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Advantages of cortical surface reconstruction using submillimeter 7 Tesla MEMPRAGE

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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 isotropic resolution data acquired in 39 volunteers and the same data downsampled to the conventional 1 mm³ 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.

Keywords

FreeSurfer; cortex; surface; MPRAGE; 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 to 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; Urbil, 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 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 mm³ 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 have 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 T₁-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 mm³ 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 mm³ 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 mm³ 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 mm³ 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 mm³ 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 T₁-weighted structural image using a 7 T Siemens 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 mm³ 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 mm³ (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 mm³ voxel sizes could be used as input, and did not address any 7T-specific processing (such as adjustments for differences in tissue contrast, stronger intensity inhomogeneity, or artifacts due to bright blood vessels). These changes are included in FreeSurfer v6.0 and details on how to perform the reconstruction at native resolution are provided online.¹

¹The FreeSurfer SubmillimeterRecon wiki page, found at <https://surfer.nmr.mgh.harvard.edu/fswiki/SubmillimeterRecon>

7 T specific processing—Due to the stronger transmit and receive field inhomogeneity at 7 T compared to 3 T, prior to cortical surface reconstruction each structural volume was intensity bias corrected using the unified segmentation routine (Ashburner and Friston, 2005) implementation in the SPM12 software using custom parameters (FWHM = 18 mm, sampling distance = 2 mm) (Uwano et al., 2014). Since custom bias correction was performed prior to the different cortical surface reconstruction streams, any differences between the results generated by the streams cannot be attributed to differences in bias correction, in addition, to account for darker gray matter intensities in the temporal lobe areas, which are likely to be due to altered transmit efficiency in these areas, we used custom values for the `mris_make_surfaces` command (e.g. `mris_make_surfaces -max_gray_at_csf_border 60 -max_csf 35` versus default values of 75 and 40, respectively). These values were identical for all processing streams and thus cannot account for the observed differences in surface placement.

Cortical surface reconstruction—Following the bias correction step each volume was processed three times, each time using different processing streams for comparison (see Fig. 1). In the first (default) FreeSurfer stream, each image was downsampled to 1 mm isotropic voxels using trilinear (default) interpolation (labeled “low-resolution stream”). In the second stream the volumes were processed at native resolution (labeled “high-resolution stream”). Because higher resolution input images consequently lead to generating surface meshes with higher vertex density, we adjusted the maximum number of iterations in the surface inflation step for both streams from the default 10 to 50. Please note that FreeSurfer’s inflation routine has an internal criterion on when to stop inflation, and the larger number here is needed only to avoid the inflation procedure exiting prematurely. Having a sufficiently inflated surface is essential for correctly projecting the surface onto a sphere and the subsequent topological defect identification and fixing (Fischl et al., 2001; Segonne et al., 2007). Otherwise the high-resolution stream was identical to the low-resolution stream, both of which were processed with identical parameters. In the third stream (“SNR-matched stream”), we used the downsampled 1 mm³ images from the low-resolution stream with added Gaussian white noise to match the image SNR of the volumes in the high-resolution stream. The third stream served as an important control because downsampling volumes to 1 mm³ leads to an increase in image SNR, and hence any difference in surface quality could be explained by SNR differences rather than differences in resolution. To match the SNR, we first measured the standard deviation of white matter voxel intensities in each high-resolution volume and then found a standard deviation of added noise that would lead to an equivalent SNR in the low-resolution volume. Otherwise the SNR-matched stream was identical to the low-resolution stream.

Note that we deliberately adopted the approach of comparing the same image at native and downsampled resolution rather than acquiring two datasets with different resolutions as has been done previously (Lüsebrink et al., 2013). The latter approach has the drawback that it is difficult to match the tissue contrast and the motion artifact levels in the two images, since higher-resolution data necessitate changing several protocol parameters that also affect contrast and require and longer acquisition durations that are more vulnerable to head motion.

Sufficient image contrast-to-noise ratio is crucial for successful surface reconstruction. While at 3 T the standard isotropic voxel size of 1 mm is common, the attempt to push the spatial resolution at higher fields is likely to result in protocols with a range of possible voxel sizes below 1 mm, resulting in a wide range of image SNR and tissue contrast. Although it is difficult to state the contrast and SNR levels that are sufficient for accurate FreeSurfer reconstruction, for future comparisons we report SNR, CNR as well as contrast values for our dataset. To determine SNR and CNR, we used volumetric segmentation provided by FreeSurfer (aseg.mgz) to determine voxels corresponding to white matter and gray matter in the image data. SNR was defined as average intensity of white matter voxels divided their standard deviation. CNR was defined as the difference between the average white matter and gray matter voxel intensities divided by the standard deviation of white matter intensities. In addition, we used “percent gray-white contrast”, expressed as $(\text{white} - \text{gray}) / (\text{white} + \text{gray}) \cdot 100\%$ at every vertex, with white intensity sampled 1 mm below the gray-white surface boundary, and gray intensity sampled at 30% cortical depth, to characterize the quality of these data. For every subject and hemisphere, we calculated the mean percent contrast as well as its variation across the cortical surface (expressed as the standard deviation of contrast values). We also repeated the same procedure for the “Buckner40”² dataset. This dataset comprises a subset of 40 images with $1 \times 1 \times 1.25 \text{ mm}^3$ resolution acquired at 1.5 T taken from a larger study (Marcus et al., 2007). It is routinely used to test and compare different FreeSurfer versions because of a wide age range of subjects included in the dataset as well as its realistic level of quality. We have chosen to use it here for comparison with our dataset because it is considered typical data for FreeSurfer.

Vertex-wise surface comparison—Comparing local cortical thickness and local surface position between low-resolution and high-resolution scans is not trivial because the low-resolution and high-resolution surface meshes do not have a natural vertex correspondence. To overcome this problem, we resampled each triangular surface mesh generated from low-resolution data onto the corresponding triangular surface mesh generated from high-resolution data and vice versa as follows: For every vertex in a low-resolution surface mesh we found the closest point on the high-resolution surface mesh (which typically fell within a triangle face of the mesh), and defined a point at that location on the high-resolution surface mesh (subsequently referred to as “sparse” meshes). This procedure is illustrated schematically in Fig. 2A. The subsequent comparisons (distance and thickness difference) were then computed between the original vertex and this newly placed point. To avoid any potential bias, we repeated the procedure in the opposite direction, i.e. by mapping the high-resolution surfaces onto the low-resolution data in the same way (subsequently referred to as “dense” meshes). This procedure yielded four pairs of surfaces: (1) sparse meshes of gray-white and gray-CSF surfaces from the low-resolution stream, (2) sparse meshes of gray-white and gray-CSF surfaces from high-resolution stream, (3) dense meshes of gray-white and gray-CSF surfaces from the low-resolution stream, (4) dense meshes of gray-white and gray-CSF surfaces from the high-resolution stream. Thus, each surface in each stream had a dense and a sparse version.

²Details on the dataset and testing are provided online at: <https://surfer.nmr.mgh.harvard.edu/fswiki/Buckner40Adni60Testing>

Low-resolution and high-resolution stream comparison—We first compared cortical thickness estimates (distance between gray–white and gray–CSF surfaces) from the two streams. In order to do this, we computed cortical thickness for each surface pair (which have a natural vertex correspondence in FreeSurfer, because the outer surface is derived from the inner surface) using the FreeSurfer command *mris_thickness* at every vertex with inner and outer surface as inputs) (Fischl and Dale, 2000). We then calculated the difference between thickness estimates from high-resolution and low-resolution streams. This we did once for the sparse meshes and once for the dense meshes. Each of the two difference maps was then projected onto the FreeSurfer *fsaverage* template with 163,842 vertices and smoothed with 3 mm FWHM 2-dimensional Gaussian kernel to identify spatial trends in the maps across subjects. After the projection onto the *fsaverage* template mesh, which equates the number of vertices, the sparser and denser thickness maps could be averaged, yielding one average thickness difference value per vertex on the *fsaverage* surface atlas (see Fig. 2B for a schematic overview of the process).

Potential differences in cortical thickness may be driven by either the gray–white surface displacement, the gray–CSF surface displacement, or by both. Therefore, to investigate what drives any observed cortical thickness differences, for each surface type we computed the distance between the surfaces derived from the low-resolution and the high-resolution streams at every vertex location to quantify the discrepancies between the positioning of the surfaces using the procedure developed in a previous study (Fujimoto et al., 2014). We employed the following convention: placement of high-resolution surfaces interiorly to the low-resolution surfaces corresponded to negative displacement, whereas placement of high-resolution surfaces outside of the low-resolution ones to positive displacement. Similar to thickness, each displacement map was then projected onto the FreeSurfer *fsaverage* template, spatially smoothed with 3 mm FWHM Gaussian kernel, and displacement maps derived from sparser and denser meshes were averaged (see Fig. 2C for a schematic overview of the process). Characterizing surface displacement also helped us to assess the relative accuracy of surface placement (see below, “Assessing accuracy of surface placement”).

Since cortical surface reconstruction at native resolution comes at a price of higher computational demands and longer processing times, in addition to the main comparisons described above we performed a surface mesh repositioning procedure similar to the one suggested by the HCP-pipeline (Glasser et al., 2013) (“surface repositioning stream”, for details see Supplemental text).

In this study we generated 1 mm isotropic image volumes from the acquired 0.75 mm isotropic data through downsampling and interpolation instead of acquiring a second dataset at native 1 mm isotropic resolution. This strategy was adopted in order to match tissue contrast levels between the two resolutions, and noise was added to the 1 mm data in order to match image SNR as well. We note that downsampling 0.75 mm data to a 1 mm grid can cause small variations over space in aliasing and in effective image resolution if the sampling grids are perfectly aligned (because the interpolation kernel weights will vary over the grid), although these variations are expected to be small relative to the final voxel size. However, in the downsampling implemented here, the low-resolution voxel grid was moved

to a new location relative to the high-resolution voxel grid, which included rotation, assuring an even spread of these downsampling artifacts throughout the image.

We used trilinear interpolation method for downsampling, because it is the default interpolation method for downsampling in FreeSurfer. Trilinear interpolation, as opposed to e.g. cubic interpolation, may result in additional blurring, which may affect surface placement. To help determine how much of the surface displacement can be attributed to blurring induced by trilinear interpolation rather than to the change in the voxel grid spacing, we conducted an additional comparison between low-resolution surfaces generated after downsampling with trilinear interpolation and those generated after cubic interpolation. The downsampling in both cases was performed using FreeSurfer's *mri_convert* command with corresponding interpolation options (e.g. *mri_convert -c -rt trilinear* or *mri_convert -c -rt cubic*). Although the main goal of our study was to determine whether there are advantages of using the native stream compared to default downsampling stream, and not to study the impact of different interpolation methods, this comparison provides a means to estimate how much of the difference in surface placement can be attributed to the blurring induced by trilinear interpolation.

Group analysis—To determine whether and at which cortical locations low-resolution and high-resolution streams systematically diverged in their cortical thickness estimates as well as in surface positioning, we conducted a group analysis across subjects. At every vertex location on the *fsaverage* surface atlas we tested whether the low-resolution and the high-resolution streams were significantly different using the one-sample t-test. This was calculated separately for the thickness difference maps, gray–white surface displacement maps, and gray–CSF displacement maps. To correct the significance level for multiple comparisons we employed the false discovery rate (FDR) correction (Genovese et al., 2002) at $q = 0.05$.

We then attempted to determine whether any systematic surface displacement we find is related to local contrast, image intensity, or surface mean curvature. We additionally established a relationship between (1) gray–white surface displacement and local percent gray–white matter contrast (defined as white intensity minus gray intensity divided by the sum of the two intensities, multiplied by 100 %), (2) gray–CSF surface placement and local gray matter intensity (because the image intensities found in voxels outside of the gray matter varies—being sometimes dark CSF, sometimes gray matter of the opposite sulcus and sometimes bright vessels—the calculation of an analogous local contrast measure equivalent to the local gray–white contrast is challenging), (3) gray–white surface displacement and local gray–white surface curvature, and (4) gray–CSF surface displacement and gray–CSF surface curvature. Gray–white contrast and gray matter intensity were drawn from the bias-field-corrected image that was used as input to the FreeSurfer reconstruction; these two parameters were considered to directly test the hypothesis that high resolution helps more accurate surface placement in regions with low tissue contrast, as suggested by Glasser et al. (2013). Local surface mean curvature was considered because our accuracy assessment (described below) suggested that, at least for the gray–CSF surface, disagreement between the high-resolution and low-resolution surfaces is most consistently observed in the sulcal fundi (see Fig. 9). All four measures were derived from the low-resolution analysis stream.

Contrast, intensity, and the two curvature maps were first projected onto *fsaverage* surface and smoothed with 3 mm FWHM Gaussian kernel prior to analysis. Following this, to identify any relationships between these metrics and surface placement we computed 2D histograms of each of the above measures versus surface displacement for every subject, and averaged the histograms across subjects. Values in each map were binned into 101 bins (curvature bin centers ranged from -1 to 1 mm^{-1} , percent gray–white matter contrast ranged from 0 to 100, the gray matter intensity ranged from 120 to 220), and the displacement values were binned into 301 bins (ranging from -1.5 to 1.5 mm). Each group average 2D histogram was then plotted using log color scale for visualization.

Assessing accuracy of the surface placement—Assessing accuracy of automatic surface placement in MRI scans is problematic due to the lack of “ground truth” data. However, in the cases where the placement of the surface is obviously erroneous one should be able to identify the error by visual inspection. Therefore to assess the accuracy of surface placement we adopted the following approach. First, for each of the statistical comparisons (gray–white displacement, gray–CSF displacement) we identified three locations with most consistent surface divergence in our sample of subjects. To identify these locations, we thresholded the significance maps at $p < 0.000001$ FDR-corrected, and examined the three most significant clusters per map (over both hemispheres). To ensure that we consider multiple distinct areas across the brain, if two clusters fell within the same anatomical parcellation label, only the single most significant cluster per label was considered. Although our improved acquisition allowed us to obtain sufficient image contrast in the problematic regions of the temporal lobe, the image quality in these regions was still inferior compared to the rest of the brain. We therefore decided not to consider clusters that fell onto one of the regions known to be affected by dielectric and off-resonance effects (according to the FreeSurfer parcellation scheme): temporal pole, entorhinal, parahippocampal, inferior temporal, fusiform, medial orbitofrontal, lateral orbitofrontal, frontal pole, altogether amounting to about 13% of the cortical surface (a map of these excluded regions is shown in Supplemental Fig. S1). For each of the three regions with the most consistent surface discrepancy in the group, we chose three *individual* subjects that showed maximal discrepancy between the streams at the *group* peak location. We then projected the location of the systematic discrepancy from the *fsaverage* group space into individual space of those subjects and inspected the surface placement at the projected location with the high-resolution image as background.

Results

Final dataset

One out of 44 volumes was excluded from analysis due to poor MR image quality. Out of the remaining 43 volumes, four failed in the SNR-matched stream due to large topological defects in the cortical surface reconstructions. The remaining volumes in all streams reconstructed successfully without manual intervention. We thus used 39 volumes, which were successfully reconstructed in *all* three streams, in further analysis [subject age (mean $\pm$ SD): 32.16 ± 7.85 , 19 females]. The average processing time for the low-resolution stream was 20.79 ± 4.36 hours (with one CPU core and 7 GB RAM), and for the high-resolution

stream 33.27 ± 8.76 hours (with two cores and 14 GB RAM). An example of high-resolution surface reconstruction is shown in Fig. 3.

The average SNR, CNR and percent contrast in our native resolution 7 T dataset after bias correction was 15.6 ± 1.1 , 3.9 ± 0.2 and $26.1 \pm 2.1\%$, respectively. For comparison, the corresponding values of the “Buckner40” 1.5 Tesla benchmarking dataset were 8.7 ± 0.6 , 3.2 ± 0.3 and $32.5 \pm 3.3\%$, respectively (see also Table 1). Hence, although the 7 T data has twice the SNR of the 1.5 T dataset, the resulting CNRs of the two datasets are comparable due to higher gray-white matter contrast of the 1.5 T data. Our data quality as determined by CNR is therefore slightly above the range of what is considered to be common for FreeSurfer surface reconstructions.

Cortical thickness differences

Comparison of cortical thickness measures derived from the two streams revealed that the high-resolution stream yielded overall smaller cortical thickness estimates (left whole-hemisphere average $\pm$ SD: -0.036 ± 0.030 mm $t(38) = -7.53$, $p < 0.001$; right hemisphere: -0.028 ± 0.026 mm $t(38) = -6.52$, $p < 0.001$), which is consistent with the previously reported result (Lüsebrink et al., 2013). This, however, was not true for all cortical areas, as evident from the vertex-wise thickness maps (Fig. 4). Although cortex was thinner in the majority of areas in the high-resolution stream, the largest differences in thickness estimates around the Calcarine sulcus, the Central sulcus and the Cingulate sulcus showed the opposite pattern. (Supplemental Table 2 in addition lists average thickness estimates derived from the two streams for every cortical region according to FreeSurfer parcellation scheme. We note, however, that some of the important vertex-wise results are not well represented in this ROI-wise analysis. For example, the opposite pattern of thickness difference between high- and low-resolution streams in the Postcentral sulcus is not reflected in this per-ROI average. This is likely due to the fact that FreeSurfer’s “postcentral” surface label includes both the Postcentral Gyrus and the posterior bank of the Central Sulcus, whereas the major change is happening in the Sulcus bank only.

The control analysis with matched SNR revealed a slight overall bias towards thicker cortex in the high-resolution stream, (left hemisphere mean 0.030 ± 0.043 mm, $t(38) = 4.30$, $p < 0.001$; right hemisphere mean 0.033 ± 0.041 mm, $t(38) = 4.97$, $p < 0.001$). However, similar to the main analysis, the thickness differences were highest around the Calcarine, the Central sulcus and the Cingulate and additionally in the Insula (see Supplemental Fig. S2 for whole-hemisphere matched SNR results). We thus confirmed that the largest thickness differences found between high-resolution and low-resolution streams are unlikely due to the superior SNR found in the downsampled/low-resolution data.

Gray–white and gray–CSF surface displacement

Thickness differences between the two streams are determined by the differences in gray–white and gray–CSF surface placement. Analysis of how surfaces generated by the high-resolution stream are displaced relative to the low-resolution stream revealed similar patterns for both surface types. High-resolution gray–white surfaces were systematically placed inside the low-resolution gray–white surfaces throughout the cortex (Fig. 5; left hemisphere

average $\pm$ SD: -0.104 ± 0.042 mm $t(38) = -15.56$ $p < 0.001$; right hemisphere: -0.112 ± 0.038 mm, $t(38) = -18.49$, $p < 0.001$). FreeSurfer thus systematically placed the surface “tighter” around white matter at higher-resolution. The control analysis with matched SNR showed a similar result (left hemisphere: -0.127 ± 0.062 , $t(38) = -12.88$, $p < 0.001$; right hemisphere: -0.124 ± 0.057 , $t = -13.57$, $p < 0.001$; see Supplemental Fig. S3A for whole-hemisphere maps).

The high resolution gray–CSF surfaces were also consistently positioned inside the low-resolution ones, with the exception of a location in the mid-anterior Cingulate sulcus, which showed the opposite pattern (left hemisphere mean displacement $\pm$ SD: -0.070 ± 0.017 mm, $t(38) = -25.27$, $p < 0.001$, right hemisphere mean -0.068 ± 0.017 mm, $t(38) = -25.50$, $p < 0.001$, Fig. 5B). The control analysis with matched SNR showed similar results (left hemisphere: -0.070 ± 0.026 mm, $t = -16.69$, $p < 0.001$; right hemisphere: -0.065 ± 0.024 mm, $t(38) = -17.058$, $p < 0.001$; Supplemental Fig. S3B).

Relationship between surface displacement and local image contrast

The relationship between gray–white surface displacement and the local gray–white matter contrast is shown in Fig. 6A. As suggested by Glasser et al. (2013), the strongest surface displacement occurs at cortical locations with low local contrast (see also Fig. 8). Notably, as the insets in Fig. 6A illustrate, low local contrast is observed around the Calcarine and the Central sulci, which also appear as areas with the largest gray–white surface displacement in Fig. 5A.

The relationship between gray matter intensity and gray–CSF surface displacement showed a similar, but less pronounced trend: the largest displacements tend to occur at locations with lower-than-average gray matter intensity values (Fig. 6B). At locations where gray matter is surrounded by CSF, which has darkest intensity values, this effect may be analogous to the low contrast effect observed for gray–white surface.

Relationship between surface displacement and surface curvature

The relationship between surface displacement and local curvature is shown in Fig. 7. The displacement of the two surfaces differs in that the gray–white surface displacement is dominated by locations with positive curvature, corresponding to the sulcal regions, while the gray–CSF surface displacement is dominated by locations with negative curvature, corresponding to the gyral regions, as can be seen by the peaks of the histograms in panel A and panel B, respectively. However, what the two histograms have in common is a trend towards the largest (negative) displacement occurring at vertices with negative curvature, which correspond to gyri.

Accuracy of surface placement

In addition to finding discrepancies in surface placement between the two streams, we also attempted to assess whether high-resolution surfaces are placed more accurately than the low-resolution ones, as has been previously suggested (Glasser et al., 2013).

For each surface type the three most significant clusters (at $p < 0.00001$ FDR-corrected, area threshold $>1 \text{ mm}^2$) of vertices where the surfaces diverged consistently in our group of subjects (as assessed by t-test) are listed in Table 2. A set of surfaces from the three subjects with the largest divergence between the low-resolution and high-resolution surfaces is displayed on a native-resolution volume for visual assessment in Fig. 8 and Fig. 9.

After visual inspection, the placement of the high-resolution gray–white matter surface deeper into the white matter appears more correct in the cingulate cortex (clusters 1 in Fig. 8). Particularly in the Cingulate sulcus high-resolution provides a clear advantage. Low-resolution surfaces may be misplaced in this area because the sulcus is very narrow and the partial volume effect at low resolution blurs the gray–white matter boundary in the depth of the sulcus. In the left Postcentral gyrus and the left Superior Parietal Cortex (Clusters 2 and in Fig. 8) the gray–white matter contrast is too low and the distance between the surfaces is too small to judge which of the surfaces is more accurate.

For the gray–CSF surface, no clear advantage can be observed for any of the examined clusters. Nevertheless, occasionally, gray–CSF surface seems to be more accurately placed at high resolution in the sulcus floor: when the sulcus is very narrow, partial volume effects cause low-resolution surfaces to be placed too superficially, whereas the surface reconstructed from high-resolution are correctly positioned deeper into the sulcus.

Effect of interpolation

To determine whether differences in surface placement between high-resolution and low-resolution streams can be explained by additional blurring due to the use of trilinear interpolation, we conducted an additional analysis comparing surfaces generated from 1 mm^3 data downsampled using trilinear and cubic interpolation methods. We found an overall tendency of the gray–white surfaces of the cubic-interpolated data to be placed inside those generated from the trilinearly-interpolated data, similar to the tendency seen in the native high-resolution stream (left hemisphere mean $\pm$ SD: $-0.022 \pm 0.029 \text{ mm}$, $t(38) = -4.81$, $p < 0.001$, right hemisphere mean $\pm$ SD: $-0.029 \pm 0.030 \text{ mm}$, $t(38) = -6.03$, $p < 0.001$). The same was true for the gray–CSF surfaces (left hemisphere mean $\pm$ SD: $-0.017 \pm 0.018 \text{ mm}$, $t(38) = -5.84$, $p < 0.001$; right hemisphere mean $\pm$ SD: $-0.019 \pm 0.014 \text{ mm}$, $t(38) = -8.32$, $p < 0.001$). Although the displacement *direction* of the low-resolution surfaces generated with cubic interpolation was overall similar to the high-resolution surfaces, the *magnitude* of this displacement was much smaller ($10\text{--}30 \text{ }\mu\text{m}$ displacement due to interpolation alone versus $100\text{--}130 \text{ }\mu\text{m}$ displacement due to interpolation and resolution). The differences in effect size are more prominent in the vertex-wise displacement maps provided in supplemental Fig. S7. Nevertheless, from this we can conclude that while there were detectable effects of the interpolation method on the surface placement seen across our group of subjects, these effects were small compared to the effect of voxel size.

Discussion

Our study shows that even a modest improvement in image resolution from 1 mm to 0.75 mm isotropic can significantly affect the position of reconstructed cortical surfaces and cortical thickness estimates derived from them. When processed at native resolution, most

cortical areas, and especially the Cingulate Cortex, Inferior Frontal and Temporal regions, were estimated to be thinner than these same regions in reconstructions from the low-resolution stream. However, a few areas, such as those around the Calcarine sulcus and the Postcentral gyrus, were systematically estimated to be thicker at high resolution. Analysis of surface displacement showed that the thickness differences in the Cingulate cortex, visual cortex and the Postcentral gyrus were mostly driven by the gray–white surface, which was placed “tighter” around the white matter at high resolution. Thickness estimates of the temporal lobe areas, in contradistinction, were driven more by the gray–CSF surface being placed “tighter” around the gray matter.

Relation to previous studies

Although there is increasing interest in comparing surface reconstruction results across software packages (Jeon et al., 2017; Lepage et al., 2017; Lewis et al., 2017), up to now only a few studies systematically examined the effect of resolution on cortical surface reconstruction. One of them used real, manually labeled scans to synthesize artificial MP2RAGE datasets with varying resolutions and SNR to study the impact of both parameters on the accuracy of segmentation and surface placement, while evaluating the performance of a newly developed processing pipeline “CBS tools” (Bazin et al., 2014). Perhaps unsurprisingly, this study found that higher resolution increases the overlap and reduces the average surface distance between the hand-labeled and automatically generated segmentations and surfaces. However, it left unclear how the individual surfaces are displaced relative to ground truth and whether there was any regional variation in the direction of surface placement akin to what we have observed in the current study. Interestingly, a comparison of the CBS processing pipeline with FreeSurfer revealed a comparably smaller effect of resolution on FreeSurfer-generated surfaces. One potential reason is that until version 6.0 FreeSurfer resampled any input to 1 mm isotropic voxel size. This study also revealed that FreeSurfer surface placement is relatively robust to SNR changes, which is consistent with our control analysis results using downsampled scans with matched SNR.

Another previous study attempting to examine differences in cortical thickness estimates used real human data acquired at different resolutions (Lüsebrink et al., 2013). This study found overall thinner cortex in high-resolution images. Lüsebrink et al. computed average thickness values over three lobes (frontal, parietal and occipital), leaving the temporal lobe out of their analysis due to poor image quality. We examined cortical thickness difference on a vertex-by-vertex basis. When averaged over the whole hemisphere, our results are consistent with the findings of Lüsebrink et al., despite the fact that this prior study compared different protocols with different resolutions, while here we compared the resolutions within the same protocol. However, our more detailed analysis reveals that differences in cortical thickness can go both ways, with surfaces generated from high-resolution data yielding consistently thicker or thinner cortical thickness estimates depending on the exact anatomical location. When averaging over the whole lobe, thinner values may drive the overall lobe-level mean, thus hiding the effect of smaller voxels producing thicker estimates as well.

Importantly, our study shows that both gray–white and gray–CSF surface placement can contribute to the final differences in cortical thickness between the two streams, and that the relative contribution of each surface depends on the brain area. Specifically, thicker cortex around the Central and Calcarine sulci in the high-resolution stream is primarily due to the gray–white surface being placed further into the white matter. In regions of the temporal lobe, in contrast, thinner cortex in the high-resolution stream is due to gray–CSF surface being positioned further into the gray matter.

We found that throughout each hemisphere high-resolution gray–white matter surfaces were displaced relative to the low-resolution surfaces, and were consistently placed further into the white matter. This agrees with a previous report by Glasser et al. (2013). Glasser et al. suggested that this effect is strongest in thin areas with high myelin content such as S1 and V1 (Glasser and Van Essen, 2011; Shafee et al., 2015) and is due to the fact that thin cortex, high myelin content, and stronger partial volume effects at lower resolution together cause gray matter in these regions to appear brighter and more similar to white matter. Our data confirm that throughout each hemisphere the most consistent across-subject gray–white surface displacement tends to happen in areas with low gray–white matter contrast. Both large gray–white surface displacement and the low gray–white contrast indeed coincided with the Calcarine and the Central sulci.

In addition to differences in gray–white matter surface placement, we also observed consistent displacement of the gray–CSF surfaces. Similar to the gray–white surfaces, high-resolution gray–CSF surfaces were mostly placed inside the low-resolution surfaces. This effect is particularly strong in the temporal lobe regions. One reason for this effect may be the same partial volume effects that influence the gray–white surface placement. We observed particularly low intensity of the gray matter in the temporal lobes, which may be due to the well-known issue of low transmit efficiency of excitation pulses at ultra-high field within the temporal cortex in the adult brain caused by dielectric effects. In particular, dark gray matter leads to reductions in the local gray–CSF contrast, which affects surface placement. Although the quality of our images was sufficient to perform surface reconstruction in the temporal lobes, further improvements need to be made in image acquisition techniques and caution must be taken when comparing cortical thickness data from ultra-high field scanners in the temporal lobe. Emerging technologies such as parallel transmit can help to increase RF transmit efficiency in these regions (Cloos et al., 2012).

Accuracy and precision of high-resolution surfaces

Our attempt to assess the accuracy of high-resolution surfaces revealed that in some cortical locations the surface divergence is so small that visual examination cannot resolve whether high-resolution surfaces are placed with higher accuracy than the standard resolution ones. A more substantial increase in image resolution (e.g. to $(0.5 \text{ mm})^3$ or higher) may potentially permit a better assessment of the accuracy of surface placement (Federau and Gallichan, 2016; Lüsebrink et al., 2017; Tisdall et al., 2013). It is also possible that, due to FreeSurfer's demonstrated capability for submillimeter precision at 1 mm^3 resolution, in our dataset surfaces were already placed accurately in most areas, and hence higher resolution did not lead to further improvement. Another potential reason may be the fact that

anatomical macrostructure of the adult human brain captured by FreeSurfer exists at a scale for which 1 mm^3 resolution is fully sufficient in most cortical areas (Fischl and Dale, 2000). Finally, we note that if the resolution is high enough to resolve cortical layers, laminar or intracortical contrast may result in local minima in the surface deformation procedures yielding inaccurate surfaces, although this has not been observed in resolutions as high as 0.5 mm isotropic.

Despite a modest increase in resolution, we were nevertheless able to capture aspects of surface reconstruction in which higher resolution may be beneficial. First, as already discussed above, higher resolution can help to correctly place the gray–white surface in areas with high myelin content. Second, surfaces derived from the high-resolution data appear to more faithfully capture the tissue boundary in the sulcal regions where the sulcus is particularly narrow, and the distinction of the opposing banks in the depth of the sulcus is difficult. It is worth pointing out that the observed advantages of the high-resolution stream were present despite the fact that low-resolution stream used downsampled images, and hence had superior SNR. High resolution can therefore improve the placement of both gray–white and gray–CSF surfaces despite the SNR loss.

In high-resolution functional MRI studies, extracting functional signal from cortical microstructures such as layers and columns using cortical surfaces represents a major challenge (Polimeni et al., 2017). Partial volume effects in boundary voxels as well as EPI distortions and signal dropouts significantly reduce the sensitivity of data analysis. In addition to these major challenges, our findings on surface displacement show that the resolution of structural scans used for surface reconstruction can also the sensitivity of high-resolution fMRI studies. For example, if the gray–CSF surface is inaccurately placed too far from the actual outer gray matter boundary, the gray matter signal will be more contaminated by physiological noise stemming from the CSF and the surface vessels (Polimeni et al., 2015, 2010; Triantafyllou et al., 2005). Correctly placed gray–CSF surface, in contrast, can help to avoid overall signal reduction stemming from erroneously included “silent” white matter voxels. Erroneous surface placement may affect the results of studies that examine signal variation across cortical depths or cortical layers. In particular, our data show that if a low-resolution scan is used, the gray–white surface location, and hence the location of deeper cortical layers, may be erroneously placed too superficially. Depending on the amount of displacement this may lead to the increased contamination of signal coming from different cortical layers. For example, in laminar fMRI studies the most popular areas being examined are the primary sensory cortices, and in particular the early visual cortex, which is relatively thin ($\sim 2\text{ mm}$) (Fischl and Dale, 2000). Our analysis shows that the gray–white surface at 1 mm^3 resolution can be displaced by up to 0.25 mm in some areas (including VI). If the gray–CSF surface is unchanged, and the cortical depth is subdivided into three compartments, the relatively small surface displacement of 0.25 mm can have a significant effect on where the compartment boundaries are placed relative to ground truth.

Despite the fact that we found consistent and significant differences in surface placement between data processed at native resolution and the downsampled data throughout the cortical surface, in most locations these differences were extremely small and can hardly be seen as a clear advantage of submillimeter voxels. The only regions where high resolution

clearly led to an improvement of surface placement was the Cingulate for gray–white surface, and various narrow sulci for the gray–CSF surface. Other studies reported more substantial differences between high-resolution and downsampled data (Bazin et al., 2014), which we have not observed here. This may be due to a relatively small resolution change from 1 mm³ to (0.75 mm)³. Structural scans acquired with higher resolution (Federau and Gallichan, 2016; Lüsebrink et al., 2017) may provide better insights into advantages of submillimeter voxels. Given the fact that the accuracy of surface placement depends on a number of factors such as specific brain area, software used, as well as image artifacts (such as motion ringing, inversion-recovery blurring effects, or resolution loss accompanying the use of partial Fourier reconstruction along one or more encoding axes), image SNR and tissue CNR, and that submillimeter surface reconstruction is associated with increased computational demands, all of these factors need to be considered and carefully weighed before choosing submillimeter reconstruction. Because submillimeter acquisitions may require longer acquisition protocols that are more vulnerable to motion and may also result in lower tissue CNR, higher resolution data will not always translate into increased reconstruction accuracy. In addition, it is important to emphasize that the high-resolution stream implemented in FreeSurfer is freely available and remains a work in progress, and therefore should be used with caution while considering all of the above.

While the *accuracy* (i.e. “correctness”) of surface placement is crucial for cortical laminar analysis, it may be less important for studies examining cortical thickness differences (Fujimoto et al., 2014). Typically such studies are focused on the change in thickness relative to some reference value (either relative to subject’s own values in longitudinal studies, or relative to a control sample in e.g. clinical cross-sectional studies). In such studies it is the *precision* (i.e. scan-to-scan consistency) of surface placement rather than accuracy that is more critical. Currently it is not known whether high resolution also improves the precision of surface placement. Future studies will be necessary to answer this question. Absolute thickness values, and hence the accuracy of thickness estimates, are nevertheless relevant for neuroanatomy. Correctly determining cortical thickness variation within the same brain is important for understanding the functional organization of the cortex (Wagstyl et al., 2015) as well as for characterization of brain networks using thickness-based connectivity measures (Chen et al., 2008; He et al., 2007; Lerch et al., 2006). A move towards higher resolution is therefore crucial for achieving better accuracy of cortical thickness estimation as well.

While increasing resolution can improve the accuracy—and potentially the precision—of cortical thickness measurements through reducing partial volume effects, it is also worth considering whether improving the methods of cortical thickness estimation could provide a similar increase in accuracy and precision. There are many established methods for estimating cortical thickness, both surface-based and volume-based (Fischl and Dale, 2000; Han et al., 2004; Hutton et al., 2008; Jones et al., 2000; MacDonald et al., 2000). A full evaluation and comparison of these techniques will be needed to empirically assess their performance, although realistic quantification of accuracy and precision will require appropriate ground-truth data. Only combining the state-of-the-art image acquisition methods with the most accurate computational methods will allow taking full advantage of the benefits provided by high resolution.

High-resolution and high-field data processing

Modern MR technology has enabled increases in the spatial resolution of structural MRI to an unprecedented degree. These resolution increases have been mostly driven by the wide use of ultra-high field scanners, which provide higher SNR and hence allow smaller voxels. However, there are specific acquisition and analysis challenges faced with ultra-high field anatomical data and also with high-resolution data at any field strength. Apart from SNR, one of the major constraints on the resolution of structural scans is subject motion, which is inevitable. Because the longer scan times required for high resolution make these scans more vulnerable to overt head motion, some correction strategy is required. Recent advancements in methods such as prospective motion correction (Maclaren et al., 2013; Tisdall et al., 2013; Lüsebrink et al., 2017) and retrospective motion correction (Federau and Gallichan, 2016) can provide high-quality submillimeter data despite the long acquisition times required, even at conventional magnetic field strengths.

Data acquired at ultra-high field often suffer from increased transmit and receive field inhomogeneity, causing the need for more aggressive bias correction algorithms or alternative approaches to reduce or eliminate the bias. In this study, we used an intensity bias correction procedure originally designed for lower magnetic fields, but with adjusted parameters to take into account the more rapid spatial variation in the bias seen at higher field strengths. Alternative approaches have been to normalize an MPRAGE scan by an additionally acquired gradient echo scan (Van de Moortele et al., 2009; Lüsebrink et al., 2013), or to using the MP2RAGE method, which similarly can remove this bias (Marques et al., 2010). However, these alternate acquisition schemes can influence the positioning of the cortical surface reconstruction (Fujimoto et al., 2014), and, due to nonlinear combination of the two inversion images used in MP2RAGE, assumptions of partial volume estimation algorithms used in morphometry studies may be violated (Duché et al., 2017). Nevertheless, these bias correction methods can greatly improve the robustness of the surface reconstruction.

Another property of ultra-high field structural scans, which is not usually seen at conventional MRI scanners, is signal enhancement within the major blood vessels, specifically the arterial vessels. The vessels appear bright not because of the field strength per se, but due to head-only transmit coils used at ultra-high field—this causes the blood flowing into the head from the neck to avoid all of the inversion or excitation pulses, therefore the blood is at equilibrium magnetization when it enters the imaging volume (Van de Moortele et al., 2009; Grinstead et al., 2010). Bright vessels can also pose a challenge to segmentation algorithms and can lead to tissue misclassification when the vessels are adjacent to tissue. We did not observe any systematic segmentation errors associated with bright vessels in our dataset, perhaps because vessel intensity was significantly higher than that of the white matter, making the two easy to distinguish. However, a more systematic investigation of their impact, and perhaps adaptation of the existing algorithms, may be needed.

Mis-segmentation of the dura mater surrounding the cerebral hemisphere is another challenge to accurate cortical segmentation, and submillimeter voxels potentially allow the thin dura layer to be spatially resolved. Since the intensity of the dura is close to that of gray

matter in standard MPRAGE protocols, it is difficult to distinguish from gray matter, causing inaccurate surface placement and inflated thickness estimates. FreeSurfer provides a possibility to account for the dura by exploiting the different T_2^* values in dura and gray matter and use the information contained in different echoes of the multi-echo MPRAGE to distinguish the two (van der Kouwe et al., 2008). This approach has been used by the Human Connectome Project in combination with an additional T_2 -weighted image, in which the intensity of dura is low (Glasser et al., 2013). There are also purely computational approaches that use prior information to predict dura location (Bazin et al., 2014). Future studies are needed to test performance of these approaches and to determine to what extent higher resolution helps to exclude dura more reliably.

Finally, releasing the 1 mm voxel size constraint on structural images means that the resulting scans may have a range of potential acquisition parameters with various contrast, SNR, CNR and artifact level, not all of which will meet the expectations of existing software. A high-resolution scan can provide poor cortical surface reconstruction and cortical thickness estimation if it lacks sufficient SNR or has poor tissue contrast. It is therefore important to keep in mind that along with resolution, adequate SNR is similarly important for accurate surface reconstruction, and potential gains and losses must be weighed carefully when decreasing the voxel size.

Overall, both high-resolution anatomical data and anatomical data acquired at ultra-high fields can have artifacts and other image characteristics that are not present in conventional data. Addressing these challenges requires alternative acquisition strategies to reduce these artifacts and in some cases additional preprocessing steps to ensure accurate segmentation, and to fully exploit the additional anatomical information provided by high resolution.

Conclusion

In this study we found systematic differences between cortical surfaces generated from high and low-resolution scans, which are most likely due to stronger partial volume effects at low resolution. High-resolution scans offer some advantage over low resolution, which may be important in work requiring a high level of accuracy such as laminar fMRI. However, the current study assessed the advantages of high resolution only for cortex-related measures, using only one software package, and with only a modest resolution increase. More studies are needed to evaluate the potential advantage of high resolution for segmenting sub-cortical structures, to characterize the performance of other software, and to determine whether resolution even higher than the one used here can provide further advantages for cortical surface reconstruction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Data preprocessing steps and the three streams for gray-white and gray-CSF surface reconstruction.

Figure 2.

Overview of the surface analysis steps.

(A) First, to be able to compare the surfaces derived from low-resolution and high-resolution streams at every vertex, we resampled each surface onto its low- or high-resolution counterpart. This was done for every vertex on the source surface (indicated by colored dots) by finding the closest point on the target surface (indicated by black dots). This procedure generated two additional pairs of resampled surfaces (shown in the same color as the source surfaces, but with black outlines).

(B) After resampling, cortical thickness difference (defined as distance between gray–white and gray–CSF surface, indicated by red arrows) was computed twice: once on a low-density

mesh and once on a high-density mesh. Both thickness difference maps were then projected onto *fsaverage* template with 163,842 vertices and averaged across subjects.

(C) For each of the streams surface displacement (defined as distance between low-resolution stream surface and high-resolution stream surface at every vertex, indicated by red arrows) was also computed twice: once with low-density meshes and once with high-density meshes. Similar to thickness, both displacement maps were then projected onto the *fsaverage* template with 163,842 vertices and averaged across subjects.

Figure 3.

Example of a successfully completed FreeSurfer recon-all stream at native 0.75 mm³ resolution.

(A) Gray-white and gray-CSF surfaces as well as subcortical segmentation are shown on an axial slice of an MRI one volunteer.

(B) Inflated gray-white surface mesh with gyri (light gray) and sulci (dark gray) as well as the outlines of the cortical parcellation.

Figure 4. Cortical thickness differences between low-resolution and high-resolution surface reconstruction streams. Whole-hemisphere vertex-wise difference maps representing mean (top), standard deviation (middle) as well as t-values thresholded at $p < 0.05$ (FDR-corrected) significance level (bottom row) are shown on an inflated surface of the *fsaverage* template brain. LH: left hemisphere; RH: right hemisphere.

Figure 5.

Gray-white and gray-CSF surface displacement.

(A) Whole-hemisphere vertex-wise surface displacement maps representing mean (top), standard deviation (middle) as well as t-values thresholded at $p < 0.05$ (FDR-corrected) significance levels (bottom row) for the gray-white surface are shown on an inflated surface of the *fsaverage* template brain.

(B) Same as (A), but for the gray-CSF surface

LH: left hemisphere; RH: right hemisphere

Figure 6.

Relationship between surface displacement and local image contrast

(A) 2D histogram of the % gray–white matter contrast versus gray–white surface displacement for each hemisphere. Color bar shows group average number of vertices in each bin. Blue arrows indicate the peak displacement in the histogram

(B) Same as (A) but for gray–CSF surface and gray matter intensity instead of contrast.

Insets show the average per-vertex values of the gray–white contrast (in panel A) or the gray matter intensity (in panel B).

Figure 7.

Relationship between surface displacement and surface mean curvature.

(A) 2D histograms of the curvature versus surface displacement for each hemisphere. Color bars show average number of vertices in each bin across subjects. Negative curvature corresponds to gyri, positive to sulci.

(B) Same as (A) but for the gray-CSF surface.

Insets show average per-vertex mean curvature across subjects.

Figure 8.

Accuracy of gray-white surface placement.

Each panel shows three locations with most significant displacement on the group level. S1, S2 and S3 are individual subjects with largest displacement at that location (note that S1, S2 and S3 for cluster 1 are not the same subjects shown for cluster 2). The contours represent the cross-sections of the cortical surface reconstructions on the image plane from the three streams (orange – high-resolution stream; green – low-resolution stream; cyan – SNR-matched stream). For each subject we indicated whether the high-resolution surface is clearly superior relative to the low-resolution surface (“High > Low”), clearly inferior (“High < Low”), about the same or difficult to determine (“High ~ Low”).

Figure 9.
Accuracy of gray–CSF surface placement. Same convention as in Fig. 8.

Table 1

SNR, CNR and percent gray-white contrast and its variation $\pm$ SD for 7 T dataset at native resolution, the downsampled 7 T dataset as well as for the “buckner40” dataset (1.5 T) used to test FreeSurfer.

	SNR	CNR	% contrast	% contrast variation
7 T native resolution	15.6 $\pm$ 1.1	3.9 $\pm$ 0.2	26.0 $\pm$ 2.1	9.7 $\pm$ 0.7
7 T downsampled	18.0 $\pm$ 1.3	4.6 $\pm$ 0.3	23.1 $\pm$ 1.8	8.0 $\pm$ 0.5
1.5 T “buckner40”	8.7 $\pm$ 0.6	3.2 $\pm$ 0.3	32.5 $\pm$ 3.3	9.4 $\pm$ 0.6

Table 2

Peak clusters for surface displacement examined in Fig. 8 and 9

Significance ($-\log_{10}(p)$)	Average displacement $\pm$ SD (mm)	Cluster size (mm ²)	X	Y	Z	Annotation
Gray–white surface displacement						
14.25	0.22 $\pm$ 0.11	84.16	−8.7	−30.4	27.8	Left Isthmus of the Cingulate gyrus
13.675	0.16 $\pm$ 0.09	1711.90	−32.1	−27.1	57.6	Left Postcentral gyrus
11.435	0.09 $\pm$ 0.05	164.01	−11.3	−51.0	57.4	Left Superior Parietal
Gray–CSF surface displacement						
14.14	0.13 $\pm$ 0.06	775.76	43.5	48.0	−12.2	Right Inferior frontal gyrus (p. Orbitalis)
12.45	0.12 $\pm$ 0.07	1604.98	−63.4	−53.6	6.4	Left Middle Temporal gyrus
12.22	0.05 $\pm$ 0.03	7.34	−25.1	39.9	17.2	Left Rostral Middle Frontal gyrus