NeuroImage 165 (2018) 11–26

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Advantages of cortical surface reconstruction using submillimeter 7 T MEMPRAGE

Natalia Zaretskaya [a,b,c,d,*], Bruce Fischl [d,e,f], Martin Reuter [d,e,f,g], Ville Renvall [h], Jonathan R. Polimeni [d,e,i]

[a] Centre for Integrative Neuroscience, University of Tuebingen, Tuebingen, Germany
[b] Department of Psychology, University of Tübingen, Tübingen, Germany
[c] Max Planck Institute for Biological Cybernetics, Tübingen, Germany
[d] Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA
[e] Department of Radiology, Harvard Medical School, Boston, MA, USA
[f] Computer Science and AI Lab (CSAIL), Massachusetts Institute of Technology, Cambridge, MA, USA
[g] German Center for Neurodegenerative Diseases, DZNE, Bonn, Germany
[h] Department of Neuroscience and Biomedical Engineering, Aalto University School of Science, Espoo, Finland
[i] Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA, USA

ARTICLE INFO

Keywords:
FreeSurfer
Cortex
Surface
MPRAGE
Thickness

ABSTRACT

Recent advances in MR technology have enabled increased spatial resolution for routine functional and anatomical imaging, which has created demand for software tools that are able to process these data. The availability of high-resolution data also raises the question of whether higher resolution leads to substantial gains in accuracy of quantitative morphometric neuroimaging procedures, in particular the cortical surface reconstruction and cortical thickness estimation. In this study we adapted the FreeSurfer cortical surface reconstruction pipeline to process structural data at native submillimeter resolution. We then quantified the differences in surface placement between meshes generated from (0.75 mm)^3 isotropic resolution data acquired in 39 volunteers and the same data downsampled to the conventional 1 mm^3 voxel size. We find that when processed at native resolution, cortex is estimated to be thinner in most areas, but thicker around the Cingulate and the Calcarine sulci as well as in the posterior bank of the Central sulcus. Thickness differences are driven by two kinds of effects. First, the gray–white surface is found closer to the white matter, especially in cortical areas with high myelin content, and thus low contrast, such as the Calcarine and the Central sulci, causing local increases in thickness estimates. Second, the gray–CSF surface is placed more interiorly, especially in the deep sulci, contributing to local decreases in thickness estimates. We suggest that both effects are due to reduced partial volume effects at higher spatial resolution. Submillimeter voxel sizes can therefore provide improved accuracy for measuring cortical thickness.

Introduction

Two major recent advances in Magnetic Resonance Imaging (MRI) hardware and methodology have allowed researchers to considerably increase the spatial resolution of functional and structural brain images. First, the magnetic field strength of the modern MRI systems has increased from the standard 3 T–7 T and higher, allowing for higher signal-to-noise ratio and (in some cases) enhanced contrast of the acquired data (Budinger et al., 2016; Budinger and Bird, 2017; Ertürk et al., 2017; Pohmann et al., 2016; Uğurbil, 2012). Second, significant improvements in the receiver coil design have enabled the use of accelerated parallel imaging, which allows one to reduce image distortions that are particularly prominent at ultra-high field (Setsompop et al., 2016). Together, these major advances permit routine measurement of MRI signal from voxels that are less than a cubic millimeter in size.

Improved spatial resolution of MRI scans is expected to benefit several fields of neuroscience. First, it can potentially improve the accuracy of quantitative morphometric imaging procedures, in particular cortical thickness estimation, which is an important marker of cortical plasticity (Anderson et al., 2002; Bermudez et al., 2009; Engvig et al., 2010; Lazar et al., 2005), healthy aging (Salat et al., 2004) as well as neurodegeneration (Du et al., 2007; Lerch et al., 2005). Second, it can

* Corresponding author. Centre for Integrative Neuroscience, University of Tübingen, Otfried-Müller-Str. 25, 72076 Tübingen, Germany.
E-mail address: natalia.zaretskaya@cin.uni-tuebingen.de (N. Zaretskaya).

https://doi.org/10.1016/j.neuroimage.2017.09.060
Received 7 June 2017; Received in revised form 9 September 2017; Accepted 28 September 2017
Available online 29 September 2017
1053-8119/

allow improved imaging of smaller brain structures like the subthalamic nucleus (Keuken et al., 2013), hypothalamus (Schindler et al., 2013), and various midbrain and brainstem nuclei (Satpute et al., 2013). Finally, smaller voxels allow researchers to non-invasively record structural signals (Cohen-Adad et al., 2011; Fracasso et al., 2016; Trampel et al., 2011), including diffusion imaging (Kleinnijenhuis et al., 2015; McNab et al., 2013), as well as functional signals (Huber et al., 2015; Kok et al., 2016; Maass et al., 2014; Muckli et al., 2015; Nasr et al., 2016; Olman et al., 2012; Polimeni et al., 2010) at different cortical depths in order to examine functional and structural changes imparted by the cortical laminar architecture. Correct measurement of these signals in a depth-resolved manner depends critically on accurate and reliable determination of the inner and outer boundaries of the gray matter sheet.

Higher resolution is expected to improve the accuracy of cortical surface reconstruction for both laminar imaging and thickness analysis, and several software tools have recently been newly developed or adjusted to process high resolutions structural data (Bazin et al., 2014; Goebel, 2012). However, an explicit demonstration and detailed characterization of the advantages of high resolution scans is sparse. In fact, submillimeter voxel resolution is not always necessary to detect differences in cortical thickness that are only a fraction of a voxel. In particular, due to the fact that both the radius of curvature and thickness of the human cortex are greater than 1 mm, surface-based approaches for measuring cortical thickness such as those used in FreeSurfer or CIVET (Kim et al., 2005), can achieve submillimeter accuracy with conventional 1 mm^3 voxel size by interpolation and partial volume modeling (Fischl and Dale, 2000). Indeed the accuracy (Kuperberg et al., 2003; Rosas et al., 2002) and scan-rescan precision (Fujimoto et al., 2014; Han et al., 2006) for FreeSurfer-generated surfaces and thickness estimates has been reported to be well below 1 mm.

Nevertheless, there have been some reports that even with surface-based thickness measures such as those provided by FreeSurfer, spatial resolution may influence surface placement and cortical thickness estimation, presumably because of reduced partial volume effects at higher resolution. For example, Glasser et al. (2013) first processed the downsampled version of their high-resolution (0.7 $mm)^3$ isotropic structural scans using FreeSurfer, and then used the original high-resolution images to adjust the position of the surfaces as a part of the standard processing pipeline for the Human Connectome Project (Fig. 13 in Glasser et al., 2013). They noticed that in thin and densely myelinated regions, such as the Calcarine or the Central sulci, the inner surface at the gray–white matter intersection (hereafter called the gray–white surface) can be placed too far into the gray matter if the conventional low-resolution 1 mm data are used, but the position of this surface appears to be correct after surface adjustment using a high-resolution scan. They further hypothesized that in heavily myelinated regions low-resolution images produce stronger partial volume effects, because more myelin leads to stronger bias of the T_1-weighted gray matter voxel intensities towards brighter values, which, in turn, leads to surface displacement. This observation was based on a few individual examples and has neither been investigated systematically nor quantified. Another, more systematic study found that the image resolution directly affects cortical thickness estimates (Lüsebrink et al., 2013). High-resolution images yielded smaller cortical thickness values compared to a conventional 1 mm^3 resolution in frontal, parietal and occipital lobes. This study left unclear whether these differences in thickness are due to altered definition of the inner surface between gray and white matter, due to altered definition of the outer surface between gray matter and the cerebrospinal fluid (CSF), or both. In addition, because frontal, parietal and occipital lobes were each analyzed in this study as a whole, it remains unclear whether there are more fine-grained regional variations in thickness difference, e.g. due to known variability in myelin content, as suggested by Glasser et al. (2013). Finally, the temporal lobe was not analyzed in this study because of the poor data quality at ultra-high field strengths due to a combination of RF transmit effects (caused by dielectric effects found near the temporal pole) (Collins et al., 2005; Collins and Smith, 2001) and off-resonance effects (caused by the susceptibility gradient imparted by the nearby ear canals) (Jezzard and Balaban, 1995; Wrede et al., 2012) typically found within the temporal lobe of the adult human brain.

In the present study we aimed at systematically quantifying the differences in surface reconstruction and cortical thickness estimation derived from images processed at standard 1 mm^3 and native submillimeter resolutions across the whole cortical surface. We adapted the full FreeSurfer cortical surface reconstruction pipeline (Fischl, 2012), which was originally designed to process 1 mm^3 structural images, to process structural data at native submillimeter resolution. We then quantified the differences in surface placement between meshes generated from high-resolution data and the same data downsampled to the conventional 1 mm^3 voxel size. We found systematic differences in thickness estimates across 39 subjects that varied with cortical location, with high-resolution estimates being larger in some areas and smaller in others. In addition, we determined that resolution-induced variations in the cortical thickness estimates are due to the different placement of both the gray–white matter surface, which is placed tighter around the white matter volume at high resolution, and gray–CSF surface, which is placed tighter around the gray matter at high resolution. Visual comparison of surfaces generated from 1 mm^3 resolution and submillimeter resolution suggests that high-resolution gray–white surface placement may be consistently more accurate in thin regions with high myelin content, and the gray–CSF surface may be consistently more accurate deep in the more compact sulci.

Materials and methods

Data

Forty-four healthy adults volunteered to participate in the study. Written informed consent was obtained from each participant before the experiment in accordance with our institution's Human Research Committee. For each subject we acquired a T_1-weighted structural image using a 7 T S whole-body scanner (Siemens Healthcare, Erlangen, Germany) equipped with body gradients and a custom-made 31-channel brain receive coil array and bandpass circularly-polarized birdcage volume transmit coil (Keil et al., 2010). The images were acquired using the multi-echo MPRAGE (MEMPRAGE) method (van der Kouwe et al., 2008) with a 13 ms FOCI adiabatic inversion pulse (Hurley et al., 2010) and non-selective excitation pulse at (0.75 $mm)^3$ resolution in a sagittal acquisition with the following imaging parameters: TI = 1100 ms, two echoes at TE = 1.76, 3.70 ms, TR = 2530 ms, flip angle = 7°, 208 slices per slab, matrix size 320 × 320, echo spacing = 6.2 ms, bandwidth = 651 Hz/pixel, A≫P primary phase encode and L≫R secondary phase encode, and $R = 2$ acceleration (32 reference lines) with online GRAPPA reconstruction (total acquisition time: 7 min 24 s).

Data analysis

Updates to FreeSurfer

Because FreeSurfer was originally designed to process images at 1 mm^3 resolution, previous attempts to assess cortical surface reconstruction for submillimeter resolution had to partly rely on the standard FreeSurfer processing pipeline, which downsamples any submillimeter input image data to 1 mm^3 (Glasser et al., 2013; Lüsebrink et al., 2013). For the current study, several modifications to the FreeSurfer software have been made to process the data at native submillimeter resolution. In particular, the following FreeSurfer routines were adjusted: registration to the Gaussian classifier atlas (*mri_em_register*, *mri_ca_register*) (Fischl et al., 2002), intensity normalization (*mri_normalize*) (Dale et al., 1999), and skull stripping (*mri_watershed*) (Ségonne et al., 2004). These modifications were related exclusively to removing the constraint in the software that only 1 mm^3 voxel sizes could be used as input, and did not address any 7 T-specific processing (such as adjustments for differences in tissue contrast, stronger intensity inhomogeneity, or artifacts due to