# Cortical Thickness Measurements with Buried Sulcus Recovery from MRI: An Application to Dementia

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# Introduction

Cortical thickness is a valuable clinical metric in studying neurodegenerative diseases. Thickness is usually defined using *some* distance measure between *corresponding* points on the white matter (WM) -- gray matter (GM) interface and the GM – cerebrospinal fluid (CSF) boundary. We introduce a methodology where the correspondence is defined by registering the WM and GM probability map images and thickness is defined as the Euclidean distance between corresponding pairs of points. Using diffeomorphic registration [1] to define correspondence allows us to recover deep sulci that are often mislabeled as GM due to segmentation errors [2]. We applied this methodology to a longitudinal study of thickness changes in a patient cohort diagnosed with frontotemporal dementia (FTD) spectrum disorders.

### Methods

# Image Acquisition

Twenty elderly individuals diagnosed with FTD spectrum disorders were imaged at two time points each. Patients were identified clinically in the Department of Neurology at the University of Pennsylvania School of Medicine, and clinical research diagnosis was established using a consensus mechanism where two independent investigators review the clinical chart relative to a modification of published criterion. Rare disagreements were resolved through discussion. High-resolution T1 structural data for each patient were acquired using a Siemens 3.0 T MRI scanner with TR (repetition time) = 1620 ms, TE (echo time) = 3 s, slice thickness = 1 mm, in-plane resolution =  $0.9766 \times 0.9766$  mm and matrix size =  $256 \times 256 \times 192$ . The same protocol was used at baseline (younger) and later (older) time points. *Thickness Computation* 

T1 image volumes were segmented into WM, GM and CSF probability map images using an adaptation of the FAST [3] algorithm. The WM probability map image was then mapped to the combined WM and GM probability map image (Figure 1 - left). Thickness at every WM surface point is then defined as the norm of the deformation field given by the mapping between the given point and its corresponding GM surface point. Thickness values are propagated to the GM volume along the deformation path given by the diffeomorphic mapping, thus generating a volumetric thickness map in the GM. An example is shown in Figure 1 (right).





## Longitudinal Study

Thickness maps for each subject for both earlier and later time points were warped into a template space for statistical analysis. A population-specific template was used for this purpose. Mapping between individual subject and template space was obtained by deformable registration [1]. A labeled anatomical atlas was also mapped to the template space that provides Brodmann area labels. Pairwise t-tests between thickness maps at earlier and later time points were carried out across the patient population in the template space.

## Results

Areas of significant longitudinal decrease in thickness across the patient population include language areas in the temporal lobe and areas in frontal and parietal cortices (Figure 2 -- right). Average decrease in thickness in Brodmann regions was also calculated. The diffeomorphic maps used to define corresponding points on WM and GM surfaces are topology preserving, thus preventing opposing banks of sulci from touching each other, often recovering buried sulci (Figure 2 - left (c)).



Figure 2. Left: Thickness maps in template space for a subject at earlier (a) and later (b) time point. (c) Top: Segmentation of the area inside the red box in Figure 1 (right) (a). The sulcus is mislabeled as GM. Bottom: The deformation fields emanating from WM surface points showing recovery of the sulcal boundary. Right: T-statistic showing Brodmann regions with significant decrease in thickness overlaid on the rendered template brain. False Discovery Rate of 0.05 was used to correct for multiple comparisons.

#### References

1) B.B. Avants et al., MedIA, p. 397, 2006. 2) S.R. Das, et al. MMBIA, 2007. 3) Zhang et al., IEEE TMI, p. 45, 2001.