MRI-based Simulation of Central Brain Atrophy for Evaluation of Brain Atrophy Measurement Methods

Kunio Nakamura[1], Nicolas Guizard[1], Vladimir S. Fonov[1], Sridar Narayanan[1], D. Louis Collins[1], and Douglas L. Arnold[1]
[1]*McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada*

Introduction: Several brain atrophy simulation tools are available[1,2] to aid validation of image analysis tools. These methods apply known deformations to real images. But the accuracy of gold standard is limited due to the discrete nature of model and images and due to the need to estimate volumetric change from applied deformation. In this study, we simulated MRIs from probability maps, which allowed accurate calculation of brain volumes.

Objectives: (1) To construct a brain atrophy simulation dataset with accurately known volumes and their changes, (2) to evaluate five image analysis methods in terms of their correlation, accuracy and potential bias, and (3) to compare the relative brain atrophy rates between simulated MRIs and real MRIs acquired within a multiple sclerosis (MS) clinical trial.

Methods: We used twenty previously-obtained, high-resolution (0.5mm isotropic) brain tissue probability maps (including gray matter (GM), white matter (WM), cerebrospinal fluid (CSF), skull, marrow, dura, fat, muscles, skin, and vessels)[3] as input to an MRI simulator (mrisim, BrainWeb[4], MINC tools) and altered these probability maps to simulate central brain atrophy. We progressively expanded the lateral ventricles and contracted surrounding GM and WM by (1) fully automatic segmentation of lateral ventricles from the images without simulated atrophy using a patch-based method[5], (2) grayscale dilation of ventricular CSF probability with radii of 0.5, 1.0, 1.5, and 2.0mm, treating the dilated values as the new probabilities, and (3) proportionally decreasing GM and WM probabilities. Original and modified probability maps were the input to the MRI simulator to generate 5 simulated 3D MRI images (original plus 4 levels of ventricular dilation) for each of the 20 subjects in the simulation dataset.
We analyzed these images using fully-automated, commonly-used image analysis software (SIENA[6], SIENAX[6], SPM[7], longitudinal FreeSurfer (FS)[8], and tensor-based morphometry (pairwise Jacobian integration method, PJI[9])), measured the *percent change in whole brain volume*, and compared the results to the known volume changes measured from the probability maps as the sum of GM and WM probabilities from all voxels. For the statistical analysis, we measured the correlation coefficient, absolute error, and the slope of the linear regression line as an estimate of bias. As a simple validation of the simulation dataset, we measured the relative brain atrophy rate (slope of linear regression) between PJI and SIENA and compared to the same slope obtained from real MRIs acquired from a cohort of 195 relapsing-remitting MS patients in a longitudinal clinical trial (ASSERT, NCT00203047).

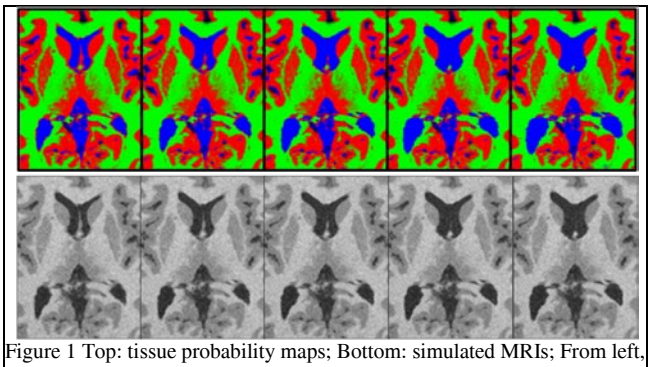

Figure 1 Top: tissue probability maps; Bottom: simulated MRIs; From left, original and 4 levels of ventricular dilations.

Results: The most precise measures of whole brain volume change (based on correlation coefficients, R^2) were provided by SIENA (0.969) and PJI (0.962) followed by FS (0.936), SIENAX (0.808), and SPM (0.589). The most accurate atrophy estimation method based on absolute error was FS with mean±SD of 0.10±0.09% followed by SIENAX (0.24±0.24%), PJI (0.25±0.16%), SPM (0.26±0.21%), and SIENA (0.34±0.24%). The slopes (bias), in ranking, were 0.97 (FS), 0.81 (SPM), 1.26 (SIENAX), 0.69 (PJI), and 1.46 (SIENA), as shown in Figure 2. Compared to SIENA, the relative brain atrophy rates for PJI were 0.46 for simulation and 0.76 for real MRIs of MS study. Thus, the pattern of larger atrophy rate for SIENA compared to PJI was found in both datasets.

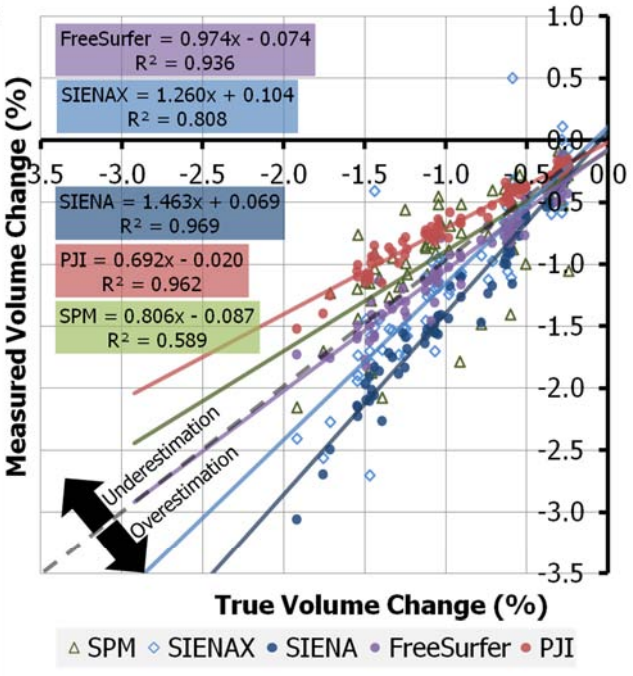

Figure 2: Results of measured brain volume change vs. gold standard.

Conclusion/Impact: The validation datasets allowed a direct comparison of accuracy among different methods. Three longitudinal methods (FS, SIENA, and PJI) performed well: SIENA and PJI on correlation, FS on accuracy. The bias pattern on simulated images appeared similar to that from real MRIs. Our simulation tool allows varying factors like intensity non-uniformity, resolution, noise level, and sequence parameters. We plan to provide these simulation MRIs to the research community to help validate future techniques and to compare directly to our results.

Reference: [1] Camara 2008 NeuroImage. [2] Davatzikos 2001 NeuroImage, [3] Aubert-Broche 2006 NeuroImage, [4] Collins 1998 IEEE TMI, [5] Coupe 2011 NeuroImage, [6] Smith 2002 NeuroImage, [7] Ashburner 2005 NeuroImage, [8] Fischl 1999 NeuroImage, [9] Nakamura 2013 NeuroImage Clinical (in press).