

UCSF FreeSurfer Methods

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***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

ADNI1 data was run with FreeSurfer version 4.3. ADNIGO and ADNI2 data are being run with FreeSurfer version 5.1. 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 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. 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.

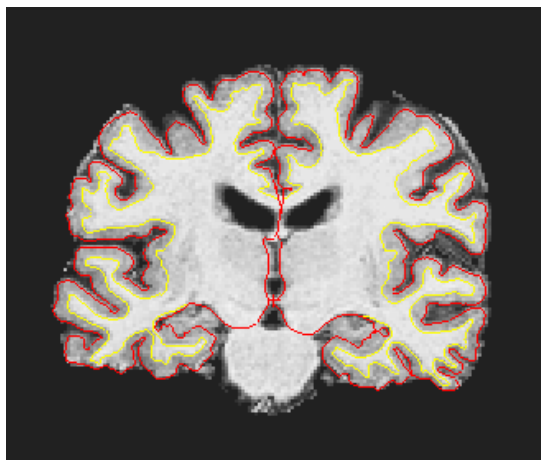


Figure 2a. FreeSurfer output after -autorecon2, Pial surface

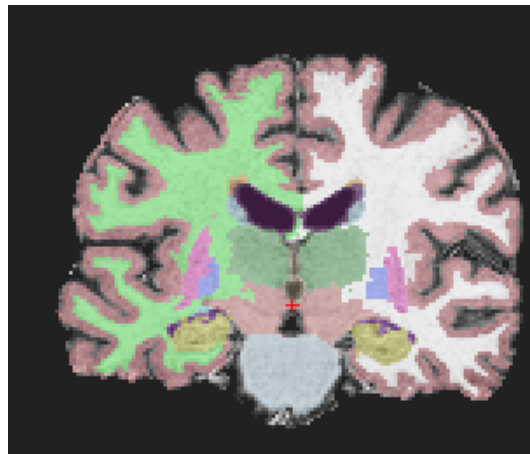


Figure 2b. FreeSurfer output after -autorecon2, Gray-White Segmentation

3rd Step: Autorecon-3

The -autorecon3 command creates the cortical parcellation.

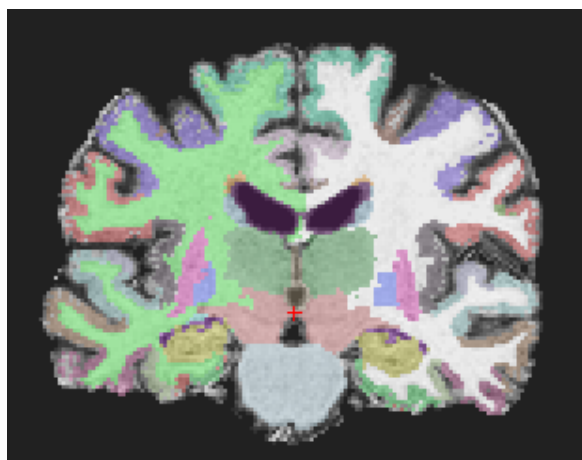


Figure 3. FreeSurfer output after -autorecon3, Segmentation/ Parcellation viewed in tkmedit

QC Guide

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

Pass indicates a good overall segmentation.

Fail indicates a global failure due to either extremely poor image quality or registration issues. 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 7 regions listed below. These 7 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 7 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:

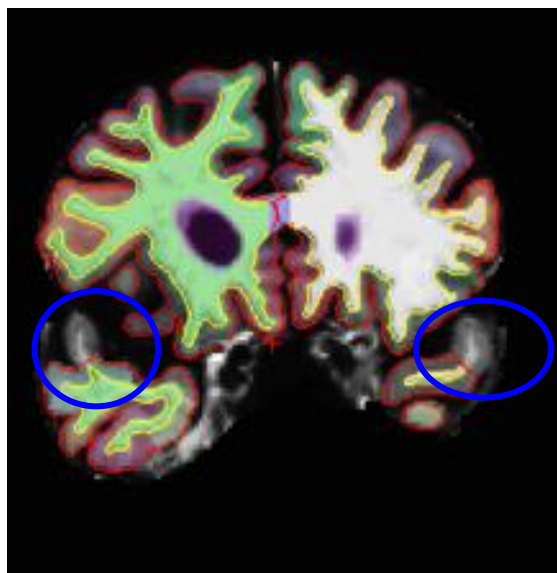


Figure 4a. Example of Temporal fail

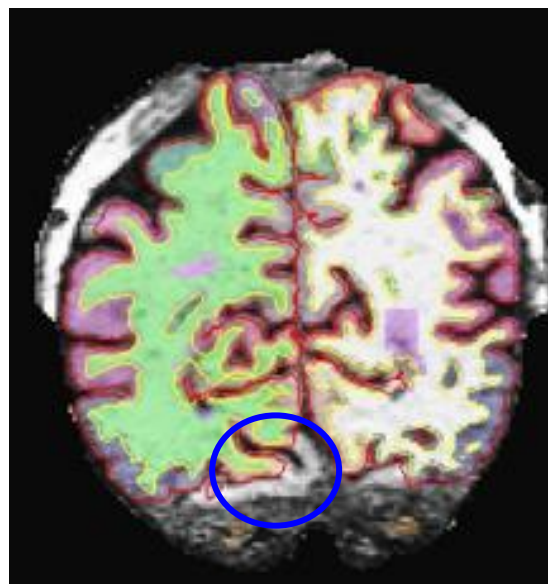


Figure 4b. Example of Occipital fail

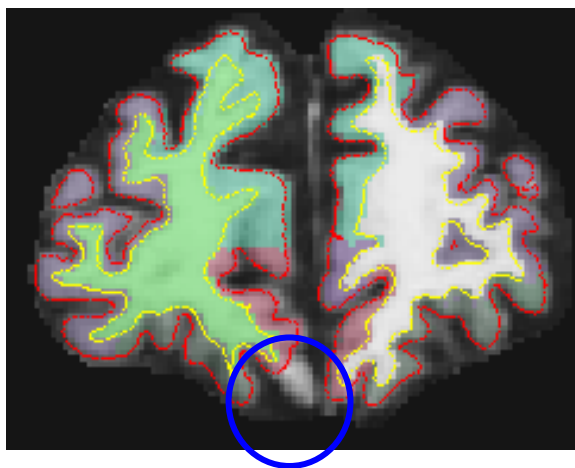


Figure 4c. Example of Frontal fail



Figure 4d. Example of Parietal fail

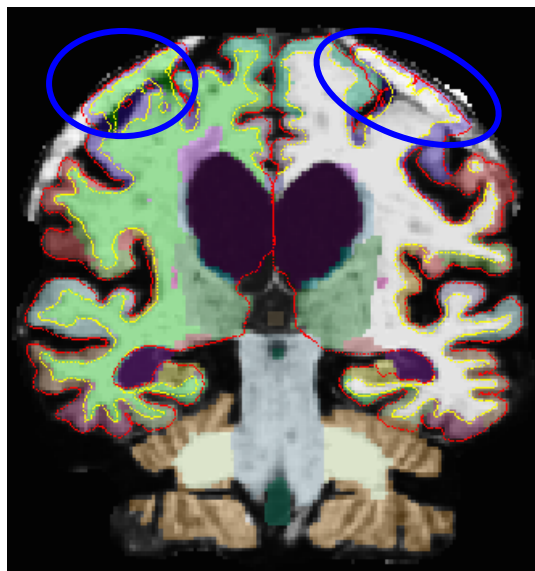


Figure 4e. Example of Cerebral WM fail

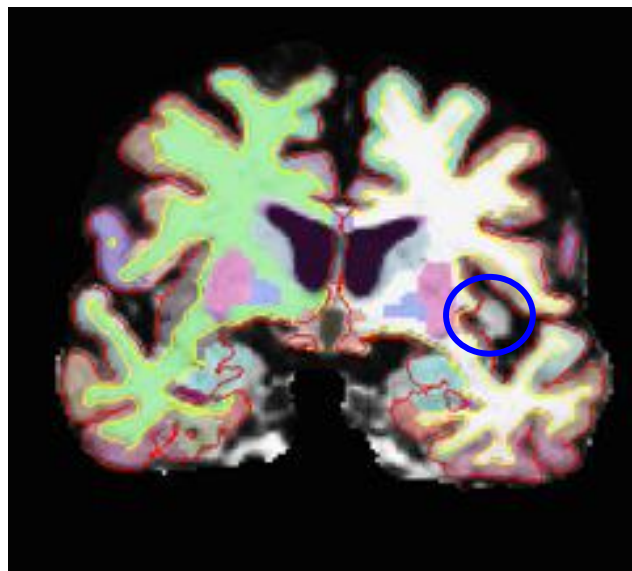


Figure 4f. Example of Insula fail

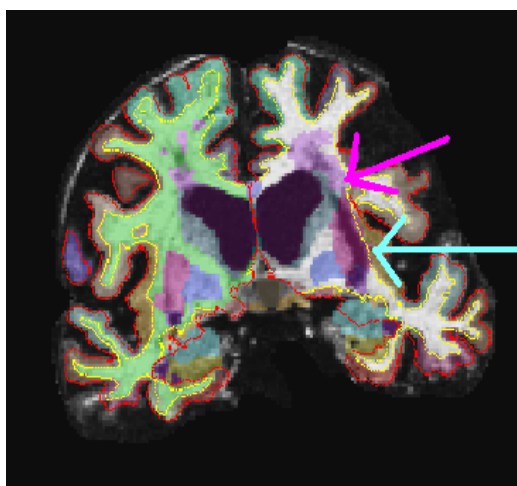


Figure 4g. Example of Basal Ganglia fail

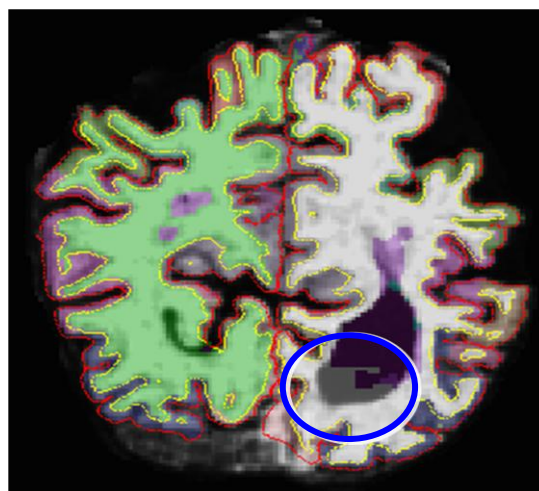


Figure 4h. Example of Ventricle fail

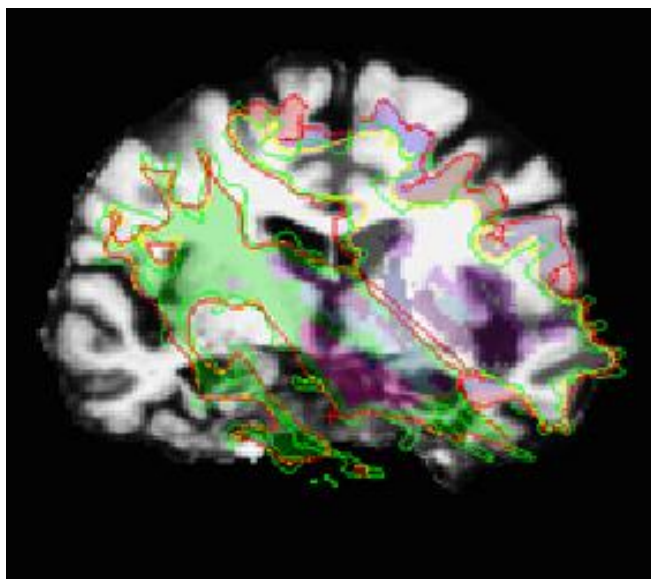


Figure 4i. Example of Overall fail

Dataset Information

Dataset Name	Date Submitted
UCSF—Cross-Sectional FreeSurfer (FreeSurfer Version 4.3)	February 2012
UCSF—Longitudinal FreeSurfer (FreeSurfer Version 4.4)	February 2012
UCSF—FreeSurfer (Version 5.1) Cross-Sectional	December 2012

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