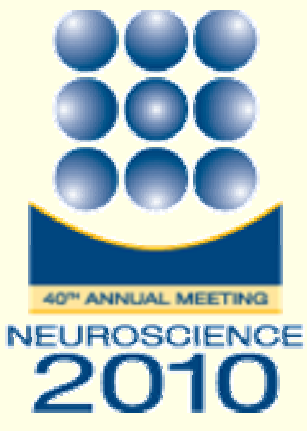


208.17 MMM8 Fully automated measurement of the human corpus callosum from MRI: Morphometry and callosal-cortical correlations



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ABSTRACT.

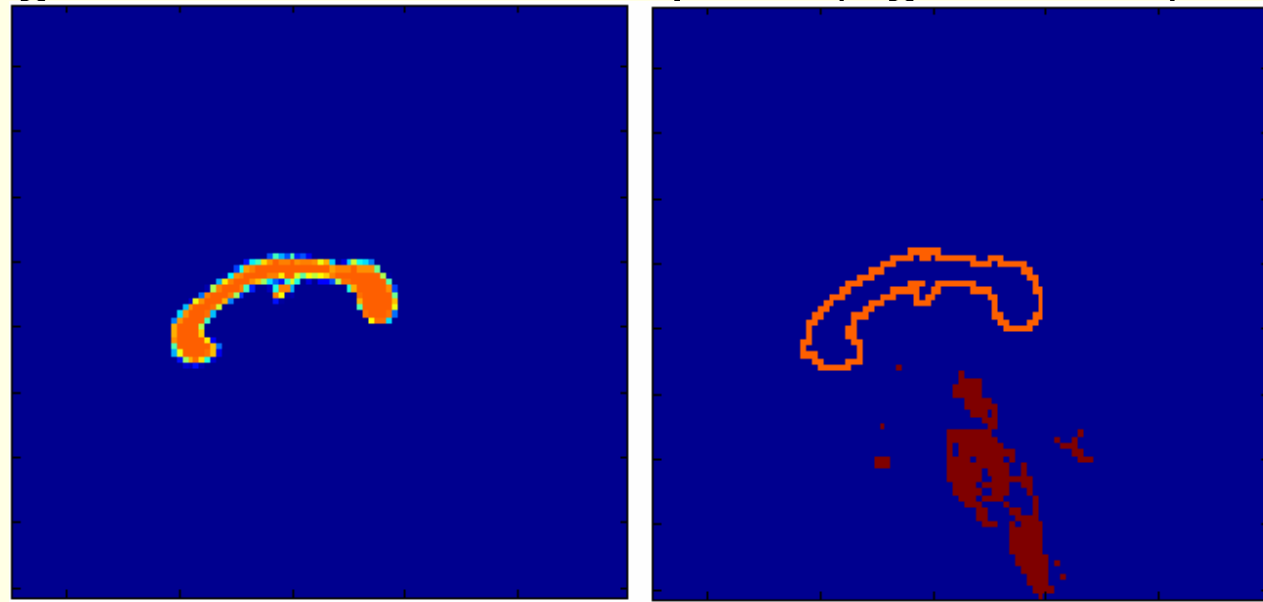
We present the open-source Matlab software package, **C8**, that measures sagittal cross-section thickness and area of the human corpus callosum from high-resolution T1 in vivo MR images. We test the method using a high-quality public image database [2] and apply C8 to a lower quality database [3].

Callosal Extraction Method

C8 quickly extracts and measures corpus callosum (CC) cross-sections by using segmented, 3D normalized brain images.

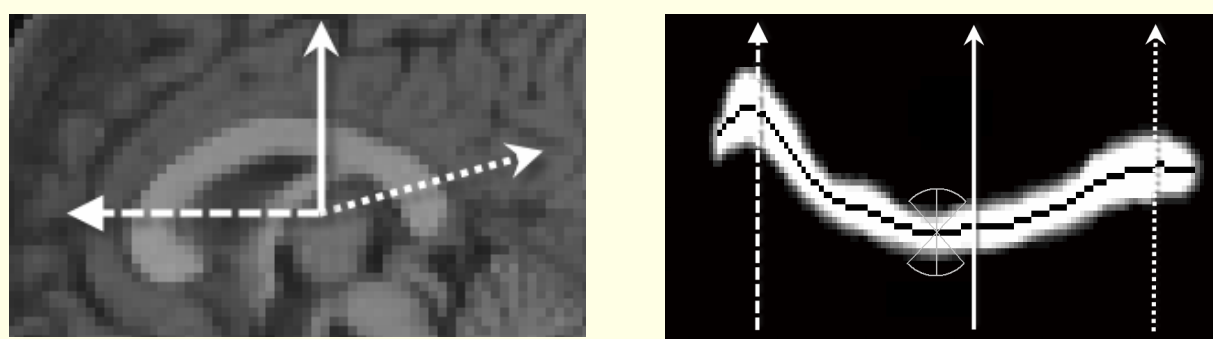


Preprocessing: High-resolution T1 anatomical images (left above) should be first processed using standard automated software (e.g. SPM, FSL, AFNI): align the T1 images to MNI space using affine transformations, segment the T1s into brain matter types to obtain white matter images, and transform the white matter (WM) segmentations into MNI space (right above).



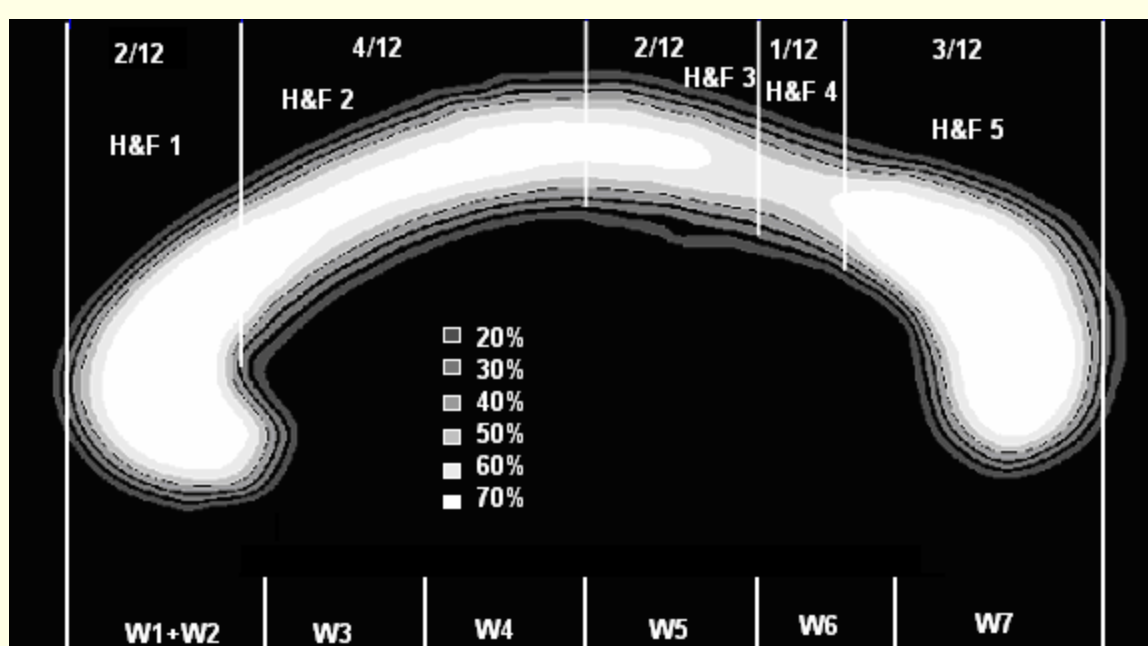
Callosum Isolation & Boundary Identification: C8 identifies the corpus callosum (CC) cluster(s) within WM, (left) usually separating the CC from most of the fornix. The CC outer boundary is identified (right) and used for partitioning below.

Thickness is computed in MNI space and in native space along an angularly spaced median line within the callosum



Quantification of callosal thickness. *Left.* The CC on the midsagittal plane with reference to a series of radial lines (three shown) emanating from a central point. *Right.* The radial lines are now oriented vertically, thus "straightening" the CC in order to define a median line and measure thickness. The median CC line (thick black) was determined as the median location of WM probabilities (white) considered vertically, and thickness was computed at each point along the median CC line using the shortest line segment crossing the CC and passing through that point (thin light gray).

Areas are computed for geometrically defined callosal compartments [1].



Partitioning of the callosum into compartments for quantification of size and tissue properties. Segmentations of the CC identified in MNI space for subjects are subdivided into five compartments along its maximal extent along the anterior-posterior axis using geometric ratios (top) according to Hofer and Frahm [1]. Percentage shadings show the probabilistic locations of the CC for control subjects and demonstrate the variability of callosal boundaries in MNI space. Bottom labels (W) show the CC partitioned according to Witelson [1].

Verification of Callosal Measurements

C8's performance is tested on the OASIS image database [2] and produces consistent, reliable callosal measurement estimates over both repeated scans and compared to manual measurements.

Study	W1+W2+W3	W4+W5	W6	W7
OASIS [2] database analysis using C8 (n=152, age: 23.2±4.2)	239 ± 39 mm ²	136 ± 30 mm ²	49 ± 14 mm ²	163 ± 3-0 mm ²
Jaencke et al., 1997 (n=54, age: 27.8 ± 5.2)	274 ± 34 mm ²	162 ± 24 mm ²	66 ± 12 mm ²	186 ± 31 mm ²
Bermudez & Zattore, 2001 (n=136, age: 24.6±4.8)	294 ± 34 mm ²	169 ± 12 mm ²	67 ± 14 mm ²	190 ± 27 mm ²
Luders et al., 2003 (n=30, age: 23.3±3.9)	254 ± 38 mm ²	149 ± 11 mm ²	57 ± 13 mm ²	191 ± 29 mm ²

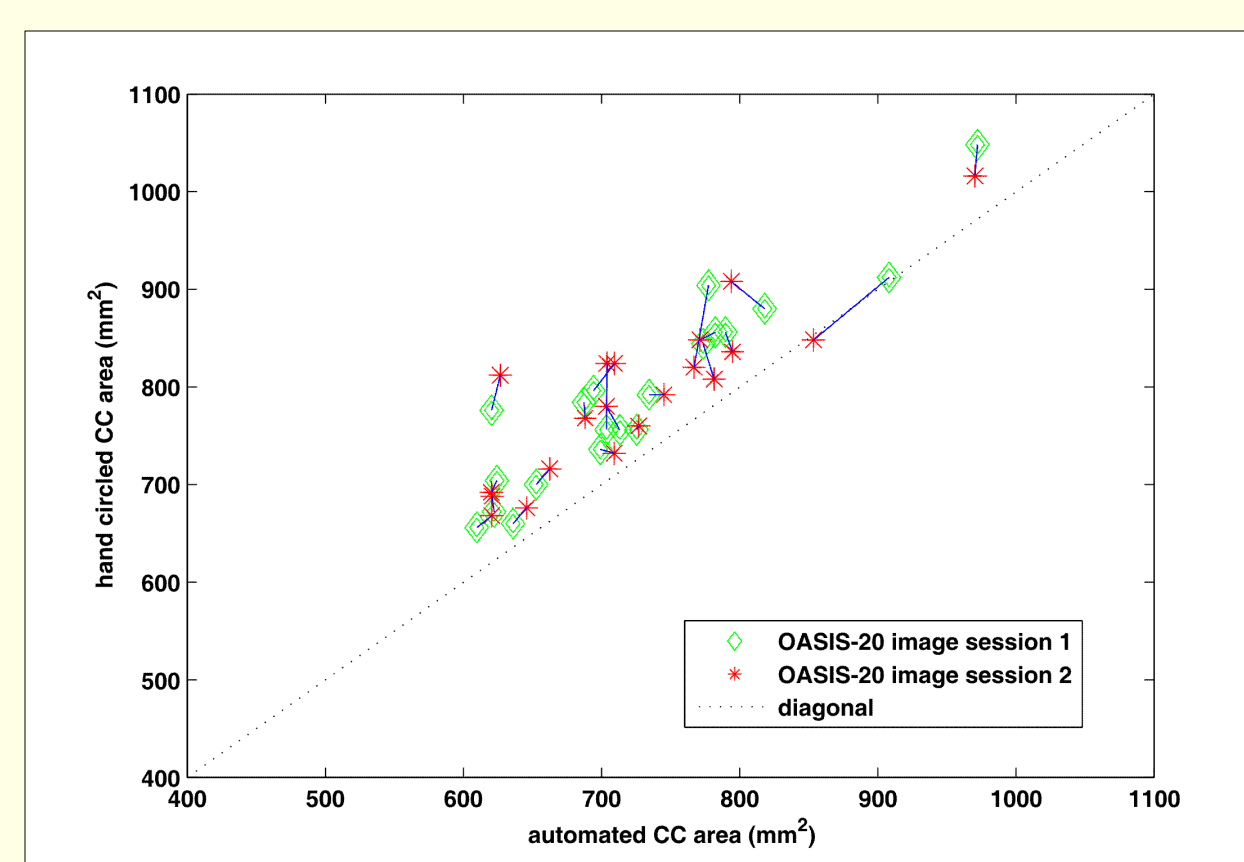
Corpus callosum area measurements (mean and standard deviations) for callosal Witelson compartments: From the OASIS anatomical image database [2] using the present method and compared to results reported in three earlier studies [5] all using manual CC delineation.

Midbody CC Thickness Measures: C8 produces thicknesses of 4.9 ± 0.8 mm for young, normal subject images in [2]. Studies in [6] show mid body thickness from 6 to 7 mm ; e.g. mean of 7.2 ± 1.9 mm in Raine et al 2003.

Our reduced values are due to our thickness definition, segmentation algorithm artifacts, and our use fractional voxel measurements.

	H&F 1	H&F 2	H&F 3	H&F 4	H&F 5
Thickness variation	3.2%	4.3%	5.8%	4.2%	3.2%
Area variation	5.1%	6.5%	7.1%	5.9%	1.5%

Repeatability: Mean absolute % difference in the mean thickness and area of the five Hofer and Frahm compartments from session 1 to session 2 for 20 subjects who underwent repeated scans in the OASIS database [2].



Scatterplot comparing manually delineated corpus callosum total cross-sectional areas (y-axis) with the present automated area analysis (x-axis) for 20 normal subjects in the OASIS database [2]. Diamonds = session 1, asterisks = session 2. Solid lines connect a single subject's 2 different sessions, while the dotted line is the area diagonal.

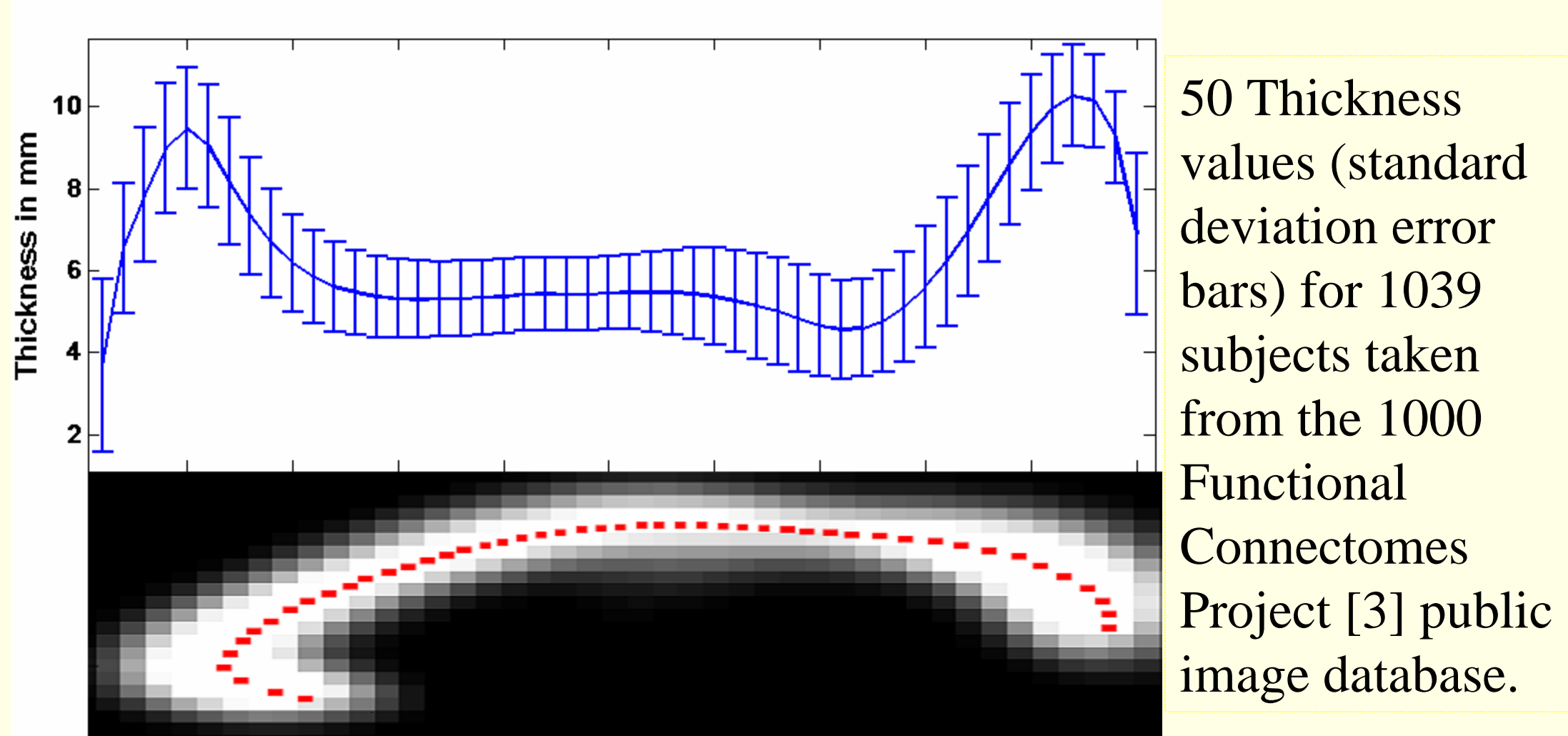
Conclusion.

C8 produces reliable estimates of mid-sagittal callosal thickness and subpartition areas that are, by design, slight underestimates of those obtained by manual delineation of MR images.

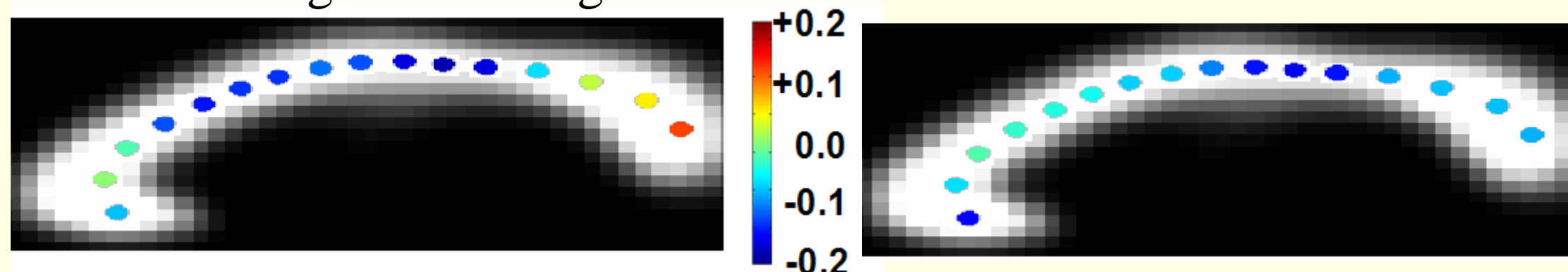
References.

- [1] Hofer & Frahm, *NeuroImage*, 32(3) 2006; Witelson, *Brain*, 112(3), 1989.
- [2] www.oasis-brains.org; Marcus et al, *J. Cog. Neuro.*, 19(9), 2007.
- [3] www.nitrc.org/projects/fcon_1000
- [4] Pannek et al, *NeuroImage*, 50, 2010. Chao et al, *HBM*, 30(10), 2009.
- [5] Jancke et al, *Cereb Cortex*, 7(1), 1997; Bermudez & Zattore, *Neuroimage*, 13(6 pt 1), 2001; Luders et al *Cereb Cortex*, 13(10), 2003.
- [6] Luders et al *Neuroreport*, 18(3), 2007; Luders et al, *Neuroimage*, 37(4), 2007; Raine et al, *Arch Gen Psych*, 60(11), 2003.

Callosal Thickness Measurements



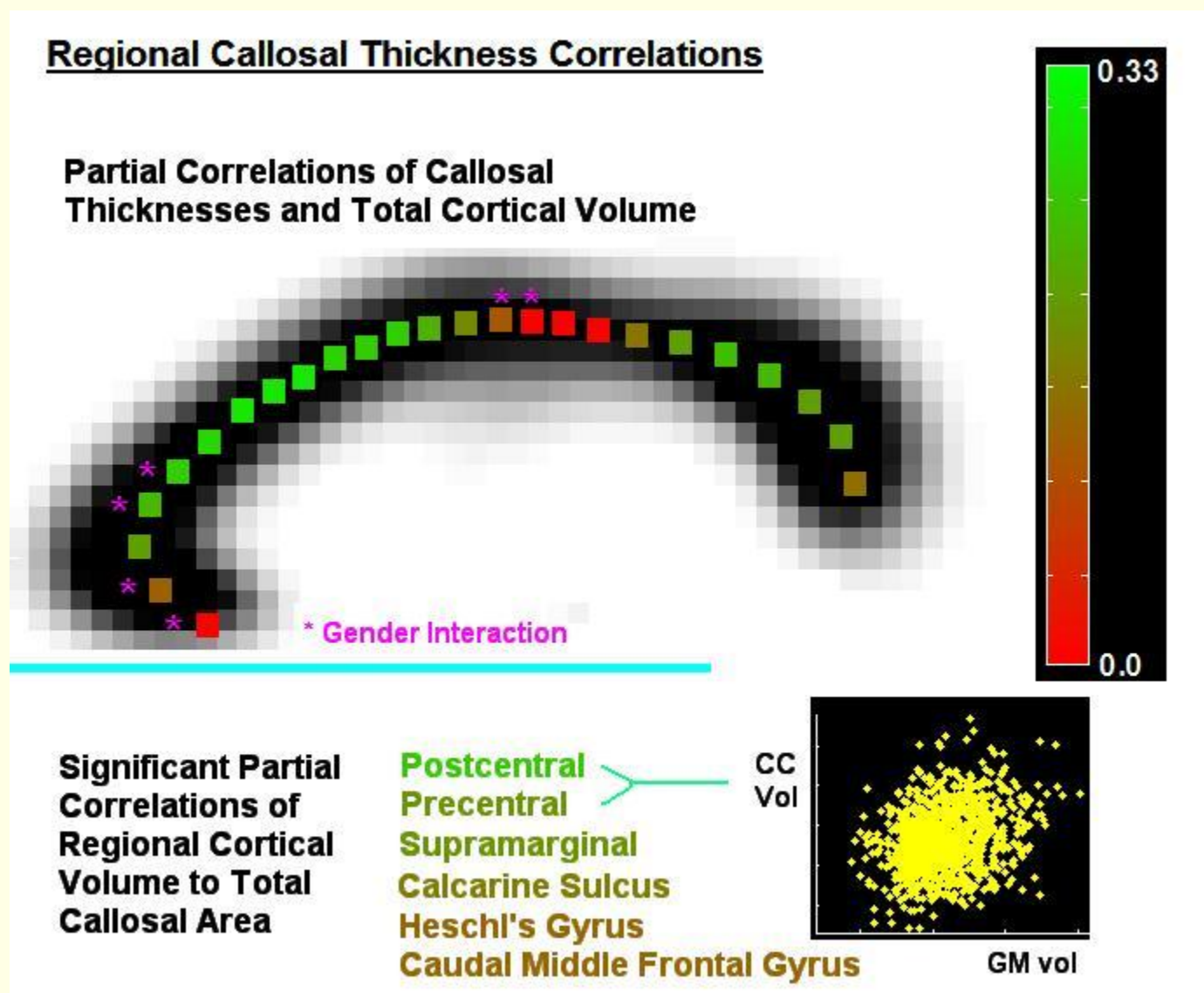
The thicknesses of the corpus callosum sagittal cross-section also correlate with gender and age.



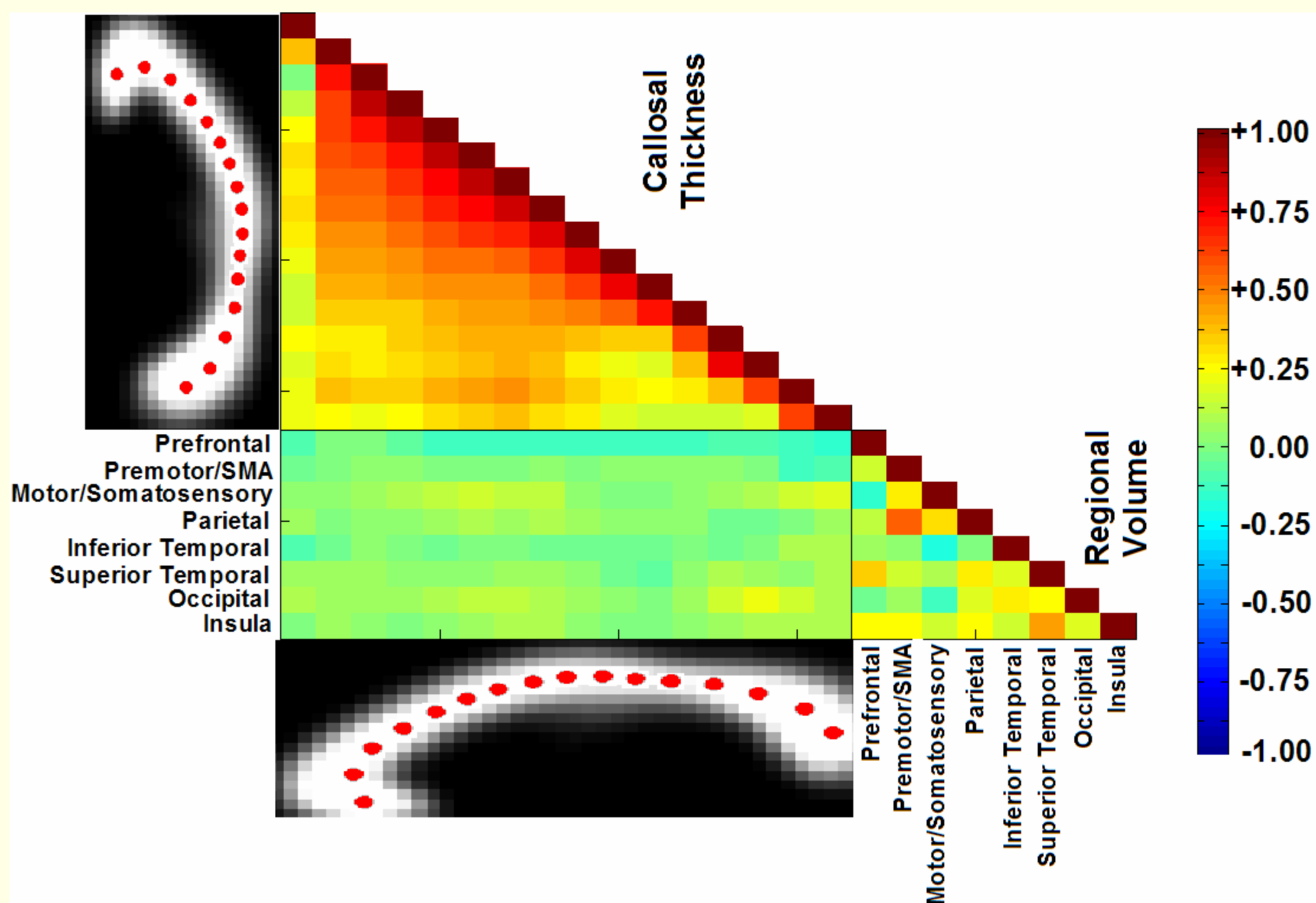
Partial Spearman correlations of regional callosal thickness with age (left) and being female (right) covarying over gender or age (respectively) and total brain GM volume. Correlations of age with CC geometric partition *areas* show the same pattern, but being female does not partially correlate with callosal *area* except in partition H&F#3.

Callosal-Cortical Correlations

We correlated callosal thicknesses with regional cortical gray matter density using an atlas of 34 cortical ROIs for 1039 subjects from the 1000 Functional Connectomes Project [3].



Global-Regional correlations: Anterior mid-body callosal thickness correlated best with total cortical gray matter (GM) volume.

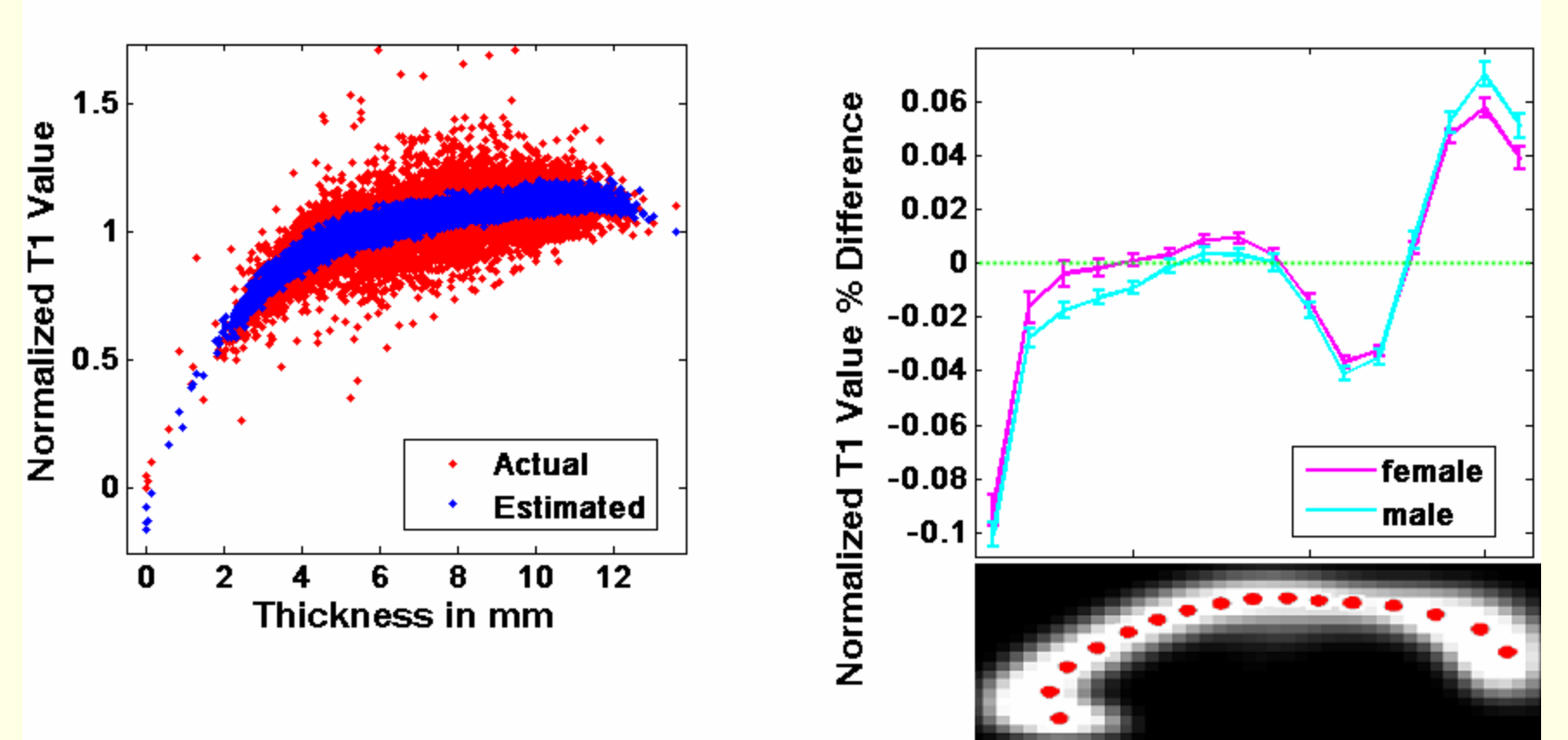


Partial Pearson correlations of regional callosal thickness and regional cortical volume covarying out age, gender, total brain GM volume, and scanning cohort membership for subjects in [3].

Cortical ROI volume/callosal thickness correlations show significant differences compared with cortical-based callosal parcellations identified using DTI tractography [4]. Splenium thicknesses are also relatively independent of other CC thicknesses.

Callosal T1 Density Measurements

C8 is able to sample other images that are coregistered to the WM segmented MNI space images. E.g. here we look at regional differences in T1 values within the callosum to see if there are regional differences in callosal myelination.

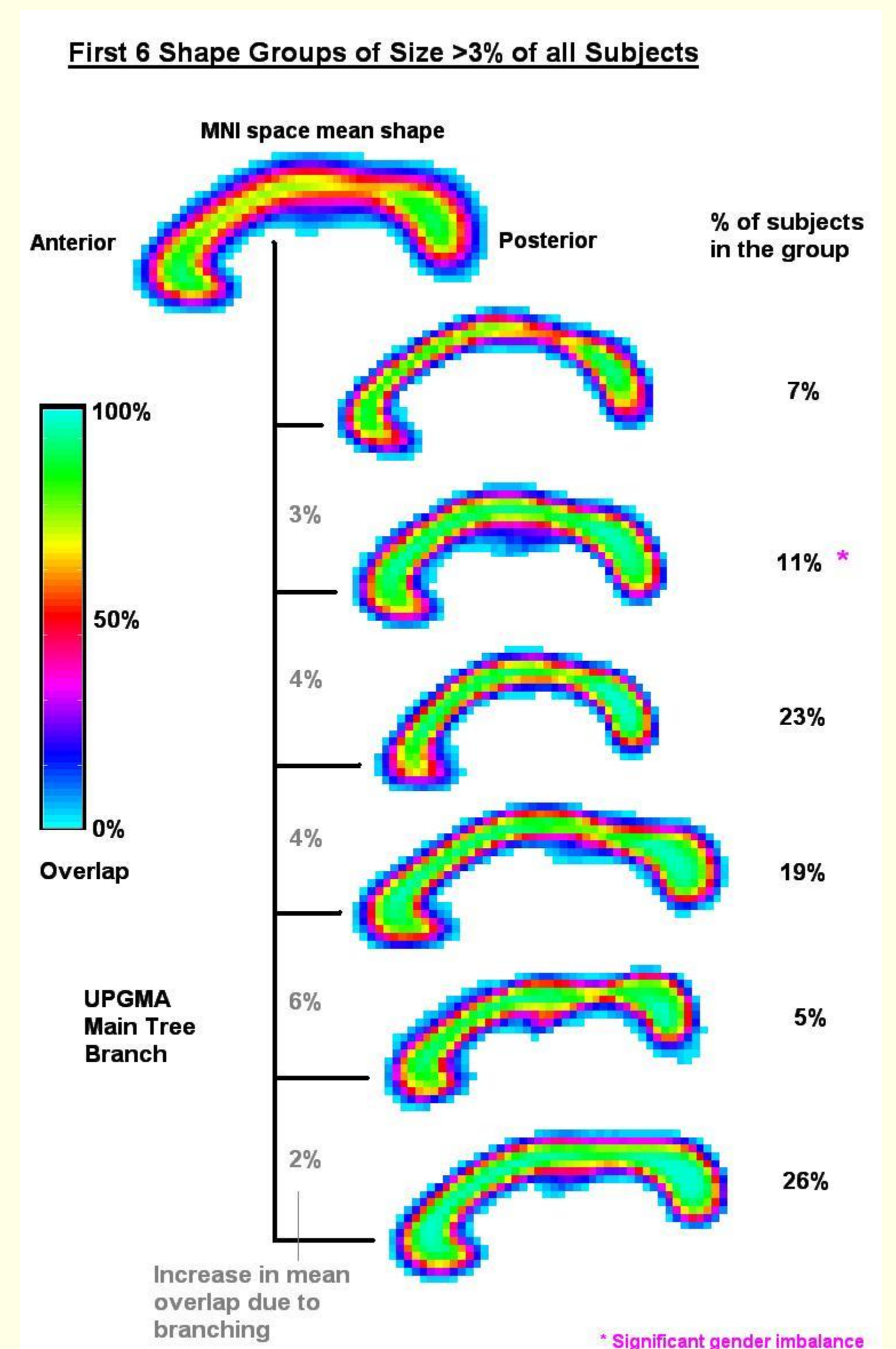


Variation in T1 values across the Corpus Callosum: T1 3D images from [3] were stripped of all linear value gradients (x,y, and z directions), and the T1 values were then sampled by C8 on the median CC line at 16 angularly-spaced locations. *Left:* Normalized T1 values (mean =1 over every subject) varied with cortical thickness (red) and were parameterized nicely using a quartic polynomial function of thickness plus age, gender, whole brain GM volume and cohort membership (blue). *Right:* Plot with standard errors of the difference between actual T1 values and predicted T1 values.

Splenium T1 values are quite high while inferior genu and posterior mid-body are lower than average. End point T1 values are likely low due to 3 sides worth of partial voluming.

Callosal Shape Analysis

We used 1039 T1 anatomical images from the 1000 Functional Connectomes Project [3] to evaluate the incidence of different callosal shapes and group them into clusters.



Shape Analysis: Callosal shapes were analyzed by extracting cross-section pairs and applying translation, polar coordinate, and joint y/z scale transformations to achieve maximal pair overlap. The resulting overlap similarity matrix was used to form groups via both k-means and agglomerative (e.g. UPGMA) clustering. Similar callosal shape groups resulted using both methods.