

## Comparison of two spatial normalization methods in the elderly brain

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**Introduction:** Brain volume and local cortical structures have different atrophy rates as people age, while localized cortical structures are affected by neurodegenerative diseases such as Alzheimer's disease (AD). Spatial normalization involves transforming all of the subjects' data to the same stereotactic space to facilitate the comparison of different subjects [1]. One of the most popular normalization software packages for brain analysis is Statistical Parametric Mapping (SPM2, Wellcome Department of cognitive Neurology), in which the geometric transformation model adopts the discrete cosine transformation (DCT) as its basis functions. Alternatively, Chen's normalization method computes the displacements of each voxel without any constraints and is claimed as a fully deformable normalization method [2,3]. However, no studies to date have compared the performance and accuracy of these two normalization methods as applied to brain functional imaging including perfusion MRI. The goal of our study was to assess the accuracy of spatial normalization with respect to the correspondence of fine cortical structures to true anatomical structures and the effects on biostatistical analysis of functional (perfusion) dementia studies.

**Methods:** We chose two initial cortical structures (hippocampus and thalamus) to assess the accuracy of the two spatial normalization methods (SPM and Chen). Coronal T<sub>1</sub>-weighted spoiled gradient-recalled echo (SPGR) images covering the whole brain were acquired (124 slices with Matrix: 256 × 192; Thickness: 1.5 mm and zero spacing, TE: min Full, TR: 25 ms, FOV: 24 × 18 cm, rBW: 16 kHz) from a 1.5 T GE Signa scanner. The SPGR images were regridded into 240 × 186 × 180 matrix with voxel size 1 × 1 × 1 mm<sup>3</sup>. We registered the corresponding template image to a subject SPGR image, and then used the resultant geometric transformation to transfer the hippocampi masks and thalami masks from the corresponding template image to the subject image. The following template images were found to optimize the performance of each registration method and adopted for this study: Chen's template used the colin27 brain image with voxel size 1 × 1 × 1 mm<sup>3</sup>; the SPM template used a smoothed image with voxel size 2 × 2 × 2 mm<sup>3</sup>.

We evaluated the effects of these two normalization methods on dementia group comparisons of perfusion maps acquired with arterial spin labeled MRI. First, we registered a subject image to the template image, then used the resultant geometric transformation to transfer the gray matter perfusion map from the subject image to the template image, smoothed the resulting map using a 6 mm Gaussian kernel, and performed an ANOVA analysis to make inferences about group differences (19 Normal controls of age 81.9 ± 3.2, 20 MCI of age 83.6 ± 3.9, and 22 AD subjects of age 83.3 ± 2.9).

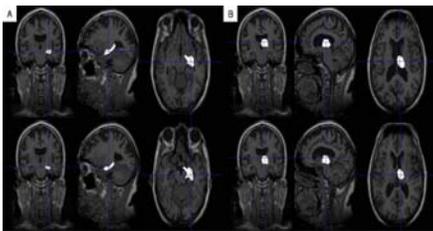
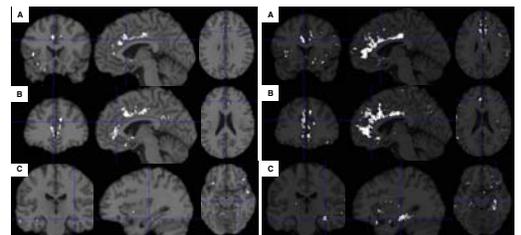


Figure 1: Comparison of automatic ROI detection (left) from SPM (top row) and Chen's method (bottom row) for the left hippocampus (A) and left thalamus (B). ROIs are shown projected onto the individual's SPGRs. Statistically significant regions (white) from SPM (left) and Chen's registrations (right). A)  $CBF_{AD} > CBF_{Control}$ ; B)  $CBF_{AD} > CBF_{MCI}$ ; C)  $CBF_{MCI} > CBF_{Control}$ .



**Results & Discussion:** The segmentation results for two cortical structures of the same subject image from SPM and Chen's normalization techniques are shown in Fig. 1. SPM caused the left hippocampus to be shifted up from its true anatomical position while the thalamus was erroneously located within the ventricles. Chen's normalization method provided more precision to match cortical structures between the subject images and the template image. The results for group differences in cerebral blood flow (CBF) of normal controls, MCI and AD subjects from SPM and Chen's techniques are shown in Fig. 2. Chen's method shows markedly larger regions of statistical significance than SPM for 13 of 14 brain regions of interest. The regions of statistical significance increased in area by 230% on average with Chen's method.

**References:** 1. Ashburner et. al., Neuroimage. 11(6 Pt 1): 805-21 (2000). 2. Chen. PhD dissertation, CMU (1999). 3. Carmichael et. al., Neuroimage. 27(4): 979-90 (2005).