

Cortical Thickness Estimation

In vivo measurements of cortical thickness from MR images have potentially widespread utility in the characterisation of normal brain development and maturation as well as in diagnosing and measuring the progress of a number of cortical pathologies. The literature describes several approaches to this problem, which may be divided into two groups: those relying on deformable models of the inner and outer cortical surfaces, and those relying on image intensities alone. Results from the former may be largely model driven at points deep within sulci, where no apparent channel of cerebrospinal fluid can be seen at the resolution of typical MR images, potentially introducing bias.

The TINA cortical thickness measurement algorithm is based on a modified version of the Canny edge detector. The TINA segmentation algorithm is applied initially to find the mean intensities of grey matter, white matter and cerebro-spinal fluid, and to produce a map of the grey matter. A ‘z-score’ measure of the grey-level of each voxel being consistent with the GM/WM midpoint value is used to construct a likelihood image which highlights the GM/WM boundary. This is then used as a replacement for the conventionally used sum-squared image gradient (edge strength) map in the Canny edge detector in order to produce well localised connected edge strings to sub-pixel accuracy. The 3D surface normal at each voxel on the GM/WM boundary is determined by taking the local grey-level gradient of the 3D, Gaussian-smoothed, grey-level data. The GM tissue probability maps and the GM/WM boundary and edge orientations are used to determine the distance from the boundary, at each voxel on the boundary, along the orientation direction to another GM edge. This edge can either be a GM/CSF boundary or, if no CSF is visible in the intervening sulcus, a GM/WM boundary, and is determined by comparing the value of the voxel in the original grey-level image to the mean GM value. If it is a WM boundary it is assumed that the opposing banks of a sulcus have been traversed and the sulcal thickness is taken to be half this length: this approach has been shown to have little effect on subsequent regional thickness measurements [6]. Histograms of the cortical thickness measurements in various regions are then produced and their median values taken to produce the final regional thickness measurements.

In order to compare the TINA cortical thickness algorithm to other techniques, a meta-study of thickness measurements in the pre-central gyrus was performed. This application was chosen due to its clinical relevance (the pre-central gyrus is the thickest region of the cortex, and the location of the primary motor cortex) and the number of previous measurements available in the literature. Figure 1 shows the average cortical thickness measurements for the pre-central gyrus in 119 subjects (52 male, mean age = 70.3 years, range = 19-86 years) produced using the algorithm presented here, plotted against age. A quadratic fit to the data is shown: the dashed curves either side of the fit show the upper and lower standard error bounds. Also shown are a number of measurements of pre-central gyrus thickness from the literature. The details of the studies involved are given in Table 1. With the exception of the results from Kabani et. al. [2], the data were read from graphical representations¹. The results presented by von Economo [8] were measured manually post-mortem: brain volume decreases by approximately 10% during postmortem fixation. However, the thickness measurement was performed only on the gyral cap, which is known to be thicker than the sulcal fundi. Similarly the presentation of the results in Sowell et. al. [5] and Thompson et. al. [6] as projections onto the outer cortical surface prevented identification of the thickness in the sulcal fundi. These three data therefore represent upper limits on the average thickness in the region. Overall, the studies represented in Fig. 1 represent the widest possible range of methods for defining the inner and outer cortical surfaces, the thickness metric, and the presentation of the results. Some variation between the measurements, introduced by these differences in experimental procedure, might therefore be expected. However, the data show a remarkable level of agreement both with each other and the results from this study. If the errors on the results quoted by Kabani et. al. [2] can be taken as representative of the errors on the other studies, then there is no statistically significant difference between any of these results and our own. The remaining paper included in this study, Salat et. al. [4], was the only one to study variation in cortical thickness with age, and the only model-based study to cover the whole age range between adolescence and senescence. A significant disagreement between this study and the others included in the meta-study can be seen, with Salat et. al. suggesting a much lower rate of cortical thickness change with age. Given the level of agreement between the other studies, and the fact that the algorithm used by Salat et. al. was based on deformable modelling of the inner and outer cortical surfaces, we suggest that this may be due to the possibility for bias identified by [3] in such algorithms. The constraints applied to prevent self-intersection of the models and to aid in the modelling of the surfaces in tightly folded gyri tend to bias

¹With the exception the results from Salat et. al. [4] and von Economo [8] these were presented as views of the outer cortical surface, in some cases partially inflated to reveal the sulcal fundi, with colour coding to represent the thickness at each point. This method of data display is popular in the literature as it avoids the need for parcellation of the data into particular regions. However, the calculation of regional average thicknesses from such representations is difficult and the calculation of errors on the averages impossible. Hence, these points are shown without error bars.

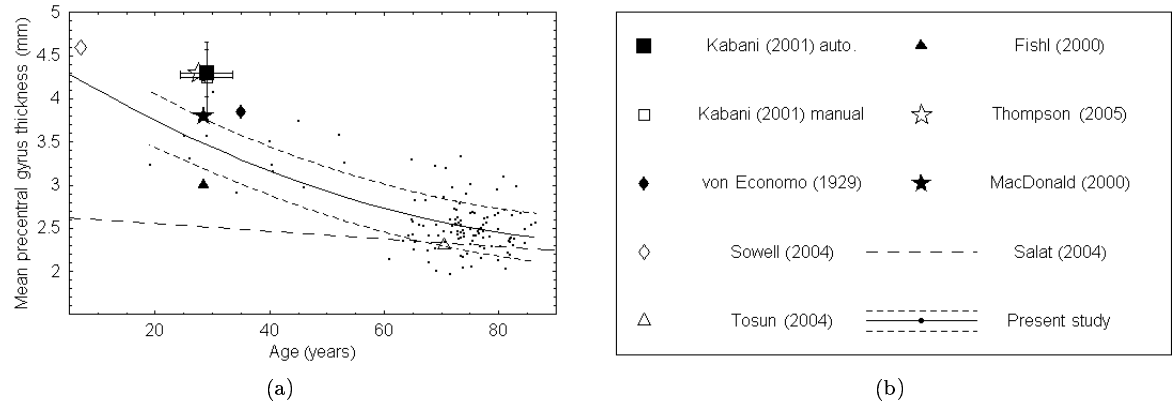


Figure 1: Measurements of the average cortical thickness in the pre-central gyrus: see main text for description.

the model towards a fixed thickness, suppressing the observation of age-related changes. Overall, the meta-study confirms that the TINA medical image segmentation algorithm produces accurate and bias-free regional thickness measurements.

Reference	No. subjects	Age range (years)	Algorithm type
Kabani et. al. 2001 [2]	40	18-40	Model based
von Economo 1929 [8]	-	30-40	Manual measurement
Sowell et. al. 2004 [5]	45	5-11	Intensity based
Tosun et. al. 2004 [7]	105	59-84	Model based
Fishl et. al. 2000 [1]	30	20-37	Model based
Thompson et. al. 2005 [6]	40	18-48	Intensity based
MacDonald et. al. 2000 [3]	150	18-40	Model based
Salat et. al. 2004 [4]	106	18-93	Model based

Table 1: Details of the studies included in the meta-study of the dependence of pre-central gyrus thickness on age.

References

- [1] Fischl, B. and Dale, A. M. (2000). Measuring the thickness of the human cerebral cortex from magnetic resonance images. *PNAS*, 97:11050–11055.
- [2] Kabani, N., Le Goualher, G., MacDonald, D., and Evans, A. C. (2001). Measurement of cortical thickness using an automated 3-D algorithm: A validation study. *NeuroImage*, 13:375–380.
- [3] MacDonald, D., Kabani, N., Avis, D., and Evans, A. C. (2000). Automated 3-D extraction of inner and outer surfaces of cerebral cortex from MRI. *NeuroImage*, 12:340–356.
- [4] Salat, D. H., Buckner, R. L., Snyder, A. Z., Greve, D. N., Desikan, R. S. R., Busa, E., Morris, J. C., Dale, A. M., and Fischl, B. (2004). Thinning of the cerebral cortex in aging. *Cerebral Cortex*, 14:721–730.
- [5] Sowell, E. R., Thompson, P. M., Leonard, C. M., Welcome, S. E., Kan, E., and Toga, A. W. (2004). Longitudinal mapping of cortical thickness and brain growth in normal children. *J. Neurosci.*, 24:8223–8231.
- [6] Thompson, P. M., Lee, A. D., Dutton, R. A., Geaga, J. A., Hayashi, K. M., Eckert, M. A., Bellugi, U., Galaburda, A. M., Korenberg, J. R., Mills, D. L., Toga, A. W., and Reiss, A. L. (2005). Abnormal cortical complexity and thickness profiles mapped in Williams syndrome. *J. Neurosci.*, 25:4146–4158.
- [7] Tosun, D., Rettmann, M. E., Han, X., Tao, X., Xu, C., Resnick, S. M., Pham, D. L., and Prince, J. L. (2004). Cortical surface segmentation and mapping. *NeuroImage*, 23:S108–S118.
- [8] von Economo, C. (1929). *The Cytoarchitectonics of the Human Cerebral Cortex*. Translated by S. Parker. Oxford University Press, Oxford.