Corpus Callosum Thickness in Multiple Sclerosis

C. Sander[1], M. P. Sampat[1], A. M. Berger[1], P. Hildenbrand[1], R. Bakshi[1], S. Khoury[2], H. Weiner[2], D. S. Meier[1], and C. R. Guttmann[1]

[1]Center for Neurological Imaging, Brigham and Womens Hospital, Boston, Massachusetts, United States, [2]Partners MS Center, Brigham and Womens Hospital, Boston, Massachusetts, United States

Objective: To measure the width of the corpus callosum (CC) in mid-sagittal brain MR images and assess differences between clinical subtypes of MS and correlate the average width with the functional clinical scores.

Background: Quantitative measurements of brain atrophy in multiple sclerosis (MS) patients have shown to be of significant clinical relevance. Regional atrophy of the CC depends on the type and severity of the disease. In previous work, we found that the Secondary Progressive (SP) MS patients have a significantly smaller CC than Relapsing-Remitting (RR) or Primary Progressive (PP) MS patients. Various parcellation schemes have been implemented to quantitatively compare data from patients and classify the disease progress accordingly. However, precise width measurements are essential to compare data and to draw relevant conclusions.

Methods: A set of 69 MS patients (30 RR, 19 SP, and 20 PP) was selected from the Comprehensive Longitudinal Investigation of MS at the Brigham and Women's Hospital (CLIMB) study. Callosal outlines were obtained manually from sagittal T1-weighted images and used to compute the width of the CC at all points along the boundary. Implementing a new method for calculating the width profile, the approach was to apply a Fourier parameterization [1] to the curve, describing the boundary of the CC. Each coordinate pair in the image was treated as a complex number, thus reducing the 2-D problem to 1-D. The Fourier descriptors a(u) were defined by the Discrete Fourier Transform (DFT): $a(u) = \frac{1}{N}\sum_{k=0}^{N-1} s(k)e^{-j2\pi uk/N}$ .The original boundary can be obtained by applying the inverse DFT: $s(k) = \sum_{u=0}^{N-1} a(u)e^{-j2\pi uk/N}$. Taking only the first P coefficients (P<N) for reconstruction implements an effective and robust form of shape smoothing. A Fourier parameterization with a low number of harmonics was implemented to give a smoothed boundary of the CC. Then, normal lines to the lower boundary of the parameterized curve were calculated at each reconstruction point. The matched point pairs on lower and upper half of the smooth CC boundary, resulting from the normal lines, were projected on another parameterized curve with a high number of harmonics to achieve an accurate measurement of the width. Towards the rostrum and splenium the width was measured by constructing parallel lines to the previous one (see blue colored ends in Figs. 1(b), 2(b) and Figs. 1(c), 2(c)). These vertices of the CC were defined as starting at the first point from the center at which three points form the upper boundary were connected to the same point on the lower boundary. For each reconstruction point, the width was found, with the number of reconstruction points being fixed. The algorithm generating the width profile was fully automated.
The correlation of the average CC width with the Expanded Disability Status Scale (EDSS) [2] and Ambulation Index (AI) were calculated. The correlation of the average CC width to EDSS functional sub-scores was computed. For all of these comparisons, the Spearman Correlation Coefficient was used. For each correlation coefficient a hypothesis test was performed to test whether it was significantly different from zero.

Results: Figures 1(c) and 2(c) show a width profile of the CC computed based on Fourier descriptors. The average width of the CC was 6.1736mm^2, 5.1277mm^2 and 6.1782mm^2 for the RR, SP and PP patients respectively. A two-sample t-test was used to compare each of the following pair of groups: 1) PP vs. SP, 2) PP vs. RR and 3) SP vs. RR. There was a significant difference in the average width of the CC between the SP patients and PP patients ($p = 0.002$). The average width of the SP and RR patients was also significantly different ($p < 0.001$), whereas the average width of the CC of the PP and RR patients was not significantly different. Moderate but significant correlations were observed between CC and clinical scores. The CC width showed a moderate negative correlation with EDSS and AI (Table 1). In addition, a negative correlation was found between the CC width and the sensory and cerebellar EDSS functional sub-scores (Table 1).

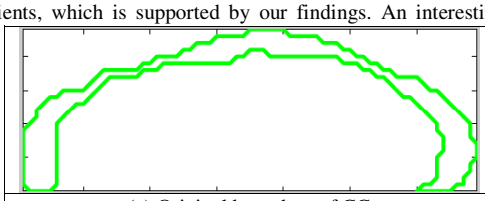
	Spearman Correlation (p-value)
1. CC & EDSS	**-0.2988 (p = 0.0126)**
2. CC & AI	**-0.2932 (p = 0.0160)**
3. CC & Pyramidal FS	-0.1961 (p = 0.1117)
4. CC & Sensory FS	**-0.3679 (p = 0.0022)**
5. CC & Cerebellar FS	**-0.4844 (p < 0.001)**
6. CC & Visual FS	-0.0485 (p = 0.6967)

Table 1: Rows 1 to 2: Correlation of average CC width and clinical scores (EDSS and AI). Rows 3 to 6: Correlation of average CC width and EDSS functional sub-scores).

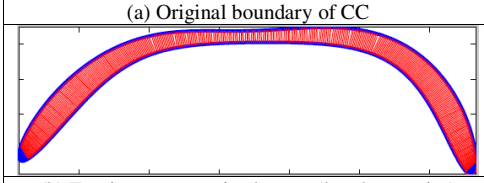
Discussion: (a) Differences in CC width in different disease sub-groups: There is a greater degree of neuro-degeneration in SPMS patients than in RRMS patients, which is supported by our findings. An interesting finding was that the CC of the PP patients appears to remain relatively preserved. This finding is in agreement with the clinical observation that in PP patients dominant involvement is spinal and cortical.

(b) Correlation with clinical scores: The CC width showed a moderate negative correlation with EDSS, AI, and the sensory and cerebellar EDSS functional sub-scores. This was an intriguing result since certain sections of the CC are associated with white matter tracts from the sensory regions. As expected, the visual functional sub-score did not correlate with CC thickness.

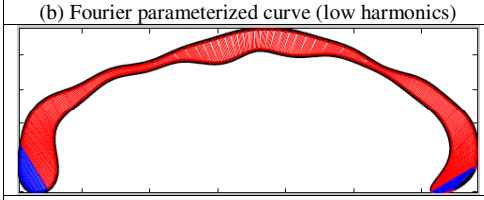
As different segments of the CC have been associated with specific functions, future work will involve looking at the correlation of the EDSS functional scores with width measurements in respective segments of the CC.



(a) Original boundary of CC

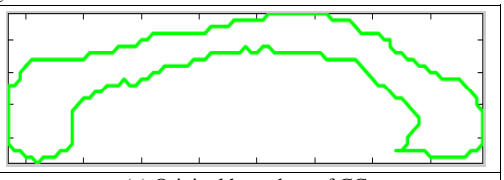


(b) Fourier parameterized curve (low harmonics)

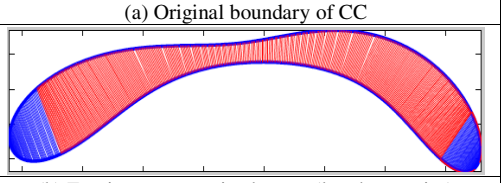


(c) Fourier parameterized curve (high harmonics)

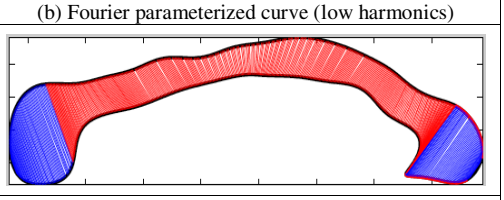
Figure 1: Corpus Callosum of SPMS patient



(a) Original boundary of CC



(b) Fourier parameterized curve (low harmonics)



(c) Fourier parameterized curve (high harmonics)

Figure 2: Corpus Callosum of RRMS patient

In Figs. 1 and 2 the red and blue lines along the boundary, measure the width of the CC at those points.

References:

1. Staib and Duncan et al. IEEE-PAMI, 1992.
2. Kurtzke, Ann Neurology, 1994.