# Accurate Mapping of Brains with Severe Atrophy Based on Multi-Channel Non-linear Transformation

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#### INTRODUCTION

Voxel-based analysis applied on transformed MR images is widely used for quantification of brain anatomy, which has been successful in studies with normal, adult brain images. However, accurate transformation could be difficult for subjects with enlarged ventricles due to severe brain atrophy, such as Alzheimer's disease patients (AD). Although the simple shape transformation between a small and a large ventricle (Fig. 1) is mathematically straightforward, such deformation does not provide an anatomically correct transformation field (red arrows). This is because a substantial part of ventricle enlargement is not due to the expansion shown in Fig. 1a but due to "opening" of spaces that are closed in young adult brains (Fig. 1b). Without modeling the anatomically correct transformation, voxel-based analysis could lead to inaccurate biological conclusions. In this study, we use multi-channel LDDMM[1] to improve the mapping process of AD subject brains by introducing a second source, or channel, of information comprised of the segmentation maps of the lateral ventricles. Our hypothesis is that the second channel would reinforce the representation of an existing anatomical structure and guide the transformation of the subject to the template.

#### **METHODS**

Images from AD patients (n=9) were acquired using T1WI (MPRAGE, matrix 256x256, FOV 240x240, slice thickness 1.2mm, TE 3.2ms, TR 6.85ms). Linear (AIR) and nonlinear transformations (LDDMM) between each subject's data and a template atlas[2] were obtained using DiffeoMap software [3]. The first channel for LDDMM consisted of T1-weighted images; the second channel consisted of segmentation maps of the lateral ventricles (LV) of both template and subject. In the

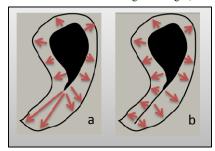


Figure 1: (a) Expansion of lateral ventricle with mesial part of occipital horn not visible. (b) Expansion of ventricle with ventricular extension included.

normal, adult brain, the mesial parts of the occipital and temporal horns of the lateral ventricles are not visible in T1-weighted images at the given resolution. In AD brains, parenchymal atrophy leads to an evident enlargement of the ventricles, including these mesial portions. The requirement for an accurate representation of the expansion process was met by adding a ventricular extension to the LV segmentation map of the template, which reinforced the existence of these ventricular areas (Fig. 1b). The LV segmentation maps of subjects were obtained using two different methods: (1) semi-automatically, by using an intensity-based 2-D region growing approach with ROIEditor[3], with manual correction at each slice, and (2) automatically, with intensity-based segmentation in Statistical Parametric Mapping (SPM5). For testing the accuracy of these two methods as well as single-channel LDDMM based on T1WI only, we compared the results of each of these registration-based segmentations with manual segmentation of LV and of the left lingual gyrus, located next to LV. Segmentation comparison was performed in 2-D axial slice number 71 in three subject images after linear transformation and repeated three times to calculate intra-rater agreement. Reliability of segmentation was quantified by Kappa analysis [4].

## RESULTS

Fig. 2 shows results of (a) single-channel LDDMM with T1-weighted images, (b) dual-channel LDDMM with semi-automatically derived LV segmentation maps, and (c) dual-channel LDDMM with automatically derived LV maps. Qualitatively, dual-channel LDDMM with semi-automatically derived LV maps and automatically derived LV maps yield comparable results, with single-channel LDDMM giving the worst results. This difference is evident in the portions of LV which are not mapped as LV and which are sometimes mapped as left lingual gyrus, in the single-channel method. Compared with manual segmentation, Kappa values [5] for registration-based segmentation of LV and left lingual gyrus are 0.79 and 0.77, 0.91 and 0.80, and 0.88 and 0.82 for single-channel, dual-channel with semi-automatic LV maps, and dual-channel with automatic LV maps, respectively. In addition, intra-rater Kappa values are 0.93 for LV and 0.94 for the left lingual gyrus.

### DISCUSSION AND CONCLUSION

Our findings show that including a second channel of information, in this case LV segmentation maps, improves the registration of images. By accounting for an existing anatomical structure in our template and including it as a second channel, we obtained higher Kappa values than by using single-channel LDDMM. We also showed that we can automate the process by using automated segmentation methods to derive the segmentation maps of guiding structures (LV) in subjects and achieve good results. Multi-channel LDDMM with segmentation maps is a powerful tool for improving registration of images.

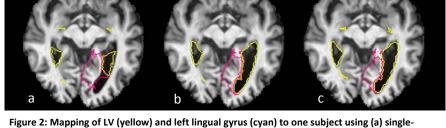


Figure 2: Mapping of LV (yellow) and left lingual gyrus (cyan) to one subject using (a) single-channel LDDMM, (b) dual-channel LDDMM with semi-automatically derived LV maps, and (c) dual-channel LDDMM with automatically derived LV maps. Axial slice 71. K= Kappa values for average of three subjects.

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