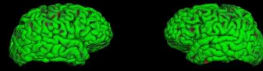
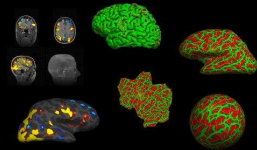


FreeSurfer: Automated Anatomical Analysis

surfer.nmr.mgh.harvard.edu



FreeSurfer



MASSACHUSETTS
GENERAL HOSPITAL



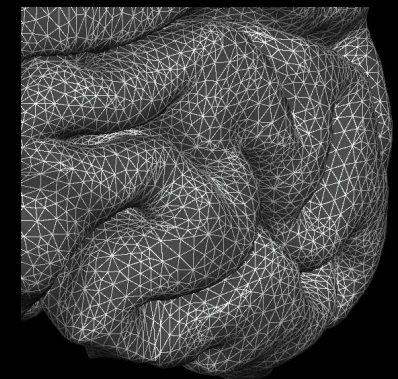
Administratia

- surfer.nmr.mgh.harvard.edu
 - Register
 - Download
 - Mailing List
- Wiki: surfer.nmr.mgh.harvard.edu/fswiki
- Platforms: Linux and Mac
- Important! How to report a bug!
 - Version
 - Command-line
 - Error description
 - \$subjid/scripts/recon-all.log
 - freesurfer@nmr.mgh.harvard.edu

Surface Reconstruction Theory

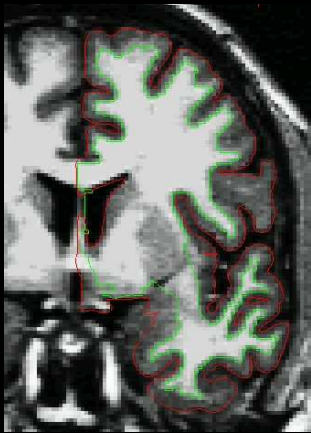
- Input: T1-weighted (MPRAGE,SPGR)
- Segment white matter from rest of brain.
- Find white/gray surface
- Find pial surface
- “Find” = create mesh
 - Vertices, neighbors, triangles, coordinates
 - Accurately follows boundaries between tissue types
 - “Topologically Correct”
 - closed surface, no donut holes
 - no self-intersections
- Subcortical Segmentation along the way

Surface Model



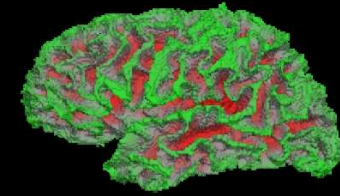
- Mesh (“Finite Element”)
- Vertex = points shared by adjacent triangles
- XYZ at each vertex
- Triangles/Faces ~ 300,000
- Area, Distance, Curvature, Thickness
- Moveable (vertex index is invariant)

Find “Subcortical Mass”

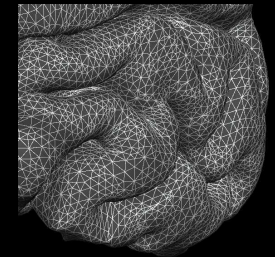


- All White Matter
- Array of Subcortical Structures (basal ganglia, thalamus, etc....)
- Ventricles
- Excludes brain stem and cerebellum
- Hemispheres separated
- Connected (no islands)
- Many Stages ... More Later ...

Tessellation and Topology Fixing

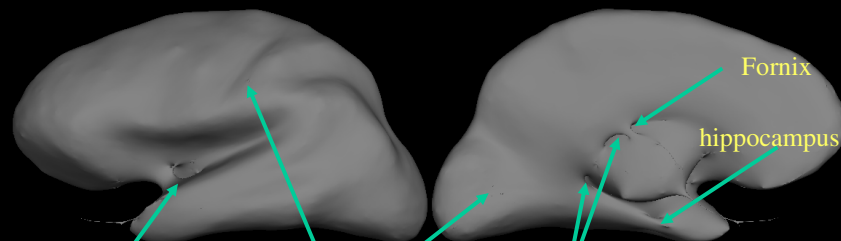


orig surface
surf/lh.orig
surf/rh.orig

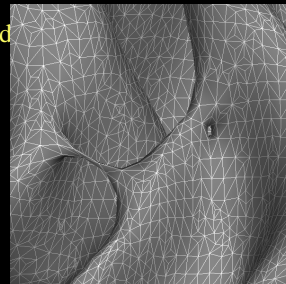


- Mosaic of triangles (“tessellation”)
- Errors: Donut holes, handles
- Automatic topology fixer

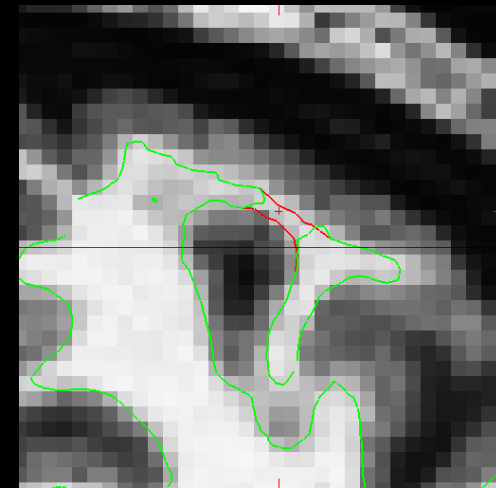
Topological Defects



- Holes
- Handles
- Automatically Fixed



Surface Correction

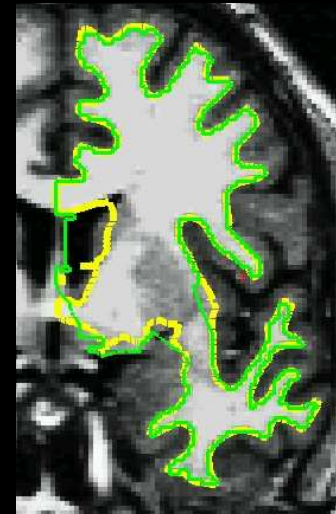


Difference between uncorrected (green) and corrected (red)

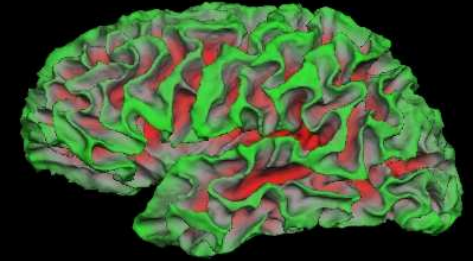
Topology Correction



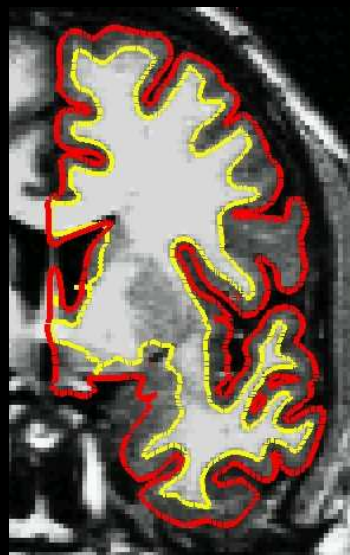
White Matter Surface



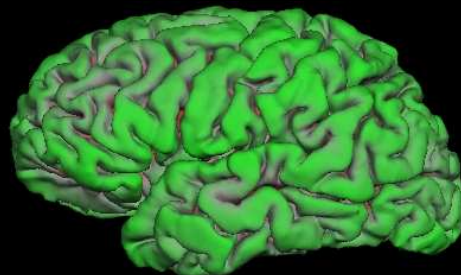
- Deform orig surface
- Follow T1 intensity gradients
- Smoothness and self-intersection constraints
- Vertex Identity (index) Preserved



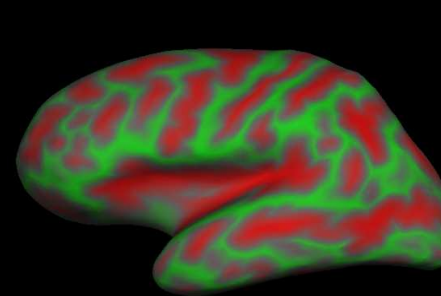
Pial Surface



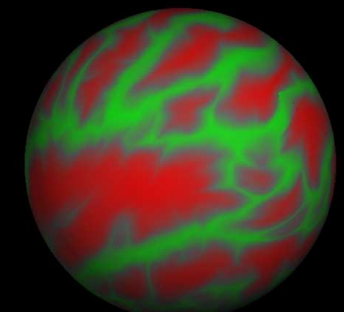
- Deform white surface
- Follow T1 intensity gradients
- Vertex Identity (index) Preserved



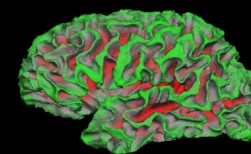
Surface “Inflation”



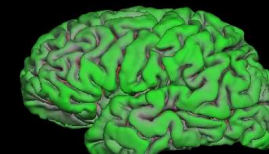
Inflated



Sphere



White

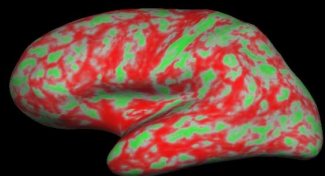


Pial

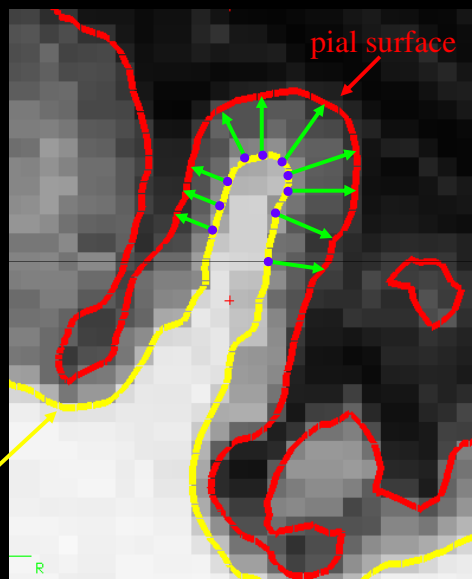
- Vertex Identity (index) Preserved

Cortical Thickness

- Distance between white and pial surfaces
- One value per vertex
- Vertices much denser!

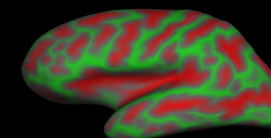
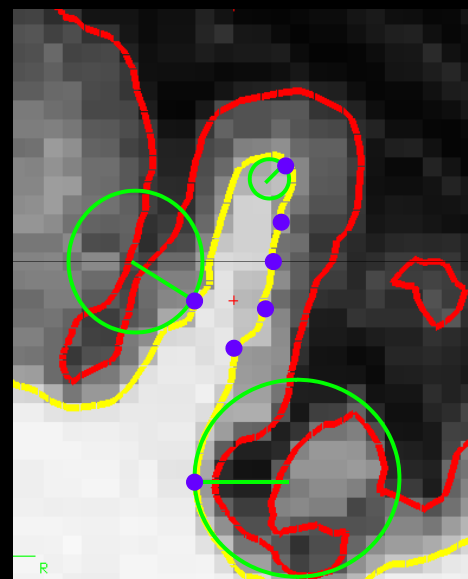


white/gray surface
lh.thickness, rh.thickness



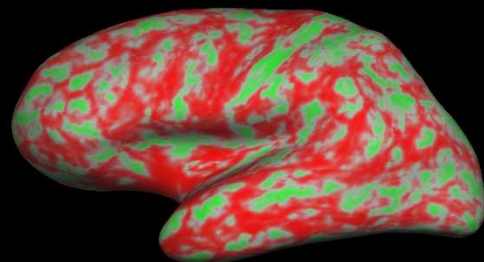
Curvature (Radial)

- Circle tangent to surface at each vertex
- Curvature measure is $1/\text{radius of circle}$
- One value per vertex
- Signed (sulcus/gyrus)
- Actually use mean curvature
- Signed value (gyri < 0)
- Vertices much denser!

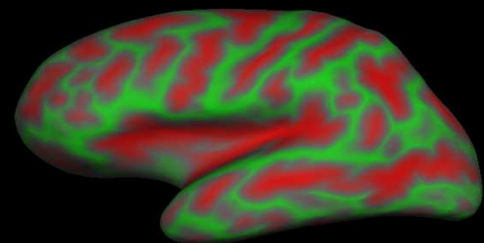
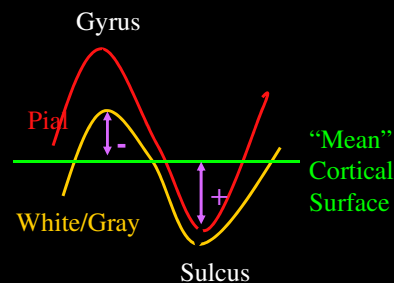


lh.curv, rh.curv

Cortical Morphometry

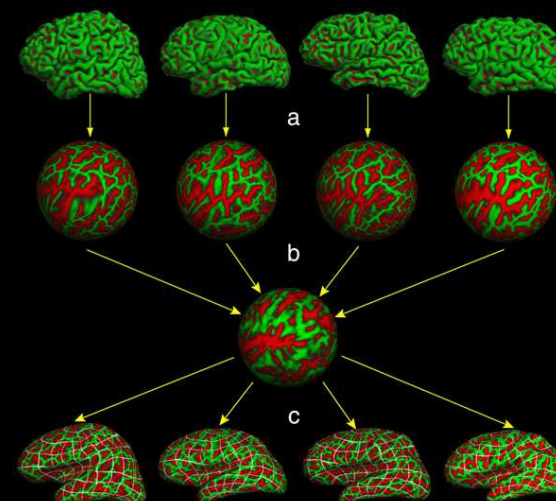


Thickness

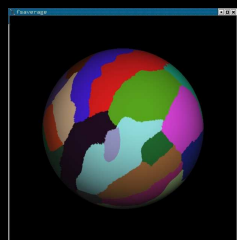


Sulcal Curvature

Inter-Subject Registration of Cortical Folding Patterns

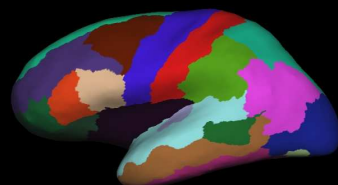


Automatic Cortical Parcellation

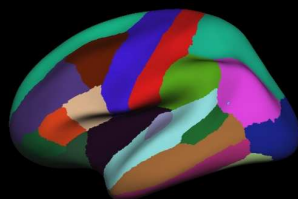


Spherical Template
based on Manual
Parcellation

Segment Individual
Using Spherical Reg



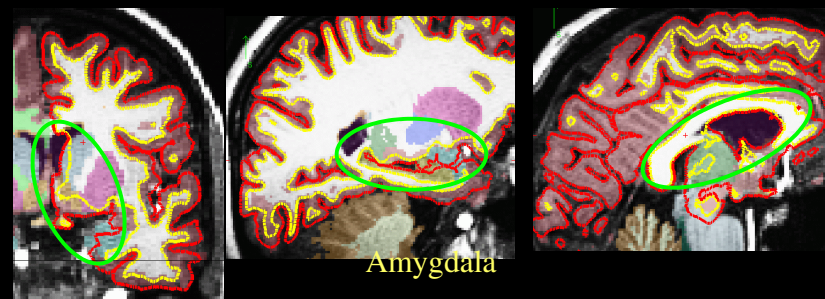
Fine-tune based on
individual anatomy



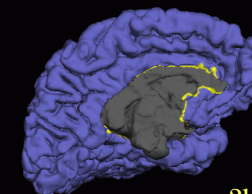
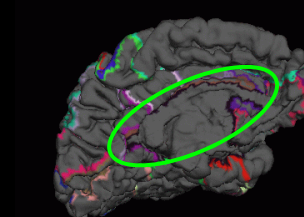
Note: Volume labeling done
in a similar way.

Atlases: curvature.buckner40filled.desikan_killiany, atlas_2005_simple

Non-Cortical Areas of Surface



Amygdala, Putamen, Hippocampus, Caudate, Ventricles, CC

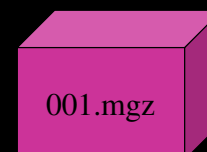


?h.cortex.label

Reconstruction Details

- Installation directory:
\$FREESURFER_HOME
- Unix command-line (Linux, MacOSX)
- File Formats
- Directory structure, naming conventions

MGZ File Format



- mgz = compressed MGH file
- Can store 4D (like NIFTI)
- cols, rows, slices, frames
- Generic: volumes and surfaces

- Eg, Typical Anatomical volume: 256 x 256 x 128 x 1

“Volume-encoded” Surface Overlay Files



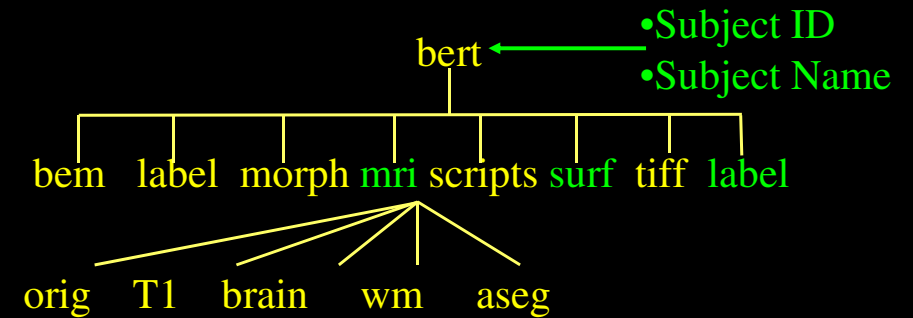
- nvertices, 1, 1, frames (eg, 163214 x 1 x 1 x 40)
- No geometry information

Other File Formats

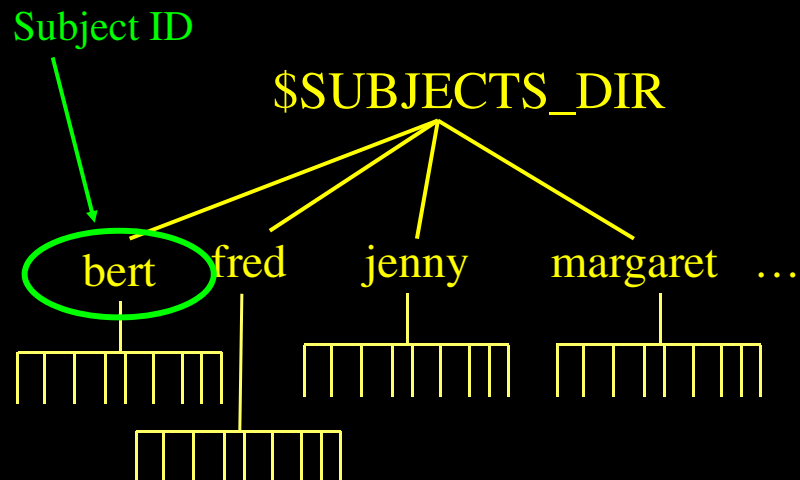
- Surface: lh.white
- Curv: lh.curv, lh.sulc, lh.thickness
- Annotation: lh.aparc.annot
- Label: lh.pericalcarine.label
- Unique to FreeSurfer
- FreeSurfer can read/write:
 - NIFTI, Analyze, MINC
 - Careful with NIFTI!
- FreeSurfer can read:
 - DICOM, Siemens IMA, GE, AFNI

FreeSurfer Directory Tree

Each data set has its own unique SubjectId (eg, bert)



SUBJECTS_DIR Environment Variable



Fully Automated Reconstruction

Launch reconstruction:

```
recon-all -s bert -i run1_slice1.dcm -i run2_slice1.dcm -autorecon-all
```

Come back in 30 hours ...

Check your results – do the white and pial surfaces follow the boundaries?
Are the folds labeled properly?

\$\$SUBJECTS_DIR

\$\$SUBJECTS_DIR

bert

?h.cortex.label ?h.aparc.annot, ? h.aparc.a2005s.annot

?h.white ?h.pial ?h.inflated ?h.curv ?h.sulc ?h.thickness...

orig.mgz norm.mgz aseg.mgz T1.mgz brain.mgz wm.mgz filled.mgz...

001.mgz 002.mgz

Volumetric Processing Stages (subjid/mri):

1. Motion Cor, Avg, Conform (orig.mgz)
2. Talairach transform computation
3. Non-uniform inorm (nu.mgz)
4. Intensity Normalization 1 (T1.mgz)
5. Skull Strip (brain.mgz)

6. EM Register (linear volumetric registration)
7. CA Intensity Normalization
8. CA Non-linear Volumetric Registration
9. CA Label (Volumetric Labeling) ([aseg.mgz](#))

10. Intensity Normalization 2 (T1.mgz)
11. White matter segmentation (wm.mgz)
12. Edit WM With ASeg
13. Fill and cut (filled.mgz)

Green = Manual Intervention?

recon-all -help

Note: ?h.orig means lh.orig or rh.orig

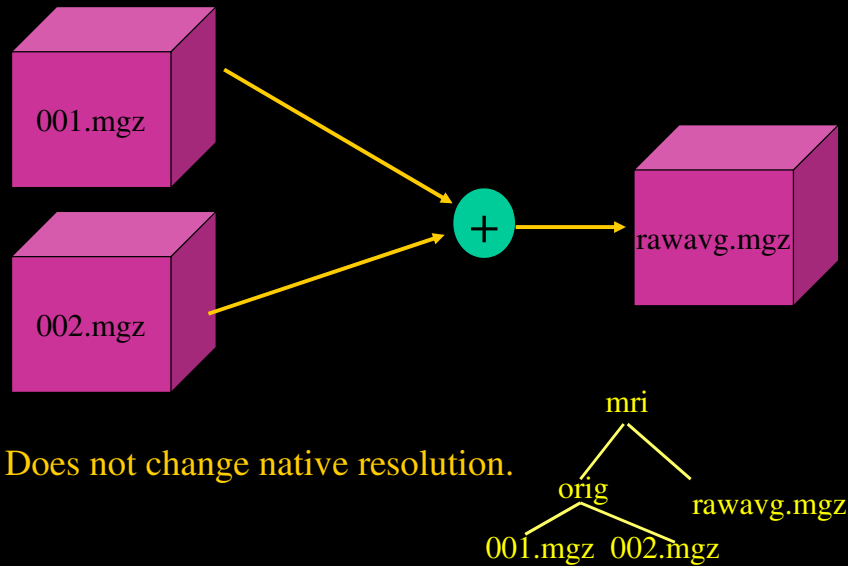
Surface Processing Stages (subjid/surf):

14. Tessellate (?h.orig)
15. Smooth1 (?h.smoothwm)
16. Inflate1 (?h.inflated)
17. QSphere (?h.qsphere)
18. Automatic Topology Fixer (?h.orig)
19. Euler Number
20. Smooth2
21. Inflate2
22. Final Surfs (?h.white,?h.pial)
23. Cortical Ribbon Mask
24. Spherical Morph
25. Spherical Registration
26. Spherical Registration
27. Map average curvature to subject
28. Cortical Parcellation (Labeling)
29. Cortical Parcellation Statistics
30. Cortical Parcellation mapped to ASeg

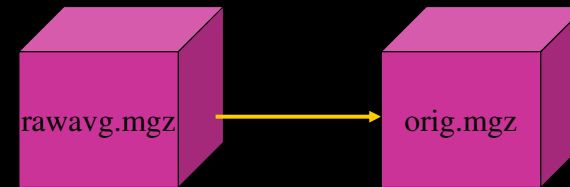


WMSeg includes `mri_segment`, `edit_wm_with_aseg`, and `mri_pretext`
 CP = Control Points
 Fill can have (`aseg.mgz&tal.lta`) or (`tal.xfm,cutting planes`) as input, but not both

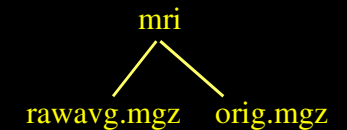
Motion Correction and Averaging



Conform

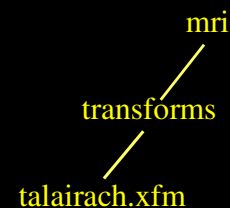


Changes to 256^3 , 1mm³, 8-bit
All volumes will be conformed.



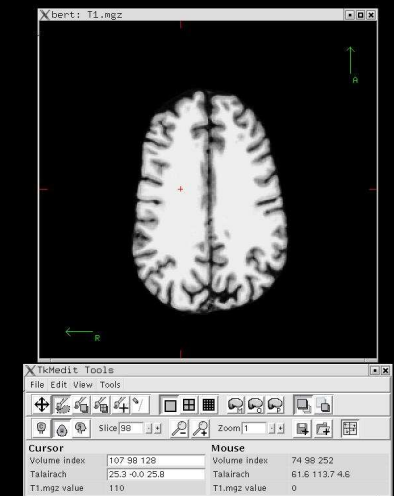
Talairach Transform

- Computes 12 DOF transform matrix
- Does NOT resample
- MNI305 template
- Used to help find structures (eg, CC)
- Can also be used to localize functional activation
- `mri/transforms/talairach.xfm`



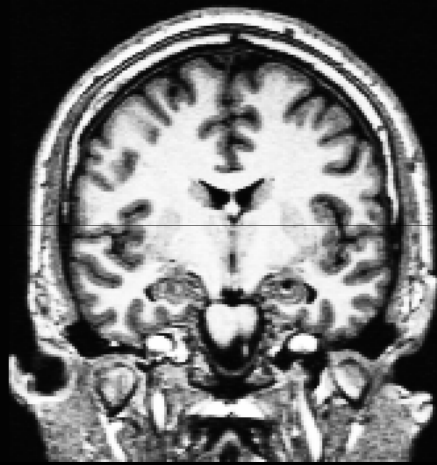
Intensity Normalization

- Removes (receive) B1 and coil bias field
- NU (N3 from MNI) `nu.mgz`
- Presegmentation (`T1.mgz`)
 - All WM close to 110 intensity
 - Pre- and Post-Skull Strip



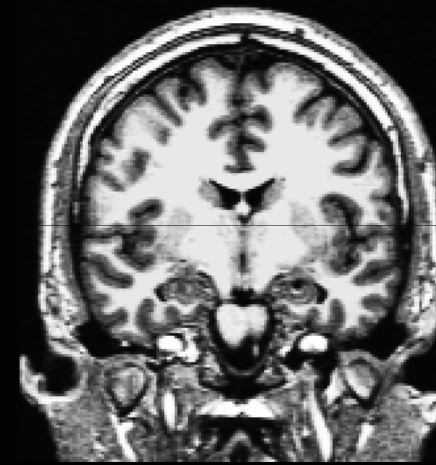
T1 Volume

Intensity Normalization (before)



mri
T1.mgz

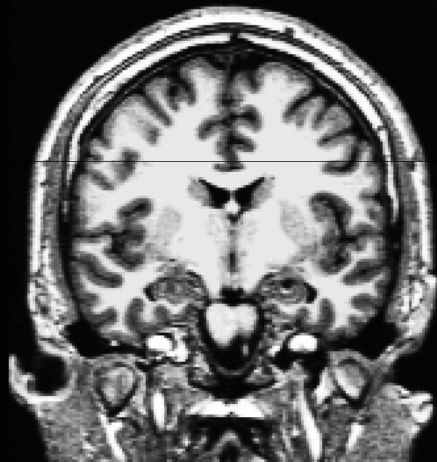
Intensity Normalization (after)



mri
T1.mgz

Skull Stripping (before)

Removes all non-brain (Skull, Eyes, Neck, Dura)



mri
brain.mgz
brainmask.mgz

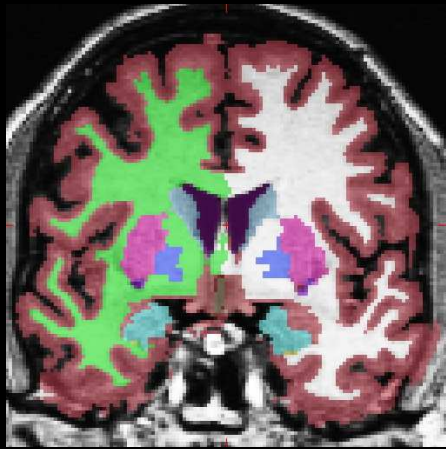
Skull Stripping (after)

Removes all non-brain (Skull, Eyes, Neck, Dura)



mri
brain.mgz/
brainmask.mgz

Automatic Volume Labeling



aseg.mgz volume

Atlas: RB_all_2006-2-15

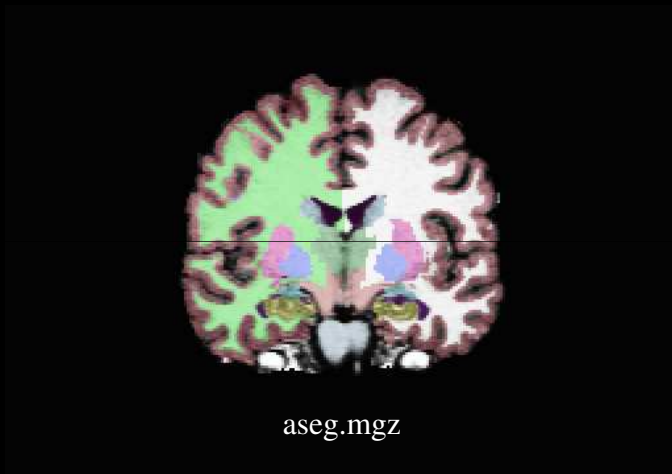
- Complete description of macroscopically observable neural structures.
- Used to fill in subcortical structures for creating subcortical mass (automates surface reconstruction).

Subcortical Segmentation (before)



norm.mgz

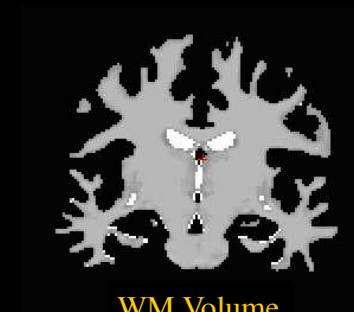
Subcortical Segmentation (after)



aseg.mgz

White Matter Segmentation

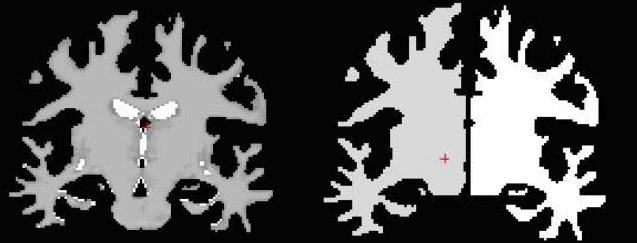
- Separates white matter from everything else
- “Fills in” subcortical structures using aseg
- Somewhat redundant with aseg (fault tolerance!)
- wm.mgz



WM Volume

Fill and Cut

- Fills in any voids
- Removes any islands
- Removes brain stem and cerebellum
- Separates hemispheres (each hemi has different value)
- filled.mgz (“Subcortical Mass”)



WM Volume

Filled Volume

Troubleshooting

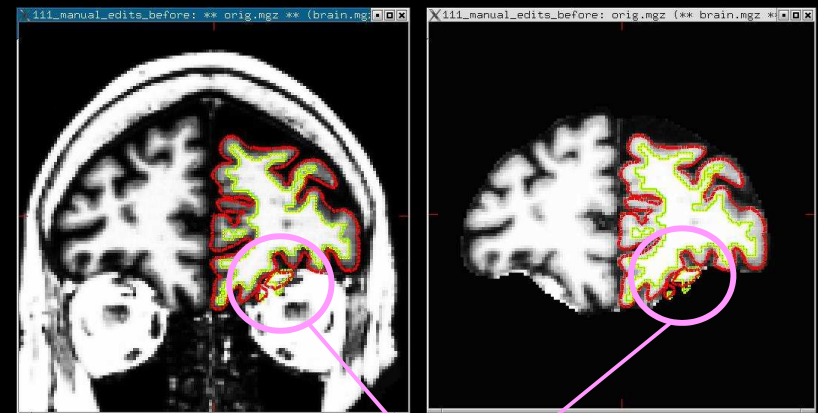
- Segmentation Errors
- Skull Strip Errors
- Intensity Normalization
- Pial Surface

Troubleshooting – Common Cases

(<10% of cases for good data)

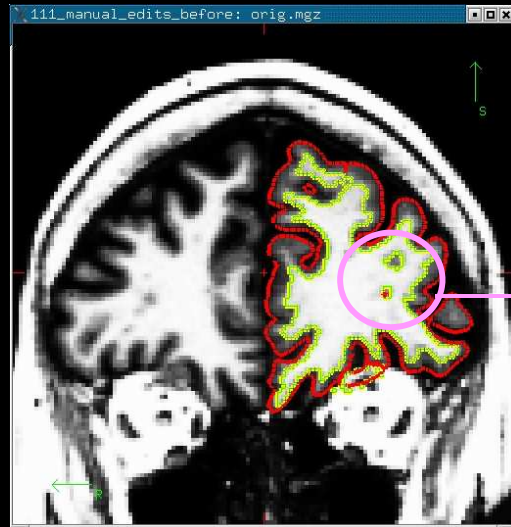
- **Symptom:** wm.mgz not accurate
- **Interventions**
 - add control points (if $wm \ll 110$).
 - Expert opts to set intensity thresholds in segmentation (almost never).
 - Manually erase/draw wm
- **Symptom:** skull strip not accurate
- **Interventions**
 - Check/fix talairach.
 - Adjust mri_watershed parameters
 - Manually erase skull/clone T1.mgz to recover brain
- **Symptom:** surfaces are not accurate.
- **Interventions:**
 - Add control points (if white matter $\ll 110$).
 - Erase dura/blood vessels
 - Check topology on ?h.inflated.nofix (if ?h.orig surface doesn't follow wm.mgz)

Troubleshooting: Segmentation Error



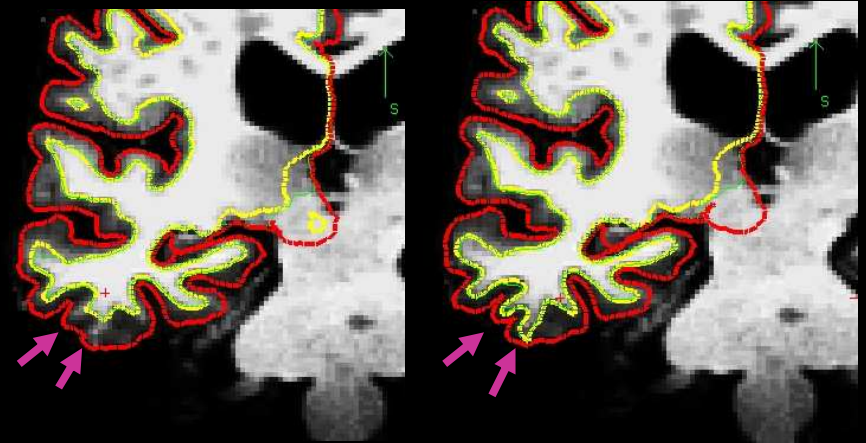
Eye Socket classified as WM.
Skull Strip Failure.

Troubleshooting: Segmentation Error



“Hypo-Intensities”
White Matter Lesions
Misclassified as gray
matter

Troubleshooting: Intensity Normalization



Intensity Normalization Failure.
Most WM in T1 volume (T1.mgz) should be close to 110.
Can fix by adding “Control Points”. Beware partial voluming!

Troubleshooting: Skull Strip

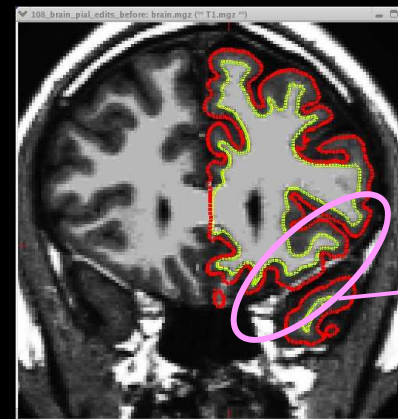


orig.mgz



brainmask.mgz

Troubleshooting: Skull Strip/Pial Surface Error



Dura or Blood Vessel
White/Gray OK, but
Pial Inaccurate

Individual Stages

Volumetric Processing Stages (subjid/mri):

1. Motion Cor, Avg, Conform (orig.mgz)
2. Talairach transform computation
3. Non-uniform inorm (nu.mgz)
4. Intensity Normalization 1 (T1.mgz)
5. Skull Strip (brain.mgz)
6. EM Register (linear volumetric registration)
7. CA Intensity Normalization
8. CA Non-linear Volumetric Registration
9. CA Label (Volumetric Labeling) (aseg.mgz)

10. Intensity Normalization 2 (T1.mgz)
11. White matter segmentation (wm.mgz)
12. Edit WM With ASeg
13. Fill_and cut (filled.mgz)

Green = Manual Intervention?

recon-all -help

Note: ?h.orig means lh.orig or rh.orig

Surface Processing Stages (subjid/surf):

14. Tessellate (?h.orig)
15. Smooth1 (?h.smoothwm)
16. Inflate1 (?h.inflated)
17. QSphere (?h.qsphere)
18. Automatic Topology Fixer (?h.orig)
19. Euler Number
20. Smooth2
21. Inflate2
22. Final Surfs (?h.white,?h.pial)
23. Cortical Ribbon Mask
24. Spherical Morph
25. Spherical Registration
26. Spherical Registration
27. Map average curvature to subject
28. Cortical Parcellation (Labeling)
29. Cortical Parcellation Statistics
30. Cortical Parcellation mapped to ASeg

Actual Workflow

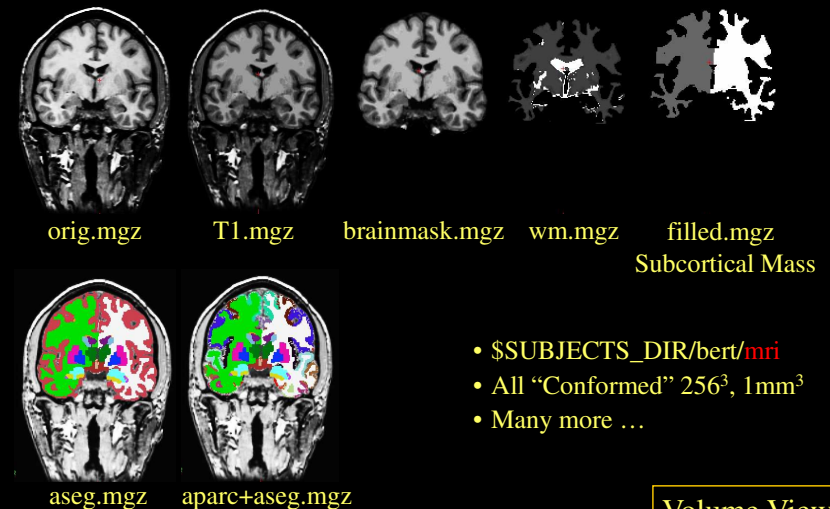
1. recon-all -all (Stages 1-30)
2. Check talairach transform, skull strip, normalization (?)
3. Check surfaces. Possible interventions:
 - 3a. Add control points: recon-all -autorecon2-cp (Stages 10-23)
 - 3b. Edit wm.mgz: recon-all -autorecon2-wm (Stages 13-23)
 - 3c. Edit brain.mgz: recon-all -autorecon2-pial (Stage 23)
 - 3d. (if anything changed) recon-all -autorecon3 (Stages 24-30)

Note: all stages can be run individually

Results

- Volumes
- Surfaces
- Surface Overlays
- ROI Summaries

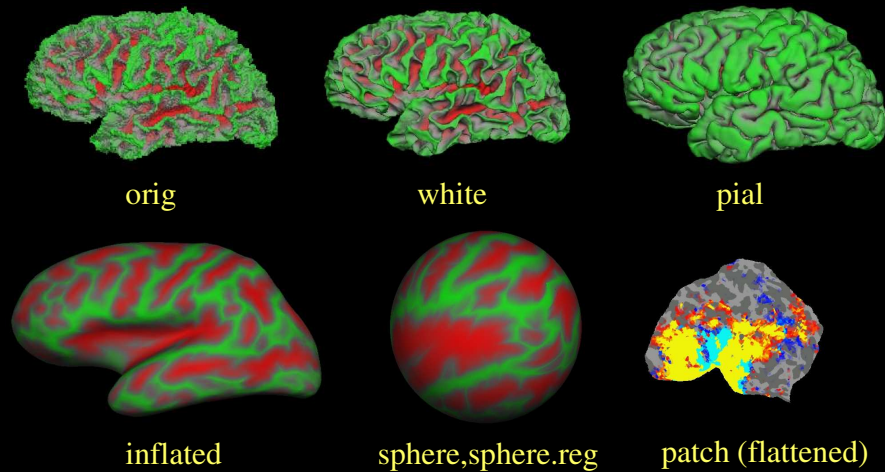
Volumes



- \$\$SUBJECTS_DIR/bert/mri
- All “Conformed” 256³, 1mm³
- Many more ...

Volume Viewer:
tkmedit

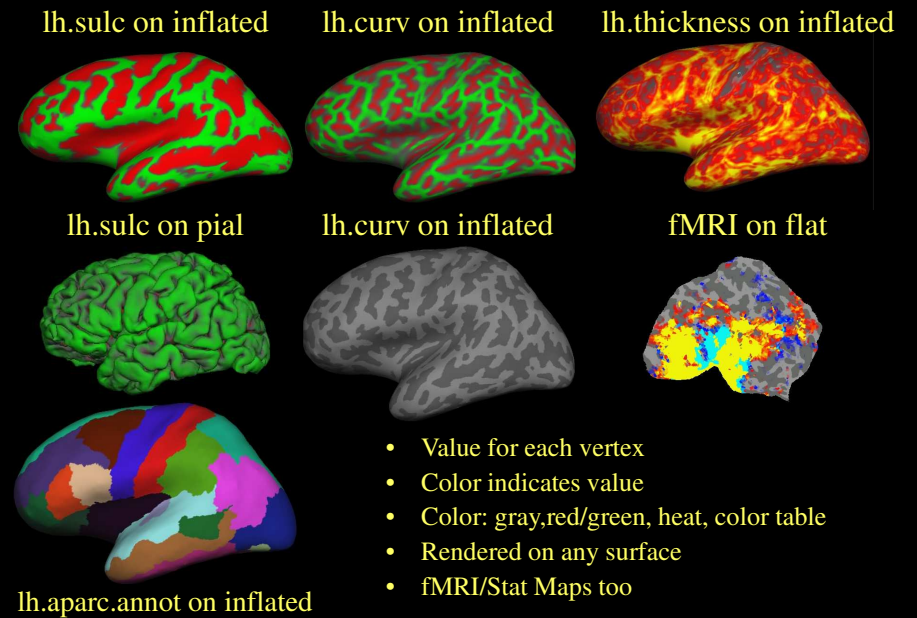
Surfaces



- `$SUBJECTS_DIR/bert/surf`
- Number/Identity of vertices stays the same (except patches)
- XYZ Location Changes
- Flattening not done as part of standard reconstruction

Surface Viewer:
tksurfer

Surface Overlays



- Value for each vertex
- Color indicates value
- Color: gray, red/green, heat, color table
- Rendered on any surface
- fMRI/Stat Maps too

ROI Summaries:

`$SUBJECTS_DIR/bert/stats`

aseg.stats – volume summaries

?h.aparc.stats – desikan/killiany parcellation summaries

?h.aparc.2005.stats – destrieux parcellation summaries

wmparc.stats – white matter parcellation

Index	SegId	NVoxels	Volume_mm3	StructName	normMean	normStdDev	normMin	normMax	normRange
1	1	0	0.0	Left-Cerebral-Exterior	0.0000	0.0000	0.0000	0.0000	0.0000
2	2	265295	265295.0	Left-Cerebral-White-Matter	106.6763	8.3842	35.0000	169.0000	134.0000
3	3	251540	251540.0	Left-Cerebral-Cortex	81.8395	10.2448	29.0000	170.0000	141.0000
4	4	7347	7347.0	Left-Lateral-Ventricle	42.5800	12.7435	21.0000	90.0000	69.0000
5	5	431	431.0	Left-Inf-Lat-Vent	66.2805	11.4191	30.0000	95.0000	65.0000
6	6	0	0.0	Left-Cerebellum-Exterior	0.0000	0.0000	0.0000	0.0000	0.0000

Routines to generate spread sheets of group data

- `asegstats2table --help`
- `aparcstats2table --help`

Demo

1. tkmedit – volume viewer
2. tksurfer – surface viewer

On to the Practical!

1. Open Firefox browser
(surfer.nmr.mgh.harvard.edu/fswiki/Tutorials)
2. Click on “FreeSurfer tutorial”
3. Session 1a and 1b (Session 2 tomorrow)
1a Using visualization tools
1b Troubleshooting
4. Open a terminal window.
5. Cut-and-paste

Acknowledgements

MGH

Jenni Pacheco
Nick Schmansky
Brian T Quinn
Andre van der Kouwe
Doug Greve
David Salat
Evelina Busa
Lilla Zollei
Koen Van Leemput
Xiao Han
Kevin Teich

MGH

Niranjini Rajendran
Dennis Jen
Allison Stevens

BWH

Wendy Plesniak
Nicole Aucoin
Kathryn Hayes
Haiying Liu
Steve Pieper

UC San Diego

Anders Dale

UCL

Marty Sereno

