

Introduction to Freesurfer



Repronim workshop 3/30/2021

Learning leads to brain changes

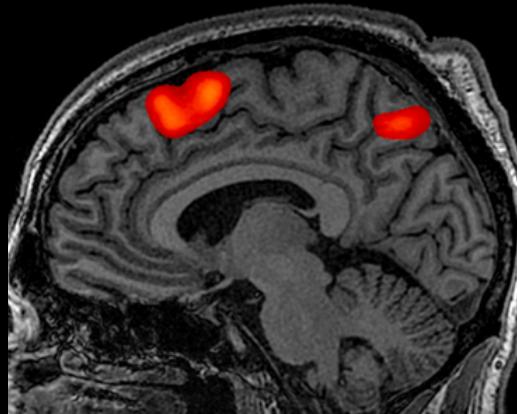
- Learning new tasks is associated with brain changes



Learning leads to brain changes

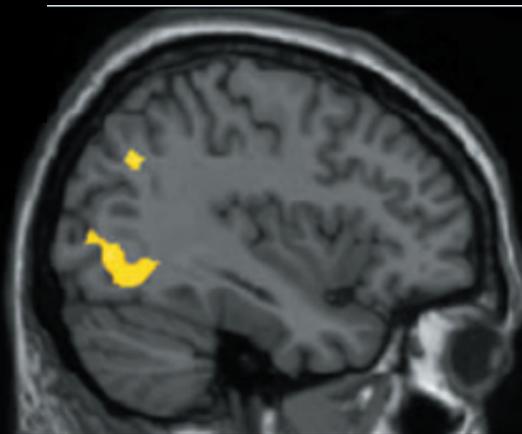
- Learning new tasks is associated with changes in:

Functional activity
(Green & Bavelier, 2008;
Karni et al., 1995)



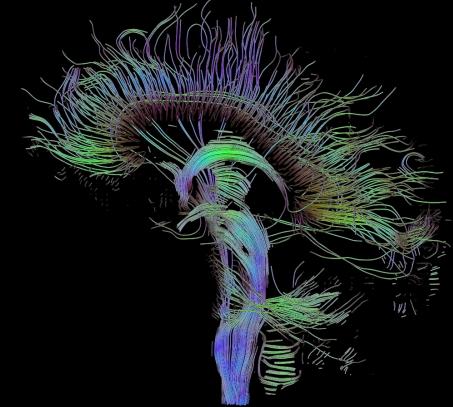
fMRI

Gray matter structure
(Draganski et al., 2004;
Maguire et al., 2000)



sMRI

White matter microstructure
(Draganski et al.,
2004)



DTI

Tissues of the brain

- Gray Matter (GM)

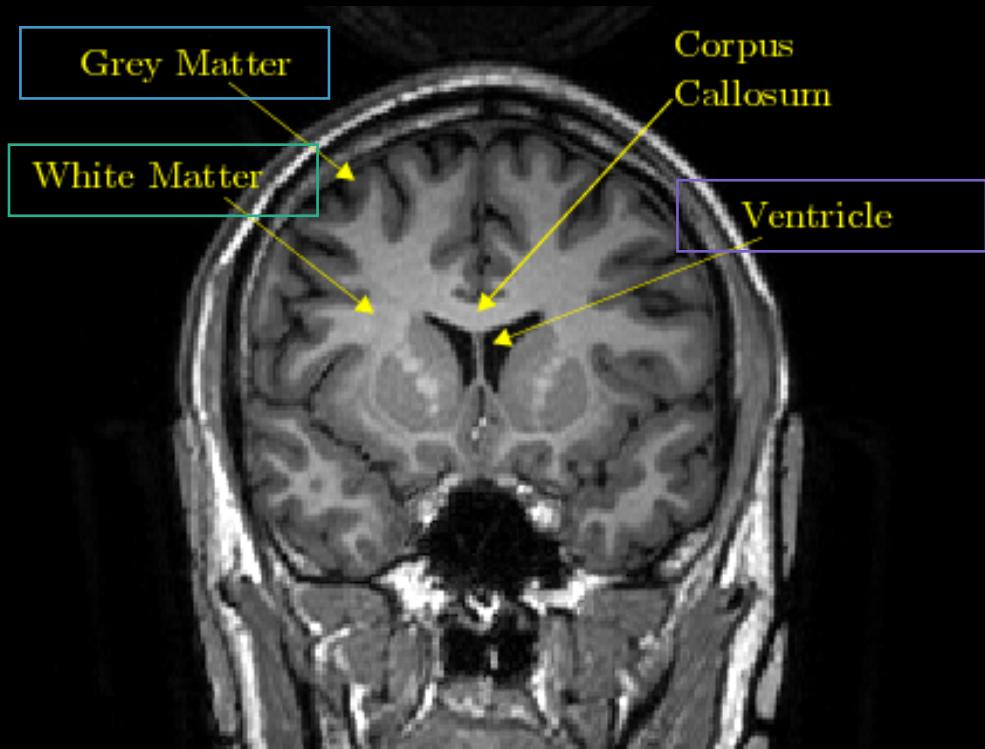
- Cell bodies & dendrites

- White Matter (WM)

- Neural axons

- Cerebrospinal fluid (CSF)

- Fluid that the brain is suspended in

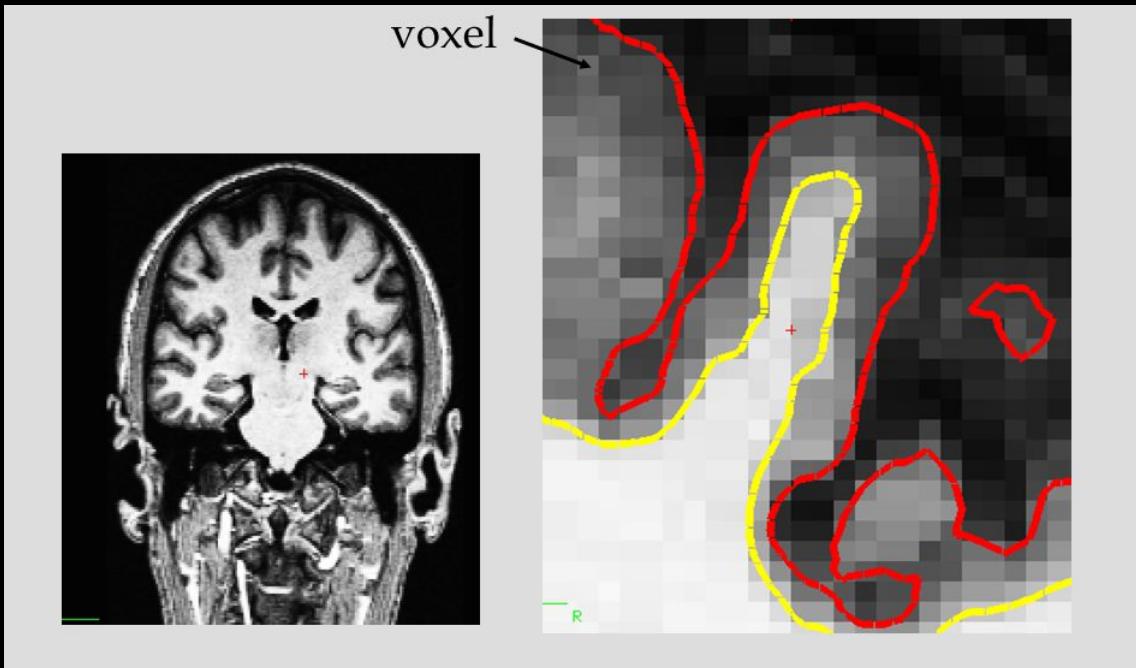


Why examine gray matter?

- Provides a high-resolution picture of the brain
- sMRI findings are not task-dependent
 - Can compare findings across various studies
- When used in a longitudinal paradigm, can provide a concrete measure of neural plasticity
- When combined with other MRI scans, can provide a more comprehensive understanding of neural mechanisms

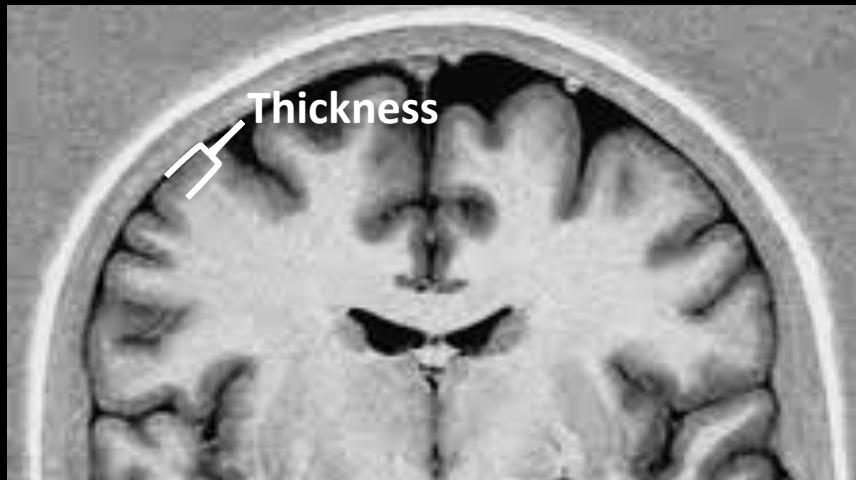
Brain structure measures

- Gray matter volume (GMV)
 - Aggregate measure of synaptogenesis, axon sprouting, dendritic branching (Zatorre et al., 2012)
 - Extensive literature to draw upon
 - Limited by size of voxel



Brain structure measures

- Cortical thickness (CT)
 - Measured as closest distance between gray/CSF boundary and gray/white matter boundary
 - Can detect submillimeter level differences and accounts for cortical folding
 - Posited to reflect cognitive processes more accurately than GMV (Narr et al., 2007)



How do we examine gray matter?

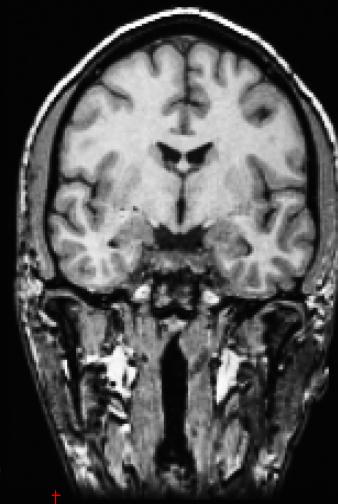
- Voxel - Based Morphometry (VBM)
 - Available with SPM or FSL
 - Easy to use with GUI, appropriate for clinical studies expecting large differences
 - Not as appropriate for longitudinal data or for examining small individual differences

How do we examine gray matter?

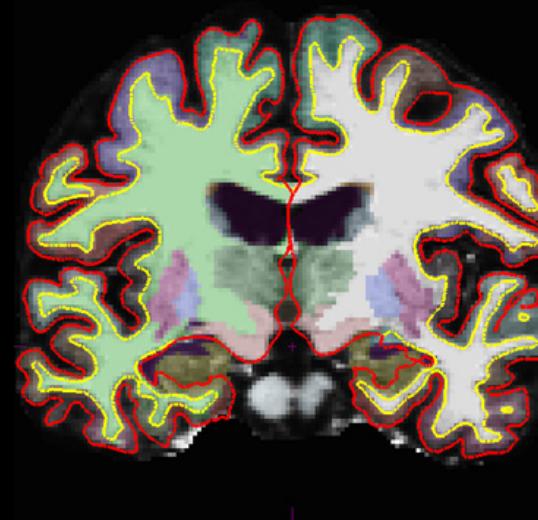
- Cortical surface registration
 - Available with Freesurfer
 - More complex processing requiring bash scripting and commands
 - Can tailor commands to your specific data needs
 - Most appropriate for longitudinal data and for examining small individual differences

What FreeSurfer Does...

FreeSurfer creates computerized models of the brain from MRI data.



Input:
T1-weighted (MPRAGE)
1mm³ resolution
.dcm



Output:
Segmented & parcellated conformed
volume
.mgz

Registration

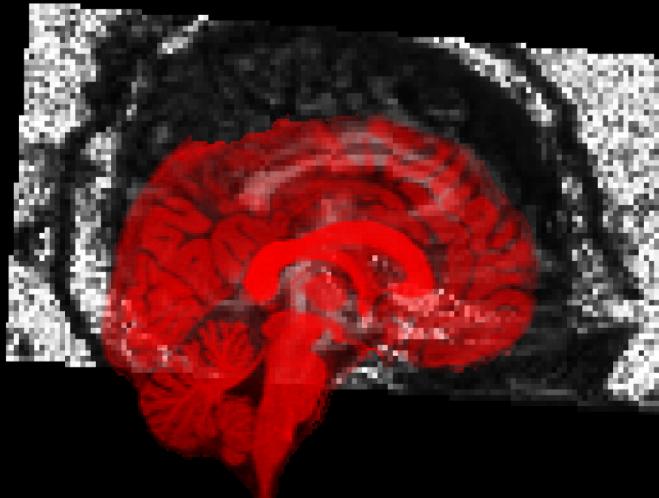
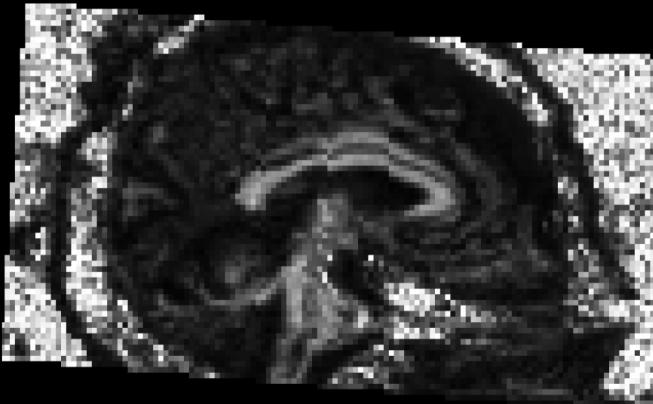
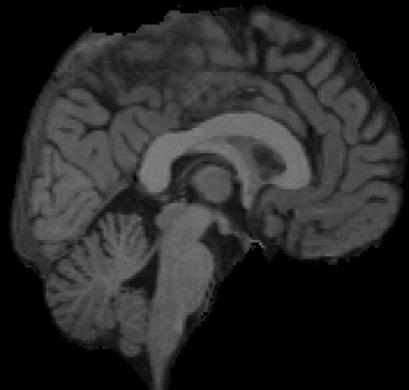
Goal:

To find a common coordinate system for the input data sets

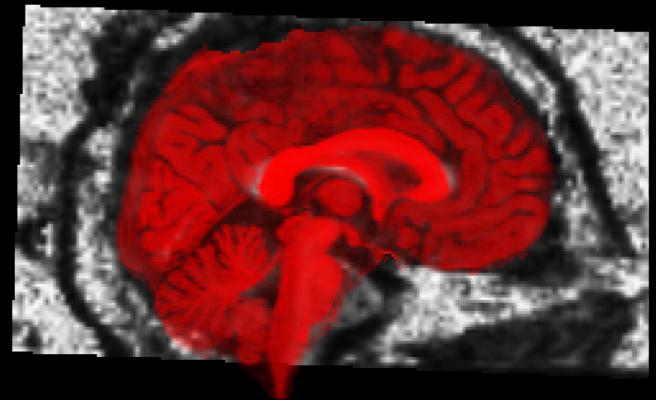
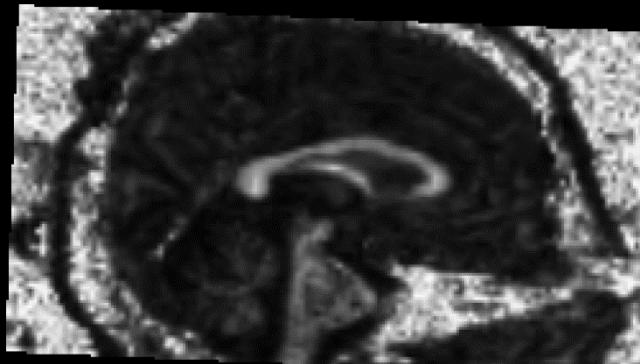
Examples:

- Comparing different MRI images of the same individual
 - Longitudinal scans, diffusion vs functional scans
- Comparing MRI images of different individuals

Examples of registration



before spatial alignment



after spatial alignment

Robust Registration

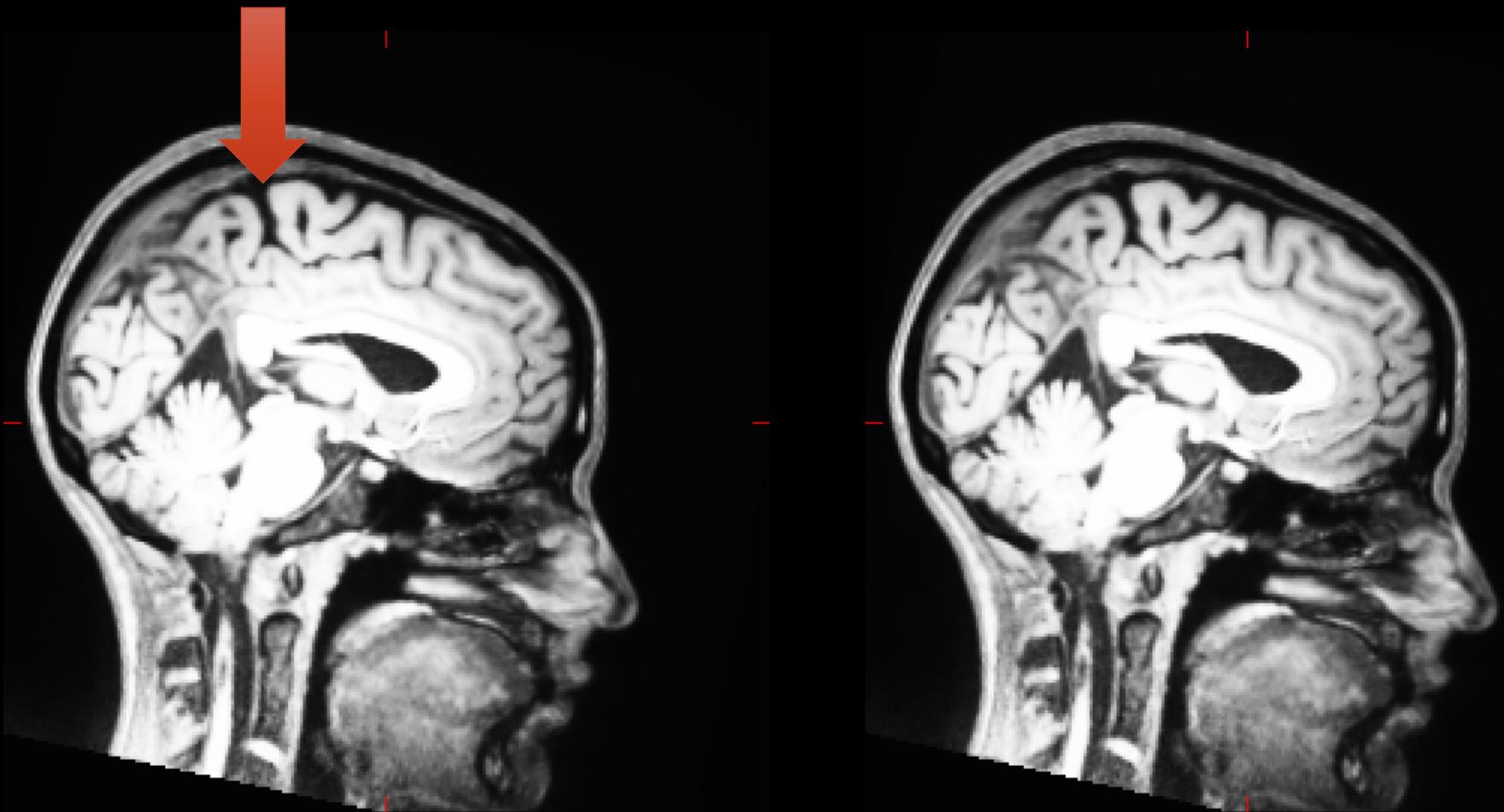


Target



Target

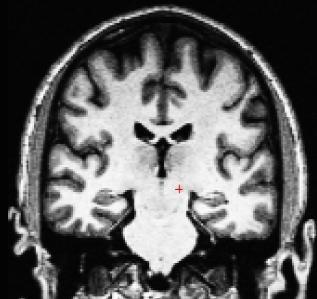
Robust Registration



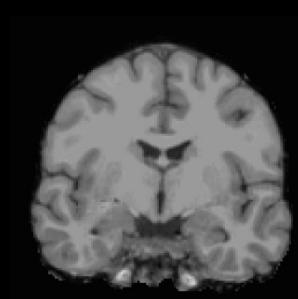
Registered Src correlation ratio

Registered Src Robust

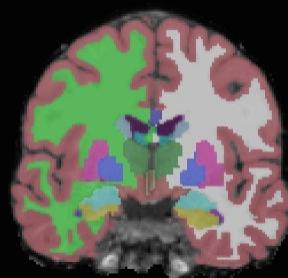
Processing Stream Overview



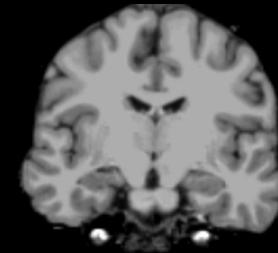
T1 Weighted
Input



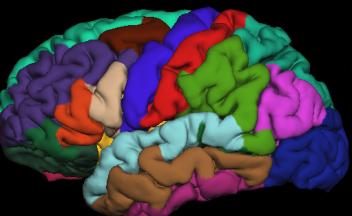
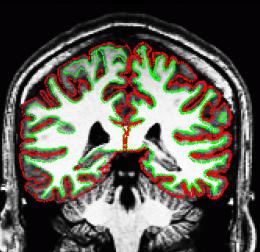
Skull Stripping



Volumetric Labeling



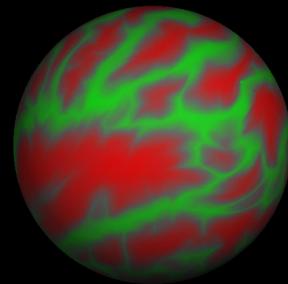
Intensity
Normalization



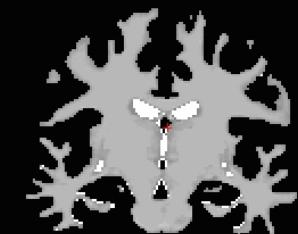
Gyral Labeling



Surface Extraction



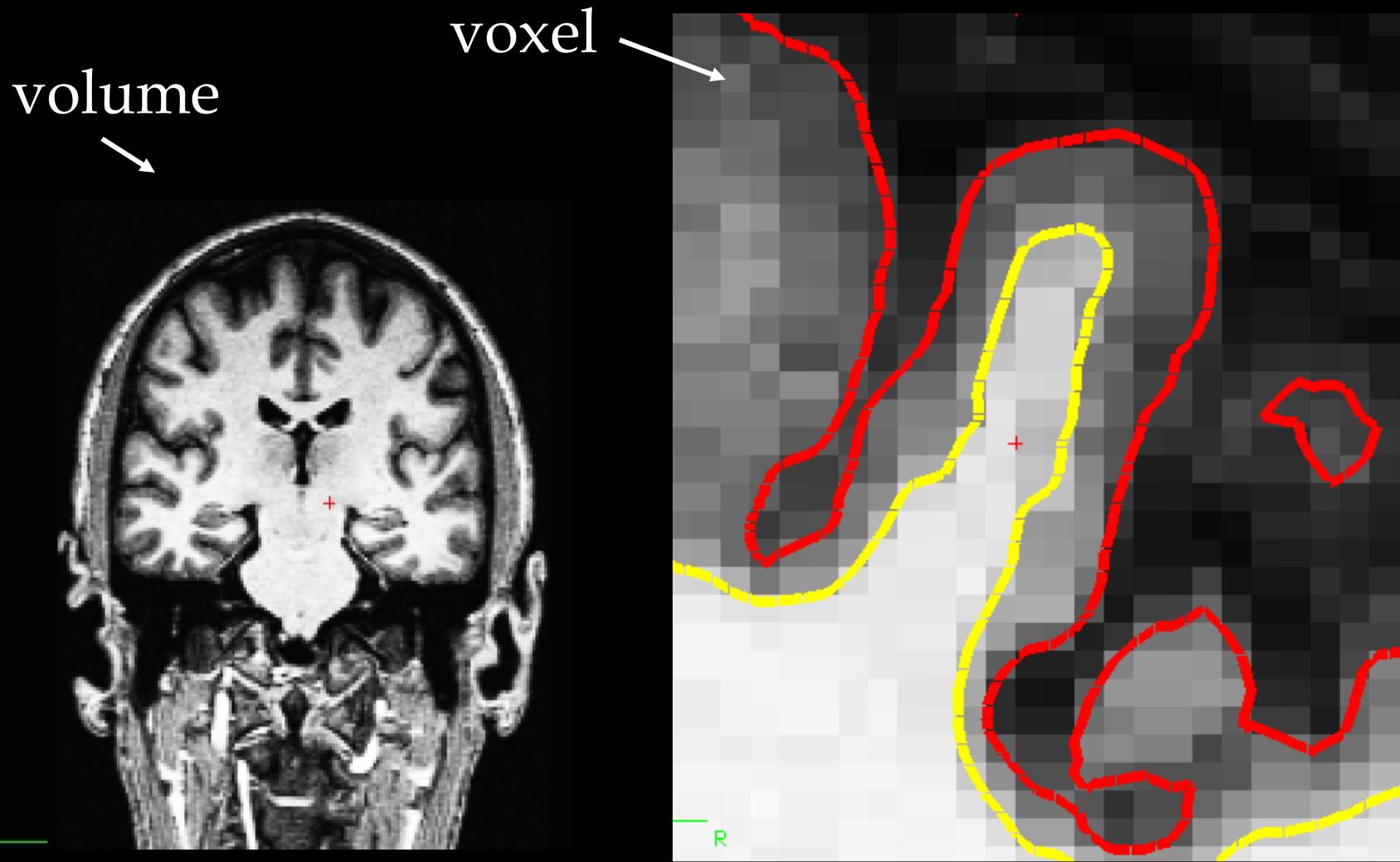
Surface Atlas
Registration



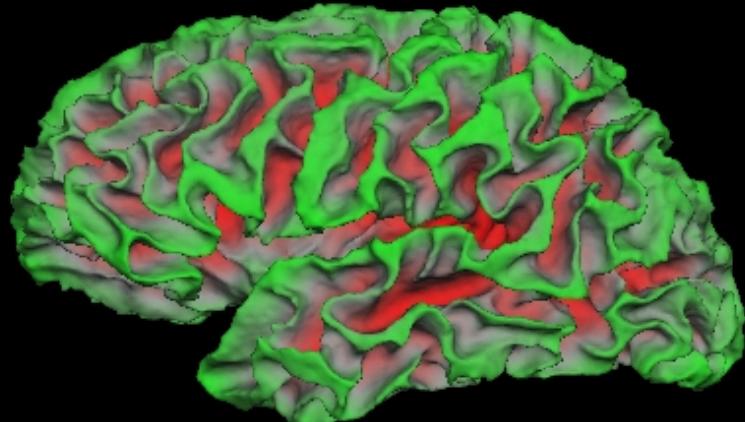
White Matter
Segmentation

Stats!

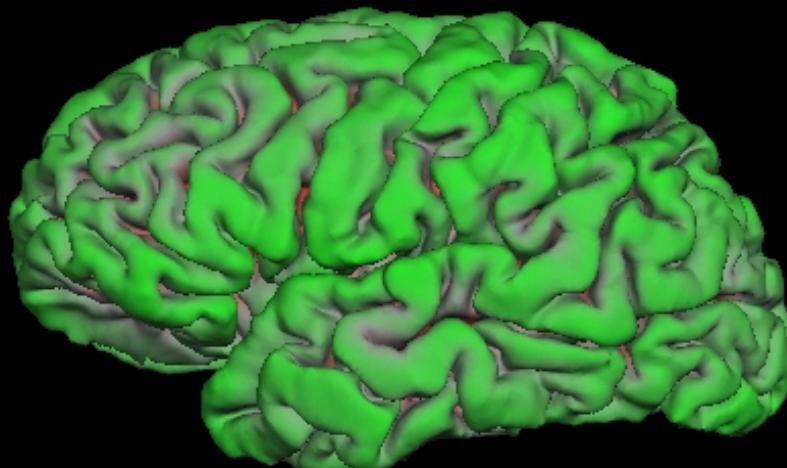
Intro to FreeSurfer Jargon



Intro to FreeSurfer surfaces

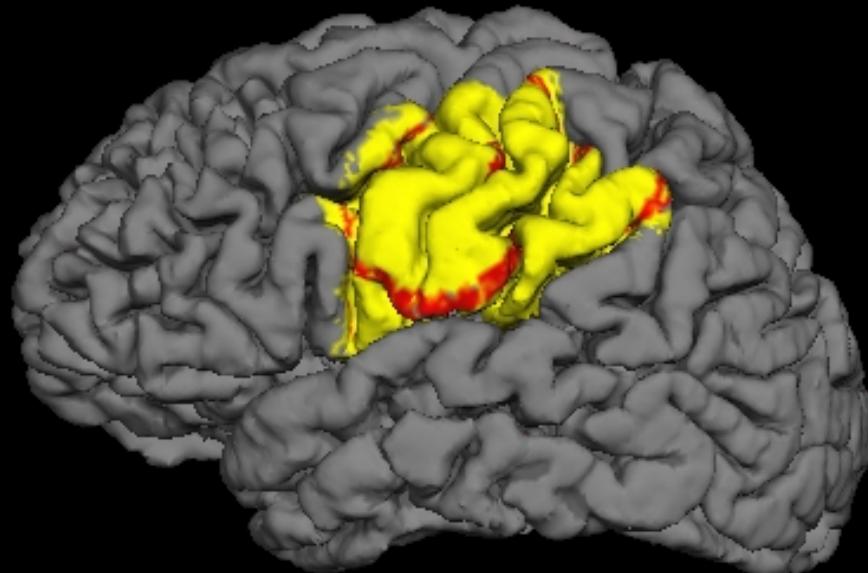


White matter
surface



Pial surface

Intro to FreeSurfer surfaces



Inflated surface
lets you see
areas hidden by
sulci ↓



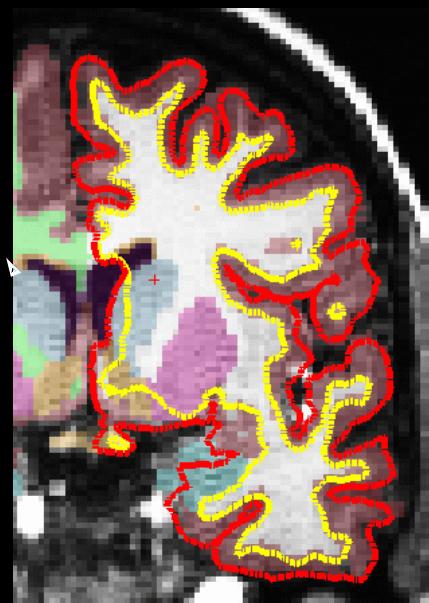
Most significance maps are added as overlays on the inflated surface

Cortical vs. Subcortical GM

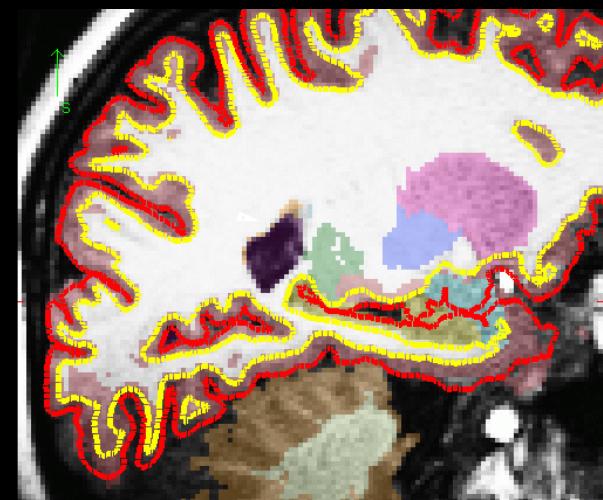
cortical gm



subcortical gm



coronal

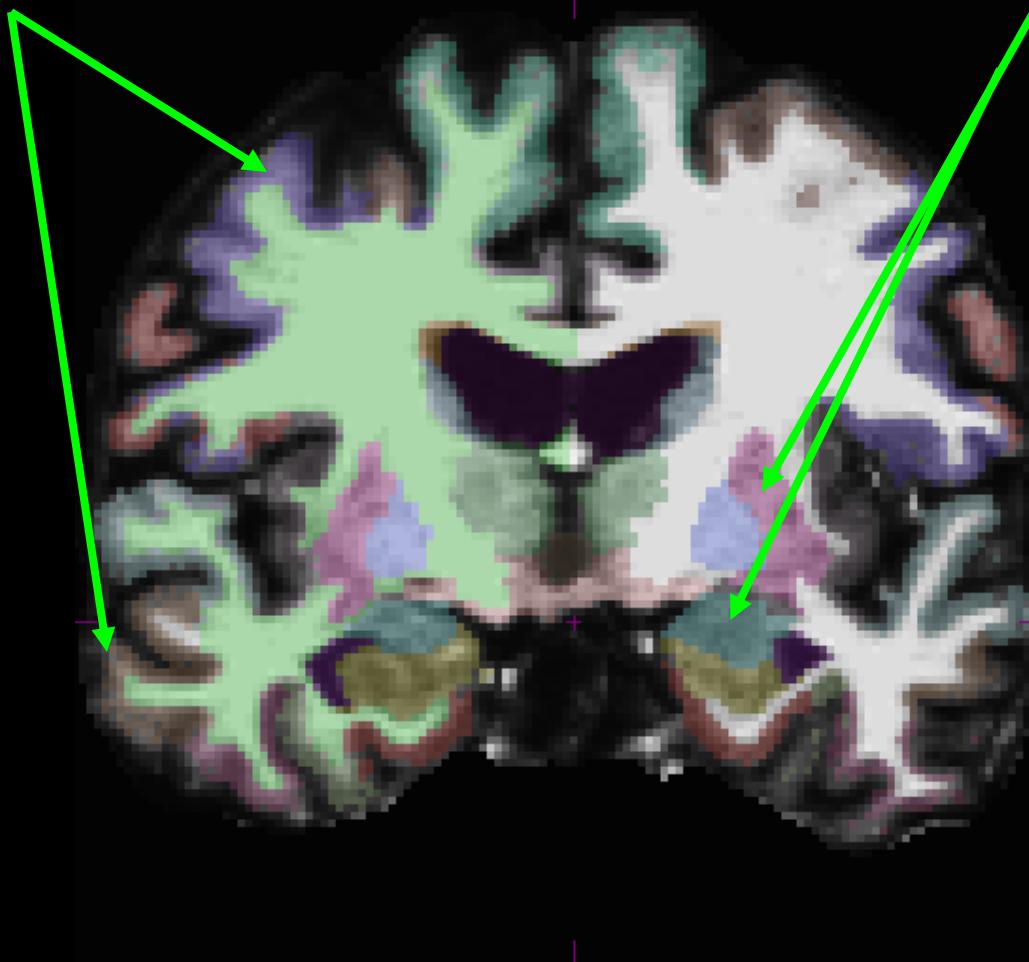


sagittal

Parcellation vs. Segmentation

(cortical) parcellation

(subcortical) segmentation

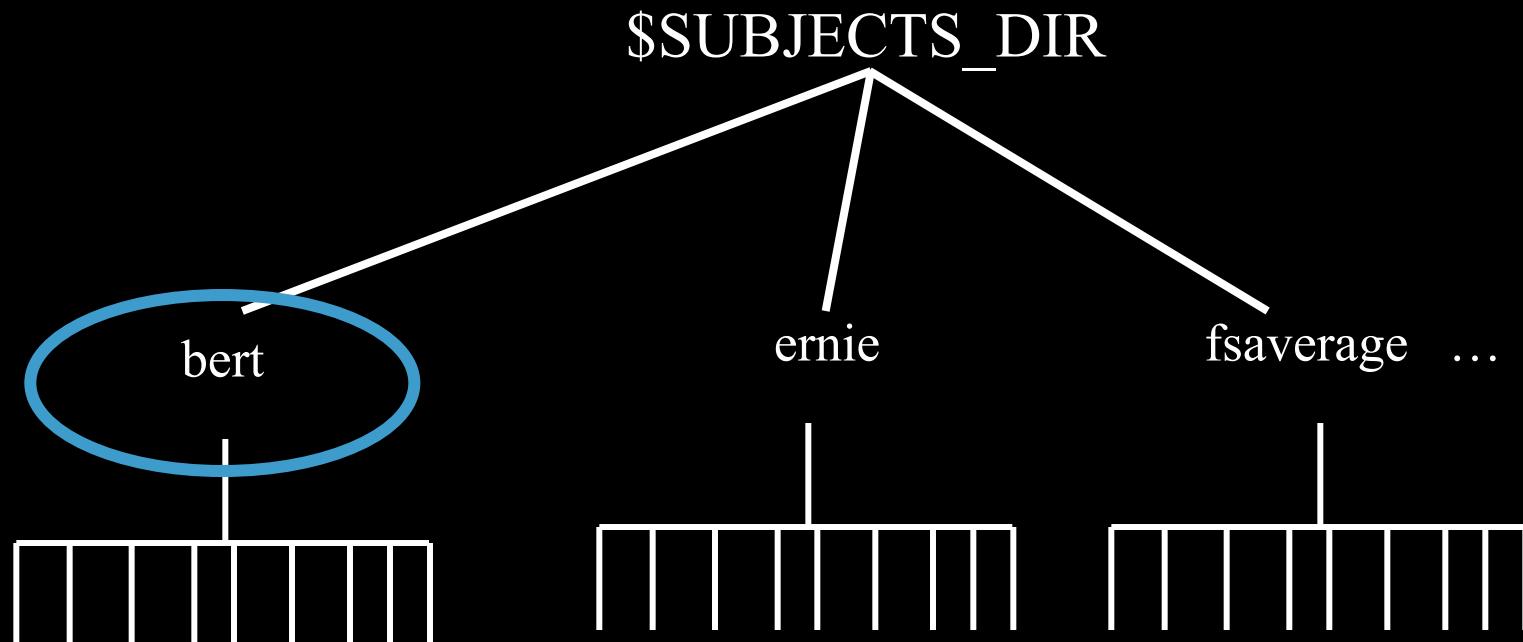


Reconstruction steps

```
recon-all
```

```
  -i sMRI.nii  
  -subject bert  
  -all
```

- The first recon-all command creates a subject-specific folder in a structure that Freesurfer can read for all further steps
- “bert” is the “name” of the subject
- Creates a folder in \$SUBJECTS_DIR
- All output goes in this folder (~400MB)
- Other subjects in \$SUBJECTS_DIR

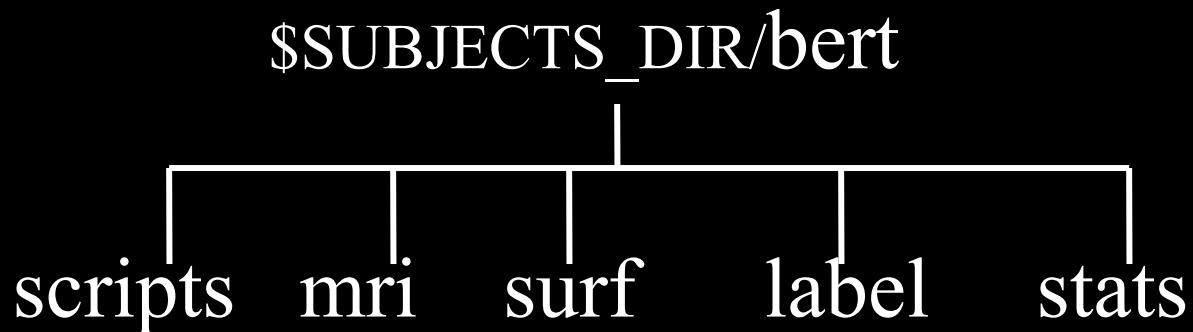


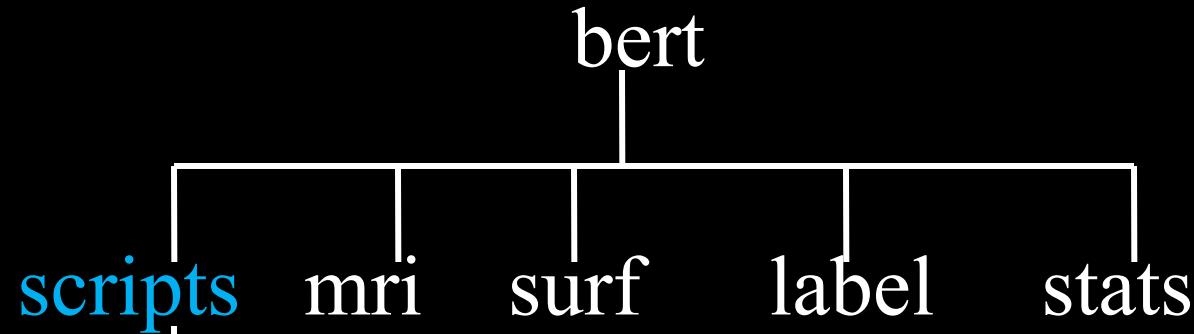
```
export SUBJECTS_DIR /path/to/space
```

Upon Completion...

```
recon-all autorecon-all -i sMRI.nii -  
subject bert
```

This does the actual reconstruction





recon-all.log
recon-all.done

Just because it finishes
“without error” does not mean
that everything is ok!

```

Terminal
File Edit View Search Terminal Help

limiting computations to label ./rh.entorhinal_exvivo.label.
reading volume /autofs/cluster/freesurfer/test/dng/v5.3/b40/045/mri/wm.mgz...
reading input surface /autofs/cluster/freesurfer/test/dng/v5.3/b40/045/surf/rh.white...
reading input pial surface /autofs/cluster/freesurfer/test/dng/v5.3/b40/045/surf/rh.pial...
reading input white surface /autofs/cluster/freesurfer/test/dng/v5.3/b40/045/surf/rh.white...
INFO: assuming MGZ format for volumes.

table columns are:
  number of vertices
  total surface area (mm^2)
  total gray matter volume (mm^3)
  average cortical thickness +- standard deviation (mm)
  integrated rectified mean curvature
  integrated rectified Gaussian curvature
  folding index
  intrinsic curvature index
  structure name

  236      152      759   3.117  0.598     0.141      0.035      3      0.4 ./rh.entorhinal_exvivo.label

#-----#
Started at Fri Apr 26 19:18:47 EDT 2013
Ended   at Sat Apr 27 12:07:26 EDT 2013
#Q#%# recon-all-run-time-hours 16.811
recon-all -s 045 finished without error at Sat Apr 27 12:07:26 EDT 2013
[t:D:~->]
  
```

Send freesurfer recon-all.log when you have
problems! freesurfer@nmr.mgh.harvard.edu

Upon Completion...

bert

scripts

mri

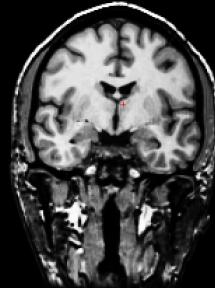
surf

label

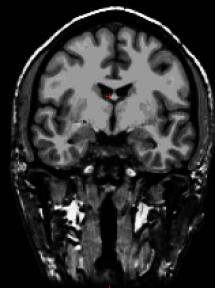
stats



rawavg.mgz



orig.mgz



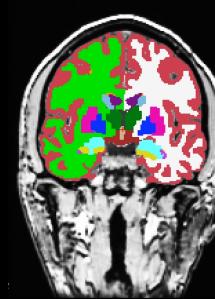
T1.mgz



brainmask.mgz



wm.mgz



aseg.mgz

others: nu.mgz, norm.mgz, wmparc.mgz, aparc+aseg.mgz, ribbon.mgz

Upon Completion...

bert

scripts

mri

surf

label

stats



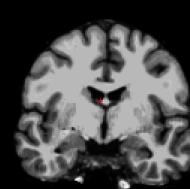
rawavg.mgz



orig.mgz



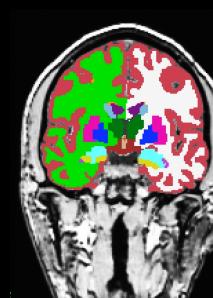
T1.mgz



brainmask.mgz



wm.mgz



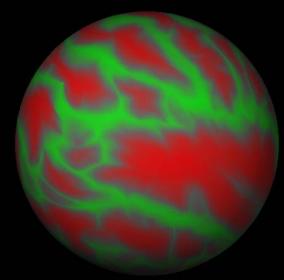
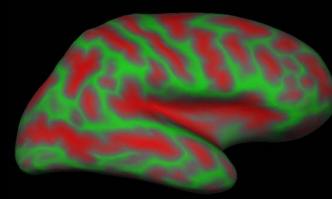
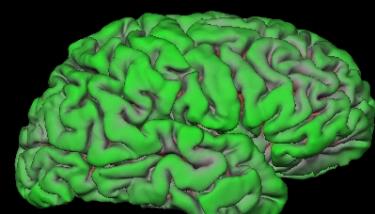
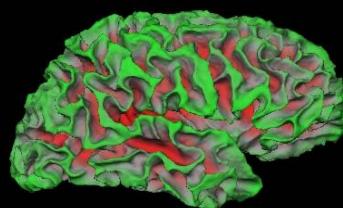
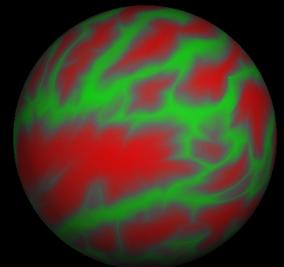
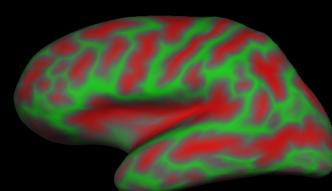
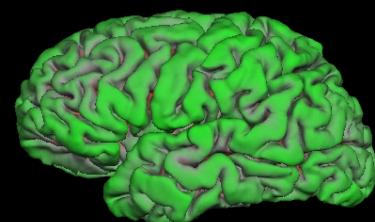
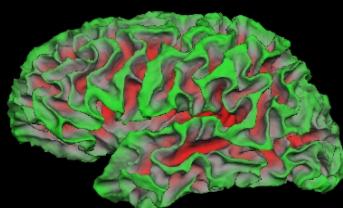
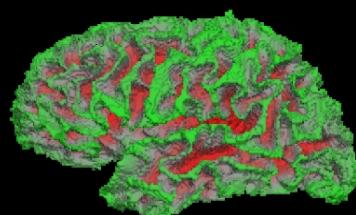
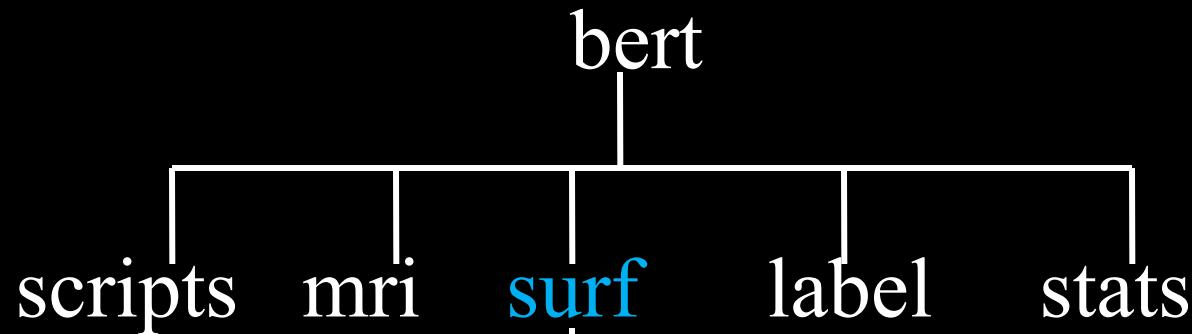
aseg.mgz



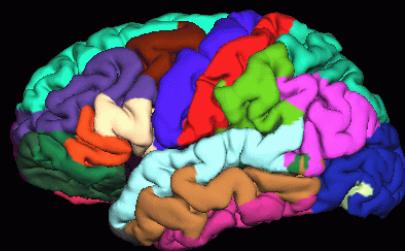
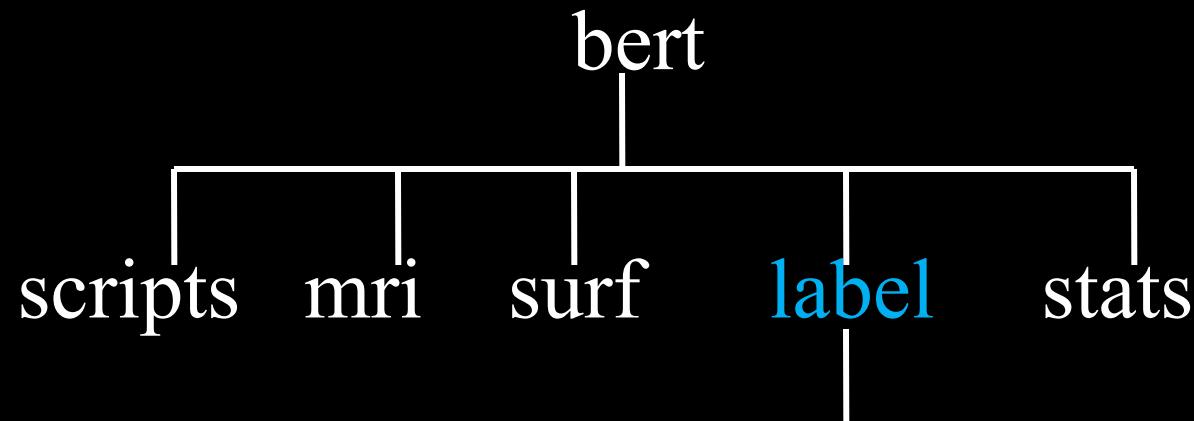
Native Anatomical Space
eg, $1 \times 1 \times 1.2 \text{ mm}^3$, $256 \times 256 \times 128$



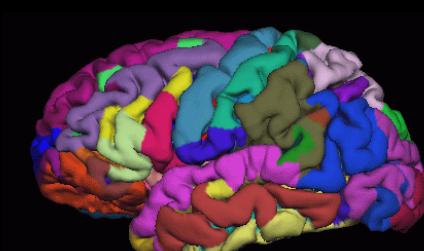
Conformed" Anatomical Space
 $1 \times 1 \times 1 \text{ mm}^3$, $256 \times 256 \times 256$



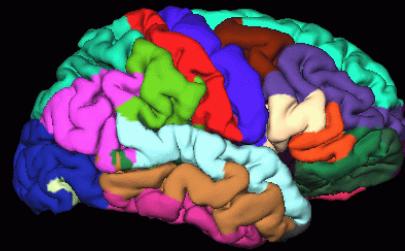
Lh/rh.thickness, lh/rh.curv, lh/rh.sulc



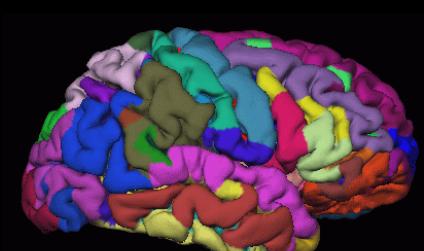
lh.aparc.annot



lh.aparc.a2009s.annot



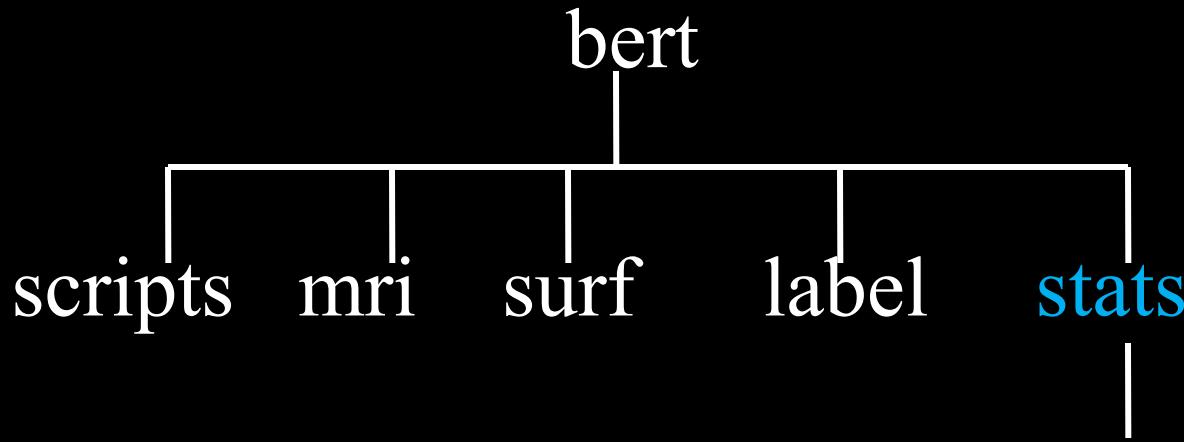
rh.aparc.annot



rh.aparc.a2009s.annot

Desikan/Killiany Atlas

Destrieux Atlas



aseg.stats – subcortical volumetric stats

wmparc.stats – white matter segmentation volumetric stats

lh.aparc.stats – left hemi Desikan/Killiany surface stats

rh.aparc.stats – right hemi Desikan/Killiany surface stats

lh.aparc.a2009.stats – left hemi Destrieux

rh.aparc.a2009.stats – right hemi Destrieux

stats files are text files with summary information, eg:

volume of left amygdala

average thickness in superior temporal gyrus

After registration

Make sure files are properly reconstructed

- Especially for child populations
 - Children tend to move a lot
 - Their brains are more difficult to model due to high variation between children

Using Qoala-T for QA

- How do we know which files need fixing?
 - High inter-rater differences in deciding what needs to be fixed
- We will use Qoala-T to help us decide which files to include/exclude and/or fix
 - A supervised-learning tool to assess accuracy of manual quality control of automatic segmented MRI data
 - Particularly intended for use in developmental datasets

Using Qoala-T

Predicting scan Qoala-T score by using
Braintime model

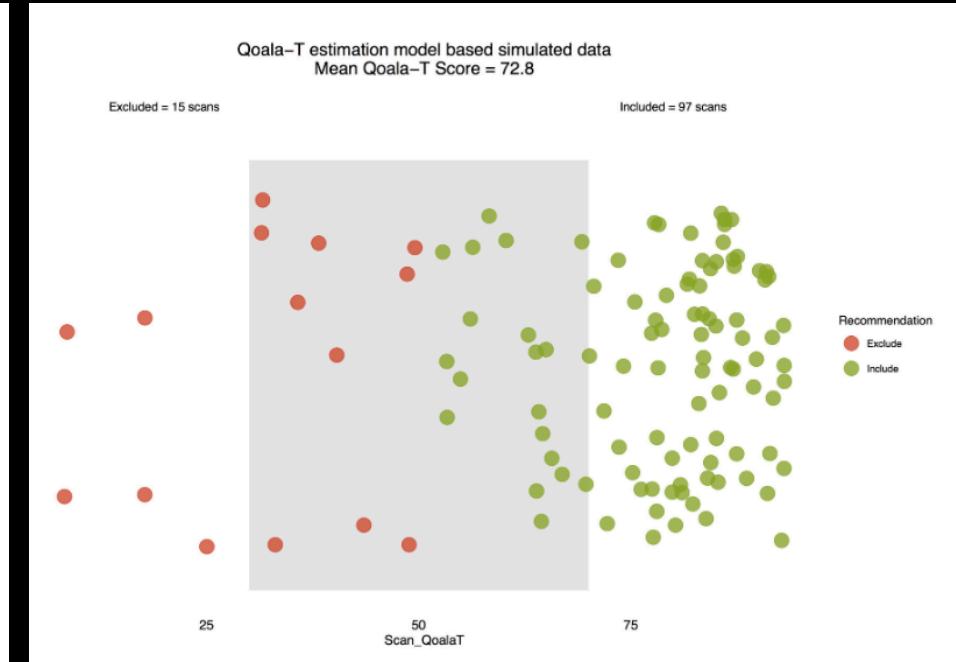
- R script: Qoala-T scores for a dataset are estimated using a supervised- learning model
- Model based on 784 T1-weighted imaging scans of subjects aged between 8 and 25 years old (53% females)
- Only counts errors if they are seen in 3 consecutive slices

Using Qoala-T

Braintime model output

- Provides recommendation for inclusion/exclusion and whether QC is advised

VisitID	Scan_QoalaT	Recommendation	manual_QC_advised
Simulated_98	8	Exclude	no
Simulated_85	9	Exclude	no
Simulated_109	18	Exclude	no
Simulated_25	18	Exclude	no
Simulated_65	25	Exclude	no
Simulated_10	32	Exclude	yes
Simulated_112	32	Exclude	yes
Simulated_22	33	Exclude	yes
Simulated_6	36	Exclude	yes
Simulated_5	38	Exclude	yes
Simulated_51	40	Exclude	yes



Using Qoala-T

Make your own quality control file

- Each row should contain information for each participant
 - Which types of errors were found, whether/how they were fixed, etc..
 - Sample spreadsheet provided in this github repo for this tutorial

Subject	Final_Score	Excessive_movement	Temp_pole_miss_LH	Temp_pole_miss_RH	Dura_LH	Dura_RH	Missing_Anterior_LH	Missing_Anterior_RH	Missing_Superior_Medial_LH	Missing_Superior_Medial_RH	Missing_Posterior_LH	Missing_Posterior_RH	Notes
Subject001	1	0	0	0	0	0	0	0	0	0	0	0	
Subject002	1	0	1	1	0	0	1	1	1	1	0	0	0 Minor parts anterior and temporal lobe missing

Using Qoala-T

Four criteria are used to assess scan quality:

- 1) Is the reconstructed image affected by movement?
- 2) Is (part of) the temporal pole missing in the reconstruction?
- 3) Is non-brain tissue (e.g. dura/skull) included in the reconstruction of pial surface (red line)?
- 4) Are parts of the cortex missing in the reconstruction (other than temporal poles)?

Qoala-T criterion

1) Movement assessment

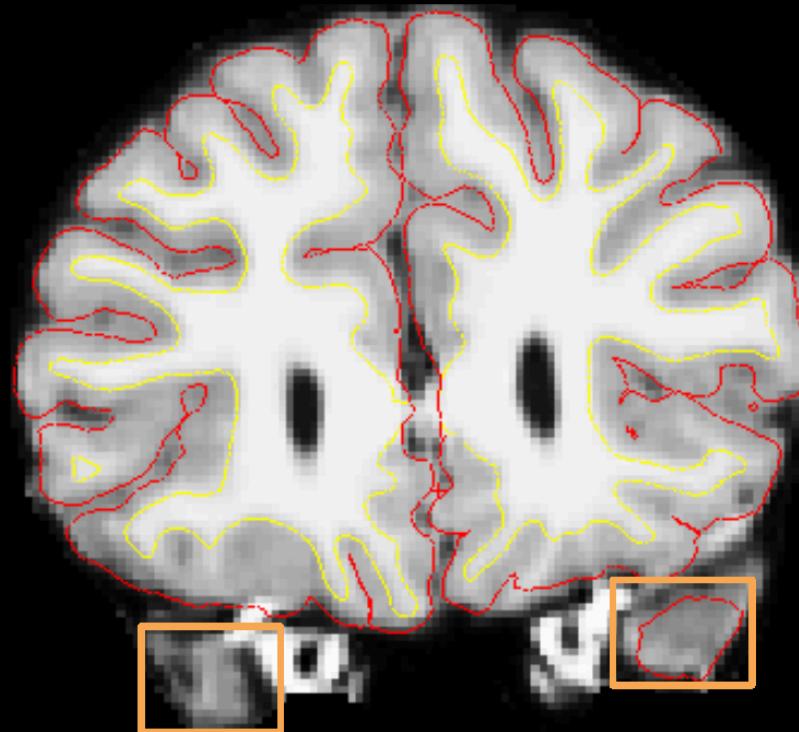
1) If it looks like there are “rings” around the brain, that’s a tell-tale sign of movement



Qoala-T criterion

2) Temporal pole assessment

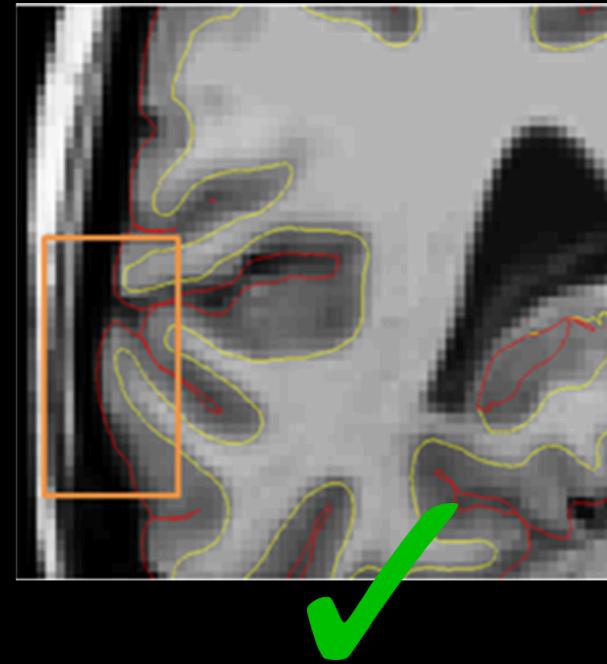
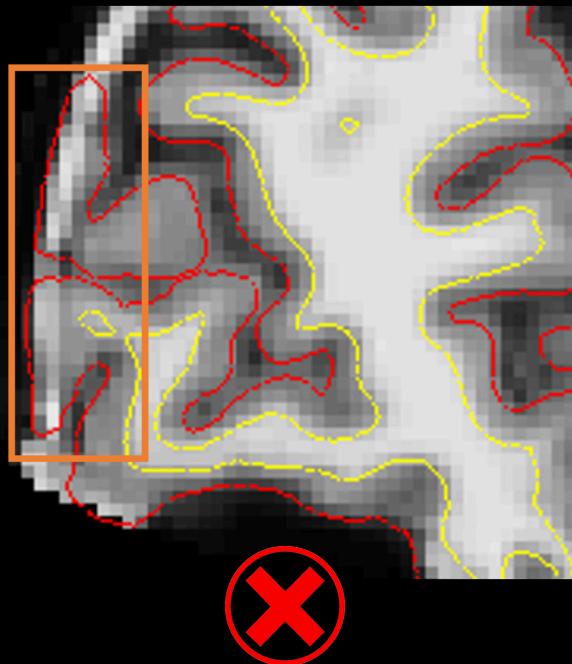
Error: When there is a whole section of temporal lobe not included in red



Qoala-T criterion

3) Non-brain tissue included in pial surface

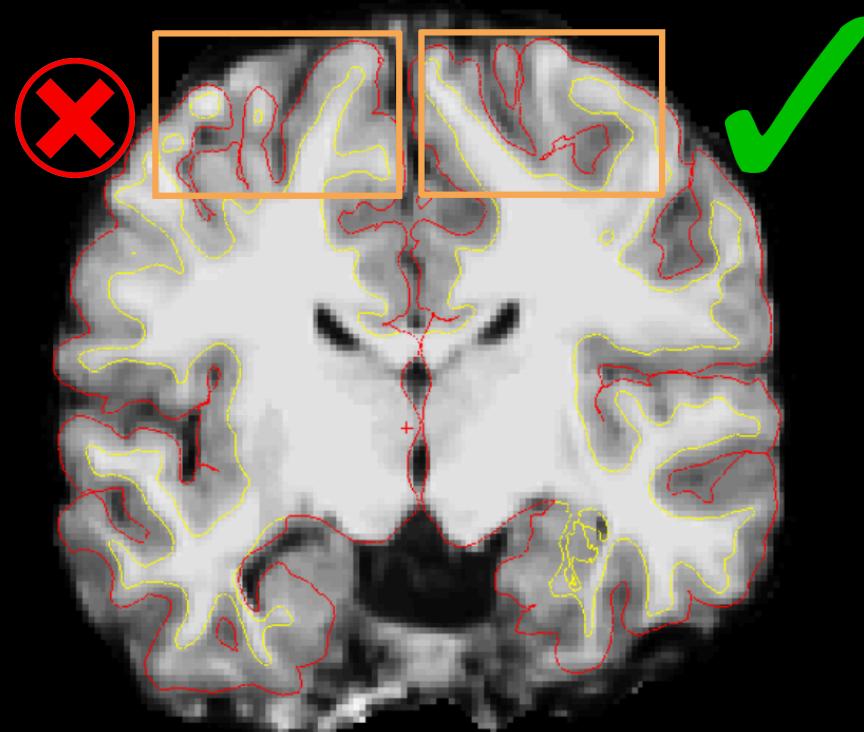
Example of dura included (left) and not included (right) in pial surface reconstruction



Qoala-T criterion

2) Other parts of brain not included

Where there is a whole section of temporal lobe not included in red



How do we use Qoala-T?

- 1) Extract gray matter volume, cortical thickness, and surface area (SA) for each participant in Freesurfer
- 2) Insert extracted .txt files into Qoala-T app
- 3) Look at output recommendations

Extracting GM measures

- 1) Navigate to folder with FS reconstructed data
- 2) Make output folder
- 3) Set subject's directory
- 4) Set list of which subjects you want to run the extraction for
- 5) Execute FS commands for GMV, CT, and SA

Extracting GM measures

- 1) Navigate to folder with FS reconstructed data

```
cd /path/to/FS_reconstructed_files
```

- 2) Make your own specific folder where the outputs will go

```
mkdir <folder_name>
```

- E.g. cd /users/documents/jdoe/FS_recon_data
 mkdir qt_outputs

Extracting GM measures

3) Set subject's directory

```
Export SUBJECTS_DIR =/path/to/where/you/created/folder  
echo $SUBJECTS_DIR
```

- E.g Export
 SUBJECTS_DIR=/users/documents/jdoe/FS_recon_data/qt_o
 utputs

Extracting GM measures

- 4) Set list of which subjects you want to run the extraction for

```
list=`ls -d <beginning_name_of_files_you_want_to_include>*/*`
```

- To include all FS recon participants starting with the name “sub-” (fmriprep standard), you can do the following:

```
list=`ls -d sub-*/*`
```

Extracting GM measures

- 5) First work on extracting GMV (does this for both hemispheres of the brain, includes eTIV)

```
asegstats2table --subjects $list --meas volume --skip --tablefile  
/path/to/where/you/created/folder/aseg.stats.txt
```

- This will create a file named `aseg.stats.txt`
- For Qoala-T to work in R, you have to name the files exactly as stated here

Extracting GM measures

Double-check you did this correctly

```
[17:08]qigroup@sylvian:Freesurfer_edits_tutorial$ cd Jen/
[17:09]qigroup@sylvian:Jen$ ls
aseg_stats.txt
[17:09]qigroup@sylvian:Jen$ cat aseg_stats.txt
Measure:volume Left-Lateral-Ventricle Left-Inf-Lat-Vent      Left-Cerebellum-White-Matter  Left-Cerebellum-Cortex]
  Left-Thalamus-Proper   Left-Caudate   Left-Putamen      Left-Pallidum   3rd-Ventricle  4th-Ventricle  Brain-Stem ]
  Left-Hippocampus Left-Amygdala    CSF      Left-Accumbens-area  Left-VentralDC Left-vessel    Left-choroid-plexus
  Right-Lateral-Ventricle Right-Inf-Lat-Vent  Right-Cerebellum-White-Matter Right-Cerebellum-Cortex Right-]
Thalamus-Proper  Right-Caudate   Right-Putamen      Right-Pallidum  Right-Hippocampus Right-Amygdala  Right-Accumbens-area
  Right-VentralDC Right-vessel    Right-choroid-plexus 5th-Ventricle WM-hypointensities  Left-WM-hy
pointensitiesRight-WM-hypointensities non-WM-hypointensities Left-non-WM-hypointensities Right-non-WM-hypointensit
ies  Optic-Chiasm CC_Posterior  CC_Mid_PosteriorCC_Central  CC_Mid_Anterior CC_Anterior  BrainSegVol
  BrainSegVolNotVent  BrainSegVolNotVentSurf lhCortexVol  rhCortexVol  CortexVol    lhCerebralWhiteMat
terVol rhCerebralWhiteMatterVol  CerebralWhiteMatterVol SubCortGrayVol TotalGrayVol  SupraTentorialVol
  SupraTentorialVolNotVenSupraTentorialVolNotVentVox MaskVol BrainSegVol-to-eTIV  MaskVol-to-eTIVlhSurfac
eHoles  rhSurfaceHoles SurfaceHoles  EstimatedTotalIntraCranialVol
sub-blastc019/ 7058.0 388.4 11721.3 52777.7 7096.2 3336.0 4548.0 1965.3 901.2 2124.0 15643.1 3733.8 1297.4
  799.1 436.1 3631.8 30.3 474.9 5982.3 874.1 11227.1 50644.2 6498.1 3392.3 4711.7 1612.5 3625.2 1568
  .0 455.3 3645.1 18.8 332.0 0.0 376.3 0.0 0.0 0.0 0.0 0.0 157.9 895.8 339.8 37
  7.2 425.7 904.6 1020839.0 1002319.0 1002791.48444 243642.591178 245312.592207 488955.183385
167014.433407 167879.867651 334894.301058 52836.0 645954.183385 893229.484443 878434.484443 876091.0
  1368600.0 0.75661 1.014358 28.0 30.0 58.0 1349227.9561
sub-blastc122/ 3443.5 389.4 11637.5 56429.9 7624.4 2960.5 5535.8 1862.1 665.6 1425.6 16723.5 3442.2 1284.5
  778.5 630.5 3577.8 40.7 300.4 2416.6 300.2 11659.1 57174.8 7801.6 3482.3 5742.8 1801.5 3697.4 1781
  .0 710.3 3734.8 20.2 362.3 0.0 2462.8 0.0 0.0 0.0 0.0 0.0 112.9 625.2 367.8 43
  9.9 378.7 755.0 1020217.0 1010704.0 1009873.4321 250144.584449 240081.046668 490225.631118
167059.747551 158670.053426 325729.800978 57565.0 661644.631118 882745.432095 875973.432095 874316.0
  1353857.0 0.679579 0.90182 385.0 298.0 683.0 1501249.32584
```

Extracting GM measures

- 5) Next you can extract CT and SA for right and left hemispheres separately

```
aparcstats2table --subjects $list --hemi lh --meas thickness --skip --  
tablefile /path/to/where/you/created/folder/aparc_thickness_lh.txt
```

```
aparcstats2table --subjects $list --hemi rh --meas thickness --skip --  
tablefile /path/to/where/you/created/folder/aparc_thickness_rh.txt
```

```
aparcstats2table --subjects $list --hemi lh --meas area --skip --tablefile  
/path/to/where/you/created/folder/aparc_area_lh.txt
```

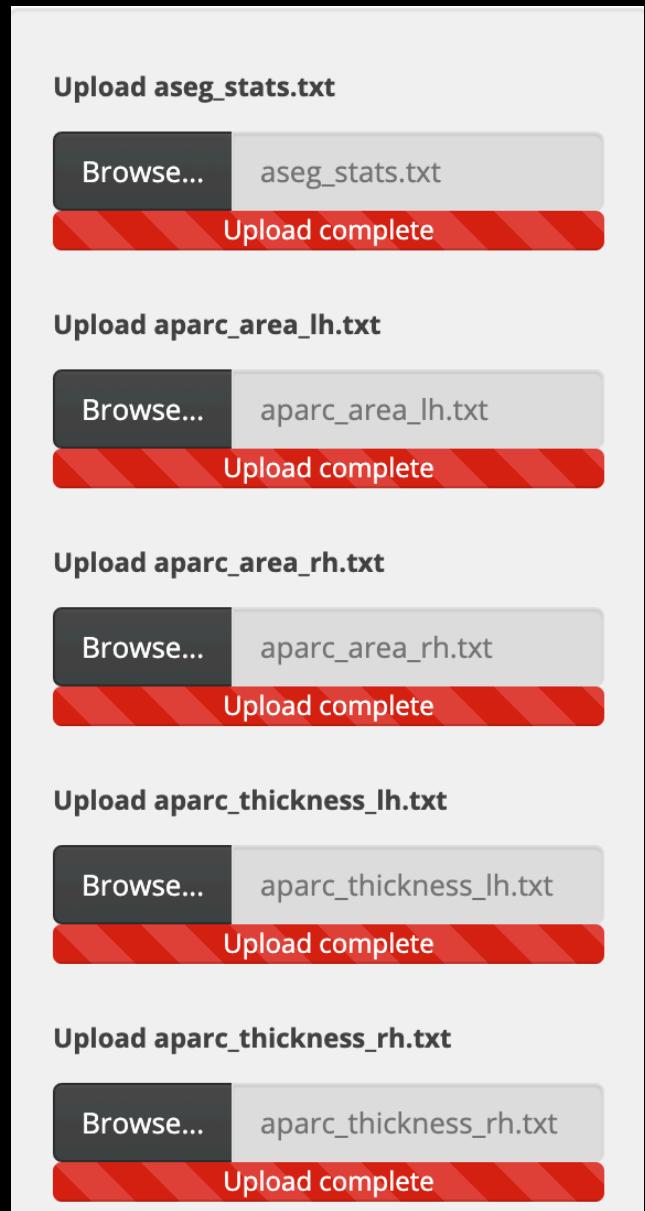
```
aparcstats2table --subjects $list --hemi rh --meas area --skip --tablefile  
/path/to/where/you/created/folder/aparc_area_rh.txt
```

Extracting GM measures

- 6) Check that your files are in your folder
- 7) Congrats! You extracted Qoala-T ready files!!

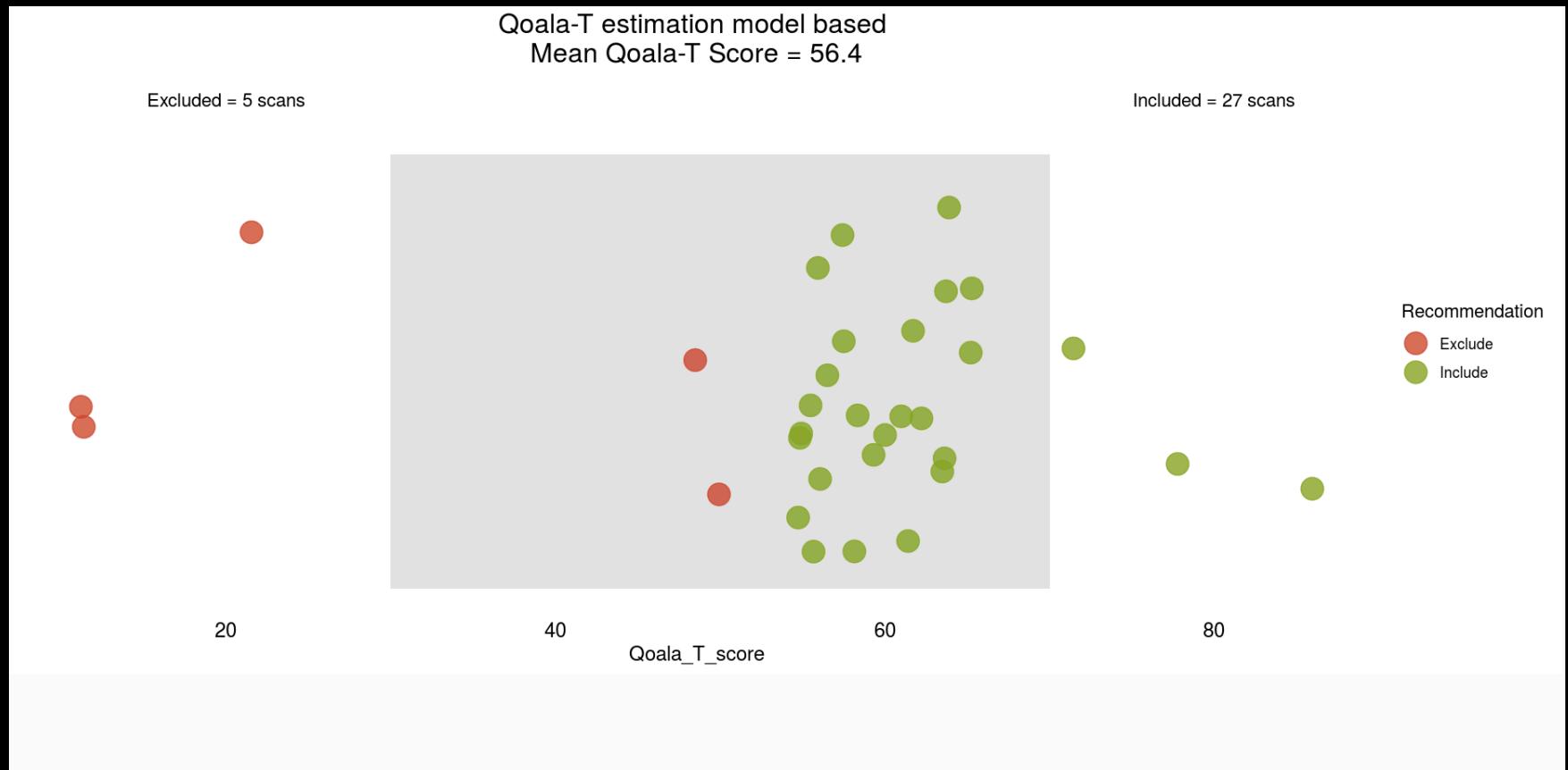
Using Qoala-T

- 1) Go to: https://qoala-t.shinyapps.io/qoala-t_app/
- 2) Insert .txt extracted files in respective locations



Using Qoala-T

1) Look at graph output



Using Qoala-T

1) Look at Table output and download .csv

Once the Qoala-T scores are displayed here, hit 'Download csv' to download a csv file of this table.

[Download csv](#)

Scan_ID	Qoala_T_score	Recommendation	Manual_QC_advised
sub-blastc034	11.18	Exclude	no
sub-blastc034_Nicolo	11.38	Exclude	no
sub-blastc122	21.56	Exclude	no
sub-blasta013	48.50	Exclude	yes
sub-blasta023	49.90	Exclude	yes
sub-blasta029	54.69	Include	yes
sub-blasta008	54.89	Include	yes
sub-blasta021	54.89	Include	yes
sub-blastc071	55.49	Include	yes
sub-blasta024	55.69	Include	yes
sub-blasta012	55.89	Include	yes
sub-blasta001	71.46	Include	no
sub-blastc019	77.84	Include	no
sub-blasta002	86.03	Include	no

These are probably due to motion in the scanner, which cannot be corrected for if there is too much

These might be reparable with FS edits

These should still be inspected for possible FS edits

These are likely good, but should still be inspected

Next week

Go over quality control file, using
Freesurfer's Freeview, and how to make
Freesurfer edits