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Consistent cortical reconstruction and multi-atlas brain segmentation

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ABSTRACT

Whole brain segmentation and cortical surface reconstruction are two essential techniques for investigating the human brain. Spatial inconsistences, which can hinder further integrated analyses of brain structure, can result due to these two tasks typically being conducted independently of each other. FreeSurfer obtains self-consistent whole brain segmentations and cortical surfaces. It starts with subcortical segmentation, then carries out cortical surface reconstruction, and ends with cortical segmentation and labeling. However, this "segmentation to surface to parcellation" strategy has shown limitations in various cohorts such as older populations with large ventricles. In this work, we propose a novel "multi-atlas segmentation to surface" method called Multi-atlas CRUISE (MaCRUISE), which achieves self-consistent whole brain segmentations and cortical surfaces by combining multi-atlas segmentation with the cortical reconstruction method CRUISE. A modification called MaCRUISE$^+$ is designed to perform well when white matter lesions are present. Comparing to the benchmarks CRUISE and FreeSurfer, the surface accuracy of MaCRUISE and MaCRUISE$^+$ is validated using two independent datasets with expertly placed cortical landmarks. A third independent dataset with expertly delineated volumetric labels is employed to compare segmentation performance. Finally, 200 MR volumetric images from an older adult sample are used to assess the robustness of MaCRUISE and FreeSurfer. The advantages of MaCRUISE are: (1) MaCRUISE constructs self-consistent voxelwise segmentations and cortical surfaces, while MaCRUISE$^+$ is robust to white matter pathology. (2) MaCRUISE achieves more accurate whole brain segmentations than independently conducting the multi-atlas segmentation. (3) MaCRUISE is comparable in accuracy to FreeSurfer (when FreeSurfer does not exhibit global failures) while achieving greater robustness across an older adult population. MaCRUISE has been made freely available in open source.

Introduction

Whole brain segmentation and cortical surface reconstruction are two essential automatic techniques for quantitatively investigating MR images (Balafar et al., 2010; Cootes et al., 2001; Lim and Haron, 2014; Pham and Prince, 1999; Van Leemput et al., 1999). Magnetic resonance (MR) images provide morphometric measurements such as region of interest volume (Brewer, 2009; Brewer et al., 2009; Fischl et al., 2002; Keshavan et al., 1995), cortical thickness (Fischl and Dale, 2000; Han et al., 2006; MacDonald et al., 2000), and surface area (Fan et al., 2012; Winkler et al., 2012) using either manual delineation or automatic medical image processing methods (Feczko et al., 2009; Symms et al., 2004). Manual investigation is extremely resource consuming, so validated automatic methods (Cocosco et al., 2003; Van Leemput et al., 1999; Wells et al., 1996) are overwhelmingly preferred.

Atlas-based segmentation assigns tissue labels to the voxels of unlabeled images using a pairing of an anatomical MR image and a corresponding manual segmentation (Cabezas et al., 2011). The pair of images is commonly referred as an atlas. Initially, labels were transferred from a single atlas to a target by image registration (Gass et al., 2013; Guimond et al., 2000; Wu et al., 2007). However, single-atlas segmentation has difficulty capturing large inter-subject anatomical variation (Doan et al., 2010). As reviewed in (Iglesias and Sabuncu, 2015) the *de facto* standard atlas-based segmentation paradigm, has become to use multiple atlases and carry out label combination (Aljabar et al., 2009; Artaechevarria et al., 2009; Asman et al., 2014; Asman and

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Landman, 2013; Coupé et al., 2011; Heckemann et al., 2006; Iglesias and Sabuncu, 2015; Isgum et al., 2009; Rohlfing et al., 2004; Sabuncu et al., 2010; Wang et al., 2013; Warfield et al., 2004).

Cortical reconstruction, the localization and representation of human cortical surfaces, is another widely used automatic technique in neuroscience (Dale et al., 1999; Kim et al., 2005; Liu et al., 2008; MacDonald et al., 2000; Shattuck and Leahy, 2002; Xu et al., 1999). Cortical reconstruction has been key to surface based registration (Fischl et al., 1999b; Lyttelton et al., 2007; Tosun and Prince, 2008; Tosun et al., 2004; Yeo et al., 2010), cortical labeling (Desikan et al., 2006; Destrieux et al., 2010; Fischl et al. 2004b), population-based probabilistic atlas generation (Thompson et al., 2001), and surface based morphometry (Chung et al., 2003; Fornito et al., 2008).

Spatial inconsistences that can hinder further brain morphometry analyses might develop because brain segmentation and cortical reconstruction are typically conducted separately. There are limited reports of methods for consistent whole brain volumetric segmentation and cortical surface reconstruction (Fischl, 2012; Han et al., 2004; Stewart et al., 2012). FreeSurfer is a well-known method for whole brain segmentation and cortical reconstruction that has been widely accepted as the *de facto* standard of brain segmentation (Dale et al., 1999; Fischl, 2012; Fischl et al., 1999a). FreeSurfer first automatically labels whole brain image volumes as gray matter (GM), white matter (WM), cerebrospinal fluid (CSF), and subcortical regions by combining a Markov random field (MRF) and probabilistic atlases into a Bayesian framework (Fischl et al., 2002; Fischl et al. 2004a; Han and Fischl, 2007). Then, an outer (or pial) surface is reconstructed based on the GM/CSF boundaries while an inner surface is reconstructed based on the GM/WM interface (Dale et al., 1999). Finally, the cortical GM regions are labeled based on a surface parcellation that forces the cortical segmentations to be consistent with the surfaces (Desikan et al., 2006; Fischl et al., 2004c). However, since the latter steps strongly rely on the former steps in this "segmentation to surface reconstruction to parcellation" strategy, the cortical parcellation fails when the segmentations and surfaces are reconstructed incorrectly. FreeSurfer has yielded inaccurate whole brain segmentations and cortical surfaces in older adults typically with larger ventricles. When this happens, the resulting surface reconstruction and parcellation are inaccurate.

Cortical surface measurements from FreeSurfer have been evaluated against manual measurements in Alzheimer's disease (Lehmann et al., 2010) and post-mortem histologic measurements (Cardinale et al., 2014). In both cases, FreeSurfer surface estimates showed a high level of correspondence with the manual estimates. Thus, alternative cortical surface algorithms should be consistent with FreeSurfer as long as FreeSurfer operates as intended. Substantial differences would indicate a failure of either FreeSurfer or the novel method. FreeSurfer is not the only approach for segmenting cortical surfaces. Cortical Reconstruction using Implicit Surface Evolution (CRUISE) (Han et al., 2004; Landman et al., 2013; Shiee et al., 2014) is a well-validated method that reconstructs consistent cortical surfaces and fuzzy segmentation (Bazin and Pham, 2007, 2008; Han et al., 2002).

In this paper, we propose a novel "multi-atlas segmentation to surface" method called Multi-atlas Cortical Reconstruction Using Implicit Surface Evolution (MaCRUISE). MaCRUISE simultaneously obtains 133 volumetric labels from a single multi-atlas segmentation and achieves volume consistent and robust cortical surfaces based on the same segmentation. Multi-atlas segmentation is performed with Nonlocal Spatial Staple (NLSS) (Asman and Landman, 2012, 2013). The main contribution of this work is to integrate cortical reconstruction and multi-atlas segmentation. Specifically: (1) MaCRUISE obtains self-consistent whole brain multi-atlas segmentation (133 labels) and cortical surfaces without compromising surface accuracy. (2) MaCRUISE achieves more accurate volumetric segmentations than a traditional multi-atlas framework. (3) While both deriving consistent whole brain segmentations and cortical surfaces, MaCRUISE is comparable in accuracy to FreeSurfer while achieving greater robustness across an elderly population. Notably, we do not seek to "outperform" FreeSurfer or CRUISE in terms of absolutely accuracy for cases in which these methods work as designed since they have both been extensively validated with respect to human expertise.

This work extends previous conference work (Huo et al., 2016). Herein, we present a more complete description of the MaCRUISE and a more thorough analysis of the performance on an extended dataset. Additionally, we introduce MaCRUISE$^+$ (by extending MaCRUISE using the CRUISE$^+$ approach (Shiee et al., 2014)) as a method to reconstruct accurate cortical surfaces and volumetric segmentations when multiple sclerosis (MS) lesions are present.

Theory and implementation

MaCRUISE is a method that produces consistent multi-atlas segmentations and cortical reconstruction from T1-weighted MR images (Fig. 1). First, cortical surfaces are reconstructed based on estimated tissue class memberships and multi-atlas boundary information. Second, multi-atlas segmentations are refined by the reconstructed cortical surfaces.

Preprocessing

Images are bias corrected with N4 (Tustison et al., 2010) prior to being used as inputs for multi-atlas segmentation. The bias corrected images are skull stripped with SPECTRE (Carass et al., 2011) and processed by dura stripping (Shiee et al., 2014) in preparation for TOADS.

Segmentation

Multi-atlas segmentation

Multi-atlas segmentation is performed with 45 MPRAGE images from the Open Access Series on Imaging Studies (OASIS) dataset (Marcus et al., 2007). The images are expertly delineated using 133 labels (132 brain regions and 1 background) according to the BrainCOLOR protocol (Klein et al., 2010). All of the 45 OASIS atlases are available from Neuromorphometrics Inc. (http://www.neuromorphometrics.com/) and 35 of the atlases are freely available from the MICCAI 2012 Grand Challenge and Workshop on Multi-Atlas Labeling (Landman and Warfield, 2012) (https://masi.vuse.vanderbilt.edu/workshop2012/).

Briefly, each target image is first affinely registered (Ourselin et al., 2001) to the MNI305 atlas (Evans et al., 1993). Following (Asman et al., 2015; Asman and Landman, 2013), the 15 closest atlases for each target image are selected from the 45 OASIS atlases using PCA projection. The 15 selected atlases are non-rigidly registered to the target image (Avants et al., 2008) and non-local spatial staple label fusion (NLSS) (Asman and Landman, 2012, 2013) is used to combine the labels from each atlas to the target image. For non-rigid registration, we use symmetric image normalization (SyN), with a cross correlation similarity metric convergence threshold of 10^{-9} and convergence window size of 15, provided by the Advanced Normalization Tools (ANTs) software (Avants et al., 2008). After multi-atlas labeling, each voxel in the brain is assigned to one of the 133 labels in the BrainCOLOR protocol.

To assist with the cortical reconstruction framework in CRUISE, all cortical GM labels are combined into a single GM segmentation (M_{GM}). All WM labels and several subcortical labels (nucleus accumbens, amygdala, lateral ventricle, pallidum, putamen, thalamus, and ventral diencephalon) are combined into a single "pseudo-WM" segmentation (M_{WM}). The "pseudo-WM" subcortical labels are used to define M_{WM} to mimic the CRUISE "Autofill" procedure (Han et al., 2004). Finally, M_{GM}, M_{WM}, and the remaining subcortical labels (hippocampus, amygdala, basal forebrain, and inferior lateral ventricle) are grouped together to form a cerebrum segmentation M_{Cerebrum} (Fig. 2).

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