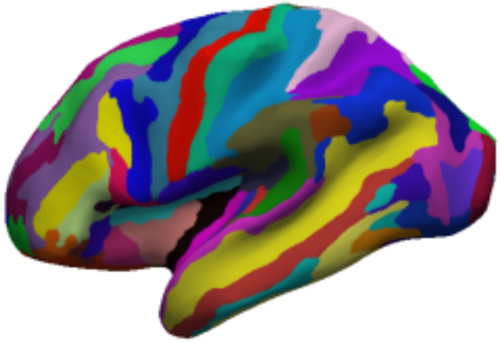
FREESURFER TUTORIAL

Kevin Aquino & Lauren Gascoyne

2016

Outline

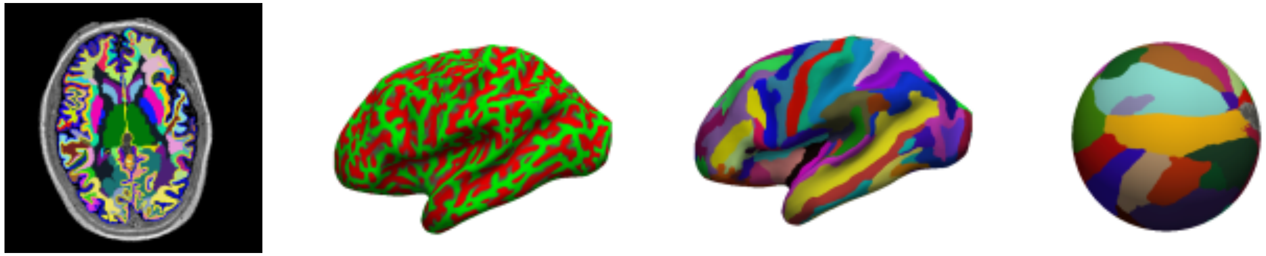


- What is Freesurfer?
- Getting started
- Freesurfer workflow
- Running Freesurfer
- Using PSIRs from SPMIC
- Fixing bad segmentations
- High resolution data
- Tips and tricks
- Freesurfer in action (Lauren Gascoyne)

Advanced topics

What is Freesurfer?

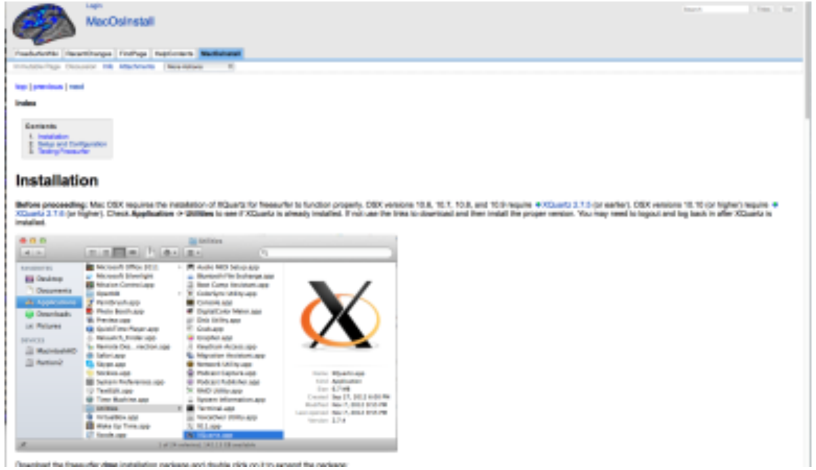
- Automatic segmentation
- Uses intensity gradients, surface constraints and registration to talairach atlases
- Generates:
  - Surfaces at: WM/GM (white), GM/CSF (pial)
  - Automatic Volume parcellations
  - Automatic surface parcellations (and can import Lausanne et al. Atlases)
  - Surface-based registrations



generated using from 7T PSIR from Notts

Getting started

- Only runs on Linux, and Mac (El capitan users beware)
- Open software available from http://freesurfer.net/
- Which version to choose from?
  - v5.3 Stable release well suited to 1mm isotropic MPRAGE
  - beta version “v6” can work with high-resolution data
- Freesurfer wiki explains installation steps well
- Understanding shell operations helps!
- - versions OS same



MacOsInstall

Installation

Freesurfer workflow

Autorecon Processing Stages (see -autorecon# flags above):

1. Motion Correction and Conform
2. NU (Non-Uniform intensity normalization)
3. Talairach transform computation
4. Intensity Normalization 1
5. Skull Strip

`autorecon1`
Volume pre-processing

1. EM Register (linear volumetric registration)
2. CA Intensity Normalization
3. CA Non-linear Volumetric Registration
4. Remove Neck
5. LTA with Skull
6. CA Label (Volumetric Labeling, ie Aseg) and Statistics
7. Intensity Normalization 2 (start here for control points)
8. White matter segmentation
9. Edit WM With ASeg
10. Fill (start here for wm edits)
11. Tessellation (begins per-hemisphere operations)
12. Smooth1
13. Inflate1
14. QSphere
15. Automatic Topology Fixer
16. Final Surfs (start here for brain edits for pial surf)
17. Smooth2
18. Inflate2

`autorecon2`
Segmentation, surface reconstruction, toplogical fixes and inflation

19. Spherical Mapping
20. Spherical Registration
21. Spherical Registration, Contralateral hemisphere
22. Map average curvature to subject
23. Cortical Parcellation - Desikan_Killiany and Christophe (Labeling)
24. Cortical Parcellation Statistics
25. Cortical Ribbon Mask
26. Cortical Parcellation mapping to Aseg

`autorecon3`
Spherical registration, between-subject registration maps, cortical parcellations

`recon-all`
everything

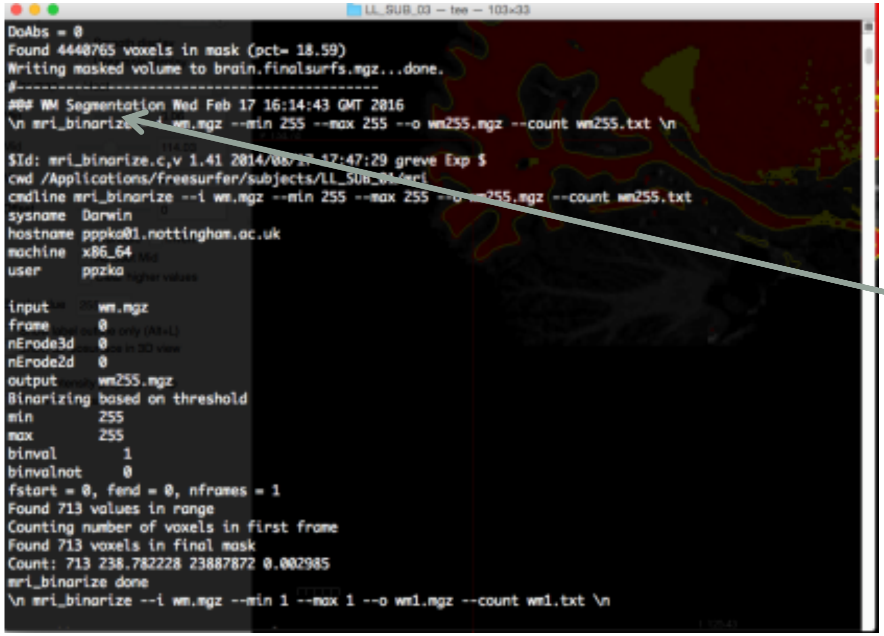
Freesurfer Inputs

- MPRAGE/MP2RAGE T1-weighted data
- PSIR (Nottingham's standard)
  - Positive, mulitplied by 200 (from standard output)
- T2-weighted data
- Whole brains only!
- Formats:
  - Nifti (.nii)
  - Analyze (.hdr/.img)

Running freesurfer

- To run recon-all with all the stages (1,2,and 3) simply type:

```
recon-all –all –s SUBJECT –I INPUTIMAGE
```



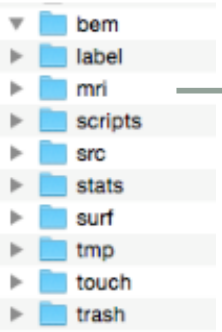
```
DoAbs = 0
Found 4440765 voxels in mask (pct= 18.59)
Writing masked volume to brain.finalsurfs.mgz...done.
#--------------------------------------------
#@# WM Segmentation Wed Feb 17 16:14:43 GMT 2016
\n mri_binarize --i wm.mgz --min 255 --max 255 --o wm255.mgz --count wm255.txt \n

$Id: mri_binarize.c,v 1.41 2014/08/17 17:47:29 greve Exp $
cwd /Applications/freesurfer/subjects/LL_SUB_03/mri
cmdline mri_binarize --i wm.mgz --min 255 --max 255 --o wm255.mgz --count wm255.txt
sysname  Darwin
hostname pppka01.nottingham.ac.uk
machine  x86_64
user     ppzka

input      wm.mgz
frame      0
nErode3d   0
nErode2d   0
output     wm255.mgz
Binarizing based on threshold
min        255
max        255
binval        1
binvalnot     0
fstart = 0, fend = 0, nframes = 1
Found 713 values in range
Counting number of voxels in first frame
Found 713 voxels in final mask
Count: 713 238.782228 23887872 0.002985
mri_binarize done
\n mri_binarize --i wm.mgz --min 1 --max 1 --o wm1.mgz --count wm1.txt \n
```

- Freesurfer will run displaying information in the terminal screen

WM Segmentation
Stage: 12
Part of auto-recon2

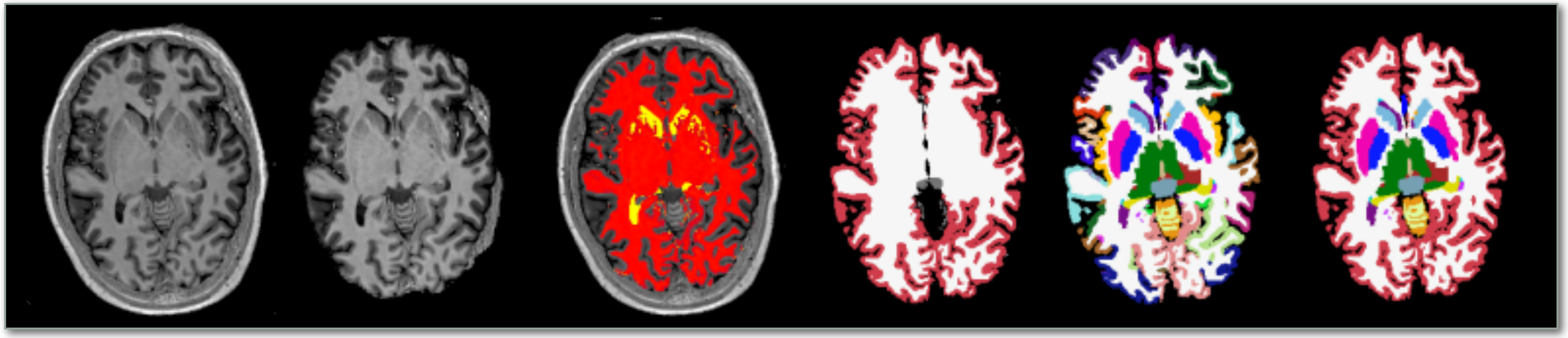
- Can take up to~40 hours

What does freesurfer output?



- bem
- label
- mri
- scripts
- src
- stats
- surf
- tmp
- touch
- trash

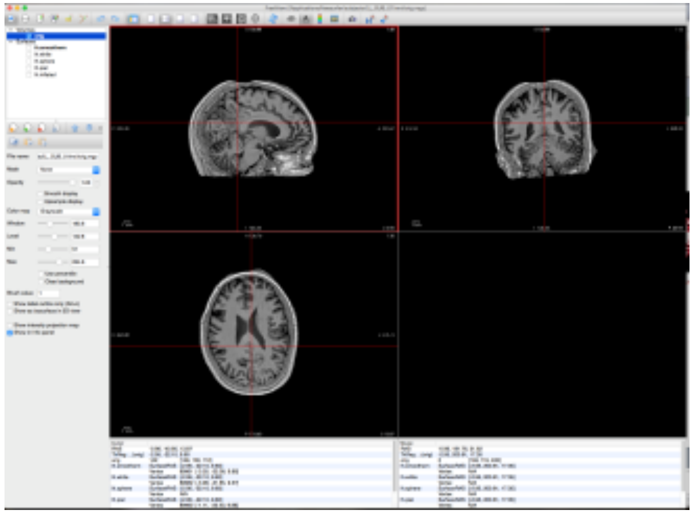
Volumes



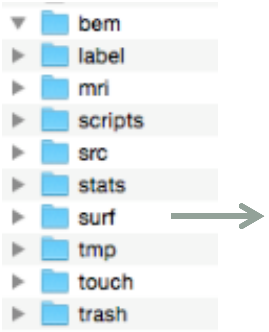
`orig.mgz` `brain.mgz` `wm.mgz` `ribbon.mgz` `aseg.mgz` `aparc+aseg.mgz`

Outputs from freesurfer can be viewed in freeview
Load volume -> mri -> …

And spheres etc.

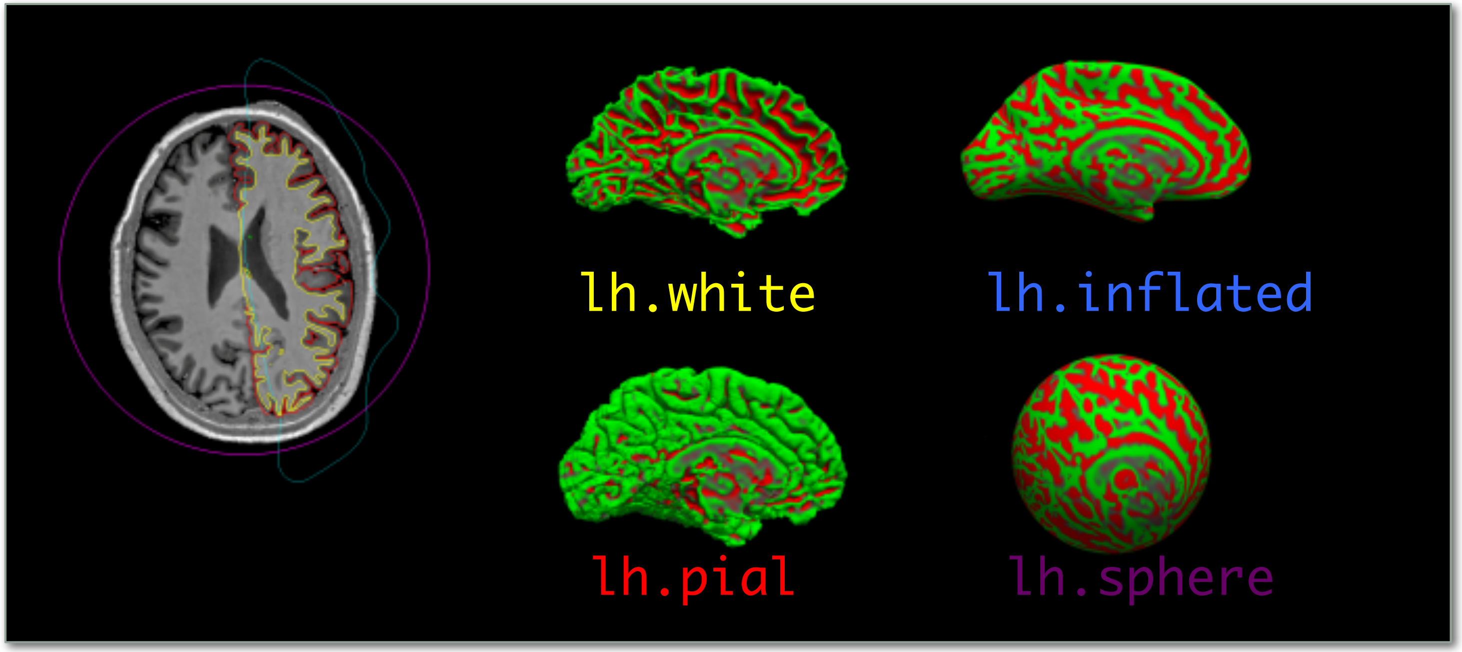


What does freesurfer output?



bem
label
mri
scripts
src
stats
surf
tmp
touch
trash

Surfaces

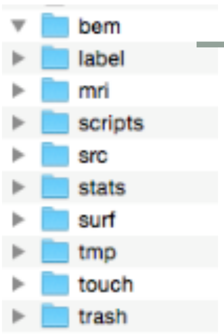


White and pial surfaces follow boundaries of WM/GM and GM/CSF respectively

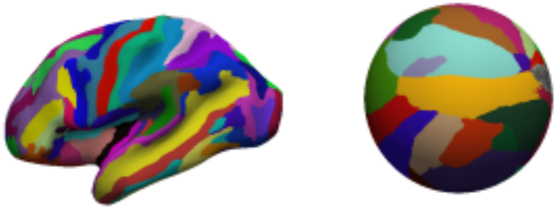
Inflated surface = smoothed and inflated to approach sphere, using fixed contraints
Sphere surface = surface inflated all the way to a sphere

All surfaces are generated from lh.white, and have the same number of vertices. Hence mapping of each vertex along the way.

What does freesurfer output?



bem
label
mri
scripts
src
stats
surf
tmp
touch
trash



Atlas registrations

- Deskilany atlas
- Destriux atlas
- Lausanne atlas (you can apply this)

From these outputs you can calculate properties such as:

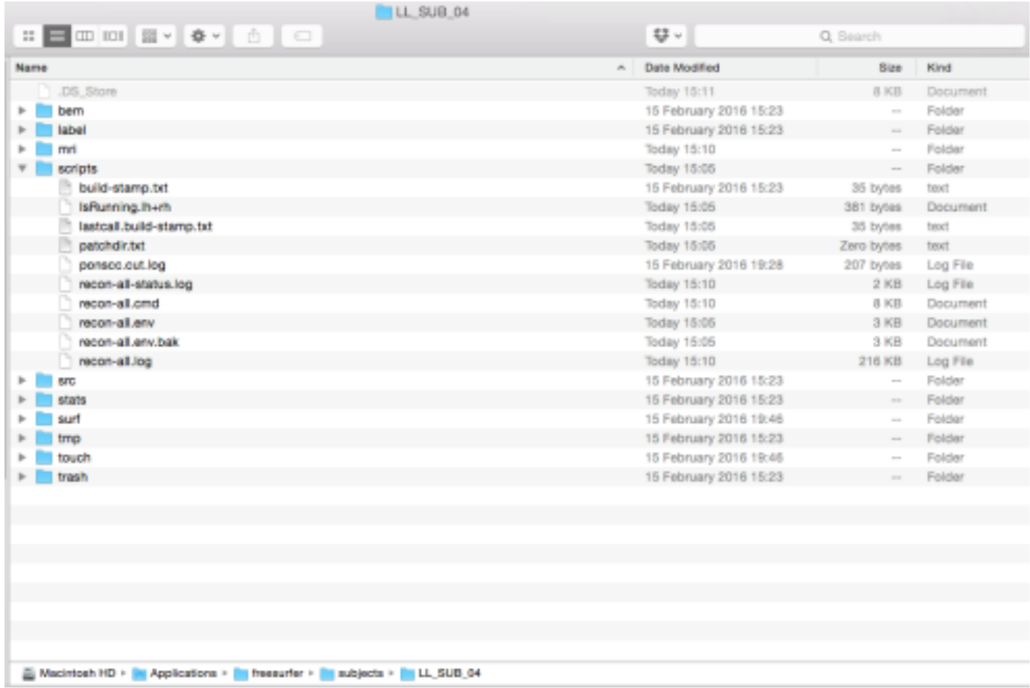
- surface area
- Gaussian/intrinsic curvature
- Mean curvature
- cortical thickness
- local gyrification index

(As described at the end of this talk)

Freesurfer logs

Logs stored in:

```
+ SUBJECTFOLDER
  + SUBJECT
    + scripts
     + recon-all.log
```

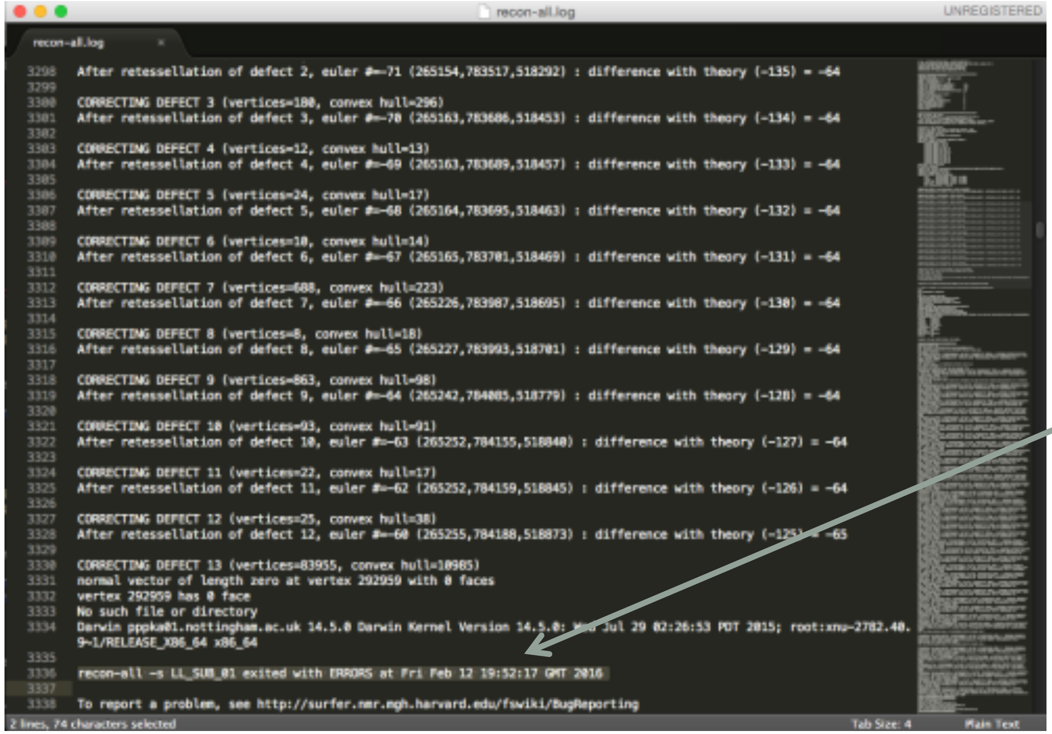


Name	Date Modified	Size	Kind
.DS_Store	Today 15:11	8 KB	Document
bem	15 February 2016 15:23	--	Folder
label	15 February 2016 15:23	--	Folder
mri	Today 15:10	--	Folder
scripts	Today 15:05	--	Folder
build-stamp.txt	15 February 2016 15:23	35 bytes	text
IsRunning.lh+rh	Today 15:05	381 bytes	Document
lastcall.build-stamp.txt	Today 15:05	35 bytes	text
patchdir.txt	Today 15:05	Zero bytes	text
ponscc.cut.log	15 February 2016 19:28	207 bytes	Log File
recon-all-status.log	Today 15:10	2 KB	Log File
recon-all.cmd	Today 15:10	8 KB	Document
recon-all.env	Today 15:05	3 KB	Document
recon-all.env.bak	Today 15:05	3 KB	Document
recon-all.log	Today 15:10	216 KB	Log File
src	15 February 2016 15:23	--	Folder
stats	15 February 2016 15:23	--	Folder
surf	15 February 2016 19:46	--	Folder
tmp	15 February 2016 15:23	--	Folder
touch	15 February 2016 19:46	--	Folder
trash	15 February 2016 15:23	--	Folder

Macintosh HD ▸ Applications ▸ freesurfer ▸ subjects ▸ LL_SUB_04

Diagnosing errors

- Freesurfer can crash for any number of reasons, the way to diagnose is to look at the log file (very important)



```
After retessellation of defect 2, euler #=-71 (265154,783517,518292) : difference with theory (-135) = -64

CORRECTING DEFECT 3 (vertices=180, convex hull=296)
After retessellation of defect 3, euler #=-70 (265163,783686,518453) : difference with theory (-134) = -64

CORRECTING DEFECT 4 (vertices=12, convex hull=13)
After retessellation of defect 4, euler #=-69 (265163,783689,518457) : difference with theory (-133) = -64

CORRECTING DEFECT 5 (vertices=24, convex hull=17)
After retessellation of defect 5, euler #=-68 (265164,783695,518463) : difference with theory (-132) = -64

CORRECTING DEFECT 6 (vertices=10, convex hull=14)
After retessellation of defect 6, euler #=-67 (265165,783701,518469) : difference with theory (-131) = -64

CORRECTING DEFECT 7 (vertices=608, convex hull=223)
After retessellation of defect 7, euler #=-66 (265226,783987,518695) : difference with theory (-130) = -64

CORRECTING DEFECT 8 (vertices=8, convex hull=18)
After retessellation of defect 8, euler #=-65 (265227,783993,518701) : difference with theory (-129) = -64

CORRECTING DEFECT 9 (vertices=863, convex hull=98)
After retessellation of defect 9, euler #=-64 (265242,784085,518779) : difference with theory (-128) = -64

CORRECTING DEFECT 10 (vertices=93, convex hull=91)
After retessellation of defect 10, euler #=-63 (265252,784155,518840) : difference with theory (-127) = -64

CORRECTING DEFECT 11 (vertices=22, convex hull=17)
After retessellation of defect 11, euler #=-62 (265252,784159,518845) : difference with theory (-126) = -64

CORRECTING DEFECT 12 (vertices=25, convex hull=38)
After retessellation of defect 12, euler #=-60 (265255,784188,518873) : difference with theory (-125) = -65

CORRECTING DEFECT 13 (vertices=83955, convex hull=10985)
normal vector of length zero at vertex 292959 with 0 faces
vertex 292959 has 0 face
No such file or directory
Darwin pppka01.nottingham.ac.uk 14.5.0 Darwin Kernel Version 14.5.0: Wed Jul 29 02:26:53 PDT 2015; root:xnu-2782.40.
9~1/RELEASE_X86_64 x86_64

recon-all -s LL_SUB_01 exited with ERRORS at Fri Feb 12 19:52:17 GMT 2016

To report a problem, see http://surfer.nmr.mgh.harvard.edu/fswiki/BugReporting
```

Open up recon-all.log (or look in the terminal screen) and search for the 1ST instance of `“exited with ERRORS”`

This information is useful to report bugs!

In this case (as often with sub mm data) Topological correction hanging.

Diagnosing errors

- https://mail.nmr.mgh.harvard.edu/mailman/listinfo/freesurfer

[Freesurfer] Using freesurfer on a partial brain

Bruce Fischl fischl at nmr.mgh.harvard.edu
Tue Jan 19 10:07:22 EST 2016

- Previous message: [Freesurfer] Using freesurfer on a partial brain
- Next message: [Freesurfer] Little cluster after FDR correction
- **Messages sorted by:** [date] [thread] [subject] [author]

```
Hi Kevin

we have used it on hemispheres, but I don't think it will work on partial
brains. It violates too many assumptions (e.g. topology,etc...)
sorry
Bruce


On Tue, 19 Jan 2016, Kevin Aquino wrote:

> Dear Freesurfer list,
> I was wondering if anyone here has used freesurfer on anatomical scans acquired on a partial brain?
>
> I realise that recon-all and many of the tools are suited for a full brain, but I was wondering if anyone out there has had
> experience making the tools work for this scenario? Not necessarily the parcellations and the full set-up, but other tools such
> as segmentation, creating a white and pial surface and topology fixes.
>
>
> Cheers,
>
>
> Dr Kevin Aquino
> Research fellow,
> Sir Peter Mansfield Magnetic Resonance Center, The University of Nottingham.
>
> Honorary Research Fellow
> School of Physics, Faculty of Science, University of Sydney
>
> E Kevin.aquino at nottingham.ac.uk, aquino at physics.usyd.edu.au | W www.physics.usyd.edu.au/~aquino/
>
> -------------------------------------------
>
> The brain is a wonderful organ. It starts working the moment you get up and does not stop until you get into the office.
> -
> Robert Frost
>
> CRICOS 00026A
> This email plus any attachments to it are confidential. Any unauthorised use is strictly prohibited. If you receive this email
> in error, please delete it and any attachments.
>
> Please think of our environment and only print this e-mail if necessary.
>
>
>
```

- Previous message: [Freesurfer] Using freesurfer on a partial brain
- Next message: [Freesurfer] Little cluster after FDR correction
- **Messages sorted by:** [date] [thread] [subject] [author]

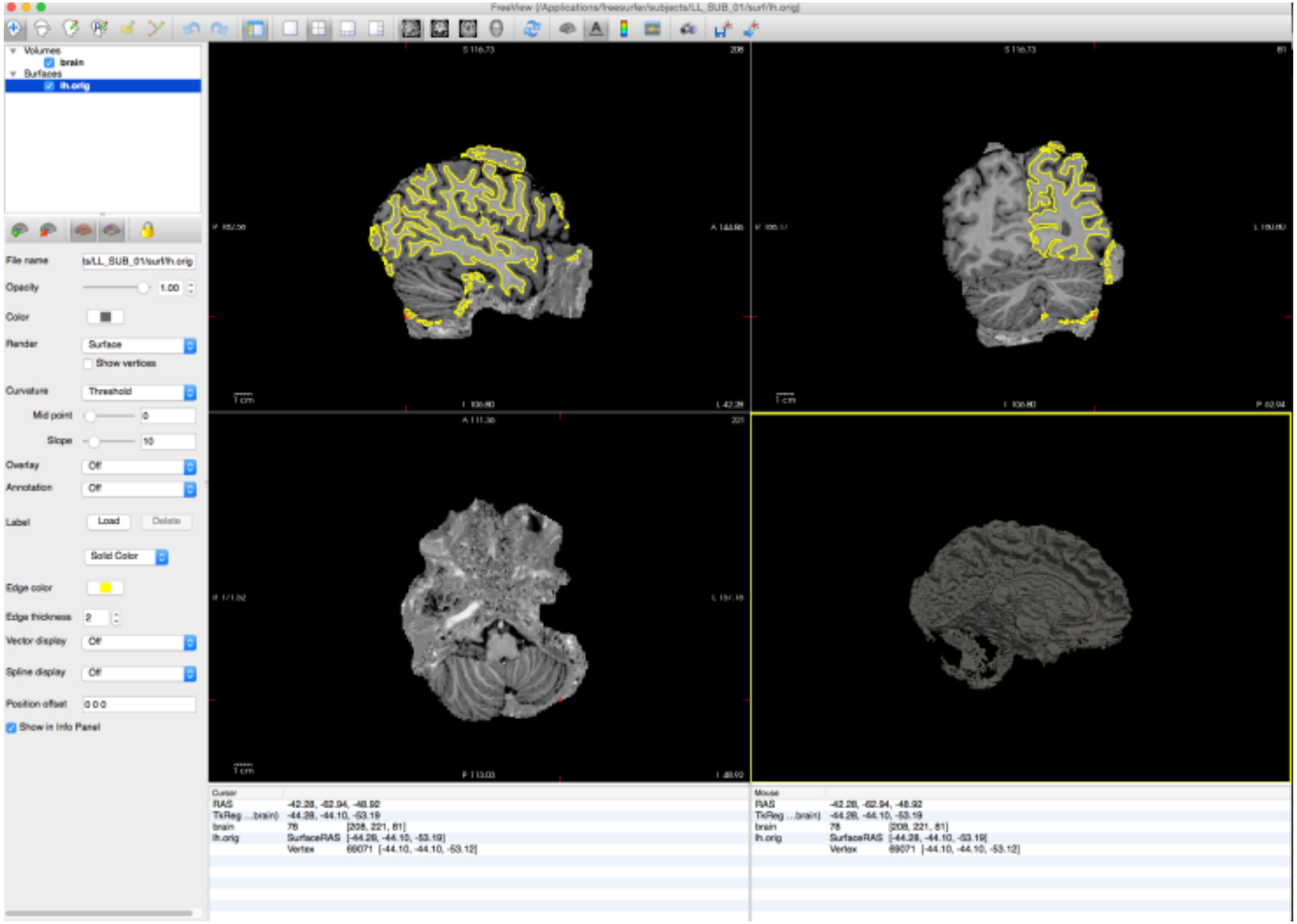
More information about the Freesurfer mailing list

Checking segmentation quality

- Does the white surface follow the WM/GM boundary?
- Does the pial surface follow the GM/CSF boundary?
- Is the surface distorted?

- If these are not correct can impact:
  - Thickness measurements
  - Gyrification measures
  - Surface area
  - Cortical layering

Fixing bad segmentations



FreeView (/Applications/freesurfer/subjects/LL_SUB_01/surf/lh.orig)

- Volumes
  - ☑ **brain**
- Surfaces
  - ☑ **lh.orig**

File name: ts/LL_SUB_01/surf/lh.orig

Opacity: 1.00

Render: Surface

☐ Show vertices

Curvature: Threshold

Mid point: 0

Slope: 10

Overlay: Off

Annotation: Off

Label: Load Delete

Solid Color

Edge thickness: 2

Vector display: Off

Spline display: Off

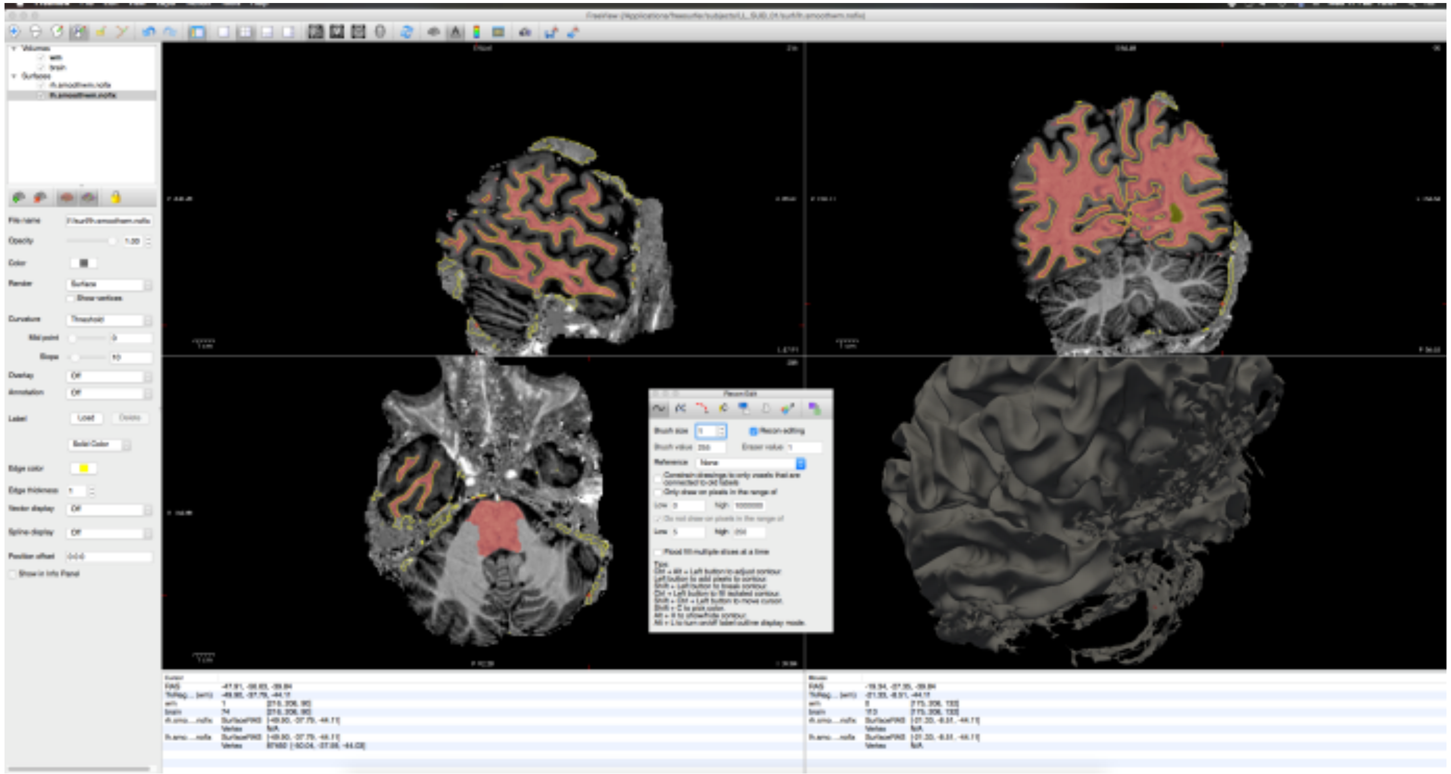
Position offset: 0 0 0

☑ Show in Info Panel

Cursor		
RAS	-42.28, -62.94, -48.92	
TkReg ...brain)	-44.28, -44.10, -53.19	
brain	78	[208, 221, 81]
lh.orig	SurfaceRAS	[-44.28, -44.10, -53.19]
	Vertex	69071 [-44.10, -44.10, -53.12]

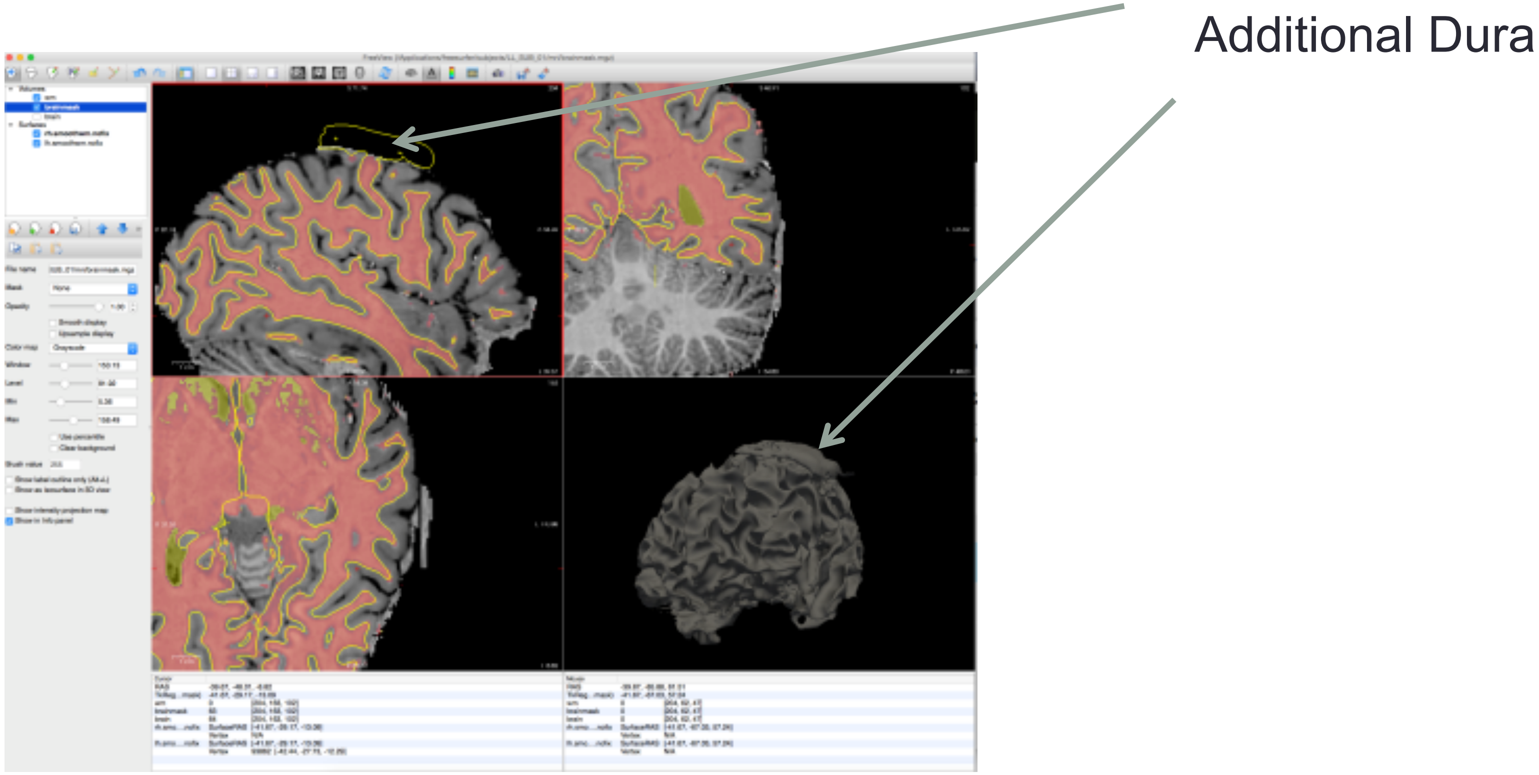
Mouse		
RAS	-42.28, -62.94, -48.92	
TkReg ...brain)	-44.28, -44.10, -53.19	
brain	78	[208, 221, 81]
lh.orig	SurfaceRAS	[-44.28, -44.10, -53.19]
	Vertex	69071 [-44.10, -44.10, -53.12]

Fixing WM segmentations



- Open freeview, load brain.mgz, wm.gz, lh and rh surfaces
- Highlight wm -> Recon edit -> shift click to remove. Page up/down go through slices
- Remove unnecessary voxels

Fixing segmentations #2



Additional Dura

- Open freeview, load brain.mgz, brainmask.mgz, lh and rh surfaces
- Highlight brainmask -> Recon edit -> shift click to remove. Page up/down go through slices
- Remove unnecessary voxels (dura)

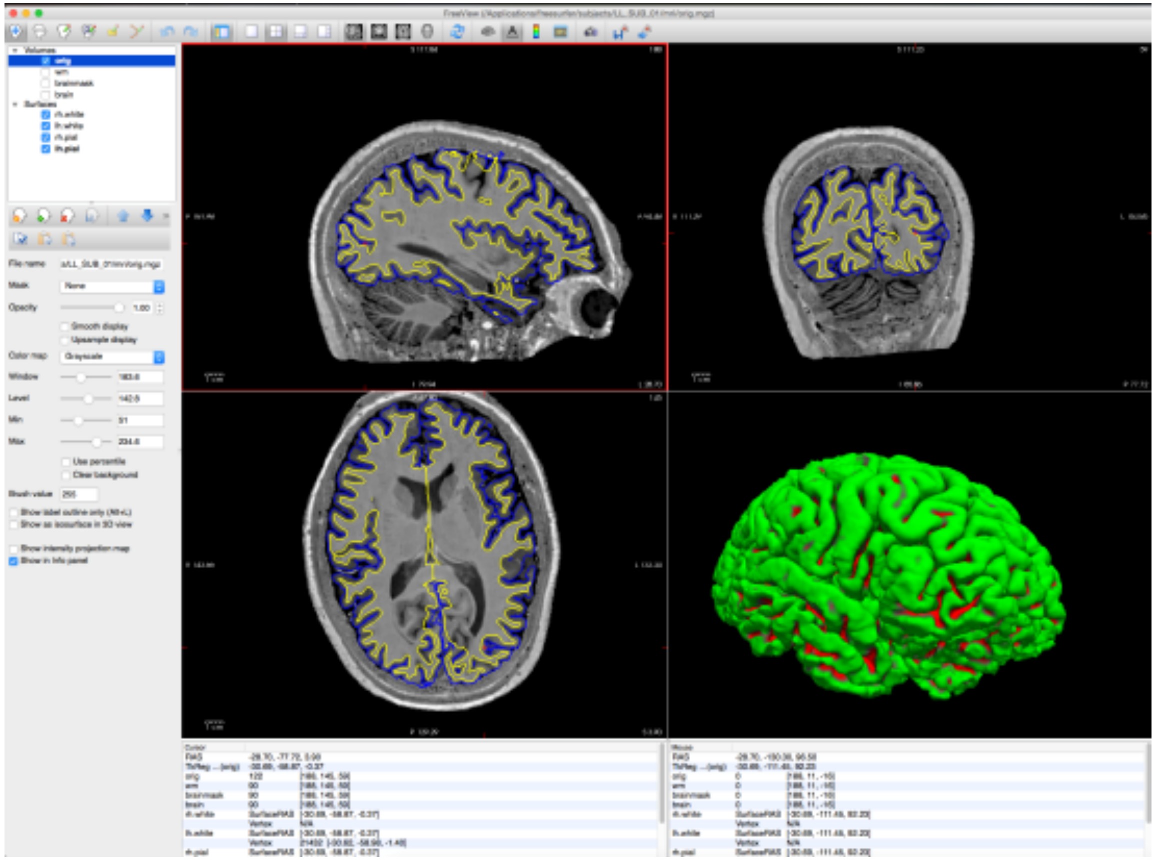
Fixing bad segmentations

- After you have fixed the segmentation run the following commands:

```
recon-all -autorecon2-wm -autorecon3 –subjid $SUBJECT
```

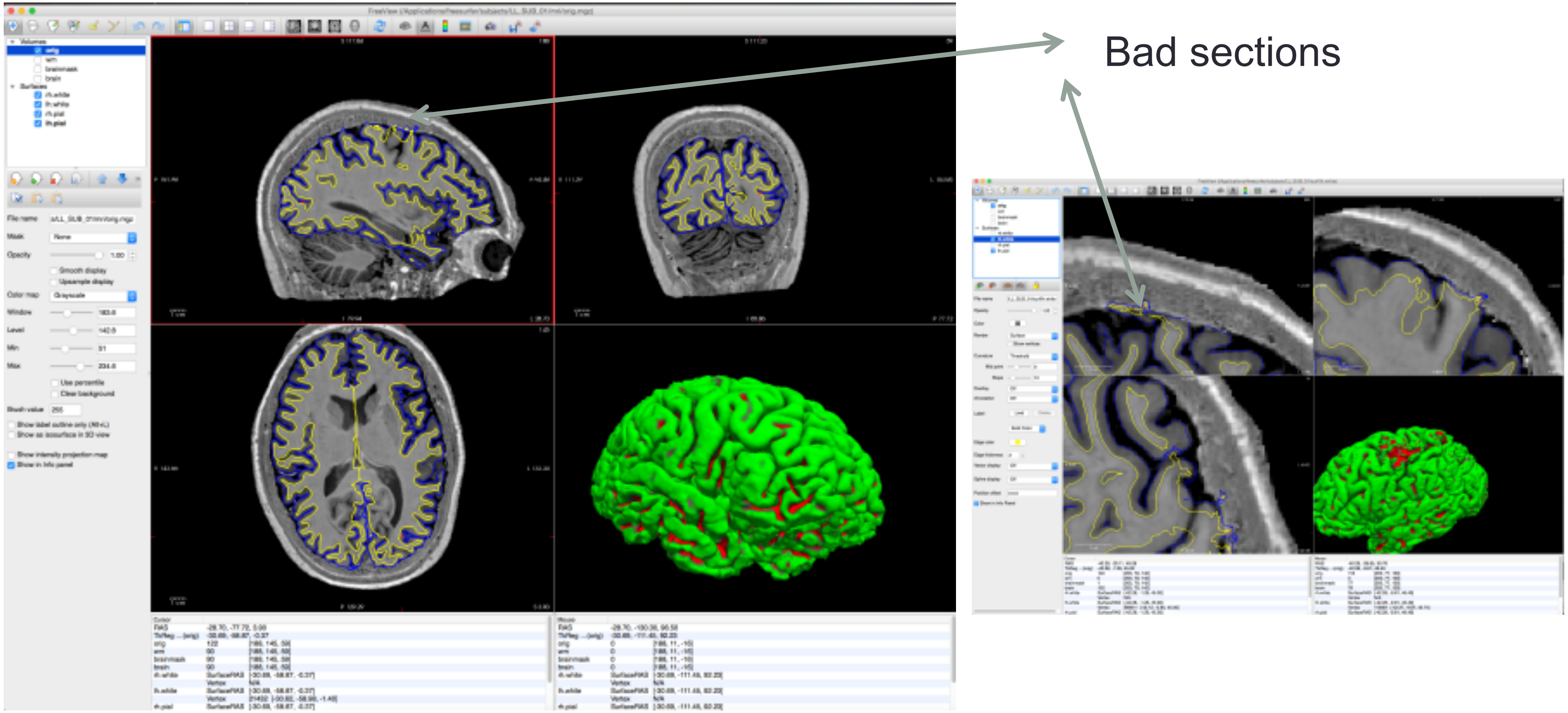
- This will run steps 15-23
  - (starting from fillling in WM),

Fixing bad segmentations



- Finished updated segmentation
- Inspect the surfaces again!

Finished result


Bad sections

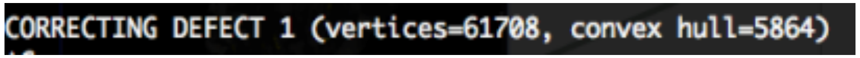
- Segmentation can still be updated!
- Up to projects (in the absence of time restraints).

High resolution (<1mm Images)

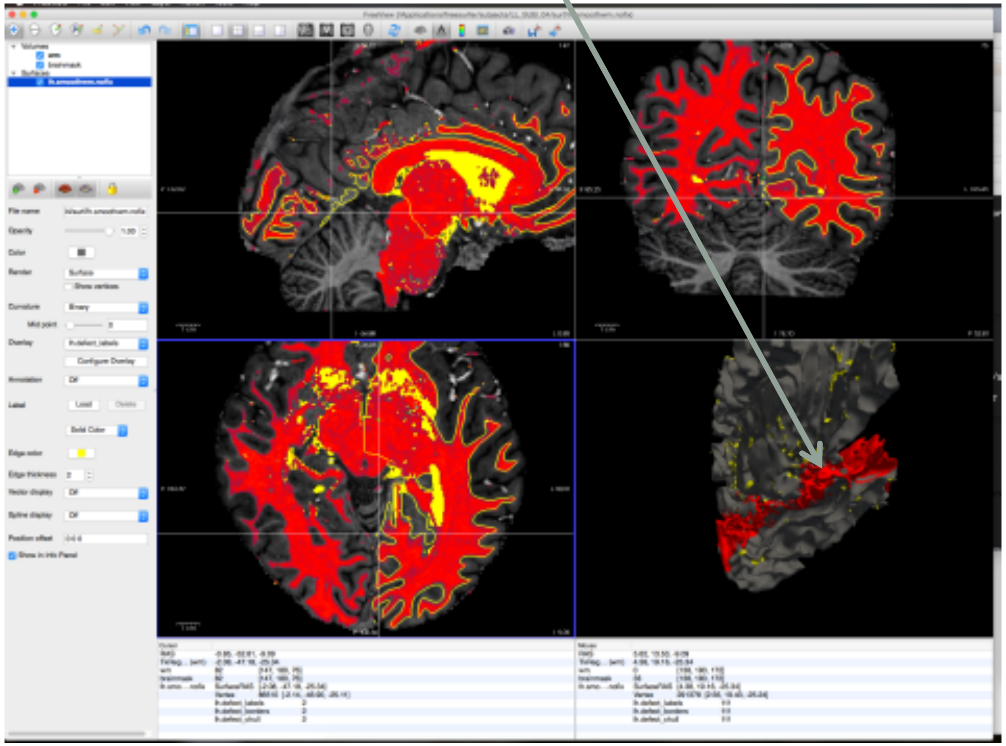
- For <1mm isotropic resolution data Freesurfer’s toplogical checks might fail
- Freesurfer V5.3
  - Use HiResRecon-all script (can provide)
- Freesurfer V6 (beta)
  - Works out of the box

- With either version, failure due to toplogical defects is a common occurrence.

Toplogical errors (high res problems)



```
CORRECTING DEFECT 1 (vertices=61708, convex hull=5864)
```



- If Freesurfer hangs at toplogical defects as shown here.
- Vertices in the order of 200,000
- Large number means Freesurfer will hang
- Find defects
  - Surface = `lh.smoothwm.nofix`
  - Overlay = `lh.defect_labels`
- Continue as before

Personal experiences in freesurfer

Should you fix these defects?

- Whole brain analyses (possibly)
- Large group analyses (less likely)
- Only if it affects your brain region of interest

FREESURFER IN ACTION

Lauren Gascoyne

QDEC Query, Design, Estimate, Contrast

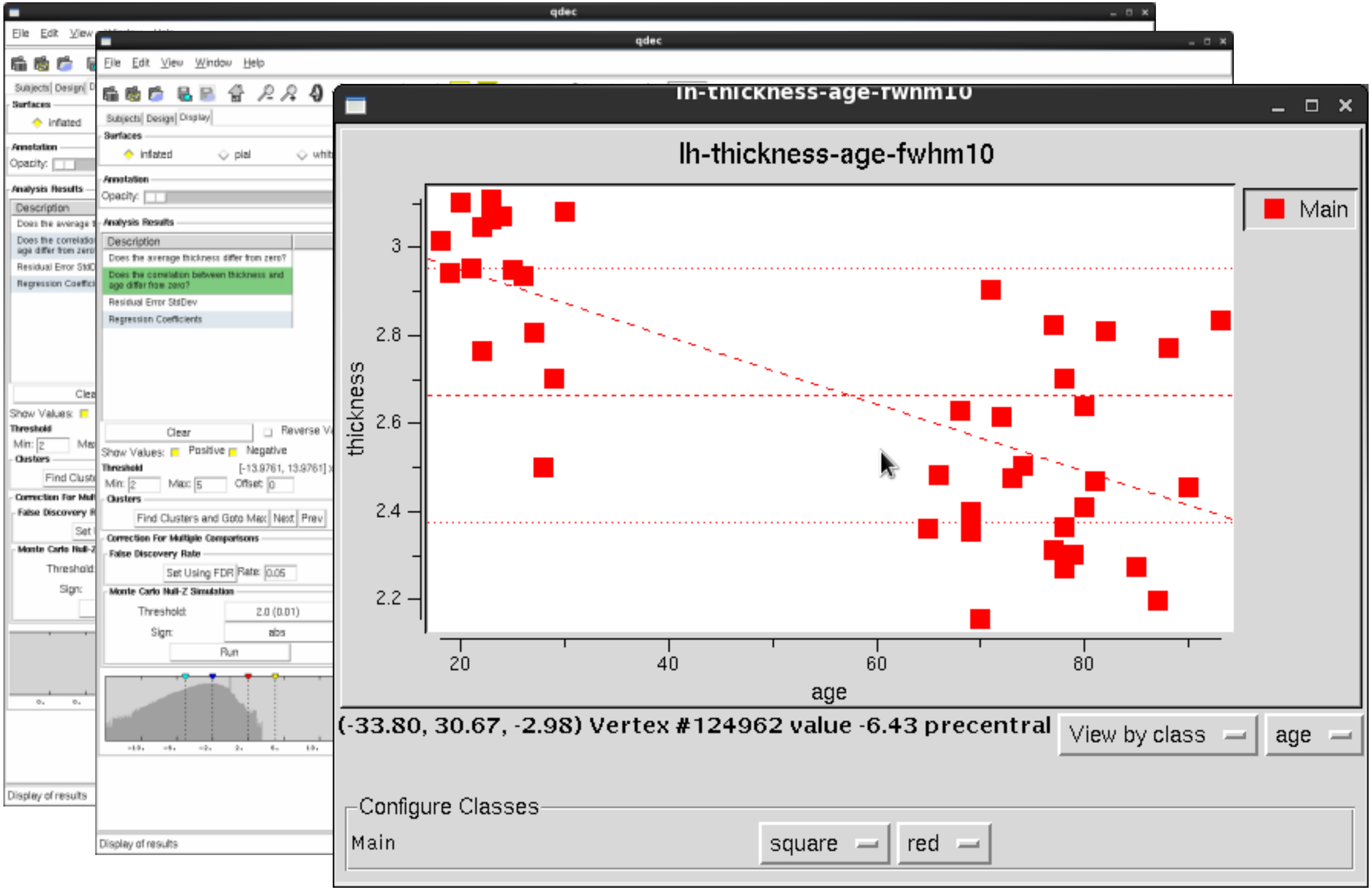
Group analysis of morphometry data

thickness, area, volume, sulc, curv, jacobian_white

Steps:

- smooth the cortical surfaces for each individual
  - **recon-all –s <subjid> -qcache**
- input subject demographics in a table format e.g. age, gender, other covariates
- open qdec and import the table
- choose a design and run the stats engine

QDEC



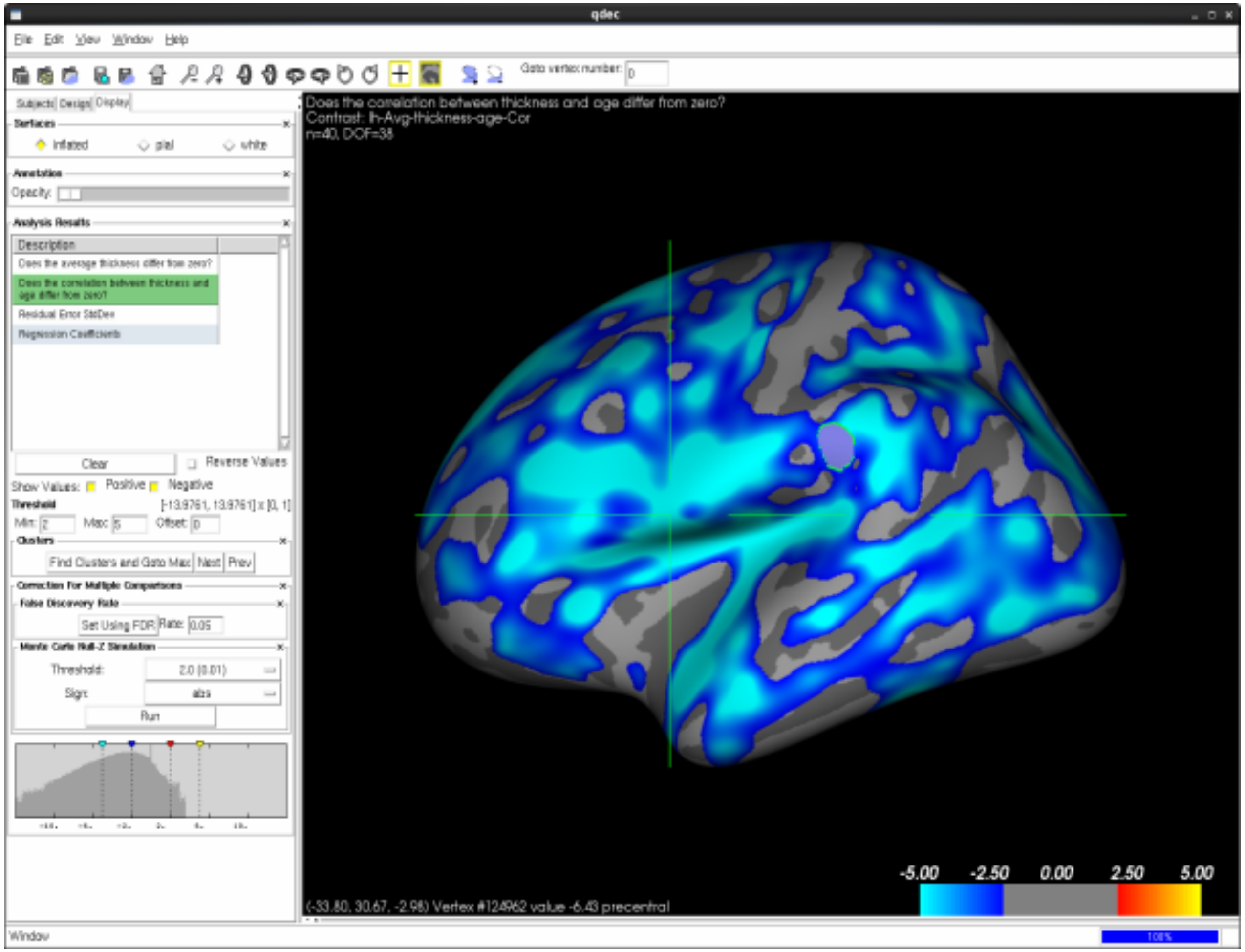
(-33.80, 30.67, -2.98) Vertex #124962 value -6.43 precentral

Labels

Easy to draw

Use QDEC, tkmedit, tksurfer, freeview

Can do it using for a group (using fsaverage) or on an individual level



Goto vertex number: 0

Does the correlation between thickness and age differ from zero?
Contrast: lh-Avg-thickness-age-Cor
n=40, DOF=38

Opacity:

Description
Does the average thickness differ from zero?
Does the correlation between thickness and age differ from zero?
Residual Error StdDev
Regression Coefficients

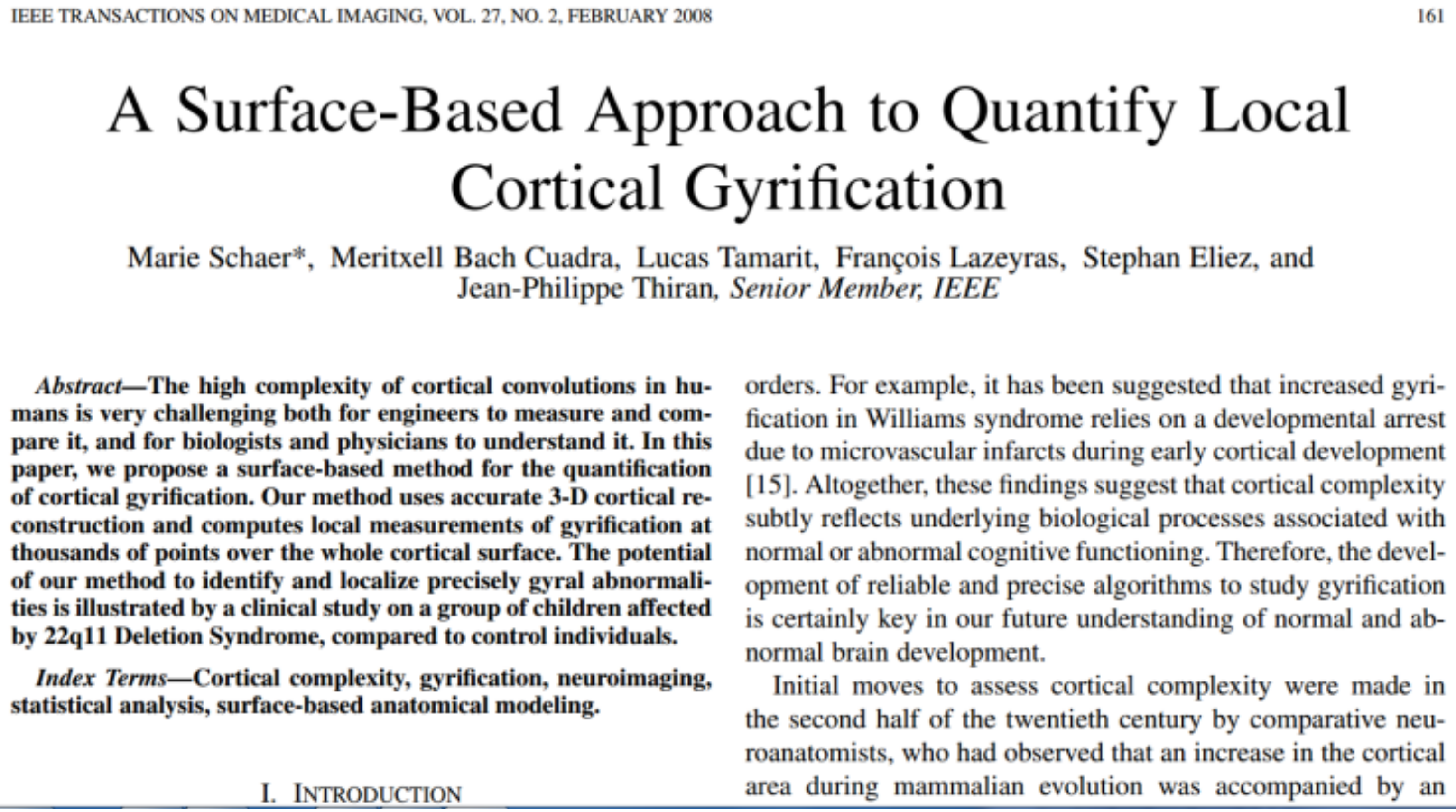
Threshold [-13.9761, 13.9761] x [0, 1]
Min: 2 Max: 5 Offset: 0

Rate: 0.05

Threshold: 2.0 (0.01)
Sign: abs

(-33.80, 30.67, -2.98) Vertex #124962 value -6.43 precentral

Local Gyrification Index



IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 27, NO. 2, FEBRUARY 2008 161

A Surface-Based Approach to Quantify Local Cortical Gyrification

Marie Schaer*, Meritxell Bach Cuadra, Lucas Tamarit, François Lazeyras, Stephan Eliez, and
Jean-Philippe Thiran, *Senior Member, IEEE*

***Abstract*—The high complexity of cortical convolutions in humans is very challenging both for engineers to measure and compare it, and for biologists and physicians to understand it. In this paper, we propose a surface-based method for the quantification of cortical gyrification. Our method uses accurate 3-D cortical reconstruction and computes local measurements of gyrification at thousands of points over the whole cortical surface. The potential of our method to identify and localize precisely gyral abnormalities is illustrated by a clinical study on a group of children affected by 22q11 Deletion Syndrome, compared to control individuals.**

***Index Terms*—Cortical complexity, gyrification, neuroimaging, statistical analysis, surface-based anatomical modeling.**

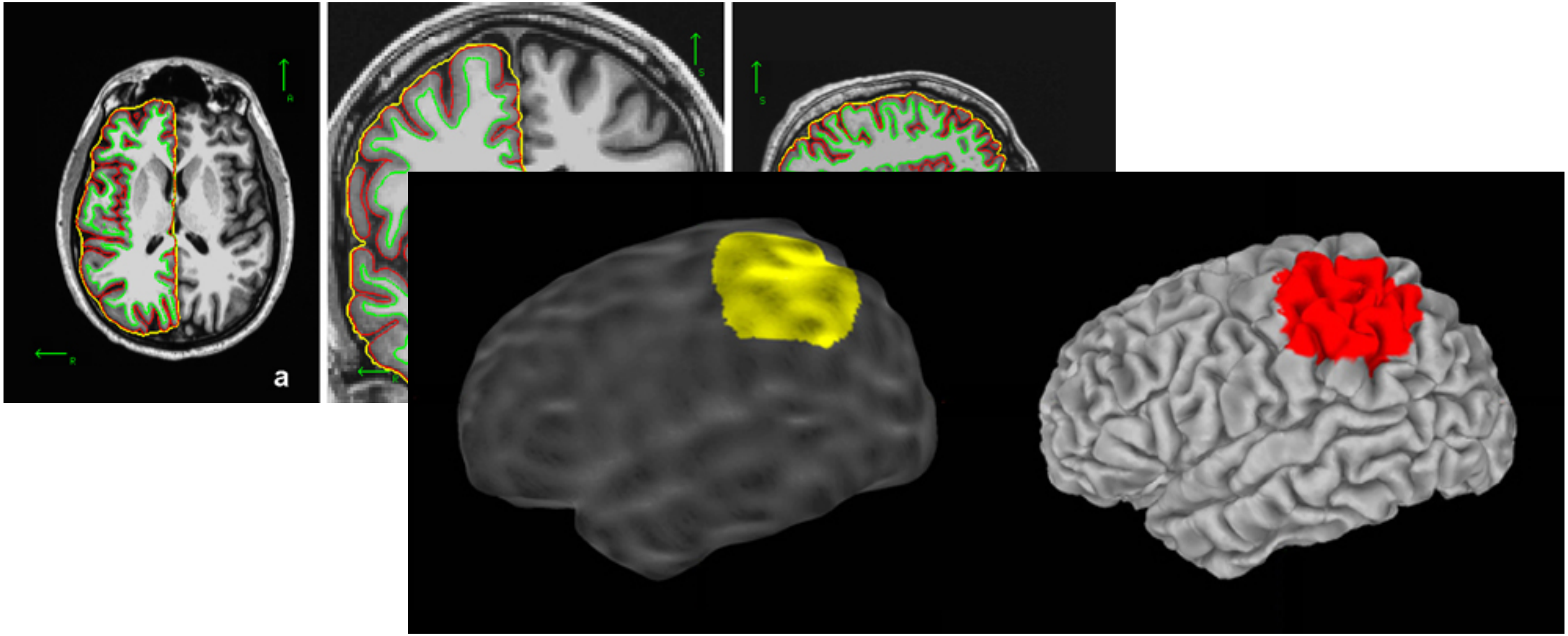
I. INTRODUCTION

orders. For example, it has been suggested that increased gyrification in Williams syndrome relies on a developmental arrest due to microvascular infarcts during early cortical development [15]. Altogether, these findings suggest that cortical complexity subtly reflects underlying biological processes associated with normal or abnormal cognitive functioning. Therefore, the development of reliable and precise algorithms to study gyrification is certainly key in our future understanding of normal and abnormal brain development.

Initial moves to assess cortical complexity were made in the second half of the twentieth century by comparative neuroanatomists, who had observed that an increase in the cortical area during mammalian evolution was accompanied by an

Local Gyrification Index

- Ratio of sulcal (buried) and gyral (visible) cortex across a 25mm area surrounding each vertex

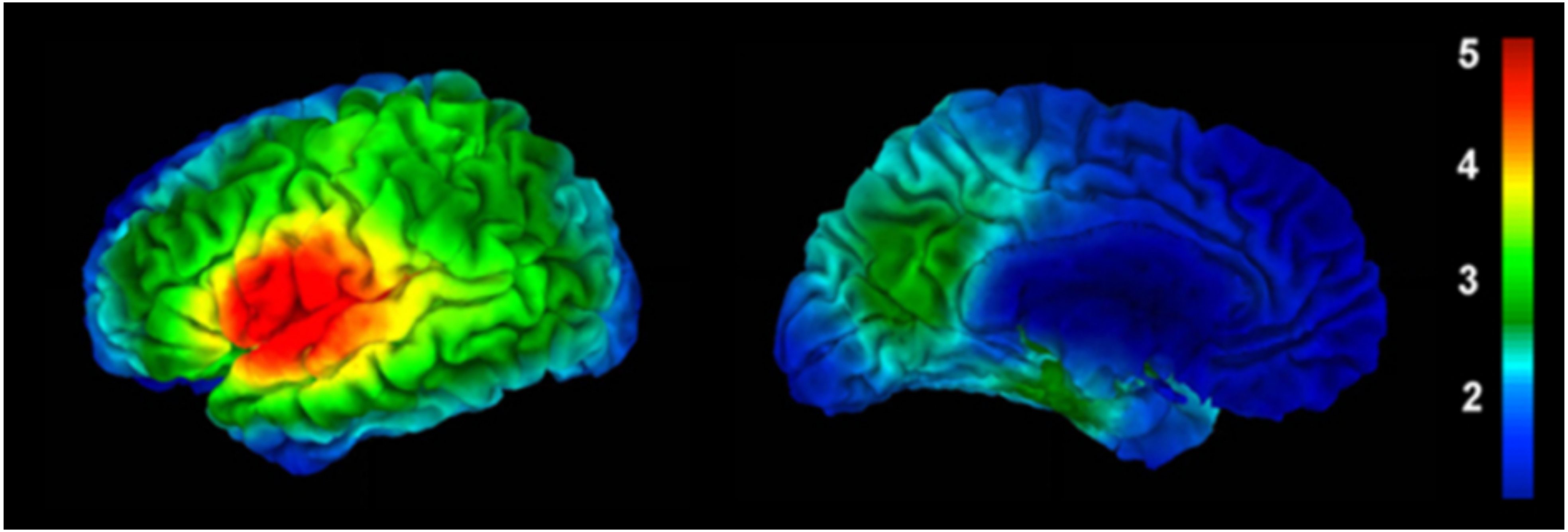


```
recon-all  –s <subj>  -localGI
```

Takes about 3 hours per subject – measures 150,000 vertices per hemisphere

Local Gyrification Index

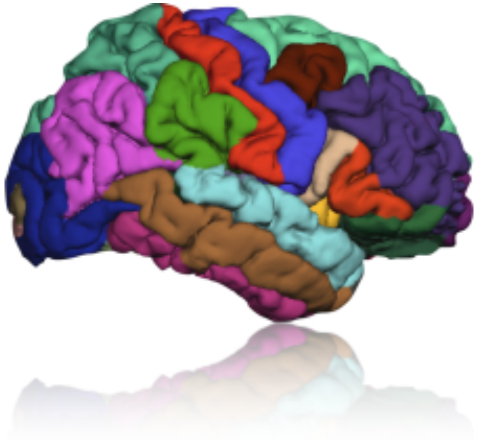
- 25mm area surrounding each vertex



Group-comparison

- Input to QDEC for statistical comparison between groups

- Vertex- vs Parcel-based analysis
  - Parcel-based analysis – this can be useful for exploratory analysis, but the LGI incorporates some of the surrounding regions, so there may be some overlap with other parcels.
  - Vertex-based analysis – allows examination of small areas of cortex, which would likely be more informative when examining pathological differences.



Thanks for listening!

- Questions?