

MRI Data Processing

Course on signal and image
processing (FFYS7086)

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**UNIVERSITY
OF TURKU**

Learning goals

Basic understanding in:

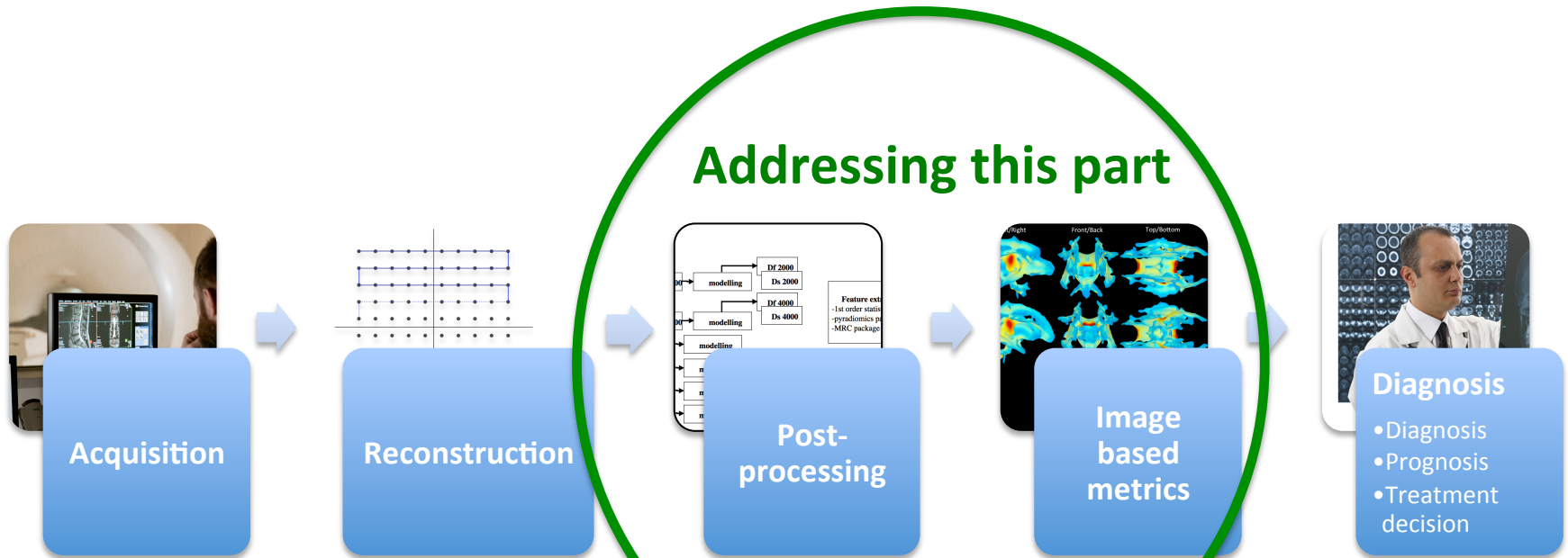
- How MRI data is organized
- Goals of MR image processing
- Concepts of common MRI data processing steps

- Tool(s) useful for each particular processing step, are marked with ***blue bold font***

In zoom session, please leave questions/comments to the chat, I will answer them at the end of the talk



What is post-processing and why it is important?



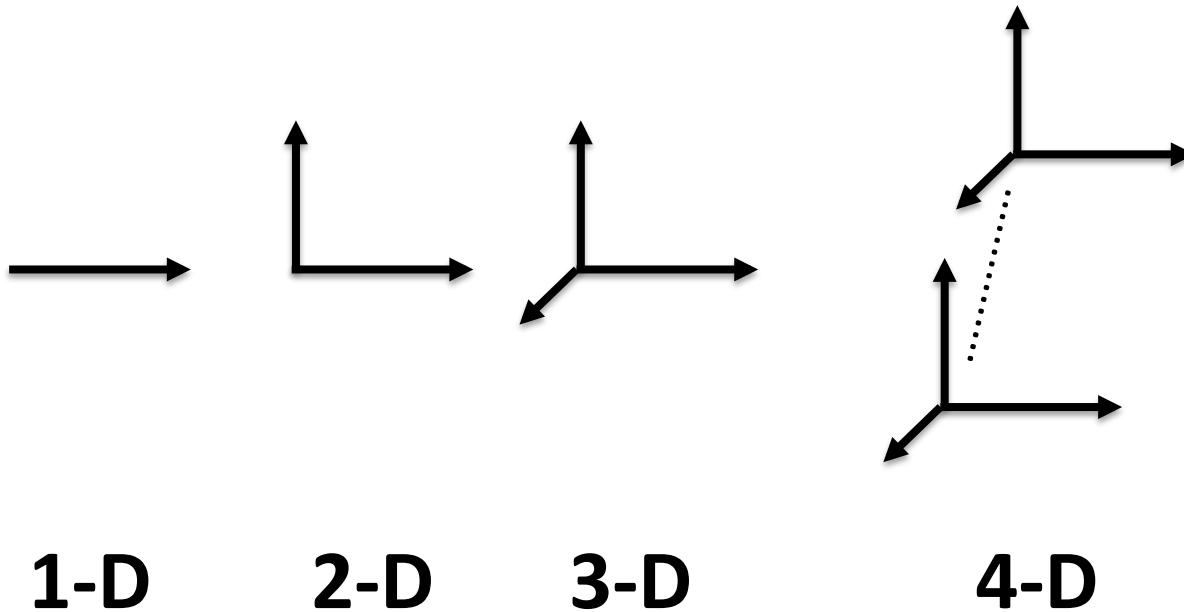
Goals of post-processing:

- Assure data quality
- Salvage otherwise unusable or dubious data
- Apply model fitting to obtain their specific parameters
- Compose information not available with mere manual inspection

Outline

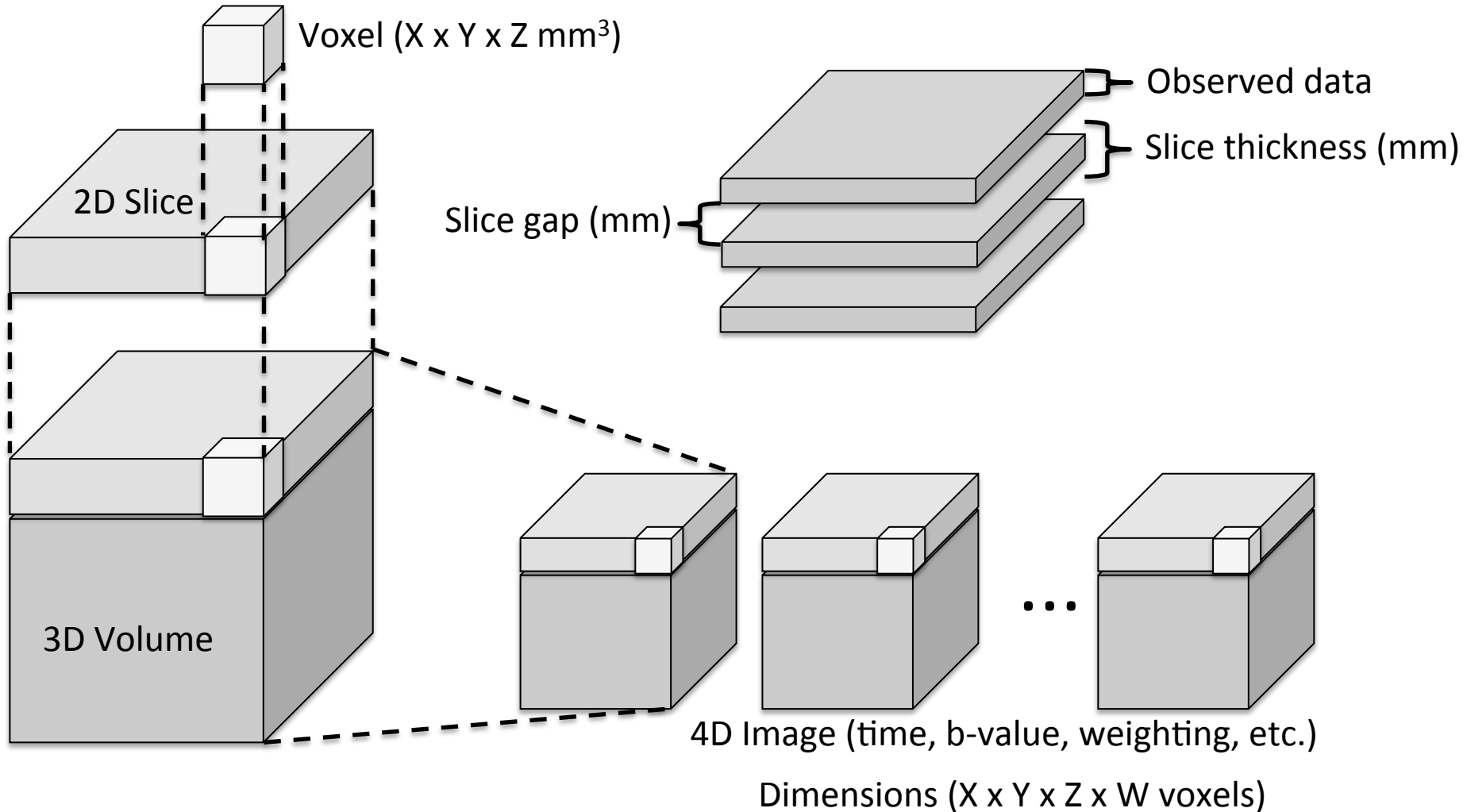
- 1 Data organization
- 2 MR Data modalities
- 3 Image formats
- 4 Quality Assurance
- 5 Image processing steps
- 6 Radiomics
- 7 Artificial Intelligence

1 Data organization



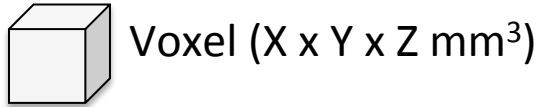
Data organization: Components

Medical imaging data is multi-dimensional signal

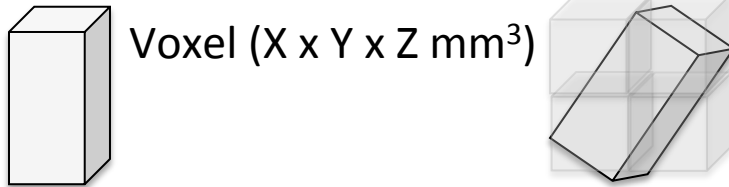


Data: Continued

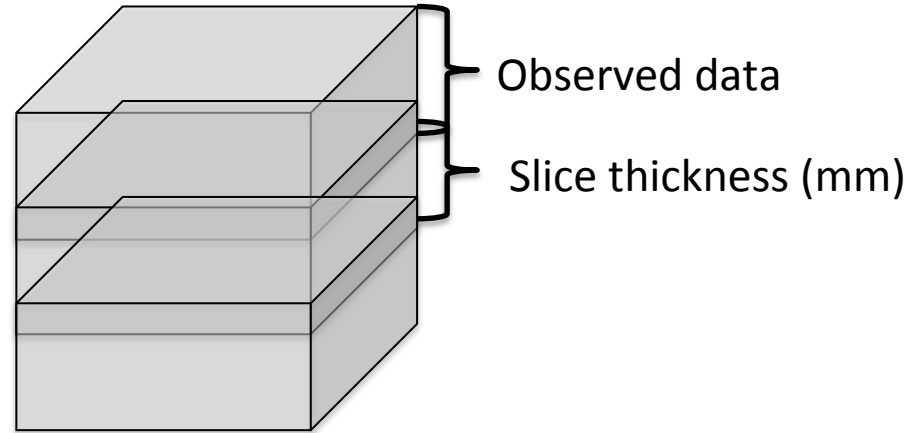
Isotropic voxel



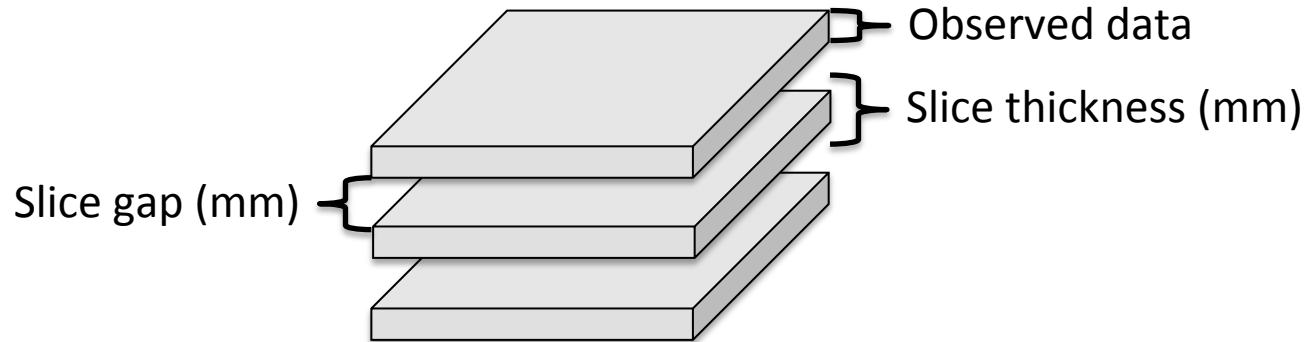
Anisotropic voxel



Oversampled acquisition



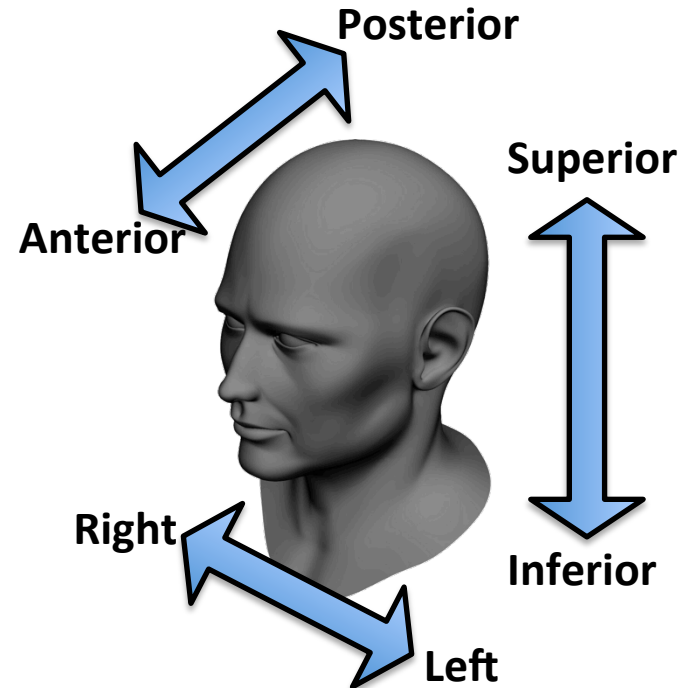
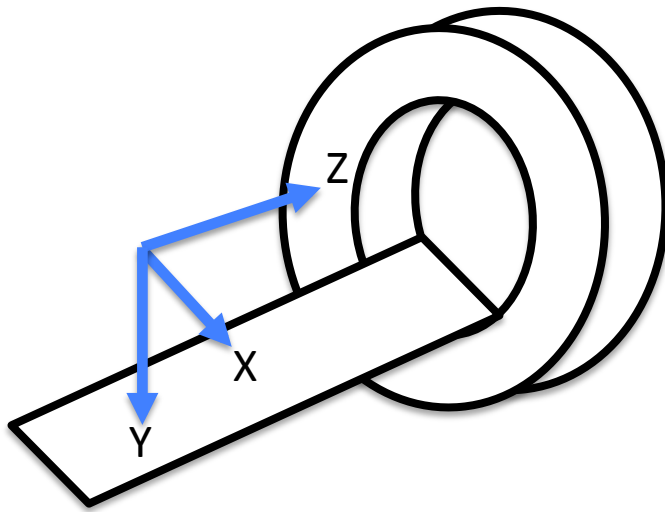
Undersampled acquisition



- Voxel shape and sampling is important when analysis considers information in 3D
- Slice gap and anisotropic voxel cause extra data loss when image is rotated

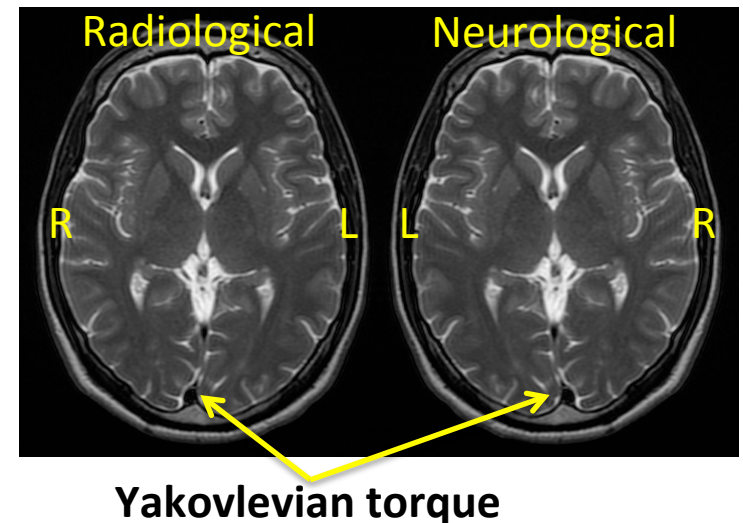
Data: Orientation

- Image data is collected in **transaxial/coronal/sagittal** slices in respective to the scanner
- In addition, subject may be positioned in various orientations into the scanner, depending on the acquisition procedure



Data: Orientation

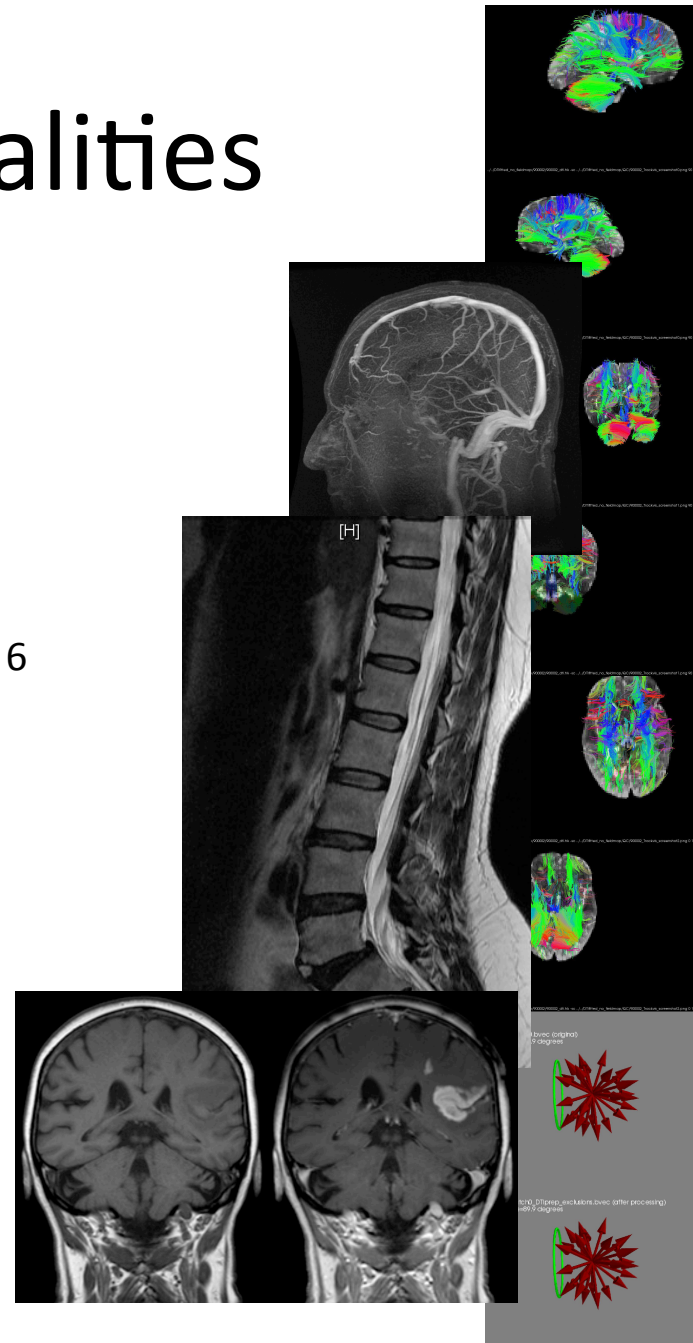
- Visualization conventions:
 - Radiological convention: Subject right is on the left
 - Neurological convention: Subject right is on the right
- How do I know which way is up/left/front in the image?
 - localize anatomical landmarks (e g Yakovlevian torque, heart etc.)
 - consult data (e g DICOM tags (0018,5100), (0020,0020), (0020,0037))
 - localize stereotaxic marker (e g fish oil capsule)
 - consult person responsible for acquisition



2 MR Data modalities

MR Image modalities

- **T1W (3D)**, T1 relaxation time
 - gadolium contrast agent (paramagnetic)
- **T2W (3D)**, T2 relaxation time
- **DWI**, Diffusion Weighted Imaging (4D)
- **DTI**, Diffusion Tensor Imaging (4D)
 - DWI with diffusion encoding directions, minimum of 6
- **Others**
 - fMRI (BOLD signal)
 - FLAIR (FLuid Attenuation Inversion Recovery)
 - Contrast enhanced images (injected contrast agent enhances signal, 3D/4D)
- **Non-invasive** (apart from contrast agent)
 - Comparison to X-ray, CT, PET, SPECT no radiation
 - Magnetic field may limit use



Group - Element	Description	Type	Length	Value
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0002 0003	Media Storage SOP Instance UID	UI	54	1.2.826.0.1.3680043.2.1208.34948545565201041914916296
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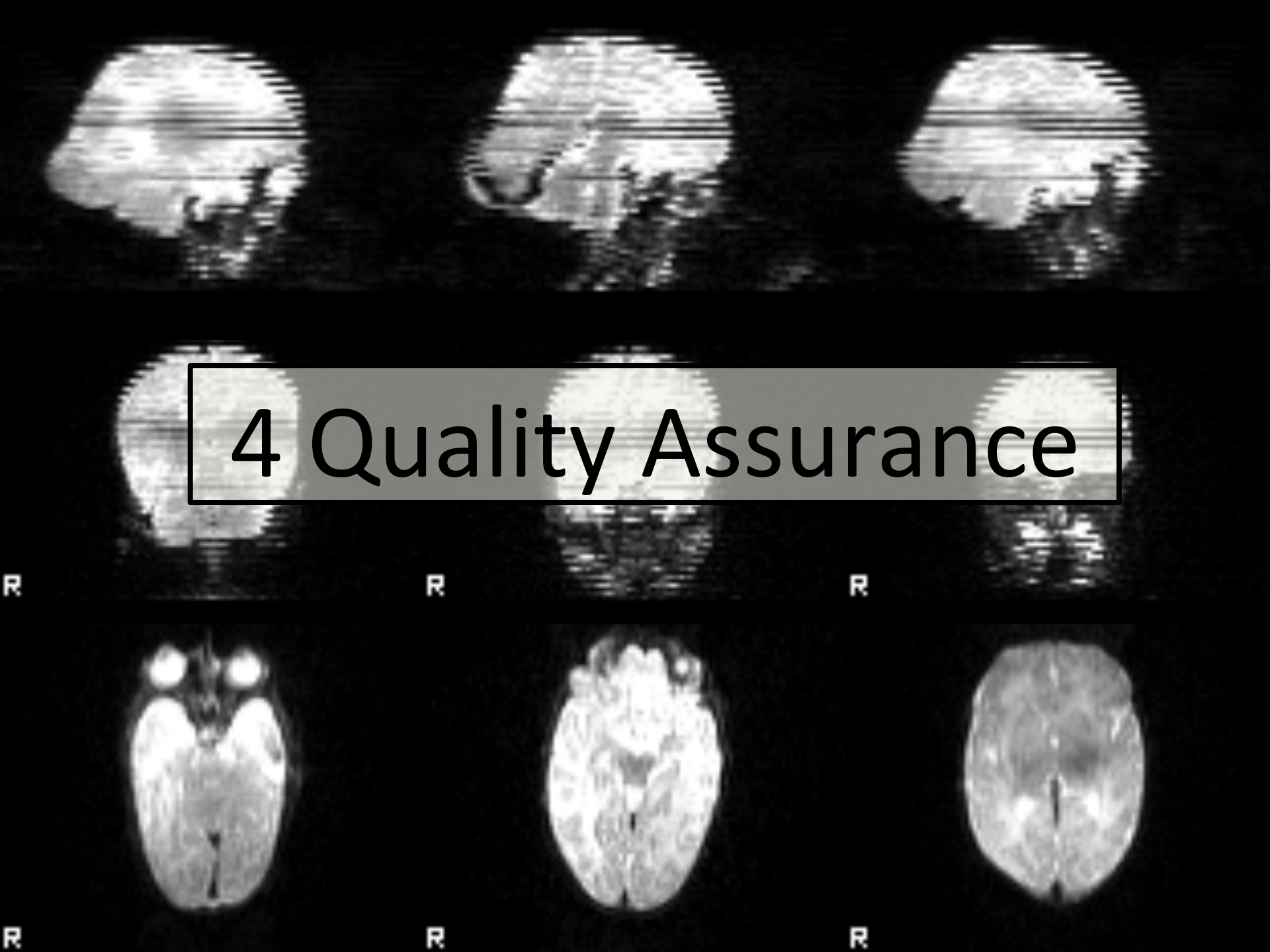
3 Image formats

Image data formats

- DICOM (Digital Imaging and Communications in Medicine, *pydicom, matlab*)
 - Most common image format in hospitals
 - Used in both storing and transferring image data
 - Data stored is commonly as one file/slice
 - Original image data acquired at the MR scanner is usually DICOM, possible that some data loss occur in conversions
- Nifti (*nibabel, matlab*, all main visualization tools support this)
 - Convenient for image processing
 - One file per 3D/4D image
- Others: mnc (*MINC toolkit*), vtk (*visualization toolkit*), nrrd, mhd (*Slicer3D*)

Summary

- Most important things to understand before analysis:
 - What is the modality
 - Isotropic or anisotropic voxel, spatial resolution
 - Which way is subject left/right, anterior/posterior



4 Quality Assurance

R

R

R

R

R

R

Quality Assurance

- Quality Assurance composes of automatic or semi-automatic methods to verify that the data is valid **for particular use**
 - While target region ultimately determine if the data is acceptable, artefacts outside it may indicate that the target region may be compromised
- Image Quality consists of
 - Spatial resolution
 - Image Contrast
 - Signal to Noise Ratio (SNR)
 - Artefacts
 - Motion
 - Susceptibility
 - Inhomogeneity
 - Other
 - Please see <https://radiopaedia.org/articles/mri-artifacts-1> for more exhaustive list

Quality Assurance

- Quality Assurance methods
 - Visual inspection for artefacts (by one or more persons)
 - Sanity checks for data integrity (data organization, reference region)
 - Noise profile
 - Artefact detection (automatic/manual)
- Things to consider in addition to image quality
 - Fit for particular use (e g in clinical application)
 - Repeatability (needs specific measurements, with test-retest setting)
 - Reproducibility (needs specific measurements, e g with phantom)
- MRI scan is a compromise between scan time and quality
 - In practice we need to compromise
- Image quality is not good enough, then what?
 - Some problems can be addressed afterwards, others not

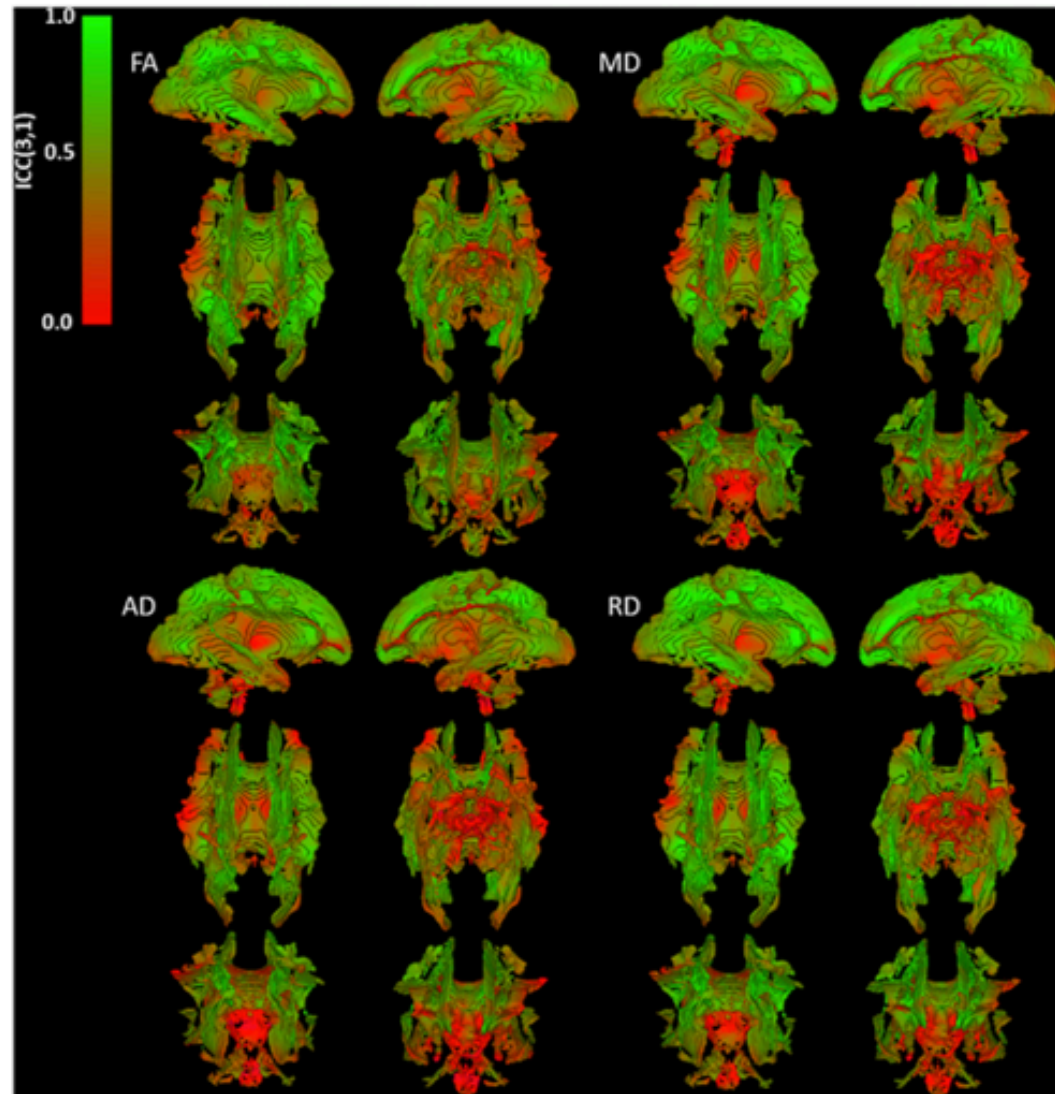
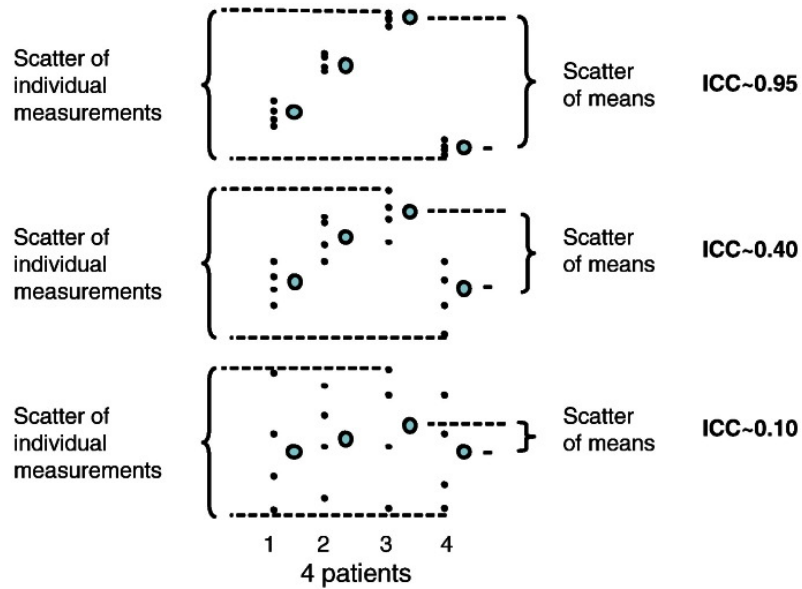
Quality Assurance: Tools

- Vendor (Siemens, Philips, GE, etc) specific visualization at workstation (DICOM, 3D/4D)
 - limited scalability
 - fit for particular use
- **fsleyes** (fsl toolbox's visualization tool Nifti, 3D)
 - part of fsl tools (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki>), designed mainly for brain
 - fusion imaging, support for DTI
- **eddyQC** (fsl quality control tool for DTI)
 - creates quality control report for DTI data
- **MRICron** (Nifti, 3D)
- **Slicer3D** (DICOM, Nifti, 3D/4D)
 - most extensive list of features
 - learning curve more steep
- **ITK-SNAP** (DICOM, Nifti, 3D/4D)
 - light-weight viewer opening almost any image
- **DTIprep** (nrrd)
 - DTI specific quality assurance tools
- **DSIstudio**
 - DTI specific visualization, contains tracktography pipeline
- **Carimas** (developed at Turku PET Centre)
 - PET specific tool can be used with MRI data as well

In addition to QC of individual image: image quality at group level

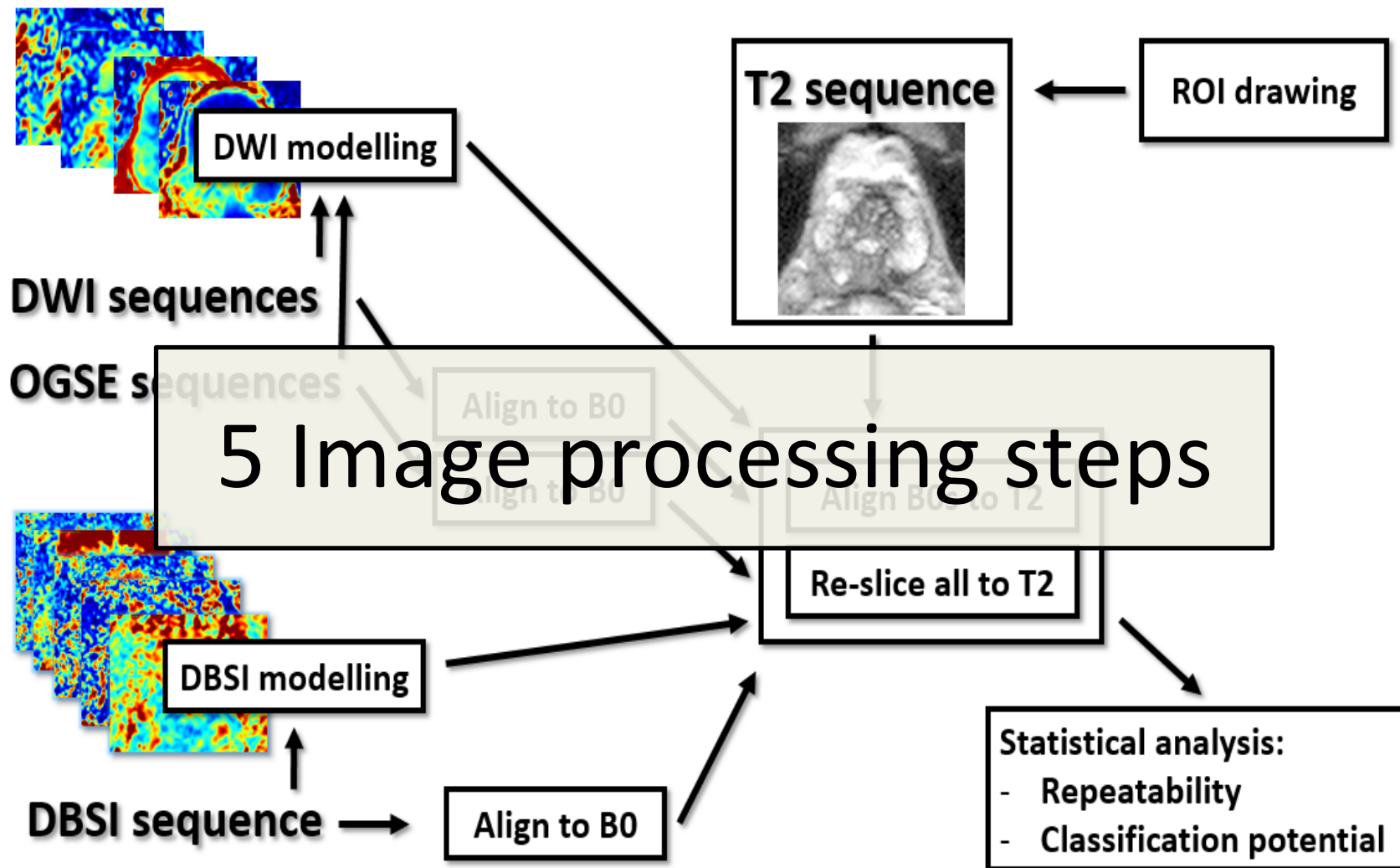
Intraclass Correlation coefficient (ICC)

Contrast between measurement variance and difference between individuals



Summary

- Early detection of problems is less costly
 - In best scenario, the acquisition can be repeated
 - In worst scenario, diagnosis quality is compromised
- When doing quality control, things to look for:
 - Missing data
 - Artefacts
 - Correct if possible
 - Signal-to-Noise ratio
 - Is a data quality problem occurring at random?
 - e.g. patients may express more motion artefact than healthy > measurement is about artefact rather than actual target tissue



Where to process the data

- In practise, large data/processing is run on servers
- Standardized image visualization may need specific monitors
- The trend is towards OS independent processing
- Patient anonymity!

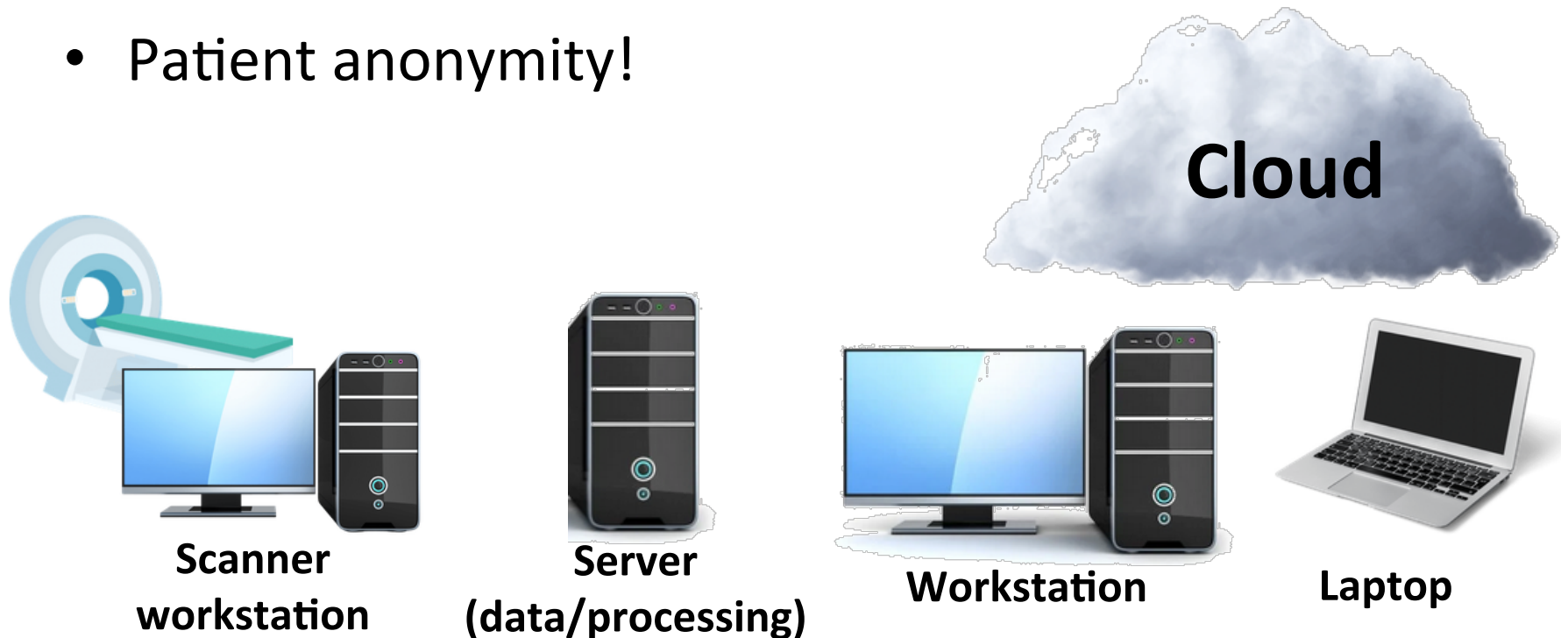


Image processing steps

- Artefact removal
- Signal modelling
- Region of Interest (ROI) placement
- Radiomics
- Computation of diagnostic/prognostic scores

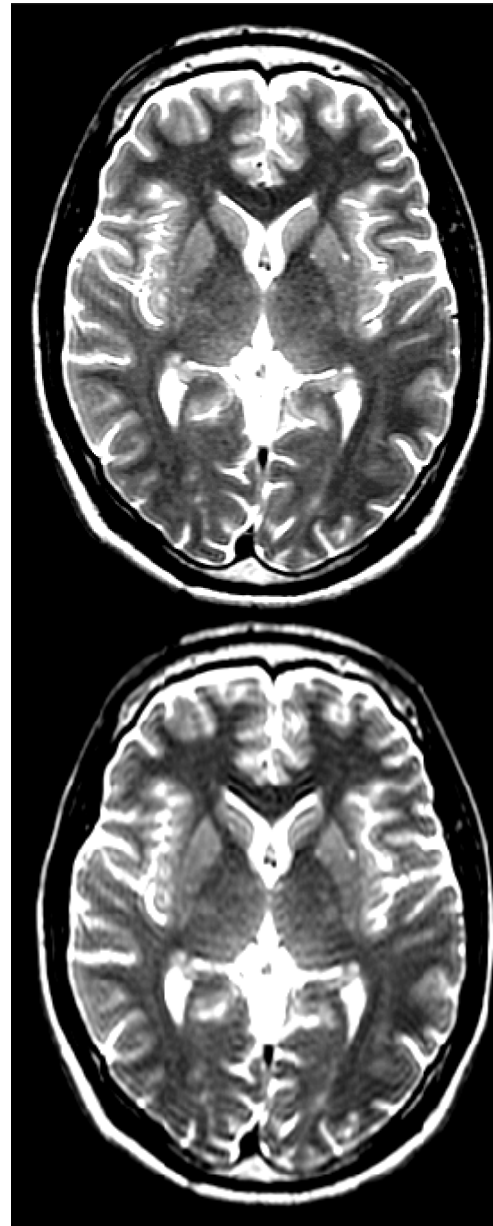
Artefact removal



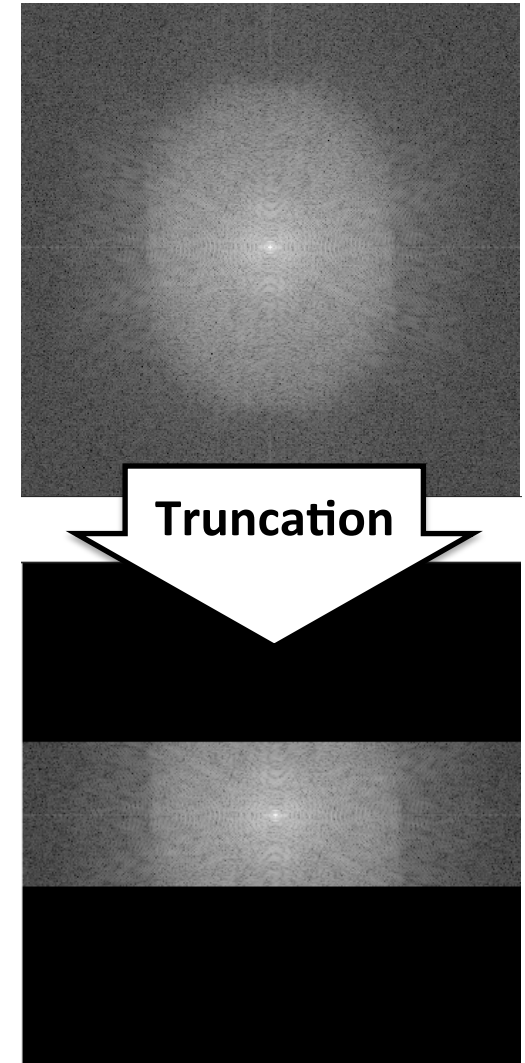
Gibbs Ringing

- Abruptly truncating signal in k -space introduces “ringing” to the image
- To fix: `mrxtrix degibbs`
 - Removes ringing artefact if present

native slice

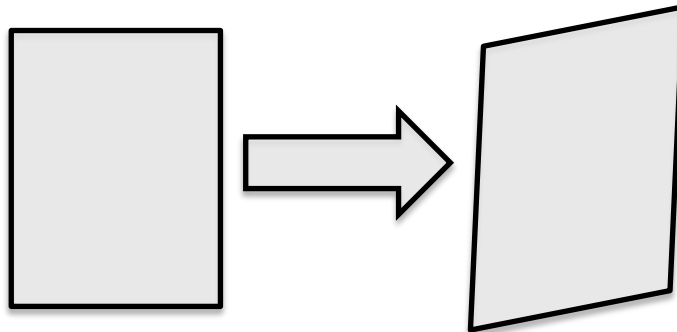


fft space



Eddy Current correction

- **Eddy currents** result from gradient magnetic fields
 - Eddy currents generate their own magnetic fields, which distort the spatial and temporal performance of the overall desired magnetic field.



Eddy current distortion in DTI

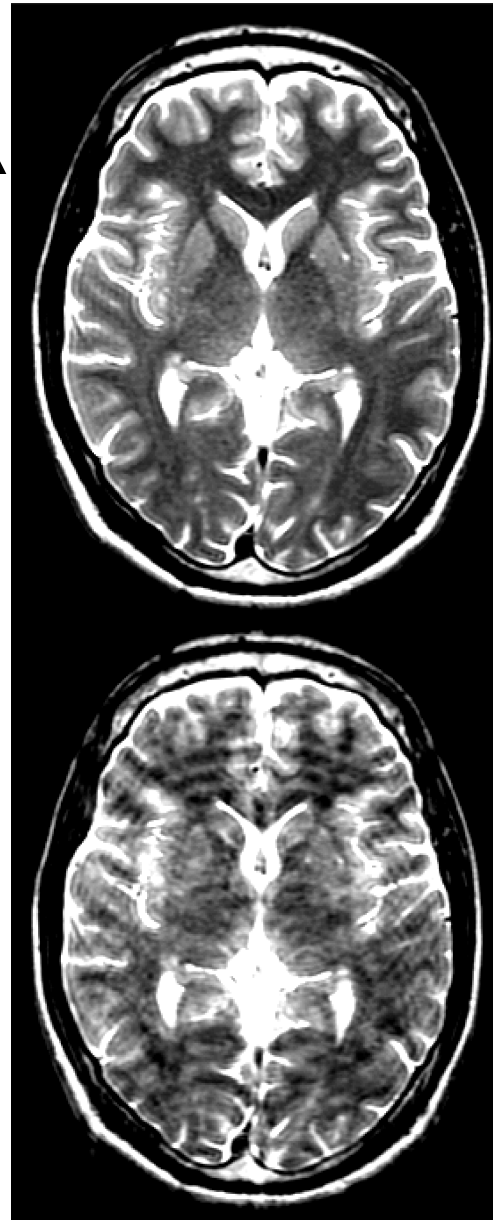
Motion artefact

- Occurs **within** (see right) and **between slices and volumes**
- Tools (between volumes motion correction): *fsl eddy, mcflirt, ANTs*

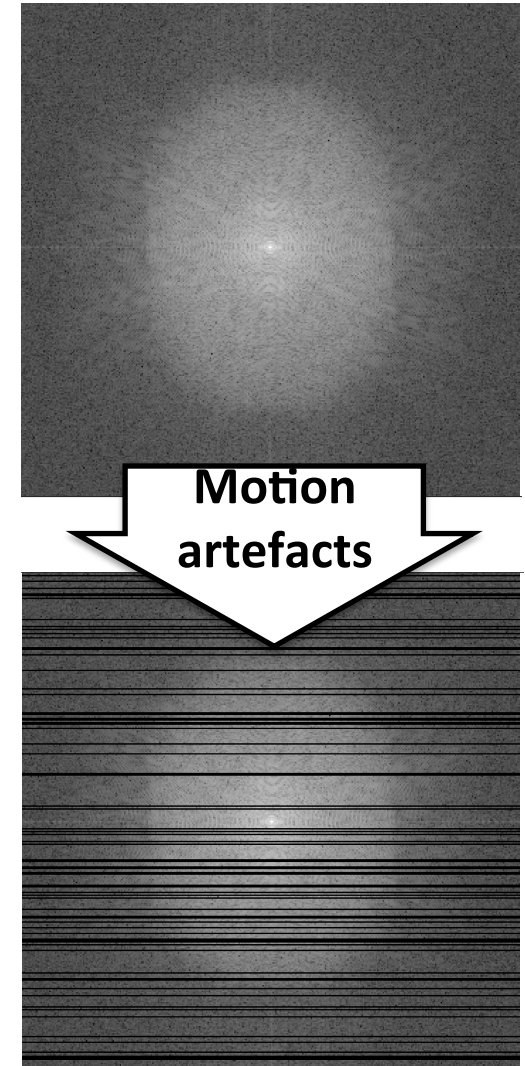
Phase
Encoding
direction



native slice



fft space



Motion correction

- Approaches for assessing motion
 - Motion suppression by means of acquisition setting (positioning, pillows etc)
 - Protocols/sequences optimized to address motion (PROPELLER, navigator images, oversampling etc.)
 - **Post-processing**
 - If possible, estimate occurred motion, and use as covariate
- With multi-volume MRI data, eddy current distortion is corrected at the same time with motion

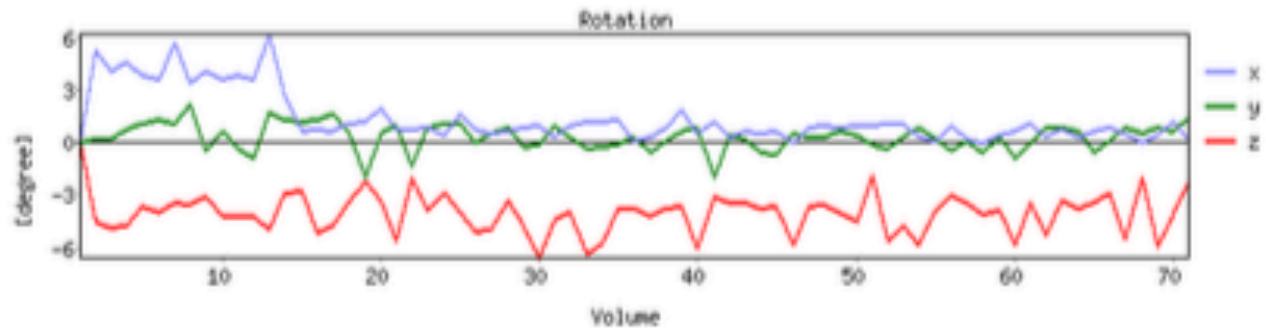
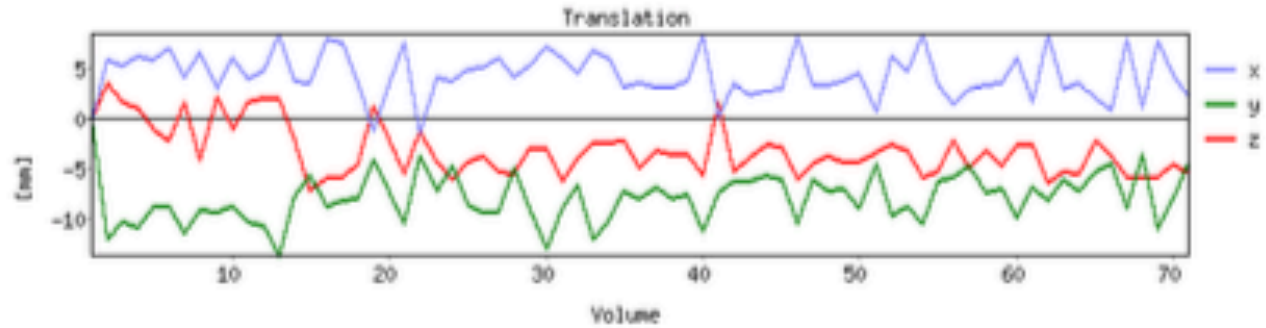
Motion correction example

Estimated motion

Mean dislocation : 9.976763 [mm]

Mean translation: (x y z)=(4.531128, -7.783876, -3.033722) [mm]

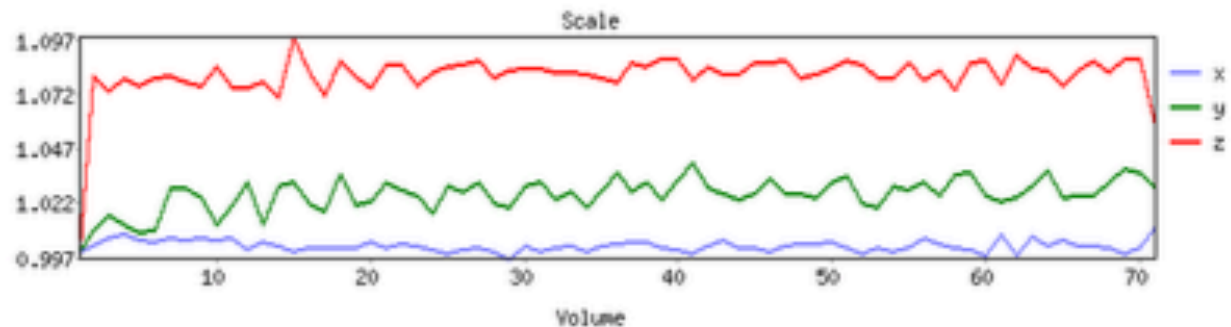
Mean rotation: (x y z)=(1.405032, 0.362363, -3.988247) [degree]



Estimated distortion

Mean scale: (x y z)=(1.002559, 1.026221, 1.081162)

Mean skew: (x y z)=(0.029569, -0.001893, -0.016641)



N/2 Ghosting artefact

- Shifted trajectory is sum of 2 shifted undersampled trajectories (or single undersampled trajectory)
- Causes aliasing (“N/2 ghosting”)
- To fix: measure shifts with reference scan, shift back in reconstruction

Effect of 1 voxel shift

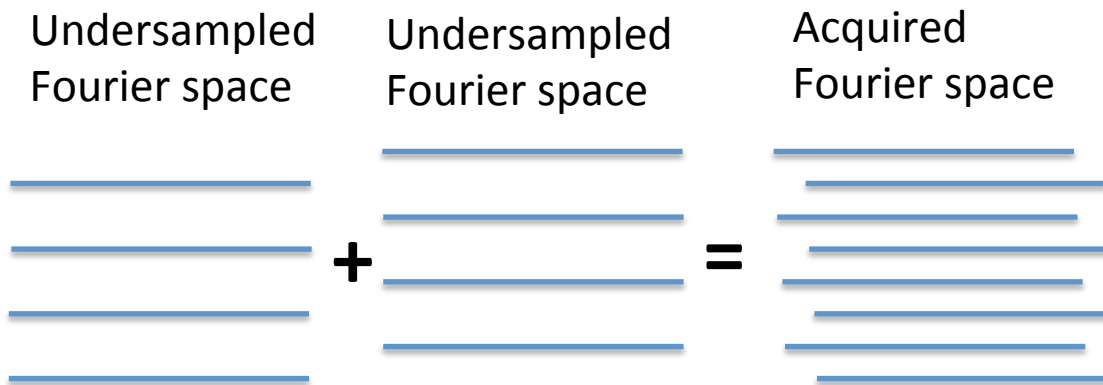
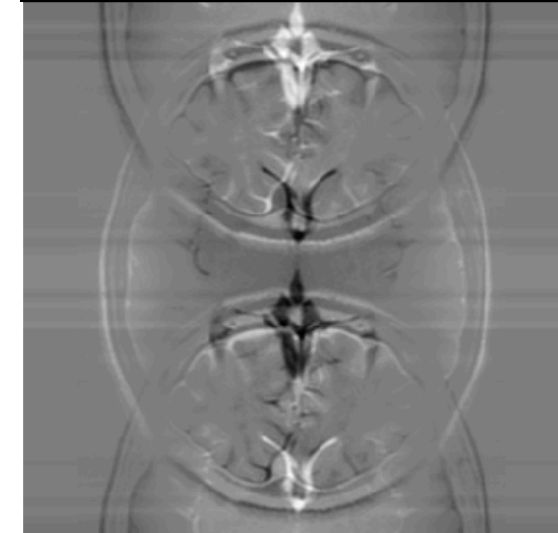
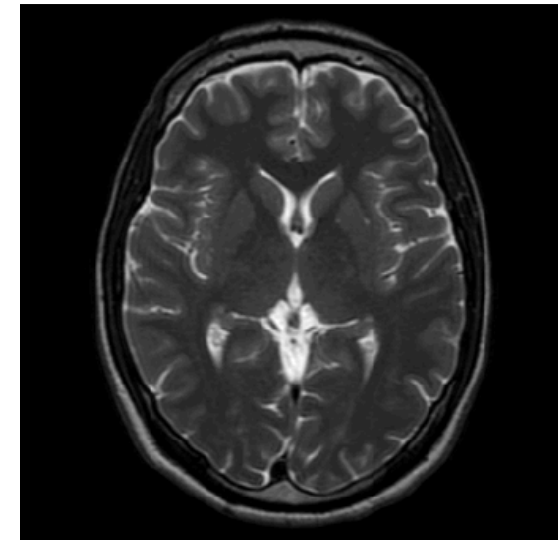
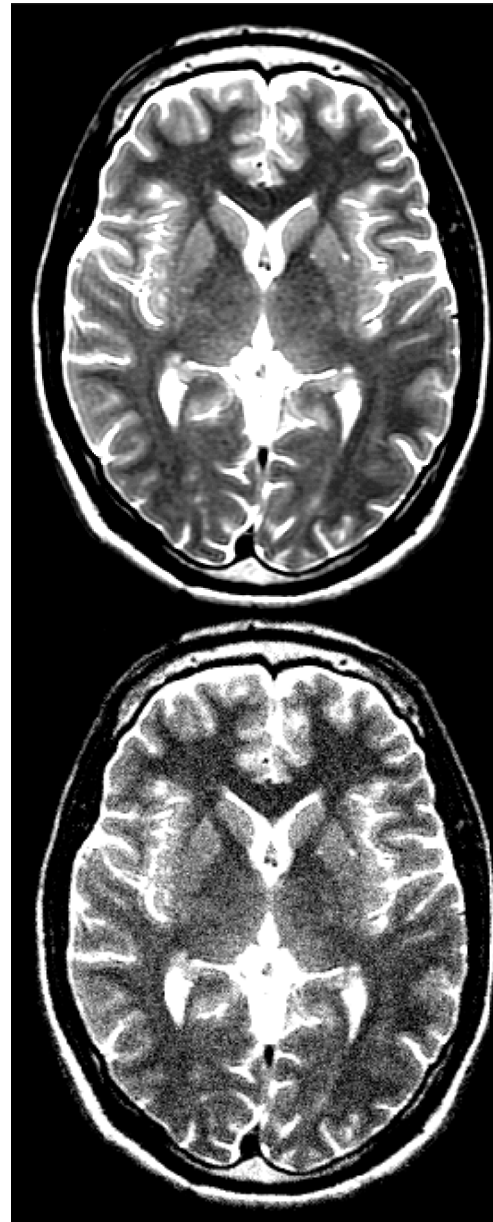


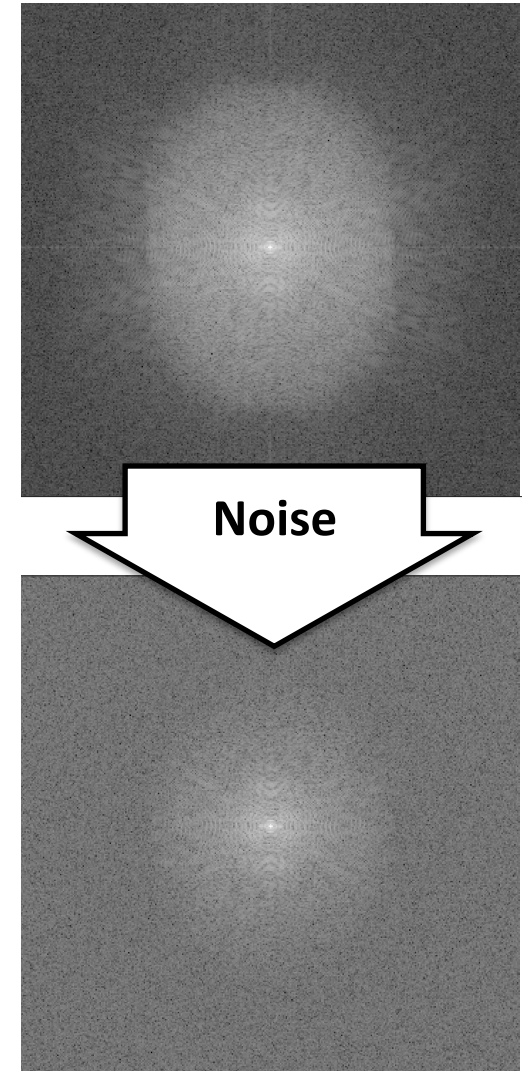
Image Noise

- Noise arises from target tissue and scanner
- Noise is additive in phase and magnitude data, theoretically resulting Rician noise in reconstructed image
- To fix: mrtrix ***dwidenoise***
 - Aims to remove noise according to Marchenko-Pastur theorem for image data components, in separation signal from noise

native slice



fft space

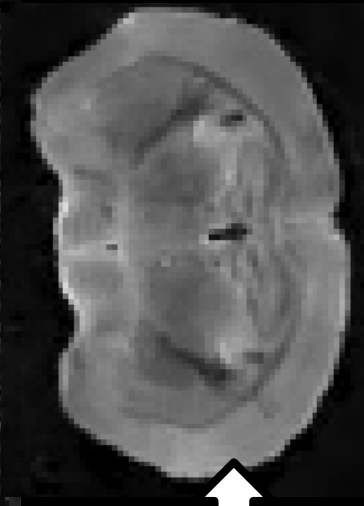


DTI Noise removal example: Pre-clinical murine with PCA

B_0 A02
117x117x200



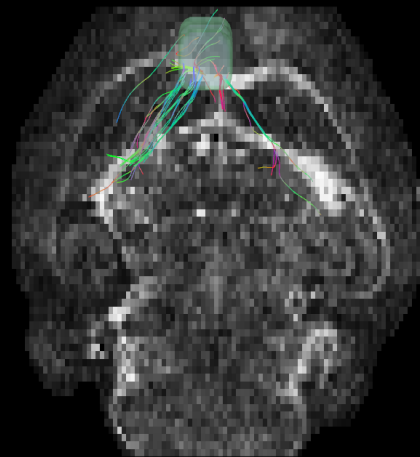
B_0 A02
117x117x200
LPCA



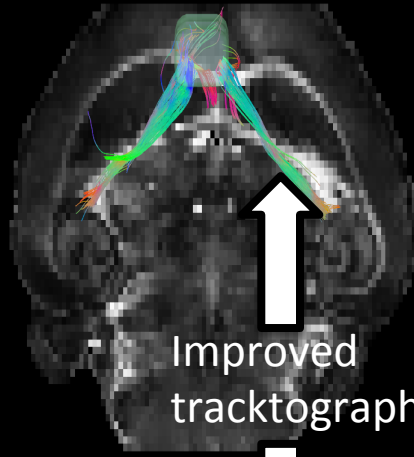
Improved B_0
image

LPCA = Localized
Principal
Component Analysis
noise removal

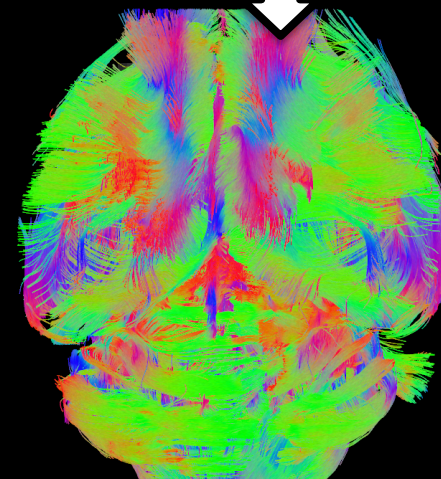
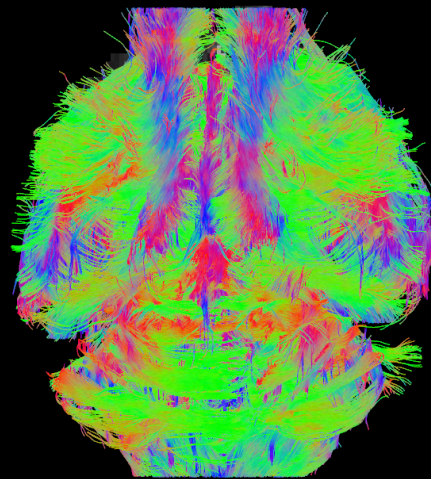
A02 117x117x200



A02 117x117x200 LPCA



Improved
tractography



Distortion correction

Magnetic susceptibility

- Degree of magnetization in response to applied magnetic field
- Magnetization varies between air, bone, tissue



Inhomogeneity of B0 field



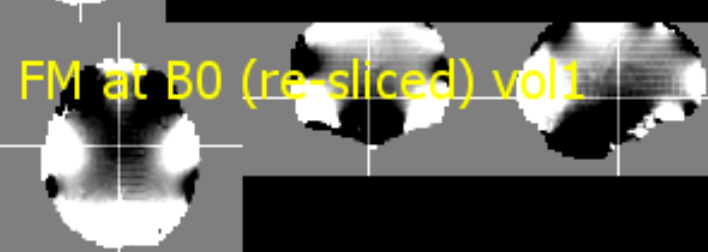
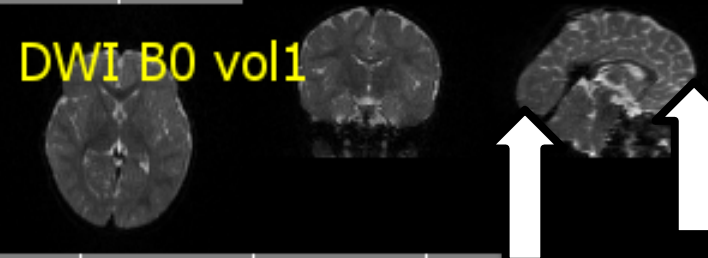
Geometric distortions



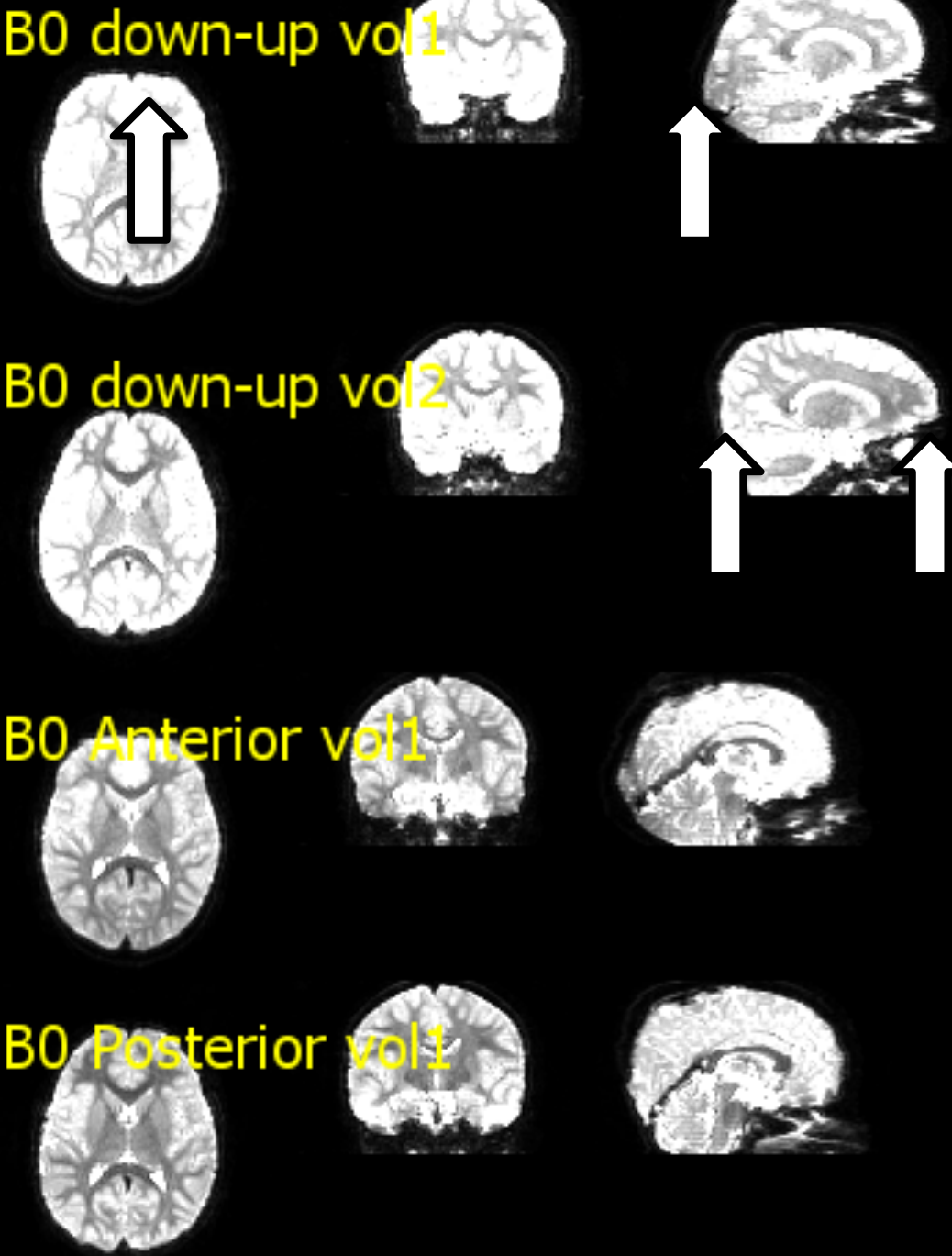
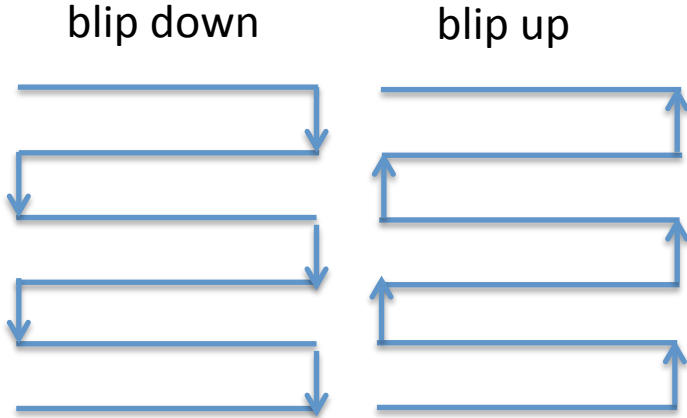
Anatomical inaccuracies

- Magnetization processes at a different rate than expected, and reconstruction places the signal at the wrong location
- Correction options
 - 1) Specifically acquired field maps
 - 2) **Acquire opposite blip direction image, fsl *topup***
 - 3) Estimate distortion using anatomical reference e g T1W image ***SynB0*** tool

Distortion
correction
example:
Separately
acquired field
map

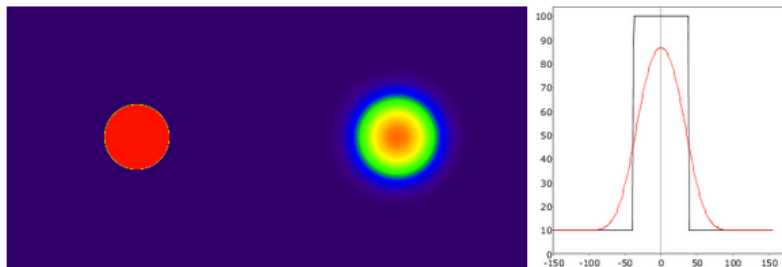
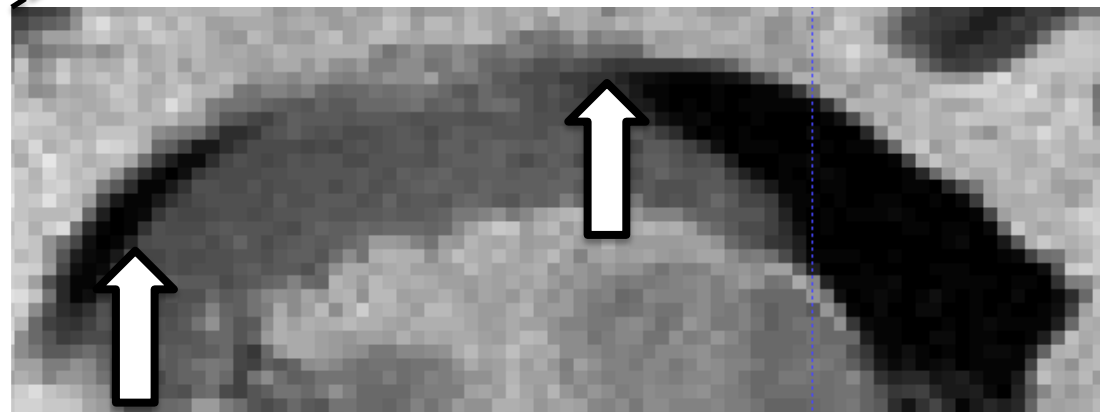
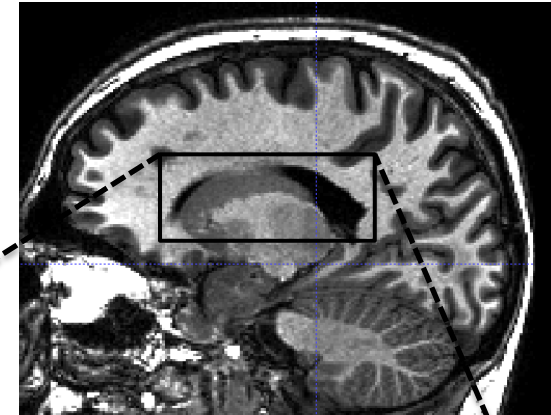


Distortion correction example: TOPUP



Partial Volume Effect

- Correct for Partial Volume Effect (PVE)
 - Potential spill-over from e.g. cerebrospinal fluid to juxtaposed region
 - Tools *fslmaths*
python *skimage*



Summary

- Many of the artefacts in the image can be avoided by better optimization of acquisition
- Motion, susceptibility and noise may need to be addressed with post-processing

Signal Modelling

At this point we assume data is all good,
now doing the actual image processing

"All models are wrong, but some are useful"

- George Box, statistician



Signal Modelling

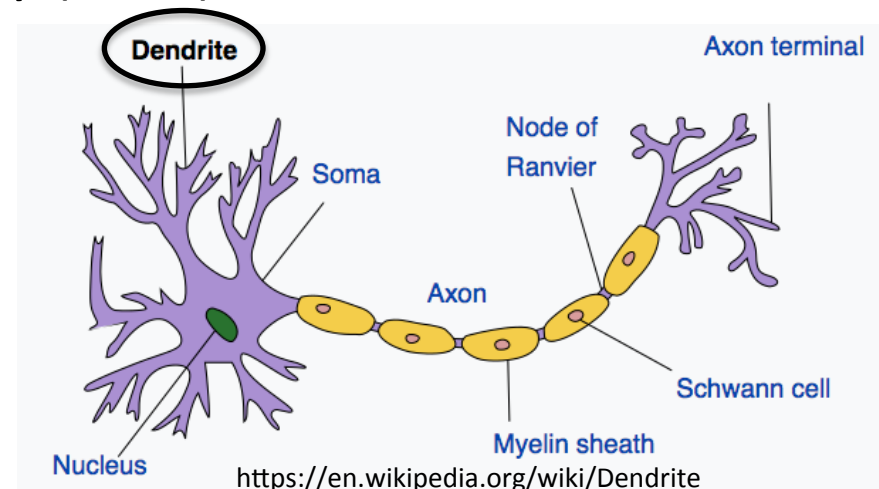
- Modelling is usually done for each *individual voxel* in the image, although sometimes for *ROI mean values*
- Parameter estimates in medical imaging can be used as *biomarkers* - objective measure capturing of what is happening in a cell or an organism at a given moment
- Model parameters have a level of *unspecificity*: Parameter value may have multiple different physiological interpretations at cell or organism level
- In medicine, ultimate criteria for good parameter is usefulness in *clinical context*

Modelling T1W/T2W

- T1W
 - T1 times depend strongly upon magnetic field strength 1.5T, 3T, 7T etc.
 - In brain, T1 have support to detect changes in water content, myelin, fiber orientation, iron
- T1W/T2W ratio
 - can be used a measure for myelin, axon/dendrite density, iron content
matlab, python
- T1W: Voxel Based Morphometry (VBM) *SPM*
 - gray matter 'density'



Mechelli A, Price CJ, Friston KJ, Ashburner J. Voxel-based morphometry of the human brain: methods and applications. Current Medical Imaging. 2005 Jun 1;1(2):105-13.



Modelling DWI

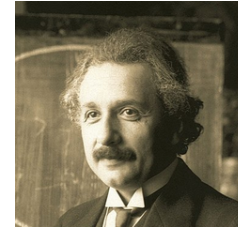


<https://en.wikipedia.org/wiki/Diffusion>

Brown, 1827: Continuous and spontaneous random motion of pollen grains suspended in water, with microscope

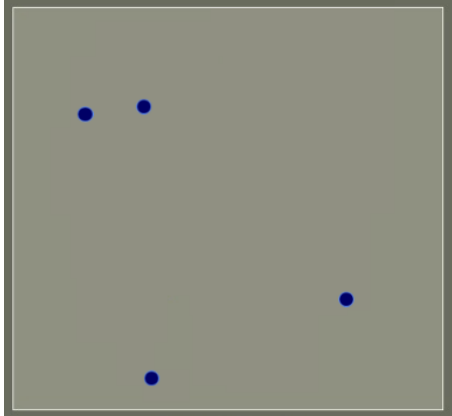


Einstein, 1905: Brownian motion, i. e. random motion of particles in a fluid

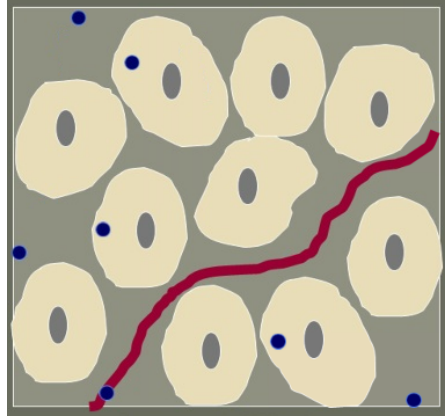


Tools: C code *dlib*
www.github.com/haanme,
matlab, *Carimas*, *python dipy* etc.

Modelling DWI



Free diffusion



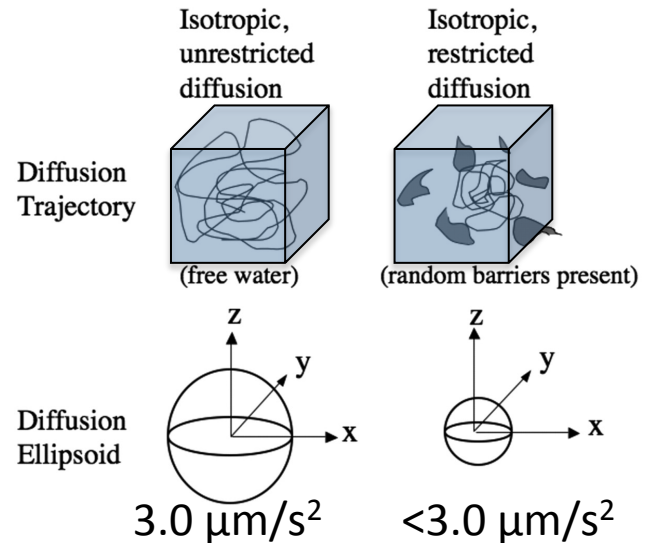
Restricted/Hindered diffusion

• Most common DWI measure is Apparent Diffusion Coefficient (ADC):

- Microcapillary perfusion
- Fluid homogeneity
- Macromolecules
- Cellular **density**
- Cell membranes integrity
- Microstructural organisation

Physiological example values of ADC

- $0 \mu\text{m}^2/\text{s}$ - No diffusion
- $3.0 \mu\text{m}^2/\text{s}$ - Free water (e.g. water in a glass)

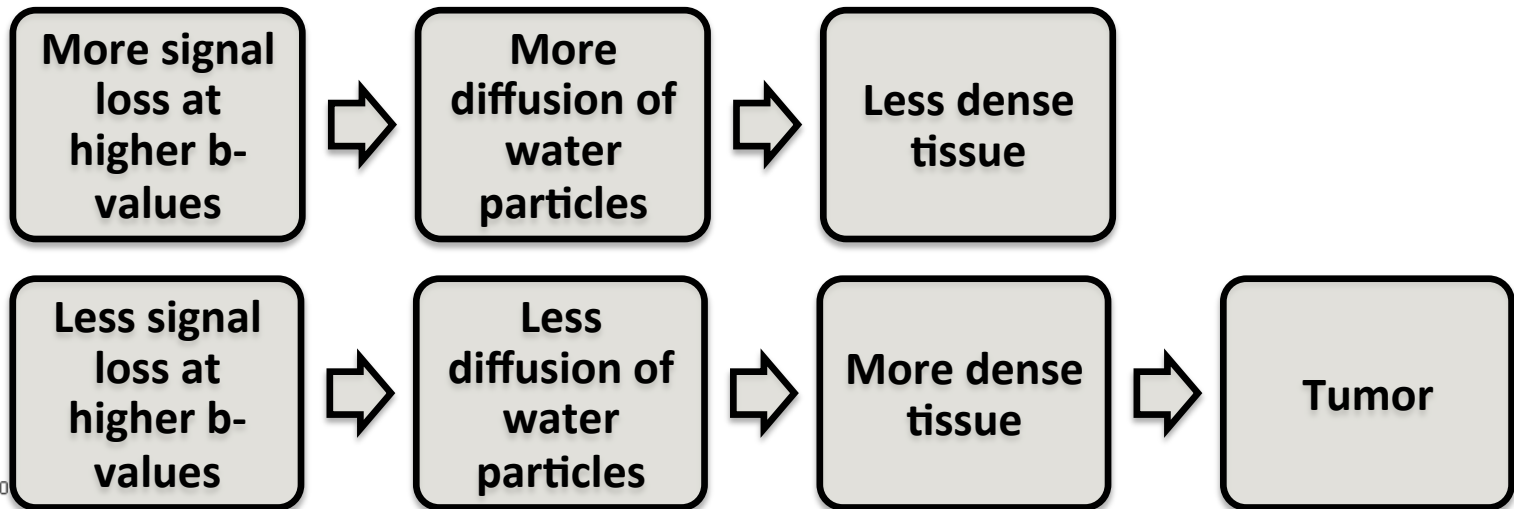
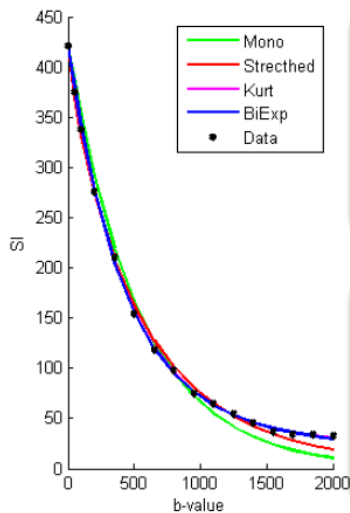
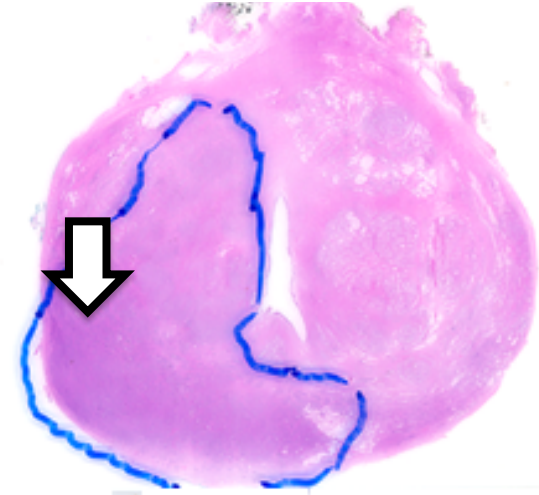
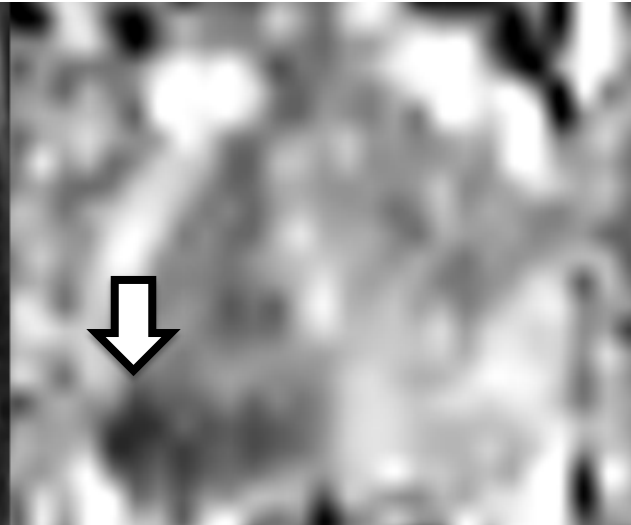
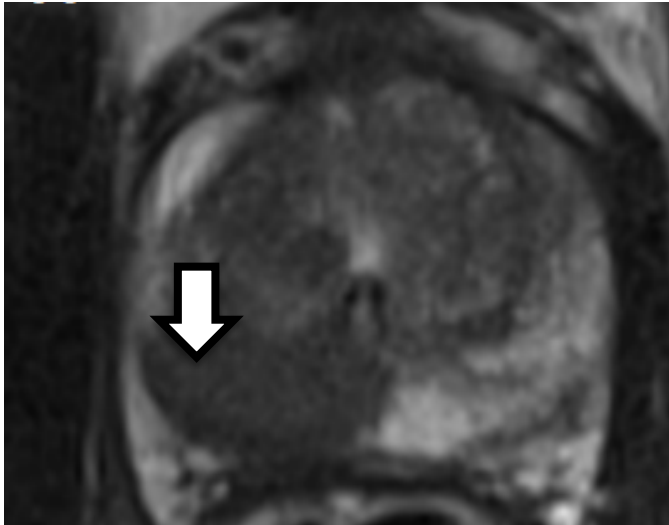


Apparent Diffusion Coefficient example: Prostate Cancer

T2W

ADC

Histology



Modelling DWI: Monoexponential

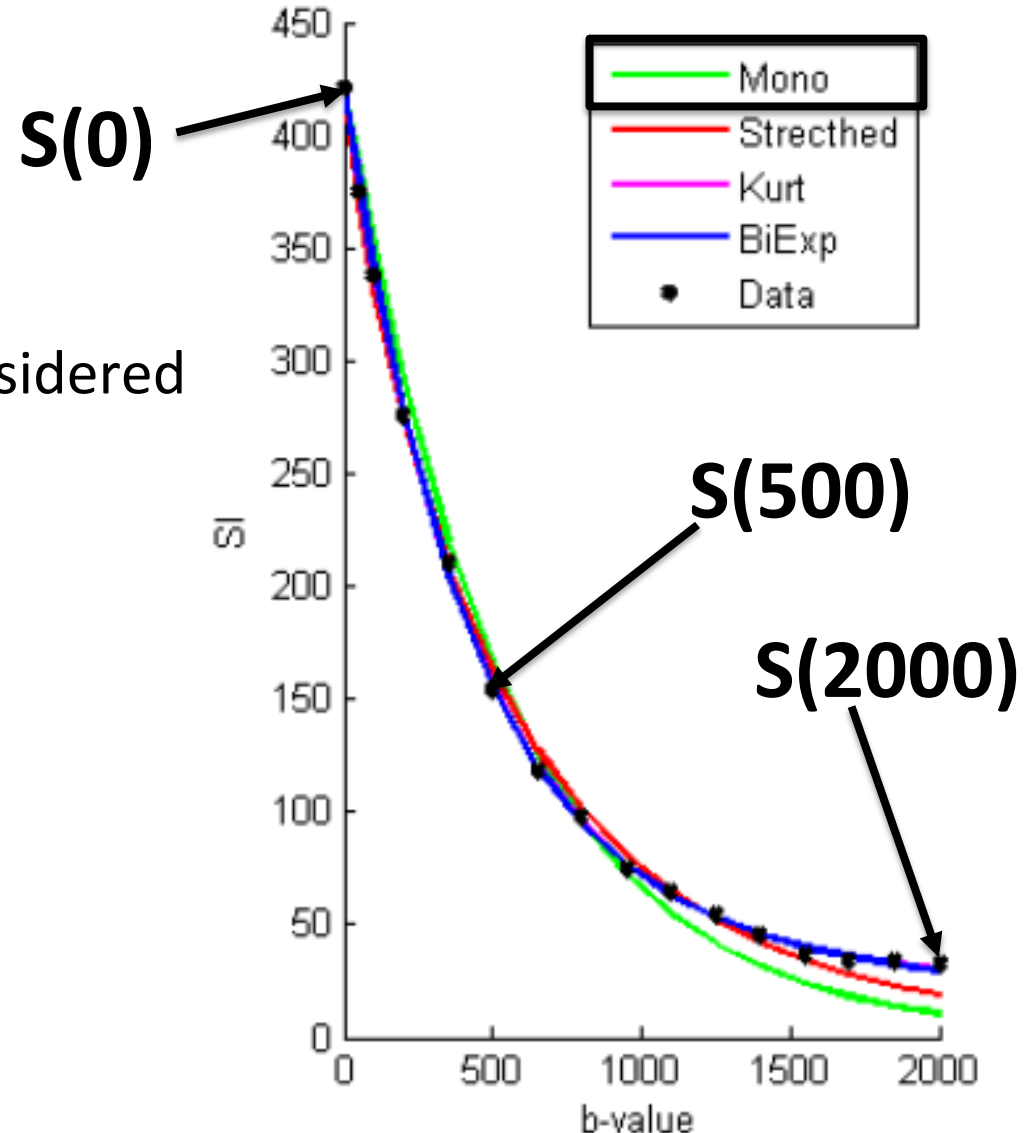
$$S(b) = S_0 e^{-bADC_{mono}}$$

Monoexponential:

- Single exponential decay
- ADC can be generally considered to reflect tissue density:

↑ less dense tissue

↓ more dense tissue



Modelling DWI: Other models

Stretched exponential

$$S(b) = S_0 e^{-(bADC_{stretched})^\alpha}$$

Kurtosis model

$$S(b) = S_0 e^{(-bADC_{kurtosis} + \frac{1}{6}b^2 ADC_{kurtosis}^2 K)}$$

Intra-voxel Incoherent Motion (IVIM)

Biexponential

$$S(b) = S_0 ((1-f)e^{-bD_s} + fe^{-bD_f})$$

Modelling: Stretched exponential

$$S(b) = S_0 e^{-(bADC_{stretched})^\alpha}$$

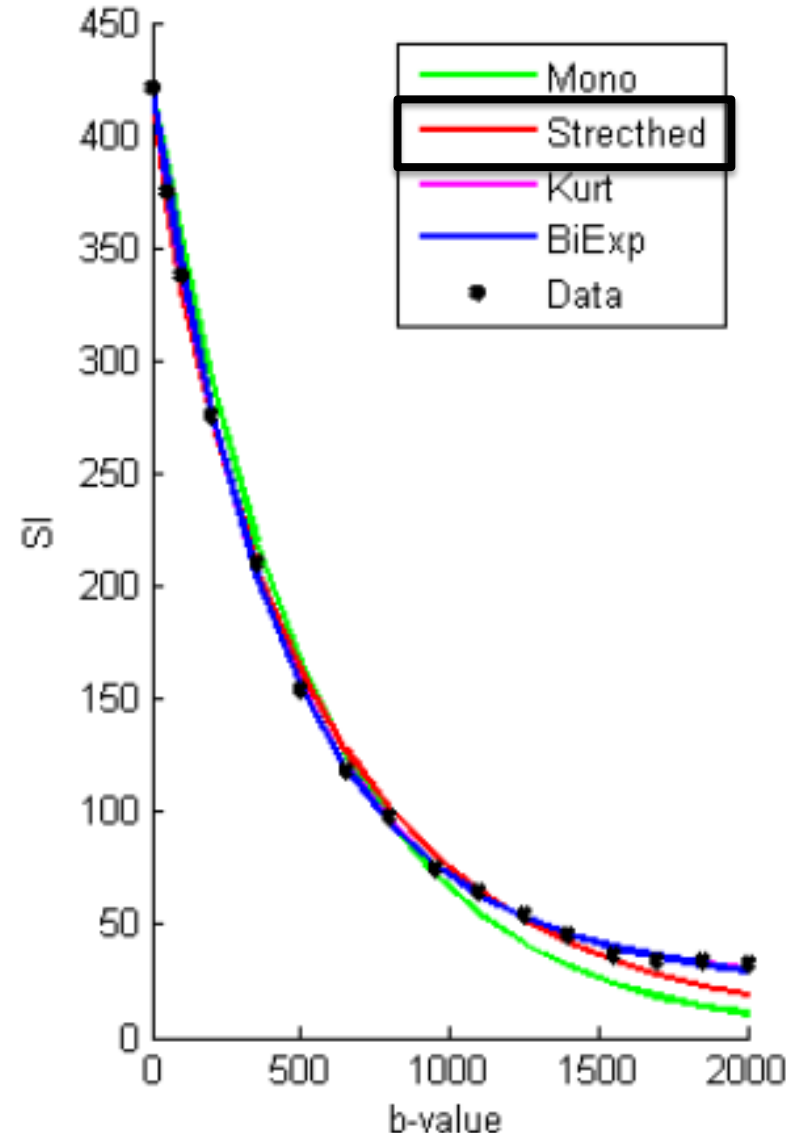
Stretched exponential:

- Heterogeneity index α reflects composition of multiple exponentials

- $\alpha < 1$ for more than one exponential present

- ↑ more homogenous tissue

- ↓ more heterogenous tissue



Modelling DWI: Kurtosis model

$$S(b) = S_0 e^{(-bADC_{kurtosis} + \frac{1}{6}b^2 ADC_{kurtosis}^2 K)}$$

Kurtosis:

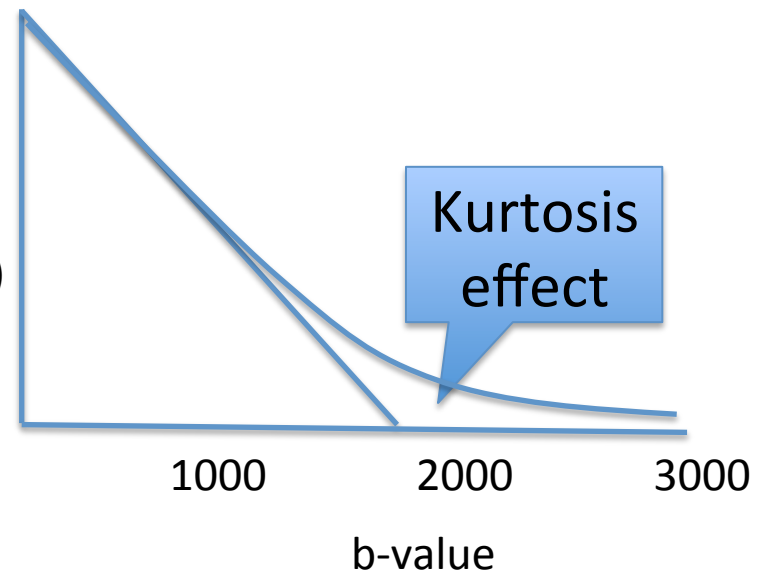
- K reflects deviation from Gaussian shape, physically associated with structure

- Based on Taylor series expansion of signal

↑ more structures in tissue

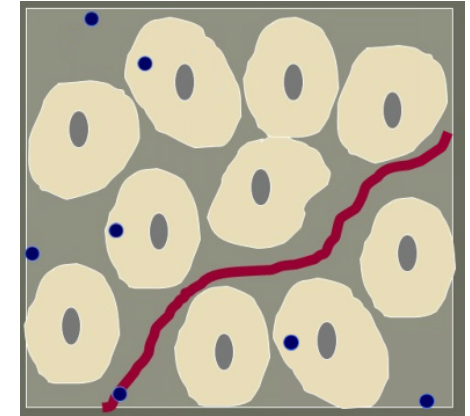
↓ less structure

DWI Signal
 $\ln(S(b)/S(0))$



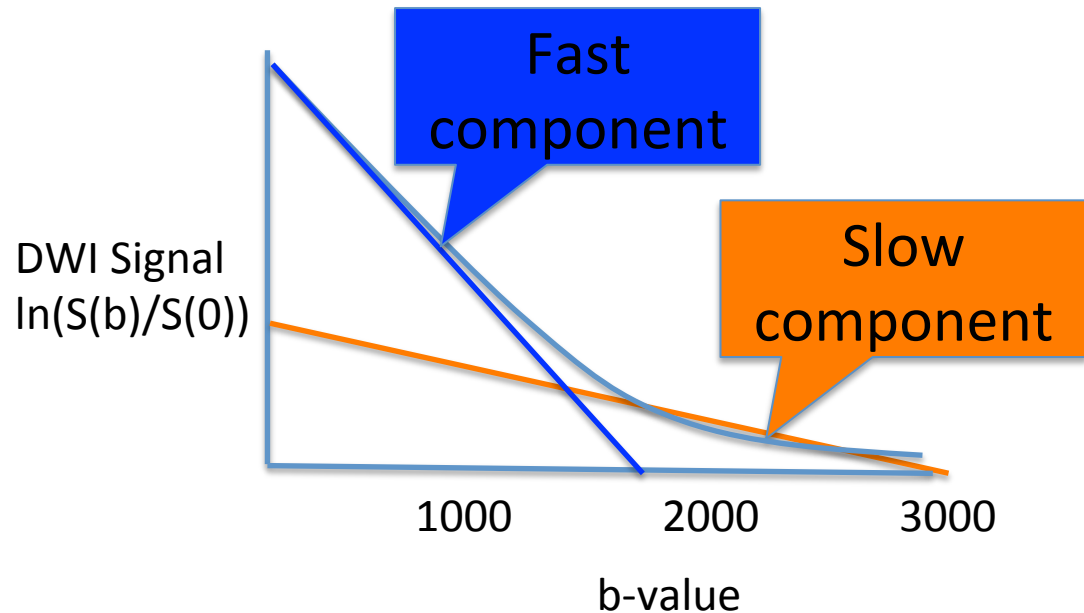
Modelling DWI: Bi-exponential

$$S(b) = S_0((1-f)e^{-bD_s} + fe^{-bD_f})$$



Biexponential:

- D_f and D_s reflect fast and slow exponential decays
- Interpretation depends on used b -values, and the tissue under study



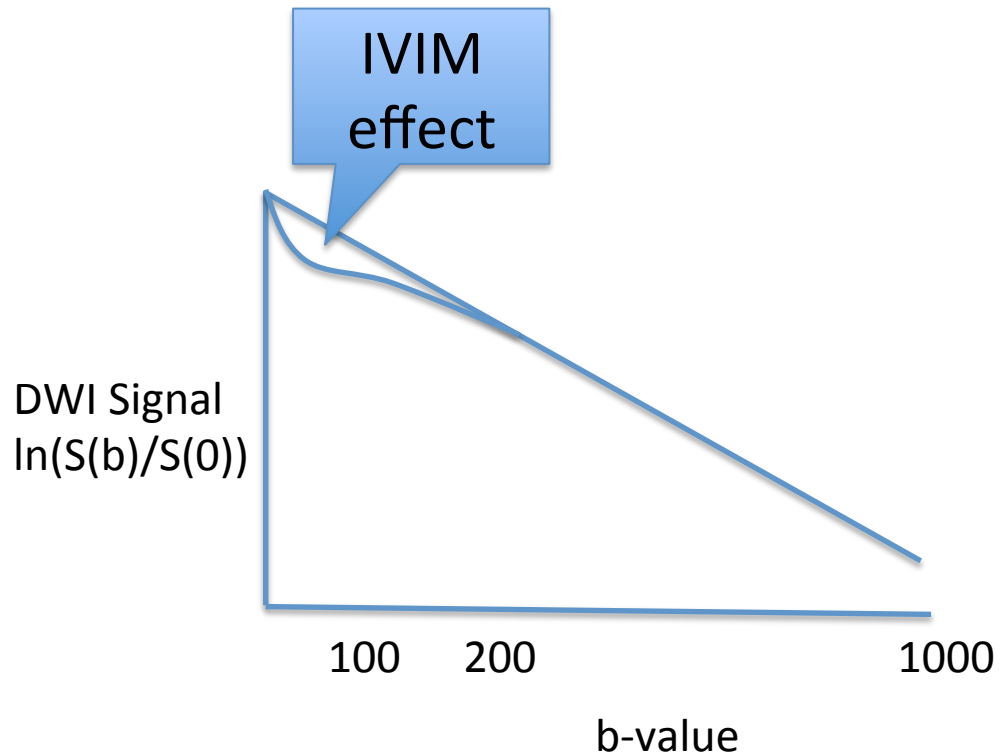
Modelling IVIM (IntraVoxel Incoherent Motion)

$$S(b) = S_0 \left[(1-F_p) e^{-ADC_D b} + F_p e^{-b(ADC_P + ADC_D)} \right]$$

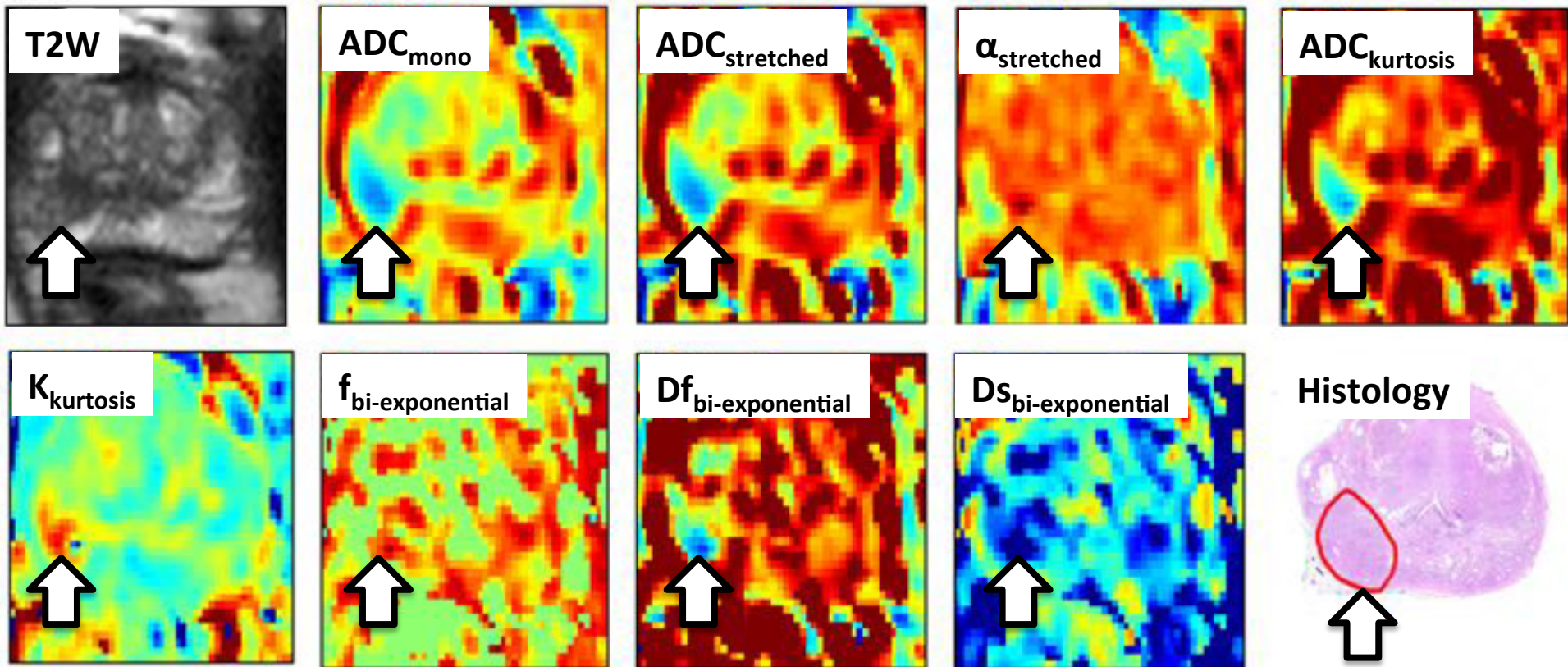
Le Bihan D, Radiology 1988

IVIM:

- Mathematically the same as a bi-exponential model
- Difference arises from the acquired b-value samples at range of IVIM effect
- $b\text{-value} < 200 \text{ s/mm}^2$
- D^* (pseudodiffusion) reflects blood perfusion



Modelling DWI: Example of prostate cancer parameter maps



DWI models reveal different contrast with tumour and within tumour, with data from the same DWI acquisition

Modelling DTI

- DTI model assumes one 3D ellipsoid instead of sphere

- Convention is to use DTI in brain white matter (WM)

- Tools: fsl *dtifit*, *DSIstudio*, *mrtrix*, *diffusion toolkit*

- DTI scalar interpretations:

Fractional Anisotropy (FA):

↑ high integrity of fibers ↓ low integrity

Mean Diffusivity (MD):

↑ less dense tissue

↓ more dense tissue

Axial Diffusivity (AD):

↑ healthy fibers

↓ axonal injury

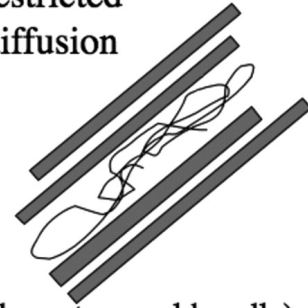
Radial Diffusivity (RD):

↑ myelin loss

↓ more myelin

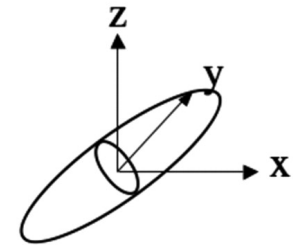
Diffusion Trajectory

Anisotropic, restricted diffusion



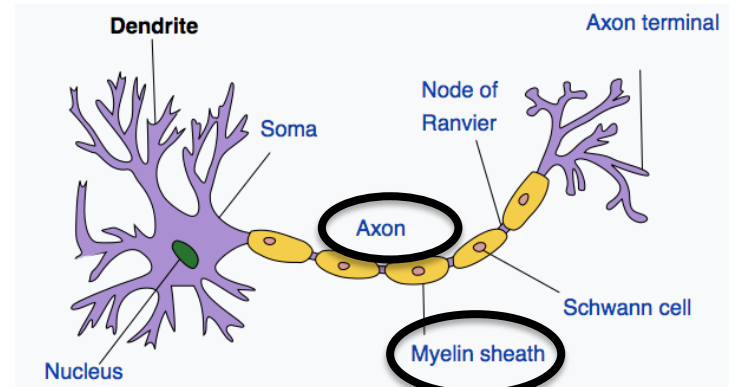
(coherent axonal bundle)

Diffusion Ellipsoid

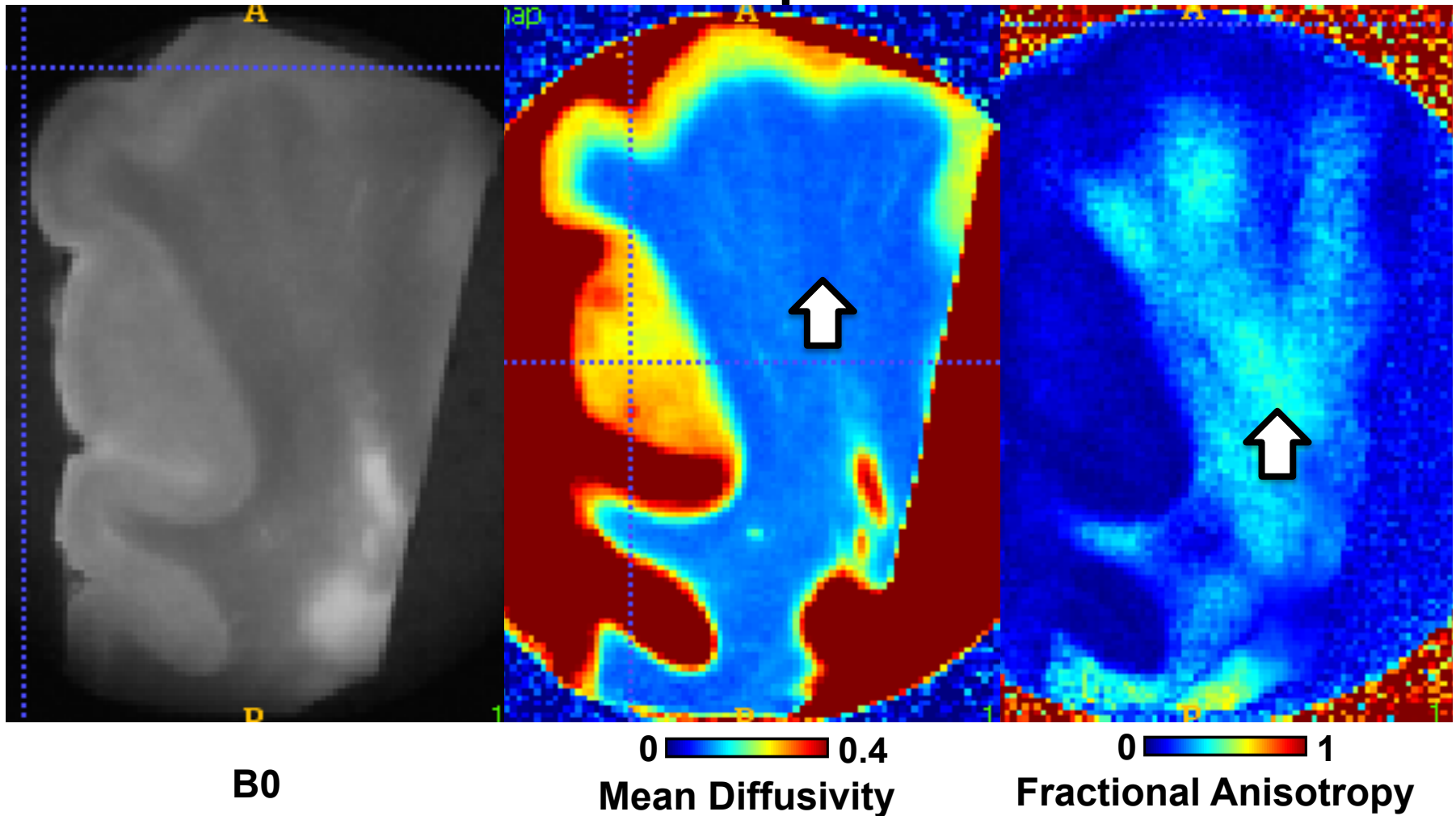


Diffusion Tensor

$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{yz} & D_{zz} \end{bmatrix}$$



Modelling DTI: Example brain sample

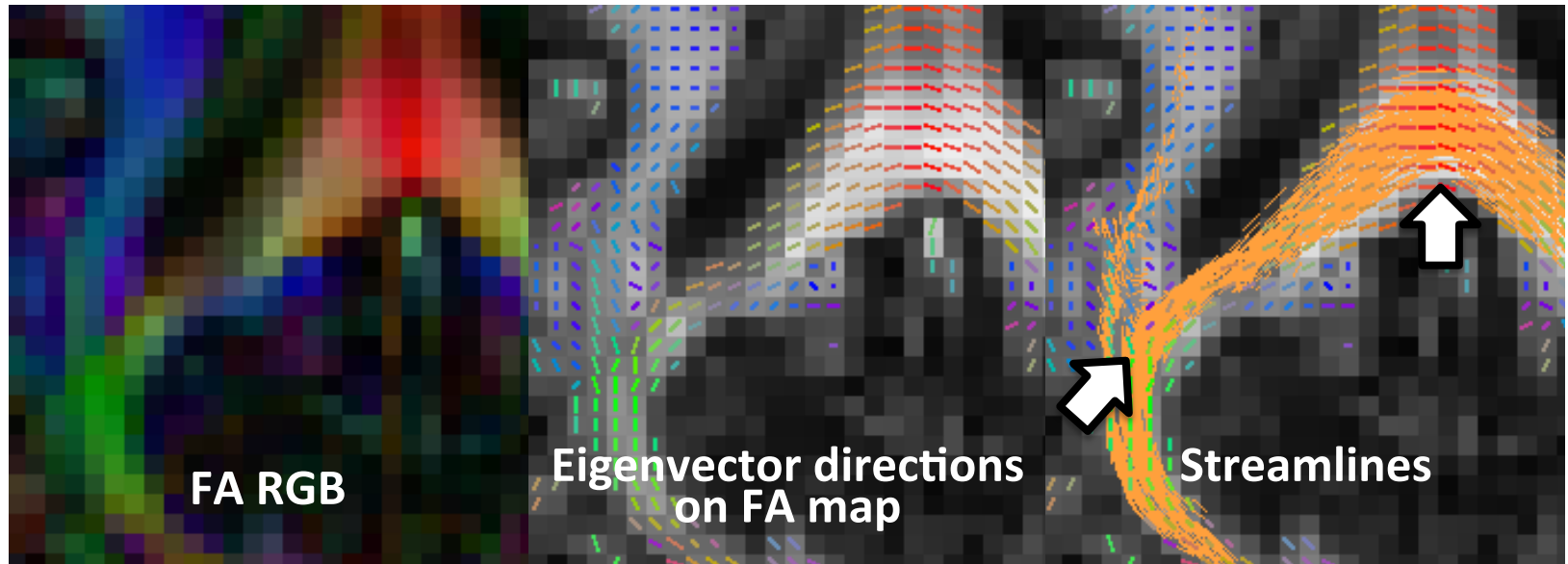
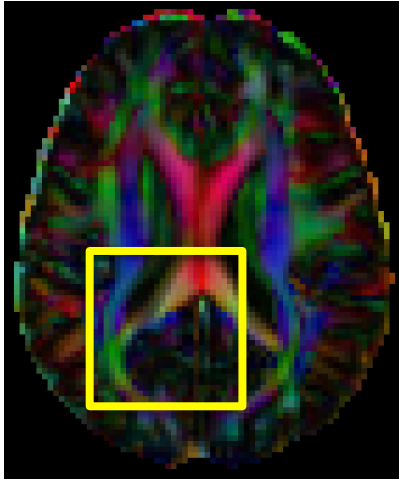


Mean Diffusivity shows dense white matter (blue, middle)

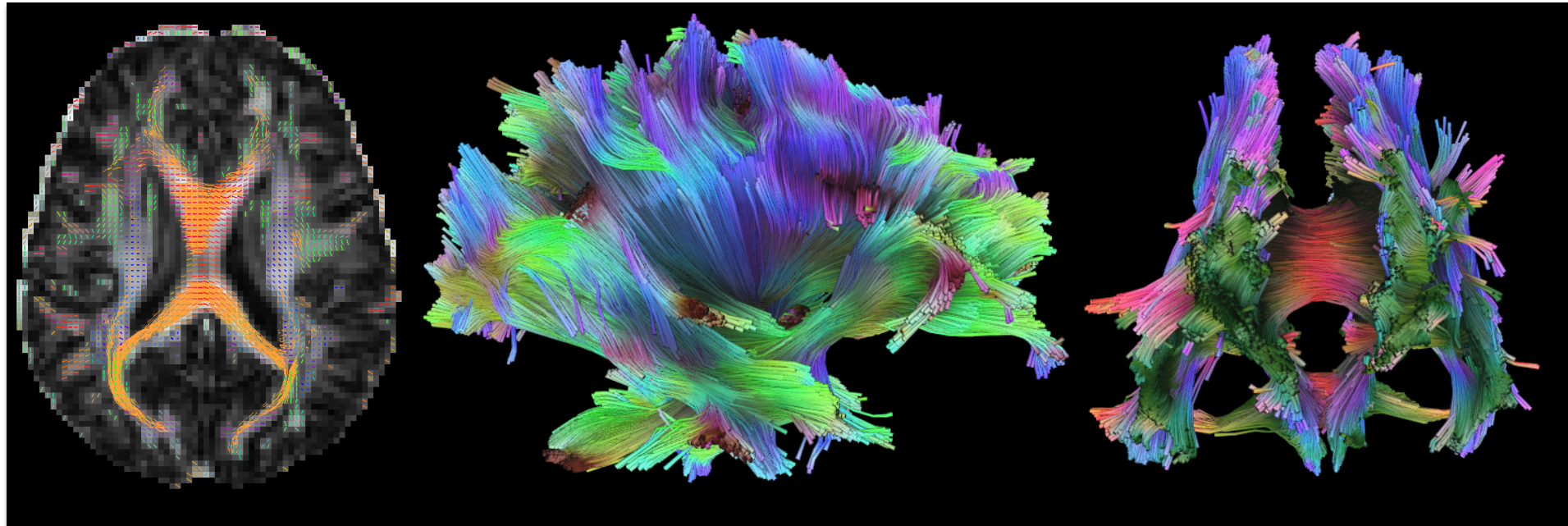
Fractional Anisotropy map highlighting white matter integrity (bright blue, right)

DTI Tracktography

- **Streamline** algorithm (repeat to cover seed region, e.g. 10k times):
 1. Start from a location in source region
 2. Move along voxels along their major eigenvector
 3. End when stop region is reached
 4. Repeat from step 1.
- **Deterministic** tracktography: One streamline per seed location *DSIstudio, trackvis*
- **Probabilistic** tracktography: Distribution of all streamlines from all seed voxels fsl *bedpostx, probtrackx*



DTI Tractography: Example of Deterministic tractography



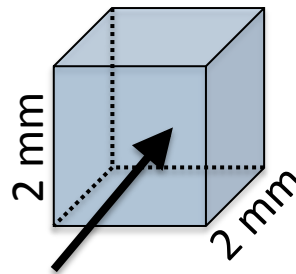
Eigenvectors on FA map

Tractogram sagittal view

2 mm

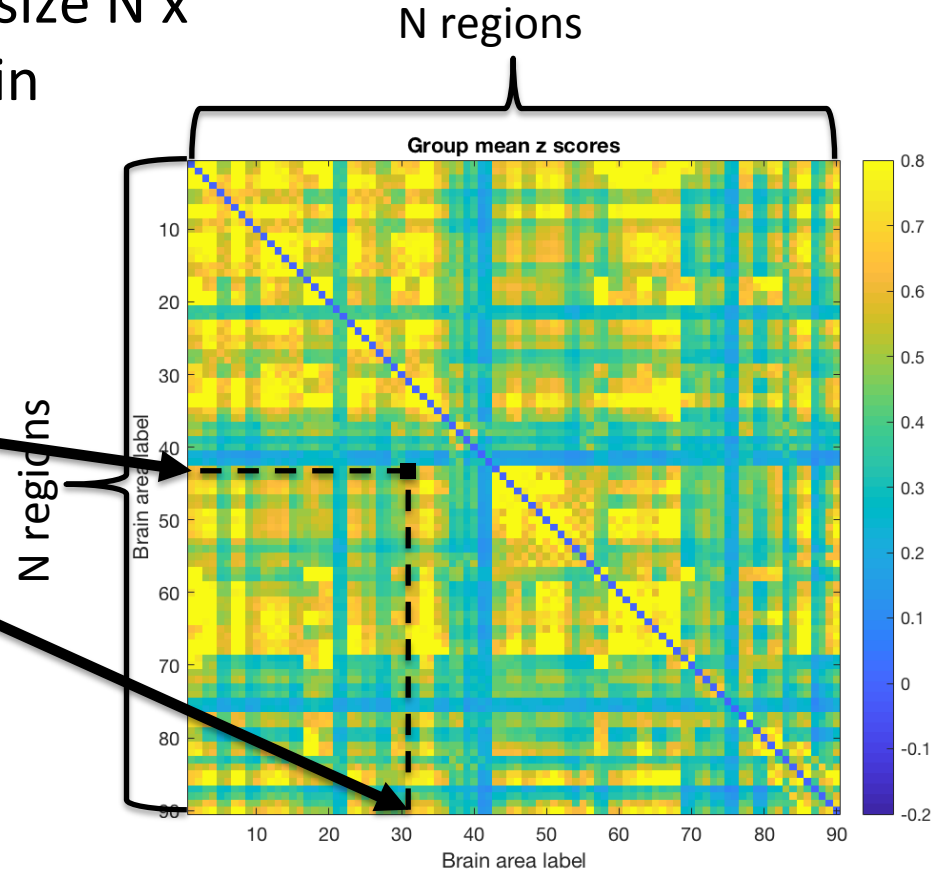
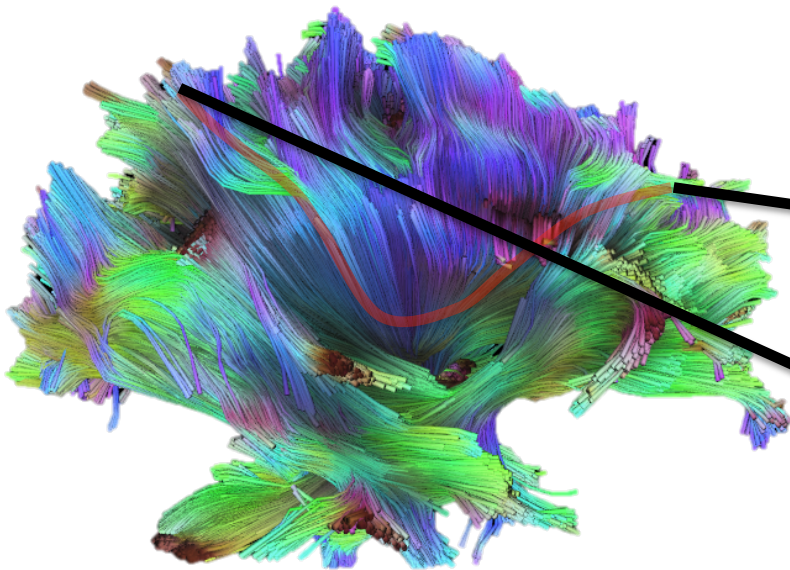
Tractogram coronal view

Voxel of size $2 \times 2 \times 2 \text{ mm}^3$ can contain approximately from ~ 0.5 million axons to >5 million axons!



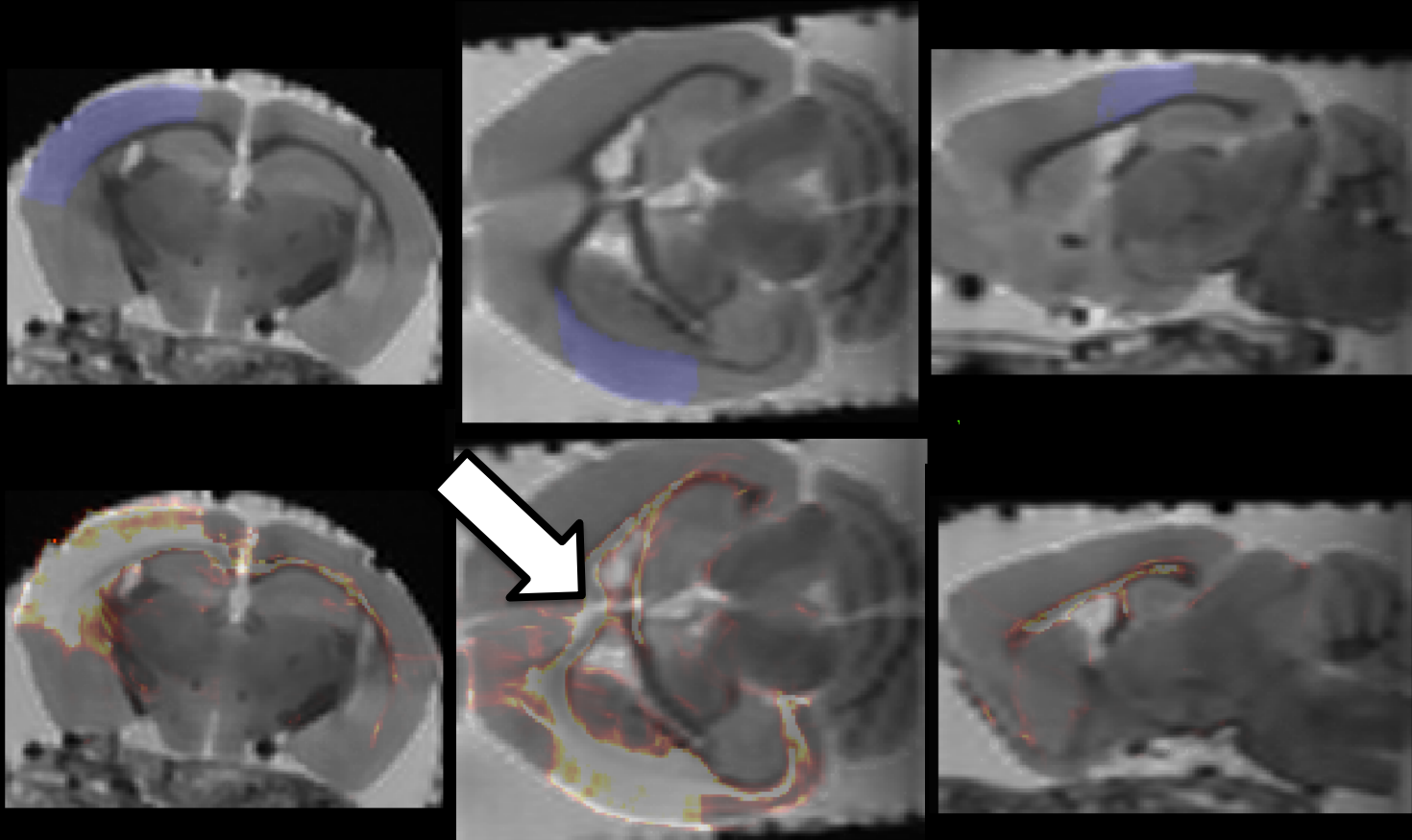
DTI Tractography: Connectomy matrix

Tractography can be executed e.g. between pairs of gray matter regions, creating **connectomy matrix**, of size $N \times N$, where N is the number of brain regions *matlab*, *python*



DTI Tractography: Example of Probabilistic tractography

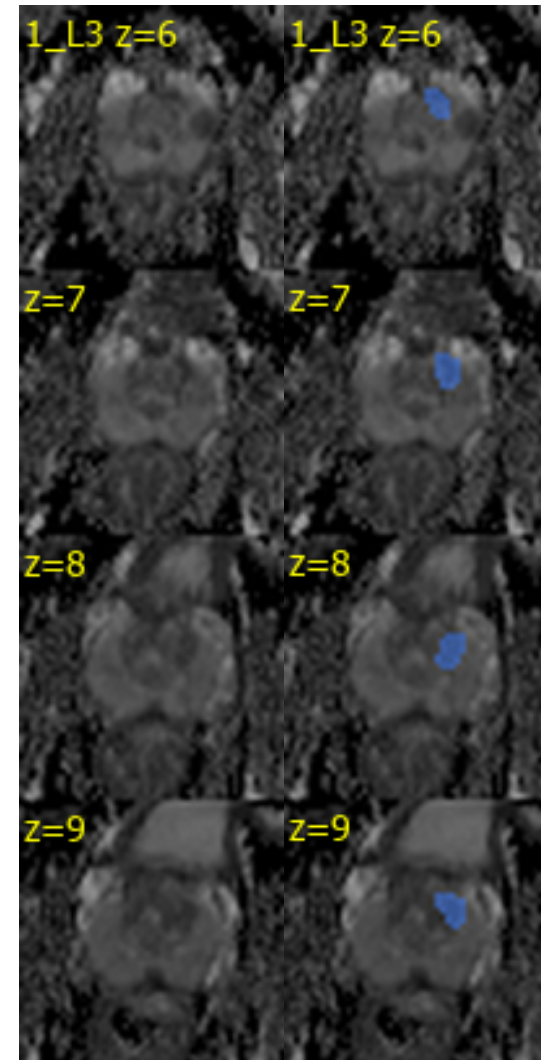
Murine TBI model right somatosensory cortex as seed region, arrow points corpus callosum where seed region connects to the opposite side



Region of Interest (ROI) placement

Region of Interest (ROI) placement

- Manual delineation
 - laborous
 - intra/inter-reader variability
- Automatic delineation
 - Atlas-based *ANTs*, *elastix*, *SPM*,
fsl *fnirt*, *Freesurfer*:
 - Procedure: 1) align image to template 2)
bring atlas to individual space 3) may
require manual edits/QA
 - Surface segmentation
Freesurfer



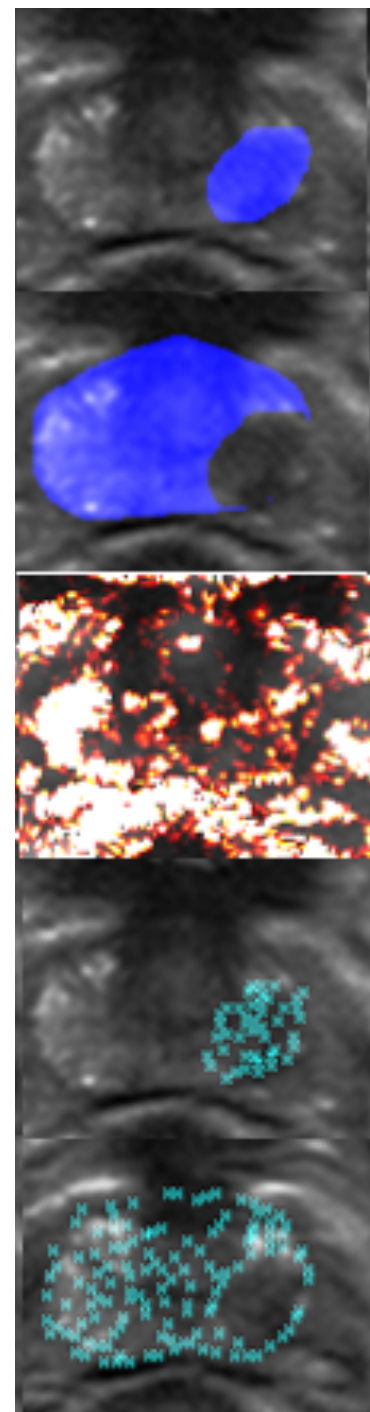
6 Radiomics

A radiomic feature is an extracted measure value from radiology data

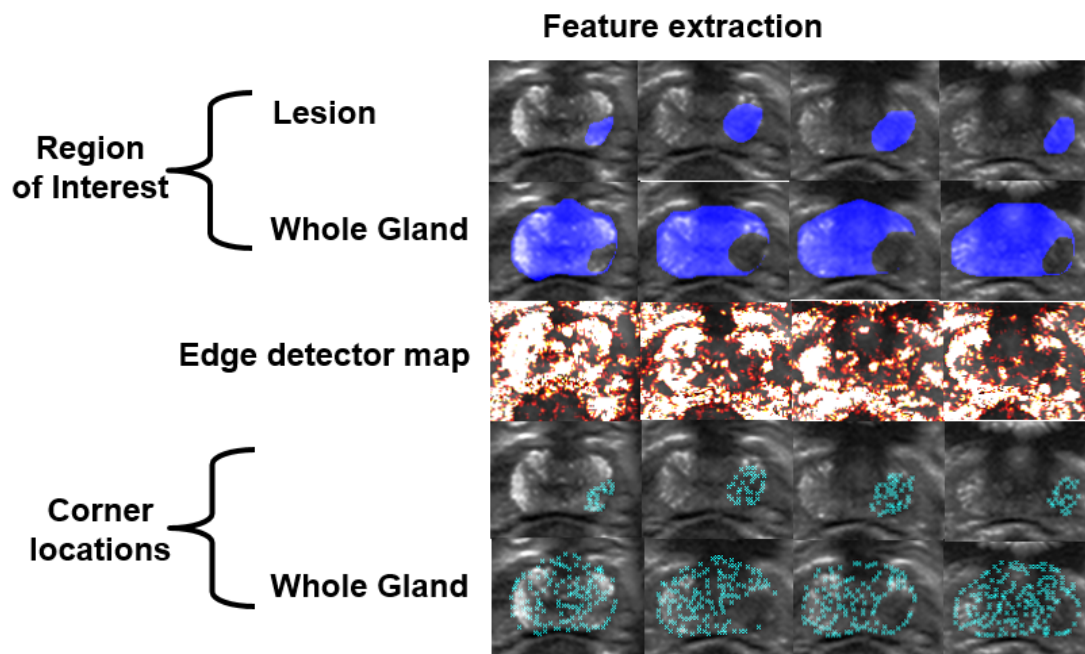
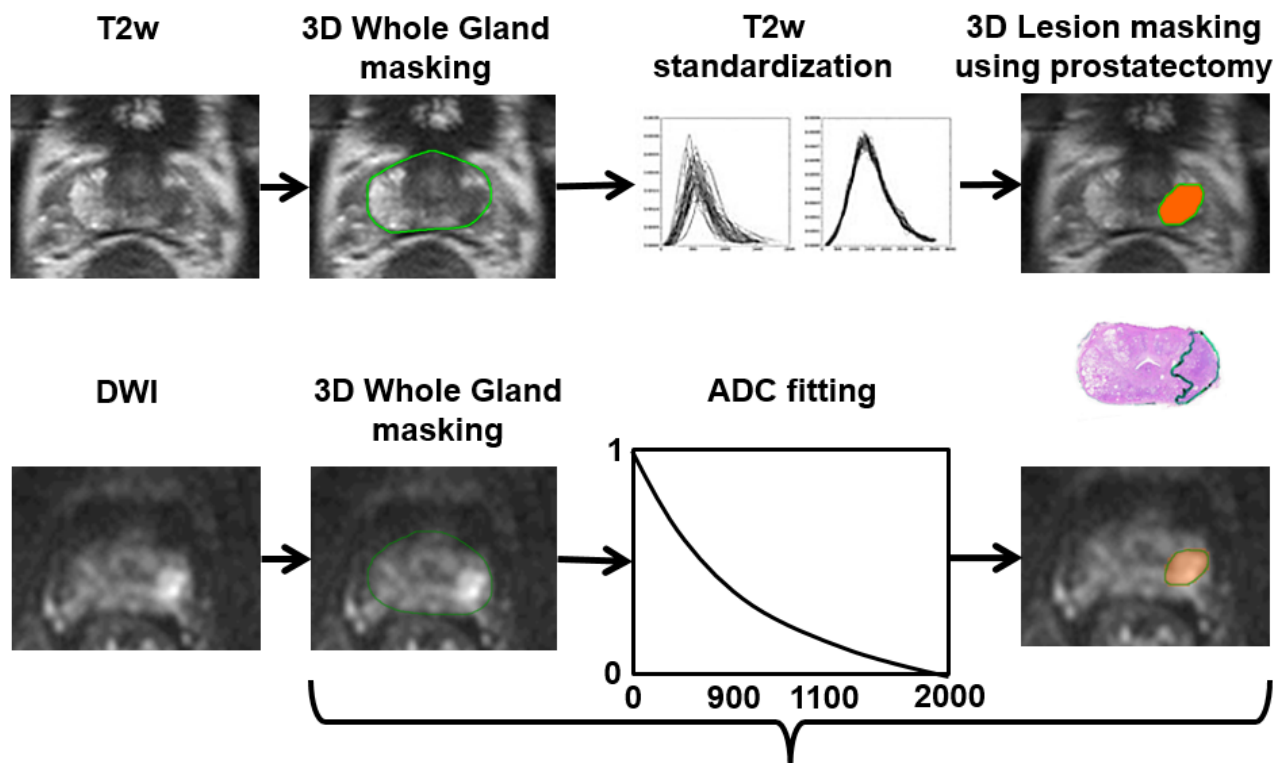
Field of study about radiomic features is ***Radiomics***

Radiomics

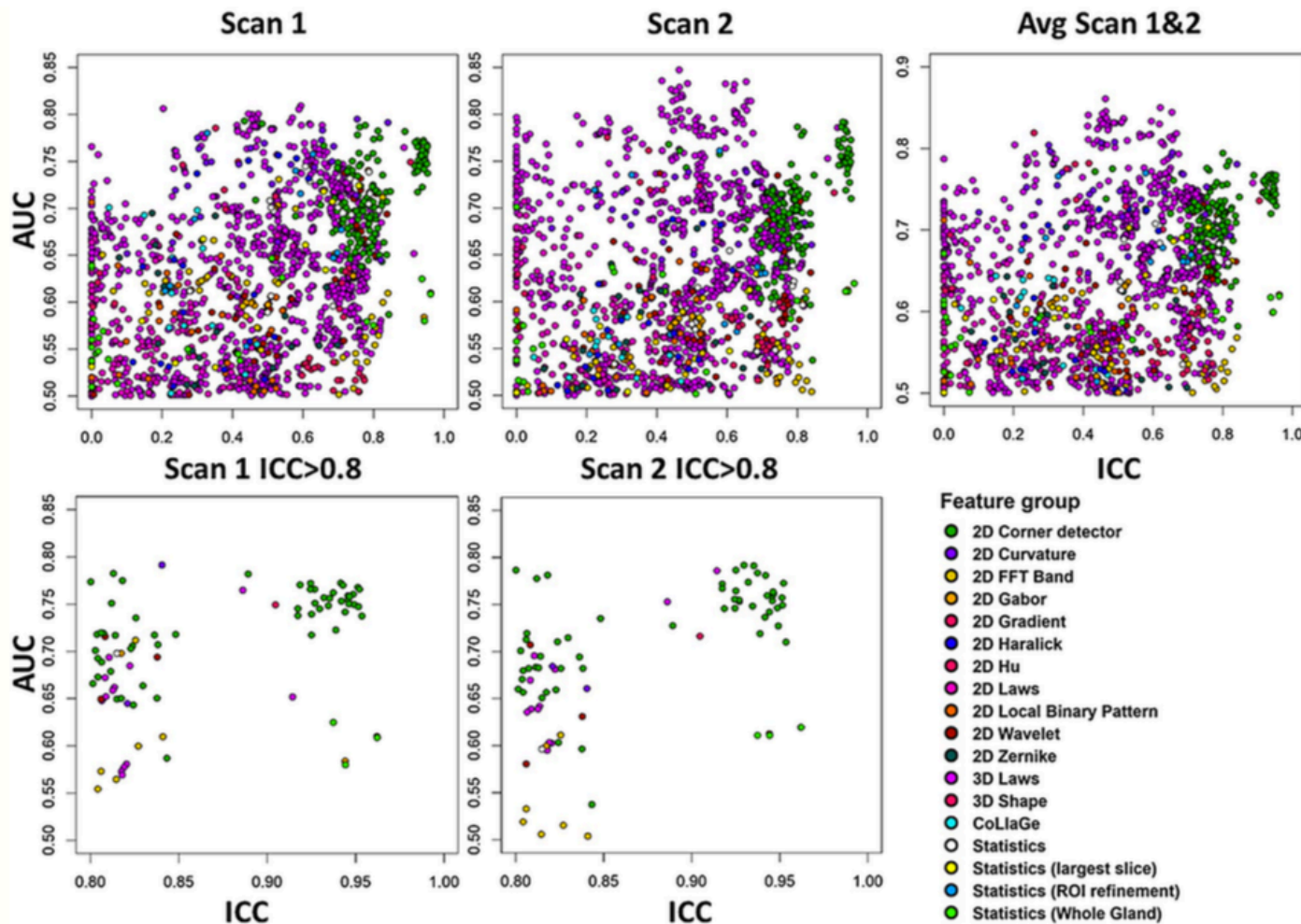
- Conventional analysis method is to take mean intensity (or median) in the ROI
- Radiomic feature extraction involves calculating other metrics from the voxel intensities inside ROI
 - Statistical descriptors (e.g. skewness, kurtosis percentiles)
 - Texture features (i.e. features describing textures)
 - Shape features (e.g. surface curvature, sphericity)
 - **Automatic features** (deep learning framework) or **Hand-crafted features** (by design)
- Performance in particular may depend on
 - Spatial resolution
 - Signal to noise ratio
 - Overall intensity level
- Field of study about radiomic features is called **Radiomics**
- Tools: ***pyradiomics, MRC tools, pytorch, tensorflow***



Radiomic feature extraction example: Prostate cancer



Radiomics at group level: Repeatability vs clinical performance



ICC(3,1) vs AUC for significant prostate cancer classification with ADC, optimal features are in top right corner

Radiomics: Feature selection

- Feature selection:
 - Selection of most relevant features relevant to the given problem
 - Crucial part of machine learning
 - Techniques
 - MRMR (Maximum Relevance Minimum Redundancy) algorithm
 - Univariate analysis
- Tools: R *mRMRe*, python *scikit-learn*, *pearson/spearman correlation between features*, *t-test/wilcoxon rank sum test for target groups*, *repeatability of features*

7 Artificial Intelligence

At this point all measurements are done,
now giving output for clinical use

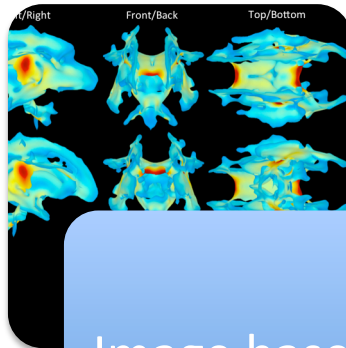
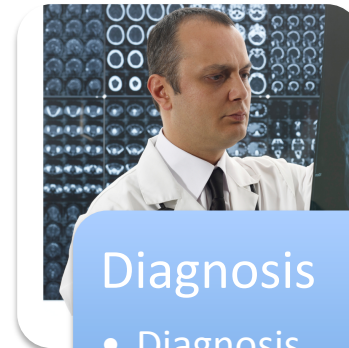


Image based
metrics

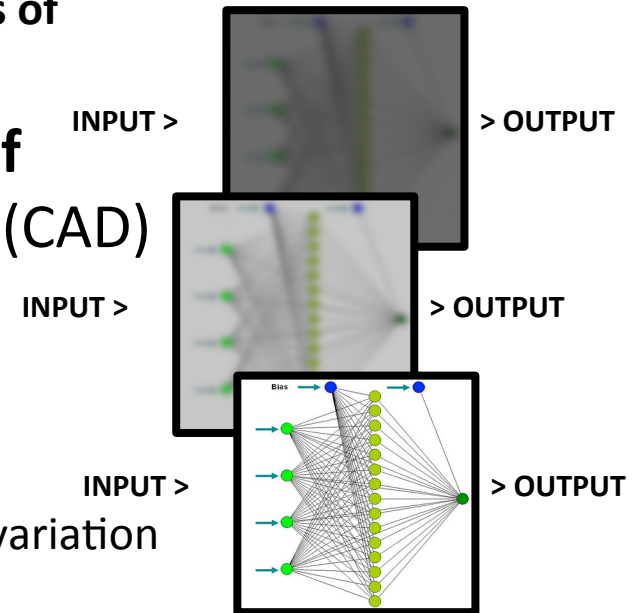


Diagnosis

- Diagnosis
- Prognosis
- Treatment decision

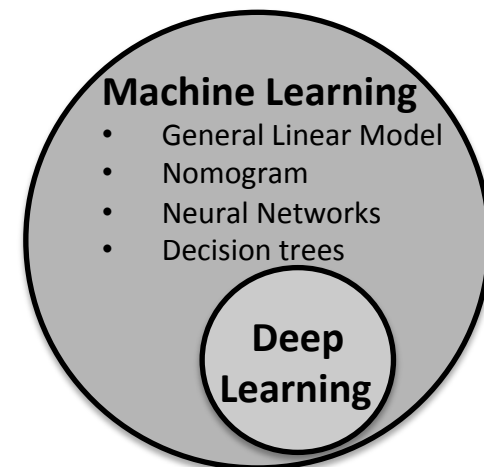
Artificial Intelligence

- Artificial Intelligence (AI) is used to tackle problem of large data
 - It is hard for human to benefit from all **large amounts of multidimensional data**
- AI can be used as a tool **assisting analysis of radiologist** in Computer Assisted Diagnosis (CAD)
 - CAD for region of interest
 - CAD for direct diagnosis/prognosis
- Pros & Cons of AI
 - Pro: AI is repeatable: no intra-reader or inter-reader variation with the same input
 - Con: ***black-box nature***
 - We do not know exactly why the AI tool gives certain specific answer – only that the answer is based on training data



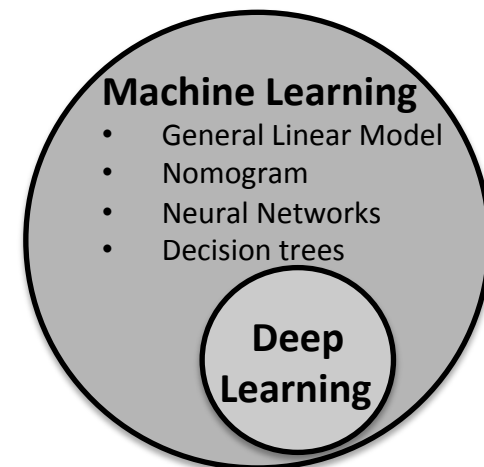
Artificial Intelligence

- **Machine learning** is generally used to train classifiers
 - Makes use of both radiomic features and clinical variables
 - Tools: R packages of: *stats* (GLM), *rms* (nomogram), *neuralnet* (ANN), *rpart* (decision trees), python *scikit-learn*
- **Deep learning** is specific type of Machine Learning, where neural networks have many internal layers, making the 'deep' architecture
 - Input is either 2D (image slice) or 3D/4D (image volume, multiple channels)
 - Require high amount of data and processing power
 - Tools: python *pytorch*, *tensorflow*, require CUDA



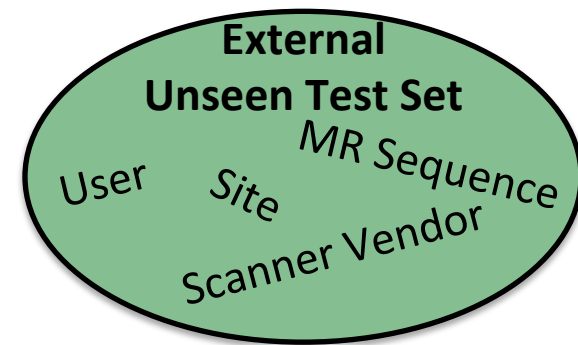
Machine Learning

- Steps for doing machine learning:
 1. Preprocessing of data to uniform format
 2. Feature Extraction
 3. Data split
 4. Training/Evaluation
 5. (Final test of fixed developed models)



Training AI

- Data is typically divided into training and testing set, used to verify that the trained model captures correct signal and is not **overfitting** to data
- Separate test data is created by dividing the available data into portions
 - **Stratification**: ensure same proportion of groups are represented in both training and testing
- **Testing set** is sometimes called '**unseen**', '**external**', or '**hold out**'
 - Not used in any method development/adjustments
- For designing training strategy and developing models use **training set**



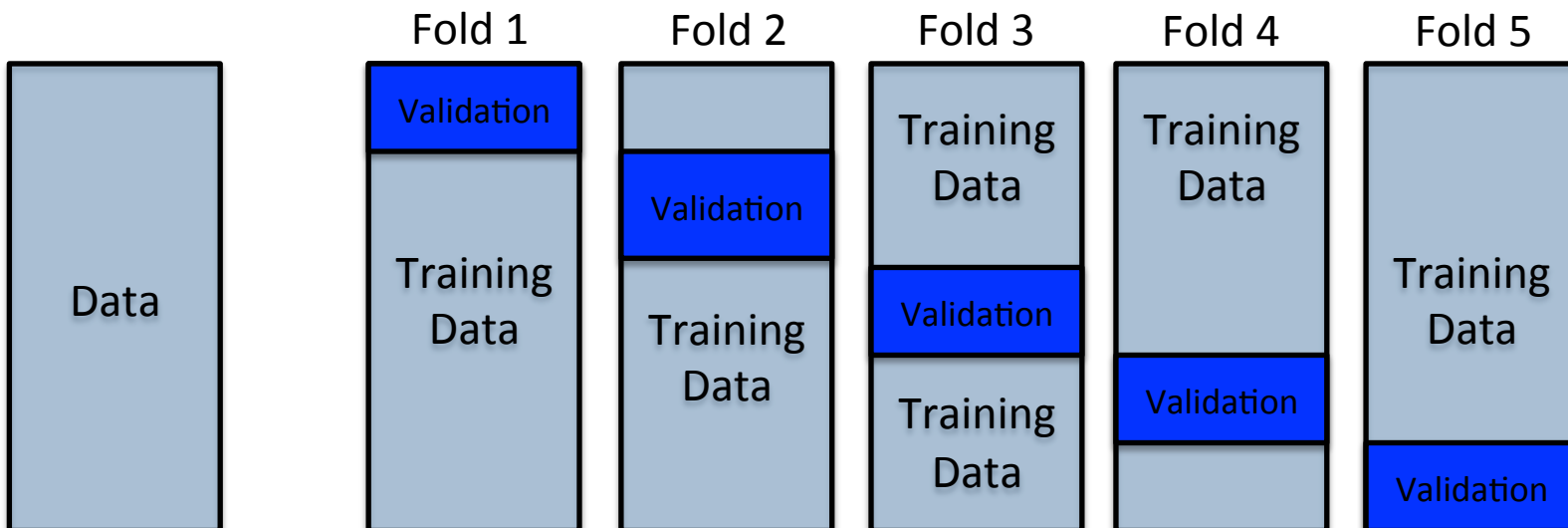
Cross-validation

- Typical N-fold cross-correlation analysis:
 - Data is split to folds
 - Each fold is used as validation set in turn to create estimate for performance
 - Running cross-validation multiple times causes multiple trials problem:
likelihood that we get good performance score by chance increases

- Cross-validation is used to obtain ***Unbiased estimation of generalization performance***

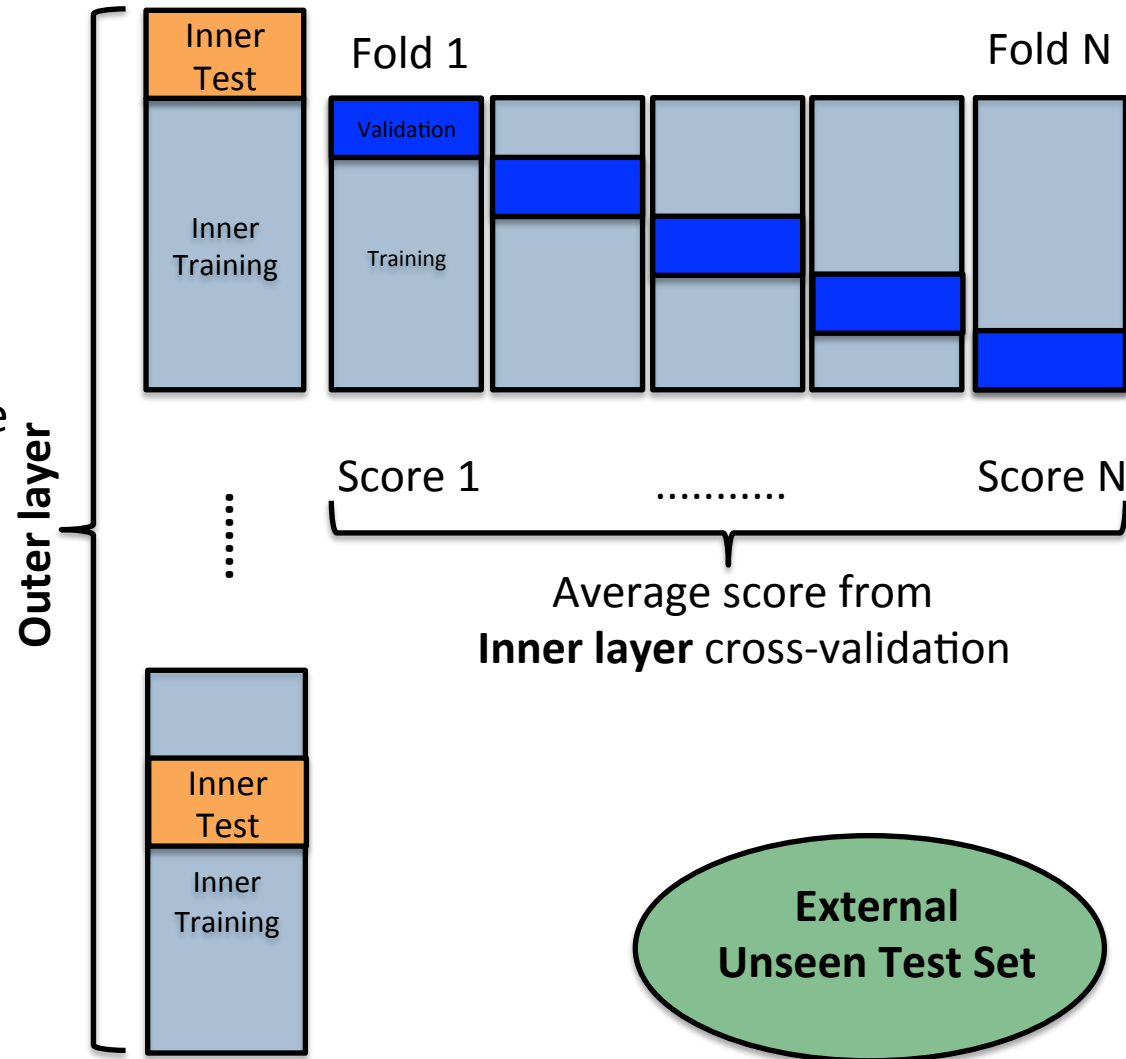
**≠
in contrast to**

Actual model for inference

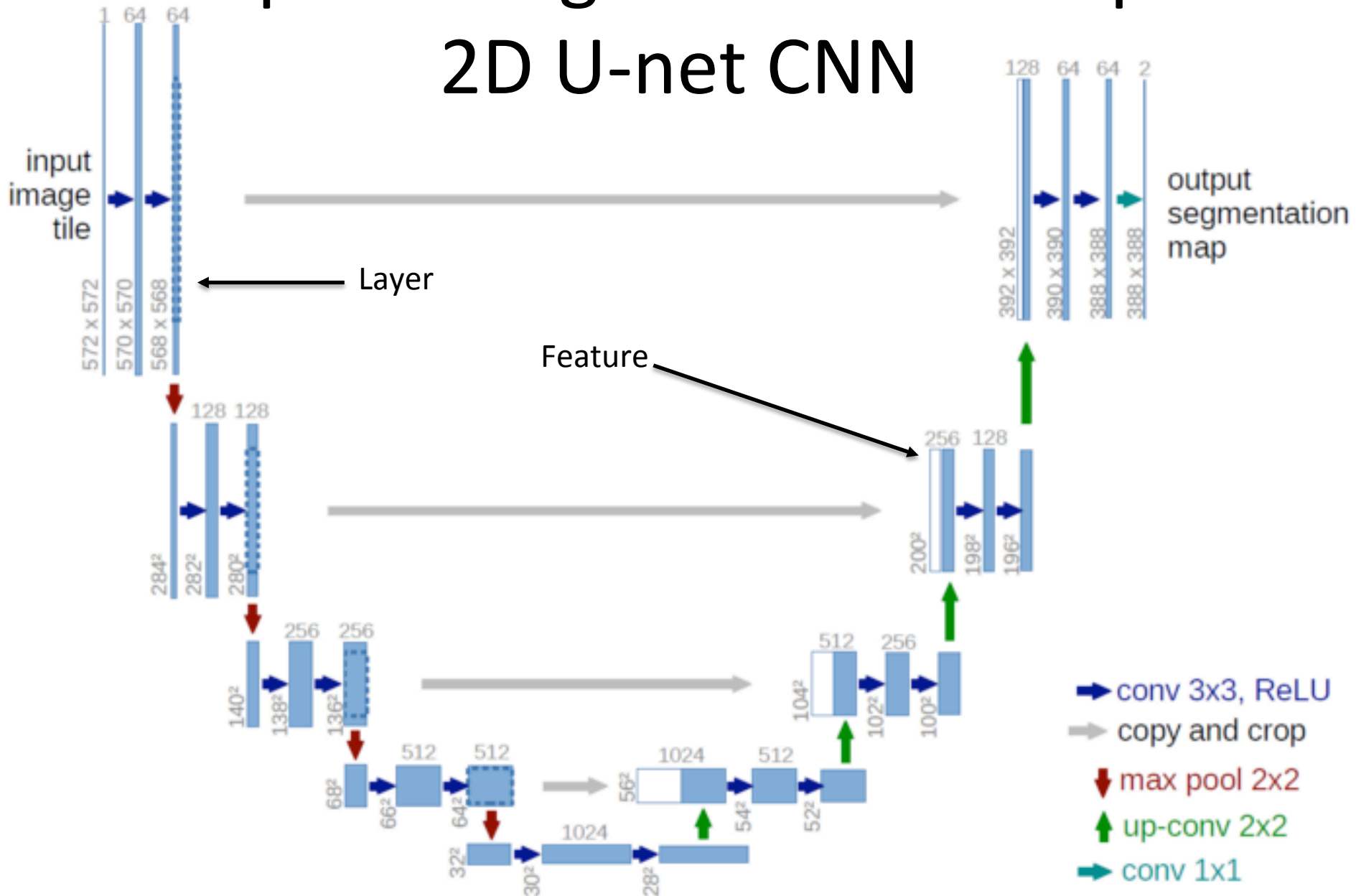


Nested Cross-validation

- Nested cross-validation (double cross-validation):
 - Cross-validation is repeated multiple times
 - Each repetition average score is calculated (as in cross-validation) with independent Test set (Inner Test)
 - **Inner layer** is used multiple times to choose model, hyperparameters, etc.
 - **Outer layer** gives unbiased estimator of generalization performance for the *whole process*

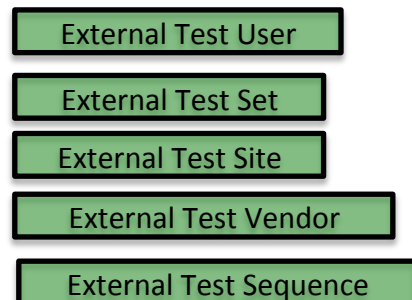
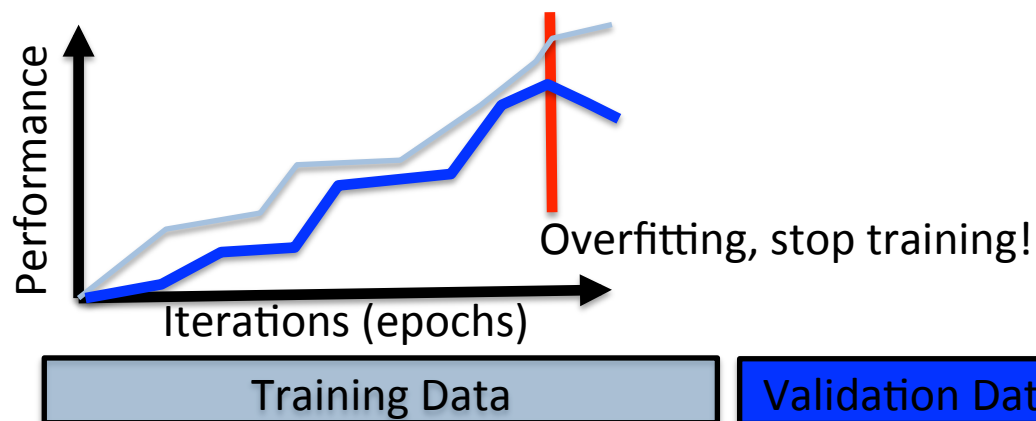


Deep learning network example: 2D U-net CNN



Deep learning

- Convention is to use one validation set since execution of evaluations is costly, even with GPU
- **Validation set** is used to see how well the model performs in external data
- When validation performance starts to drop while training performance increases, model started to **overfit to the data**
- **Ending criteria** is also part of the model development, so external test set is needed to verify the performance of trained model



Machine Learning in Medicine

- Prevalence of a condition/disease may be small
- Usually only one sample per case
- Proper Ground Truth –data not always available

Thank you!

**Any questions relating to MRI data
processing?**