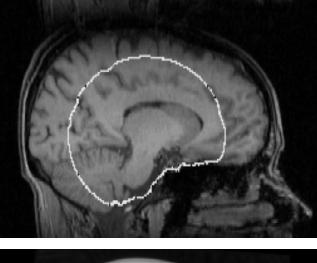
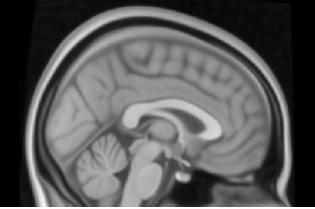
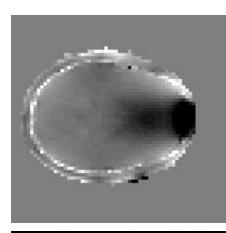
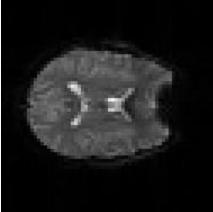
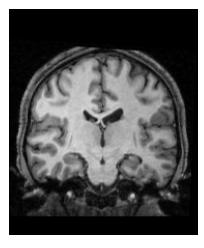
#### Introduction to Brain Extraction and Registration

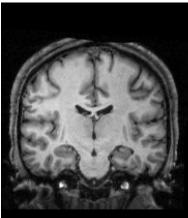






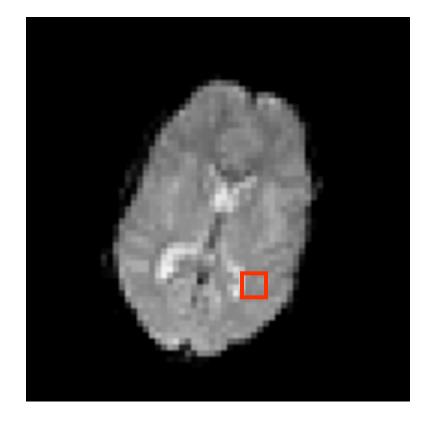


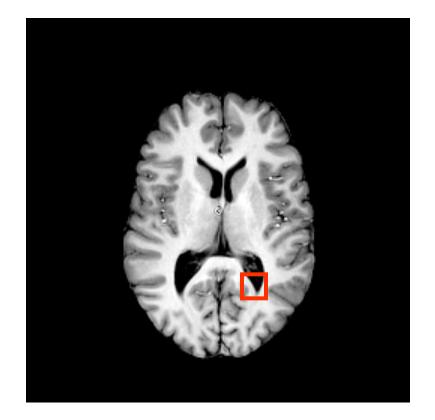






#### What is Registration?

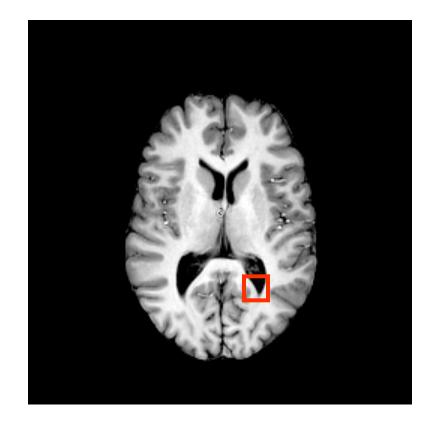






#### What is Registration?





Align images so that voxel location = anatomical location with accurate intensity values



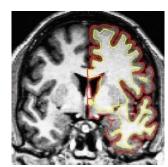
#### What use is Registration?

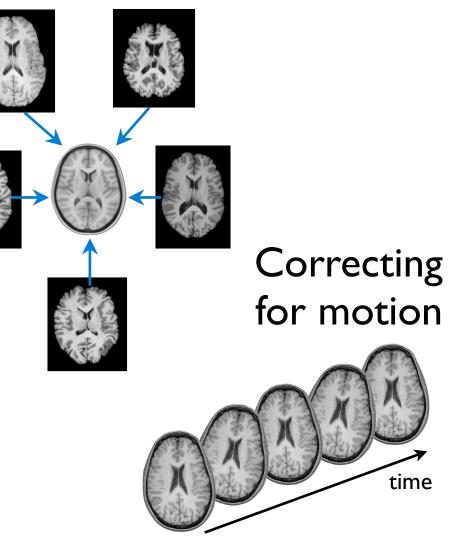
Some common uses of registration:

Combining across individuals in group studies: including fMRI & diffusion

# Quantifying structural change



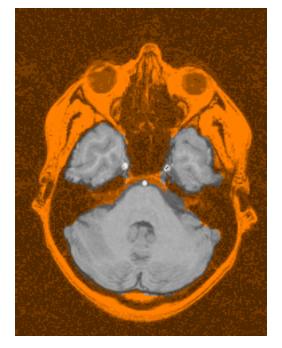






#### **BET: Brain Extraction Tool**

- Brain / non-brain segmentation
- Preparation step for registration and segmentation
- Eliminates non-brain tissues with highly variable contrast and geometry (e.g. scalp, marrow, etc.)
  - works best if some fat sat is used
- Robust to bias fields (by using local intensity changes)



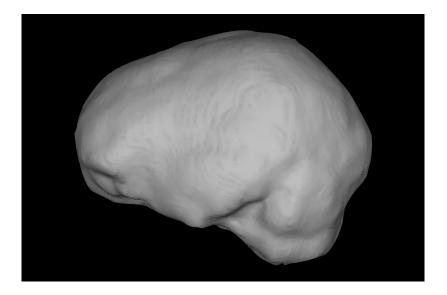
S.M. Smith; Fast robust automated brain extraction; HBM 17(3), 2002.

Works with a wide range of MRI sequences (TI,T2, etc.) and resolutions



#### **Brain Surface Model**

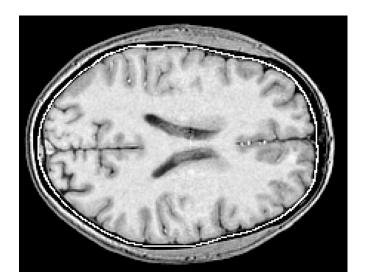
#### Extracted Brain Surface (not what we aim for here)

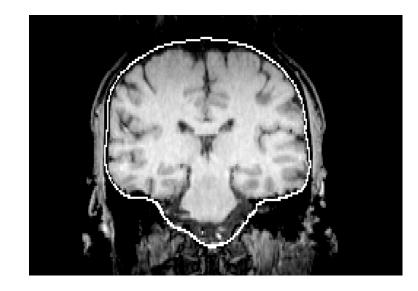


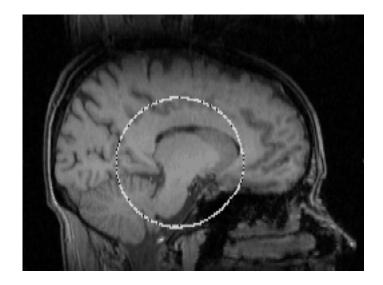






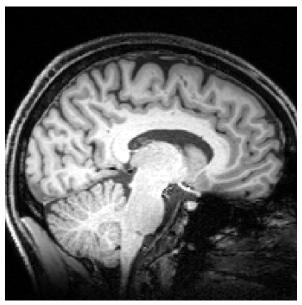




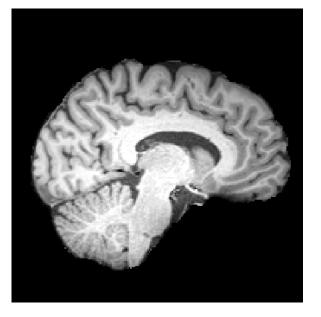




#### Original



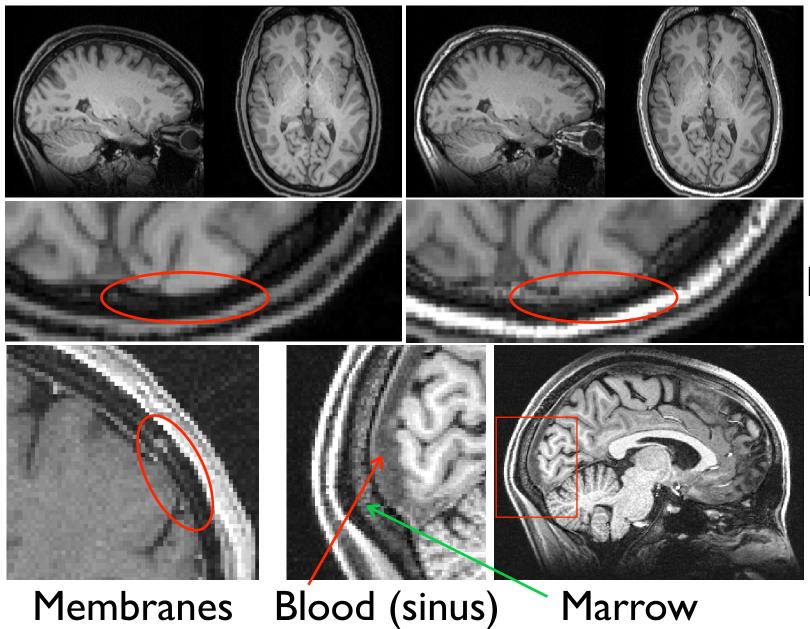
#### Brain Extracted



#### Brain Mask

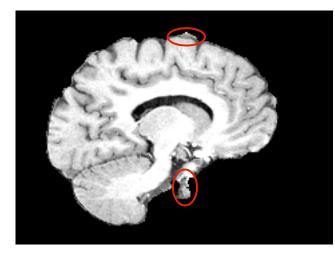


#### Difficulties



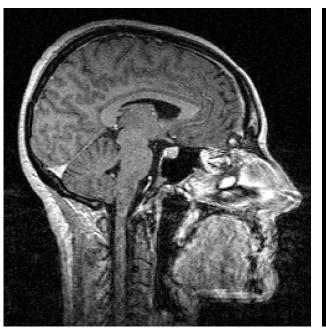
#### Marrow



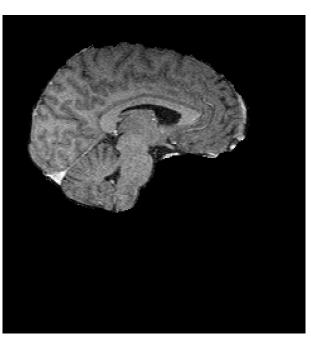


Want to remove the majority of non-brain structures, leaving all the brain intact.

Leaving small pieces of non-brain is unimportant for linear registration, but it is important for segmentation.









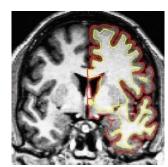
#### What use is Registration?

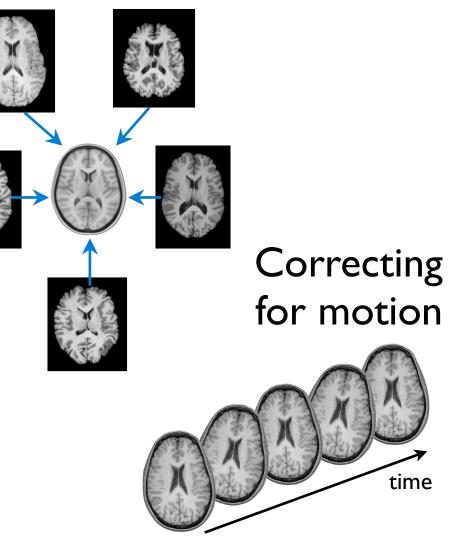
Some common uses of registration:

Combining across individuals in group studies: including fMRI & diffusion

# Quantifying structural change









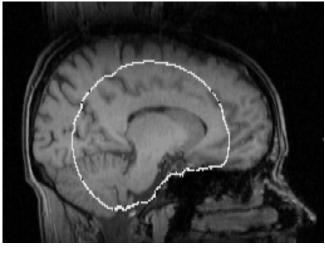
## Brain Extraction and Registration

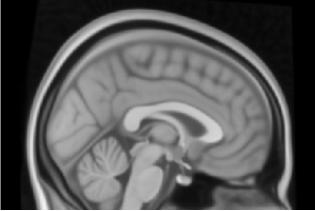
#### Summary:

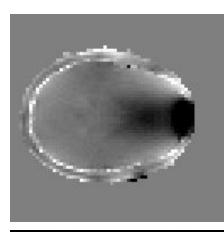
- Registration aims to align images/structures
- Can transform the image to match others
- Important component in *all* group studies
- Can measure motion or anatomical change
- Brain extraction removes bulk of non-brain
- Some errors are to be expected
- Small, isolated errors are not a problem for registration (but would be for segmentation)

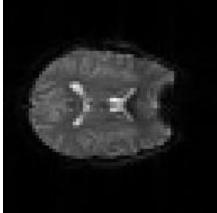


#### Registration: Image Spaces and Spatial Transformations

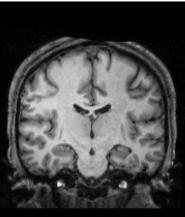






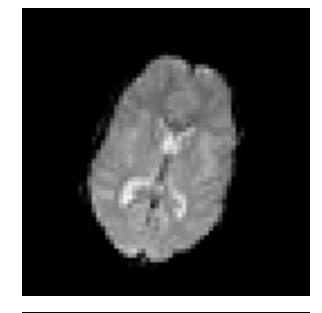






## RSIE

#### **Basic Registration Concepts**



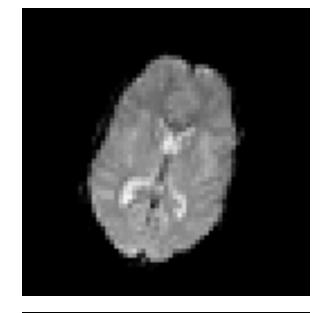


Need to understand:

- Image "spaces"
- Spatial Transformations
- Cost Functions
- Interpolation

## IRSIL

#### **Basic Registration Concepts**





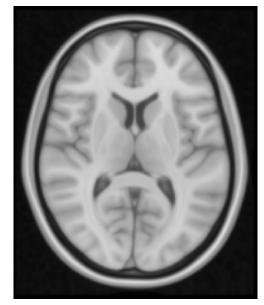
Need to understand:

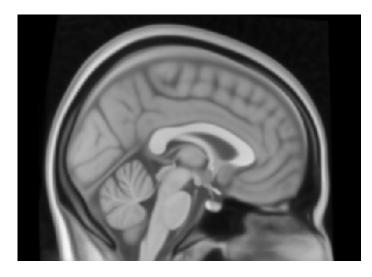
- Image "spaces"
- Spatial Transformations
- Cost Functions
- Interpolation



#### Standard Space

- Common reference coordinate system for reporting/describing
- Register all members of a group to this space for group studies
- Original Talairach & Tournoux coords based on one postmortem brain
- Now use standard images based on non-linear group average (MNI152)
- MNI is not quite Talairach

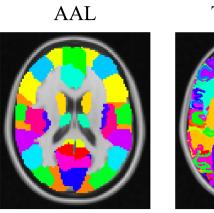




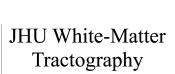


#### Standard Space: Atlases

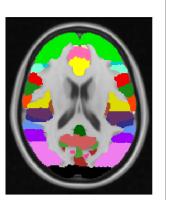
- Most atlases are in standard space (esp. MNI152)
- Information is derived from different sources, but in each case this has been brought into the standard space at some point



Talairach

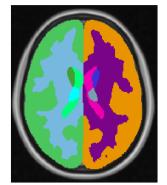


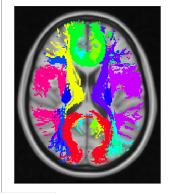
 To use atlas information for an individual (or group) study it is necessary to "get into" standard space



Cortical

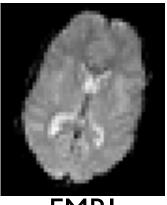
Harvard-Oxford Subcortical Summary



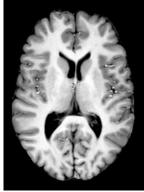




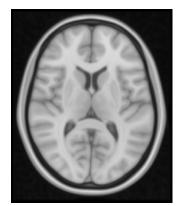
#### Other "Spaces"







Structural

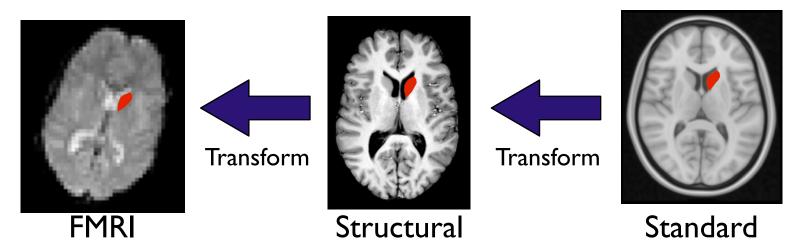


Standard

- All images in the same "space" are aligned
- Different images ⇒ different "spaces"
   e.g. standard space, structural space, functional space
- Can have different resolution images in the same space e.g. Imm and 2mm versions of standard space images
- Want to move image-related info between spaces e.g. a mask from standard space to structural space



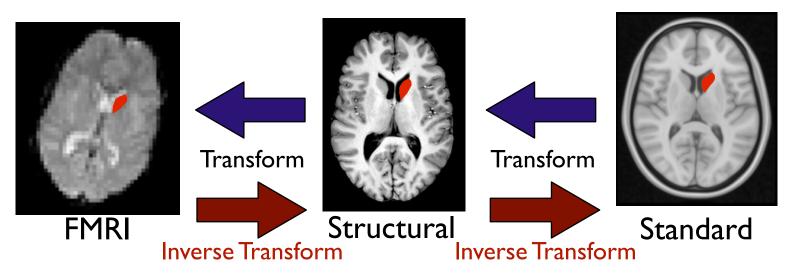
#### Other "Spaces"



- Need to registration between spaces (via images) and get the transformations before transforming/moving/resampling any image-related info (like masks or atlas ROIs)
- Can have versions of the same "image" (e.g. a mask) in several different spaces
- FSL tools (e.g. FEAT) often move things between spaces



#### Other "Spaces"



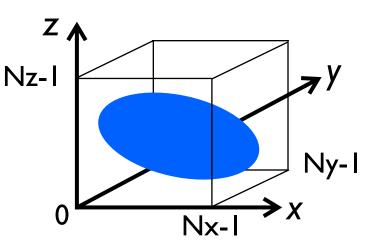
- Need to registration between spaces (via images) and get the transformations before transforming/moving/resampling any image-related info (like masks or atlas ROIs)
- Can have versions of the same "image" (e.g. a mask) in several different spaces
- FSL tools (e.g. FEAT) often move things between spaces



## Image (Voxel) Coordinates

Confusingly, there are many types of coordinates

Voxel coordinates in FSL: Integers between 0 and N-I inclusive Refer to the whole voxel Origin in the lower-left corner: (0,0,0)



location

08

4999466

location

MNI152 T1 1mm

90 108 901 543

Axes are not aligned with the anatomy Cannot distinguish left from right by voxel coordinate values

FSLeyes reports these Used by FSL commands & same as NIfTI coords

## IN

#### Standard Space Coordinates

RX

Standard Space coordinates in FSL: Real numbers, in units of *mm* Origin (0,0,0) near centre of image (anatomical landmark; e.g. anterior commisure) Axes aligned with anatomy (left and right specified)

Several standard spaces exist: MNI, Talairach, BrainWeb, etc

FSLeyes also reports these when possible

 Location

 toordinates: MNI152
 Voxel location

 -0.4999466
 90
 0

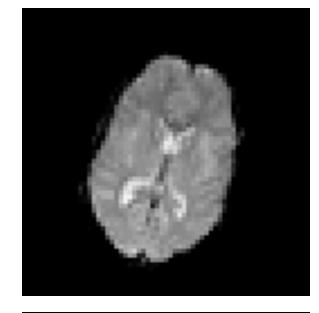
 -17.50005
 108
 0

 18.49995
 90
 0

 Volume
 0
 0

## 1.RSIL

#### **Basic Registration Concepts**





Need to understand:

- Image "spaces"
- Spatial Transformations
- Cost Functions
- Interpolation



## Spatial Transformations

😑 😑 🚫 🔀 FEAT – FMRI Expert Analysis Tool v5.97 To align images must transform them First-level analysis Full analysis 🛛 🛁 Registration Pre-stats Stats Post-stats Misc Data Many types of transformation nitial structural image Main structural image structural\_brain <u>a</u> Linear Normal search 6 DOF Degrees of Freedom (DOF) Standard space /usr/local/fsl/data/standard/MNI152\_T1\_2mm\_brain 3 partially describe transform Normal search 12 DOF Nonlinear 📃 Warp resolution (mm) 10 韋 😑 😑 📉 FLIRT - FMRIB's Linear Image Registration Tool - v5.4.2 Mode Input image -> Reference image Examples: Reference image /usr/local/fsl/etc/standard/avg152T1\_brain.hdr Model/DOF (input to ref) Affine (12 parameter model) Rigid Body (6 DOF) Input image /usr/local/feeds/data/structural.nii.gz /Users/mark/tmp/struct2avg Output image Affine (12 DOF) Number of secondary images to apply transform to 0 Non-linear (12 - millions DOF) **T** ▷ Advanced Options

Go

Exit

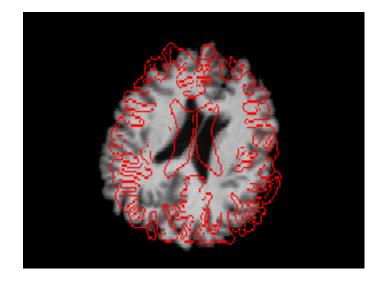
Help

Utils



## **Rigid-Body Transformations**

6 DOF in 3D Includes: 3 Rotations

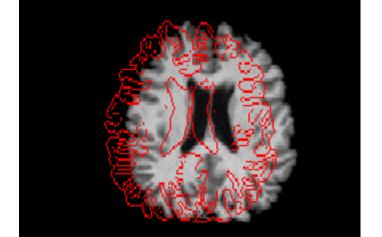




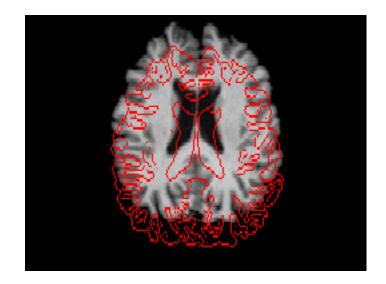
## **Rigid-Body Transformations**

6 DOF in 3D Includes: 3 Rotations

**3** Translations



Used for within-subject registrations

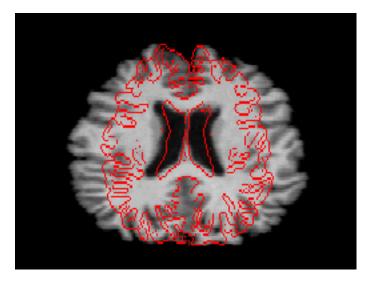


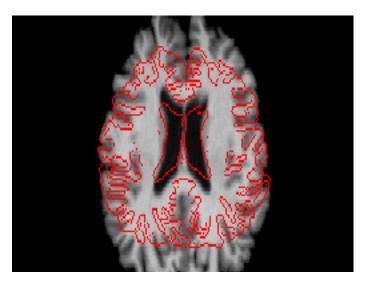


#### Affine Transformations

I2 DOF in 3DLinear Transf.Includes:

- 3 Rotations
- 3 Translations
  - 3 Scalings

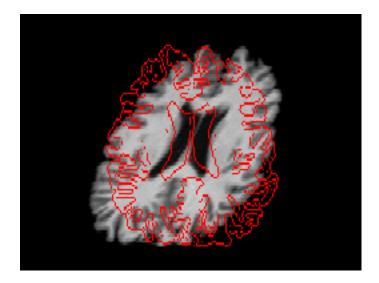






#### Affine Transformations

- I2 DOF in 3DLinear Transf.Includes:
  - 3 Rotations
  - 3 Translations



- 3 Scalings
  - 3 Skews/Shears

Used for eddy current correction and initialising non-linear registration

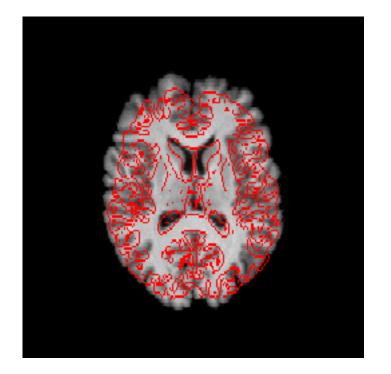


#### Non-Linear Transformations

More than 12 DOF Can be purely local

Subject to constraints:

Basis Functions e.g. B-Splines Regularisation Topology-preservation

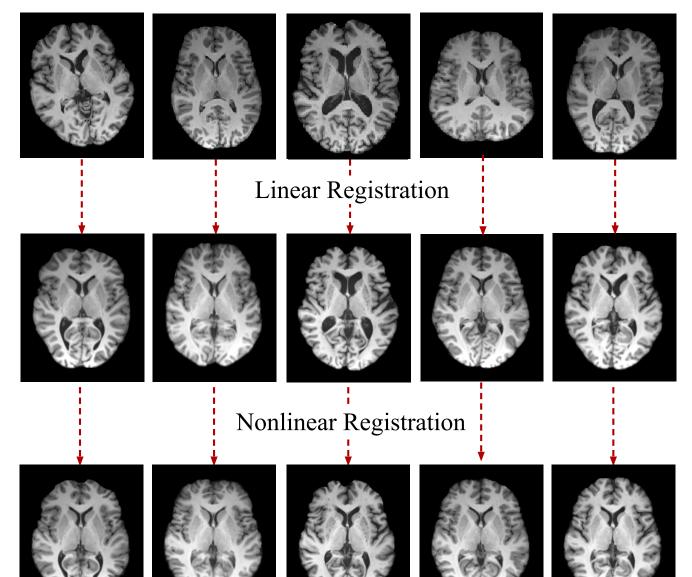


Used for good quality between-subject registrations

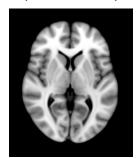


#### Non-Linear Transformations

Before Registration



Reference (MNI152)



#### What transform/DOF do I use?

#### Rigid body (6 DOF)

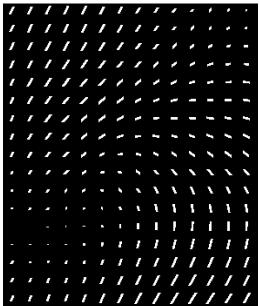
- within-subject motion
- Non-linear (lots of DOF!)
  - high-quality image (resolution, contrast) & same modality of reference/template
- better with a non-linear template (e.g. MNI152\_T1\_2mm) Affine (12 DOF)
  - needed as a starting point for non-linear
  - align to affine template, or using lower quality images, or eddy current correction
- Global scaling (7 DOF)
  - within-subject but with global scaling (equal in x,y,z)
  - corrects for scanner scaling drift in *longitudinal studies*

More DOF is **NOT** always better (e.g. within-subject)

# What do the transformations look like?

 $A = \begin{pmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ 0 & 0 & 0 & 1 \end{pmatrix}$ 

An affine transformation is represented by these 12 numbers. This matrix multiplies coordinate vectors to define the transformed coordinates.

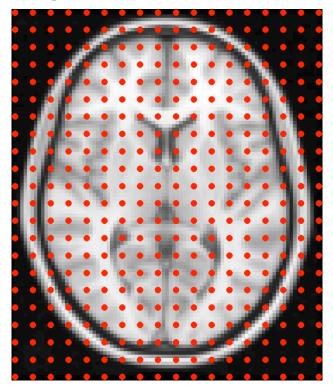


A non-linear transformation can be represented by a **deformation field**.

#### Non-linear deformation Regularisation, Warp Resolution and DOF

- Various ways of controlling warp smoothness
- Less DOF = smoother
- Lower warp resolution = smoother
- Higher regularisation = smoother

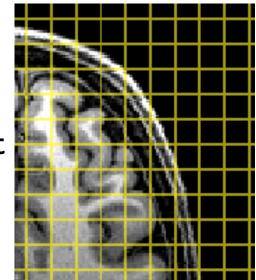
Spacing of points = warp resolution = regularisation = DOF



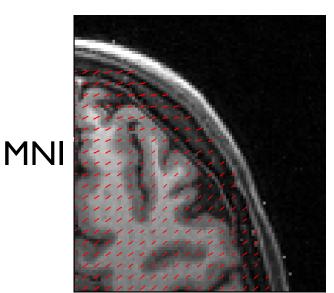


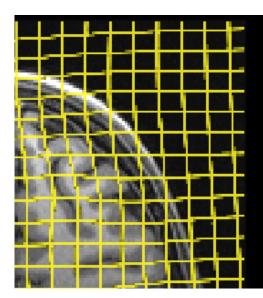
## Non-linear deformation

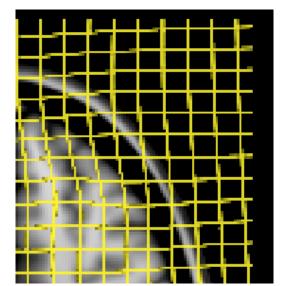
#### High Regularisation Lower Regularisation

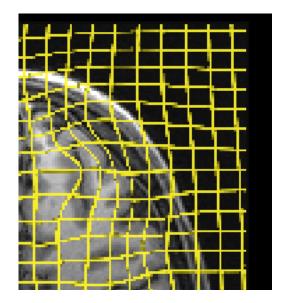


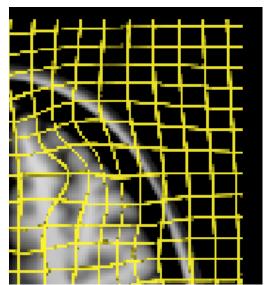








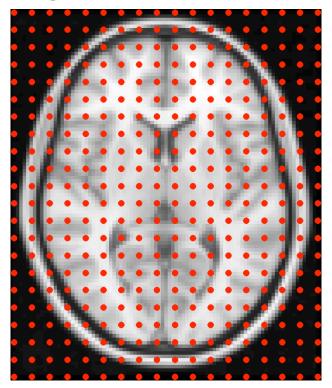




#### Non-linear deformation Regularisation, Warp Resolution and DOF

- Various ways of controlling warp smoothness
- Less DOF = smoother
- Lower warp resolution = smoother
- Higher regularisation = smoother
- Default warp resolution of 10mm is a good compromise for MNI152
- Between two subjects can use less smooth warps (less regularisation, higher warp resolution, more DOF)

Spacing of points = warp resolution = regularisation = DOF



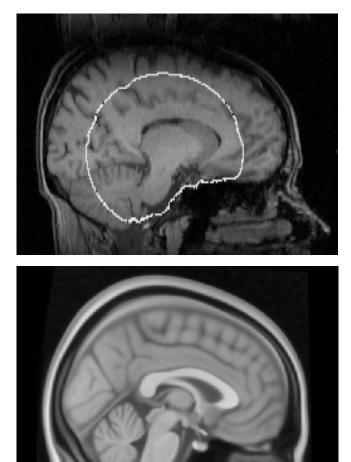
#### Registration: Image Spaces and Spatial Transformations

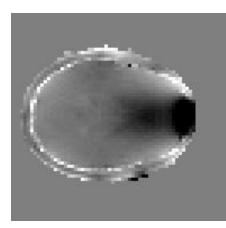
Summary:

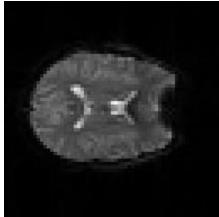
- Standard space is used as a common space
- MNI152 is a commonly used standard space
- Atlases are usually in standard space
- We often move images/info between spaces
- There are voxel and mm (standard) coordinates
- You must choose the transformation type
- Rigid is most appropriate for within-subject
- Nonlinear is most appropriate for between-subject
- Affine is needed to initialise nonlinear
- Regularisation alters flexibility of nonlinear



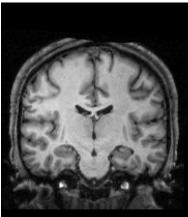
## Registration: Cost Functions, Interpolation and Masks





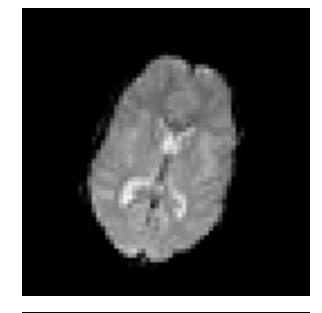






## RSIE

## **Basic Registration Concepts**



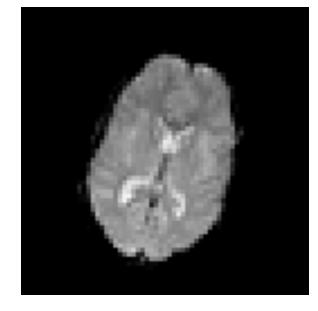


Need to understand:

- Image "spaces"
- Spatial Transformations
- Cost Functions
- Interpolation

## IRSTE

## **Basic Registration Concepts**





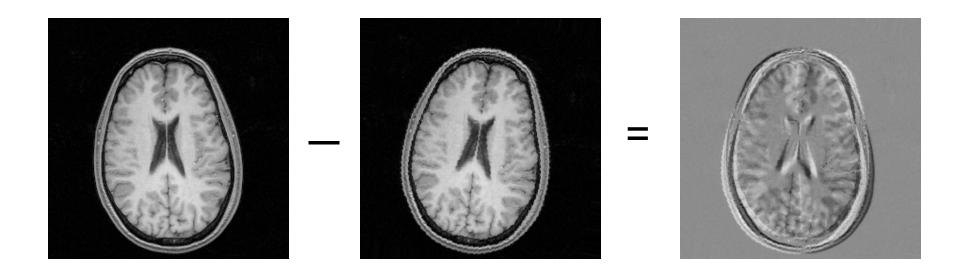
#### Need to understand:

- Image "spaces"
- Spatial Transformations
- Cost Functions
- Interpolation



### **Cost Function**

Measures "goodness" of alignment Seek the minimum value Several main varieties



Similarity function is opposite (maximum sought)



## **FLIRT: Cost Functions**

## FMRIB's Linear Image Registration Tool



## **FLIRT: Cost Functions**

### Important: Allowable image modalities Less important: Details

Least Squares	Same modality (exact sequence parameters)
Normalised Correlation	Same modality (can change brightness & contrast)
Correlation Ratio	Any MR modalities
Mutual Information	Any modalities (including CT, PET, etc.)
Normalised Mutual Info.	Any modalities (including CT, PET, etc.)
BBR	Within-subject EPI to structural (see later)



## **FNIRT: Cost Functions**

FMRIB's Non-linear Image Registration Tool

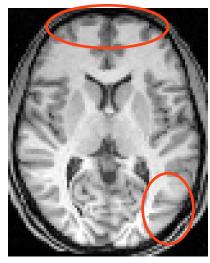
## **FNIRT: Cost Functions**

• Only uses Least Squares as cost function

so images must be of the same modality/sequence

- Also includes an explicit model for bias field (RF inhomog.)
- Estimate displacement field and RF bias field together
- Options exist to control bias field (turn off/on, smoothness)

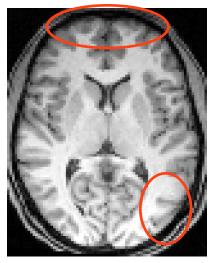
#### Without RF modelling



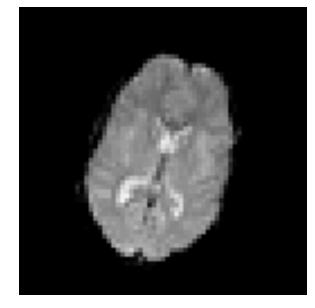
#### Template

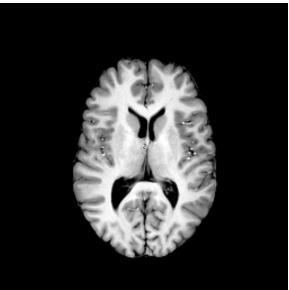


#### With RF modelling



# **Basic Registration Concepts**



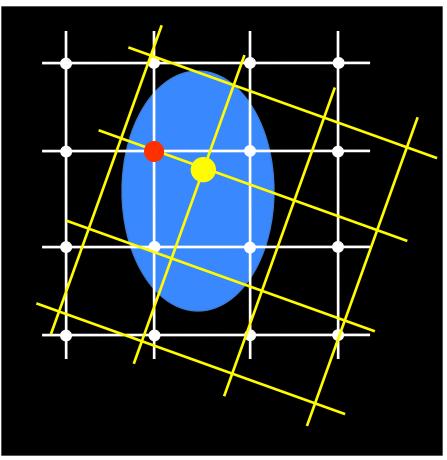


#### Need to understand:

- Image "spaces"
- Spatial Transformations
- Cost Functions
- Interpolation



### Finds intensity values between grid points



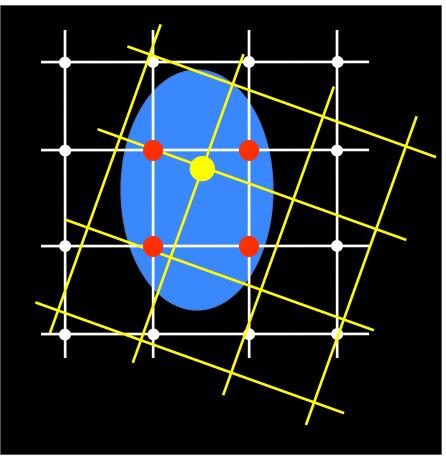
### Various types include

- Nearest Neighbour
- Trilinear
- Spline
- Sinc
- k-Space methods

Fast, but blocky - can be used for discrete labels



### Finds intensity values between grid points



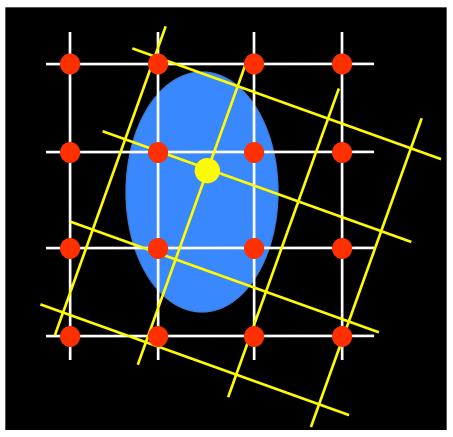
### Various types include

- Nearest Neighbour
- Trilinear
- Spline
- Sinc
- k-Space methods

Fast, with some blurring - most common option



### Finds intensity values between grid points

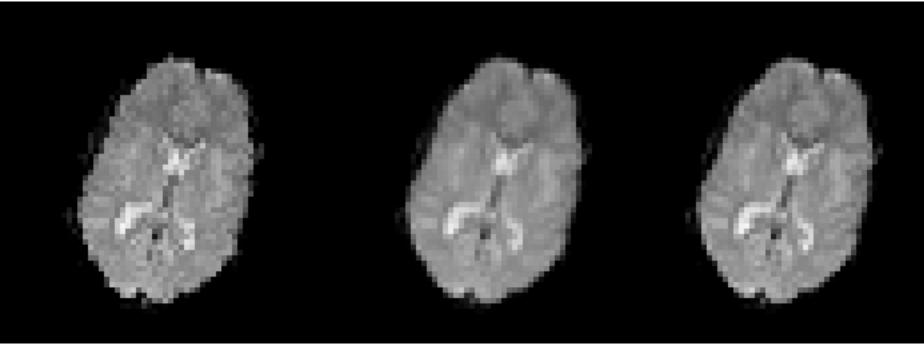


### Various types include

- Nearest Neighbour
- Trilinear
- Spline
- Sinc
- k-Space methods

Slower (spline is fairly fast) - creates sharp images but can create values outside the original range





Nearest Neighbour

Trilinear

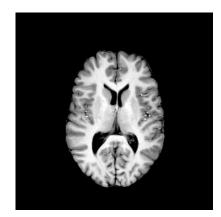
Spline

Affects accuracy of subsequent analysis Important for *quantitative imaging* Can affect size of artefacts

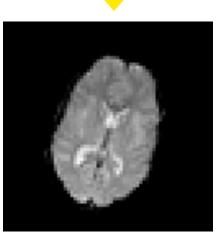


## **Applying Transformations**

- Step I: Estimating a transformation
  - finding the transformation
  - no resampling

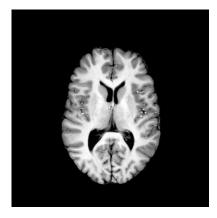


transfo<mark>rm</mark>ation

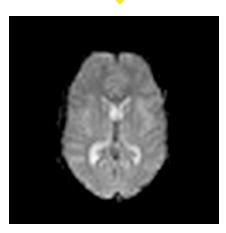


## **Applying Transformations**

- Step I: Estimating a transformation
  - finding the transformation
  - no resampling
- Step 2: Resampling
  - *applying* a transformation
  - thus creating a new, modified image
- "Registration" can mean either
- Usually delay resampling as it reduces image quality
- Other terms: coregistration & spatial normalisation



transformation





## Transforming Masks



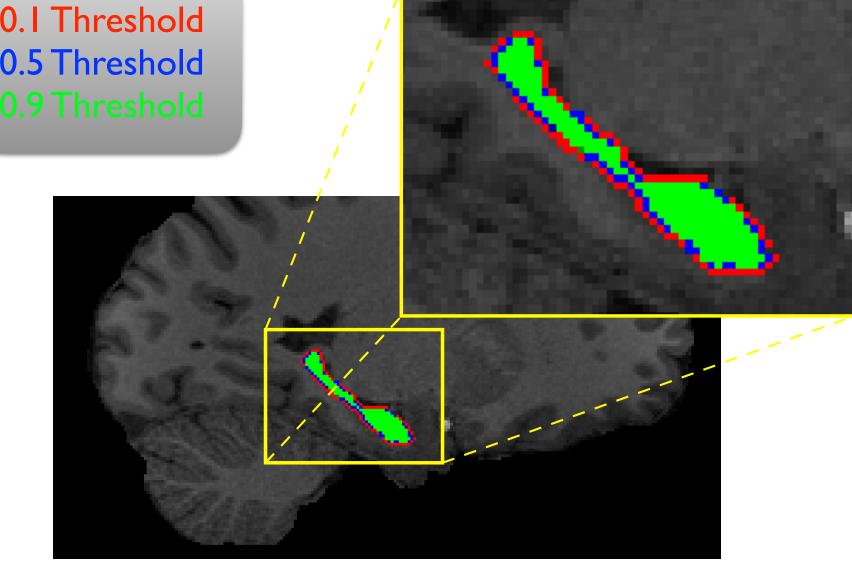
Ensure output datatype = float (applywarp & flirt default) Re-threshold (binarize) the transformed mask

"Correct" thresholding depends on the particular case Threshold near 0.0 to include partial-volume edges Threshold near 1.0 to exclude partial-volume edges Threshold at 0.5 to keep the same size (approx)



## **Transforming Masks**

**0.1** Threshold 0.5 Threshold





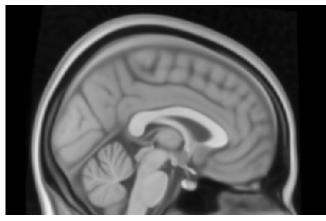
## Registration: Cost Functions, Interpolation and Masks

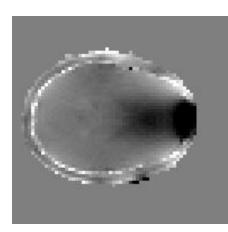
Summary:

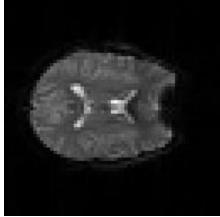
- Must choose an appropriate cost function
- Often many valid choices (depends on images)
- Interpolation used to resample images
- Often the interpolation is set within the tool
- When applying transforms want to minimise interpolation-related effects delay resampling
- Transforming masks requires attention to interpolation and thresholding - depends on task

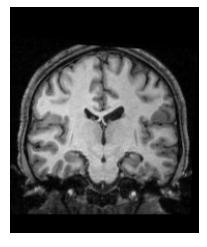


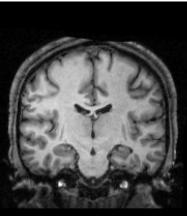
## Registration: Single-Stage and Multi-Stage Applications













## Registration with FSL

### Two main tools: FNIRT & FLIRT

(FMRIB's Non-Linear/Linear Image Registration Tool)

Misc Data Pre-stats Stats Post-stats Registration Initial structural image Main structural image structural_brain Linear Normal search = 6 DOF = Standard space /usr/local/fsl/data/standard/MNI152_T1_2mm_brain Linear Normal search = 12 DOF = Nonlinear = Warp resolution (mm) 10 =	First-level analysis 🥏 Full analysis 🚽						
Main structural image structural_brain Linear Normal search - 6 DOF - Standard space Ausr/local/fsl/data/standard/MNI152_T1_2mm_brain Linear Normal search - 12 DOF -	Misc	Data Pre-stats Sta	ts Post-stats	Registration			
Linear Normal search - 6 DOF - Standard space Ausr/local/fsl/data/standard/MNI152_T1_2mm_brain Linear Normal search - 12 DOF -		-					
Standard space          Ausr/local/fsl/data/standard/MNI152_T1_2mm_brain         Linear       Normal search	F	structural_brain		<u></u>	1		
/usr/local/fsl/data/standard/MNI152_T1_2mm_brain         Linear       Normal search			- 6 DOF -				
			/MNI152_T1_2mm	_brain 🔄			
Nonlinear 📁 Warp resolution (mm) 10 🚔	F	Linear Normal search	- 12 DOF -	1			
	Nonlinear 📁 Warp resolution (mm) 10 🚔						

#### 😑 😑 📉 FLIRT - FMRIB's Linear Image Registration Tool - v5.4.2

Mode Input image ->	Reference image 🛁	
Reference image	/usr/local/fsl/etc/standard/avg152T1_brain.hdr	
Model/DOF (input to	ref) Affine (12 parameter model) -	
Input image	/usr/local/feeds/data/structural.nii.gz	
Output image	/Users/mark/tmp/struct2avg	
Number of secondary	images to apply transform to 0	
Go	Exit	Utils

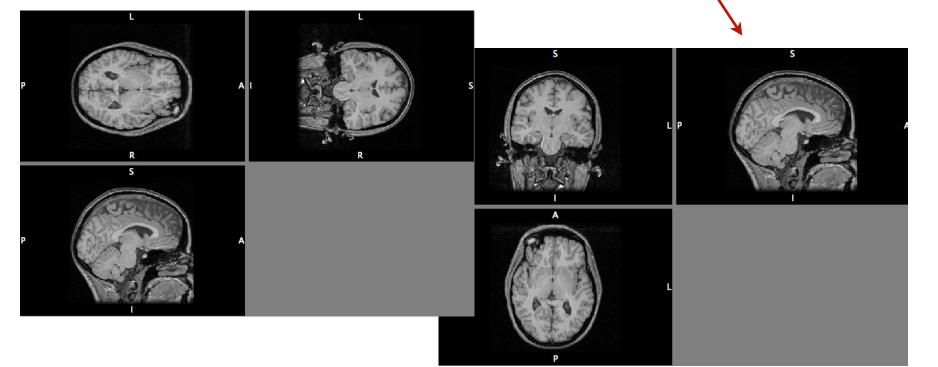
### Both tools used by FMRI and Diffusion tools (FEAT, MELODIC & FDT)



## Preliminary Steps

Recommended steps:

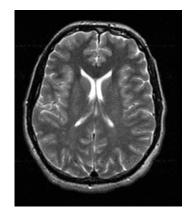
- Reorientation (fslreorient2std)
- Brain Extraction (BET)
- Bias-field correction (FAST see later)



#### Note that labels are correct in both cases



## Single-Stage Registration



Scenario:

Have two (or more) different types of images from the same subject
For example, T<sub>1</sub>-weighted and T<sub>2</sub>-weighted images

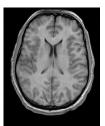
Objective:

Have images aligned so that, for example, they can be used for multi-modal segmentation

Solution: FLIRT with 6 DOF (rigid-body)



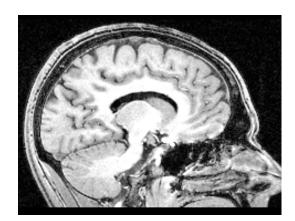
## Single-Stage Registration



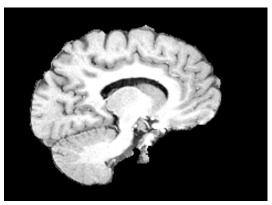
Reference

Input

- Single subject  $\Rightarrow$  6 DOF = FLIRT
- T<sub>2</sub>-wt to T<sub>1</sub>-wt ⇒ multi-modal cost function (e.g. default of correlation ratio)
- Run brain extraction on both images
- Choose image with better resolution or contrast as the reference
- Always check your output





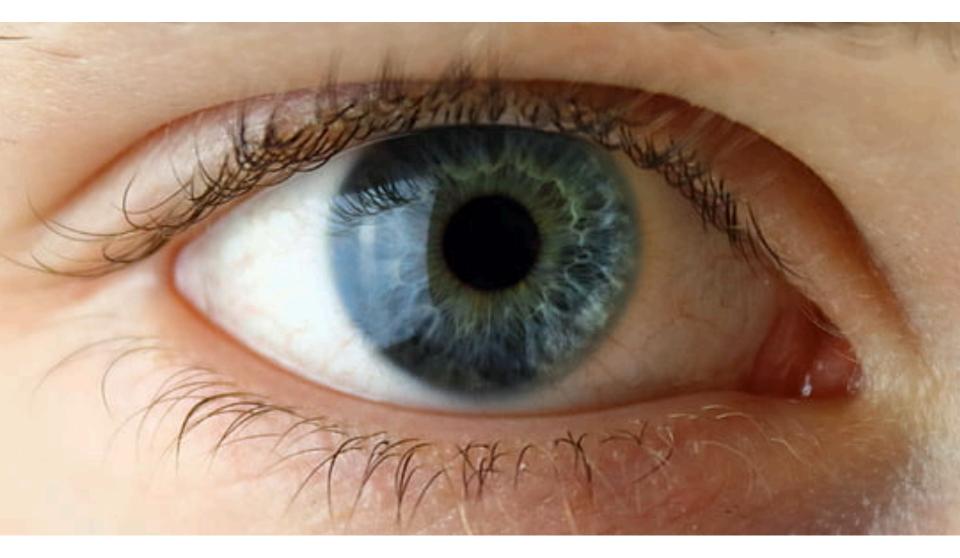




### Artefaction Detection Device



## LOOK AT YOUR DATA!





## Visual Check

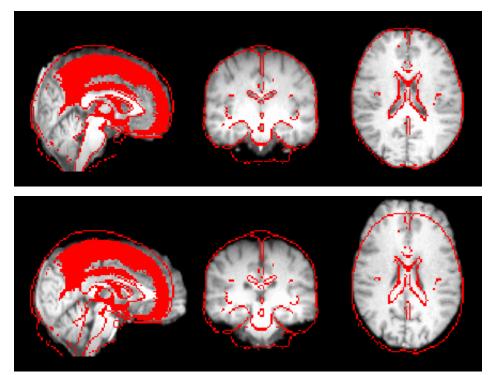
**<u>Always</u>** assess registration quality visually! Can use:

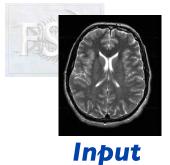
- FSLeyes (using overlay or flicking between images)
- slices for a static view use (as in FEAT)

#### slices T2\_to\_T1 im T1 im

Grayscale from first image

Red edges from second image





## **Registration in FSL**

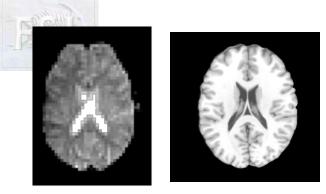


Reference

- In FSL the **reference image** controls the FOV and resolution of the output image
- Transformations are given:

from input space to reference space

- Inverse transformations can easily be calculated to go from reference space to input space when needed
- Can overlay images in FSLeyes with different FOV or resolution: i.e. images can be in different spaces and resolutions
- Images can be **resampled** into a different space by applying a previously derived transformation



Multi-Stage Registration



Scenario:

Doing a functional (or diffusion) study Have EPI and  $T_1$ -weighted of each subject

Objective:

Need to register images to a common (standard) space to allow the group study to be performed

Solution:

2-stage registration with FLIRT & FNIRT (in FEAT)



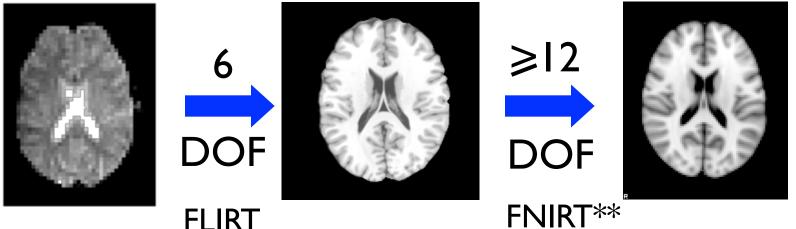
## Two Stage Registration

Registering very different images is difficult due to:

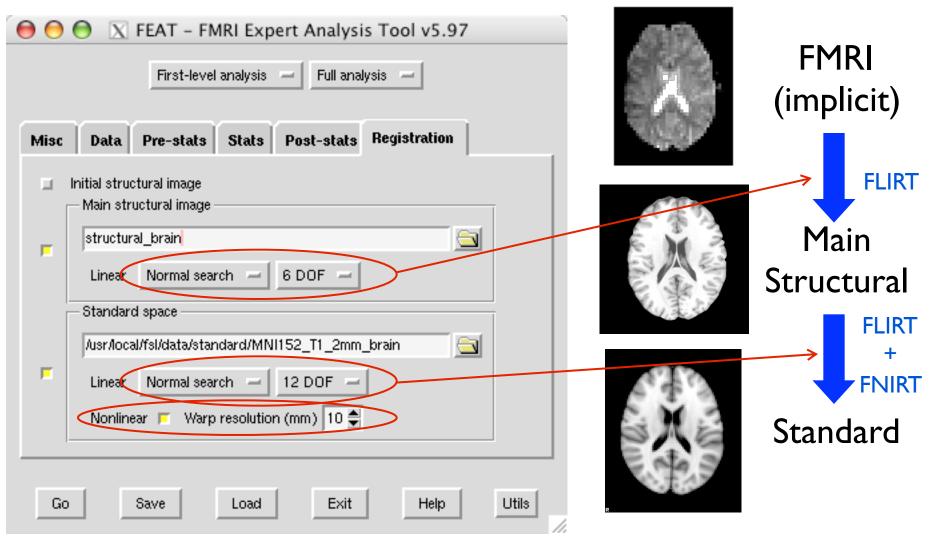
- Differences in individual anatomies
- Different contrasts in various modalities
- Distortions which differ between images

To register an EPI to a standard space template (e.g. MNII52) use a structural intermediate image

Automatically done by FEAT GUI (some user control) Need to manually run brain extraction (not on EPI usually\*)

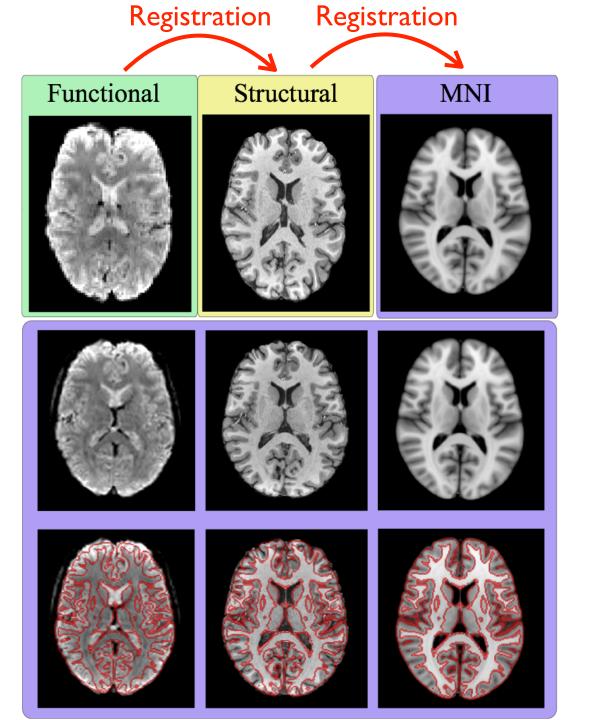


## **Registration for FMRI Analysis (FEAT)**

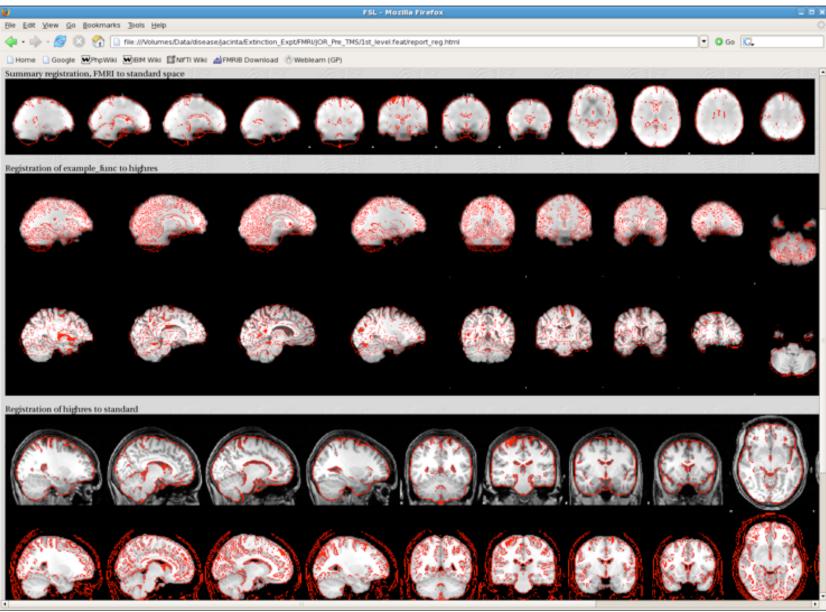


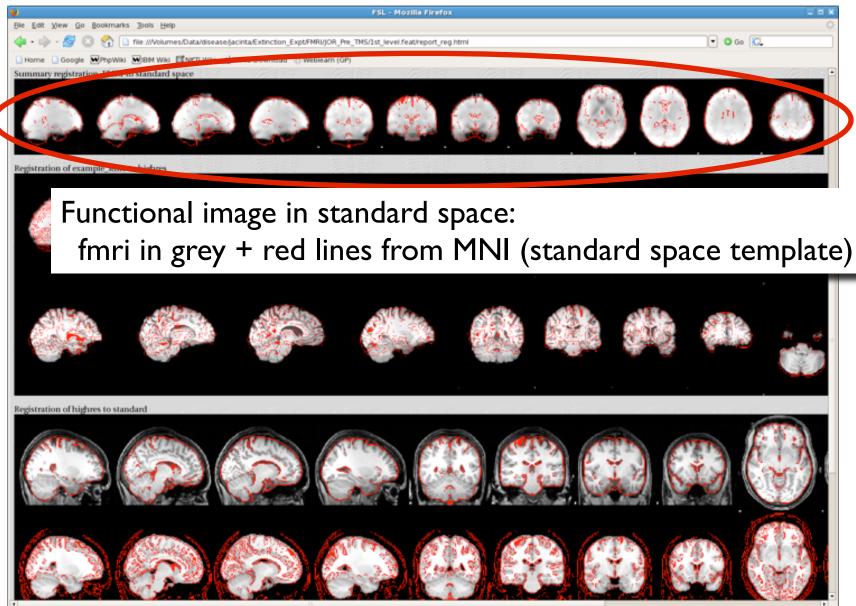
NB: actually need brain extracted **and** original images for FNIRT

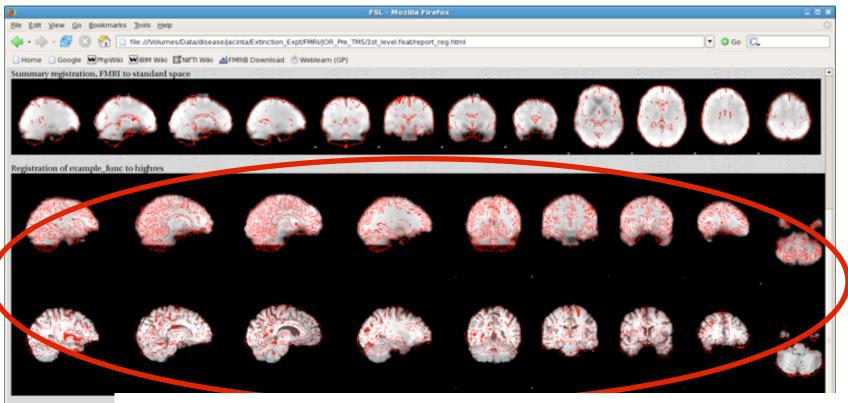


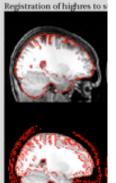


MNI Space



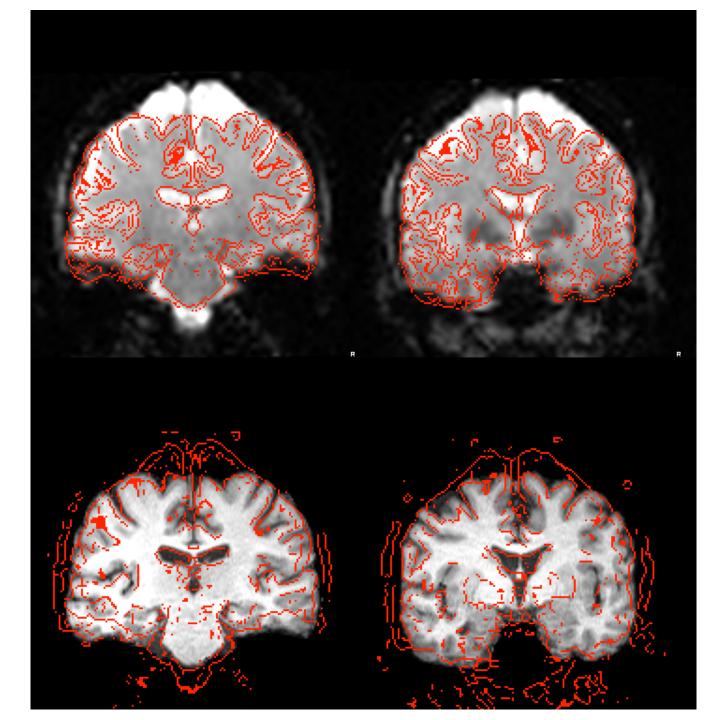


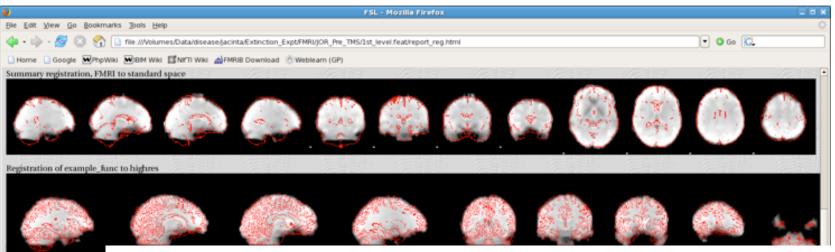


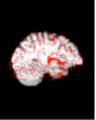


Example func (fmri) in highres (structural) space: top line = fmri in grey + red lines from structural bottom line = structural in grey + red lines from fmri Also: fsleyes highres example\_func2highres (in <u>reg</u> subdirectory of feat directory)

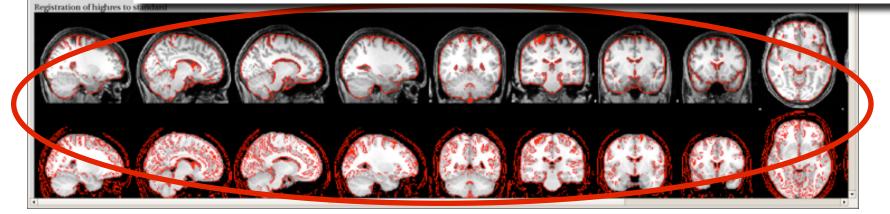




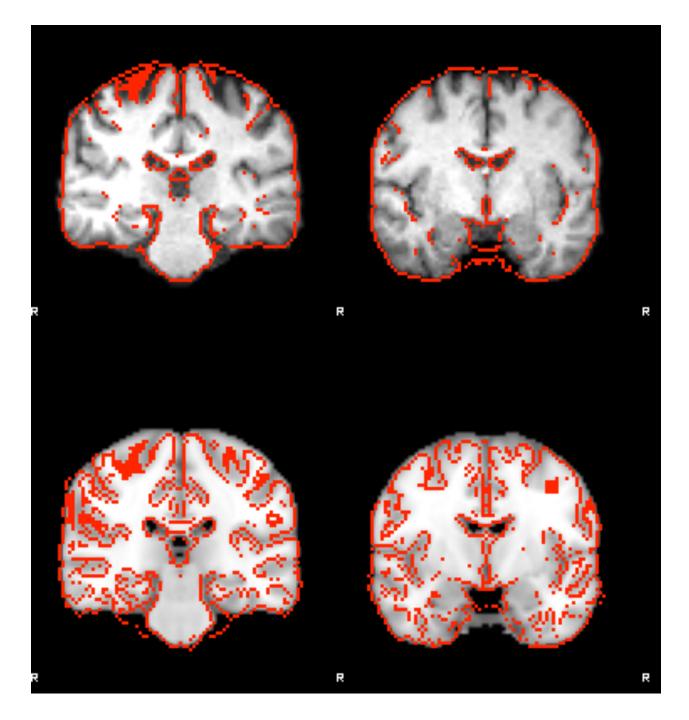




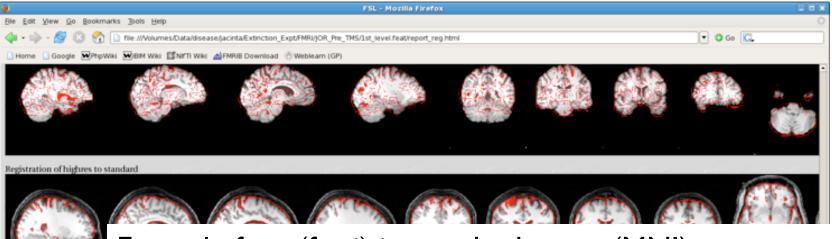
Highres (structural) in standard space (MNI) top line = structural in grey + red lines from MNI bottom line = MNI in grey + red lines from structural Also: fsleyes standard highres2standard

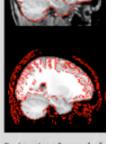




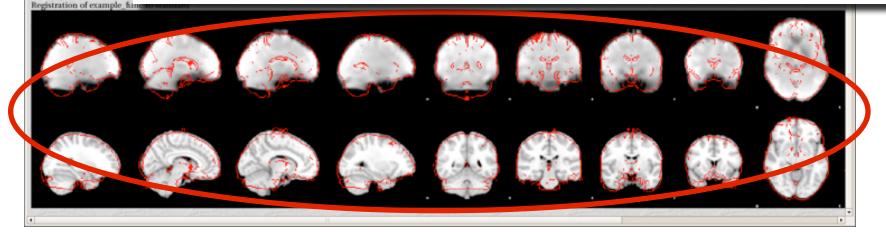


## **Registration for FMRI Analysis**

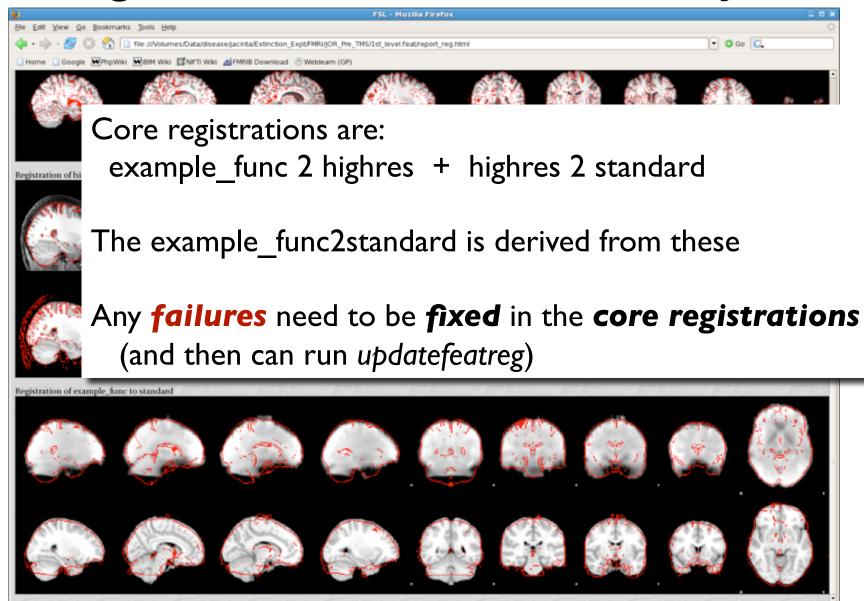




Example func (fmri) in standard space (MNI) top line = fmri in grey + red lines from MNI bottom line = MNI in grey + red lines from fmri Also: fsleyes standard example\_func2standard



## **Registration for FMRI Analysis**





## Registration: Single-Stage and Multi-Stage Applications

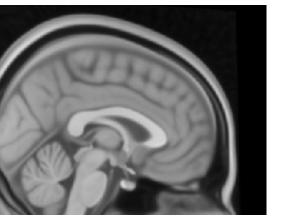
### Summary:

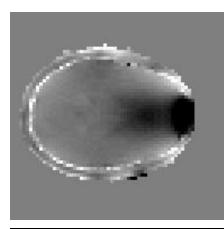
- Preliminary processing using reorientation, brain extraction and artefact correction (e.g. bias field)
- Single-stage for structural images: choose spatial transformation, cost function
- Important to **visually check** results!
- Multi-stage for multiple modalities/spaces
- Each stage benefits from fewer differences
- Evaluate results for each stage (and combined)

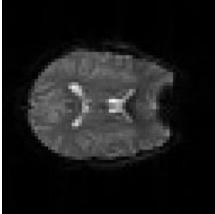


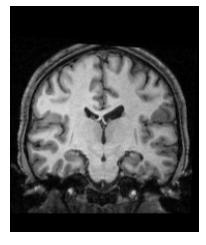
## Registration: EPI Distortion **Correction and Registration**

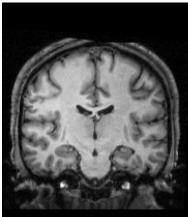


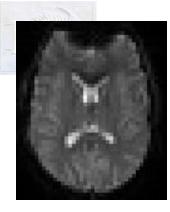




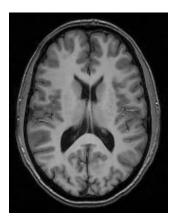








## EPI Distortion Correction



Scenario:

Doing a functional (or diffusion) study

Objective: Want to correct for distortions in EPI as otherwise the registrations are inaccurate

Solution:

Fieldmap-based correction using FUGUE/FEAT



## Registration of EPI

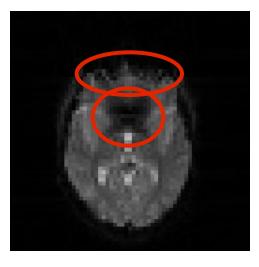
#### Problem:

- EPI images distorted and suffer signal loss
- standard registration does not work well

#### Solution:

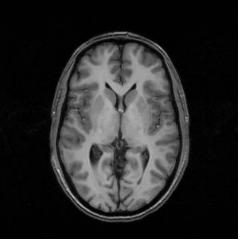
- undo distortion by "unwarping"
- ignore areas of high signal loss
- needs a **fieldmap** (special acquisition)

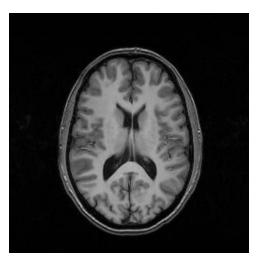
EPI





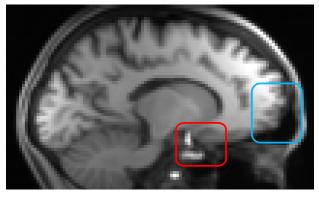
## T<sub>1</sub>-weighted anatomical

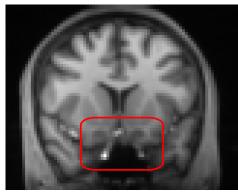


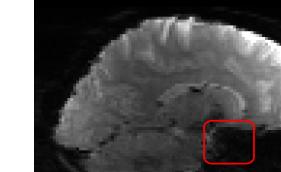




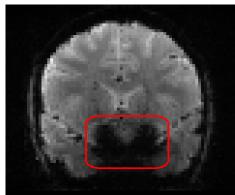
# TI-weighted (aligned)



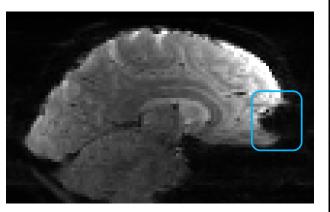


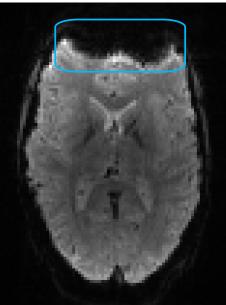






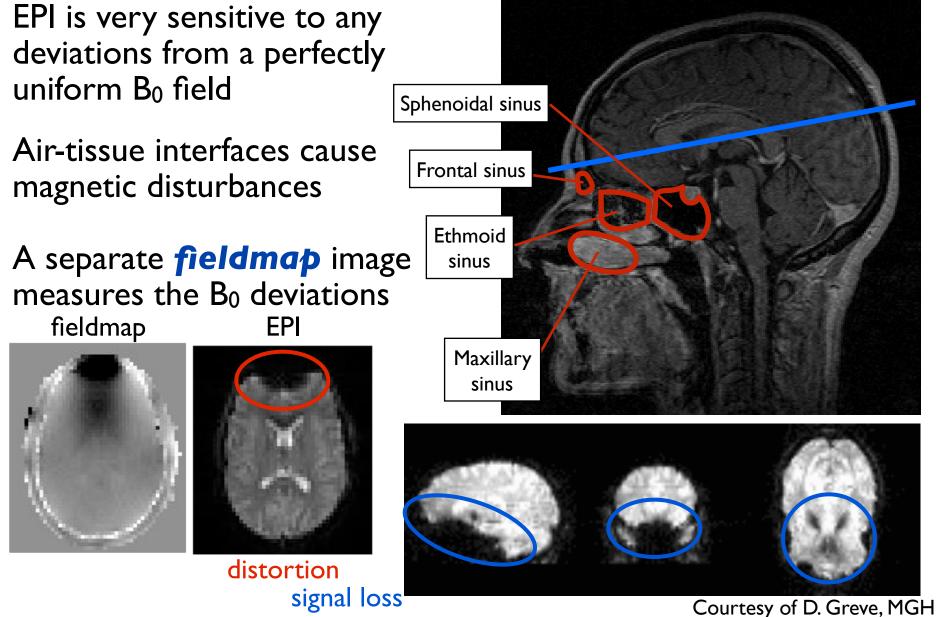
### Distortion







## **B**<sub>0</sub> Field Inhomogeneities





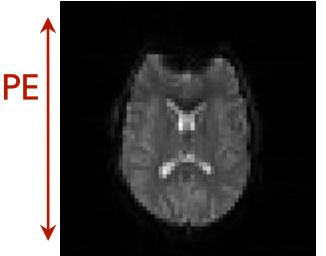
## Using Fieldmaps

From the fieldmap image we get:

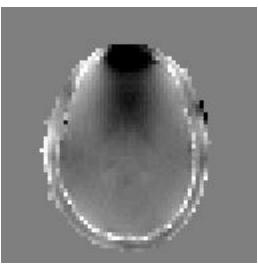
Magnitude of spatial distortions (phase-encode direction only) Estimate of signal loss

Only takes a few minutes to acquire one fieldmap - and it massively improves registration

Need a new fieldmap for each scanning session as it changes (e.g. it depends on head orientation)



EPI



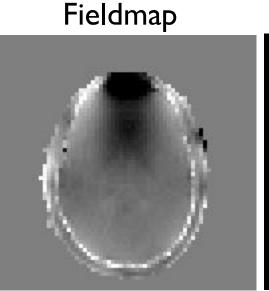
B<sub>0</sub> Fieldmap

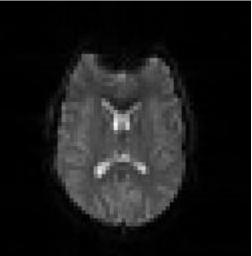


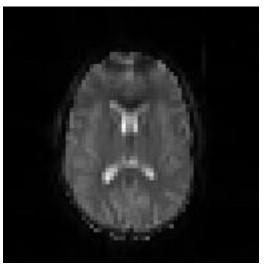
### Unwarping with Fieldmaps Fieldmap Original EPI

Used to improve **registration** of EPI and structural scan

It **does not** restore signal in the frontal lobe









#### Unwarping with Fieldmaps Fieldmap **Original EPI**

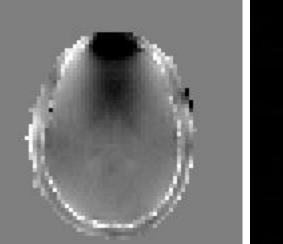
Used to improve registration of EPI and structural scan

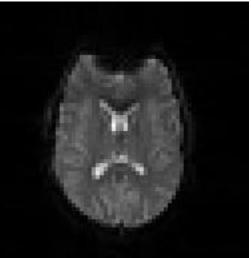
It **does not** restore signal in the frontal lobe

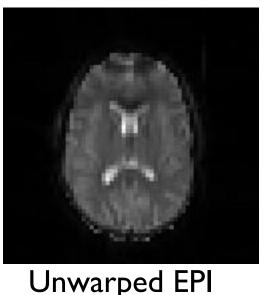
It **does not** do anything about motion correction

It **does** use fieldmap image to calculate distortion and "unwarp" EPI

It **does** deweight areas with substantial signal loss in the registration











## Fieldmap Acquisition

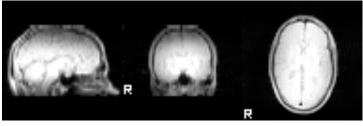
Fieldmaps are becoming standard sequences

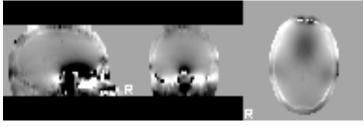
Only takes a few minutes to acquire - best either immediately before or after EPI scans (but this is not crucial)

Four main types of acquisitions:

- Gradient Echo
- Asymmetric Spin Echo
- EPI
- Blip-reversed b=0 pair (EPI)

Each based on a pair of images with different TE (record these TE values)





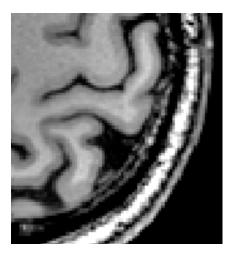
Magnitude part of fieldmap Phase difference of images Crucially requires the *phase information* (not only the magnitude, unlike the vast majority of other images)

Distortion & Signal Loss

## Boundary-Based Registration (BBR)

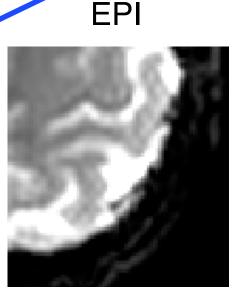
- *EPI to structural registration* (Greve & Fischl, NeuroImage, 2009)
  - incorporates *fieldmap* correction (previously FUGUE)
  - used in FEAT (B0 unwarping)
- Uses white-matter boundaries (via T1w segmentation)
  - Need good structurals (not too much bias field)
  - Also requires anatomical contrast in the EPI
  - Driven by intensity difference across boundary (samples)
- More robust to pathologies and artefacts in EPI

T1w



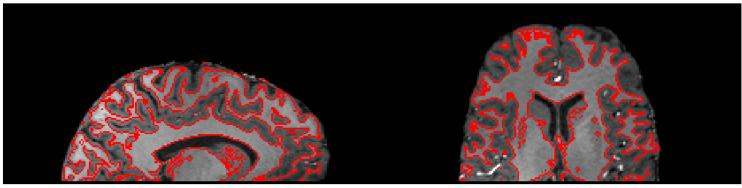
T1w + boundaries



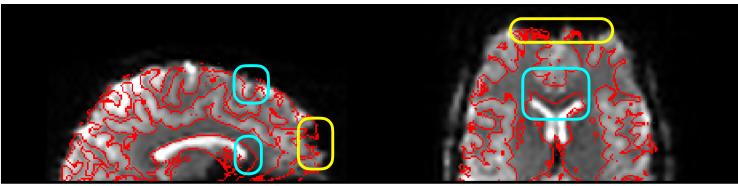


## **Distortion Correction**

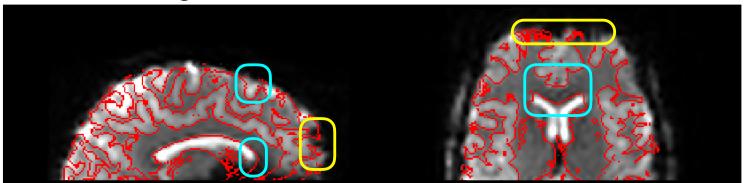
#### Structural Image



#### Registration without Distortion Correction



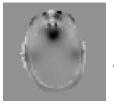
#### Registration with Distortion Correction

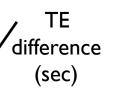


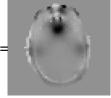
FEAT - FMRI Expert Analysis Tool v5.97			
First-level analysis – Full analysis –			
Misc Data Pre-stats Stats Post-stats Registration			
Motion correction: MCFLIRT -			
Fieldmap /home/mark/analysis/fmap_rads.nii.gz 🔄			
Fieldmap mag /home/mark/analysis/fmap_mag_brain.nii.gz			
Effective EPI echo spacing (ms) 0.68 🌻 EPI TE (ms) 40 🏺			
Unwarp direction _y % Signal loss threshold 10 🚔			
Slice timing correction: None 🛁			
BET brain extraction F			
Spatial smoothing FWHM (mm) 5			
Intensity normalization 🔲			
Temporal filtering 🛛 Perfusion subtraction 🔲 Highpass 💻 Lowpass 🔲			
MELODIC ICA data exploration 🔲			
Go Save Load Exit Help Utils			

¢		FEAT - FMRI Expert Analysis Tool v5.97	
		First-level analysis 🥏 Full analysis 🛁	
	Misc	Data Pre-stats Stats Post-stats Registration	
	Moti	B0 unwarping	
	•	Fieldmap /home/mark/analysis/fmap_rads.nii.gz	
		Fieldmap mag /home/mark/analysis/fmap_mag_brain.nii.gz 🔄	
		Effective EPI echo spacing (ms) 0.68 🚔 EPI TE (ms) 40 🚔	
		Unwarp direction 🤄 -y 🛁 % Signal loss threshold 10 🚔	
Slice timing correction: None -			
	BET	brain extraction 🗖	
	Spat	tial smoothing FWHM (mm) 5 🍧	
	Inter	nsity normalization 🔲	
		nporal filtering 🛛 Perfusion subtraction 🗔 Highpass 🗖 Lowpass 🗔	
	MEL	LODIC ICA data exploration 🔲	
	Go	o Save Load Exit Help Utils	









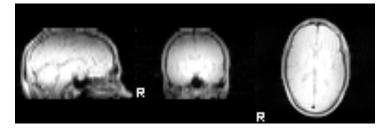
Phase difference (rad) B<sub>0</sub> Field (rad/s)

Need to prepare the fieldmap image: Fsl\_prepare\_fieldmap (for Siemens)

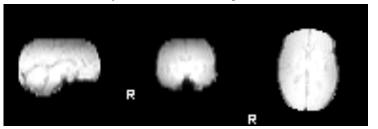


FEAT - FMRI Expert Analysis Tool v5.97			
First-level analysis — Full analysis —			
Misc Data Pre-stats Stats Post-stats Registration			
Motion correction: MCFLIRT -			
Fieldmap /home/mark/analysis/fmap_rads.nii.gz			
Fieldmap mag /home/mark/analysis/fmap_mag_brain.nii.gz			
Effective EPI echo spacing (ms) 0.68 🌻 EPI TE (ms) 40 🍧			
Unwarp direction _y % Signal loss threshold 10 🌻			
Slice timing correction: None -			
BET brain extraction 🔽			
Spatial smoothing FWHM (mm) 5			
Intensity normalization			
Temporal filtering Perfusion subtraction 🔲 Highpass 🗖 Lowpass 🗐			
MELODIC ICA data exploration			
Go Save Load Exit Help Utils			

Input file = brain extracted file ... but also needs to find original\* Fieldmap in rad/s Fieldmap Magnitude ... needs this ...



... and aggressive BET (leave **no** non-brain) for best performance



FEAT - FMRI Expert Analysis Tool v5.97	
First-level analysis – Full analysis – Misc Data Pre-stats Stats Post-stats Registration	Fieldmap in rad/s
Motion correction: MCFLIRT - B0 unwarping Fieldmap /home/mark/analysis/fmap_rads.nii.gz	Fieldmap Magnitude
Fieldmap mag /home/mark/analysis/fmap_mag_brain.nii.gz         Effective EPI echo spacing (ms)       0.68         Unwarp direction       -y         % Signal loss threshold       10	→ <u>EPI</u> echo spacing (ms)
Slice timing correction: None -	Also called dwell time
Spatial smoothing FWHM (mm) 5	Normally about 0.5-0.7ms
Temporal filtering Perfusion subtraction 🔲 Highpass 💻 Lowpass 🔲 MELODIC ICA data exploration 🔲	
Go Save Load Exit Help Utils	Time between
Divide value by any acceleration factor	space

FEAT - FMRI Expert Analysis Tool v5.97
First-level analysis — Full analysis —
Misc Data Pre-stats Stats Post-stats Registration
Motion correction: MCFLIRT - B0 unwarping
Fieldmap /home/mark/analysis/fmap_rads.nii.gz
Fieldmap mag /home/mark/analysis/fmap_mag_brain.nii.gz
Effective EPI echo spacing (ms) 0.68 CEPI TE (ms) 40
Unwarp direction 🤄 🤟 % Signal loss threshold 10 🚔
Slice timing correction: None -
BET brain extraction 📕
Spatial smoothing FWHM (mm) 5
Intensity normalization 🔲
Temporal filtering Perfusion subtraction 💷 Highpass 트 Lowpass 💷
MELODIC ICA data exploration
Go Save Load Exit Help Utils

Fieldmap in rad/s Fieldmap Magnitude EPI echo spacing (ms) EPI echo time (ms) Normally about 30-40ms at 3T

FEAT - FMRI Expert Analysis Tool v5.97	
First-level analysis 🚽 Full analysis 🚽	
Misc Data Pre-stats Stats Post-stats Registration	
Motion correction: MCFLIRT -	
B0 unwarping	
Fieldmap /home/mark/analysis/fmap_rads.nii.gz	
Fieldmap mag /home/mark/analysis/fmap_mag_brain.nii.gz	
Effective EPI echo spacing (ms) 0.68 🚔 EPI TE (ms) 40 🚔	
Unwarp direction -y - 🔀 Signal loss threshold 10 🌻	
Slice timing correction: None -	
BET brain extraction <b>F</b>	
Spatial smoothing FWHM (mm) 5	
MELODIC ICA data exploration 💷	
Go Save Load Exit Help Utils	

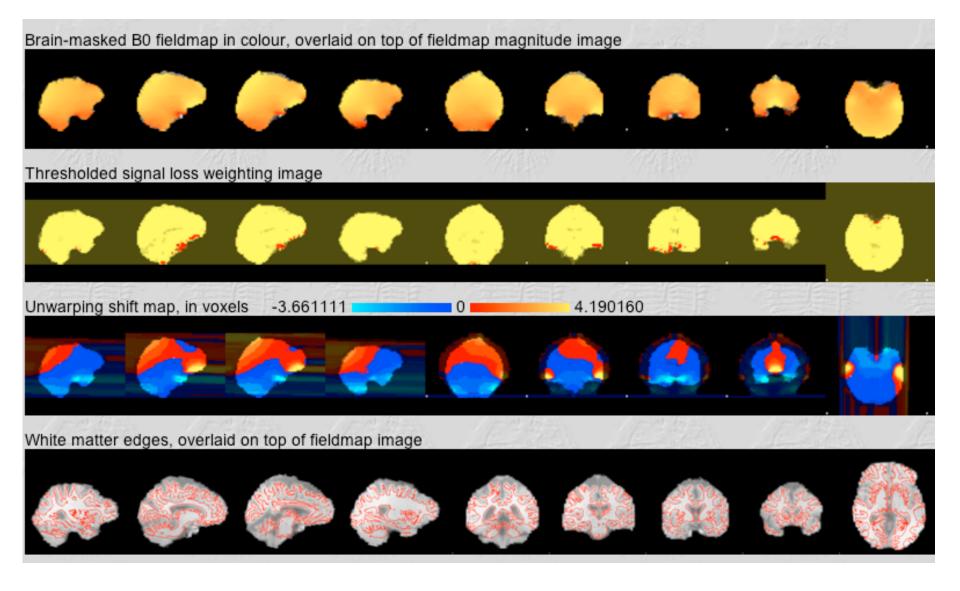
Fieldmap in rad/s Fieldmap Magnitude EPI echo spacing (ms) EPI echo time (ms) Unwarp (PE) direction - Often A-P but can be anything - Cannot tell if it is + or -- Try both and see what works (see practical)

FEAT - FMRI Expert Analysis Tool v5.97
First-level analysis 🚽 Full analysis 🚽
Misc Data Pre-stats Stats Post-stats Registration
Motion correction: MCFLIRT -
B0 unwarping
Fieldmap /home/mark/analysis/fmap_rads.nii.gz
Fieldmap mag /home/mark/analysis/fmap_mag_brain.nii.gz
Effective EPI echo spacing (ms) 0.68 🚔 EPI TE (ms) 40 🚔
Unwarp direction -y - % Signal loss threshold 10 🗧
Slice timing correction: None -
BET brain extraction F
Spatial smoothing FWHM (mm) 5
Intensity normalization 🗖
Temporal filtering Perfusion subtraction 🔲 Highpass 💻 Lowpass 💷 🗌
MELODIC ICA data exploration 💷
Go Save Load Exit Help Utils

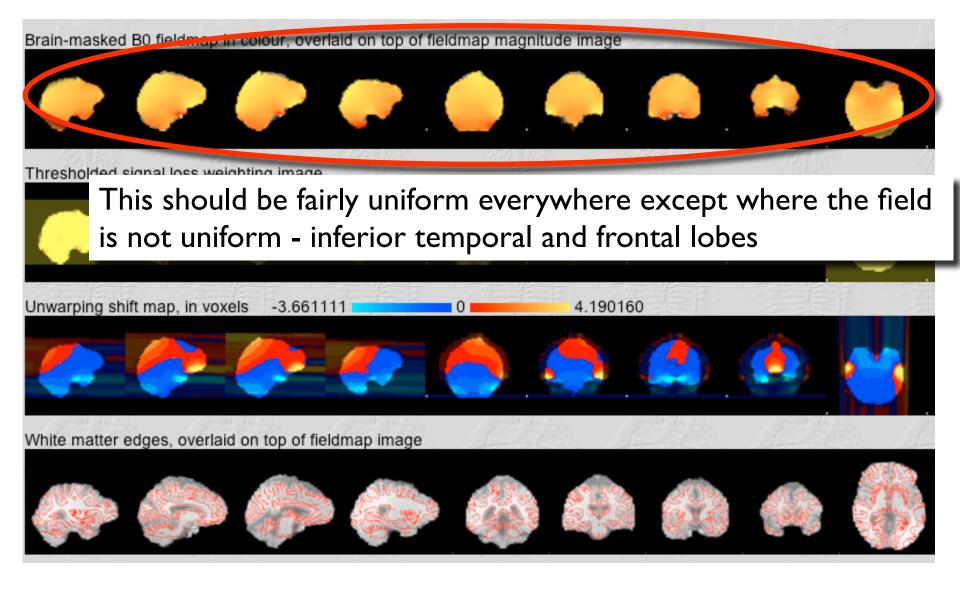
Fieldmap in rad/s Fieldmap Magnitude EPI echo spacing (ms) EPI echo time (ms) Jnwarp (PE) direction Signal loss thresh % Ignore voxels with more than

this signal loss in registration

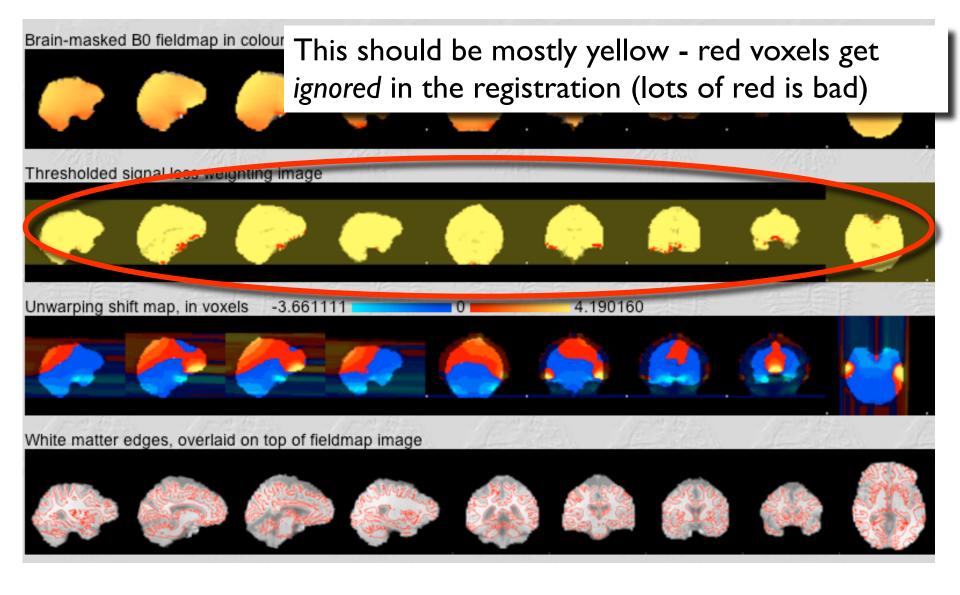




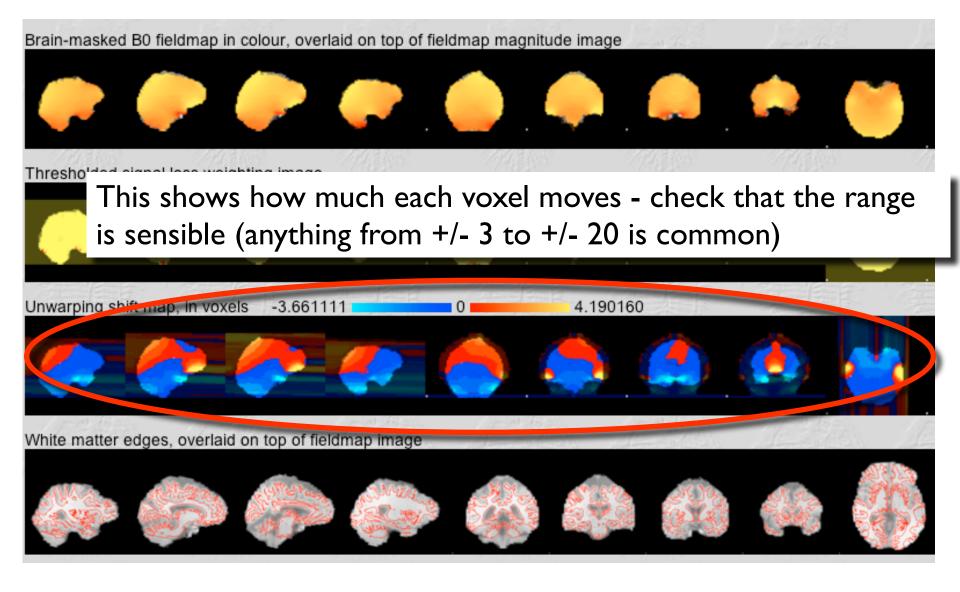




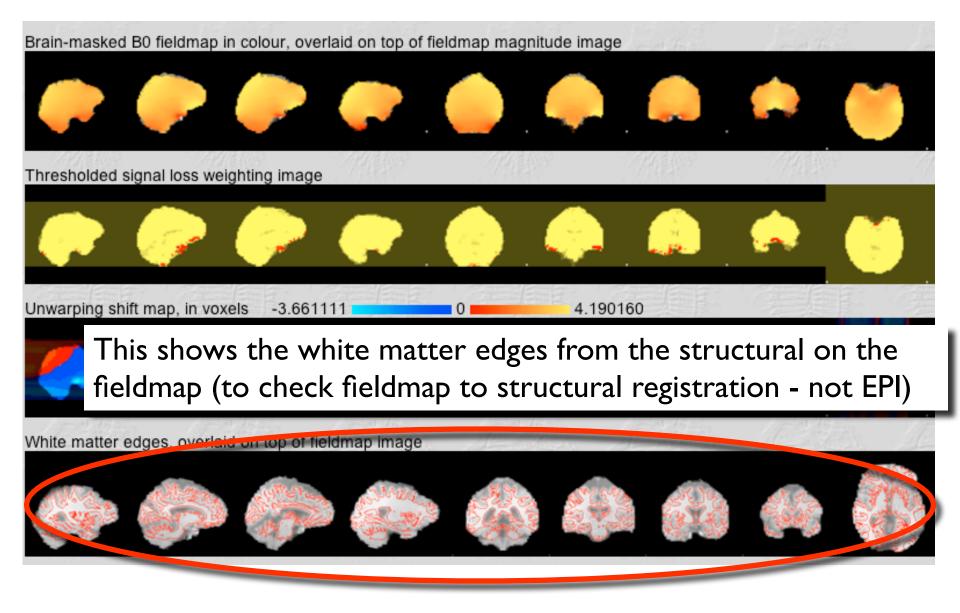




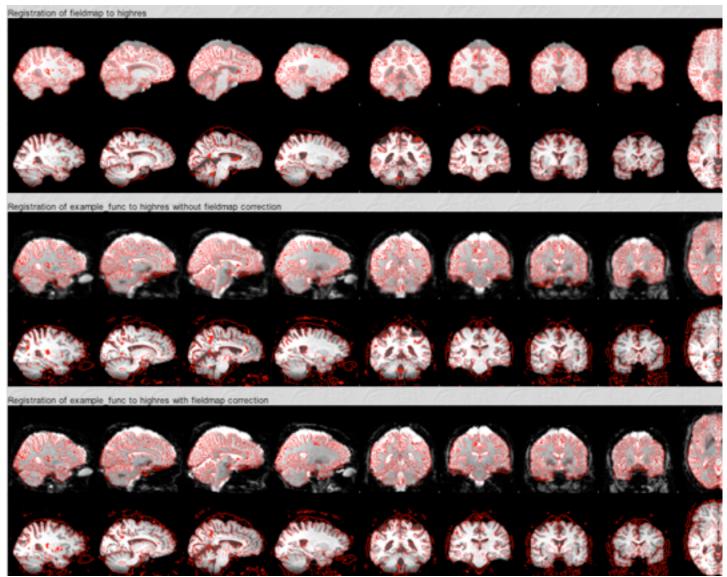










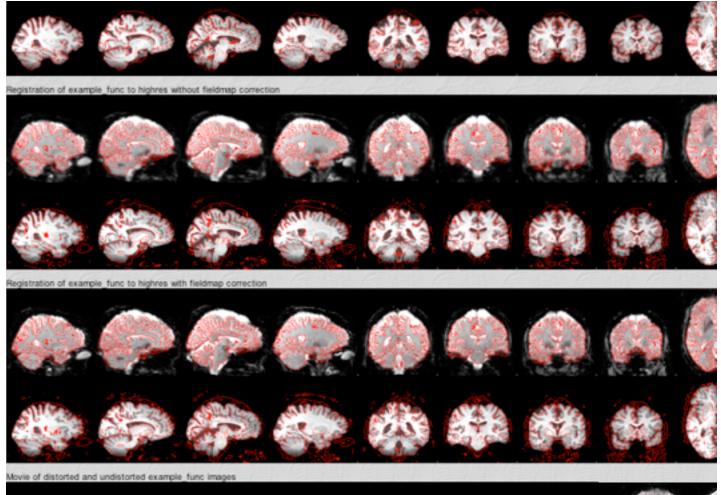


Fieldmap to highres (structural)

Functional (EPI) to highres (structural) - no correction

Functional (EPI) to highres (structural) - with fieldmap correction





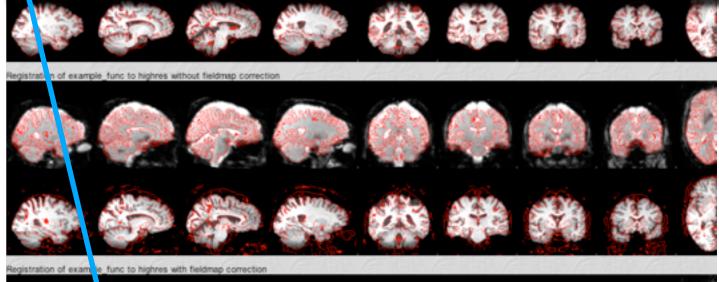
Functional (EPI) to highres (structural) - no correction

Functional (EPI) to highres (structural) - with fieldmap correction

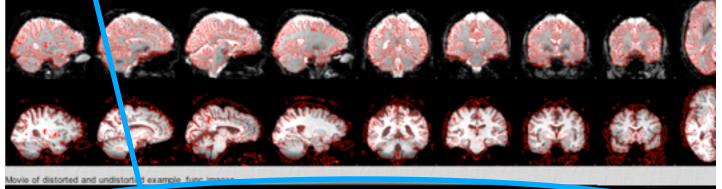
Movie of EPI with and without correction

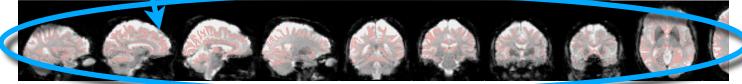


#### Look for areas where unwarping (correction) changes brain shape

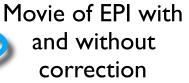


Functional (EPI) to highres (structural) - no correction





Functional (EPI) to highres (structural) - with fieldmap correction

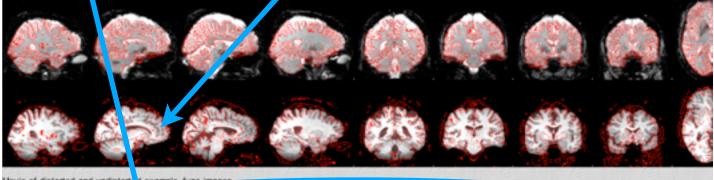




Look for areas where unwarping (correction) changes brain shape

See if these areas are better aligned with or without correction but don't trust borders with signal loss areas NB: Using FSLeyes is often better



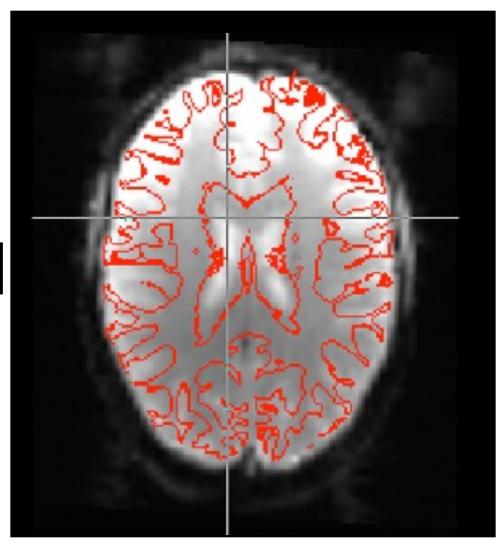


- with fieldmap correction

Functional (EPI) to highres (structural) - no correction

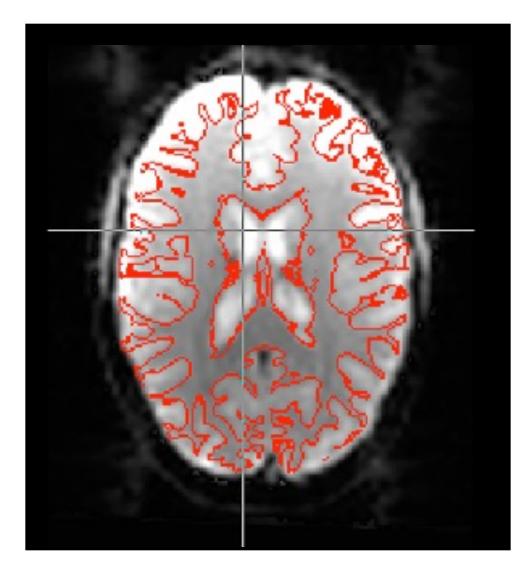
Movie of EPI with and without correction





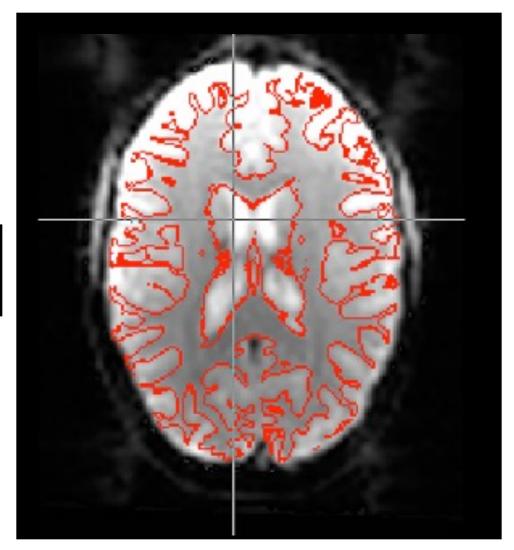
Standard FLIRT







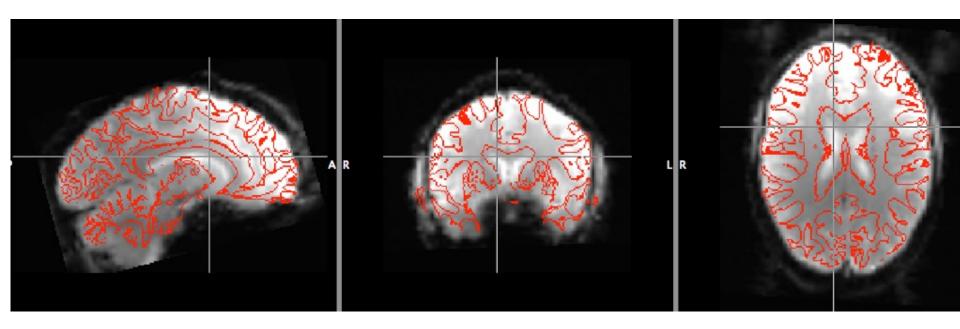




#### BBR FLIRT with Fieldmap

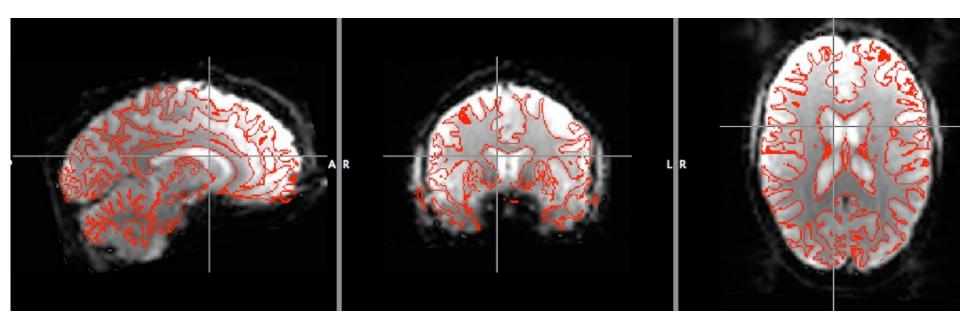


#### Standard FLIRT





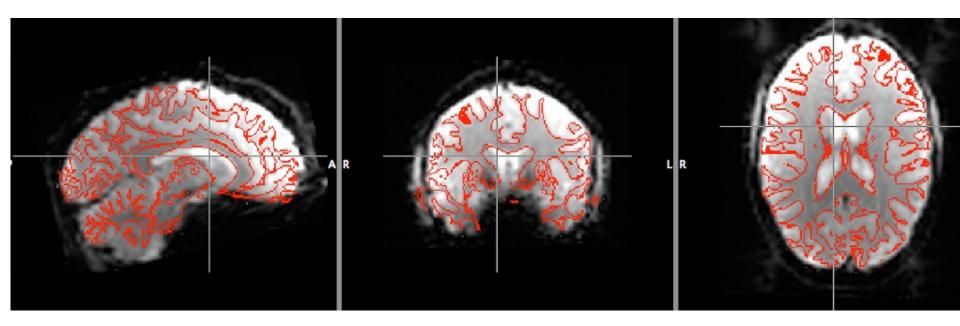






#### **BBR** and Fieldmaps

#### BBR FLIRT with Fieldmap





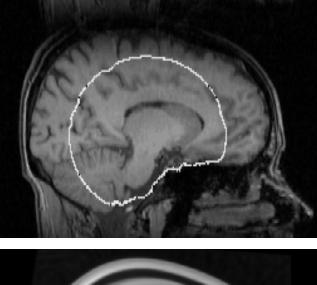
#### Registration: EPI Distortion Correction and Registration

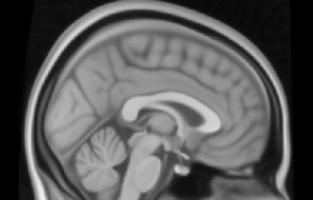
Summary:

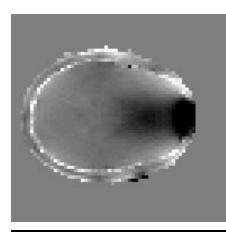
- Geometric distortions and signal dropouts affect fMRI acquisitions (using EPI)
- We can correct for geometric distortions and take account of signal loss using fieldmaps
- BBR is the cost function used for EPI-structural registration with fieldmaps
- Look at results in typical areas of distortion (inferior frontal and temporal lobes)

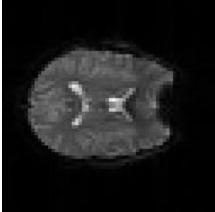


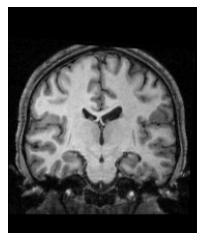
#### Registration: Cost Function Weighting and Small FOV

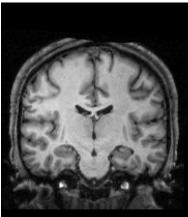














### Pathological Image Registration



Scenario:

Have images containing a known pathology (or artefact) which looks different in different imagesFor example, some sequences (e.g. FLAIR) highlight lesions that are hard to see in other sequences

Objective:

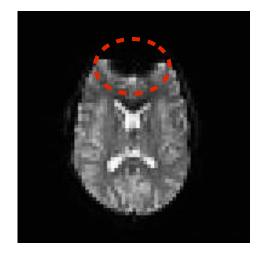
Align the images based on the healthy tissue, but "ignoring" the area of the pathology (or artefact)

Solution:

Cost-Function Weighting (FLIRT or FNIRT)



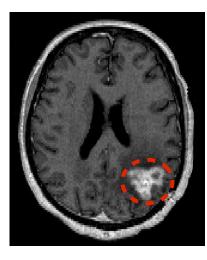
### **Cost Function Weighting**

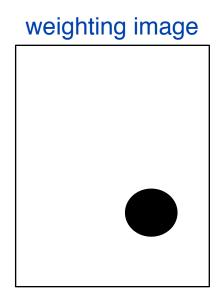


Artefacts and pathologies introduce *non-matching* image regions

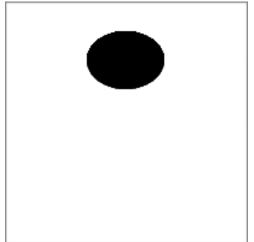
Cost (similarity) functions assume that all of the images can be matched

Use a *weighting image* to down-weight nonmatching regions





weighting image



black=0; white=1

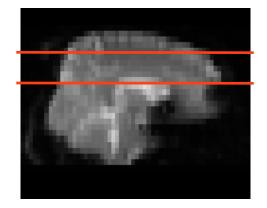


#### **Cost Function Weighting**

- All FLIRT & FNIRT cost functions can be weighted
- Weighting for reference image, input image or both
- Voxel weights are *relative*, reflecting its importance in overall matching
  - Zero, or small, values for corrupted areas e.g. gross pathology or artefact
  - Large values for important areas/regions e.g. ventricular matching
- Do not assign zero to the background as then the brain/background contrast is lost



#### Small FOV Registration



Scenario:

Functional study using a small FOV (e.g. a few slices) Often done to obtain better resolution scans over ROI

Objective:

Get activation results registered well to the full brain (and standard space)

Solution:

Scan one whole-brain EPI and use a 3-stage registration

If your FMRI scans only cover part of the brain...

Acquire one wholebrain EPI volume: it only takes a few seconds to scan but makes registration work much better

Then use the 3-stage approach

		First-level analysis — Full analysis —
	Misc	Data Pre-stats Registration Stats Post-stats
		Expanded functional image
	( _	epi_whole_brain
*		Linear Normal search - 3 DOF (translation-only)
	F	Main structural image
		structural_brain
		Linear Normal search - BBR -
	[	Standard space
		/usr/local/fsl/data/standard/MNI152_T1_2mm_brain
		Linear Normal search - 12 DOF -
		Nonlinear 🗖
	G	o Save Load Exit Help Utils

## Partial Brain EPI & Unwarping

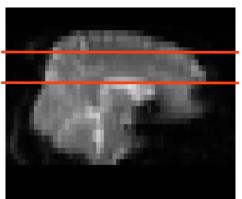
In partial FOV studies, registration is *massively* improved by multi-stage registration: I. Partial Brain to Full Brain EPI

- Desirable for full brain to contain exactly the same slices so that registration is simple (can be done without unwarping)
- If slices are different or movement is significant, then unwarping should be applied (outside of FEAT)
- 2. Full Brain EPI to Structural
  - apply unwarping (full brain field map)
- 3. Structural to Standard

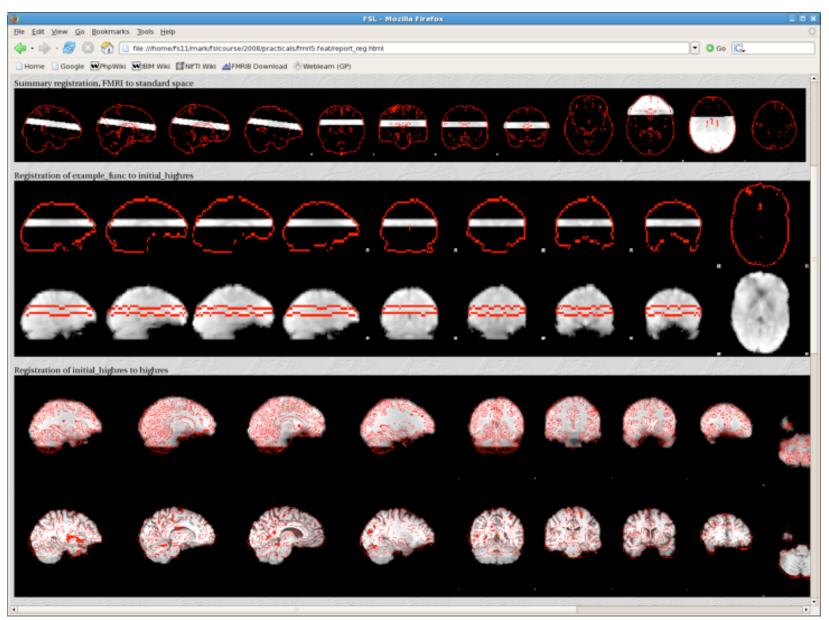
Can be run entirely within the FEAT GUI

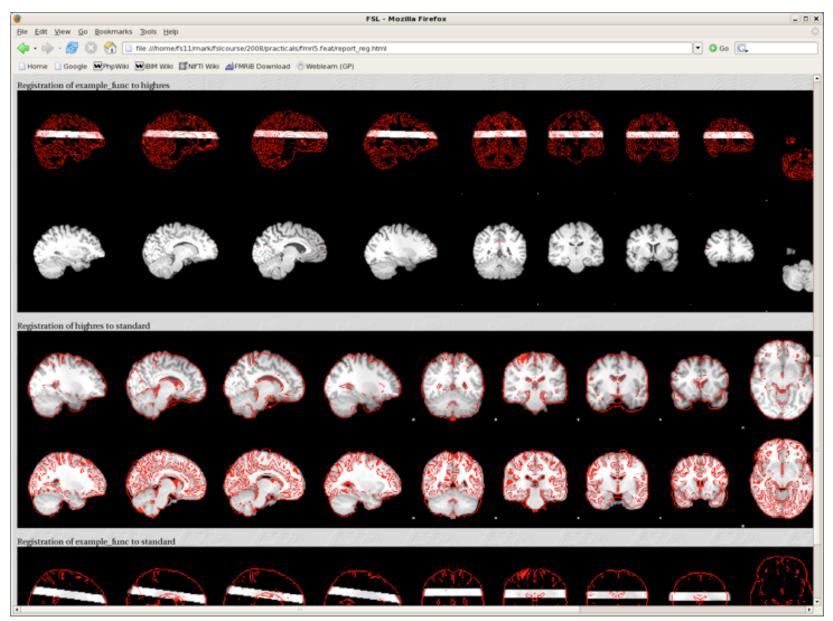


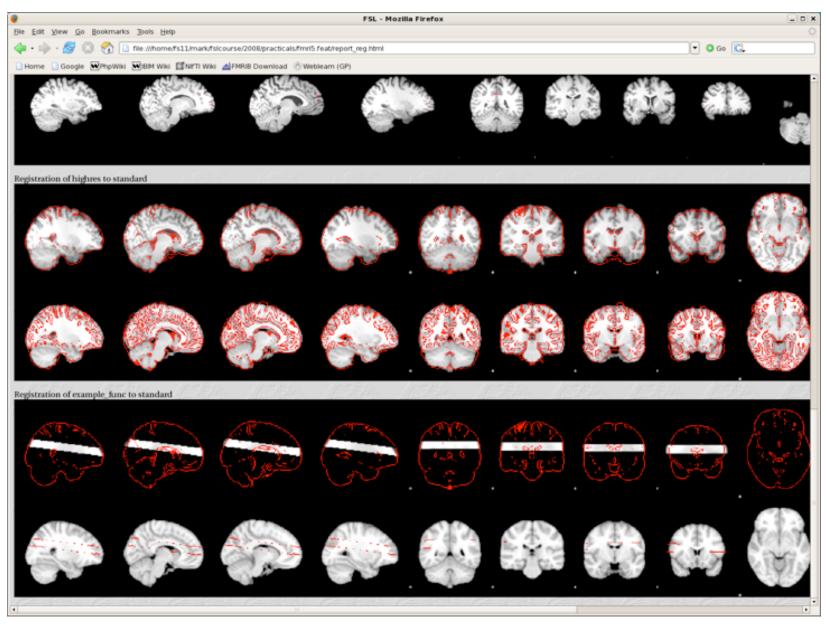
Partial Brain **FMRI** timeseries



**Full Brain** Single Image (an extra acquisition but only takes seconds!)







# BS

### **Troubleshooting Registrations**

- Check the images: voxel sizes, artefacts, large bias field
- Check the brain extraction: look for large/consistent errors
- For EPI: acquire and use fieldmap to unwarp distortion
- For FMRI or diffusion: use multi-stage registration (e.g. via GUIs) with a structural image for best results
- If pathologies/artefacts exist: use cost-function deweighting
- If images are nearly aligned: try limiting the search
- For FLIRT: can try different cost functions
- For FNIRT: check initial affine alignment is OK
- For small FOV: acquire whole-brain EPI for multi-stage reg