Estimation of total intracranial volume – a comparison of methods

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Summary

Total intracranial volume is a useful measure of inter-subject variability in pre-morbid brain volume, which has been recommended for inclusion in region of interest and voxel-based morphometric studies of dementia [1]. TIV can be estimated from structural MRI using time-consuming manual tracing or using automated methods. We show that recent improvements to the Statistical Parametric Mapping (SPM) software's unified segmentation method allow highly accurate and unbiased estimates to be obtained rapidly and without interaction.

Introduction

Regional cortical and subcortical grey matter (GM) and white matter (WM) volumes correlate with total brain volume, which in turn is correlated with total intracranial volume (TIV). In studies of neurodegenerative diseases, total brain volume typically decreases over time, while TIV remains constant as cerebrospinal fluid (CSF) expands to fill the vacated space. Controlling for TIV in statistical analyses can help to adjust for sampling imbalances in head-size, and explain some of the variability in regional measurements without removing atrophic effects, thus increasing power to detect group differences or structural correlates. Time-consuming manual estimation of TIV is unsuitable for large studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI), motivating use of automatic methods. However, inaccurate automatic methods might exhibit disease-related biases with the potential to confound analyses (for instance if the TIV measure was influenced by atrophy), implying that careful evaluation is necessary.

Methods

We compare estimates of TIV using 55 subjects (37 male, 59.9 +/- 11.4 years of age), including 22 with Alzheimer's disease and 16 with frontotemporal lobar degeneration, imaged twice (479 +/- 289 days apart). Manual tracing estimates performed with the MIDAS software [2] are compared to eight automatic methods: FreeSurfer versions 4.5 and 5 [3]; Statistical Parametric Mapping version 5, summing either native or modulated warped segmentations; SPM version 8 equivalents, which use the improved tissue prior probability maps shown in Figure 1 [4]; and Jacobian integration using either SPM8 unified segmentation or Dartel [5].

Results

Considering baseline TIV, SPM5 segmentations are highly variable and upwardly biased with respect to manual measures, while those from SPM8 are dramatically improved; FreeSurfer results lie between these (see Figure 2). The Dartel Jacobian integration method has the strongest correlation and least mean difference with respect to manual measures (see Table 1). Consideration of longitudinal changes reveals small but significant reductions in the manual measures, and in the closely correlated Dartel results (see Figure 3). The modulated warped SPM8 segmentations appear to exhibit the best balance of accuracy and stability over time.

References

[1] Barnes et al (2010) Neuroimage 53:1244-55
[2] Freeborough et al (1997) CMPB 53:15-25
[3] Buckner et al (2004) Neuroimage 23:724-38
[4] Weiskopf et al (2011) Neuroimage 54:2116
[5] Ashburner (2007) Neuroimage 38:95-113

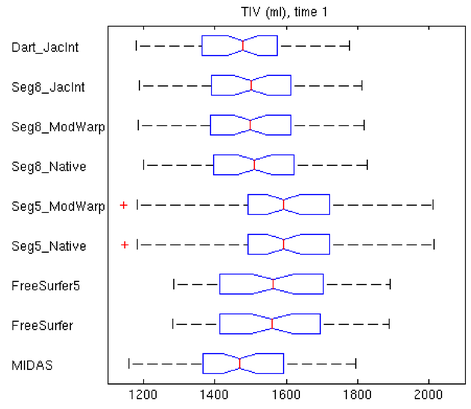

Figure 2 – Measurements at baseline
MIDAS denotes expert manual measurements. Box-plots show the median (red line), inter-quartile range (box), non-parametric test for equal medians (whether angled notches overlap), and outliers (red crosses), which are further than 1.5 times the inter-quartile range beyond the inter-quartile limits (the box-plot whiskers).

Method	Correlation (Pearson)	Mean Diff. (ml)	St. Dev. of Diff. (ml)
Dart_JacInt	0.977	-3.4	34.1
Seg8_JacInt	0.970	21.3	37.3
Seg8_ModWarp	0.974	21.8	34.8
Seg8_Native	0.974	31.4	35.0
Seg5_ModWarp	0.806	125.6	113.4
Seg5_Native	0.806	125.9	113.6
FreeSurfer5	0.911	82.5	65.3
FreeSurfer4.5	0.914	79.4	64.1

Table 1 – Correlations and differences
With respect to baseline manual/MIDAS TIV.

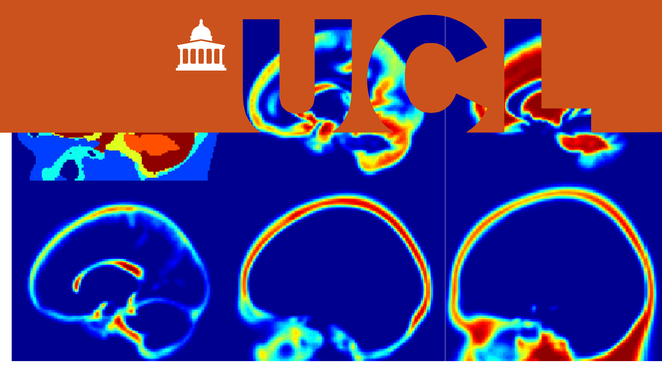

Figure 1 – SPM8's new tissue prior maps
Max-prob, GM, WM, CSF, bone and soft-tissue.

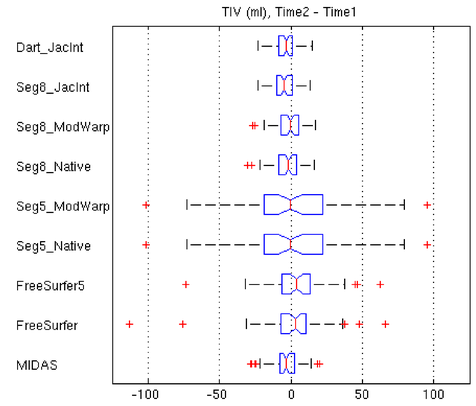

Figure 3 – Alterations across time
Change in TIV (increases positive) between baseline and repeat. See Figure 2 for plot details.

Conclusion

Accurate estimation of TIV is possible in less than 10 minutes per subject with no manual interaction, making it suitable for even the largest studies given distributed computing resources. We will use the above-selected method to estimate TIV for all subjects in ADNI, and make these publicly available.

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