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Individualized diffeomorphic mapping of brains with large cortical infarcts

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ABSTRACT

Whole brain mapping of stroke patients with large cortical infarcts is not trivial due to the complexity of infarcts' anatomical location and appearance in magnetic resonance image. In this study, we proposed an individualized diffeomorphic mapping framework for solving this problem. This framework is based on our recent work of large deformation diffeomorphic metric mapping (LDDMM) in Du et al. (2011) and incorporates anatomical features, such as sulcal/gyral curves, cortical surfaces, brain intensity image, and masks of infarcted regions, in order to align a normal brain to the brain of stroke patients. We applied this framework to synthetic data and data of stroke patients and validated the mapping accuracy in terms of the alignment of gyral/sulcal curves, sulcal regions, and brain segmentation. Our results revealed that this framework provided comparable mapping results for stroke patients and healthy controls, suggesting the importance of incorporating individualized anatomical features in whole brain mapping of brains with large cortical infarcts.

1. Introduction

Whole brain mapping has been widely used in neuroimaging research for multiple purposes, including structural segmentation, voxel-based and tensor-based morphometry, group analysis on functional magnetic resonance imaging (MRI) and positron emission tomography (PET) [1]. There has been great emphasis on developing nonlinear registration approaches for aligning healthy brains based solely on the image intensity, or on the integration of the brain image intensity and the geometry of the cortical surfaces [2–6]. Nevertheless, employing the aforementioned approaches for aligning the brain with large cortical infarcts to the healthy brain is not trivial due to the complexity of infarcts' anatomical location and appearance in the MR image.

There are only a few available brain mapping approaches that deal with brain images with large cortical infarcts. One early work [7] proposed enantiomorphic normalization that essentially creates an artificial "brain" by replacing the lesion volume with a homologous volume from its contra-lateral hemisphere and then seeks non-linear transformation based on this artificial "brain". This method, however, is only applicable to the brain with unilateral cortical infarcts and assumes, erroneously, that the brain is symmetrical, despite clear evidence saying otherwise [8]. Ashburner, J. et al. [9] introduced a unified model that combines segmentation, bias correction, and spatial normalization with the use of tissue map priors of the white matter, gray matter and cerebrospinal fluid (CSF). Multiple Gaussian models for tissue segmentation distinguish infarcted and healthy brain regions, while bias correction may model the infarcted tissue as an area of inhomogeneity. Hence, spatial normalization of cortical infarcts in this approach benefits from the segmentation and bias correction in an integrative manner. Brett and colleagues [10] extended this approach by introducing cost function masking (CFM) that first masks off the lesion voxels and then calculates differences between two brain images. This approach significantly improved the non-linear normalization results without CFM. Anderson and colleagues [11] highlighted its importance by showing that even with the use of the unified segmentation approach [9], the cost function masking remains necessary in normalizing brain images with chronic infarcts. However, both methods are based on a small deformation model, limiting its use for diffuse infarction pathology.

The aforementioned approaches for aligning brains with large cortical infarcts have thus far limited to volume-based nonlinear registration approaches. Such approaches seek the deformation that is driven by the image intensity information, and hence, provide accurate mappings in subcortical and ventricular regions where intensity contrast is clear and structural shapes are relatively simple. However, these approaches fail to accurately align the cortical region since the convoluted cortical sheet cannot be well characterized

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based on image intensity alone. There is an additional need to consider the geometric property of the cortex as functionally distinct regions are close to each other in a volume space but geometrically distant in terms of distance measured along the cortex. Such a geometric property of the cortex has been well preserved in a cortical surface model [12,13]. Registration approaches based on cortical surfaces [13–16] have shown superior performance in the alignment of highly complex cortical folding pattern over volume-based registration approaches, and thus resulted in increased statistical power for averaging of functional data in the cortical region across subjects [17].

Recent works by Postelnicu et al. [3] and Joshi et al. [18,19] have employed the spherical cortical surface mapping implemented in FreeSurfer [13] or the harmonic cortical surface mapping constrained by gyral/sulcal curves [18,19] to first seek the deformation field on the cortical boundary and then extend it to the 3D volume for further brain volume registration. These two approaches have shown tremendous improvement in mapping accuracy when compared to the advanced volume-based approach, hierarchical attribute matching mechanism for image registration (HAMMER) [5], where geometric features of the cortex have been intrinsically incorporated. Only recently, Du et al. [2] proposed the approach providing an one-to-one, differentiable, and invertible deformation field that simultaneously aligns gyral/sulcal curves, cortical surface, and intensity image volume from one subject to the other under the framework of large deformation diffeomorphic metric mapping (LDDMM). This approach with superior mapping accuracies (for both cortical and subcortical structures) as compared to LDDMM based solely on image intensity, combined volumetric and surface registration [3] and hierarchical attribute matching mechanism for elastic registration (HAMMER) [5].

In this study, we aimed to register brains with large cortical infarcts to a brain atlas, and to achieve good alignment in the intact cortical and subcortical regions of the infarcted brains. Hence, we employed the whole brain LDDMM algorithm described in [2] and proposed a brain mapping framework that individualizes anatomical features, such as cortical surfaces, sulcal/gyral curves, surfaces of the lateral ventricles, and intensity images. We incorporated these individualized anatomical features into the LDDMM algorithm to 1) mask out cortical infarct regions; 2) well constrain the boundary of cortical infarcts; 3) well align anatomical features in the intact brain regions. We quantitatively validated this mapping framework in terms of gyral/sulcal curve anatomical variation, sulcal region alignment, as well as structural segmentation in both cortical and subcortical regions using brain images with simulated cortical infarcts and brain images of stroke patients.

2. Materials and methods

The study was approved by the Institutional Review Board of National University of Singapore. All subjects gave their written informed consent.

In this section, we describe a new framework for aligning the brain with large cortical infarcts to the brain of a healthy brain using the whole brain diffeomorphic metric mapping introduced in [2]. This framework incorporates the information of subject's cortical infarcts in the image volume as well as the cortical surface to aid the mapping process. As illustrated in Fig. 1, this framework consists of three major processes: 1) whole brain segmentation and the generation of cortical and lateral ventricular surfaces; 2) the extraction of individual anatomical features, including cortical surfaces, gyral and sulcal curves; and 3) individualized large deformation diffeomorphic metric mapping (LDDMM). We detail each process in the following.

2.1. Whole brain segmentation and generation of cortical and lateral ventricular surfaces

FreeSurfer is used to label each voxel of the T1-weighted image as cerebrospinal fluid (CSF), gray matter (GM), and white mater (WM) using a Markov-Random field model [20]. An inner surface at the boundary of GM and WM is then constructed and then propagated to the boundary of GM and CSF to form an outer surface via a flow with the force based on the image labeling and gradient such that the topologies of the outer and inner surfaces are preserved [21]. The inner and outer surfaces are used to represent the geometry of the cortex (see an example in Fig. 1B). Notice that the cortical infarcted regions are labeled as CSF in FreeSurfer (red colored mask in Fig. 1B). Hence, the cortical surface corresponding to these regions is not necessary with correct topology and bounded to the cortical ribbon. In our study, the cortical surface in the infracted regions will be masked out as described below and excluded in the mapping since there is no correspondence between the cortical lesion and that in the healthy brain. Therefore, manual correction for the surface generation is not necessary.

The lateral ventricular surfaces are generated using the prior shape information of an atlas that was created from 41 manually labeled

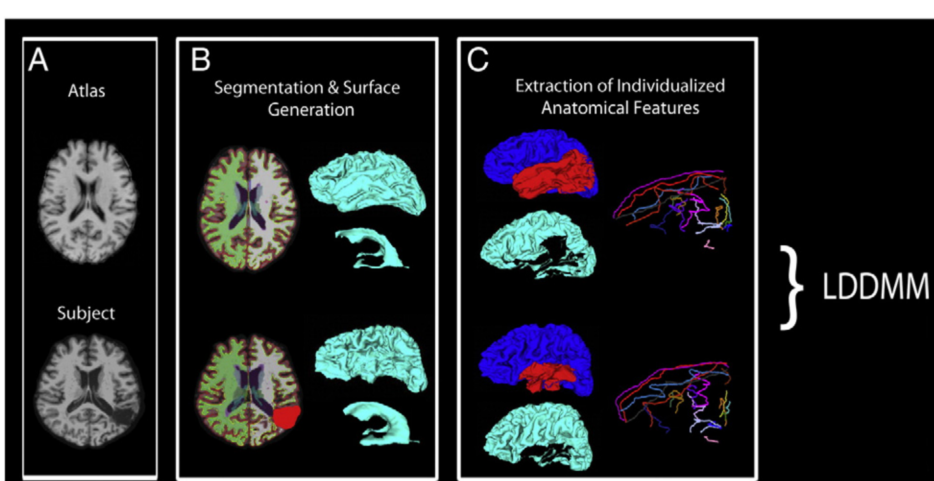

Fig. 1. The schematic diagram for individualized diffeomorphic mapping of brain with large cortical infarcts. Panel (A) shows the atlas and the subject's brain with large left temporal infarct. Panel (B) illustrates whole brain segmentation, cortical and lateral ventricular surfaces. Note that the cortical surface of the subject's brain partially misses the temporal lobe. Panel (C) shows the extracted individual anatomical features, including the cortical surface without infarcted regions (red) and gyral and sulcal curves. Lastly, these features are incorporated in large deformation diffeomorphic metric mapping (LDDMM) for aligning the infarcted brain to the atlas.