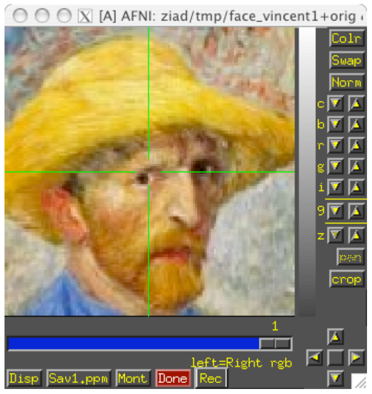
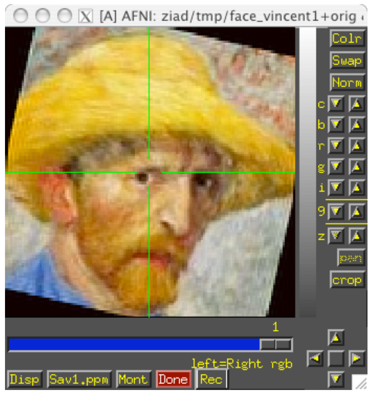
Image and Volume Registration with AFNI

- Goal: bring images collected with different methods and at different times into spatial alignment
- Facilitates comparison of data on a voxel-by-voxel basis
  - ✧ Functional time series data will be less contaminated by artifacts due to subject movement
  - ✧ Can compare results across scanning sessions once images are properly registered
  - ✧ Can put volumes in standard space such as the stereotaxic Talairach-Tournoux coordinates
- Most (all?) image registration methods now in use do pair-wise alignment:
  - ✧ Given a base image **J(x)** and target (or source) image **I(x)**, find a geometrical transformation **T[x]** so that **I(T[x]) ≈ J(x)**
  - ✧ **T[x]** will depend on some parameters
    - ➥ Goal is to find the parameters that make the transformed **I** a 'best fit' to **J**
  - ✧ To register an entire time series, each volume $\mathbf{I}_n(\mathbf{x})$ is aligned to **J(x)** with its own transformation $\mathbf{T}_n[\mathbf{x}]$, for $n=0, 1, \ldots$
    - ➥ Result is time series $\mathbf{I}_n(\mathbf{T}_n[\mathbf{x}])$ for n=0, 1, …
    - ➥ User must choose base image **J(x)**



- Most image registration methods make 3 algorithmic choices:
  - How to measure mismatch **E** (for error) between **I(T[x])** and **J(x)**?
    - **Or** … How to measure goodness of fit between **I(T[x])** and **J(x)**?
      - **E**(parameters) ≡ **–Goodness**(parameters)
  - How to adjust parameters of **T[x]** to minimize **E**?
  - How to interpolate **I(T[x])** to the **J(x)** grid?
    - So can compare voxel intensities directly
- The input volume is transformed by the optimal **T[x]** and a record of the transform is kept in the header of the output.
- Finding the transform to minimize **E** is the bulk of the registration work. Applying the transform is easy and is done on the fly in many cases.



- Next we cover various aspects of registration that are closely related:
  - Within Modality Registration
    - T1 subj1 to T1 subj 2
    - EPI timeseries to its i^{th} volume.
  - Cross Modality Registration
    - T1 subj1 to EPI subj 1
  - Registration to Standard Spaces (such as Talairach and Tournoux Atlas)
    - T1 to T1 atlas
    - EPI to EPI atlas

Within Modality Registration

- AFNI `2dImReg`, `3dvolreg` and `3dWarpDrive` programs match images by grayscale (intensity) values
  - ✧ **E** = (weighted) sum of squares differences = $\Sigma_x \, w(x) \cdot \{I(T[x]) - J(x)\}^2$
    - ➥ Only useful for registering ‘like images’:
      - ➪ Good for SPGR↔SPGR, EPI↔EPI, but **not** good for SPGR↔EPI
  - ✧ Parameters in **T[x]** are adjusted by “gradient descent”
    - ➥ Fast, but customized for the least squares **E**
  - ✧ Several interpolation methods are available:
    - ➥ Default method is Fourier interpolation
    - ➥ Polynomials of order 1, 3, 5, 7 (linear, cubic, quintic, and heptic)
  - ✧ `3dvolreg` is designed to run VERY fast for EPI↔EPI registration with small movements — good for FMRI purposes but restricted to 6-parameter rigid-body transformations.
  - ✧ `3dWarpDrive` is slower, but it allows for up to 12 parameters affine transformation. This corrects for scaling and shearing differences in addition to the rigid body transformations.

- AFNI program **2dImReg** is for aligning 2D slices
  - **T[x]** has 3 parameters for each slice in volume:
    - Shift along *x*-, *y*-axes; Rotation about *z*-axis
    - No out of slice plane shifts or rotations!
  - Useful for **sagittal** EPI scans where dominant subject movement is ‘nodding’ motion that may be faster than TR
  - It is possible and sometimes even useful to run **2dImReg** to clean up sagittal nodding motion, followed by **3dvolreg** to deal with out-of-slice motion
- AFNI program **3dvolreg** is for aligning 3D volumes by rigid movements
  - **T[x]** has 6 parameters:
    - Shifts along *x*-, *y*-, and *z*-axes; Rotations about *x*-, *y*-, and *z*-axes
  - Generically useful for intra- and inter-session alignment
  - Motions that occur within a single TR (2-3 s) cannot be corrected this way, since method assumes rigid movement of the entire volume
- AFNI program **3dWarpDrive** is for aligning 3D volumes by affine transformations
  - **T[x]** has up to 12 parameters:
    - Same as **3dvolreg** plus 3 Scales and 3 Shears along *x*-, *y*-, and *z*-axes
  - Generically useful for intra- and inter-session alignment
  - Generically useful for intra- and inter-subject alignment
- Hybrid ‘slice-into-volume’ registration (We do **not** have a program to do this):
  - Put each separate 2D image slice into the target volume with its own 6 movement parameters (3 out-of-plane as well as 3 in-plane)
  - Has been attempted, but the results are not much better than volume registration; method often fails on slices near edge of brain

- Intra-session registration example:

```
3dvolreg -base 4 -heptic -zpad 4    \
         -prefix fred1_epi_vr       \
         -1Dfile fred1_vr_dfile.1D \
         fred1_epi+orig
```

Input dataset name

- ✧ **-base 4** ⇒ Selects sub-brick #4 of dataset **fred1_epi+orig** as base image **J(x)**
- ✧ **-heptic** ⇒ Use 7th order polynomial interpolation (my personal favorite)
- ✧ **-zpad 4** ⇒ Pad each target image, **I(x)**, with layers of zero voxels 4 deep on each face prior to shift/rotation, then strip them off afterwards (before output)
  - ➥ Zero padding is particularly desirable for **-Fourier** interpolation
  - ➥ Is also good to use for polynomial methods, since if there are large rotations, some data may get 'lost' when no zero padding if used (due to the 4-way shift algorithm used for very fast rotation of 3D volume data)
- ✧ **-prefix fred1_epi_vr** ⇒ Save output dataset into a new dataset with the given prefix name (e.g., **fred1_epi_vr+orig**)
- ✧ **-1Dfile fred1_vr_dfile.1D** ⇒ Save estimated movement parameters into a 1D (i.e., text) file with the given name
  - ➥ Movement parameters can be plotted with command

```
1dplot -volreg -dx 5 -xlabel Time fred1_vr_dfile.1D
```

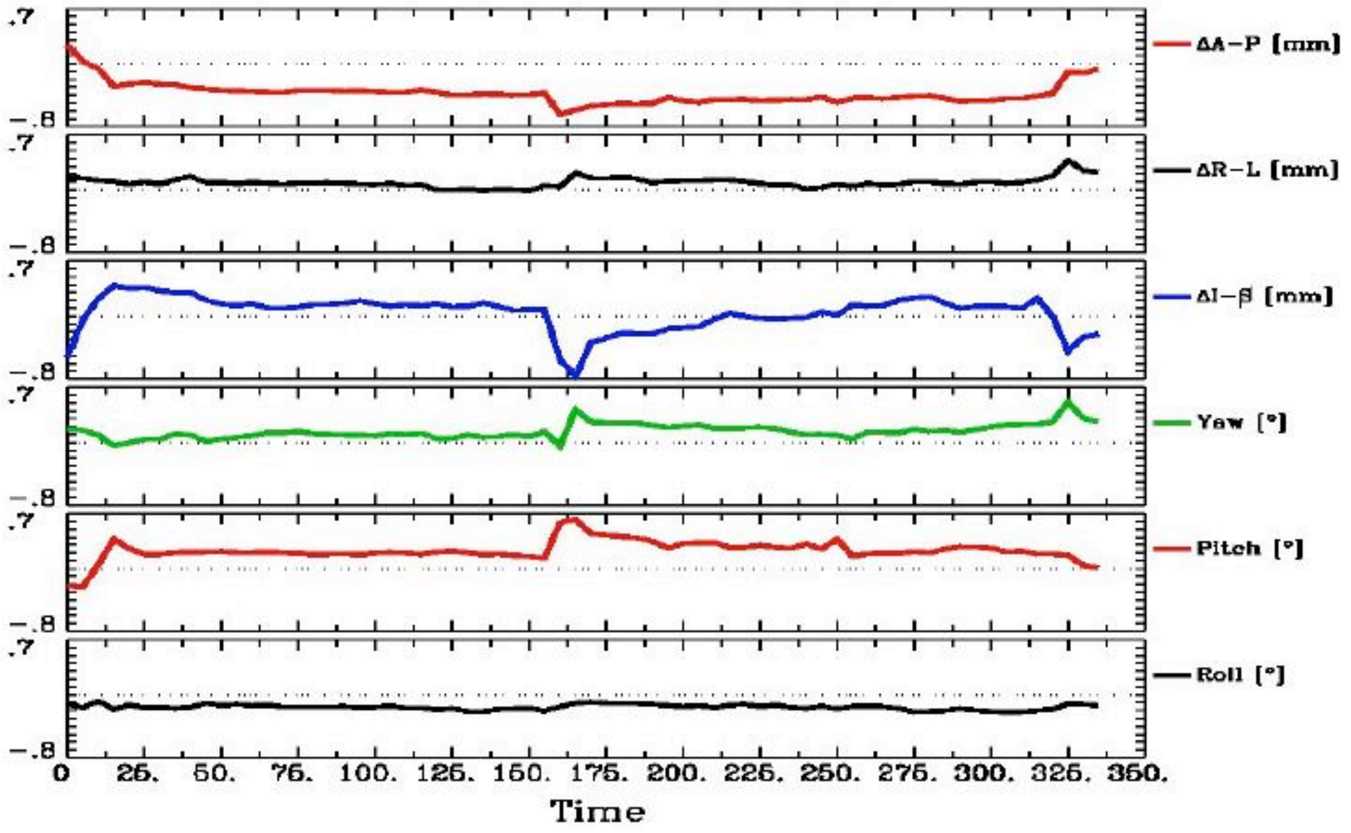
✧ Can now register second dataset from same session:

```
3dvolreg -base 'fred1_epi+orig[4]' -heptic -zpad 4      \
         -prefix fred2_epi_vr -1Dfile fred2_vr_dfile.1D \
         fred2_epi+orig
```

➥ Note base is from different dataset (**`fred1_epi+orig`**) than input (**`fred2_epi+orig`**)

➩ Aligning all EPI volumes from session to EPI closest in time to SPGR

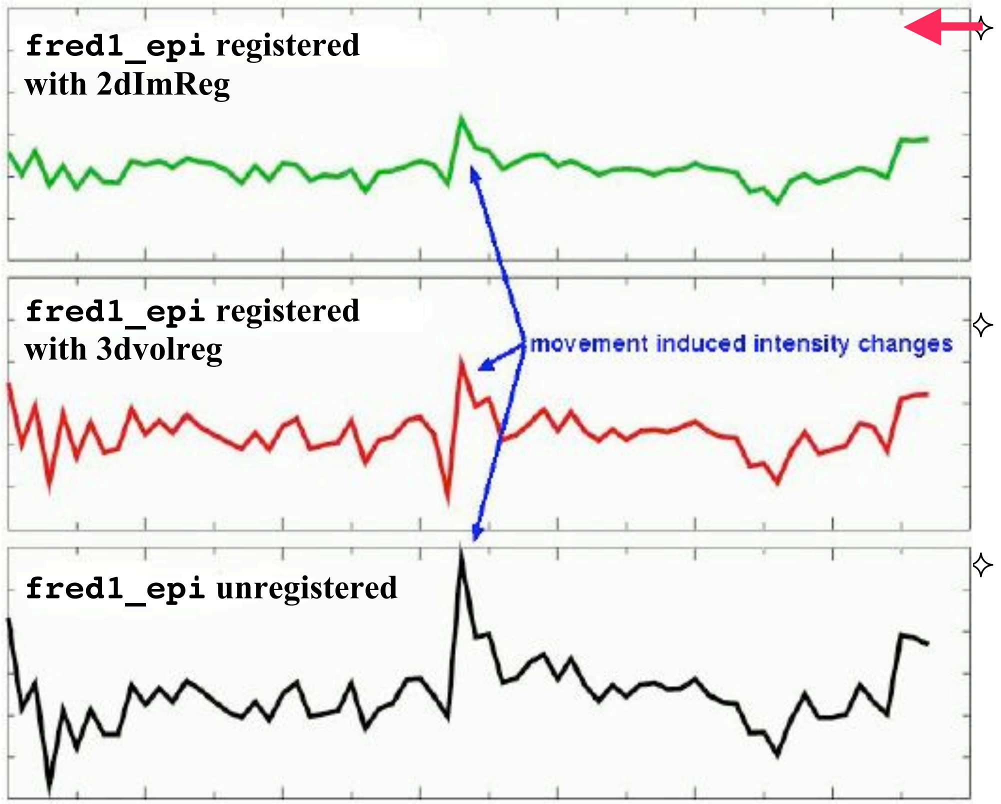
• `1dplot -volreg -dx 5 -xlabel Time fred2_vr_dfile.1D`



➥ Note motion peaks at time≈160s: subject jerked head up at that time

- Examination of time series **fred2_epi+orig** and **fred2_epi_vr_+orig** shows that head movement up and down happened within about 1 TR interval
  - Assumption of rigid motion of 3D volumes is not good for this case
  - Can do 2D slice-wise registration with command

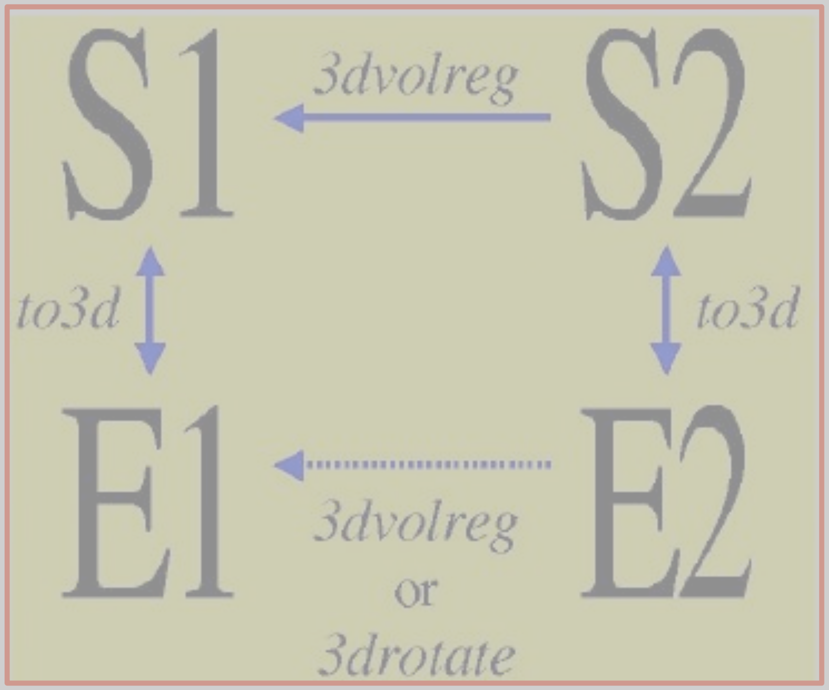
```
2dImReg -input fred2_epi+orig       \
 -basefile fred1_epi+orig           \
 -base 4 -prefix fred2_epi_2Dreg
```



- Graphs of a single voxel time series near the edge of the brain:
  - Top = slice-wise alignment
  - Middle = volume-wise adjustment
  - Bottom = no alignment
- For **<u>this</u>** example, **2dImReg** appears to produce better results. This is because most of the motion is 'head nodding' and the acquisition is sagittal
- You should also use AFNI to scroll through the images (using the **Index** control) during the period of pronounced movement
  - Helps see if registration fixed problems

No longer discussed here, see appendix A if interested

- Intra-subject, inter-session registration (for multi-day studies on same subject)
  - ✧ Longitudinal or learning studies; re-use of cortical surface models
  - ✧ Transformation between sessions is calculated by registering high-resolution anatomicals from each session
    - ➥ **`to3d`** defines defines relationship between EPI and SPGR in each session
    - ➥ **`3dvolreg`** computes relationship between sessions
    - ➥ So can transform EPI from session 2 to orientation of session 1



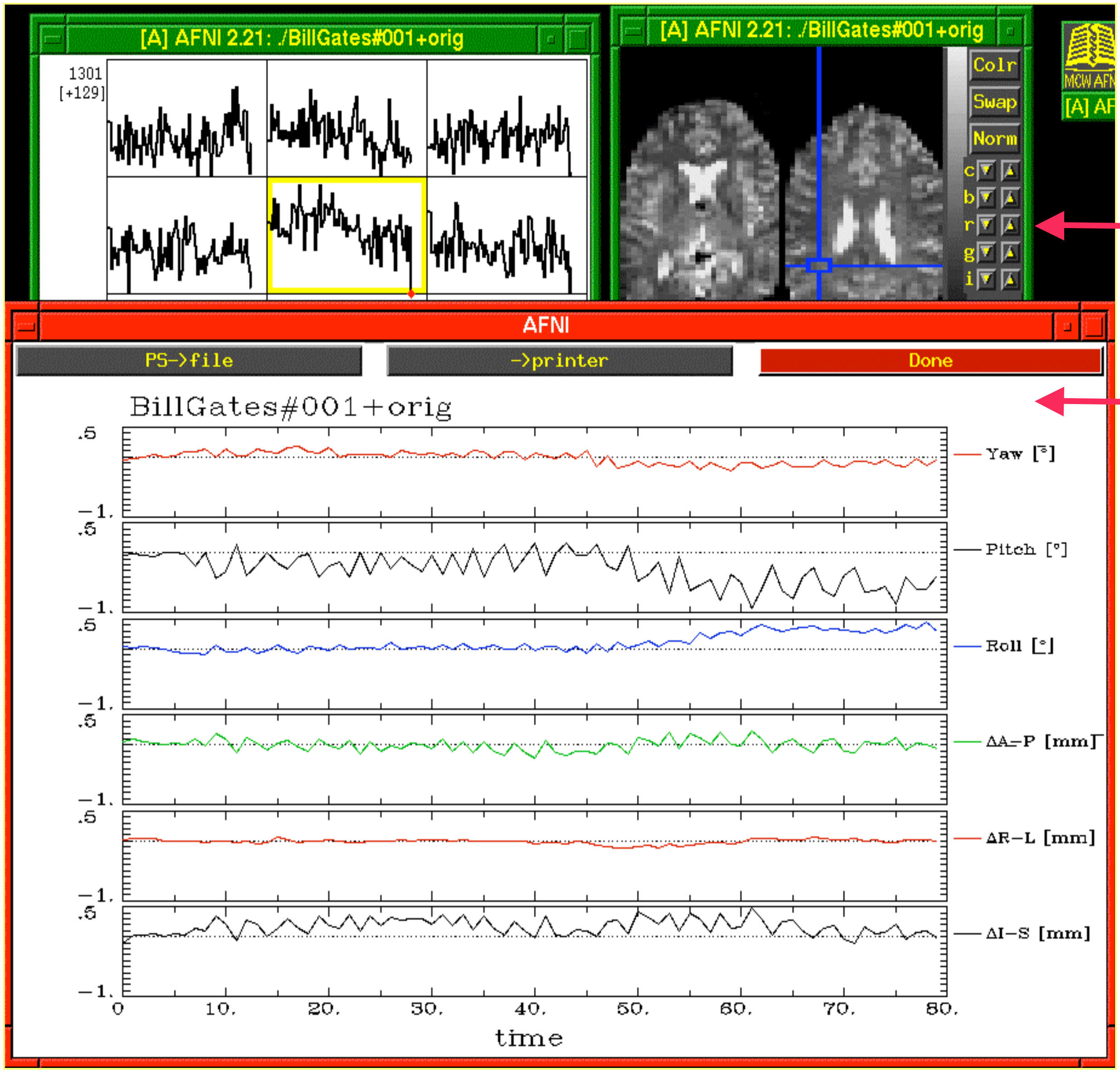
  - ✧ Issues in inter-session registration:
    - ➥ Subject’s head will be positioned differently (in orientation and location)
      - ➩ xyz-coordinates and anatomy don’t correspond
    - ➥ Anatomical coverage of EPI slices will differ between sessions
    - ➥ Geometrical relation between EPI and SPGR differs between session
    - ➥ Slice thickness may vary between sessions (try not to do this, OK?)

Real-Time 3D Image Registration

- The image alignment method using in `3dvolreg` is also built into the AFNI real-time image acquisition plugin
  - ✧ Invoke by command `afni -rt`
  - ✧ Then use `Define Datamode` → `Plugins` → `RT Options` to control the operation of real-time (RT) image acquisition
- Images (2D or 3D arrays of numbers) can be sent into AFNI through a TCP/IP socket
  - ✧ See the program `rtfeedme.c` for sample of how to connect to AFNI and send the data
    - ➥ Also see file **`README.realtime`** for lots of details
  - ✧ 2D images will be assembled into 3D volumes = AFNI sub-bricks
- Real-time plugin can also do 3D registration when each 3D volume is finished, and graph the movement parameters in real-time
  - ✧ Useful for seeing if the subject in the scanner is moving his head too much
    - ➥ If you see too much movement, telling the subject will usually help

- Realtime motion correction can easily be setup if DICOM images are made available on disk as the scanner is running.
- The script demo.realtime present in the AFNI_data1/EPI_manyruns directory demonstrates the usage:

```
#!/bin/tcsh

# demo real-time data acquisition and motion detection with afni

# use environment variables in lieu of running the RT Options plugin
setenv AFNI_REALTIME_Registration      3D:_realtime
setenv AFNI_REALTIME_Graph             Realtime

if ( ! -d afni ) mkdir afni
cd afni

afni -rt &

sleep 5

cd ..
echo ready to run Dimon
echo -n press enter to proceed...
set stuff = $<

Dimon -rt -use_imon -start_dir 001 -pause 200
```



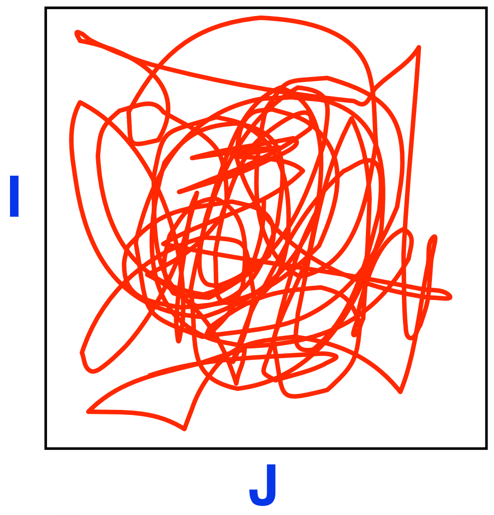
- Screen capture from example of real-time image acquisition and registration
- Images and time series graphs can be viewed as data comes in
- Graphs of movement parameters

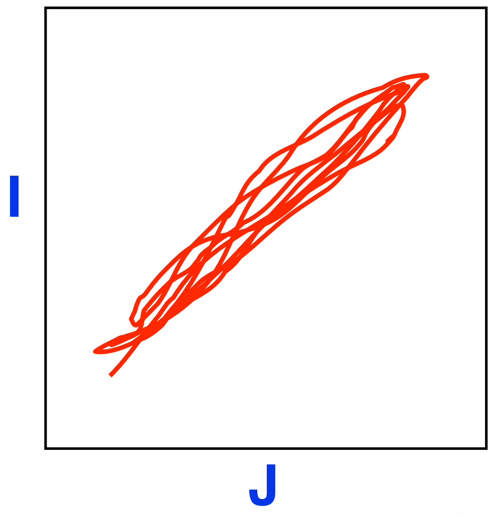
Cross Modality Registration

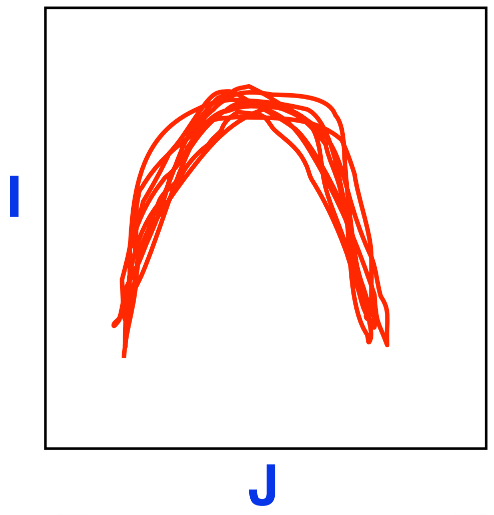
- `3dAllineate` can be used to align images from different methods
  - ✧ For example, to align EPI data to SPGR / MPRAGE:
    - ➥ Run `3dSkullStrip` on the SPGR dataset so that it will be more like the EPI dataset (which will have the skull fat suppressed)
    - ➥ Use `3dAllineate` to align the EPI volume(s) to the skull-stripped SPGR volume
    - ➥ Program works well if the EPI volume covers most of the brain
  - ✧ Allows more general spatial transformations
    - ➥ At present, 12 parameter affine: **T[x] = Ax+b**
  - ✧ Uses a more general-purpose optimization library than gradient descent
    - ➥ The **NEWUOA** package from Michael Powell at Oxford
    - ➥ Less efficient than a customized gradient descent formulation
      - ➪ But can be used in more situations
      - ➪ And is easier to put in the computer program, since there is no need to compute the derivatives of the cost function **E**

- `3dAllineate` has several different "cost" functions (**E**) available
  - ✧ **`leastsq`** = Least Squares (`3dvolreg, 3dWarpDrive`)
  - ✧ **`mutualinfo`** = Mutual Information
  - ✧ **`norm_mutualinfo`** = Normalized Mutual Information
  - ✧ **`hellinger`** = Hellinger Metric [the **default** cost function]
  - ✧ **`corrratio_mul`** = Correlation ratio (symmetrized by multiplication)
  - ✧ **`corratio_add`** = Correlation ratio (symmetrized by addition)
  - ✧ **`corratio_uns`** = Correlation ratio (unsymmetric)
- All cost functions, except "**`leastsq`**", are based on the joint histogram between images **I(T[x])** and **J(x)**
  - ✧ The goal is to make **I(T[x])** "predictable" as possible given **J(x)**, as the parameters that define **T[x]** are varied
  - ✧ The different cost functions use different ideas of "predictable"
  - ✧ <u>Perfect</u> predictability = knowing value of **J**, can calculate value of **I** exactly
    - ➥ Least squares: **I =** $\alpha\cdot$**J+**β for some constants α and β
    - ➥ Joint histogram of **I** and **J** is "simple" in the idealized case of perfect predictability

- Histogram cartoons:





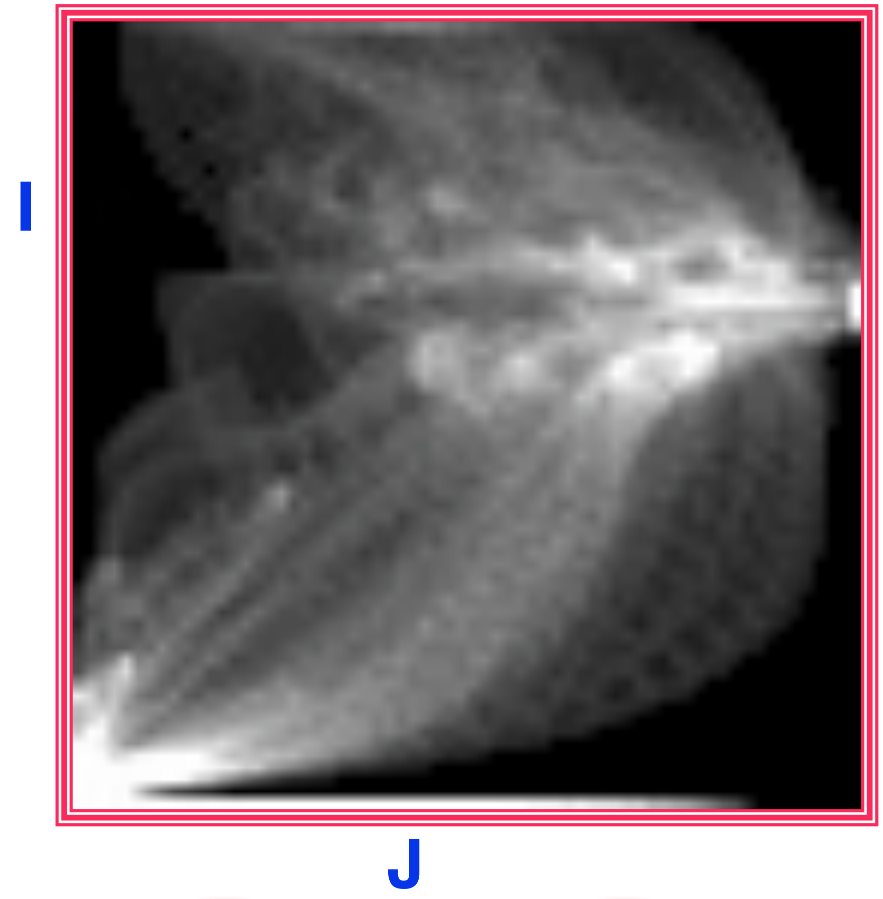


- J not useful in predicting I

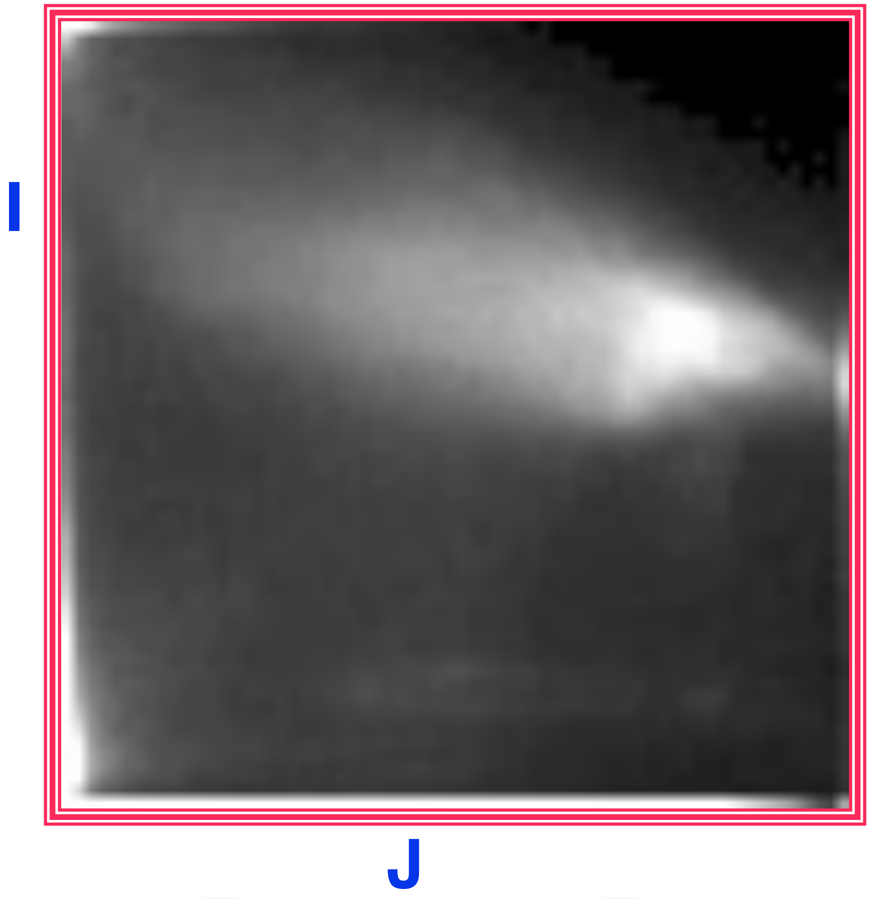
- I can be accurately predicted from J with a linear formula: **`-leastsq`** is OK

- I can be accurately predicted from J, but nonlinearly: **`-leastsq`** is BAD

- Actual histograms from a registration example
  - ✧ **J(x)** = `3dSkullStrip`-ed MPRAGE **I(x)** = EPI volume

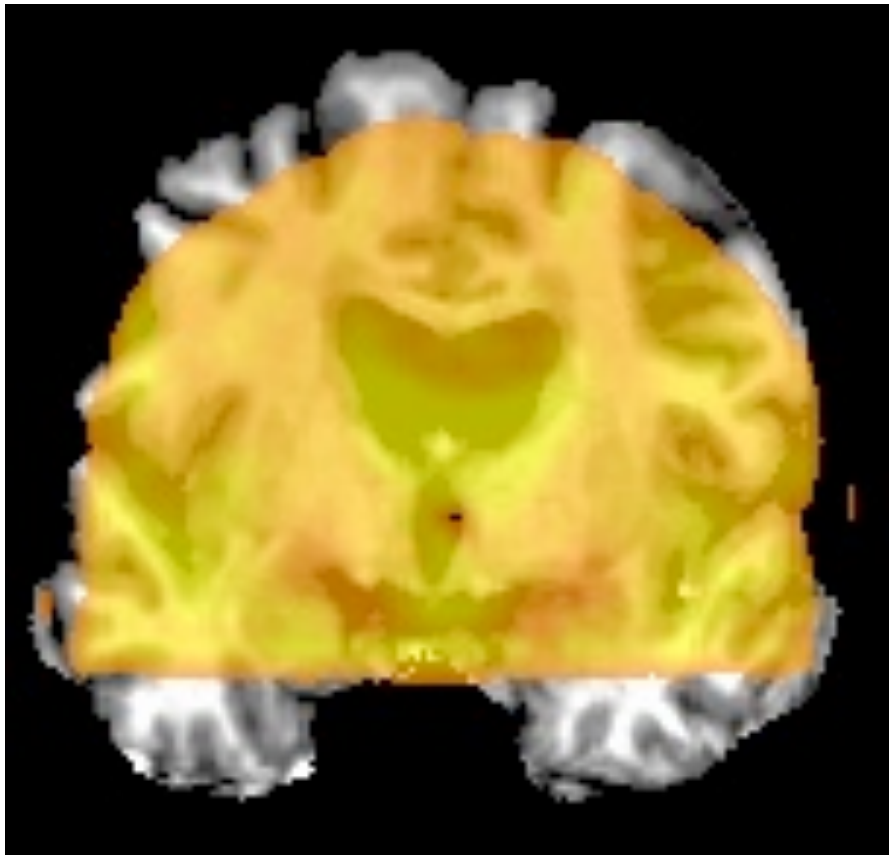


• Before alignment

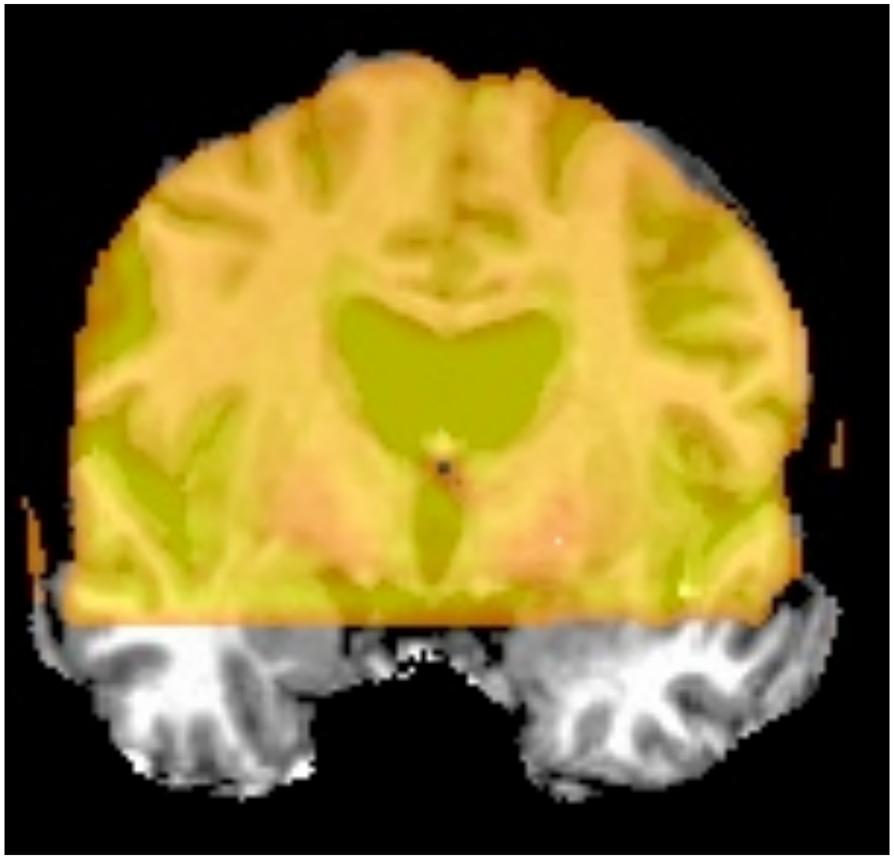


• After alignment (using **`-mutualinfo`**)

- grayscale underlay = **J(x)** = `3dSkullStrip`-ed MPRAGE
- color overlay = **I(x)** = EPI volume



• Before alignment



• After alignment (using **`-mutualinfo`**)

- Other `3dAllineate` capabilities:
  - ✧ Save transformation parameters with option `-1Dfile` in one program run
    - ➥ Re-use them in a second program run on another input dataset with option `-1Dapply`
  - ✧ Interpolation: linear (polynomial order = 1) during alignment
    - ➥ To produce output dataset: polynomials of order 1, 3, or 5
- Algorithm details:
  - ✧ Initial alignment starting with many sets of transformation parameters, using only a limited number of points from smoothed images
  - ✧ The best (smallest **E**) sets of parameters are further refined using more points from the images and less blurring
  - ✧ This continues until the final stage, where many points from the images and no blurring is used
- So why not `3dAllineate` all the time?
  - ✧ Alignment with cross-modal cost functions do not always converge as well as those based on least squares.
    - ➥ See Appendix B for more info.
    - ➥ Improvements are still being introduced

- The future for `3dAllineate`:
  - Allow alignment to use manually placed control points (on both images) ***and*** the image data
    - Will be useful for aligning highly distorted images or images with severe shading
    - Current AFNI program `3dTagalign` allows registration with control points ***only***
  - Nonlinear spatial transformations
    - For correcting distortions of EPI (relative to MPRAGE or SPGR) due to magnetic field inhomogeneity
    - For improving inter-subject brain alignment (Talairach)
  - Investigate the use of local computations of **E** (in a set of overlapping regions covering the images) and using the sum of these local **E**'s as the cost function
    - May be useful when relationship between **I** and **J** image intensities is spatially dependent
      - RF shading and/or Differing MRI contrasts
  - Save warp parameters in dataset headers for re-use by 3dWarp

Registration To Standard Spaces

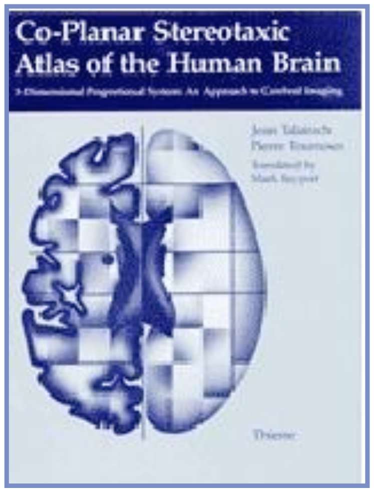
Transforming Datasets to Talairach-Tournoux Coordinates

- The original purpose of AFNI (*circa* 1994 A.D.) was to perform the transformation of datasets to Talairach-Tournoux (stereotaxic) coordinates
- The transformation can be manual, or automatic
- In manual mode, you must mark various anatomical locations, defined in

  Jean Talairach and Pierre Tournoux

  "Co-Planar Stereotaxic Atlas of the Human Brain"

  Thieme Medical Publishers, New York, 1988



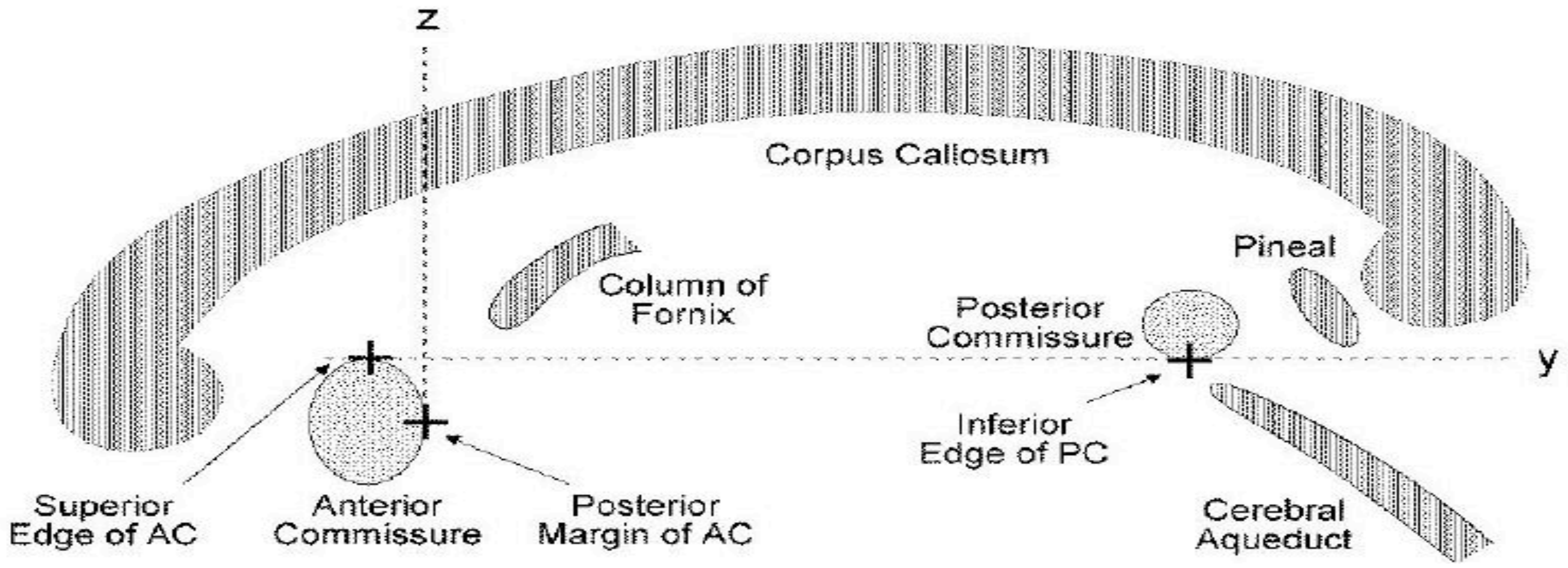
  - ✧ Marking is best done on a high-resolution T1-weighted structural MRI volume
- In automatic mode, you need to choose a template to which your data are allineated. Different templates are made available with AFNI's distribution. You can also use your own templates.
- Transformation carries over to all other (follower) datasets in the same directory
  - ✧ This is where the importance of getting the relative spatial placement of datasets done correctly in **`to3d`** really matters
  - ✧ You can then write follower datasets, typically functional or EPI timeseries, to disk in Talairach coordinates
    - ➥ Purpose: voxel-wise comparison with other subjects
    - ➥ May want to blur volumes a little before comparisons, to allow for residual anatomic variability: AFNI programs **`3dmerge`** **`or`** **`3dBlurToFWHM`**

- Manual Transformation proceeds in two stages:
    1. Alignment of AC-PC and I-S axes (to **`+acpc`** coordinates)
    2. Scaling to Talairach-Tournoux Atlas brain size (to **`+tlrc`** coordinates)

- Stage 1: Alignment to **`+acpc`** coordinates:
    - ✧ Anterior commissure (AC) and posterior commissure (PC) are aligned to be the y-axis
    - ✧ The longitudinal (inter-hemispheric or mid-sagittal) fissure is aligned to be the yz-plane, thus defining the z-axis
    - ✧ The axis perpendicular to these is the x-axis (right-left)
    - ✧ Five markers that you must place using the **`[Define Markers]`** control panel:

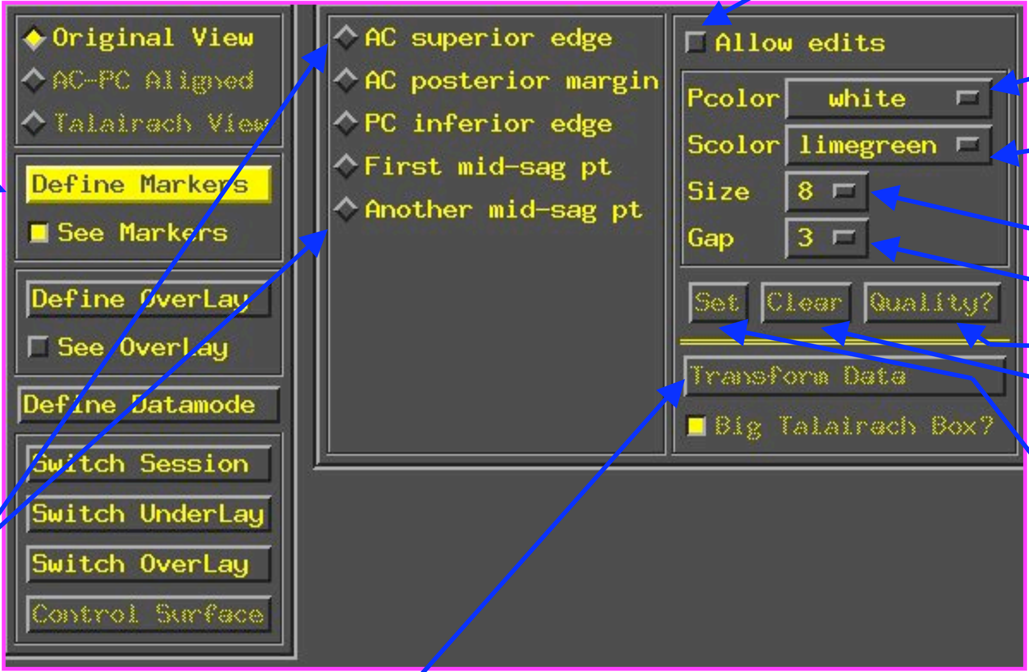
`AC superior edge`	= top middle of anterior commissure
`AC posterior margin`	= rear middle of anterior commissure
`PC inferior edge`	= bottom middle of posterior commissure
`First mid-sag point`	= some point in the mid-sagittal plane
`Another mid-sag point`	= some other point in the mid-sagittal plane

- ✧ This procedure tries to follow the Atlas as precisely as possible
    - ➥ Even at the cost of confusion to the user (e.g., you)



Press this IN to create or change markers

Click Define Markers to open the "markers" panel



Color of "primary" (selected) marker

Color of "secondary" (not selected) markers

Size of markers (pixels)

Size of gap in markers

Clear (unset) primary marker

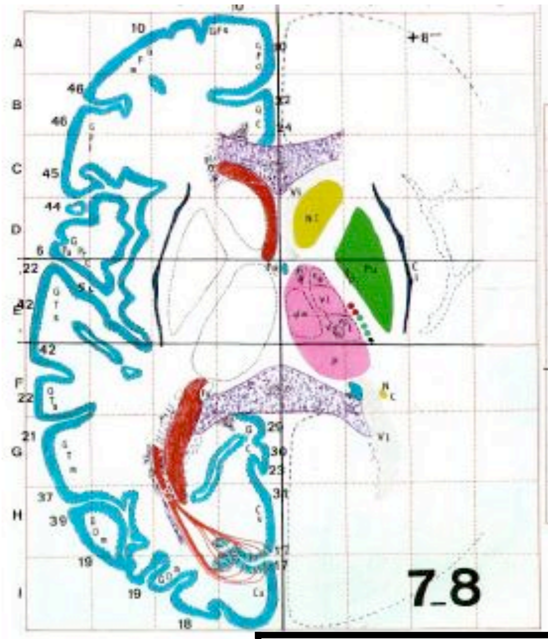
Set primary marker to current focus location

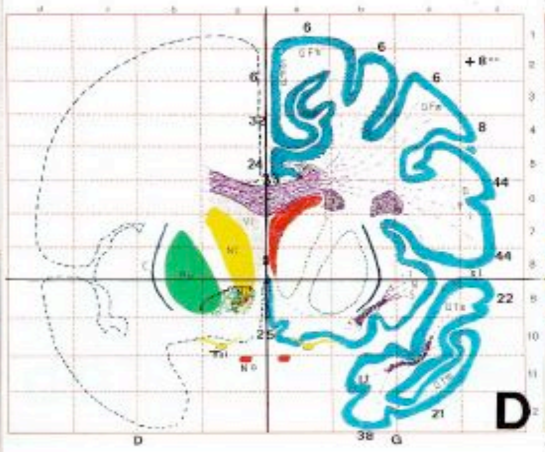
Select which marker you are editing

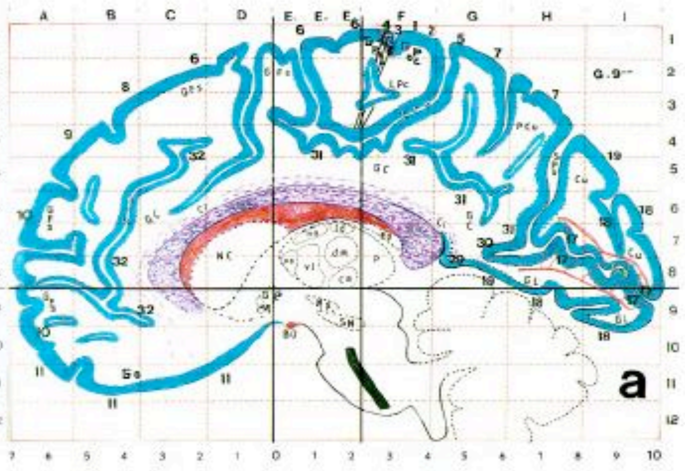
Carry out transformation to +acpc coordinates

Perform "quality" check on markers (after all 5 are set)

- **<u>Stage 2: Scaling to Talairach-Tournoux (+tlrc) coordinates</u>:**
  - ✧ Once the AC-PC landmarks are set and we are in ACPC view, we now stretch/shrink the brain to fit the Talairach-Tournoux Atlas brain size (sample TT Atlas pages shown below, just for fun)



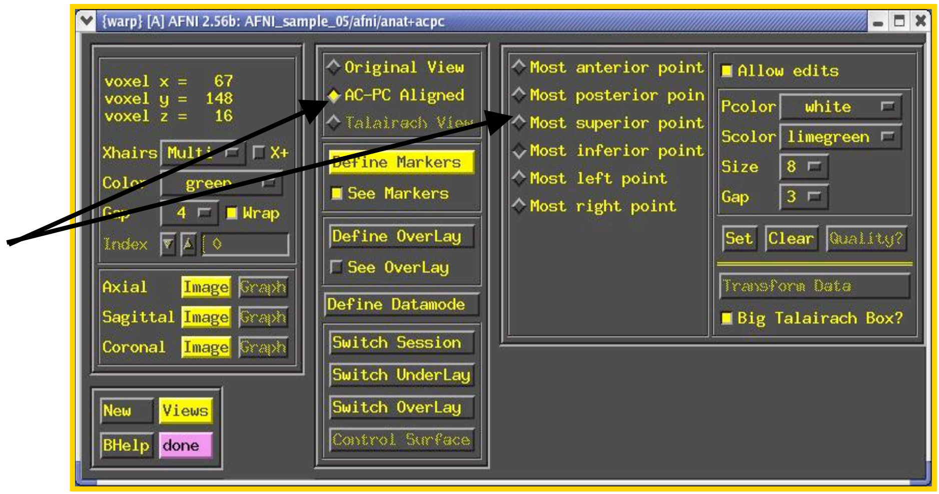




Most anterior to AC	70 mm		
AC to PC	23 mm		
PC to most posterior	79 mm	Length of cerebrum	172mm
Most inferior to AC	42 mm		
AC to most superior	74 mm	Height of cerebrum	116mm
AC to left (or right)	68 mm	Width of cerebrum	136mm

- **<u>Selecting the Talairach-Tournoux markers for the bounding box</u>:**
  - ✧ There are 12 sub-regions to be scaled (3 A-P x 2 I-S x 2 L-R)
  - ✧ To enable this, the transformed `+acpc` dataset gets its own set of markers
    - ➥ Click on the **[AC-PC Aligned]** button to view our volume in ac-pc coordinates
    - ➥ Select the **[Define Markers]** control panel
  - ✧ A new set of six Talairach markers will appear and the user now sets the bounding box markers (see Appendix C for details):

Talairach markers appear only when the AC-PC view is highlighted


{warp} [A] AFNI 2.56b: AFNI_sample_05/afni/anat+acpc

voxel x = 67
voxel y = 148
voxel z = 16

Xhairs Multi
Color green
Gap 4
Index 0

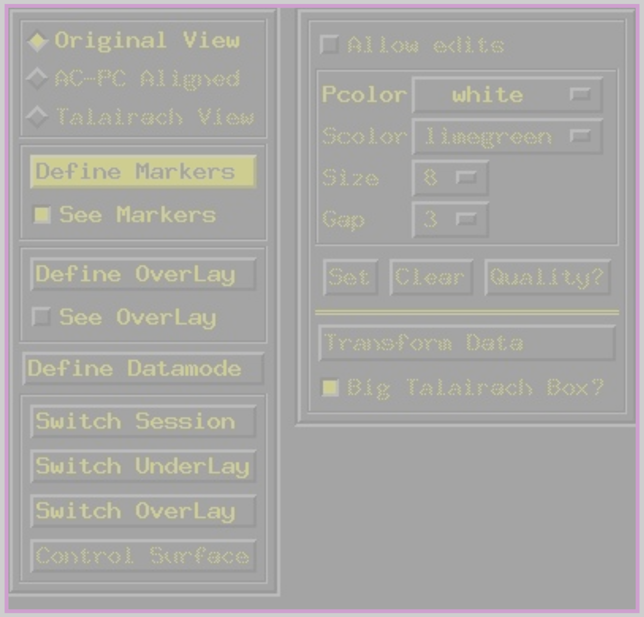
◆ AC-PC Aligned

Pcolor white
Scolor limegreen
Size 8
Gap 3

- ✧ Once all the markers are set, and the quality tests passed. Pressing **[Transform Data]** will write new ***header*** containing the Talairach transformations (see Appendix C for details)
  - ➥ Recall: With AFNI, spatial transformations are stored in the header of the output

Detailed example for manual transformation is now in appendix C

- **Listen up folks, IMPORTANT NOTE:**
  - ✧ Have you ever opened up the [**Define Markers**] panel, only to find the AC-PC markers ***missing***, like this:



Gasp! Where did they go?

- ✧ There are a few reasons why this happens, but usually it's because you've made a copy of a dataset, and the AC-PC marker tags weren't created in the copy, resulting in the above dilemma.
  - ➥ In other cases, this occurs when **afni** is launched without any datasets in the directory from which it was launched (oopsy, your mistake).
- ✧ If you do indeed have an AFNI dataset in your directory, but the markers are missing and you want them back, run **3drefit** with the **-markers** options to create an empty set of AC-PC markers. Problem solved!

```
3drefit -markers <name of dataset>
```

Automatic Talairach Transformation with @auto_tlrc

- Is manual selection of AC-PC and Talairach markers bringing you down? You can now perform a TLRC transform ***automatically*** using an AFNI script called **`@auto_tlrc`**.
  - Differences from Manual Transformation:
    - Instead of setting ac-pc landmarks and volume boundaries by hand, the anatomical volume is warped (using 12-parameter affine transform) to a template volume in TLRC space.
    - Anterior Commisure (AC) center no longer at 0,0,0 and size of brain box is that of the template you use.
      - For various reasons, some good and some bad, templates adopted by the neuroimaging community are not all of the same size. Be mindful when using various atlases or comparing standard-space coordinates.
    - You, the user, can choose from various templates for reference but be consistent in your group analysis.
    - Easy, automatic. Just check final results to make sure nothing went seriously awry. AFNI is perfect but your data is not.

- Templates in **`@auto_tlrc`** that the user can choose from:
  - **`TT_N27+tlrc`**:
    - AKA "Colin brain". One subject (Colin) scanned 27 times and averaged. (www.loni.ucla.edu, www.bic.mni.mcgill.ca)
    - Has a full set of FreeSurfer (surfer.nmr.mgh.harvard.edu) surface models that can be used in SUMA (*link*).
    - Is the template for cytoarchitectonic atlases (www.fz-juelich.de/ime/spm_anatomy_toolbox)
      - For improved alignment with cytoarchitectonic atlases, I recommend using the TT_N27 template because the atlases were created for it. In the future, we might provide atlases registered to other templates.
  - **`TT_icbm452+tlrc`**:
    - International Consortium for Brain Mapping template, average volume of 452 normal brains. (www.loni.ucla.edu, www.bic.mni.mcgill.ca)
  - **`TT_avg152T1+tlrc`**:
    - Montreal Neurological Institute (www.bic.mni.mcgill.ca) template, average volume of 152 normal brains.
  - **`TT_EPI+tlrc:`**
    - EPI template from spm2, masked as TT_avg152T1. TT_avg152 and TT_EPI volumes are based on those in SPM's distribution. (www.fil.ion.ucl.ac.uk/spm/)

Steps performed by @auto_tlrc

- For warping a volume to a template (Usage mode 1):
  1. Pad the input data set to avoid clipping errors from shifts and rotations
  2. Strip skull (if needed)
  3. Resample to resolution and size of TLRC template
  4. Perform 12-parameter affine registration using **3dWarpDrive**

  Many more steps are performed in actuality, to fix up various pesky little artifacts. Read the script if you are interested.

  - ✧ Typically this steps involves a high-res anatomical to an anatomical template
    - ➥ Example: @auto_tlrc -base TT_N27+tlrc. -input anat+orig. -suffix NONE
  - ✧ One could also warp an EPI volume to an EPI template.
    - ➥ If you are using an EPI time series as input. You must choose one sub-brick to input. The script will make a copy of that sub-brick and will create a warped version of that copy.

Applying a transform to follower datasets

- Say we have a collection of datasets that are in alignment with each other. One of these datasets is aligned to a template and the same transform is now to be applied to the other *follower* datasets
- For Talairach transforms there are a few methods:
  - ✧ Method 1: Manually using the AFNI interface (see Appendix C)
  - ✧ Method 2: With program adwarp

    ```
    adwarp -apar anat+tlrc  -dpar func+orig
    ```

    - ➥ The result will be: **`func+tlrc.HEAD`** and **`func+tlrc.BRIK`**
  - ✧ Method 3: With @auto_tlrc script in mode 2
    - ➥ ONLY when -apar dataset was created by @auto_tlrc
    - ➥ Otherwise, you can use adwarp
- Why bother saving transformed datasets to disk anyway?
  - ✧ Datasets without `.BRIK` files are of limited use:
    - ➥ You can't display 2D slice images from such a dataset
    - ➥ You can't use such datasets to graph time series, do volume rendering, compute statistics, run any command line analysis program, run any plugin…
      - ➯ If you plan on doing any of the above to a dataset, it's best to have both a `.HEAD` and `.BRIK` files for that dataset

@auto_tlrc Example

- Transforming the high-resolution anatomical:
  - ✧ (If you are also trying the manual transform on workshop data, start with a fresh directory with no +tlrc datasets)

```
@auto_tlrc                    \
   -base TT_N27+tlrc          \
   -suffix NONE               \
   -input anat+orig
```

Output:
`anat+tlrc`

- Transforming the function ("follower datasets"), setting the resolution at 2 mm:

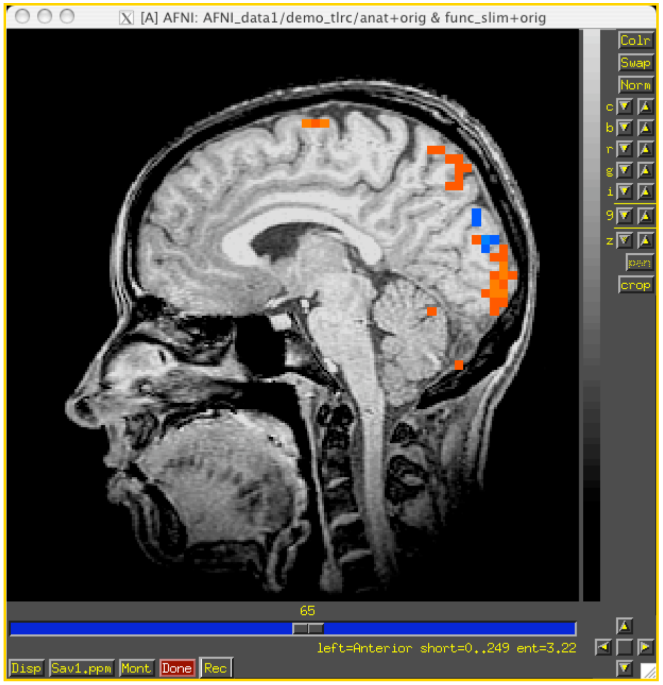
```
@auto_tlrc                    \
   -apar anat+tlrc            \
   -input func_slim+orig      \
   -suffix NONE               \
   -dxyz  2
```

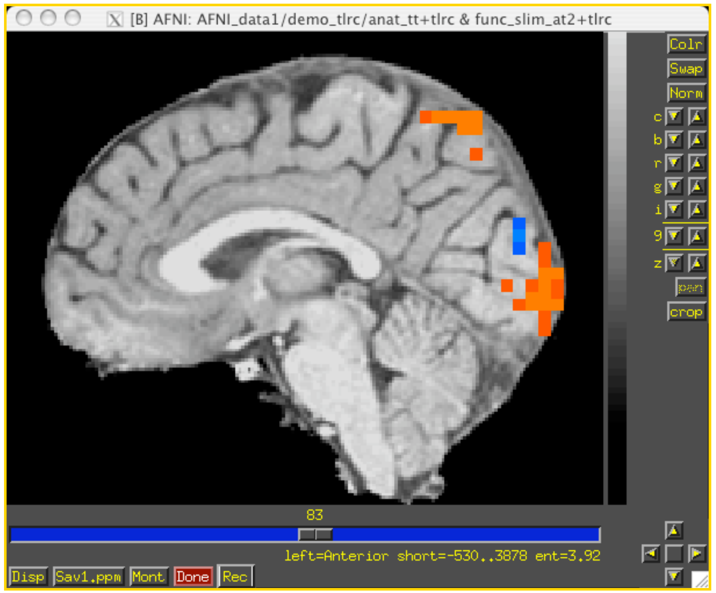
Output:
`func_slim+tlrc`

- You could also use the **icbm452** or the mni's **avg152T1** template instead of **N27** or any other template you like (see @auto_tlrc -help for a few good words on templates)

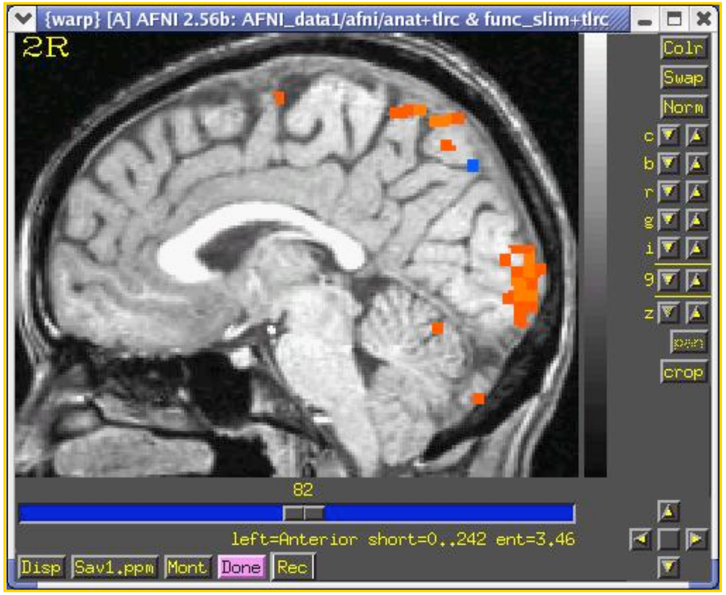
@auto_tlrc Results are Comparable to Manual TLRC:

Original


[A] AFNI: AFNI_data1/demo_tlrc/anat+orig & func_slim+orig
65
left=Anterior short=0..249 ent=3.22
Disp
Sav1.ppm
Mont
Done
Rec

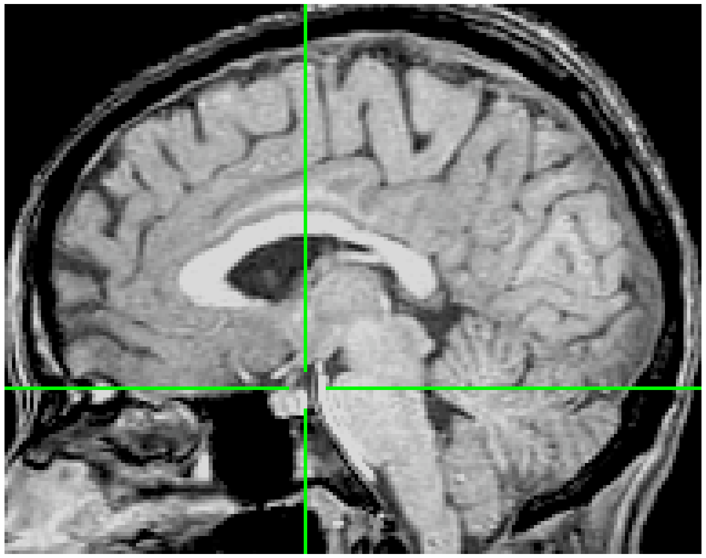

[B] AFNI: AFNI_data1/demo_tlrc/anat_tt+tlrc & func_slim_at2+tlrc
83
left=Anterior short=-530..3878 ent=3.92

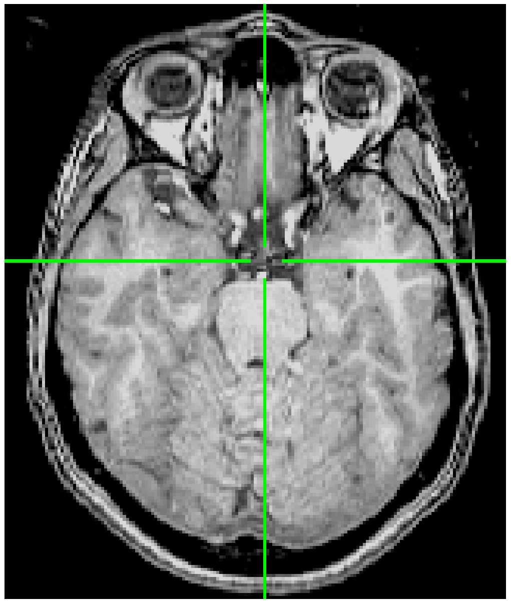
@auto_tlrc

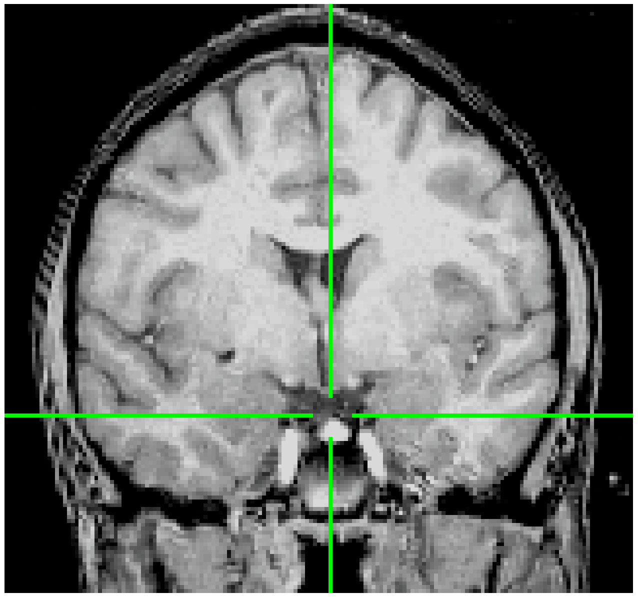

{warp} [A] AFNI 2.56b: AFNI_data1/afni/anat+tlrc & func_slim+tlrc
2R
82
left=Anterior short=0..242 ent=3.46

Manual

Manual TLRC vs. `@auto_tlrc` (e.g., N27 template)

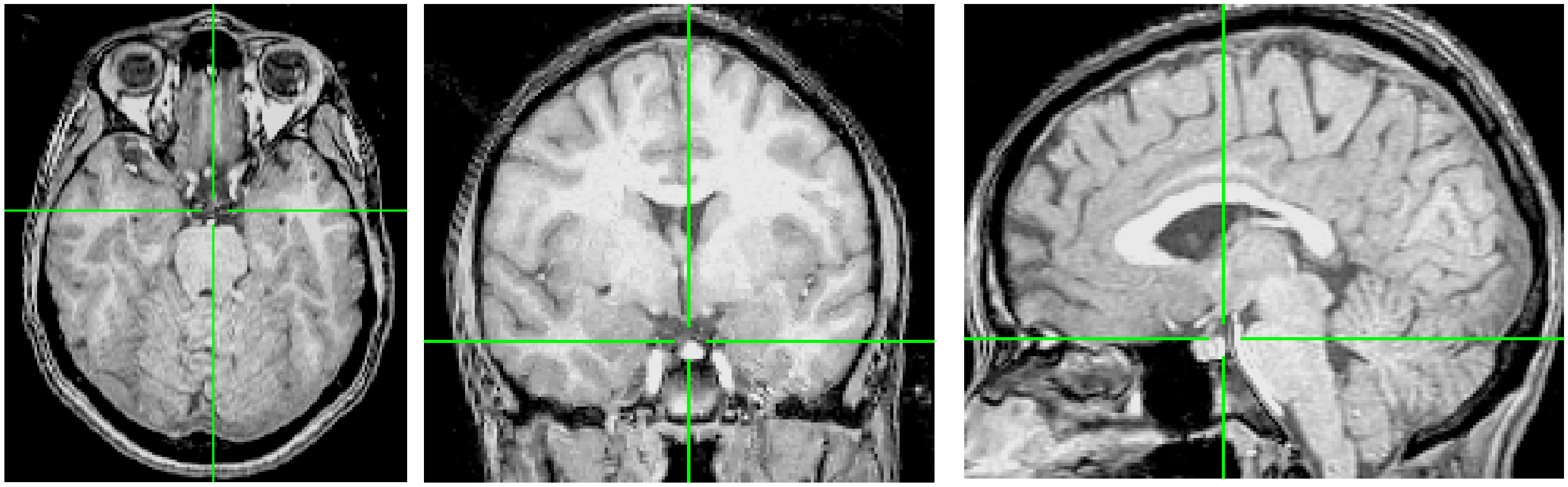




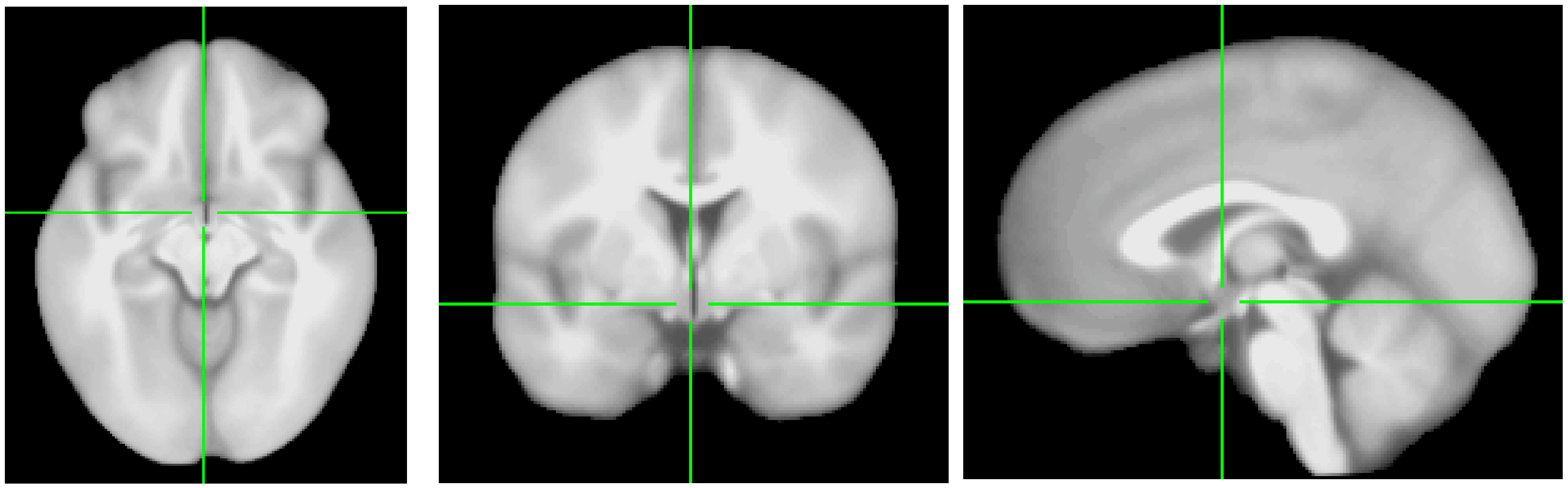


Expect some differences between manual TLRC and **`@auto_tlrc`**: The **`@auto_tlrc`** template is the brain of a different person after all.

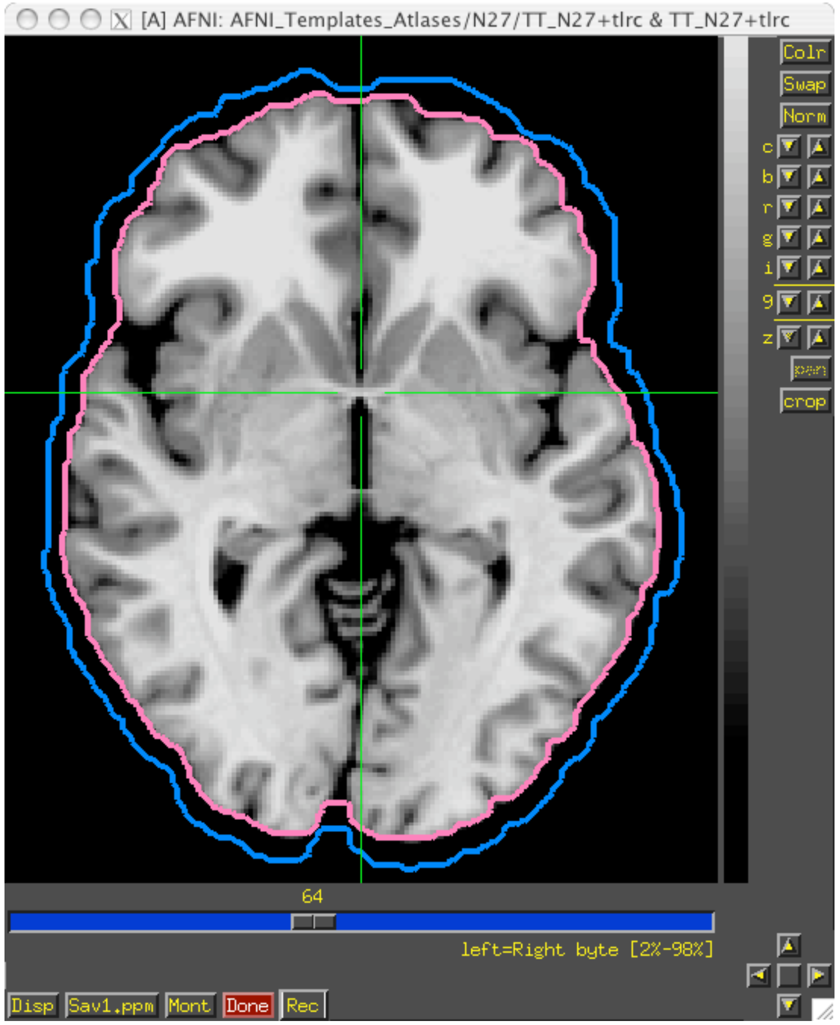
Difference Between `anat+tlrc` (manual) and `TT_N27+tlrc` template



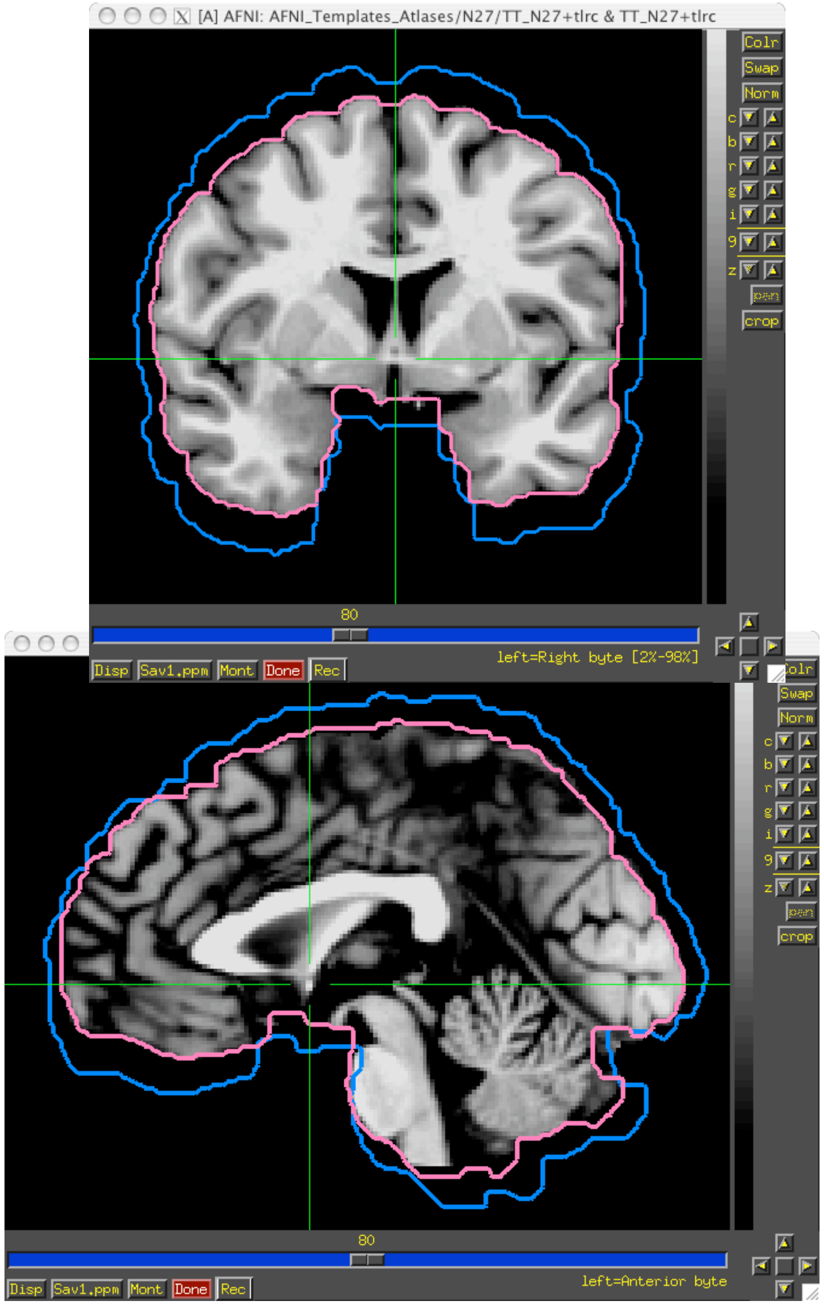
Difference between `TT_icbm452+tlrc` and `TT_N27+tlrc` templates



Atlas/Template Spaces Differ In Size

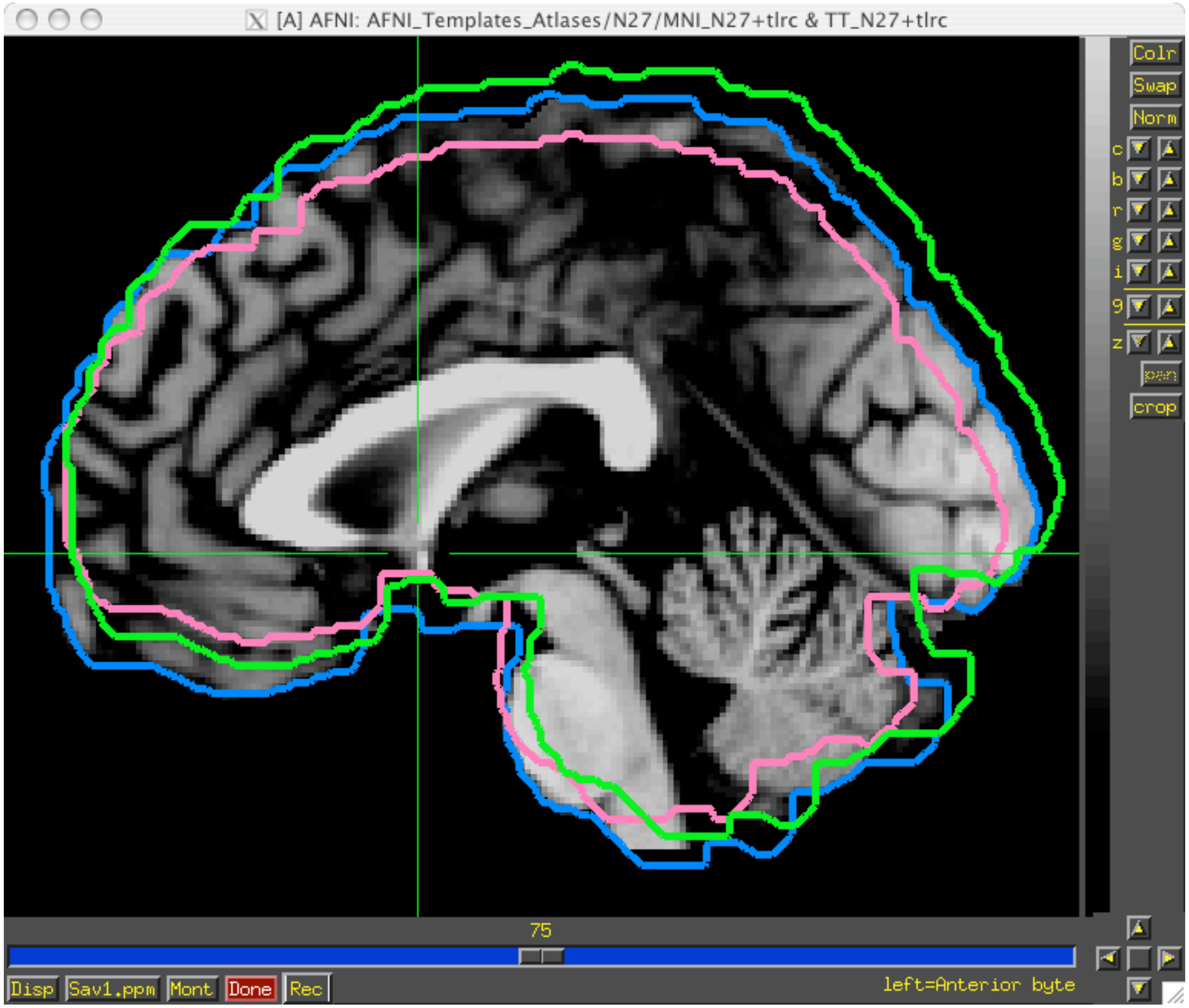


MNI is larger than TLRC space.



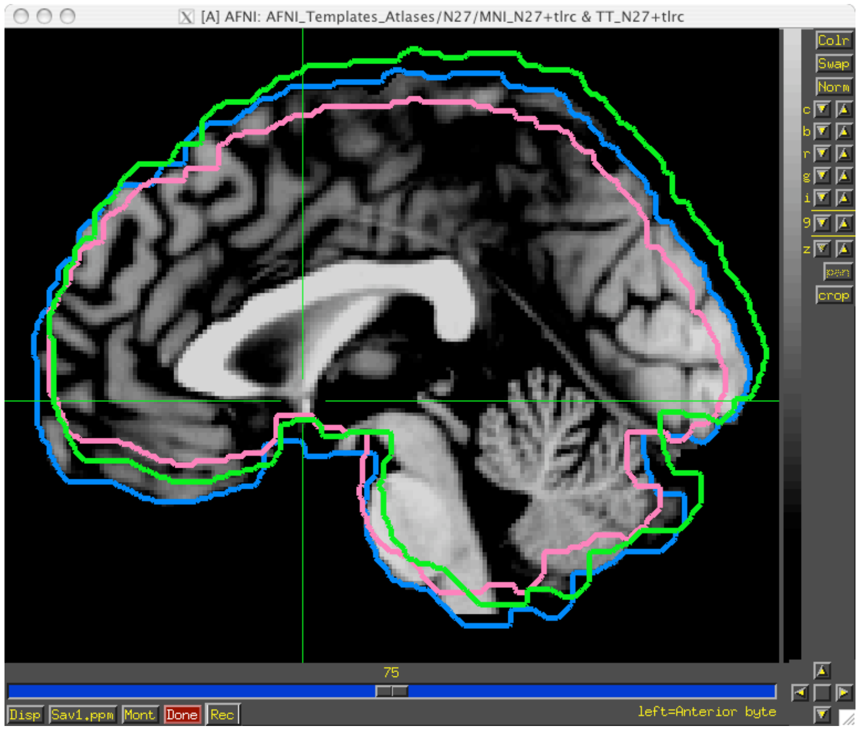
Atlas/Template Spaces Differ In Origin

TLRC
MNI
MNI-Anat.



From Space To Space

TLRC
MNI
MNI-Anat.


[A] AFNI: AFNI_Templates_Atlases/N27/MNI_N27+tlrc & TT_N27+tlrc
Colr
Swap
Norm
crop
75
Disp
Sav1.ppm
Mont
Done
Rec
left=Anterior byte

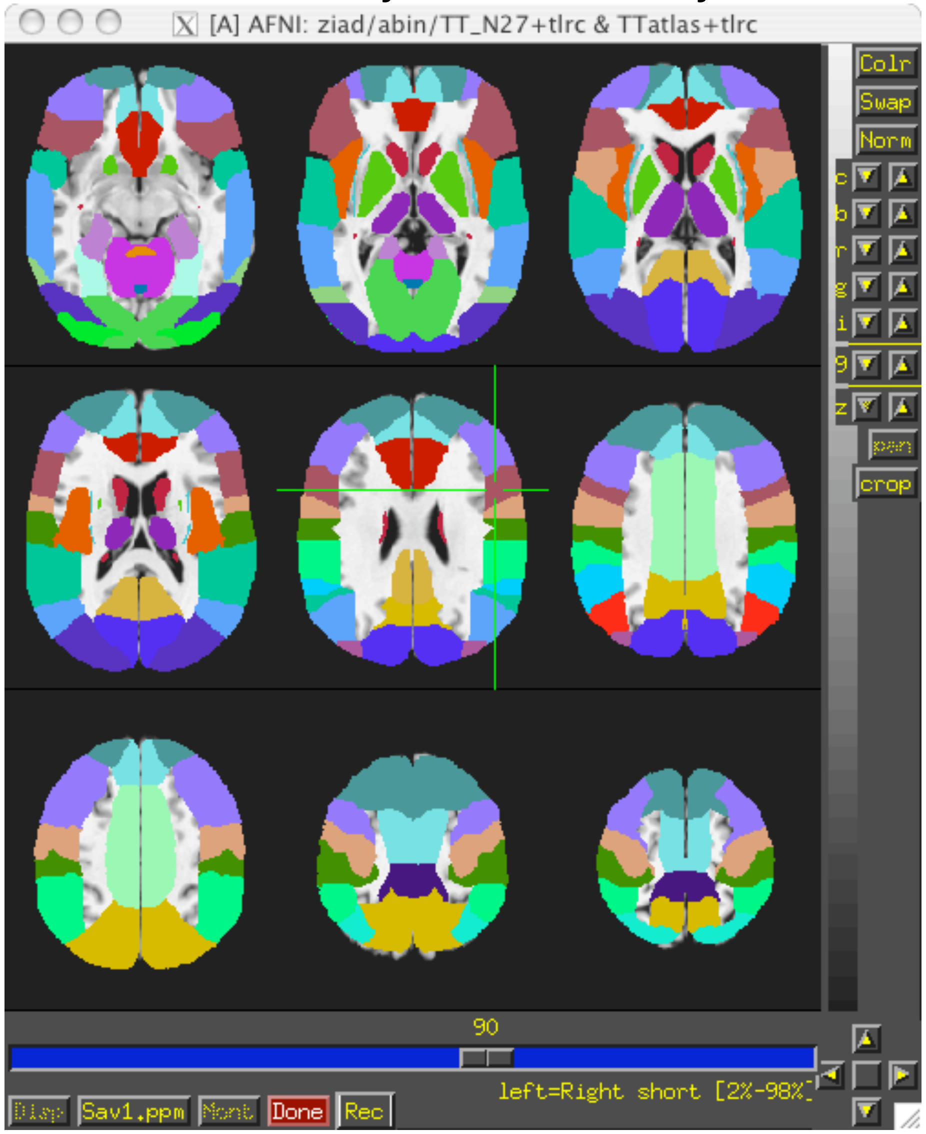
- Going between TLRC and MNI:
  - ✧ Approximate equation
    - ➥ used by **`whereami`** and **`adwarp`**
  - ✧ Manual TLRC transformation of MNI template to TLRC space
    - ➥ used by **`whereami`** (as precursor to MNI Anat.), based on N27 template
  - ✧ Automated registration of a any dataset from one space to the other
- Going between MNI and MNI Anatomical (Eickhoff et al. Neuroimage 25, 2005):
  - ✧ MNI + (0, 4, 5) = MNI Anat. (in RAI coordinate system)
- Going between TLRC and MNI Anatomical (as practiced in **`whereami`**):
  - ✧ Go from TLRC to MNI via manual xform of N27 template
  - ✧ Add (0, 4, 5)

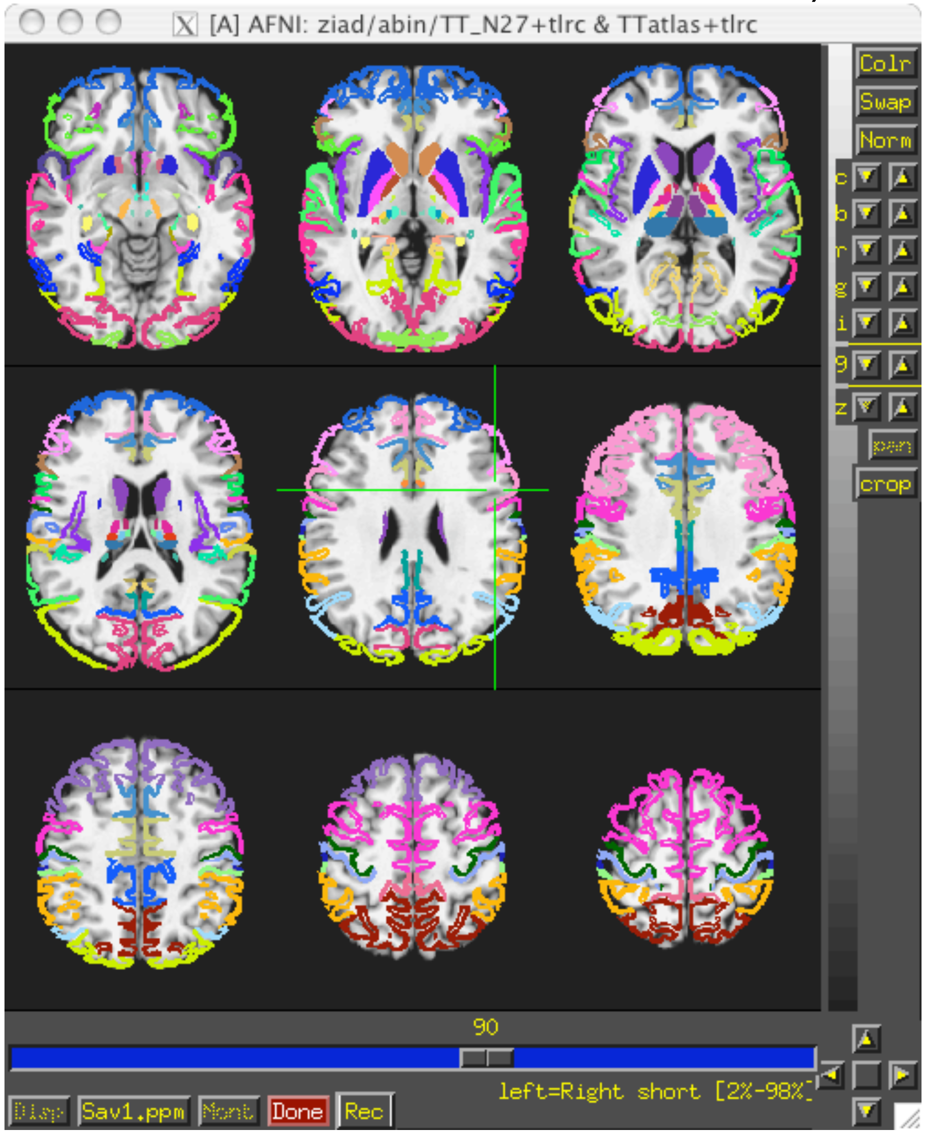
Atlases/Templates Use Different Coord. Systems

- There are 48 manners to specify XYZ coordinates
- Two most common are RAI/DICOM and LPI/SPM
- RAI means
  - ✧ X is Right-to-Left (from negative-to-positive)
  - ✧ Y is Anterior-to-Posterior (from negative-to-positive)
  - ✧ Z is Inferior-to-Superior (from negative-to-positive)
- LPI means
  - ✧ X is Left-to-Right (from negative-to-positive)
  - ✧ Y is Posterior-to-Inferior (from negative-to-positive)
  - ✧ Z is Inferior-to-Superior (from negative-to-positive)
- To go from RAI to LPI just flip the sign of the X and Y coordinates
  - ✧ Voxel -12, 24, 16 in RAI is the same as 12, -24, 16 in LPI
  - ✧ Voxel above would be in the Right, Posterior, Superior octant of the brain
- AFNI allows for all coordinate systems but default is RAI
  - ✧ Can use environment variable AFNI_ORIENT to change the default for AFNI *AND* other programs.
  - ✧ See **`whereami -help`** for more details.

Atlases Distributed With AFNI TT_Daemon

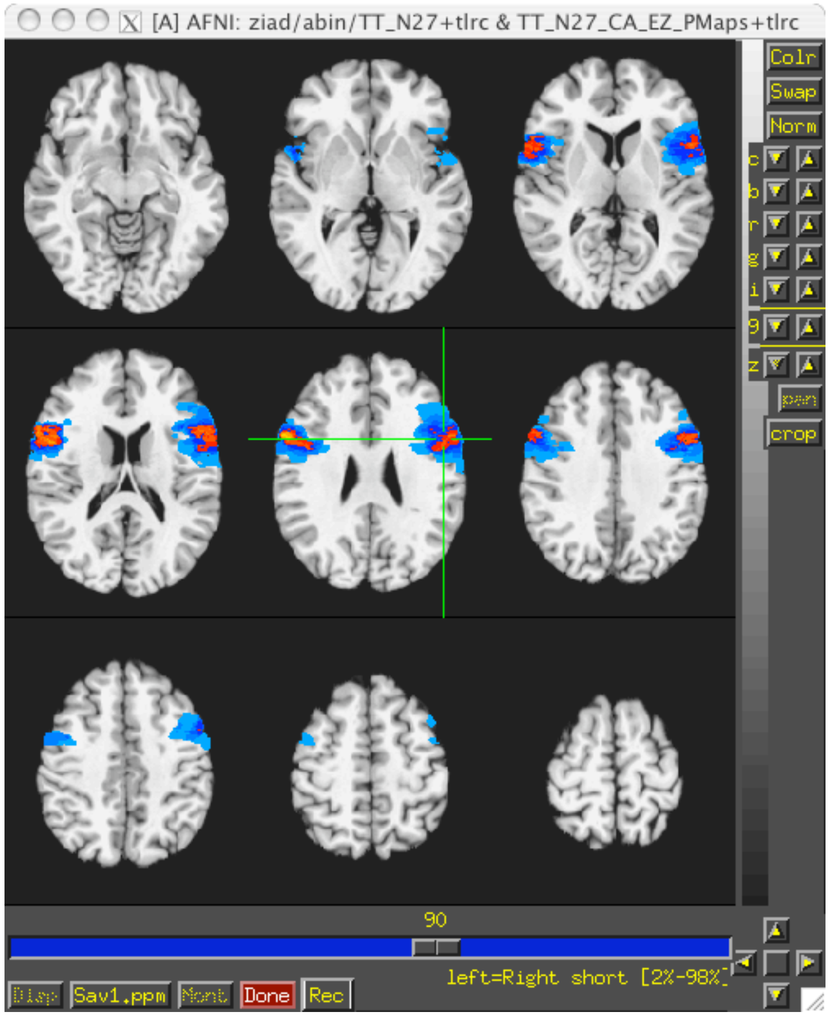
- TT_Daemon : Created by tracing Talairach and Tournoux brain illustrations.
    - ✧ Generously contributed by Jack Lancaster and Peter Fox of RIC UTHSCSA)

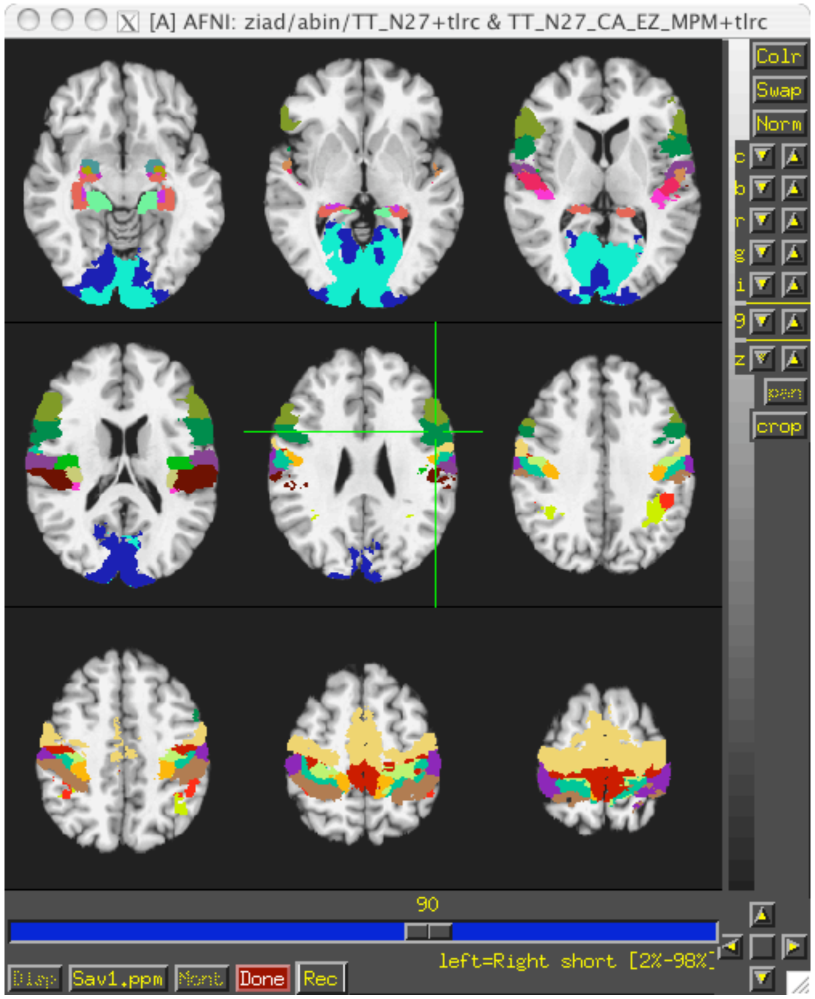

[A] AFNI: ziad/abin/TT_N27+tlrc & TTatlas+tlrc
Colr
Swap
Norm
crop
90
left=Right short [2%-98%]
Sav1.ppm
Done
Rec


[A] AFNI: ziad/abin/TT_N27+tlrc & TTatlas+tlrc
Colr
Swap
Norm
crop
90
left=Right short [2%-98%]
Sav1.ppm
Done
Rec

Atlases Distributed With AFNI
Anatomy Toolbox: Prob. Maps, Max. Prob. Maps

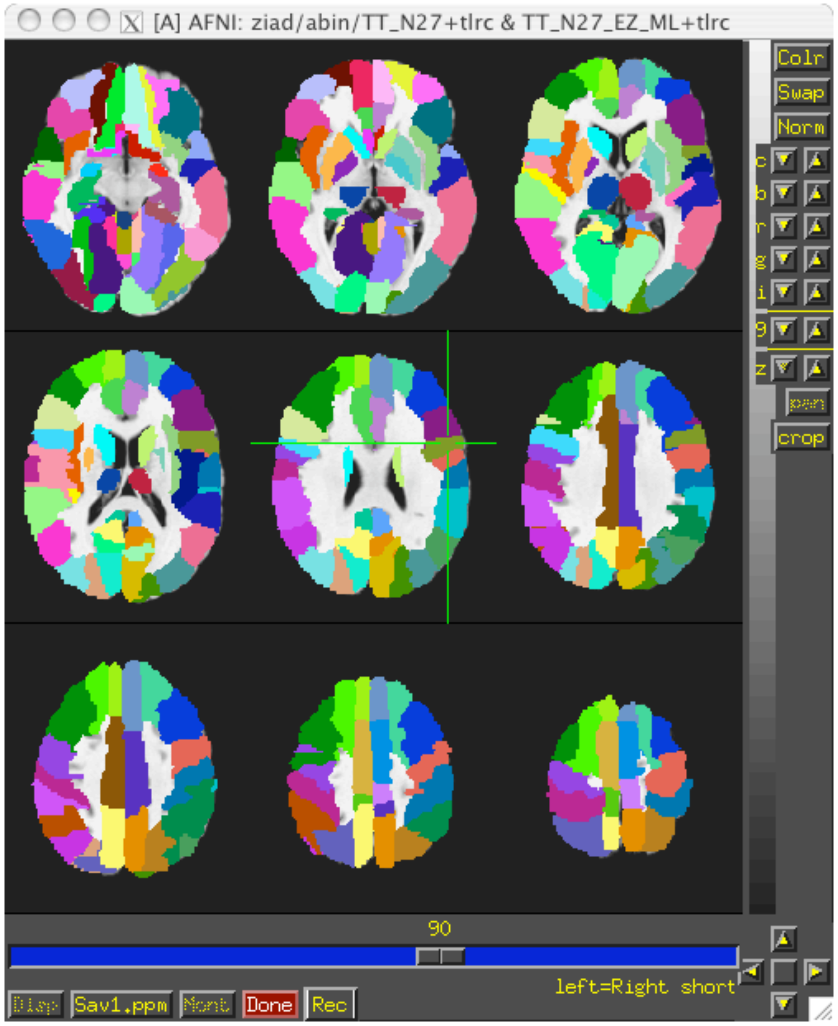
- CA_N27_MPM, CA_N27_ML, CA_N27_PM: Anatomy Toolbox's atlases with some created from cytoarchitectonic studies of 10 human post-mortem brains
  - ✧ Generously contributed by Simon Eickhoff, Katrin Amunts and Karl Zilles of IME, Julich, Germany

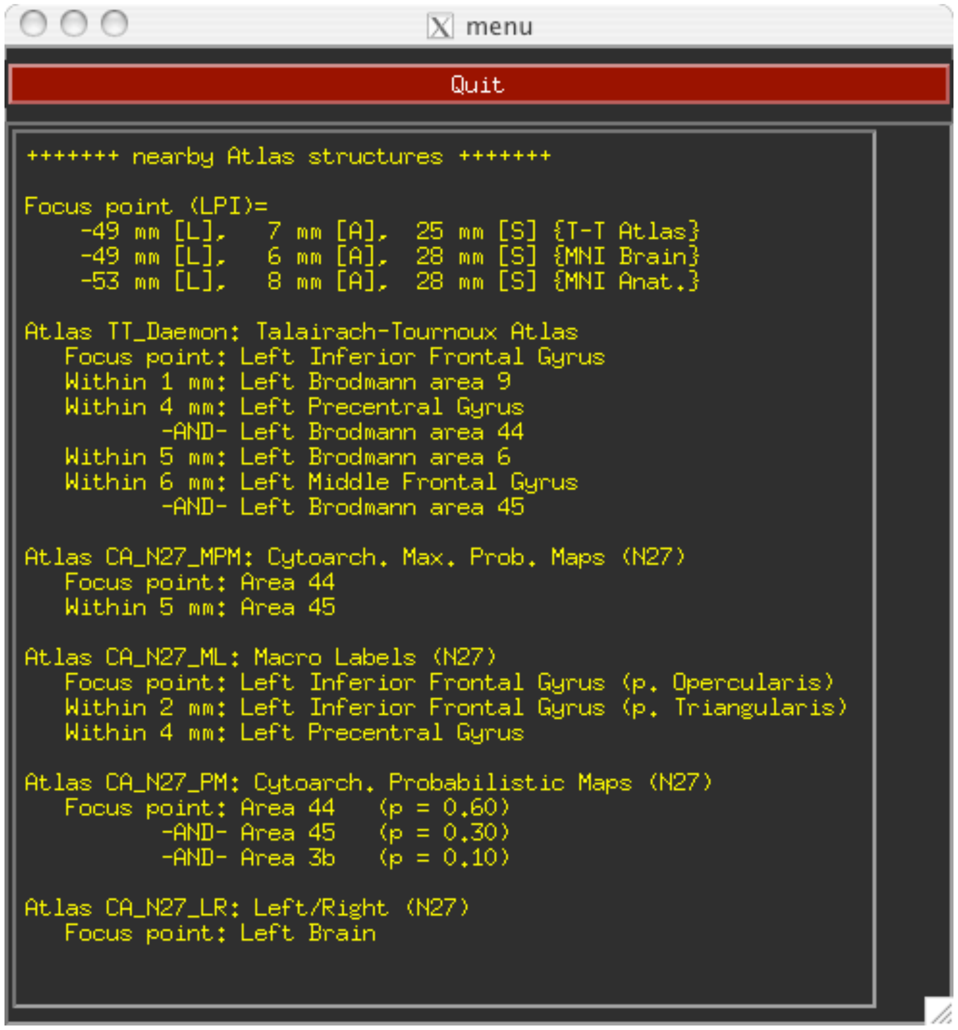

[A] AFNI: ziad/abin/TT_N27+tlrc & TT_N27_CA_EZ_PMaps+tlrc
Colr
Swap
Norm
crop
90
left=Right short [2%-98%]
Sav1.ppm
Done
Rec


[A] AFNI: ziad/abin/TT_N27+tlrc & TT_N27_CA_EZ_MPM+tlrc
Colr
Swap
Norm
crop
90
left=Right short [2%-98%]
Sav1.ppm
Done
Rec

Atlases Distributed With AFNI:
Anatomy Toolbox: MacroLabels

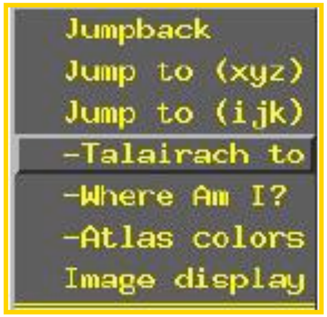
- CA_N27_MPM, CA_N27_ML, CA_N27_PM: Anatomy Toolbox's atlases with some created from cytoarchitectonic studies of 10 human post-mortem brains
  - ✧ Generously contributed by Simon Eickhoff, Katrin Amunts and Karl Zilles of IME, Julich, Germany



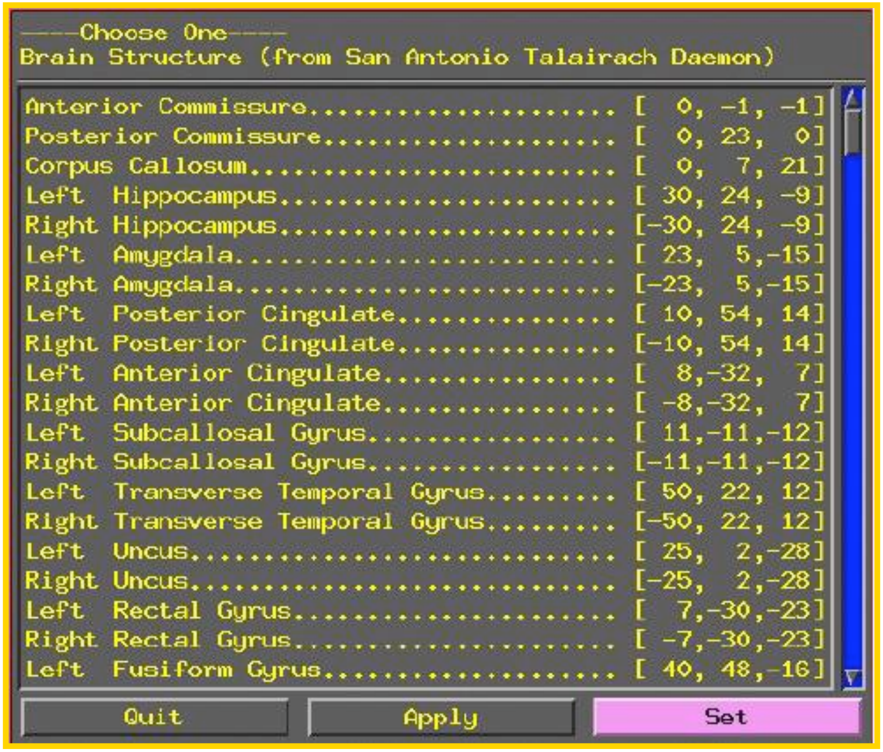


```
+++++++ nearby Atlas structures +++++++

Focus point (LPI)=
     -49 mm [L],   7 mm [A],  25 mm [S] {T-T Atlas}
     -49 mm [L],   6 mm [A],  28 mm [S] {MNI Brain}
     -53 mm [L],   8 mm [A],  28 mm [S] {MNI Anat.}

Atlas TT_Daemon: Talairach-Tournoux Atlas
   Focus point: Left Inferior Frontal Gyrus
   Within 1 mm: Left Brodmann area 9
   Within 4 mm: Left Precentral Gyrus
           -AND- Left Brodmann area 44
   Within 5 mm: Left Brodmann area 6
   Within 6 mm: Left Middle Frontal Gyrus
           -AND- Left Brodmann area 45

Atlas CA_N27_MPM: Cytoarch. Max. Prob. Maps (N27)
   Focus point: Area 44
   Within 5 mm: Area 45

Atlas CA_N27_ML: Macro Labels (N27)
   Focus point: Left Inferior Frontal Gyrus (p. Opercularis)
   Within 2 mm: Left Inferior Frontal Gyrus (p. Triangularis)
   Within 4 mm: Left Precentral Gyrus

Atlas CA_N27_PM: Cytoarch. Probabilistic Maps (N27)
   Focus point: Area 44   (p = 0.60)
           -AND- Area 45   (p = 0.30)
           -AND- Area 3b   (p = 0.10)

Atlas CA_N27_LR: Left/Right (N27)
   Focus point: Left Brain
```

- Some fun and useful things to do with `+tlrc` datasets are on the 2D slice viewer Buttton-3 pop-up menu:



✧ **[Talairach to]**



```
----Choose One----
Brain Structure (from San Antonio Talairach Daemon)

Anterior Commissure...................... [  0, -1, -1]
Posterior Commissure..................... [  0, 23,  0]
Corpus Callosum.......................... [  0,  7, 21]
Left  Hippocampus........................ [ 30, 24, -9]
Right Hippocampus........................ [-30, 24, -9]
Left  Amygdala........................... [ 23,  5,-15]
Right Amygdala........................... [-23,  5,-15]
Left  Posterior Cingulate................ [ 10, 54, 14]
Right Posterior Cingulate................ [-10, 54, 14]
Left  Anterior Cingulate................. [  8,-32,  7]
Right Anterior Cingulate................. [ -8,-32,  7]
Left  Subcallosal Gyrus.................. [ 11,-11,-12]
Right Subcallosal Gyrus.................. [-11,-11,-12]
Left  Transverse Temporal Gyrus.......... [ 50, 22, 12]
Right Transverse Temporal Gyrus.......... [-50, 22, 12]
Left  Uncus.............................. [ 25,  2,-28]
Right Uncus.............................. [-25,  2,-28]
Left  Rectal Gyrus....................... [  7,-30,-23]
Right Rectal Gyrus....................... [ -7,-30,-23]
Left  Fusiform Gyrus..................... [ 40, 48,-16]
```

Lets you jump to centroid of regions in the TT_Daemon Atlas (works in `+orig` too)

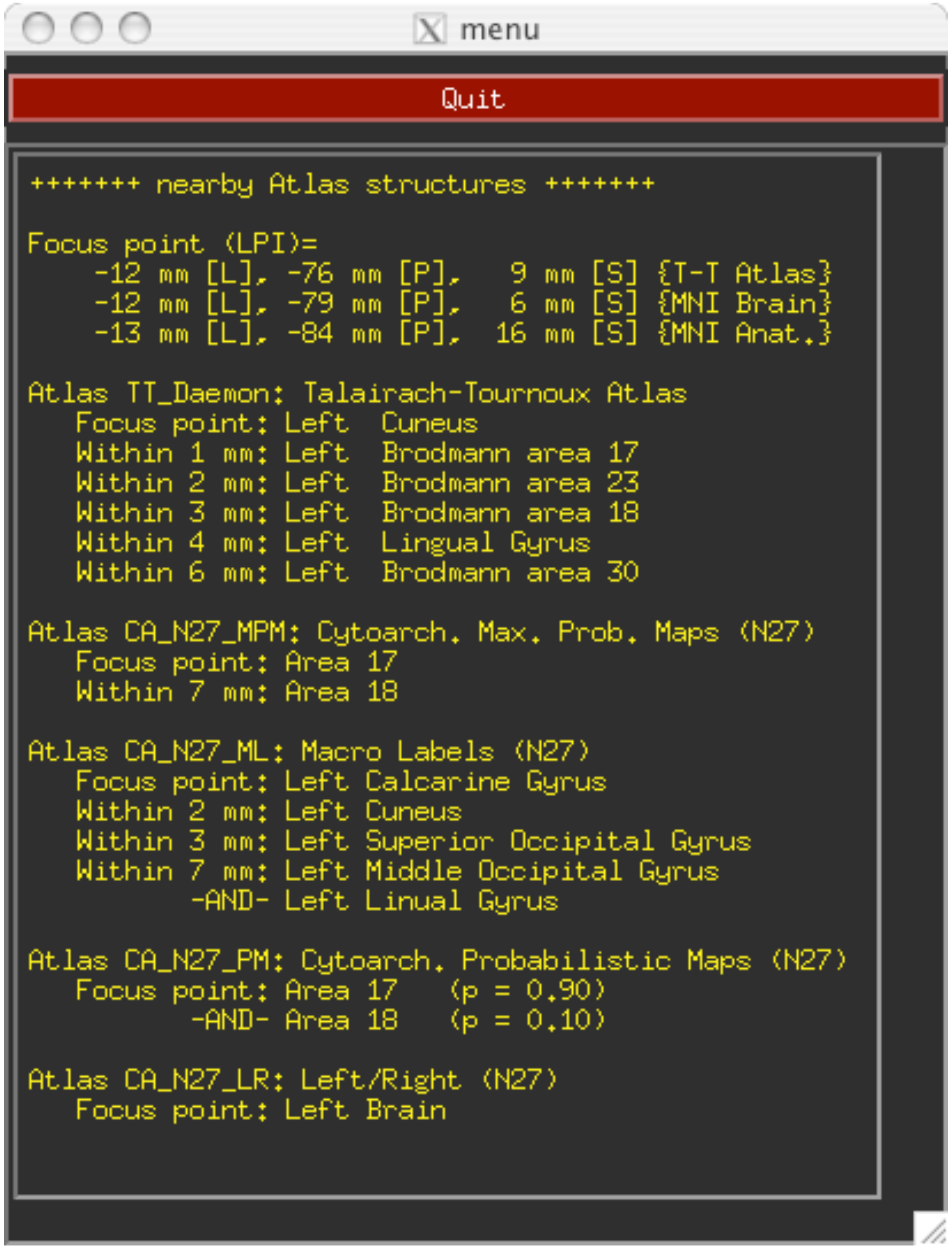
✧ **[Where am I?]**

Shows you where you are in various atlases.

(works in `+orig` too, if you have a TT transformed parent)

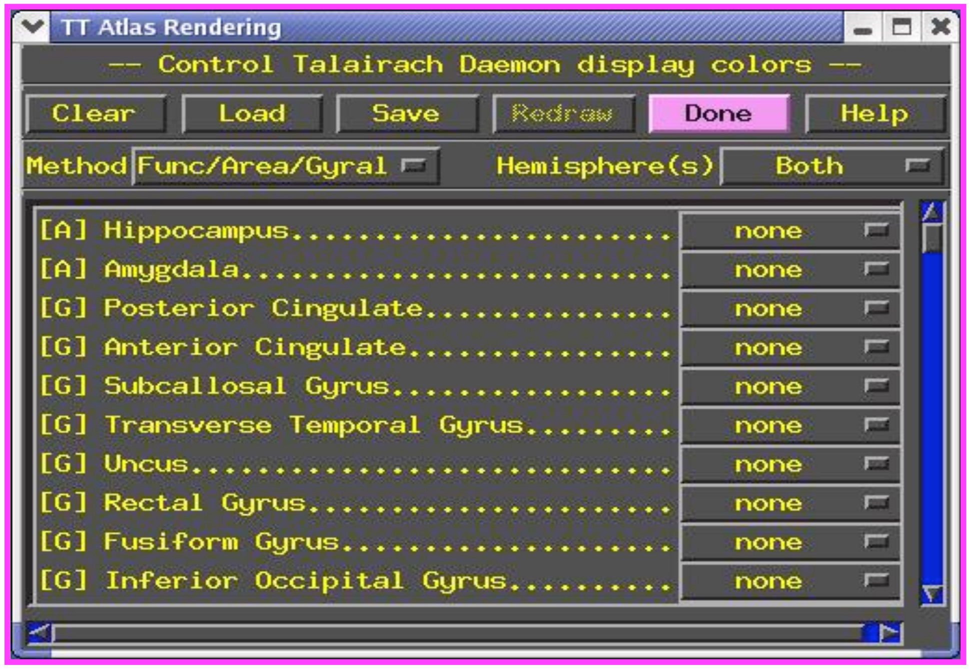
For atlas installation, and much much more, see help in command line version:

`whereami -help`



```
+++++++ nearby Atlas structures +++++++

Focus point (LPI)=
    -12 mm [L], -76 mm [P],   9 mm [S] {T-T Atlas}
    -12 mm [L], -79 mm [P],   6 mm [S] {MNI Brain}
    -13 mm [L], -84 mm [P],  16 mm [S] {MNI Anat.}

Atlas TT_Daemon: Talairach-Tournoux Atlas
   Focus point: Left  Cuneus
   Within 1 mm: Left  Brodmann area 17
   Within 2 mm: Left  Brodmann area 23
   Within 3 mm: Left  Brodmann area 18
   Within 4 mm: Left  Lingual Gyrus
   Within 6 mm: Left  Brodmann area 30

Atlas CA_N27_MPM: Cytoarch. Max. Prob. Maps (N27)
   Focus point: Area 17
   Within 7 mm: Area 18

Atlas CA_N27_ML: Macro Labels (N27)
   Focus point: Left Calcarine Gyrus
   Within 2 mm: Left Cuneus
   Within 3 mm: Left Superior Occipital Gyrus
   Within 7 mm: Left Middle Occipital Gyrus
          -AND- Left Linual Gyrus

Atlas CA_N27_PM: Cytoarch. Probabilistic Maps (N27)
   Focus point: Area 17   (p = 0.90)
          -AND- Area 18   (p = 0.10)

Atlas CA_N27_LR: Left/Right (N27)
   Focus point: Left Brain
```

✧ **[Atlas colors]**



TT Atlas Rendering

-- Control Talairach Daemon display colors --

Clear | Load | Save | Redraw | Done | Help

Method: Func/Area/Gyral   Hemisphere(s): Both

```
[A] Hippocampus......................... none
[A] Amygdala............................ none
[G] Posterior Cingulate................. none
[G] Anterior Cingulate.................. none
[G] Subcallosal Gyrus................... none
[G] Transverse Temporal Gyrus........... none
[G] Uncus............................... none
[G] Rectal Gyrus........................ none
[G] Fusiform Gyrus...................... none
[G] Inferior Occipital Gyrus............ none
```

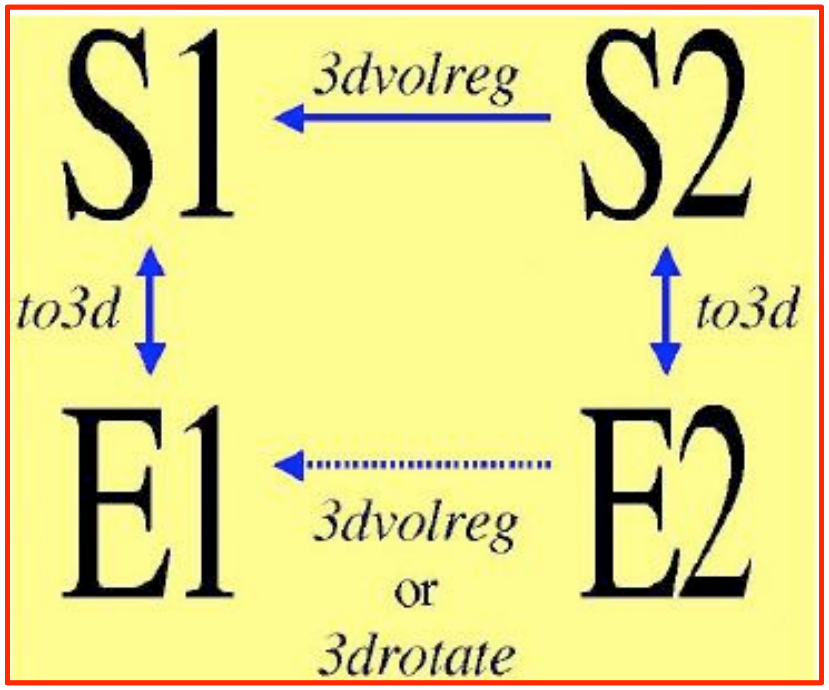
Lets you display color overlays for various TT_Daeomon Atlas-defined regions, using the Define Function See TT_Daemon Atlas Regions control (works only in `+tlrc`)

For the moment, atlas colors work for TT_Daemon atlas only. There are ways to display other atlases. See **`whereami -help`**.

Appendix A

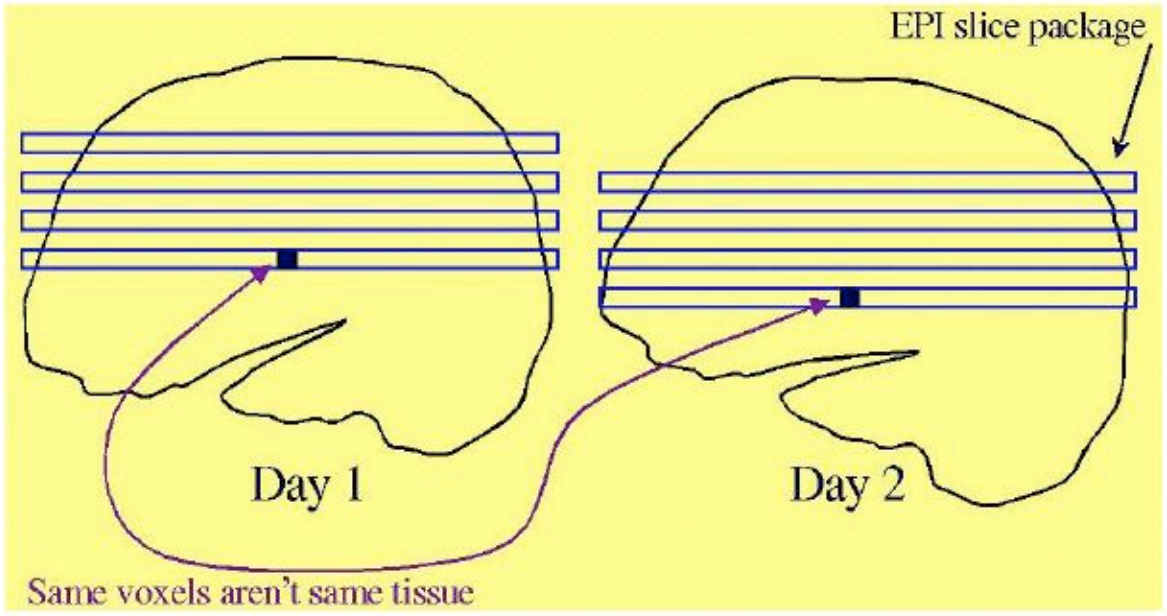
Inter-subject, inter-session registration

- Intra-subject, inter-session registration (for multi-day studies on same subject)
  - ✧ Longitudinal or learning studies; re-use of cortical surface models
  - ✧ Transformation between sessions is calculated by registering high-resolution anatomicals from each session
    - ➥ **`to3d`** defines defines relationship between EPI and SPGR in each session
    - ➥ **`3dvolreg`** computes relationship between sessions
    - ➥ So can transform EPI from session 2 to orientation of session 1

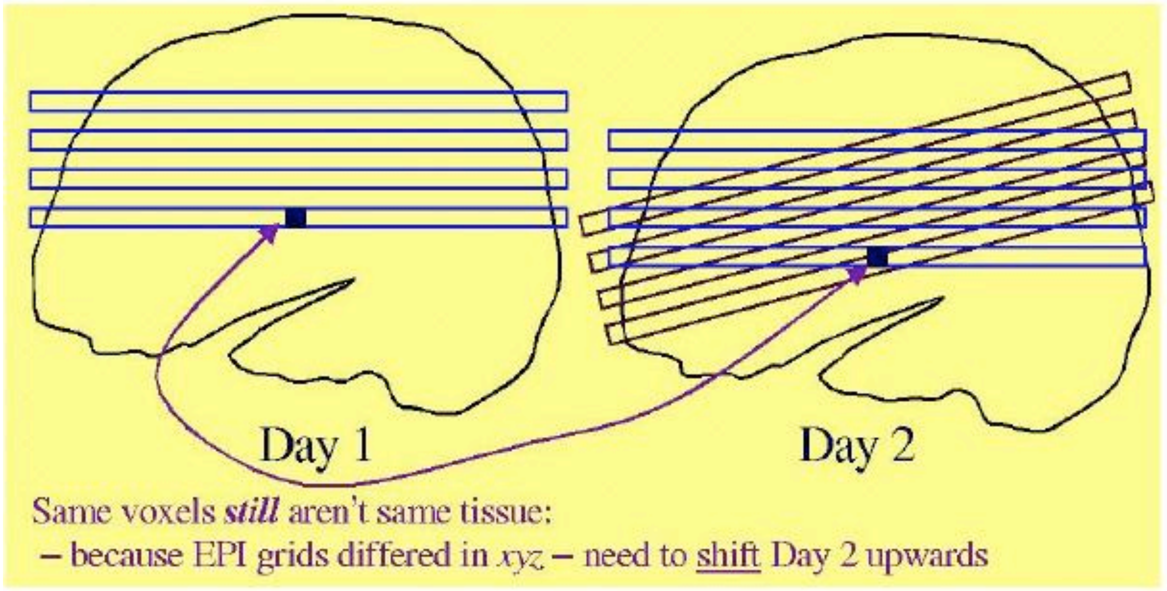


  - ✧ Issues in inter-session registration:
    - ➥ Subject's head will be positioned differently (in orientation and location)
      - ➪ xyz-coordinates and anatomy don't correspond
    - ➥ Anatomical coverage of EPI slices will differ between sessions
    - ➥ Geometrical relation between EPI and SPGR differs between session
    - ➥ Slice thickness may vary between sessions (try not to do this, OK?)

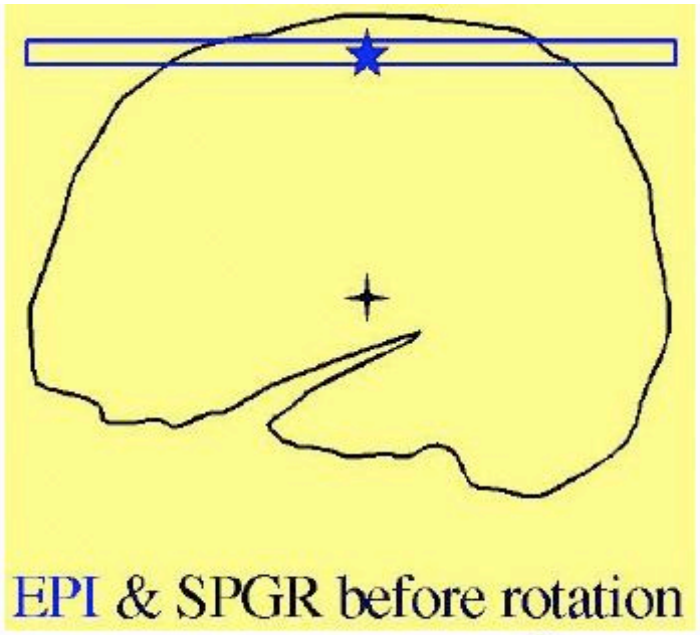
- Anatomical coverage differs



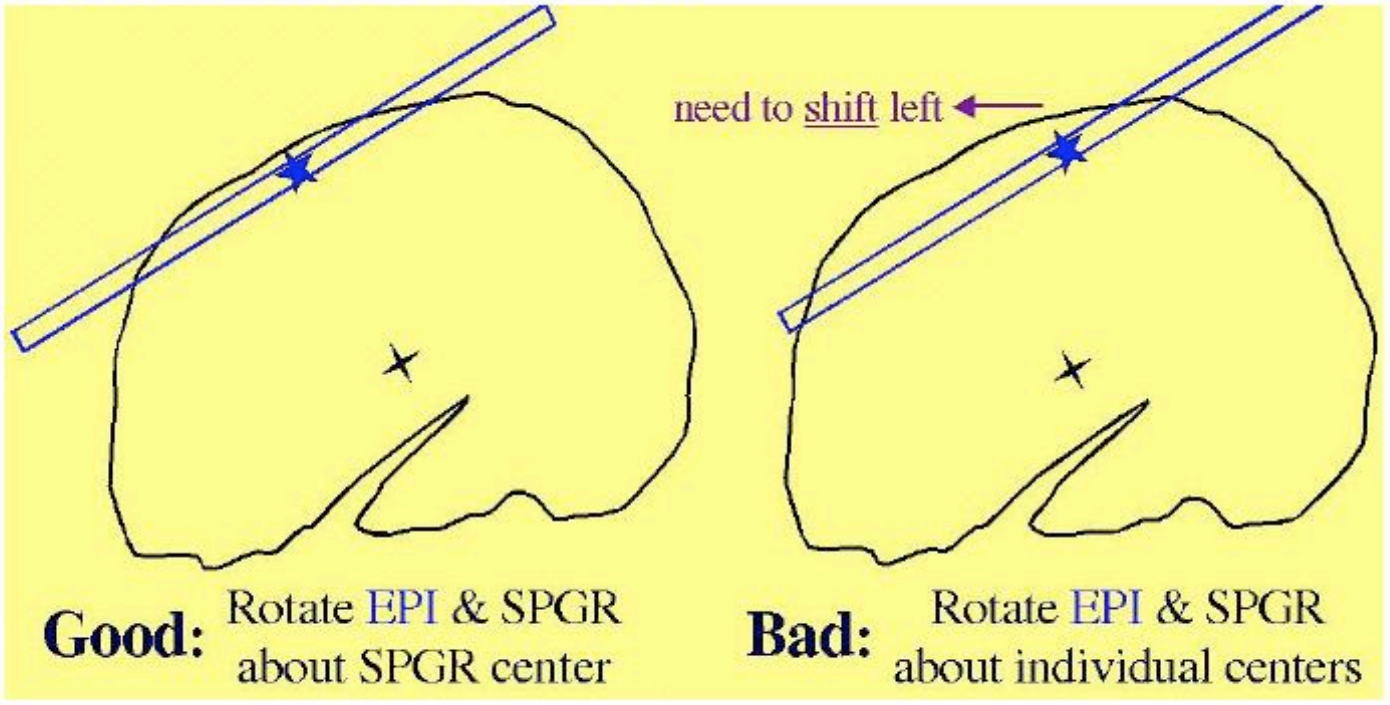
✧ At acquisition:
Day 2 is rotated relative to Day 1


Day 1
Day 2
Same voxels *still* aren't same tissue:
– because EPI grids differed in *xyz* – need to shift Day 2 upwards

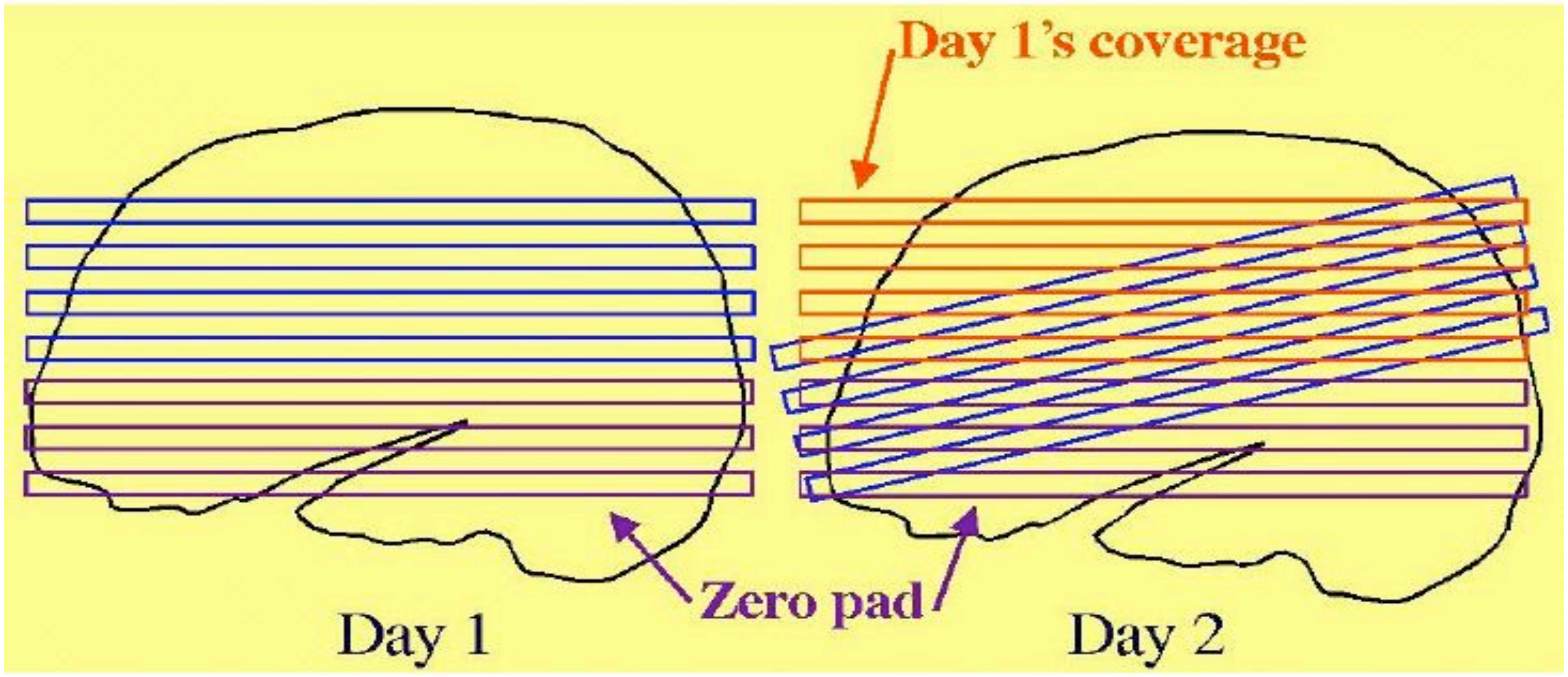
✧ After rotation to same orientation, then clipping to Day 2 xyz-grid



- ✧ Another problem: rotation occurs around center of individual datasets


need to shift left
Good: Rotate EPI & SPGR about SPGR center
Bad: Rotate EPI & SPGR about individual centers

- Solutions to these problems:
  - Add appropriate shift to E2 on top of rotation
    - Allow for xyz shifts between days (E1-E2), and center shifts between EPI and SPGR (E1-S1 and E2-S2)
  - Pad EPI datasets with extra slices of zeros so that aligned datasets can fully contain all data from all sessions
  - Zero padding of a dataset can be done in **`to3d`** (at dataset creation time), or later using **`3dZeropad`**
  - **`3dvolreg`** and **`3drotate`** can zero pad to make the output match a "grid parent" dataset in size and location



- Recipe for intra-subject S2-to-S1 transformation:
  1. Compute S2-to-S1 transformation:

```
3dvolreg -twopass -zpad 4 -base S1+orig \
         -prefix S2reg  S2+orig
```

• **-twopass** allows for larger motions

  - Rotation/shift parameters are saved in **S2reg+orig.HEAD**

  2. If not done before (e.g., in **to3d**), zero pad E1 datasets:

```
3dZeropad -z 4 -prefix E1pad  E1+orig
```

  3. Register E1 datasets within the session:

```
3dvolreg -base 'E1pad+orig[4]' -prefix E1reg \
         E1pad+orig
```

  4. Register E2 datasets within the session, at the same time executing larger rotation/shift to session 1 coordinates that were saved in **S2reg+orig.HEAD**:

```
3dvolreg -base 'E2+orig[4]' \
  -rotparent S2reg+orig     \
  -gridparent E1reg+orig    \
  -prefix E2reg  E2reg+orig
```

• These options put the aligned
• **E2reg** into the same coordinates and grid as **E1reg**

  - **-rotparent** tells where the inter-session transformation comes from
  - **-gridparent** defines the output grid location/size of new dataset
    - Output dataset will be shifted and zero padded as needed to lie on top of **E1reg+orig**

- ✧ Recipe above does not address problem of having different slice thickness in datasets of the same type (EPI and/or SPGR) in different sessions
  - ➥ Best solution: pay attention when you are scanning, and always use the same slice thickness for the same type of image
  - ➥ OK solution: use **`3dZregrid`** to linearly interpolate datasets to a new slice thickness
- ✧ Recipe above does not address issues of slice-dependent time offsets stored in data header from **`to3d`** (e.g., '**`alt+z`**')
  - ➥ After interpolation to a rotated grid, voxel values can no longer be said to come from a particular time offset, since data from different slices will have been combined
  - ➥ Before doing this spatial interpolation, it makes sense to time-shift dataset to a common temporal origin
  - ➥ Time shifting can be done with program **`3dTshift`**
    - ➩ Or by using the **`-tshift`** option in **`3dvolreg`**, which first does the time shift to a common temporal origin, then does the 3D spatial registration

- Further reading at the AFNI web site
  - ✧ File **README.registration** (plain text) has more detailed instructions and explanations about usage of **`3dvolreg`**
  - ✧ File **regnotes.pdf** has some background information on issues and methods used in FMRI registration packages

Appendix B

3dAllineate for the curious

3dAllineate: More than you want to know

Algorithmic Features

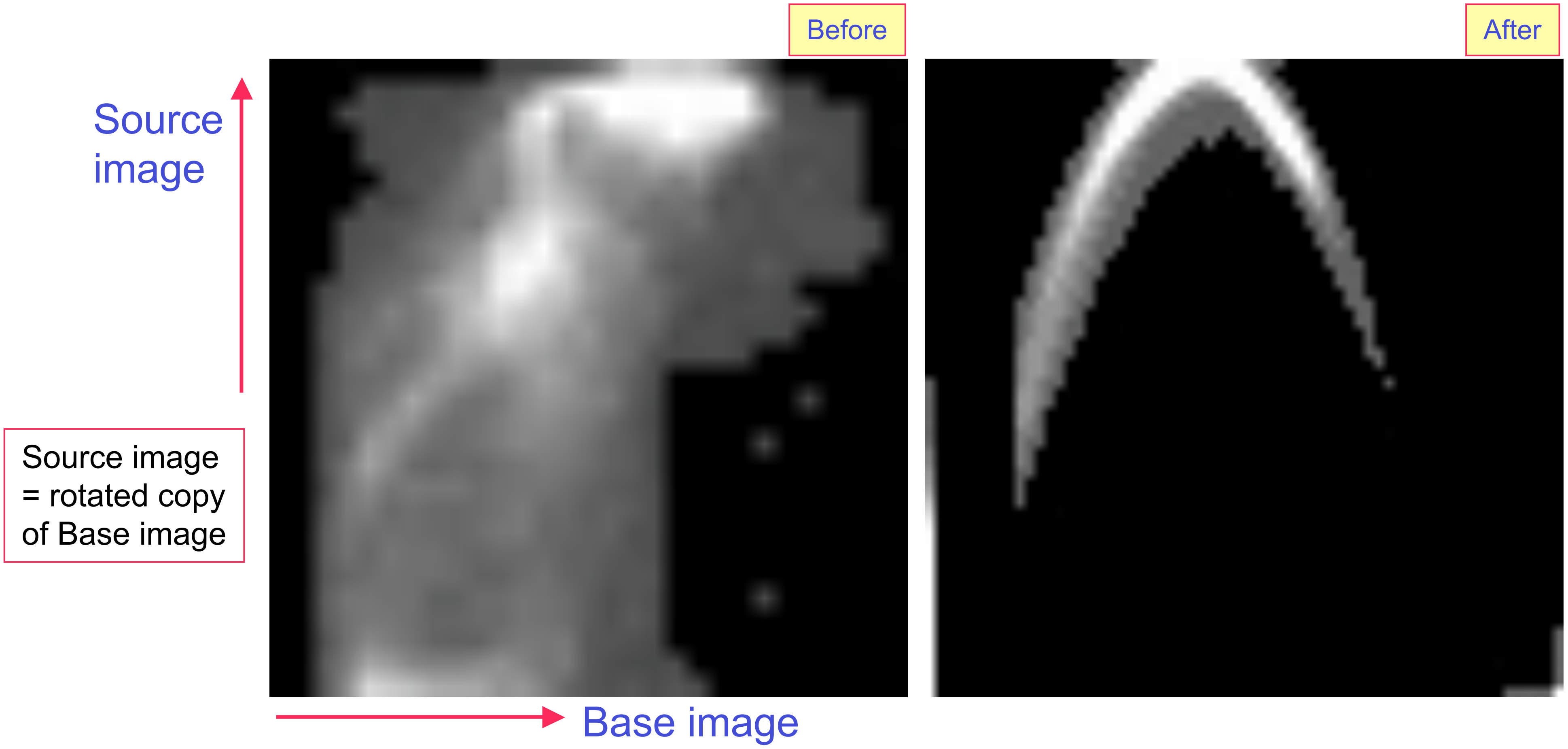
- Uses Powell's NEWUOA software for minimization of general cost function
- Lengthy search for initial transform parameters if two passes of registration are turned on [which is the default]
  - ✧ Random and grid search through hundreds of parameter sets for 15 good (low cost) parameter sets
  - ✧ Optimize a little bit from each 'good' set, using blurred images
    - ➥ Blurring the images means that small details won't prevent a match
  - ✧ Keep best 4 of these parameter sets, and optimize them some more [keeping 4 sets is the default for `-twobest` option]
    - ➥ Amount of blurring is reduced in several stages, followed by re-optimization of the transformation parameter sets on these less blurred images
    - ➥ `-twofirst` does this for first sub-brick, then uses the best parameter sets from the first sub-brick as the starting point for the rest of the sub-bricks [the default]
  - ✧ Use best 1 of these parameter sets as starting point for fine (un-blurred) parameter optimization
    - ➥ The slowest part of the program

Algorithmic Features

- Goal is to find parameter set **w** such that **E**[**J**(**x**) , **I**(**T**(**x**,**w**))] is small
  - **T**(**x**,**w**) = spatial transformation of **x** given **w**
  - **J**() = base image, **I**() = target image, **E**[ ] = cost function
- For each **x** in base image space, compute **T**(**x**,**w**) and then interpolate **I**() at those points
  - For speed, program doesn't use all points in **J**(), just a scattered collection of them, selected from an automatically generated mask
    - Mask can be turned off with `-noauto` option
    - At early stages, only a small collection of points [default=23456] is used when computing **E**[ ]
    - At later stages, more points are used, for higher accuracy
      - Recall that each stage is less blurred than the previous stages
  - Large fraction of CPU time is spent in interpolation of image **I**() over the collection of points used to compute **E**[ ]

Cost Functions

- Except for least squares (actually, `ls` minimizes $\mathbf{E} = 1.0 -$ Pearson correlation coefficient), all cost functions are computed from 2D joint histogram of $\mathbf{J}(\mathbf{x})$ and $\mathbf{I}(\mathbf{T}(\mathbf{x},\mathbf{w}))$
  - ✧ Start and final histograms can be saved using hidden option `-savehist`



Histogram Based Cost Functions

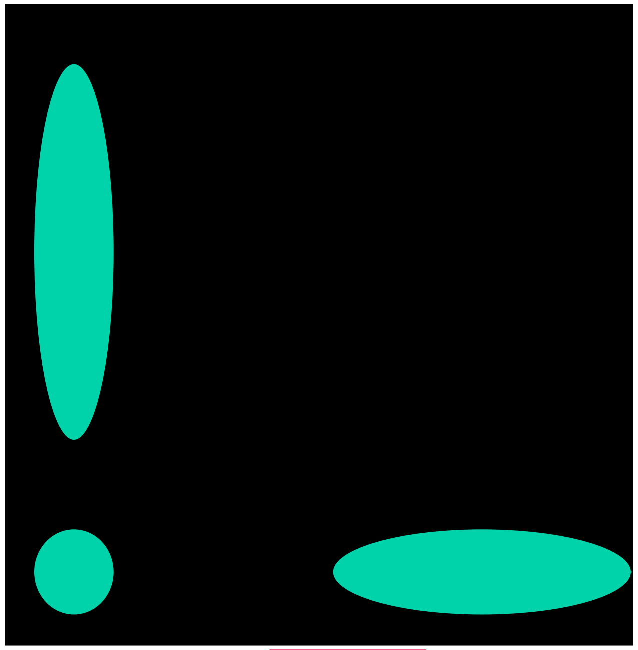
- Goal is to make 2D histogram become ‘simple’ in some sense, as a measurement of ‘predictability’ between $\mathbf{J}(\mathbf{x})$ and $\mathbf{I}(\mathbf{T}(\mathbf{x},\mathbf{w}))$
- Entropy H() of a histogram (finite number of bins):
  - ✧ $\{p_i\}$ = probabilities of index i occuring
  - ✧ $H(\{p_i\}) = -\Sigma_i\, p_i \log_2(p_i) > 0$
  - ✧ $H(\{p_i\})$ = Number of bits needed to encode a single value randomly drawn from the probabilities $\{p_i\}$
  - ✧ Smaller entropy H means the values are ‘simpler’ to encode
    - ➥ Largest H is for uniform histogram (all p_i equal)

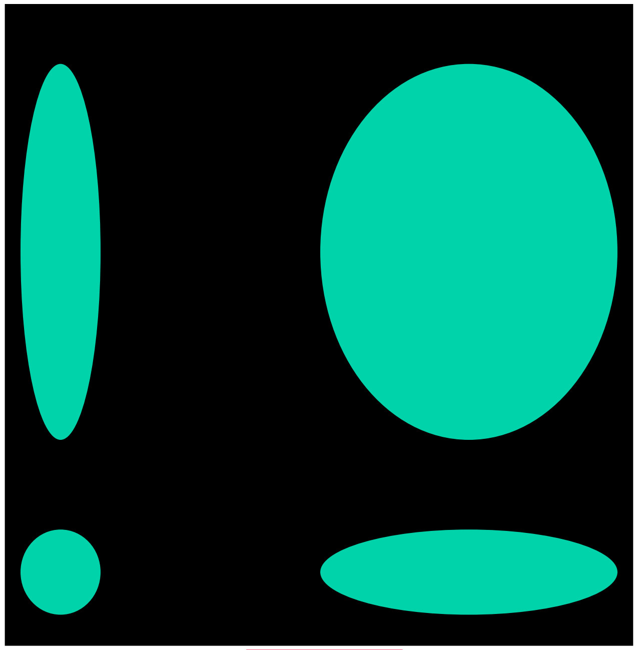
Mutual Information

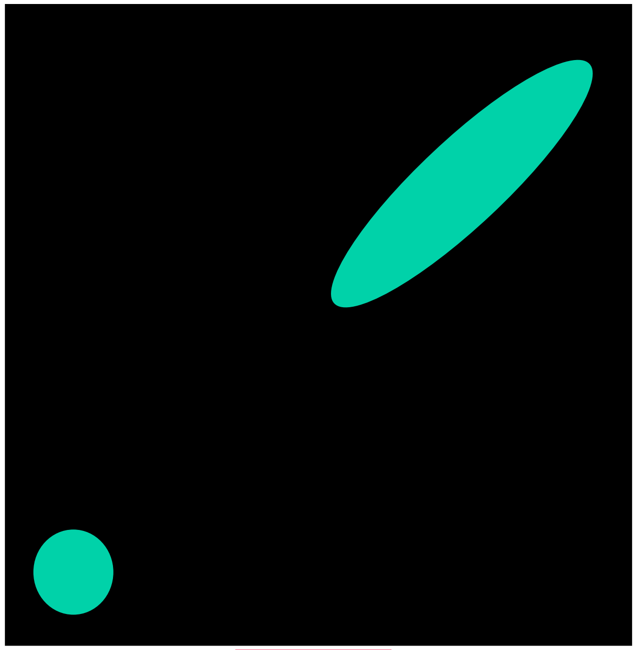
- Entropy of 2D histogram
  - ✧ $H(\{r_{ij}\}) = -S_{ij}\ r_{ij} \log_2(r_{ij})$
  - ✧ Number of bits needed to encode value <u>pairs</u> (i,j)
- **M**utual **I**nformation between two distributions
  - ✧ Marginal (1D) histograms $\{p_i\}$ and $\{q_j\}$
  - ✧ $MI = H(\{p_i\}) + H(\{q_j\}) - H(\{r_{ij}\})$
  - ✧ Number of bits required to encode 2 values separately minus number of bits required to encode them together (as a pair)
  - ✧ If 2D histogram is independent ($r_{ij} = p_i \times q_j$) then MI = 0 = no gain from joint encoding
- `3dAllineate` minimizes **E**[**J**,**I**] = –MI(J,**I**) with `-cost mi`

Normalized MI

- NMI = $H(\{r_{ij}\}) \,/\, [\, H(\{p_i\}) + H(\{q_j\}) \,]$
  - ✧ Ratio of number of bits to encode value pair divided by number of bits to encode two values separately
  - ✧ Minimize NMI with `-cost nmi`
- Some say NMI is more robust for registration than MI, since MI can be large when there is no overlap between the two images

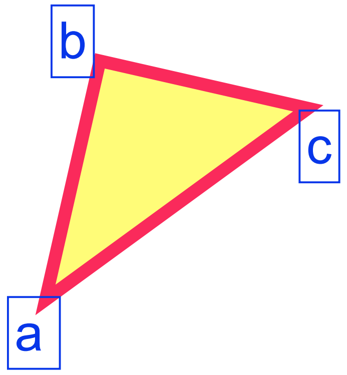

NO overlap


BAD overlap


100% overlap

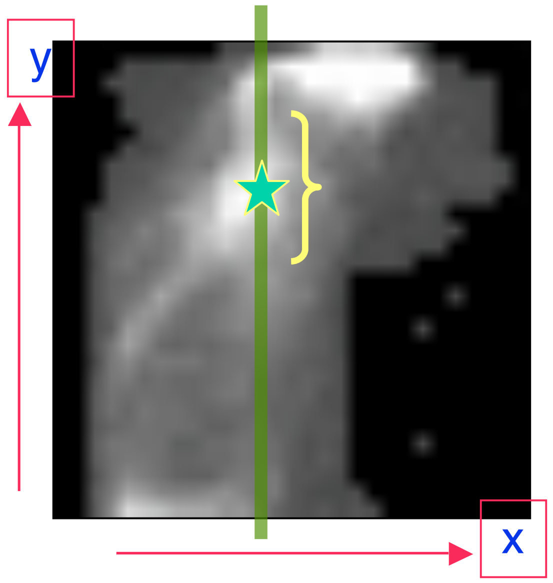
Hellinger Metric

- MI can be thought of as measuring a 'distance' between two 2D histograms: the joint distribution $\{r_{ij}\}$ and the product distribution $\{p_i \times q_j\}$
  - ✧ MI is not a 'true' distance: it doesn't satisfy triangle inequality d(a,b)+d(b,c) > d(a,c)
- Hellinger metric is a true distance in distribution "space":
  - ✧ $HM = \Sigma_{ij} [\sqrt{r_{ij}} - \sqrt{(p_i \times q_j)}]^2$
  - ✧ `3dAllineate` minimizes –HM with `-cost hel`
  - ✧ This is the default cost function



Correlation Ratio

- Given 2 (non-independent) random variables x and y
  - ✧ Exp[y|x] is the expected value (mean) of y for a fixed value of x
    - ➥ Exp[a|b] ≡ Average value of 'a', given value of 'b'
  - ✧ Var(y|x) is the variance of y when x is fixed = amount of uncertainty about value of y when we know x
    - ➥ v(x) ≡ Var(y|x) is a function of x only

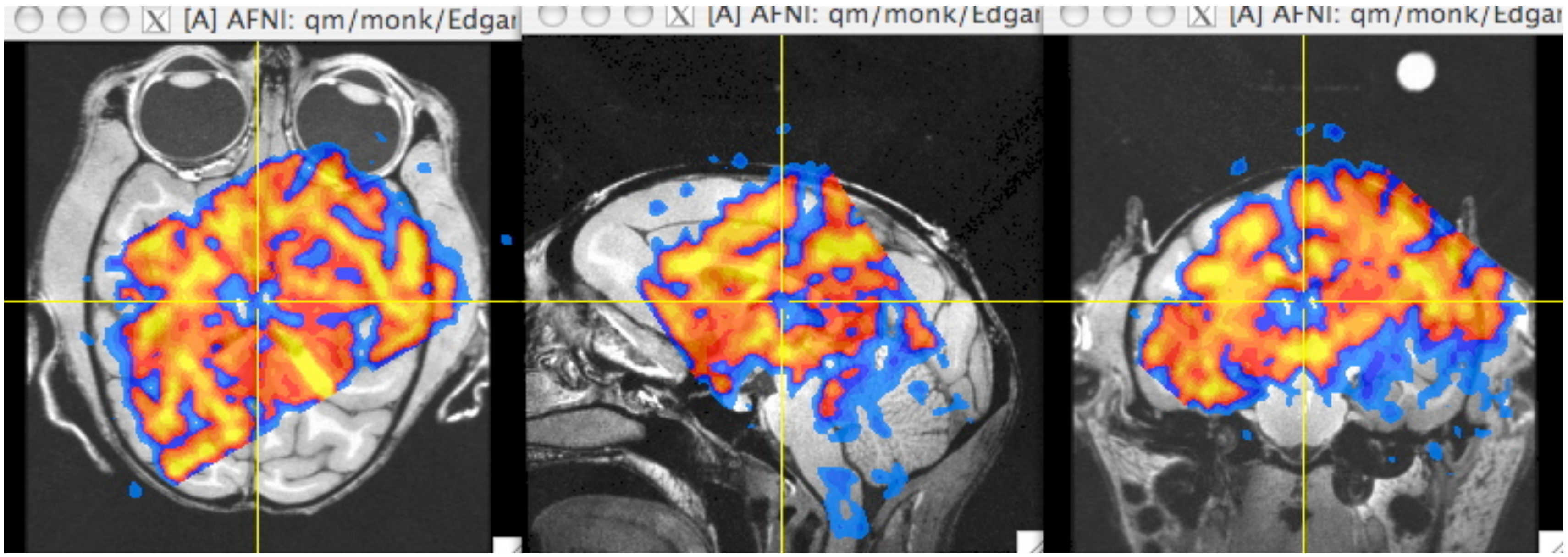


- CR(x,y) ≡ 1 – Exp[v(x)] ⁄ Var(y)
  - Relative reduction in uncertainty about value of y when x is known; large CR means Exp[y|x] is a good prediction of the value of y given the value of x
    - Does ***not*** say that Exp[x|y] is a good prediction of the x given y
  - CR(x,y) is a generalization of the Pearson correlation coefficient, which assumes that Exp[y|x] = $\alpha \cdot x + \beta$

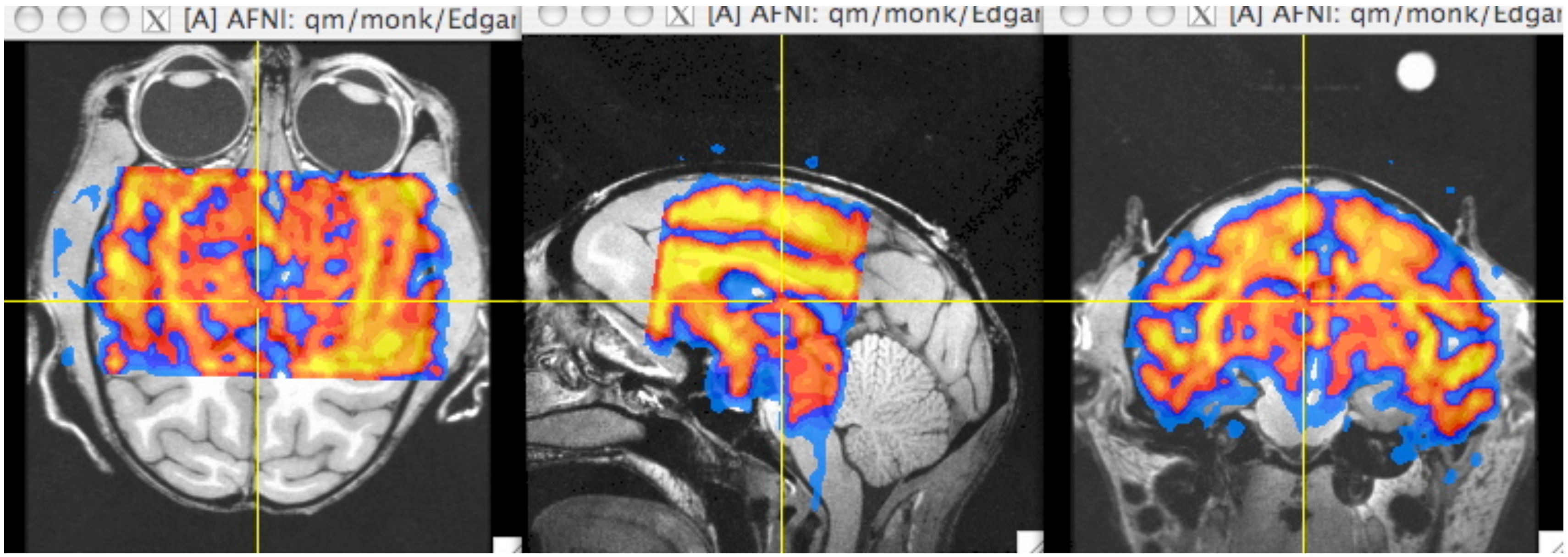
`3dAllineate`'s Symmetrical CR

- First attempt to use CR in `3dAllineate` didn't give good results
- Note asymmetry: CR(x,y) $\neq$ CR(y,x)
- `3dAllineate` now offers two different symmetric CR cost functions:
  - ✧ Compute both unsymmetric CR(x,y) and CR(y,x), then combine by Multiplying or Adding:
  - ✧ $\text{CRm}(x,y) = 1 - [\,\text{Exp}(v(x))\cdot\text{Exp}(v(y))\,] \,/\, [\,\text{Var}(y)\cdot\text{Var}(x)\,]$
    $= \text{CR}(x,y) + \text{CR}(y,x) - \text{CR}(x,y)\cdot\text{CR}(y,x)$
  - ✧ $\text{CRa}(x,y) = 1 - {}^1\!/_2\,[\,\text{Exp}(v(x)) \,/\, \text{Var}(y)\,] - {}^1\!/_2\,[\text{Exp}(v(y)) \,/\, \text{Var}(x)\,]$
    $= [\,\text{CR}(x,y) + \text{CR}(y,x)\,] \,/\, 2$
  - ✧ These work better than CR(**J**,**I**) in my test problems
- If Exp[y|x] can be used to predict y <u>and/or</u> Exp[x|y] can be used to predict x, then crM(x,y) will be large (close to 1)
- `3dAllineate` minimizes 1−CRm(**J**,**I**) with option `-cost crM`
- `3dAllineate` minimizes 1−CRa(**J**,**I**) with option `-cost crA`
- `3dAllineate` minimizes 1−CR(**J**,**I**) with option `-cost crU`

Test: Monkey EPI - Anat

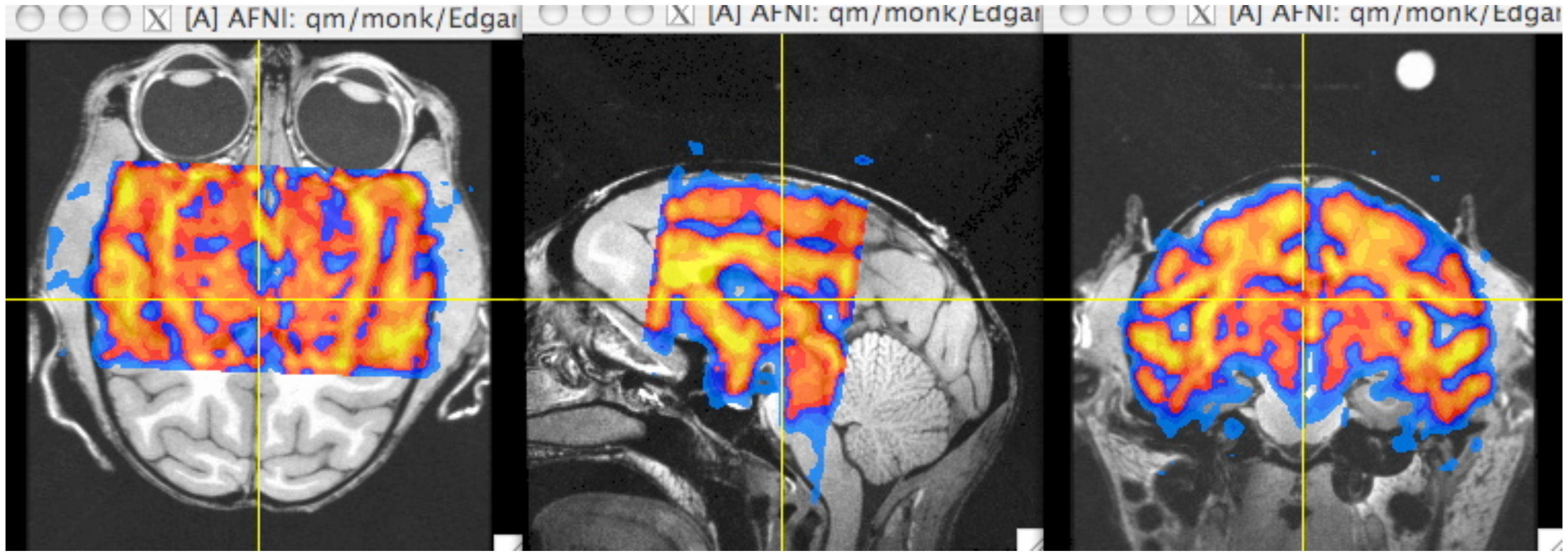


6 DOF
CRm

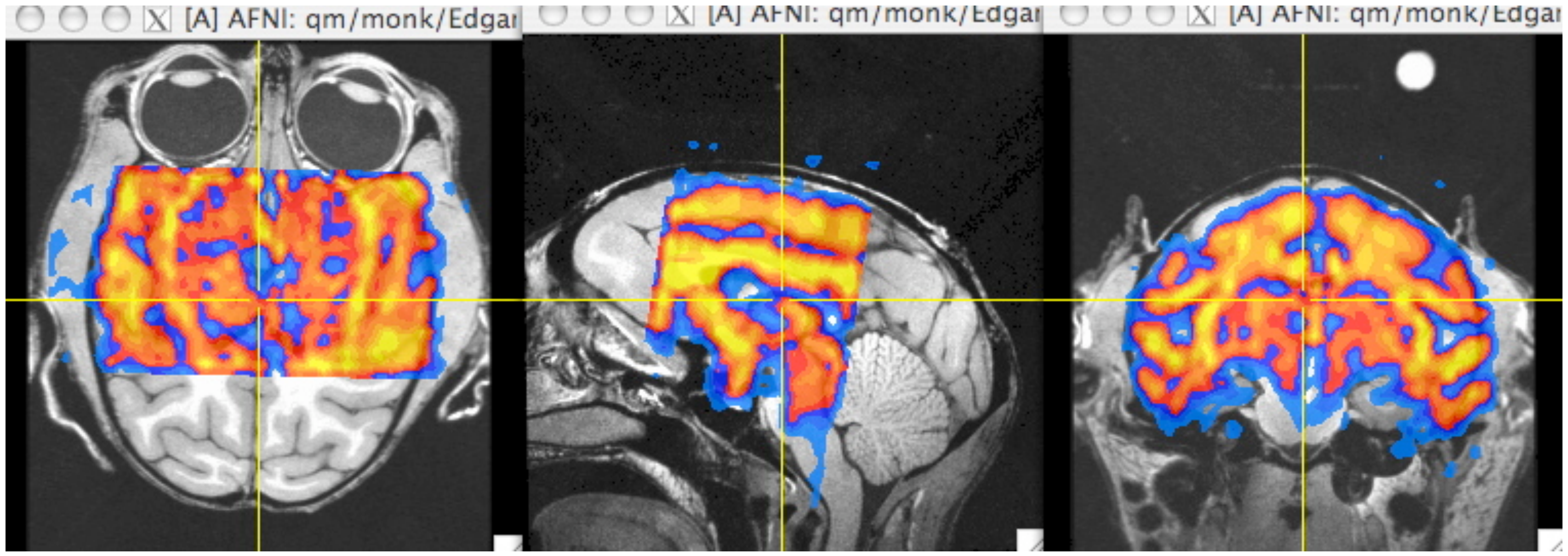


6 DOF
NMI

Test: Monkey EPI - Anat

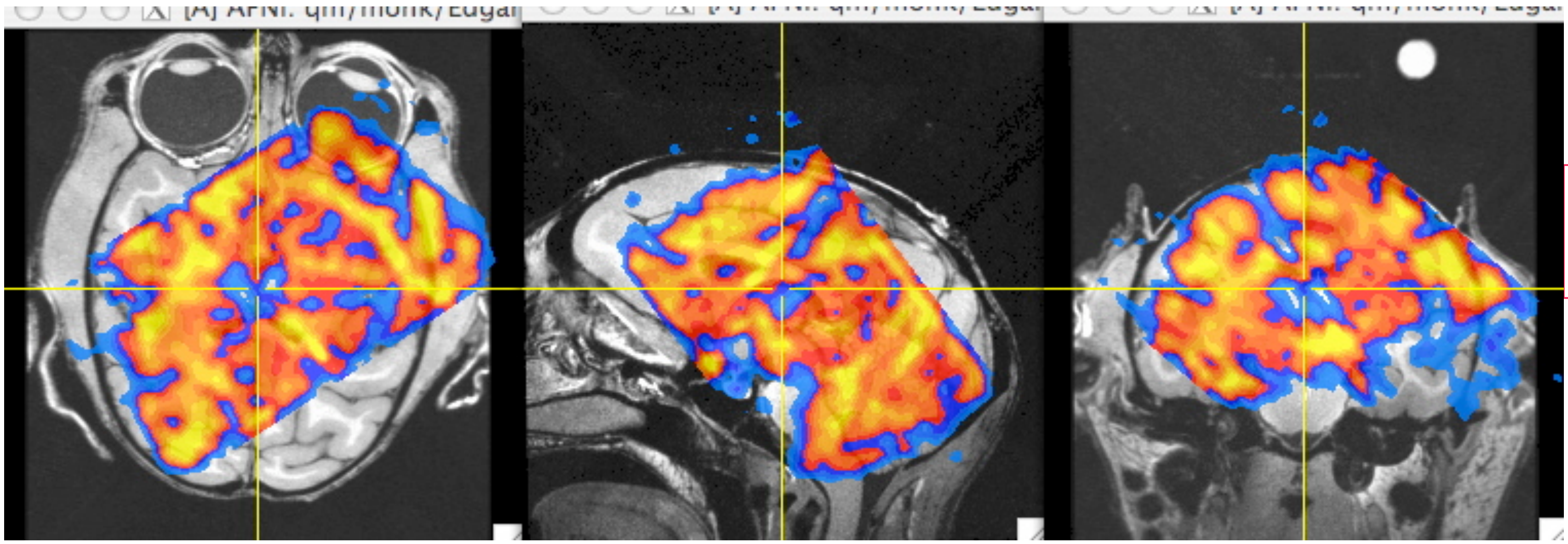


6 DOF
HEL

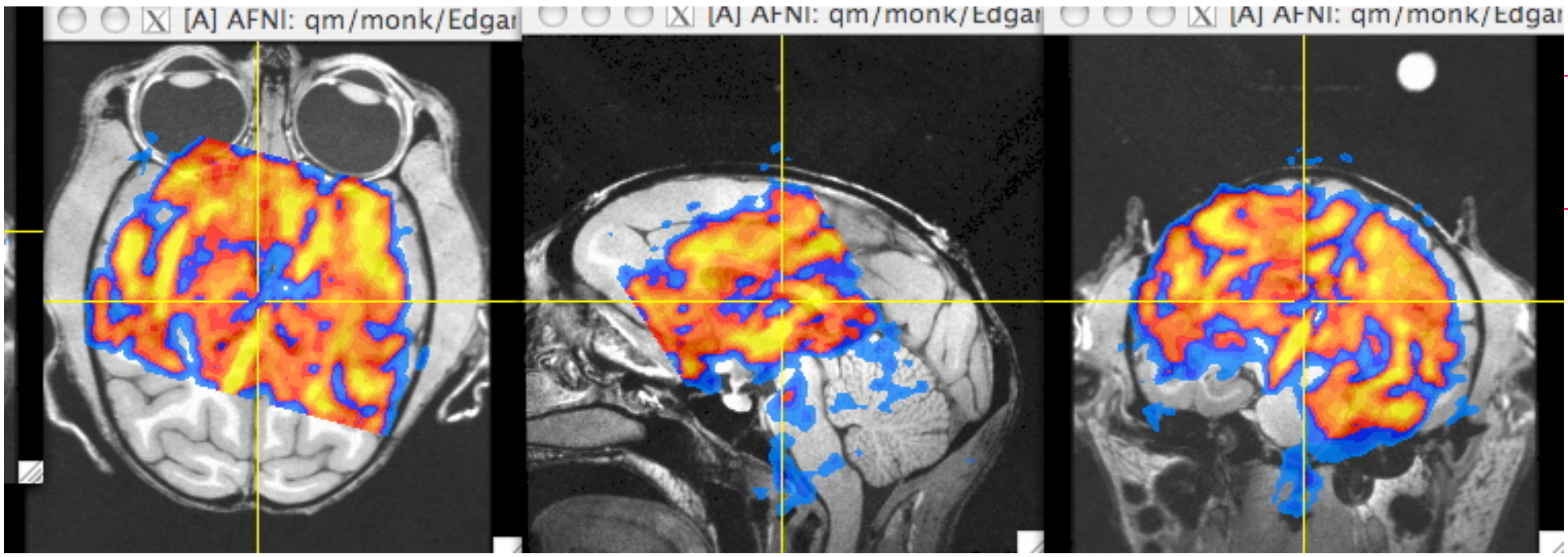


6 DOF
MI

Test: Monkey EPI - Anat

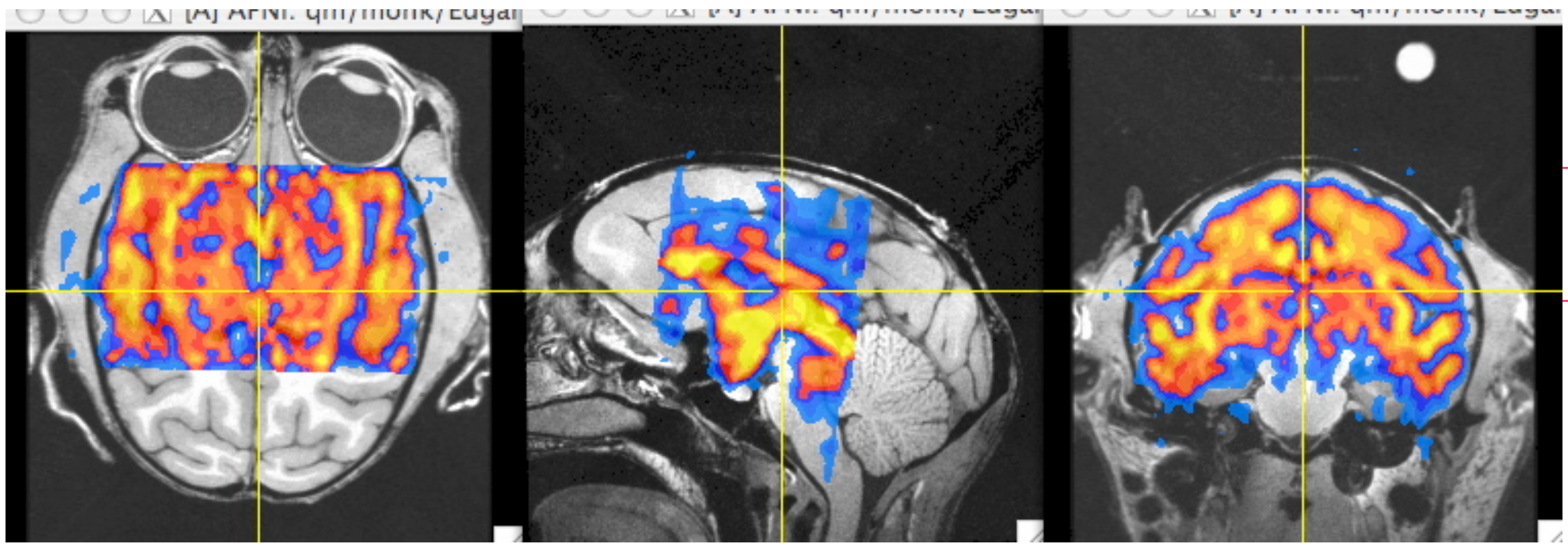


11 DOF
CRm

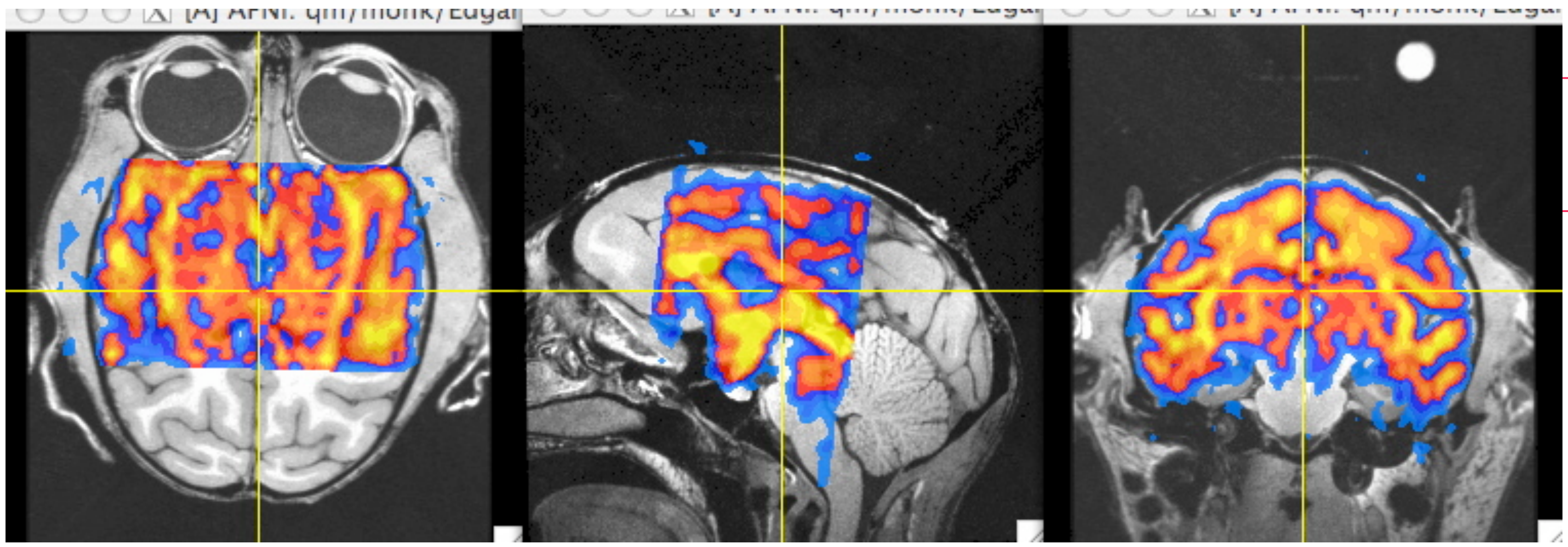


11 DOF
NMI

Test: Monkey EPI - Anat



11 DOF
HEL

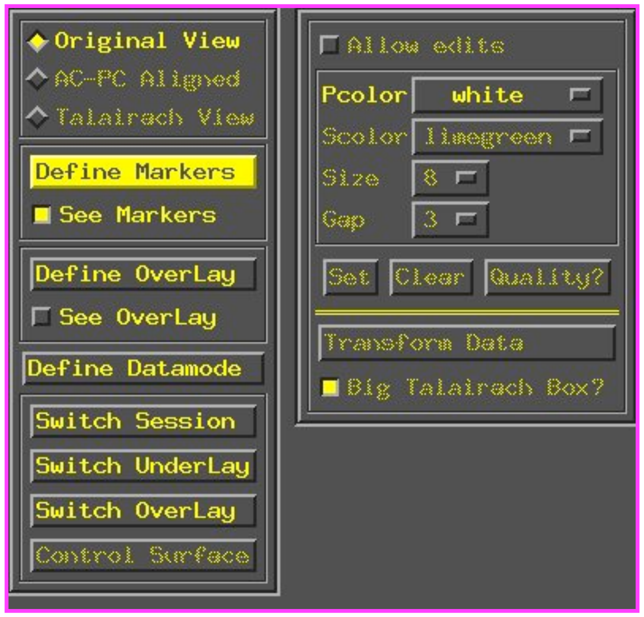


11 DOF
MI

Appendix C

Talairach Transform from the days of yore

- **Listen up folks, IMPORTANT NOTE:**
  - ✧ Have you ever opened up the **[Define Markers]** panel, only to find the AC-PC markers ***missing*** , like this:

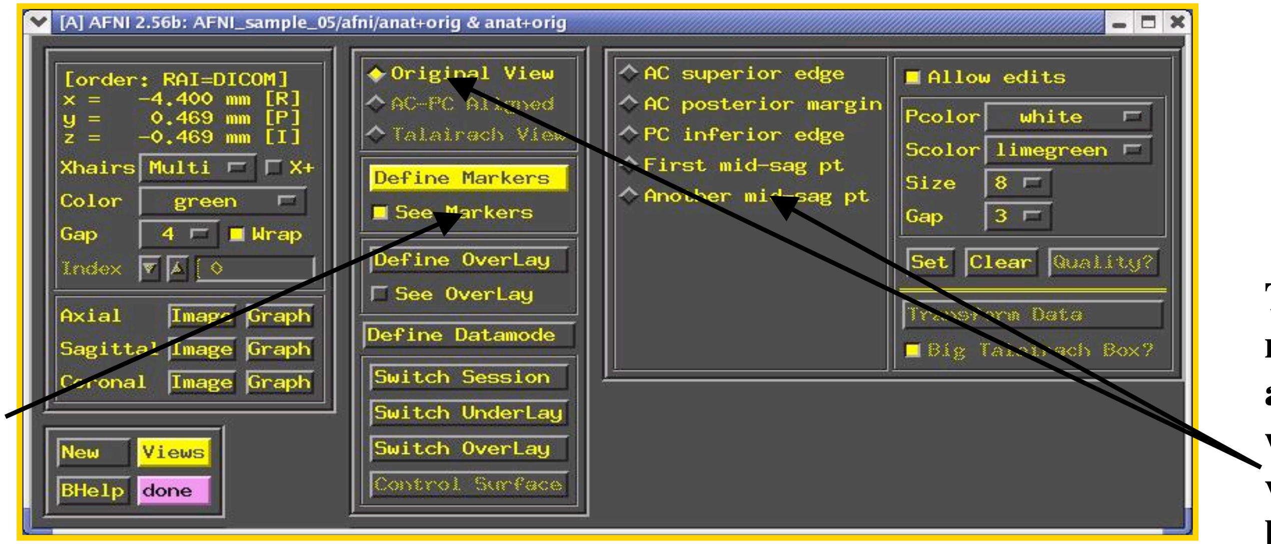


Gasp! Where did they go?

- ✧ There are a few reasons why this happens, but usually it's because you've made a copy of a dataset, and the AC-PC marker tags weren't created in the copy, resulting in the above dilemma.
  - ➥ In other cases, this occurs when **afni** is launched without any datasets in the directory from which it was launched (oopsy, your mistake).
- ✧ If you do indeed have an AFNI dataset in your directory, but the markers are missing and you want them back, run **3drefit** with the **-markers** options to create an empty set of AC-PC markers. Problem solved!

```
3drefit -markers <name of dataset>
```

- **Class Example - Selecting the ac-pc markers:**
  - ✧ `cd AFNI_data1/demo_tlrc` ⇒ Descend into the `demo_tlrc/` subdirectory
  - ✧ `afni &` ⇒ This command launches the AFNI program
    - ➥ The "`&`" keeps the UNIX shell available in the background, so we can continue typing in commands as needed, even if AFNI is running in the foreground
  - ✧ Select dataset **`anat+orig`** from the **[Switch Underlay]** control panel

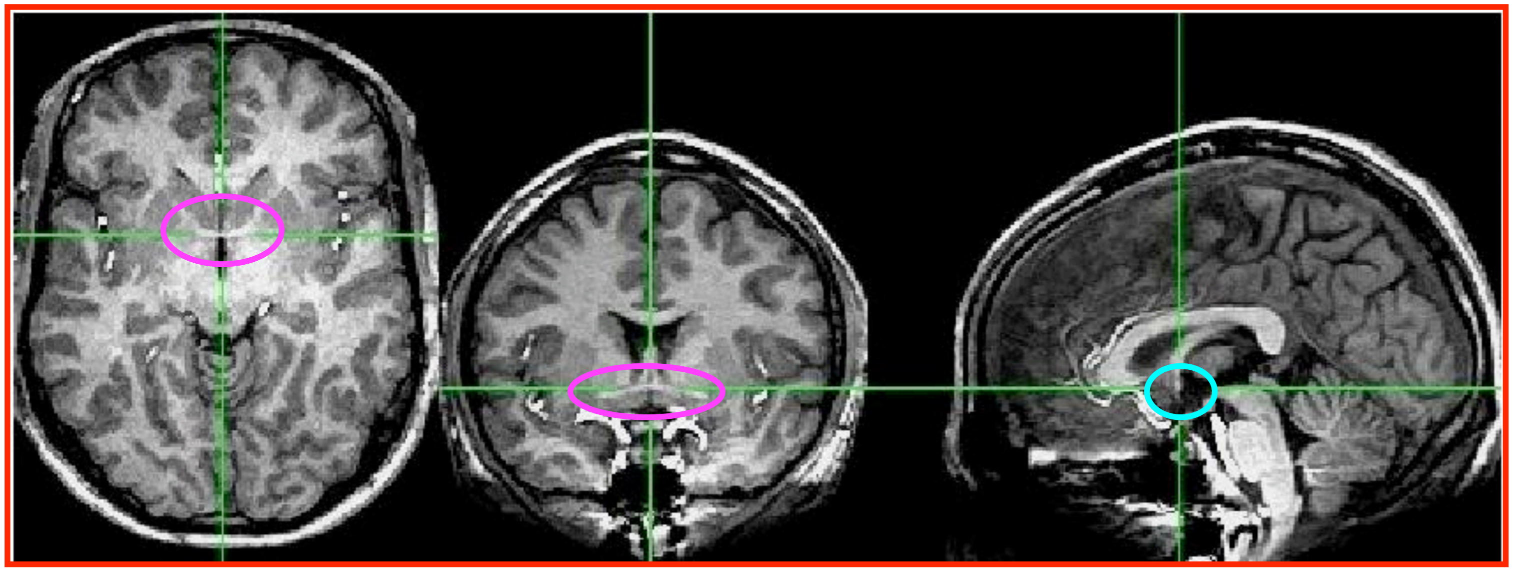


```
[order: RAI=DICOM]
x =   -4.400 mm [R]
y =    0.469 mm [P]
z =   -0.469 mm [I]
Xhairs Multi    X+
Color  green
Gap    4        Wrap
Index
Pcolor  white
Scolor  limegreen
Size    8
Gap     3
```

Press IN to view markers on brain volume

The AC-PC markers appear only when the orig view is highlighted

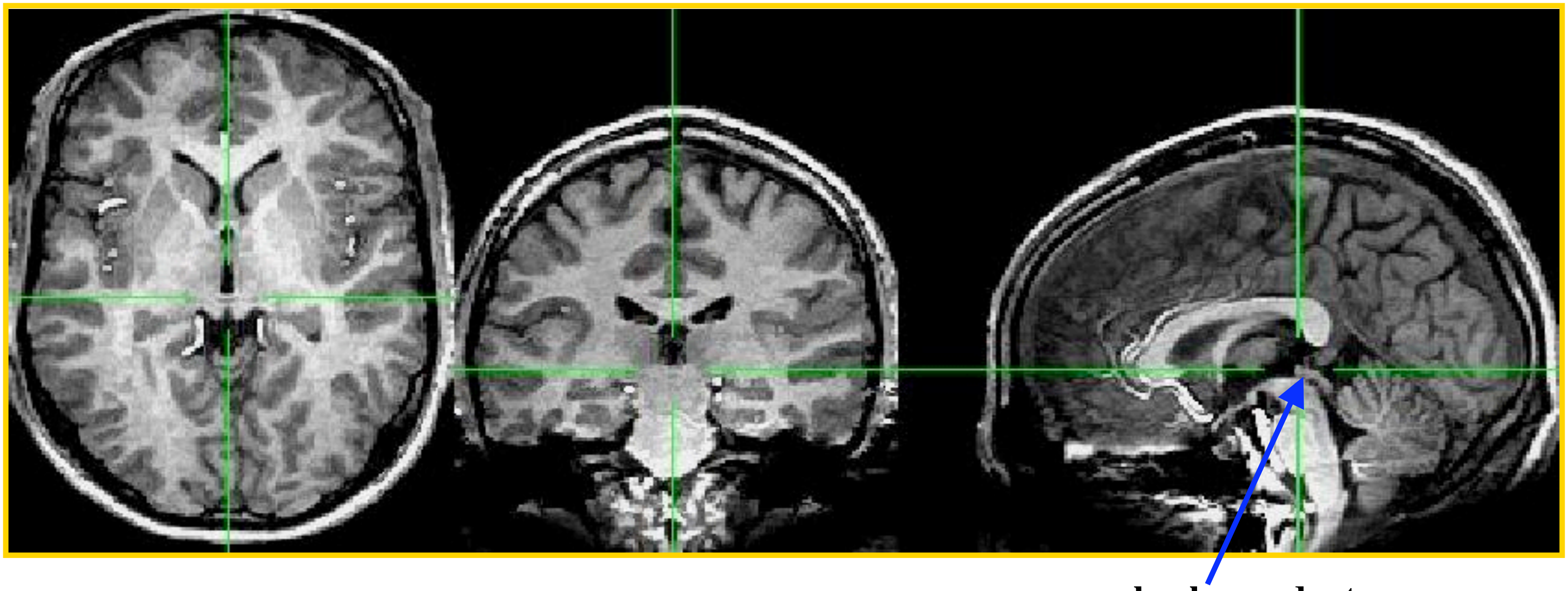
- ✧ Select the **[Define Markers]** control panel to view the 5 markers for ac-pc alignment
- ✧ Click the **[See Markers]** button to view the markers on the brain volume as you select them
- ✧ Click the **[Allow edits]** button in the ac-pc GUI to begin marker selection



✧ First goal is to mark top middle and rear middle of **AC**

- **Sagittal**: look for AC at bottom level of corpus callosum, below fornix
- **Coronal**: look for "mustache"; **Axial**: look for inter-hemispheric connection
- Get AC centered at focus of crosshairs (in Axial and Coronal)
- Move superior until AC disappears in Axial view; then inferior 1 pixel
- Press IN [AC superior edge] marker toggle, then [Set]
- Move focus back to middle of AC
- Move posterior until AC disappears in Coronal view; then anterior 1 pixel
- Press IN [AC posterior margin], then [Set]

- ✧ <u>Second goal is to mark inferior edge of **PC**</u>
  - ➥ This is harder, since PC doesn't show up well at 1 mm resolution
  - ➥ Fortunately, PC is always at the top of the cerebral aqueduct, which does show up well (at least, if CSF is properly suppressed by the MRI pulse sequence)

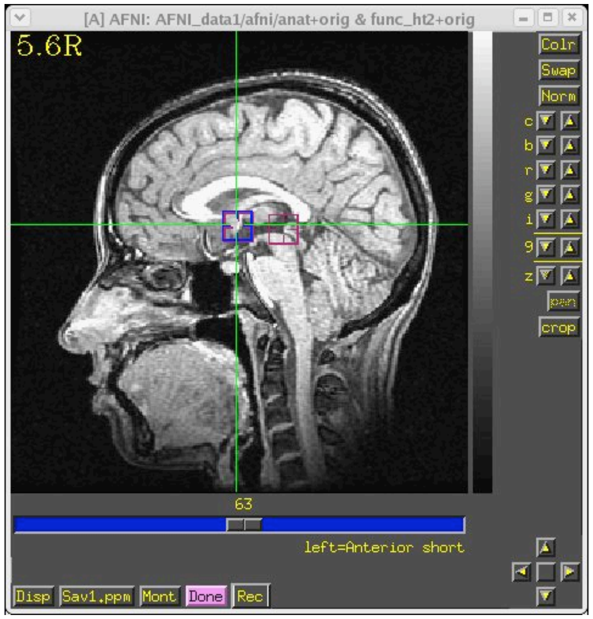


  - ➥ Therefore, if you can't see the PC, find mid-sagittal location just at top of cerebral aqueduct and mark it as `[PC inferior edge]`
- ✧ <u>Third goal is to mark **two inter-hemispheric points** (above corpus callosum)</u>
  - ➥ The two points must be at least 2 cm apart
  - ➥ The two planes AC-PC-#1 and AC-PC-#2 must be no more than **2º**

- AC-PC Markers Cheat Sheet
  - ✧ The AC-PC markers may take some time for the novice to master, so in the interest of time, we provide you with a little guide or "cheat sheet" to help you place markers on this example volume:

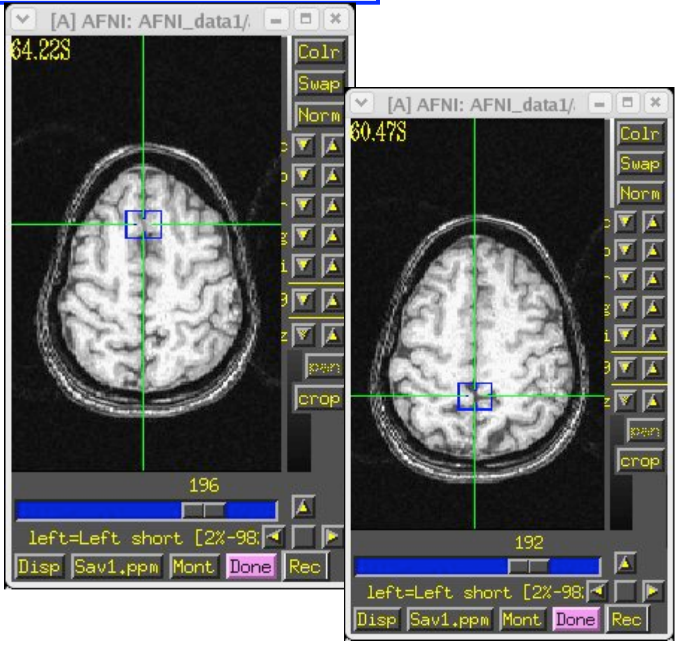
	i	j	k
AC Superior Edge:	126	107	63
AC Posterior Margin:	127	108	63
PC Inferior Edge:	152	109	63
1st Mid-Sagittal Point:	110	59	60
2nd Mid-Sagittal Point:	172	63	60

to:

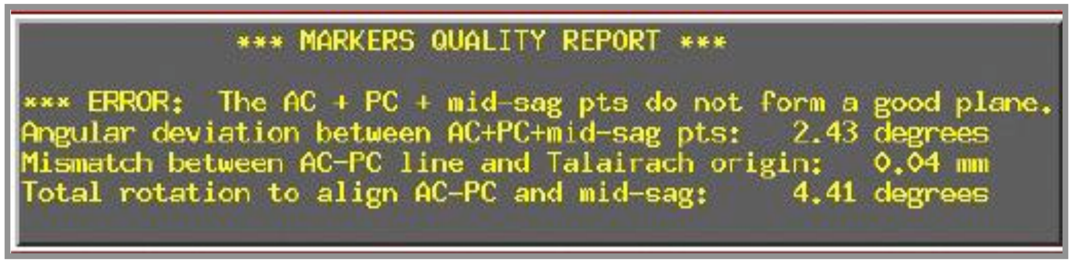


AC-PC markers

mid-sagittal markers

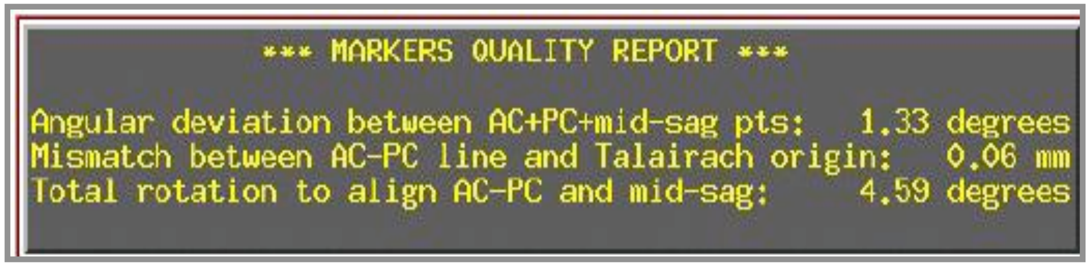


- Once all 5 markers have been set, the [Quality?] Button is ready
  - You can't [Transform Data] until [Quality?] Check is passed
  - In this case, quality check makes sure two planes from AC-PC line to mid-sagittal points are within 2^o
    - Sample below shows a 2.43^o deviation between planes ⇒ ERROR message indicates we must move one of the points a little



```
                 *** MARKERS QUALITY REPORT ***

*** ERROR:  The AC + PC + mid-sag pts do not form a good plane.
Angular deviation between AC+PC+mid-sag pts:    2.43 degrees
Mismatch between AC-PC line and Talairach origin:    0.04 mm
Total rotation to align AC-PC and mid-sag:      4.41 degrees
```

    - Sample below shows a deviation between planes at less than 2^o. Quality check is passed



```
            *** MARKERS QUALITY REPORT ***

Angular deviation between AC+PC+mid-sag pts:   1.33 degrees
Mismatch between AC-PC line and Talairach origin:   0.06 mm
Total rotation to align AC-PC and mid-sag:     4.59 degrees
```

      - We can now save the marker locations into the dataset header

- Notes on positioning AC/PC markers:
  - The structures dimensions are on the order of typical high-res images. Do not fret about a matter such as:
    - Q: Do I put the Sup. AC marker on the top voxel where I see still the the structure or on the one above it?
      - A: Either option is OK, just be consistent. The same goes for setting the bounding box around the brain discussed ahead. Remember, intra-subject anatomical variability is more than the 1 or 2 mm you are concerned about.
  - Typically, all three markers fall in the same mid-saggital plane
- Why, oh why, two mid-saggital points?
  - [Quality?] Contrary to our desires, no two hemispheres in their natural setting can be perfectly separated by a mid-saggital plane. When you select a mid-saggital point, you are defining a plane (with AC/PC points) that forms an acceptable separation between left and right sides of the brain.
  - To get a better approximation of the mid-saggital plane, AFNI insists on another mid-saggital point and uses the average of the two planes. It also insists that these two planes are not off from one another by more than 2^o
- I am Quality! How do I escape the tyranny of the [Quality?] check?
  - If you know what you're doing and want to elide the tests:
    - Set AFNI_MARKERS_NOQUAL environment variable to YES
    - This is a times needed when you are applying the transform to brains of children or monkeys which differ markedly in size from mature human brains.

✧ When [Transform Data] is available, pressing it will close the [Define Markers] panel, write marker locations into the dataset header, and create the +acpc datasets that follow from this one

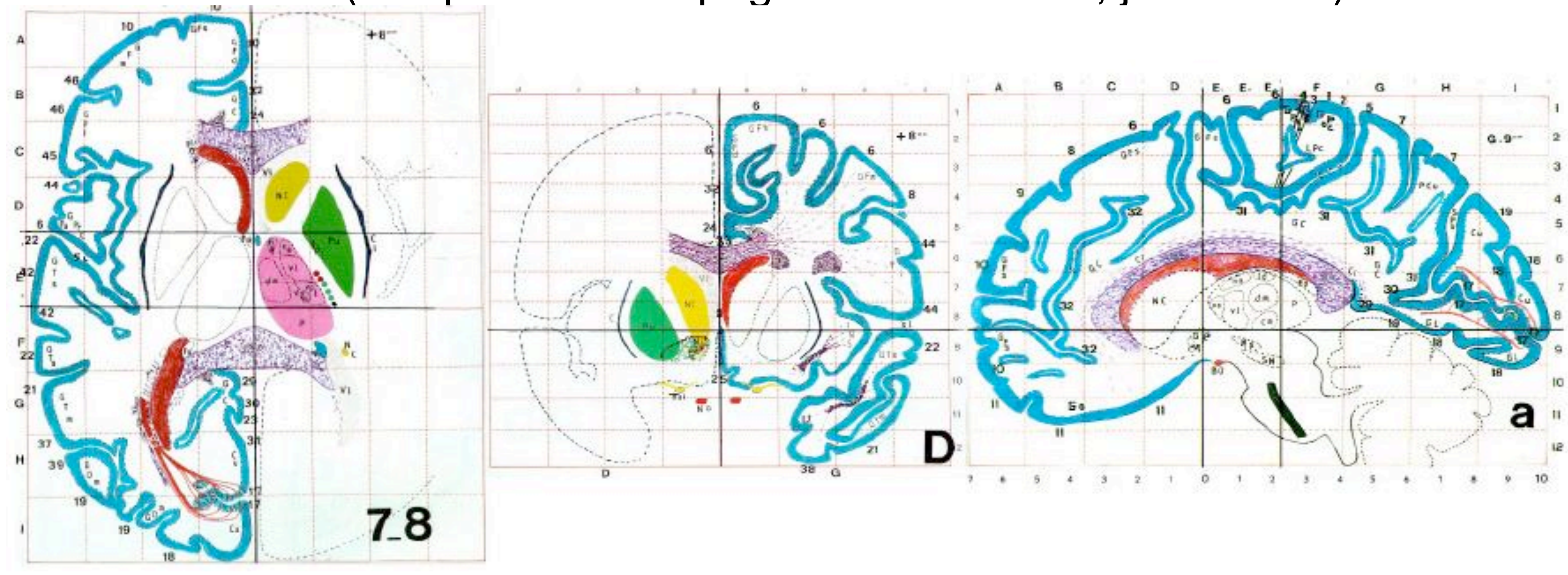
- ➥ The [AC-PC Aligned] coordinate system is now enabled in the main AFNI controller window
- ➥ In the future, you could re-edit the markers, if desired, then re-transform the dataset (but you wouldn't make a mistake, would you?)
- ➥ If you don't want to save edited markers to the dataset header, you must quit AFNI without pressing [Transform Data] or [Define Markers]

✧ **ls** ⇒ The newly created ac-pc dataset, **anat+acpc.HEAD**, is located in our demo_tlrc/ directory

✧ At this point, only the header file exists, which can be viewed when selecting the [AC-PC Aligned] button

- ➥ more on how to create the accompanying **.BRIK** file later…

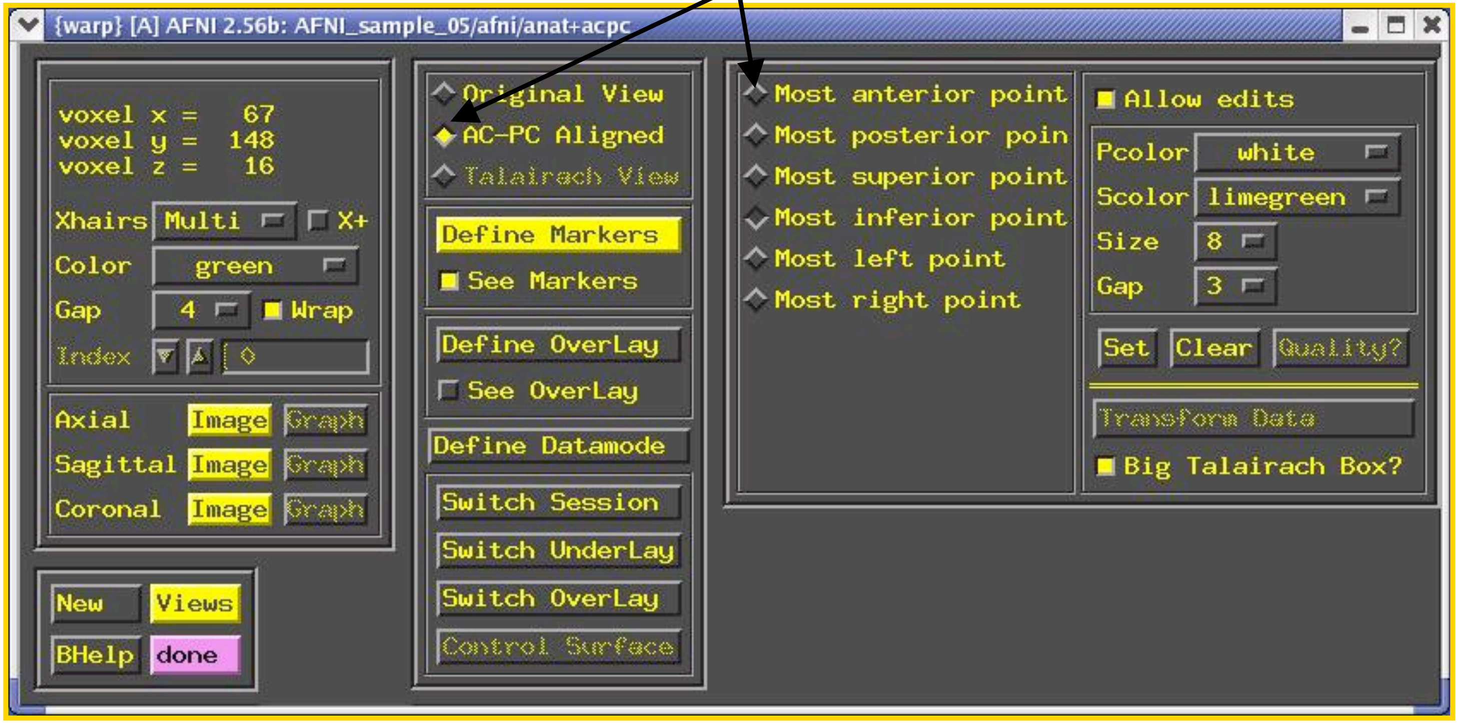
* **<u>Scaling to Talairach-Tournoux (+tlrc) coordinates</u>:**
  * We now stretch/shrink the brain to fit the Talairach-Tournoux Atlas brain size (sample TT Atlas pages shown below, just for fun)



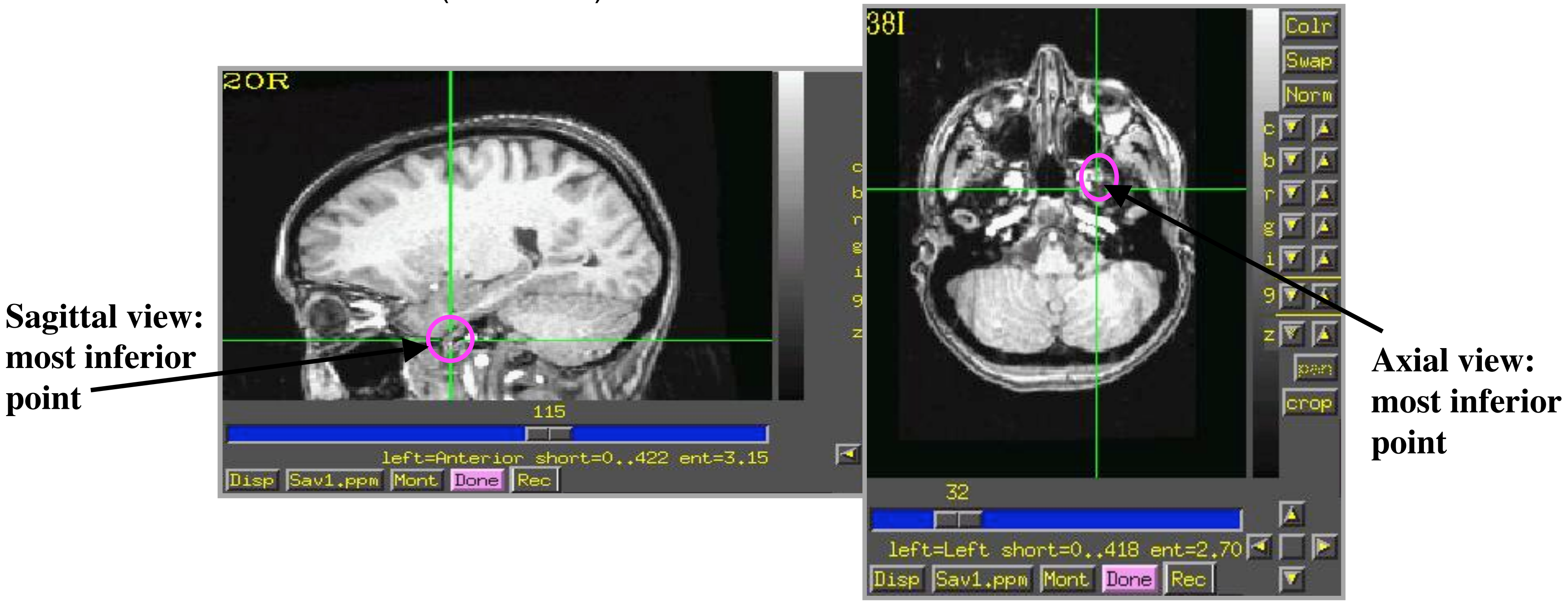
Most anterior to AC	70 mm		
AC to PC	23 mm		
PC to most posterior	79 mm	Length of cerebrum	172 mm
Most inferior to AC	42 mm		
AC to most superior	74 mm	Height of cerebrum	116 mm
AC to left (or right)	68 mm	Width of cerebrum	136 mm

- **Class example - Selecting the Talairach-Tournoux markers:**
  - ✧ There are 12 sub-regions to be scaled (3 A-P x 2 I-S x 2 L-R)
  - ✧ To enable this, the transformed +acpc dataset gets its own set of markers
    - ➥ Click on the **[AC-PC Aligned]** button to view our volume in ac-pc coordinates
    - ➥ Select the **[Define Markers]** control panel
  - ✧ A new set of six Talairach markers will appear:

The Talairach markers appear only when the AC-PC view is highlighted



- Using the same methods as before (i.e., select marker toggle, move focus there, **[Set]**), you must mark these extreme points of the cerebrum
  - Using 2 or 3 image windows at a time is useful
  - Hardest marker to select is **[Most inferior point]** in the temporal lobe, since it is near other (non-brain) tissue:


Sagittal view: most inferior point
20R
115
left=Anterior short=0..422 ent=3.15
Disp
Sav1.ppm
Mont
Done
Rec
38I
Colr
Swap
Norm
crop
32
left=Left short=0..418 ent=2.70
Axial view: most inferior point

- Once all 6 are set, press **[Quality?]** to see if the distances are reasonable
  - Leave **[Big Talairach Box?]** Pressed **IN**
  - Is a legacy from earliest (1994-6) days of AFNI, when 3D box size of `+tlrc` datasets was 10 mm smaller in `I`-direction than the current default

- ✧ Once the quality check is passed, click on **[Transform Data]** to save the `+tlrc` header
- ✧ **`ls`** ⇒ The newly created `+tlrc` dataset, **`anat+tlrc.HEAD`**, is located in our `demo_tlrc/` directory
  - ➥ At this point, the following anatomical datasets should be found in our `demo_tlrc/` directory:

    `anat+orig.HEAD`   **`anat+orig.BRIK`**

    `anat+acpc.HEAD`

    `anat+tlrc.HEAD`

  - ➥ In addition, the following functional dataset (which I -- the instructor -- created earlier) should be stored in the `demo_tlrc/` directory:

    `func_slim+orig.HEAD`   **`func_slim+orig.BRIK`**

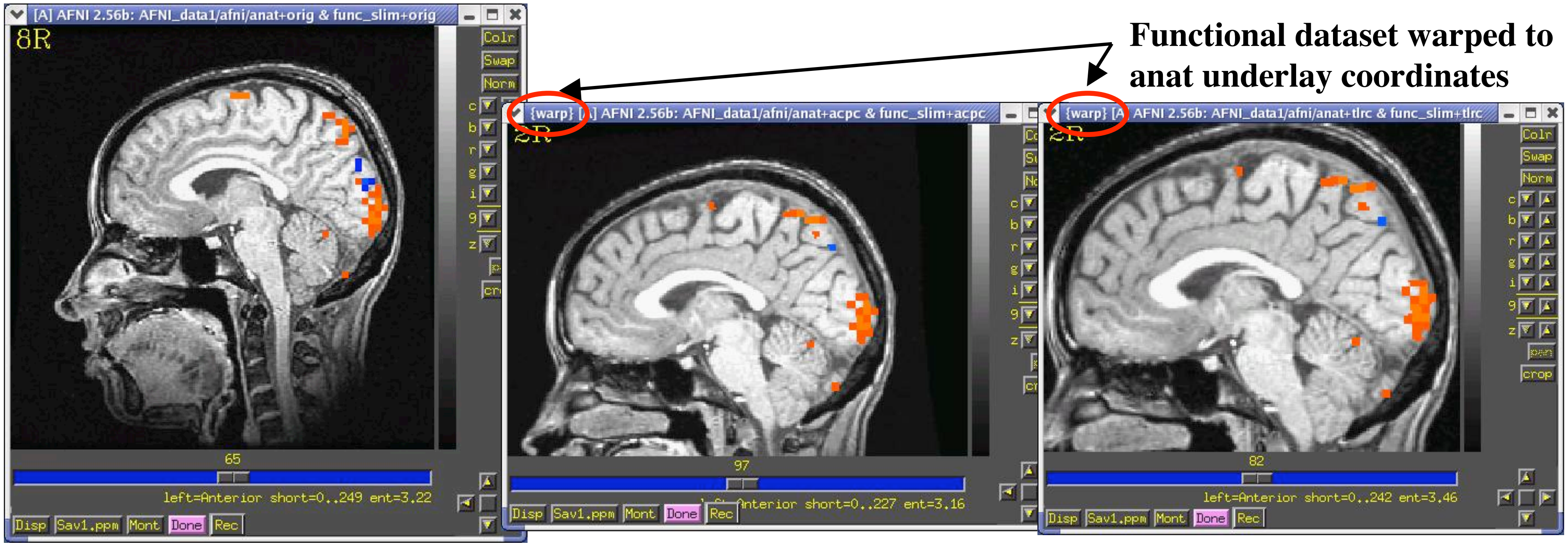
    - ➩ Note that this functional dataset is in the `+orig` format (not `+acpc` or `+tlrc`)

- **Automatic creation of "follower datasets":**
  - ✧ After the anatomical `+orig` dataset in a directory is resampled to `+acpc` and `+tlrc` coordinates, all the other datasets in that directory will *automatically* get transformed datasets as well
    - ➥ These datasets are created automatically inside the interactive AFNI program, and are not written (saved) to disk (i.e., only header info exists at this point)
    - ➥ How followers are created (arrows show geometrical relationships):

$$\begin{tikzcd}
\texttt{anat+orig} \arrow[r] & \texttt{anat+acpc} \arrow[r] \arrow[d] & \texttt{anat+tlrc} \arrow[d] \\
\texttt{func+orig} \arrow[u] & \texttt{func+acpc} & \texttt{func+tlrc}
\end{tikzcd}$$

    - ➥ In the class example, **`func_slim+orig`** will automatically be "warped" to our anat dataset's ac-pc (**`anat+acpc`**) & Talairach (**`anat+tlrc`**) coordinates
      - ➩ The result will be **`func_slim+acpc.HEAD`** and **`func_slim+tlrc.HEAD`**, located internally in the AFNI program (i.e., you won't see these files in the `demo_tlrc/` directory)
        - To store these files in `demo_tlrc/`, they must be written to disk. More on this later…

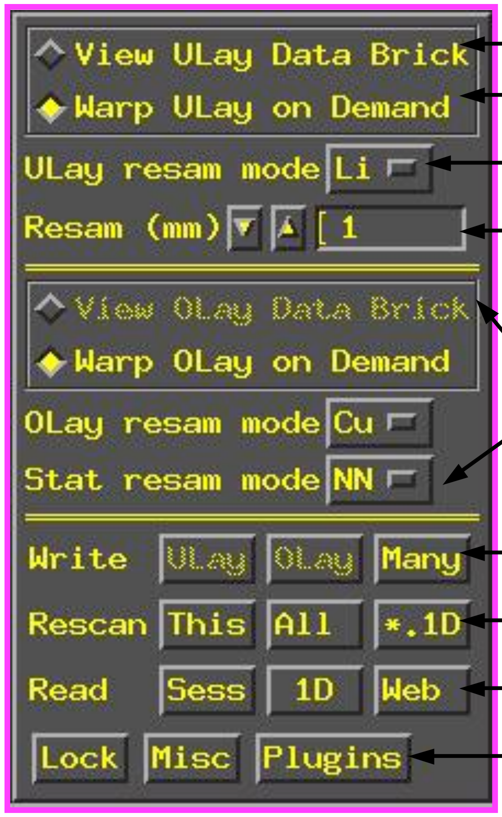
- <u>How does AFNI actually create these follower datsets?</u>
  - After **[Transform Data]** creates **anat+acpc**, other datasets in the same directory are scanned
    - AFNI defines the geometrical transformation ("warp") from **func_slim+orig** using the **to3d**-defined relationship between **func_slim+orig** and **anat+orig**, AND the markers-defined relationship between **anat+orig** and **anat+acpc**
      - A similar process applies for warping **func_slim+tlrc**
    - These warped functional datasets can be viewed in the AFNI interface:


[A] AFNI 2.56b: AFNI_data1/afni/anat+orig & func_slim+orig
{warp} [A] AFNI 2.56b: AFNI_data1/afni/anat+acpc & func_slim+acpc
{warp} [A] AFNI 2.56b: AFNI_data1/afni/anat+tlrc & func_slim+tlrc
8R
65
97
82
left=Anterior short=0..249 ent=3.22
left=Anterior short=0..227 ent=3.16
left=Anterior short=0..242 ent=3.46
Colr
Swap
Norm
crop
Disp
Sav1.ppm
Mont
Done
Rec
Functional dataset warped to anat underlay coordinates

func_slim+orig ⟶ **"func_slim+acpc"** ⟶ **"func_slim+tlrc"**

- Next time you run AFNI, the followers will automatically be created internally again when the program starts

- "Warp on demand" viewing of datasets:
  - AFNI doesn't actually resample all follower datasets to a grid in the re-aligned and re-stretched coordinates
    - This could take quite a long time if there are a lot of big 3D+time datasets
  - Instead, the dataset slices are transformed (or warped) from `+orig` to `+acpc` or `+tlrc` for viewing as needed (on demand)
  - This can be controlled from the **[Define Datamode]** control panel:



If possible, lets you view slices direct from dataset .BRIK

If possible, transforms slices from 'parent' directory

Interpolation mode used when transforming datasets

Grid spacing to interpolate with

Similar for functional datasets

Write transformed datasets to disk

Re-read: datasets from current session, all session, or 1D files

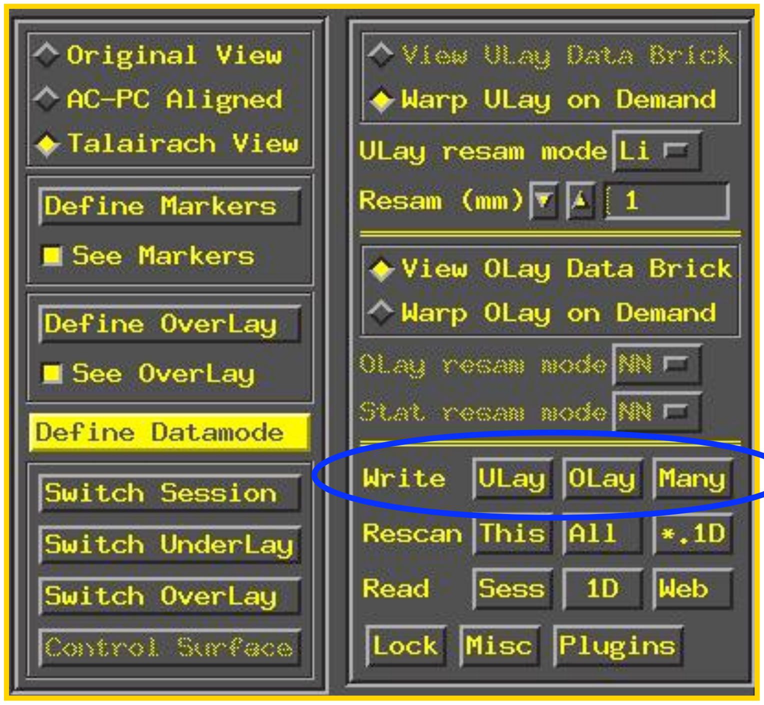
Read new: session directory, 1D file, dataset from Web address

Menus that had to go somewhere

AFNI titlebar shows warp on demand: `{warp}[A]AFNI2.56b:AFNI_sample_05/afni/anat+tlrc`

Creating follower data

- **Writing "follower datasets" to disk:**
  - ✧ Recall that when we created **anat+acpc** and **anat+tlrc** datasets by pressing **[Transform Data]**, only **.HEAD** files were written to disk for them
  - ✧ In addition, our follower datasets **func_slim+acpc** and **func_slim+tlrc** are *not* stored in our `demo_tlrc/` directory. Currently, they can only be viewed in the AFNI graphical interface
  - ✧ Questions to ask:
    1. How do we write our anat **.BRIK** files to disk?
    2. How do we write our warped follower datasets to disk?
  - ✧ To write a dataset to disk (whether it be an anat `.BRIK` file or a follower dataset), use one of the **[Define Datamode]** ⇒ **Write** buttons:



ULay writes current underlay dataset to disk

OLay writes current overlay dataset to disk

Many writes multiple datasets in a directory to disk

- **Class exmaple - Writing anat (Underlay) datasets to disk:**
  - ✧ You can use **[Define Datamode]** ⇒ **Write** ⇒ **[ULay]** to write the current anatomical dataset `.BRIK` out at the current grid spacing (cubical voxels), using the current anatomical interpolation mode
  - ✧ After that, **[View ULay Data Brick]** will become available
    - ➥ **`ls`** ⇒ to view newly created `.BRIK` files in the **`demo_tlrc/`** directory:

```
anat+acpc.HEAD   anat+acpc.BRIK
anat+tlrc.HEAD   anat+tlrc.BRIK
```

- **Class exmaple - Writing func (Overlay) datasets to disk:**
  - ✧ You can use **[Define Datamode]** ⇒ **Write** ⇒ **[OLay]** to write the current functional dataset `.HEAD` and `BRIK` files into our `demo_tlrc/` directory
  - ✧ After that, **[View OLay Data Brick]** will become available
    - ➥ **`ls`** ⇒ to view newly resampled func files in our `demo_tlrc/` directory:

```
func_slim+acpc.HEAD func_slim+acpc.BRIK
func_slim+tlrc.HEAD func_slim+tlrc.BRIK
```

- Command line program **adwarp** can also be used to write out .BRIK files for transformed datasets:

```
adwarp -apar anat+tlrc  -dpar func+orig
```

  - The result will be: **func+tlrc.HEAD** and **func+tlrc.BRIK**

- Why bother saving transformed datasets to disk anyway?
  - Datasets without .BRIK files are of limited use:
    - You can't display 2D slice images from such a dataset
    - You can't use such datasets to graph time series, do volume rendering, compute statistics, run any command line analysis program, run any plugin…
      - If you plan on doing any of the above to a dataset, it's best to have both a .HEAD and .BRIK files for that dataset