A COMPARATIVE STUDY OF VOXEL AND SURFACE BASED CORTICAL THICKNESS METHODS IN FRONTO-TEMPORAL DEMENTIA

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Cortical thickness estimation (CTE) performed in-vivo via magnetic resonance imaging is an important technique for the diagnosis and understanding of the progression of neurodegenerative diseases. Currently, two different computational paradigms exist, with methods generally classified as either surface or voxel-based. This paper provides a much needed comparison of the surface-based method FreeSurfer with two voxel-based methods using clinical data. We demonstrate that voxel-based methods can detect similar patterns of group-wise differences as well as FreeSurfer, where the lack of deformable model constraints may provide more sensitivity but with a resulting trade-off in reproducibility.

Comparison Of 3 Methods of Cortical Thickness Estimation

$$\nabla^2 \psi = \frac{\partial^2 \psi}{\partial x^2} + \frac{\partial^2 \psi}{\partial y^2} + \frac{\partial^2 \psi}{\partial z^2} = 0$$
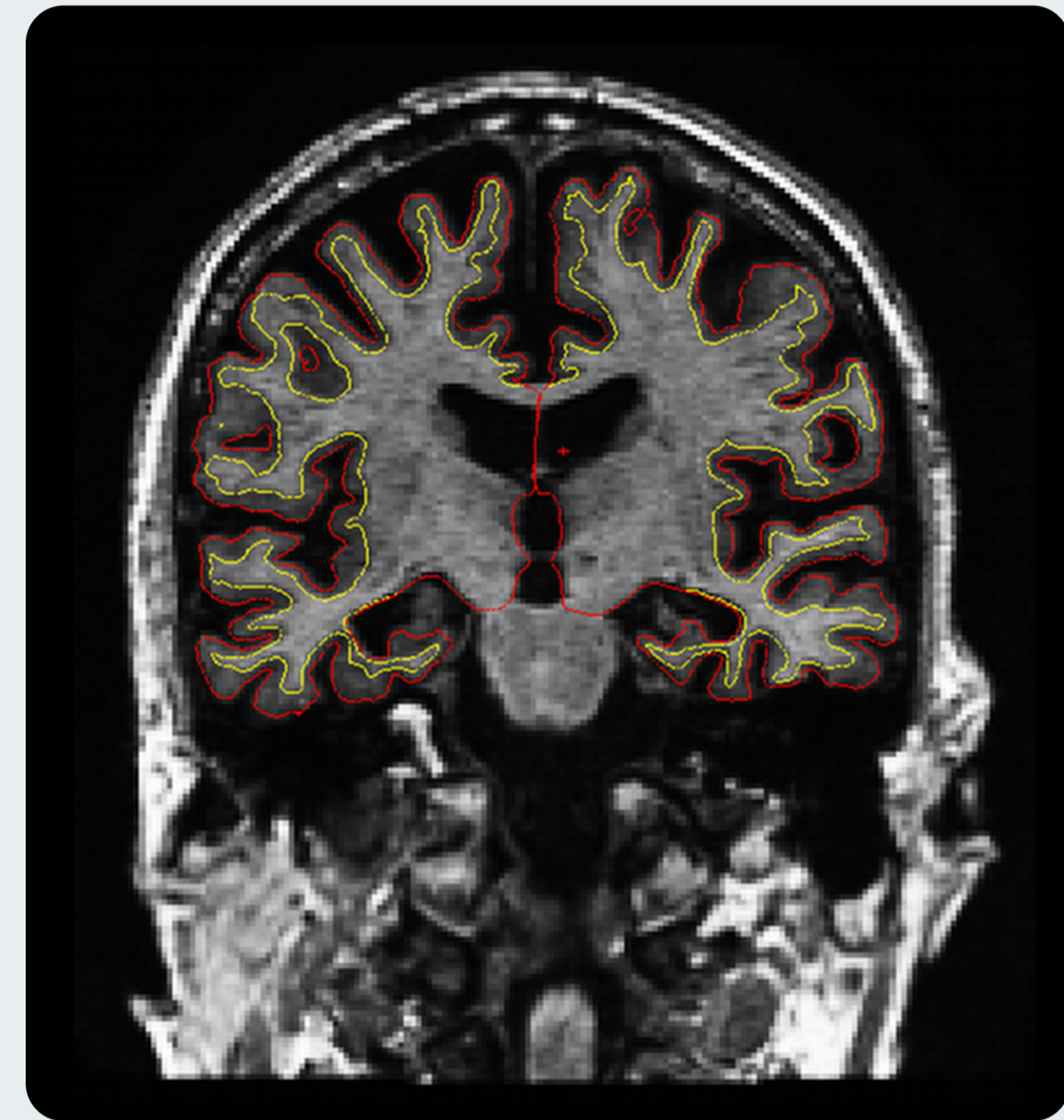
FreeSurfer [1]

Extracts the inner (yellow) surface and outer (red) surface, as triangulated meshes, and computes the average of the distance from the inner surface to the closest outer surface point and back again.
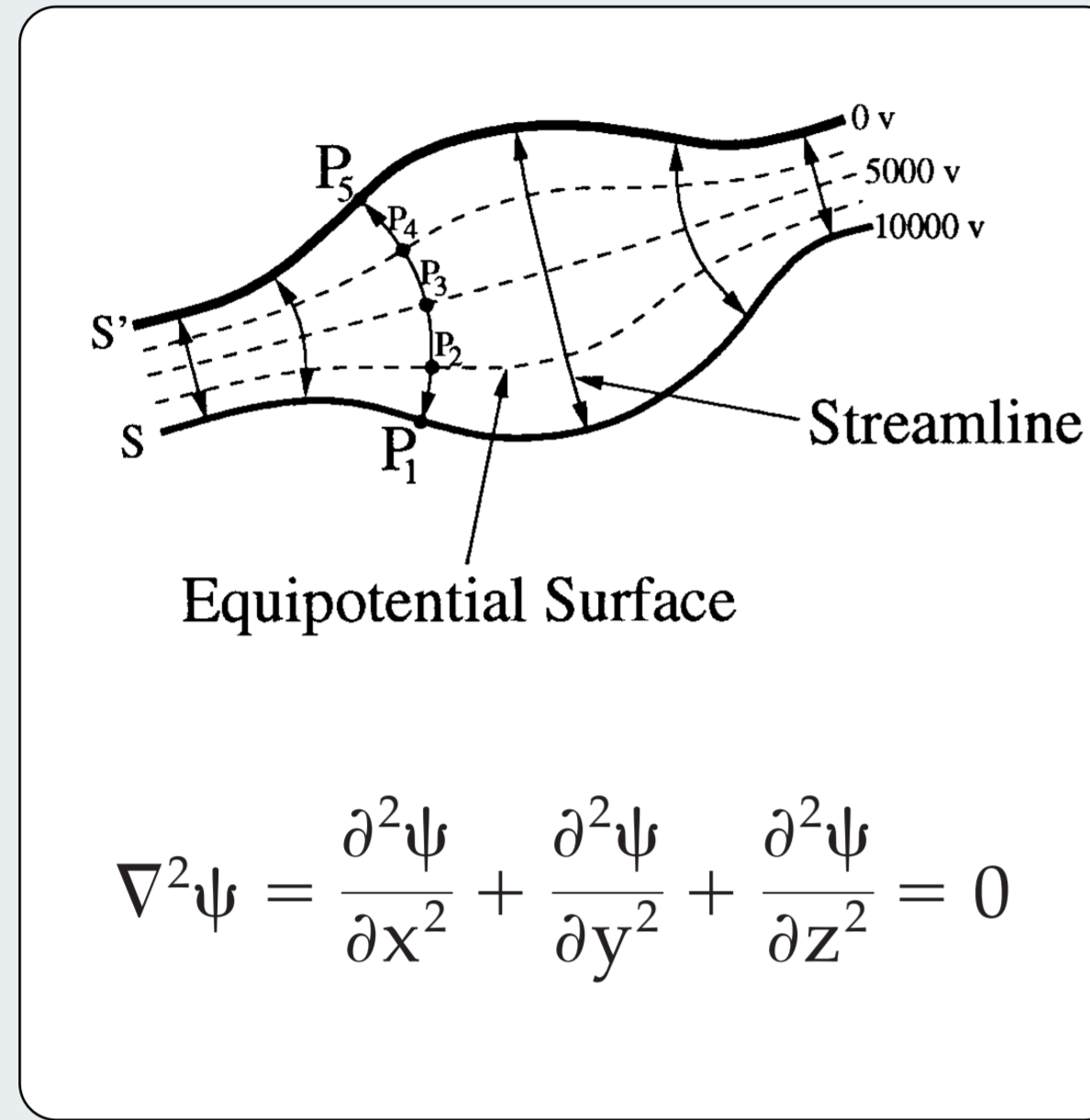
Laplacian [2,3]

From [2], imagine each side of the cortex has an electric potential. Solve the Laplace equation over the voxel grid, resulting in a smoothly varying scalar field. Cortical thickness is computed along the tangents to the equipotential lines [3].
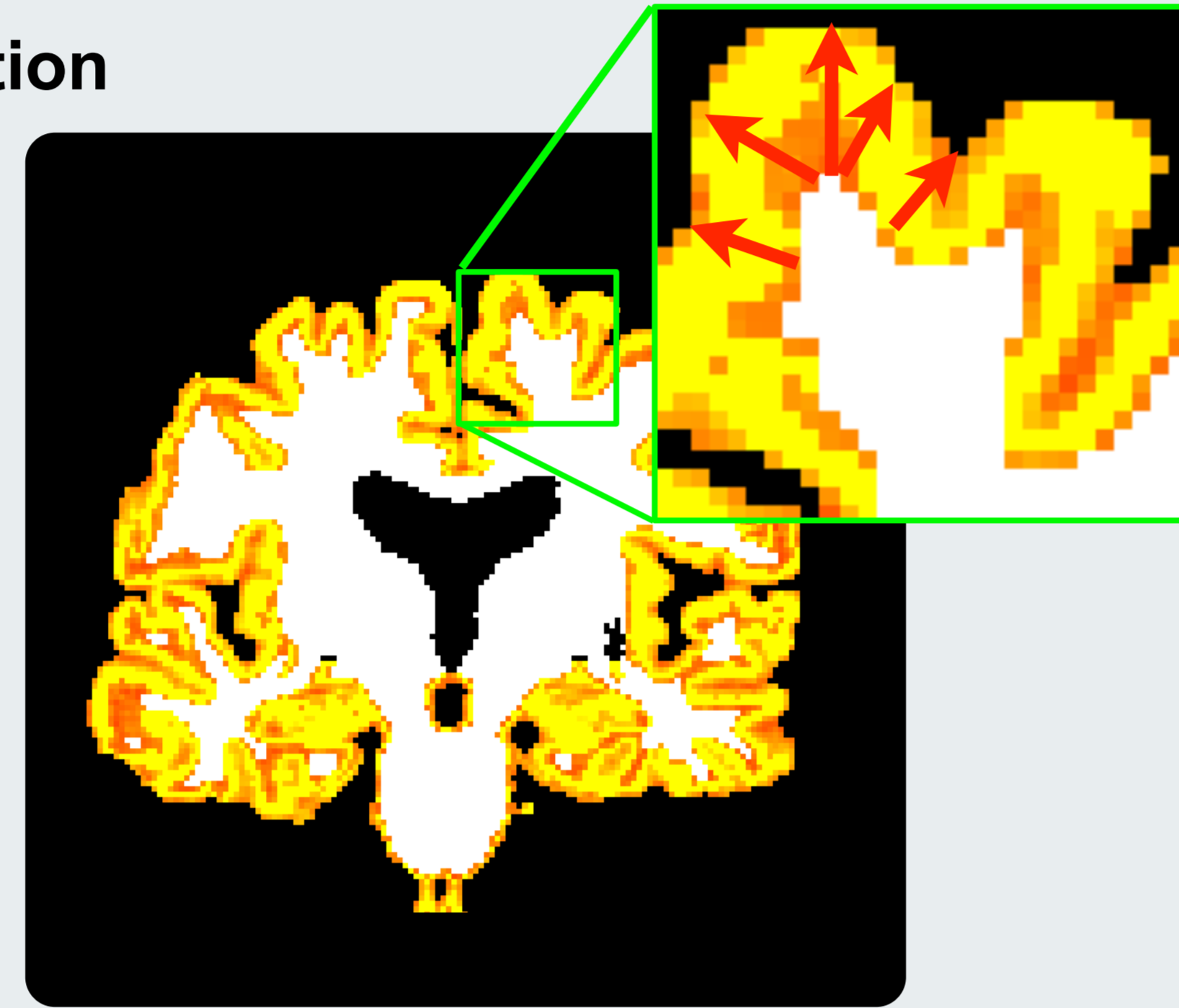
Registration [4]

Register WM mask to the WM + GM mask [4].

The thickness is the distance the GM/WM boundary moves during registration.

Experiment 1: Reproducibility

A cohort consisting of 49 subjects; 33 patients with probable AD, and 16 healthy controls, was selected from a local clinical database. All subjects had two same-day volumetric MRI scans acquired on a single 1.5T GE Signa scanner (General Electric, Milwaukee, WI). All 3 methods were run on both scans. Nine regions of interest were selected in advance on the FreeSurfer parcellation: the parahippocampal gyrus (PHG), fusiform (FUS), superior temporal gyrus (STG), precuneus (PRE), superior parietal gyrus (SPG), supramarginal gyrus (SMG), lateral occipital sulcus (LO), lingual (L) and the superior frontal gyrus (SFG). The standard deviation of the difference in the mean regional thickness was computed over all subjects.

Experiment 2: Cross-Sectional Disease Differentiation

A second cohort consisting of 101 subjects: 73 patients with clinically diagnosed frontotemporal dementia (FTD) and 28 healthy controls, was selected from a local clinical database. The FTD patients included 30 patients with progressive non-fluent aphasia (PNFA), 43 patients with semantic dementia (SD). All subjects had volumetric MRI acquired on four different 1.5T GE Signa scanners (General Electric, Milwaukee, WI).


The three thickness methods were run on all subjects, and a general linear model was used to test for statistically significant evidence of cortical thinning between patients and controls. Significance was assessed at the p=0.05 level, when corrected for multiple comparisons using the False Discovery Rate. Finally, a linear Support Vector Machine (SVM) was used to classify subjects where the comparison of interest is how well the classifier can separate the two patient groups from the control group, using the thickness data produced by each method.

Results:

Expt 1: Table shows the standard deviation of the difference in mean regional thickness for 9 anatomical regions, where an asterisk or a dagger indicate statistical significance.

Method	PHG	FUS	STG	PRE	SPG	SMG	LO	L	SFG
FreeSurfer	0.07	0.05	0.04	0.05	0.07	0.04	0.06	0.04	0.08
Laplacian	0.27*	0.39*	0.18*	0.17*	0.13*	0.16*	0.23*	0.76*	0.20*
Registration	0.16*†	0.15*†	0.15*	0.13*†	0.14*	0.16*	0.14*†	0.12*†	0.11*†

Expt 2: Methods detect similar patterns of cortical thinning for both patient groups, and the SVM experiment found no significant difference between them.
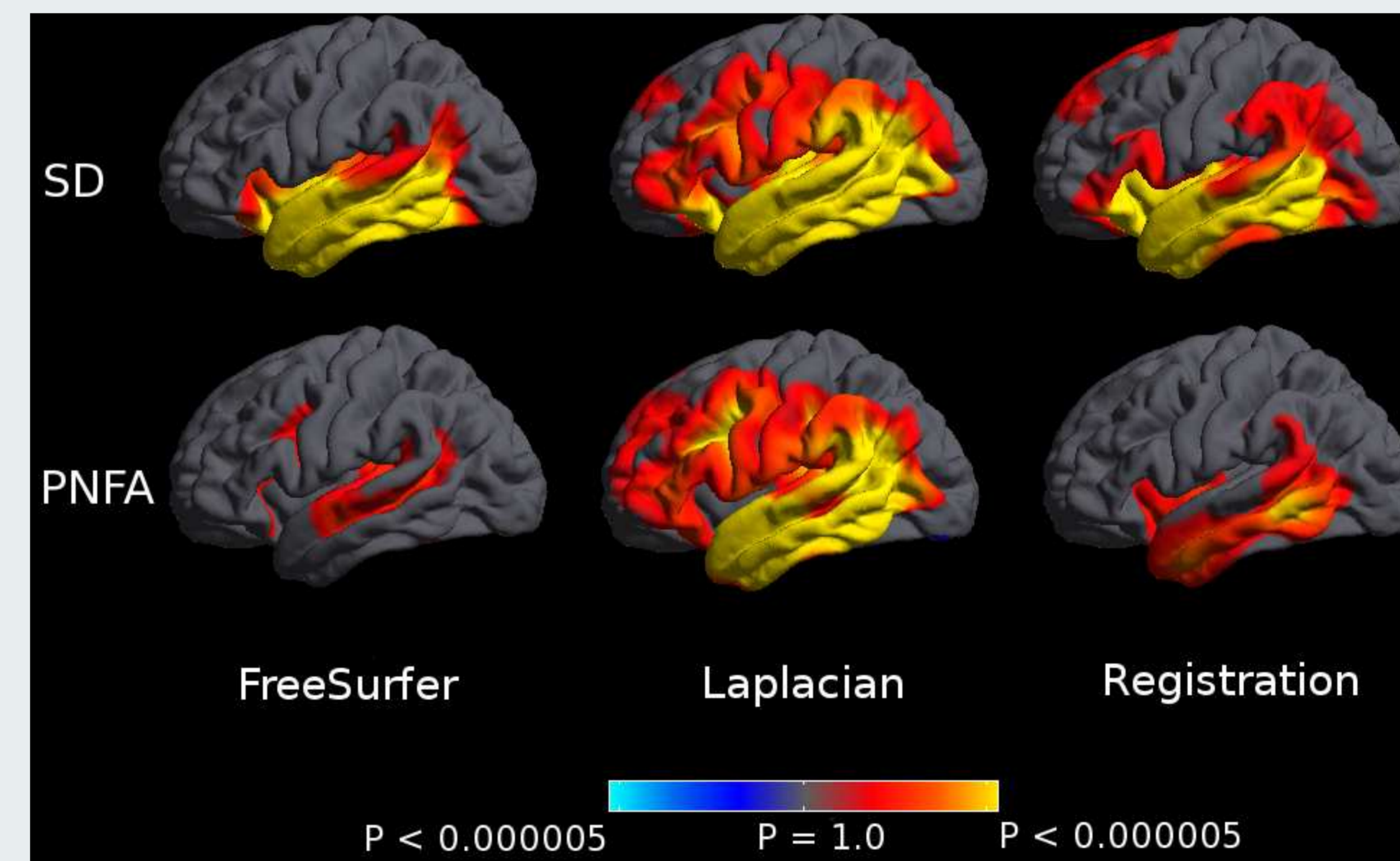
Method	Group	Accuracy (%)	-CI (%)	+CI (%)
FreeSurfer	SD	95.8	88.1	99.1
Laplacian	SD	97.2	90.2	99.2
Registration	SD	95.8	88.1	99.1
FreeSurfer	PNFA	79.3	66.6	88.8
Laplacian	PNFA	84.5	72.6	92.7
Registration	PNFA	75.9	62.8	86.1

Conclusion

FreeSurfer was shown to have a significantly lower standard deviation of regional cortical thickness for same-day scans. All 3 methods are suitable for detecting group-wise differences, displaying qualitatively similar results and more atrophy on the left than on the right side for SD and PNFA. We did not find any statistically significant evidence of a difference between methods when using an SVM to classify controls from SD patients or controls from PNFA patients. However, the SVM results indicate that the Laplacian method may be able to provide improved classification accuracy.

[1] http://surfer.nmr.mgh.harvard.edu/
[2] Jones et. al. Human Brain Mapping, 11 (12-32), 2000
[3] Acosta et. al. Medical Image Analysis 13 (730-743), 2009
[4] Das et. al. NeuroImage 45 (867-879), 2009

CMIC Centre for Medical Image Computing

Alzheimer's Research Trust

EPSRC Engineering and Physical Sciences Research Council