ADNI Alzheimer's Disease Neuroimaging Initiative

UCSF FreeSurfer Methods

Miriam Hartig, Diana Truran-Sacrey, Sky Raptentsetsang, Alix Simonson, Adam Mezher, Norbert Schuff, Michael Weiner

Contents

***All papers involving FreeSurfer data must be cited following the instructions located on the FreeSurfer methods citation webpage:*
http://surfer.nmr.mgh.harvard.edu/fswiki/FreeSurferMethodsCitation

Summary

Cortical reconstruction and volumetric segmentation is performed with the FreeSurfer image analysis suite, which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/). An early version of the longitudinal image processing framework (Reuter et al., 2012) is used to process the sequential scans. The technical details of these procedures are described in prior publications (Dale et al., 1999; Dale and Sereno, 1993; Fischl and Dale, 2000; Fischl et al., 2001; Fischl et al., 2002; Fischl et al., 2004a; Fischl et al., 1999a; Fischl et al., 1999b; Fischl et al., 2004b; Han et al., 2006; Jovicich et al., 2006; Segonne et al., 2004). Briefly, this processing includes motion correction and averaging (Reuter et al. 2010) of multiple volumetric T1 weighted images (when more than one is available), removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Segonne et al., 2004), automated Talairach transformation, segmentation of the subcortical white matter and deep gray matter volumetric structures (including hippocampus, amygdala, caudate, putamen, ventricles) (Fischl et al., 2002; Fischl et al., 2004a) intensity normalization (Sled et al., 1998), tessellation of the gray matter white matter boundary, automated topology correction (Fischl et al., 2001; Segonne et al., 2007), and surface deformation following intensity gradients to optimally place the gray/white and gray/cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue class (Dale et al., 1999; Dale and Sereno, 1993; Fischl and Dale, 2000).

Methods

ADNI11.5T data was run with FreeSurfer version 4.3 and ADNI1 3T data was run with FreeSurfer version 5.1. ADNIGO and ADNI2 data are being run with FreeSurfer version 5.1. FreeSurfer version 5.1 data is processed using the 2010 Desikan-Killany atlas and the 2009 Destrieux atlas. Only data from the Desikan-Killany atlas is made available on LONI. The input for ADNI FreeSurfer is a T1 weighted image (MPR or IR-SPGR) in NiFTI format which has been pre-processed (gradient warping, scaling, B1 correction and N3 inhomogeneity correction) by Mayo Clinic. In ADNIGO and ADNI2 two T1 weighted images are acquired for each subject—an accelerated and a non-accelerated acquisition. Mayo Clinic pre-processes both images. UCSF processed both T1 weighted images for approximately 300 subjects before determining that the sequences produced similar enough results that further comparison was not required. Currently only the non-accelerated T1 weighted image is processed with FreeSurfer. UCSF does not edit the FreeSurfer output brain mask, however a thorough visual QC is performed. For a more detailed explanation of the QC guidelines, please see the full UCSF FreeSurfer Overview and QC Guide.

ADNI scans are run through FreeSurfer using both longitudinal and cross-sectional processing:

Cross-sectional processing: Each scan is segmented according to an atlas defined by FreeSurfer. This allows for comparison between groups at a single time point. (Fischl and Dale, 2000).

Longitudinal processing: When a subject has multiple time points, a within-subject template space and average image, unbiased toward the chronological scan order (Reuter and Fischl, 2012) is created using robust, inverse consistent registration (Reuter et al., 2010). Information from each subject's template is used to initialize the longitudinal image processing to increase reliability and statistical power when measuring brain change over time. Longitudinally processed numerical outputs will change if the base image is recreated to accommodate more time points. ADNI2 3T data are being processed in separate groups of annual change and base images will be distinct for each dataset. QC ratings may change due to refinement of the QC Protocol and individual reevaluation. Any unexpected changes will be noted in the Dataset Changes section at the end of this document. For further details on longitudinal processing, please refer to the publication in NeuroImage from the FreeSurfer group (Reuter et al., 2012).

Processing Overview

1st Step: Autorecon-1

The "–autorecon1" command initiates the following tasks:

1) Motion correction and registration
2) Non-Uniform intensity normalization (NU)
3) Talairach transform computation
4) Intensity Normalization 1Skull Strip

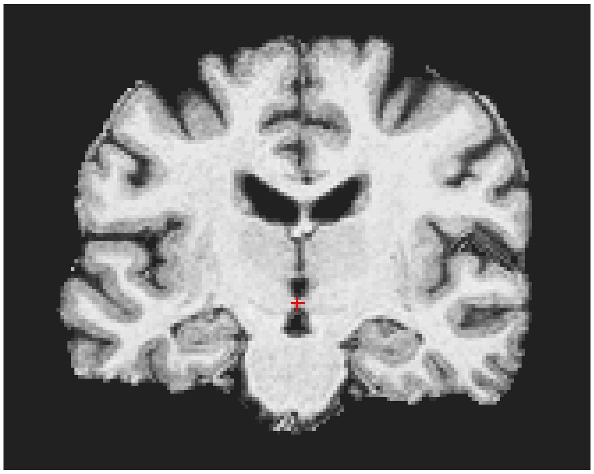

Figure 1. FreeSurfer output after –autorecon1

2nd Step: Autorecon-2

The "–autorecon-2" command creates the White-Matter and Pial surfaces. It then segments the gray and white matter, and the sub-cortical structures.

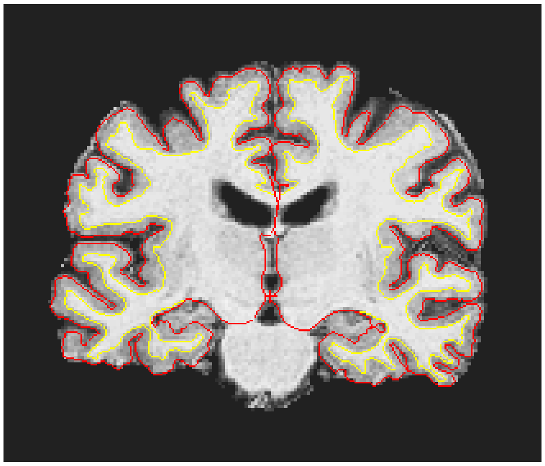

Figure 2a. FreeSurfer output after –autorecon2, Pial surface

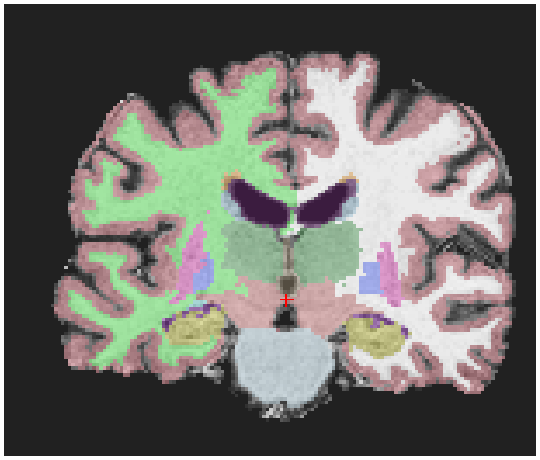

Figure 2b. FreeSurfer output after –autorecon2, Gray-White Segmentation

3rd Step: Autorecon-3

The –autorecon3 command creates the cortical parcellation.

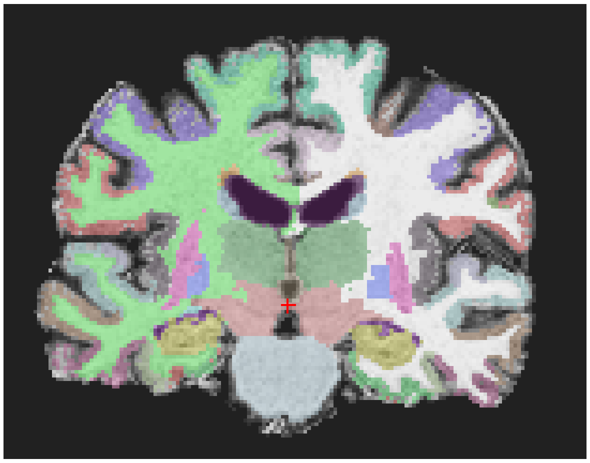

Figure 3. FreeSurfer output after –autorecon3, Segmentation/ Parcellation viewed in tkmedit

*Note: In 1.5T longitudinal processing, base images are re-created for subjects with five or fewer time points in order to include the latest time point. Once a subject has more than five time points, a new base image is **not** created. The new image is appended to the old base image.*

QC Guide

Overall Outcomes: Pass, Fail, Hippocampus-Only, and Partial.

Pass indicates a good overall segmentation.

Fail indicates a global failure due to extremely poor image quality, registration issues, or gross misestimation of the hippocampus. Fail can also indicate a processing error.

Hippocampus -Only indicates a global failure of the segmentation but the hippocampi are properly estimated.

Partial indicates a "failure" in one or more of 8 regions listed below. These 8 regions consist of several structures that are the most common sites of poor FreeSurfer segmentation.

a) **Frontal**= Frontal pole, precentral, superior frontal, caudal middle frontal, rostral middle frontal, and medial orbital frontal
b) **Temporal**= temporal pole, fusiform, superior temporal, inferior temporal, middle temporal
c) **Insula**= insula
d) **Parietal=** Postcentral, superior parietal, paracentral, supramarginal, inferior parietal
e) **Occipital**= lingual, lateral occipital, cuneus, pericalcarine

f) **Cerebral WM=** Cerebral white matter, subcortical structures
g) **Basal Ganglia=** Putamen, caudate, pallidum
h) **Ventricle**=Lateral, inferior lateral, third, fourth, fifth ventricles, choroid plexus

In cases of partial region "failures" ALL cortical regions included within that regional definition are excluded from the volumetric report regardless of which specific cortical areas were affected. For example, if a scan is rated Parietal 'fail' then the following sub-regions are excluded from the report because one or more of these sub-regions did not satisfy the QC requirements: Postcentral, superior parietal, paracentral, supramarginal, and inferior parietal. **Subjects with an overall rating of "partial" still have usable hippocampal volume data, even when the failure occurs in the Temporal region.**

Most subjects will receive an outcome of pass, partial, or hippocampus only. A fail in any of the 8 regions (Frontal, Temporal, Insula, Parietal, Occipital, Cerebral WM, or Basal Ganglia) indicates that one or more of the structures in that region did not meet our QC standards. Here are some examples of failures in each region:

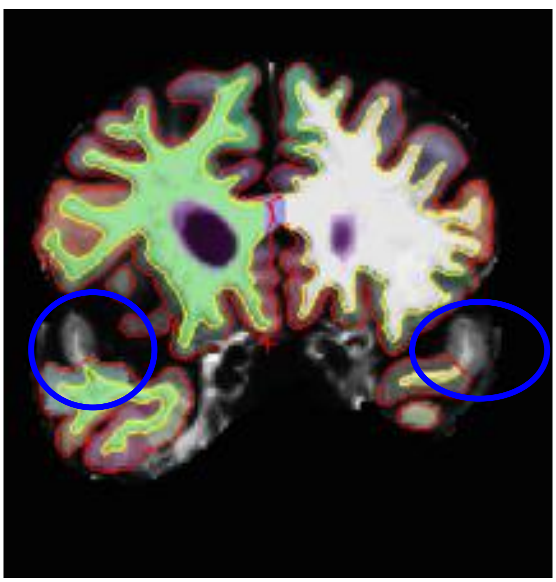

Figure 4a. Example of Temporal fail

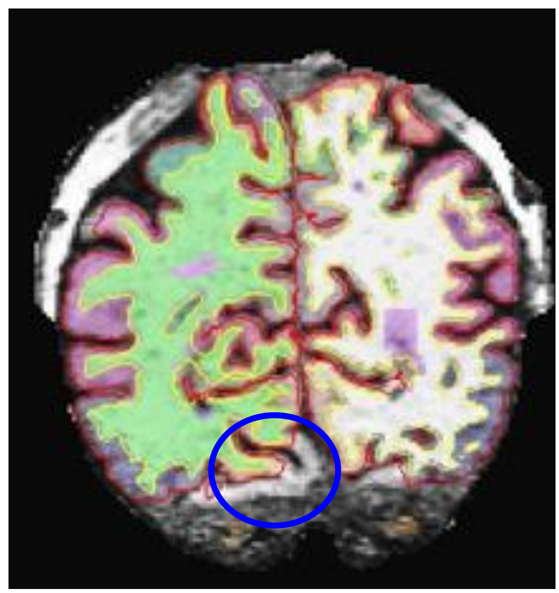

Figure 4b. Example of Occipital fail

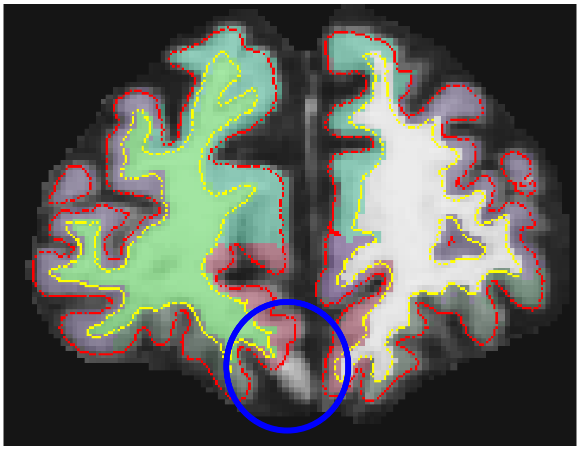

Figure 4c. Example of Frontal fail

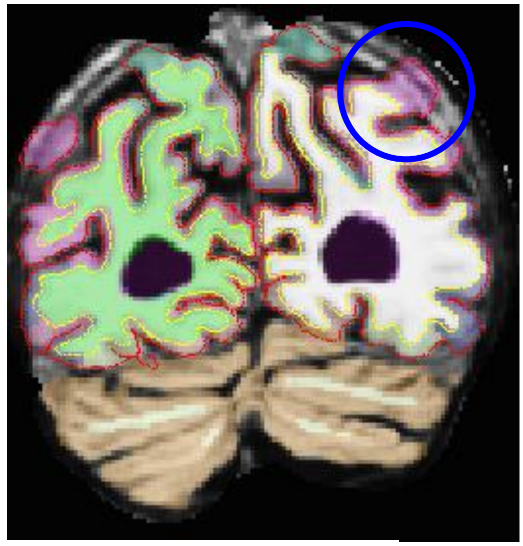

Figure 4d. Example of Parietal fail

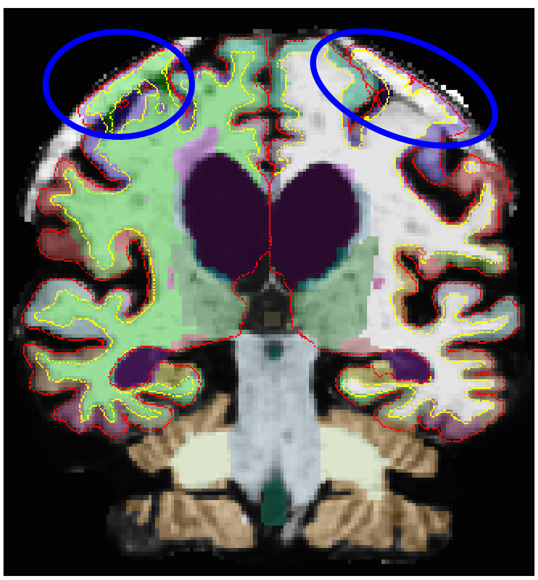

Figure 4e. Example of Cerebral WM fail

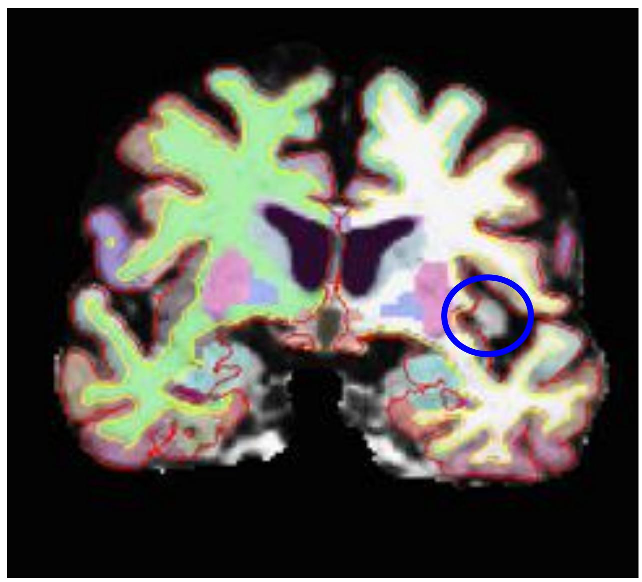

Figure 4f. Example of Insula fail

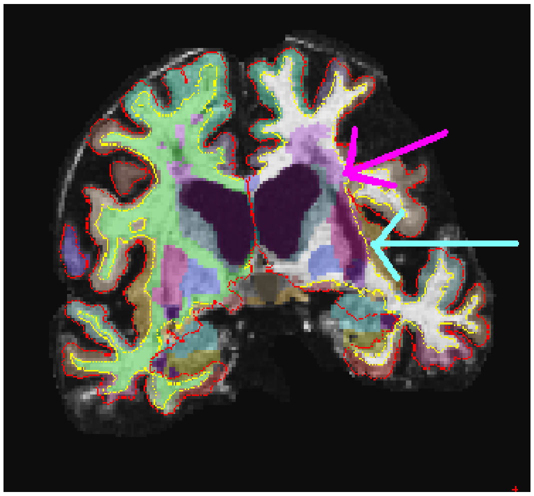

Figure 4g. Example of Basal Ganglia fail

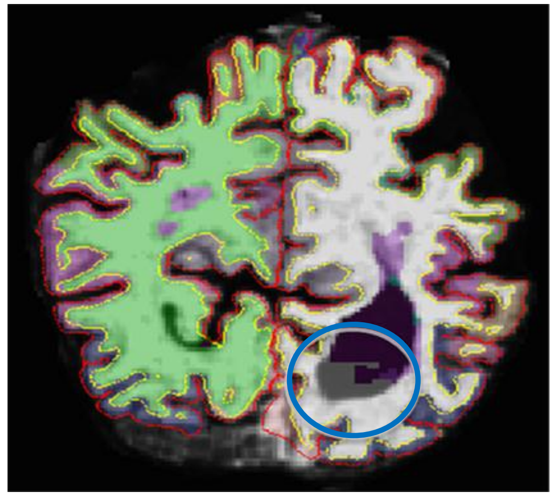

Figure 4h. Example of Ventricle fail

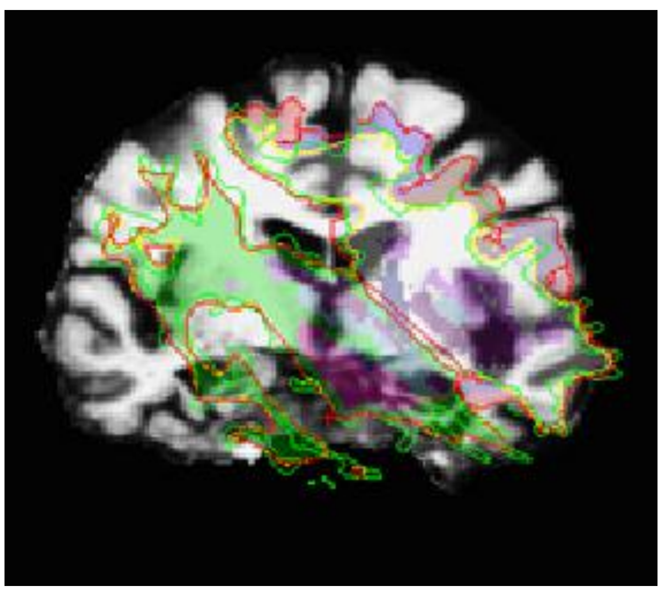

Figure 4i. Example of Overall fail

ADNI Alzheimer's Disease Neuroimaging Initiative

Version Information (1/31/2014)

This document supersedes our previous document dated 2012-12-11. Specific changes in our methods are summarized in this section and in the table below. Firstly, our QC protocol was refined to be more consistent and inclusive of usable data, with our ultimate goal being to provide the most accurate data for analyses. Secondly, regarding our 1.5T Longitudinal FreeSurfer data stream, we created new base images for subjects who previously had fewer than three time points included in their base image. Once created, we re-ran these data through FreeSurfer. Thirdly, it is sometimes the case that an image is re-QC'd if re-evaluated by another technician or by a group.

Because of these revisions, it is possible that some QC outcomes and numerical values may change from one quarterly upload to the next. As always, we recommend that users download and use the most up-to-date dataset and corresponding data dictionary for their analyses.

For a brief summary of version release notes, please see the table below:

Dataset Name	Notes	Reason	Date Submitted
All UCSF FreeSurfer datasets	Some full fail cases salvaged	Refined QC protocol to be more consistent and inclusive of usable data.	1/31/2014
All UCSF FreeSurfer datasets	Some occipital regional fails changed to passes	Refined QC protocol.	1/31/2014
UCSF—Longitudinal FreeSurfer (Version 4.4)	Slight changes in numerical outputs of some data	Created new base image for subjects who had fewer than 3 time points included in their base image. New Images were re-run and QC'd.	1/31/2014

Dataset Information

Dataset Name	**Date Submitted**
UCSF—Cross-Sectional FreeSurfer (FreeSurfer Version 4.3)	January 2014
UCSF—Longitudinal FreeSurfer (FreeSurfer Version 4.4)	January 2014
UCSF—Cross-Sectional FreeSurfer (Version 5.1)	January 2014
UCSF—Longitudinal FreeSurfer (Version 5.1)	January 2014

References

Dale, A.M., Fischl, B., Sereno, M.I., 1999. Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage 9, 179-194.

Dale, A.M., Sereno, M.I., 1993. Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: a linear approach. J Cogn Neurosci 5, 162-176.

Desikan, R.S., Segonne, F., Fischl, B., Quinn, B.T., Dickerson, B.C., Blacker, D., Buckner, R.L., Dale, A.M., Maguire, R.P., Hyman, B.T., Albert, M.S., Killiany, R.J., 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage 31, 968-980.

Fischl, B., Dale, A.M., 2000. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc Natl Acad Sci U S A 97, 11050-11055.

Fischl, B., Liu, A., Dale, A.M., 2001. Automated manifold surgery: constructing geometrically accurate and topologically correct models of the human cerebral cortex. IEEE Trans Med Imaging 20, 70-80.

Fischl, B., Salat, D.H., Busa, E., Albert, M., Dieterich, M., Haselgrove, C., van der Kouwe, A., Killiany, R., Kennedy, D., Klaveness, S., Montillo, A., Makris, N., Rosen, B., Dale, A.M., 2002. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron 33, 341-355.

Fischl, B., Salat, D.H., van der Kouwe, A.J., Makris, N., Segonne, F., Quinn, B.T., Dale, A.M., 2004a. Sequence-independent segmentation of magnetic resonance images. Neuroimage 23 Suppl 1, S69-84.

Fischl, B., Sereno, M.I., Dale, A.M., 1999a. Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. Neuroimage 9, 195-207.

Fischl, B., Sereno, M.I., Tootell, R.B., Dale, A.M., 1999b. High-resolution intersubject averaging and a coordinate system for the cortical surface. Hum Brain Mapp 8, 272-284.

Fischl, B., van der Kouwe, A., Destrieux, C., Halgren, E., Segonne, F., Salat, D.H., Busa, E., Seidman, L.J., Goldstein, J., Kennedy, D., Caviness, V., Makris, N., Rosen, B., Dale, A.M., 2004b. Automatically parcellating the human cerebral cortex. Cereb Cortex 14, 11-22.

Han, X., Jovicich, J., Salat, D., van der Kouwe, A., Quinn, B., Czanner, S., Busa, E., Pacheco, J., Albert, M., Killiany, R., Maguire, P., Rosas, D., Makris, N., Dale, A., Dickerson, B., Fischl, B.,

2006. Reliability of MRI-derived measurements of human cerebral cortical thickness: the effects of field strength, scanner upgrade and manufacturer. Neuroimage 32, 180-194.

Jovicich, J., Czanner, S., Greve, D., Haley, E., van der Kouwe, A., Gollub, R., Kennedy, D., Schmitt, F., Brown, G., Macfall, J., Fischl, B., Dale, A., 2006. Reliability in multi-site structural MRI studies: effects of gradient non-linearity correction on phantom and human data. Neuroimage 30, 436-443.

Kuperberg, G.R., Broome, M.R., McGuire, P.K., David, A.S., Eddy, M., Ozawa, F., Goff, D., West, W.C., Williams, S.C., van der Kouwe, A.J., Salat, D.H., Dale, A.M., Fischl, B., 2003. Regionally localized thinning of the cerebral cortex in schizophrenia. Arch Gen Psychiatry 60, 878-888.

Reuter, M., Schmansky,N.J., Rosas, H.D., Fischl, B., 2012.
Within-Subject Template Estimation for Unbiased Longitudinal Image Analysis. NeuroImage 61(4), 1402-1418. http://reuter.mit.edu/papers/reuter-long12.pdf

Reuter, M., Fischl, B., 2011. Avoiding asymmetry-induced bias in longitudinal image processing. Neuroimage 57 (1), 19-21. http://reuter.mit.edu/papers/reuter-bias11.pdf

Reuter, M., Rosas, H.D., Fischl, B., 2010. Highly Accurate Inverse Consistent Registration: A Robust Approach. Neuroimage 53 (4), 1181–1196. http://reuter.mit.edu/papers/reuter-robreg10.pdf

Reuter, M., Schmansky, N.J., Rosas, H.D., Fischl, B., 2012. Within-subject template estimation for unbiasted longitudinal image analysis. NeuroImage 61, 1402-1418.

Rosas, H.D., Liu, A.K., Hersch, S., Glessner, M., Ferrante, R.J., Salat, D.H., van der Kouwe, A., Jenkins, B.G., Dale, A.M., Fischl, B., 2002. Regional and progressive thinning of the cortical ribbon in Huntington's disease. Neurology 58, 695-701.

Salat, D.H., Buckner, R.L., Snyder, A.Z., Greve, D.N., Desikan, R.S., Busa, E., Morris, J.C., Dale, A.M., Fischl, B., 2004. Thinning of the cerebral cortex in aging. Cereb Cortex 14, 721-730.

Segonne, F., Dale, A.M., Busa, E., Glessner, M., Salat, D., Hahn, H.K., Fischl, B., 2004. A hybrid approach to the skull stripping problem in MRI. Neuroimage 22, 1060-1075.

Segonne, F., Pacheco, J., Fischl, B., 2007. Geometrically accurate topology-correction of cortical surfaces using nonseparating loops. IEEE Trans Med Imaging 26, 518-529.

Sled, J.G., Zijdenbos, A.P., Evans, A.C., 1998. A nonparametric method for automatic correction of intensity nonuniformity in MRI data. IEEE Trans Med Imaging 17, 87-97.

FreeSurfer Wiki. [Online]. Available: http://surfer.nmr.mgh.harvard.edu/fswiki.

ADNI Alzheimer's Disease Neuroimaging Initiative

About the Authors

This document was prepared by Miriam Hartig, UCSF/SF VA Medical Center. For more information please contact Alix Simonson at alix.simonson@va.gov or Diana Truran-Sacrey at diana.truran@ucsf.edu.

Notice: This document is presented by the author(s) as a service to ADNI data users. However, users should be aware that no formal review process has vetted this document and that ADNI cannot guarantee the accuracy or utility of this document.