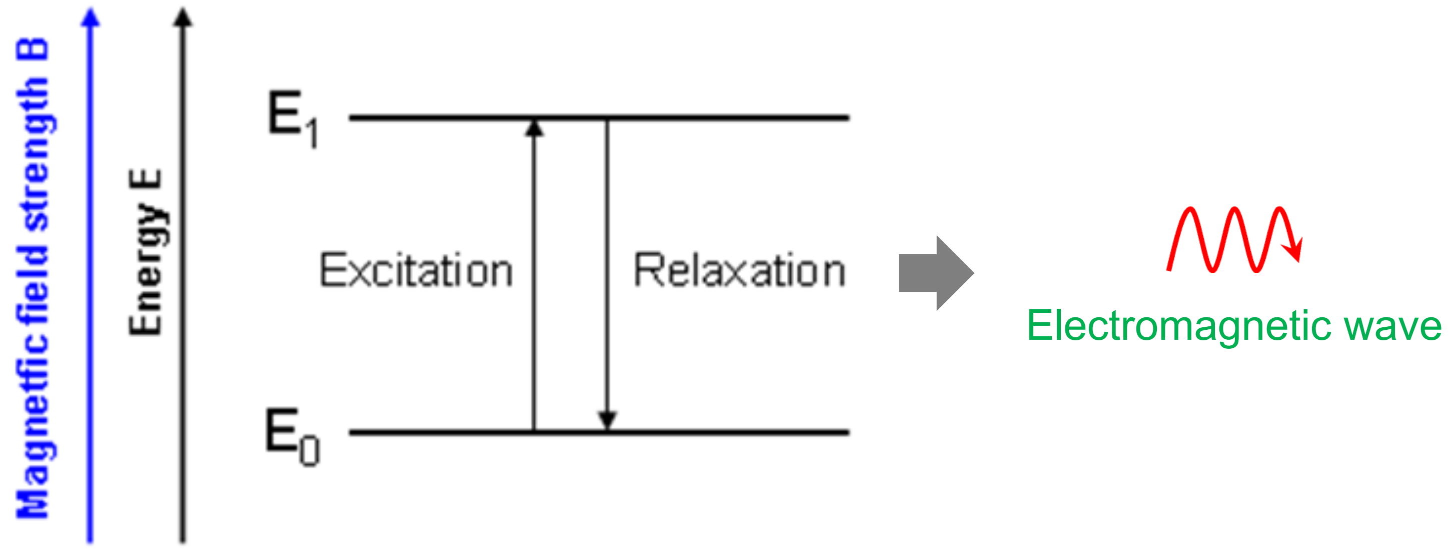
Medical/Bio Research Topics Ⅱ: Week 02 (14.09.2023)

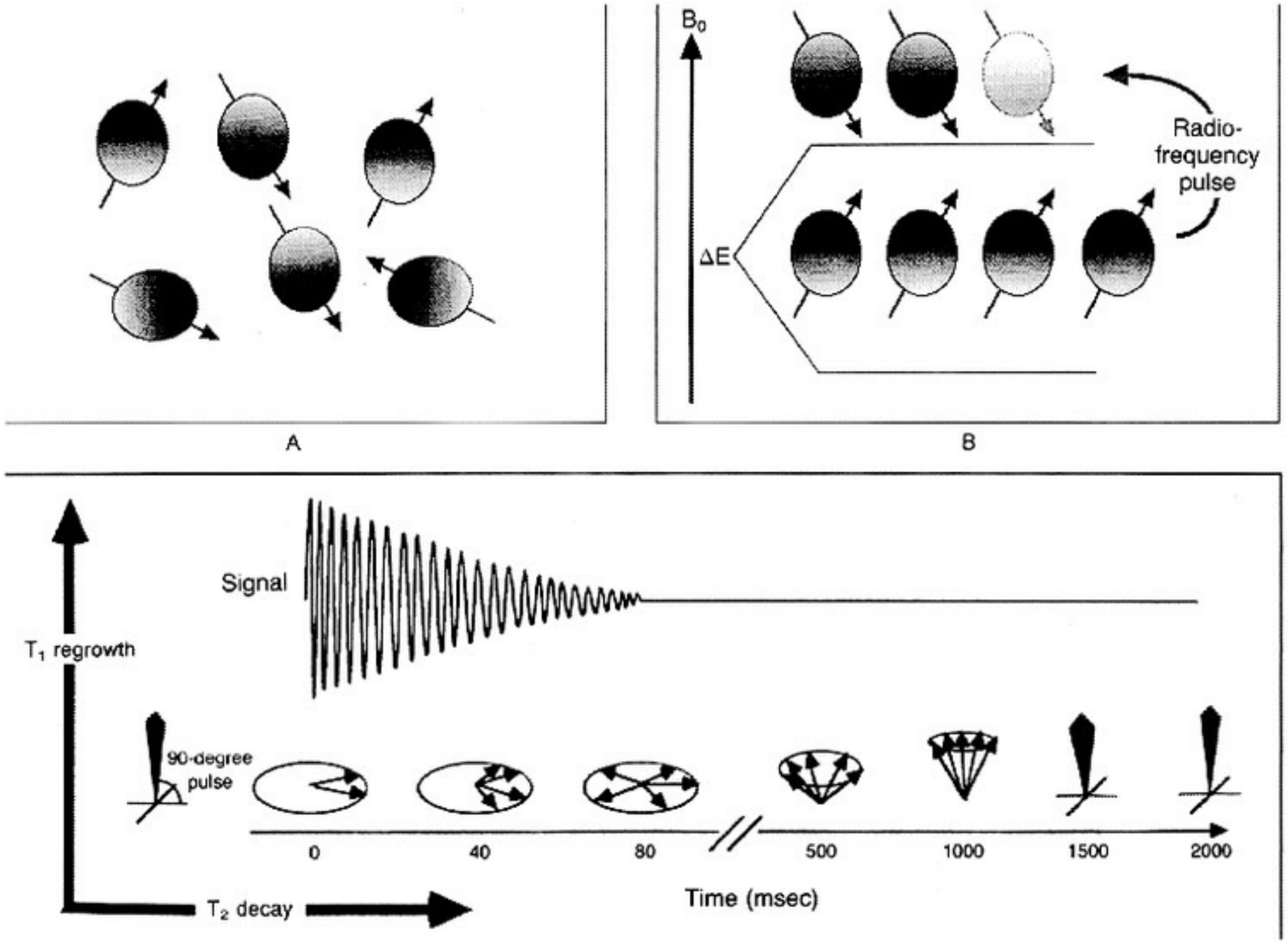
Structural MRI:
basic principles and introduction

(구조 자기공명영상: 원리 및 소개)

Principles of MRI

- Excites hydrogen nuclei (protons) into releasing electromagnetic waves (in radio frequency) and then records the locations of the waves with high accuracy





[Edelman and Warach, 1999]

Relaxation of hydrogen nuclei

- Two different relaxation times
  - T1 (longitudinal relaxation time)
    - Time taken for hydrogen nuclei to realign with the external magnetic field
    - Spin-lattice relaxation time: time taken for the longitudinal magnetization to recover 63% ($1-(1/e)$) of its initial value
    - Water-based tissues in the 400-1200 ms range; fat-based tissues in the 100-150 ms range
  - T2 (transverse relaxation time)
    - Time taken for hydrogen nuclei to lose phase coherence among the nuclei
    - Spin-spin relaxation time: time taken for the transverse magnetization to irreversibly decay to 37% ($1/e$) of its initial value
    - Water-based tissues in the 40-200 ms range; fat-based tissues in the 10-100 ms range

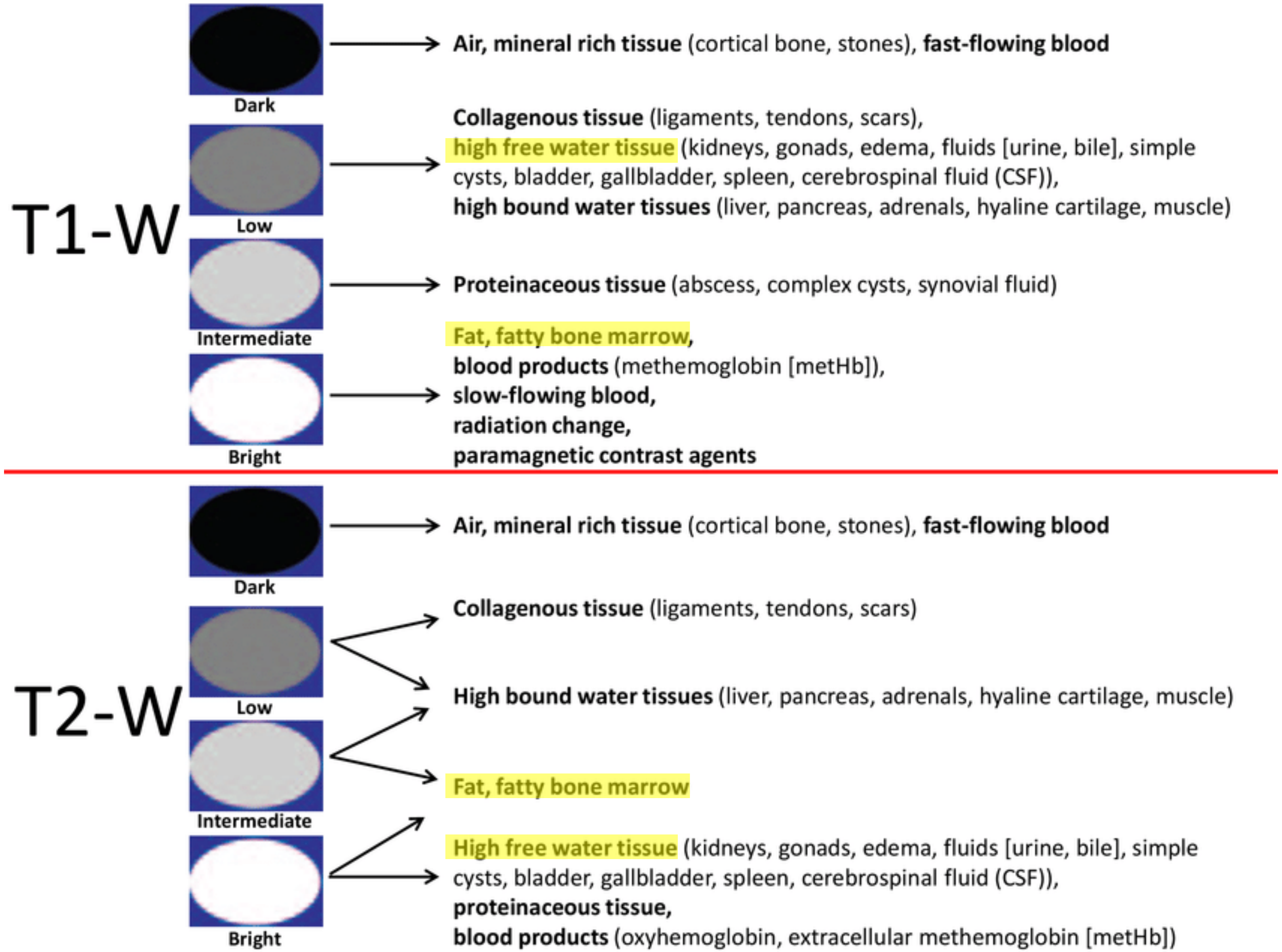
MRI Contrasts

- By varying the sequence of radio frequency electromagnetic waves (RF pulses) applied and collected
  - Repetition Time (TR): time between successive pulse sequences applied to the same slice
  - Echo Time (TE): time between the delivery of the RF pulse and the receipt of the echo signal

	TR (msec)	TE (msec)
T1-Weighted (short TR and TE)	500	14
T2-Weighted (long TR and TE)	4000	90
Flair (very long TR and TE	9000	114

[https://mriquestions.com/tr-and-te.html;
https://case.edu/med/neurology/NR/MRI Basics.htm]

MRI contrasts



[Ganiler, 2016]

Signal intensity of various tissues

- T1-weighted
  - Contrast predominately determined by T1 differences between tissues
  - Produced by using shorter TE (decreasing the T2 effect) and shorter TR (enhancing the T1 effect by rapidly exposing hydrogen nuclei to RF pulses)
  - Tissues that return to alignment faster than other tissues are bright on a T1-weighted image

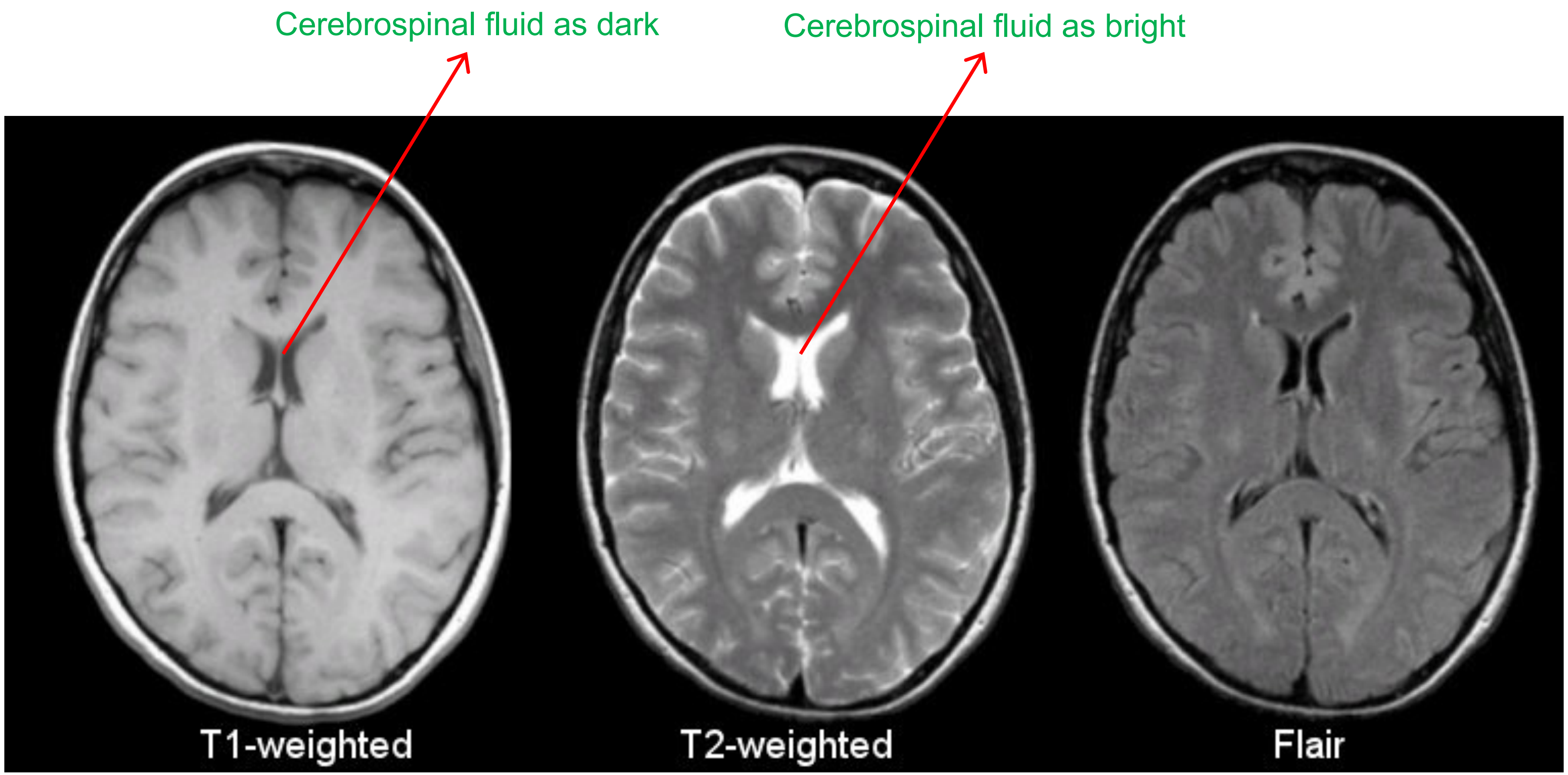
- T2-weighted
  - Contrast predominately determined by T2 differences between tissues
  - Produced by using longer TE (enhancing the T2 effect by allowing hydrogen nuclei to move away from each other) and longer TR (decreasing the T1 effect)
  - Tissues that remain in phase longer than other tissues are bright on a T2-weighted image

- Fluid Attenuated Inversion Recovery (FLAIR)
  - Heavily T2-weighted in that TE and TR are very long
  - Dampens ventricular cerebrospinal fluid signals, causing the highest signals from certain brain parenchymal abnormalities

Tissue	T1-Weighted	T2-Weighted	Flair
CSF	Dark	Bright	Dark
White Matter	Light	Dark Gray	Dark Gray
Cortex	Gray	Light Gray	Light Gray
Fat (within bone marrow)	Bright	Light	Light
Inflammation (infection, demyelination)	Dark	Bright	Bright

[https://case.edu/med/neurology/NR/MRI Basics.htm]

Different contrasts of the brain



[https://case.edu/med/neurology/NR/MRI Basics.htm]

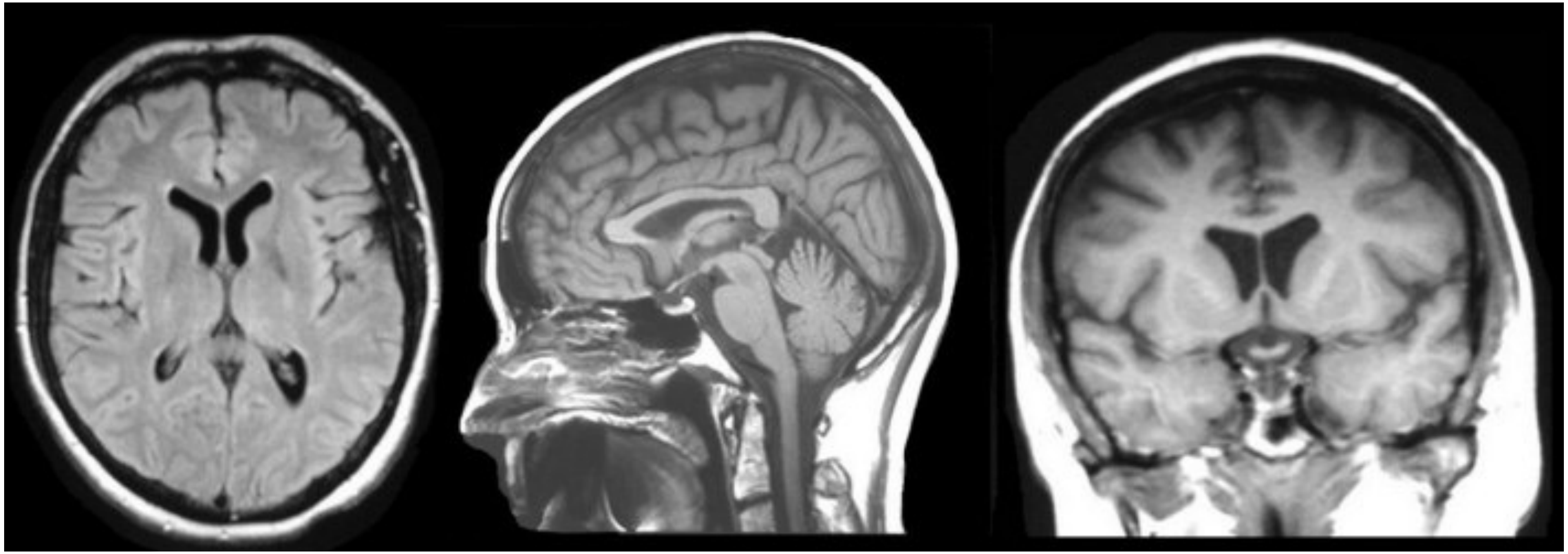
Comparison between T1-weighted, T2-weighted, and FLAIR images

T1-weighted Contrast of the Brain

- White matter (nerve fibres) has a very short T1 and relaxes rapidly
- Cerebrospinal fluid has a long T1 and relaxes slowly
- Grey matter (neuron congregations) has an intermediate T1 and relaxes at an intermediate rate

Producing an image
at a time when the curves are widely separated
between the tissues

- White matter contributes to lighter voxels
- Cerebrospinal fluid contributes to darker voxels
- Grey matter contributes to voxels with intermediate shades of grey



[https://case.edu/med/neurology/NR/MRI Basics.htm]

T1-weighted contrast of the brain

MRI Coordinate System

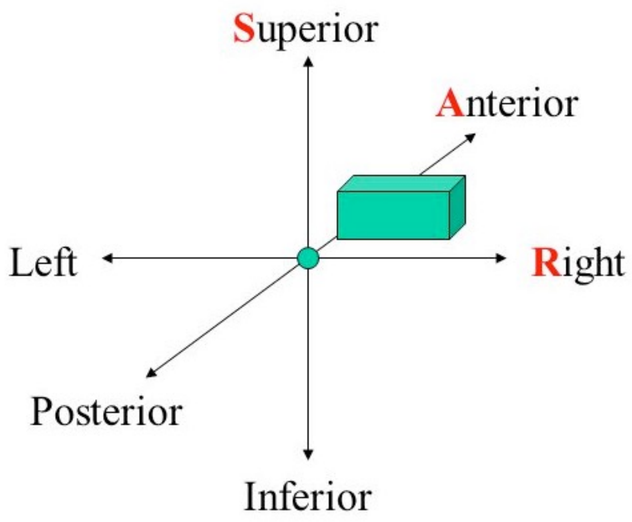
- Reference frame in a 3D space that assigns *x*, *y*, and *z* coordinates to anatomical regions [https://www.fieldtriptoolbox.org/faq/coordsys/]
  - What is the definition of the origin, *i.e.* [0, 0, 0]?
  - In which directions are the *X*-, *Y*- and *Z*-axis pointing?
  - In what units are coordinates expressed?
  - Is the geometry scaled to some template or atlas, or does it still match the individual's brain size?

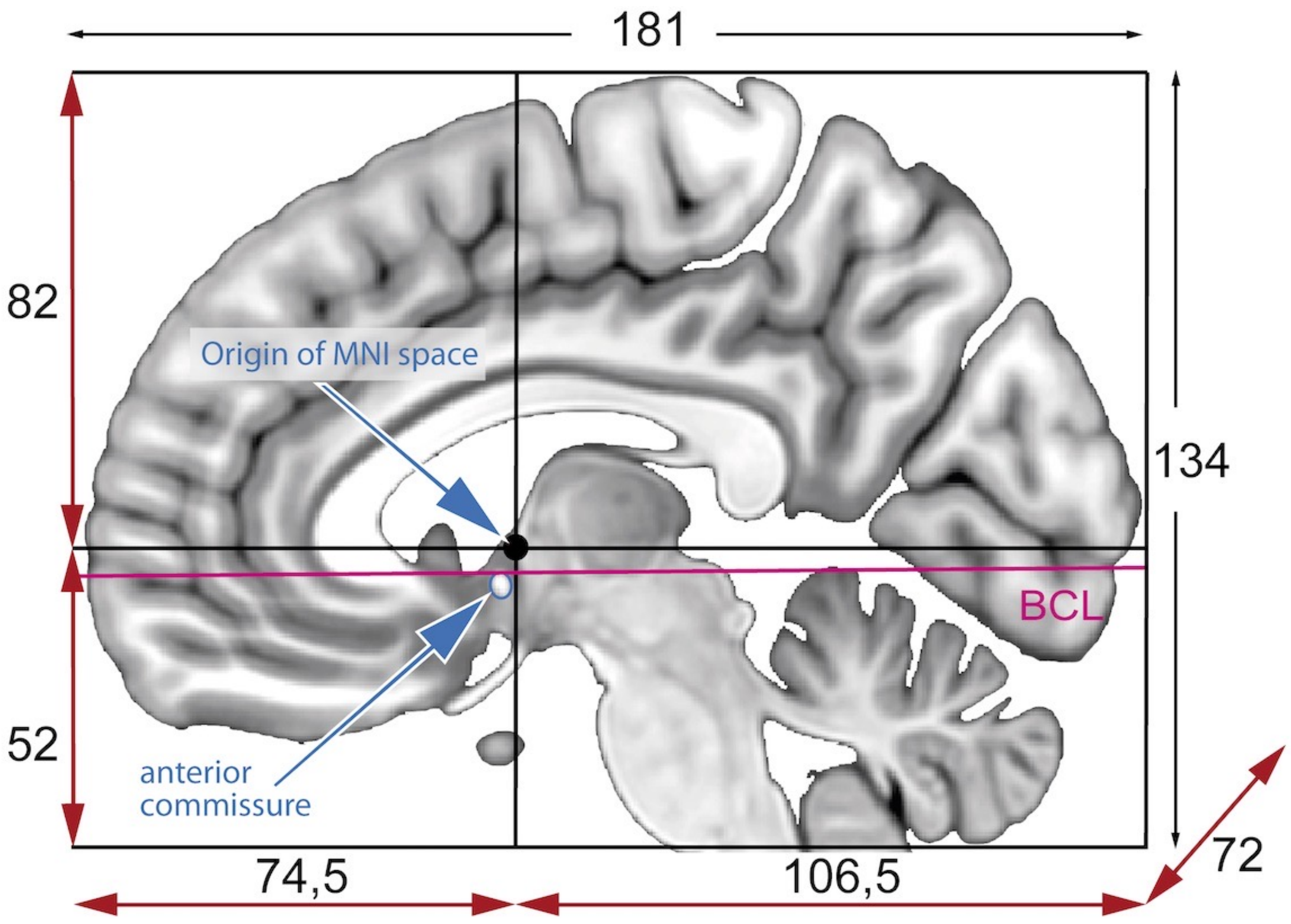
system	units	orientation	origin	scaling	notes
ACPC	mm	RAS	anterior commissure	native, i.e., not normalized to a template	
Allen Institute	mm	RAS	Bregma point		
Analyze	mm	LAS		native	
BTi/4D	m	ALS	between the ears	native	
CTF MRI	mm	ALS	between the ears	native	voxel order can be arbitrary
CTF gradiometer	cm	ALS	between the ears	native	
CapTrak	mm	RAS	approximately between the ears		
Chieti ITAB	mm	RAS	between the ears	native	
DICOM	mm	LPS	centre of MRI gradient coil	native, see here	
EEGLAB	mm	ALS	between the ears	native	
FreeSurfer	mm	RAS	center of isotropic 1 mm 256x256x256 volume		
MNI	mm	RAS	anterior commissure	scaled to match averaged template	
NIfTI	mm	RAS		see here, search for "Orientation information".	
Neuromag/Elekta/Megin	m	RAS	between the ears	native	
Paxinos-Franklin	mm	RSP	Bregma point		
Scanner RAS (`scanras`)	mm	RAS	scanner origin	native	
Talairach-Tournoux	mm	RAS	anterior commissure	scaled to match atlas	
Yokogawa		ALS	center of device		

[https://www.fieldtriptoolbox.org/faq/coordsys/]

Different MRI coordinate systems

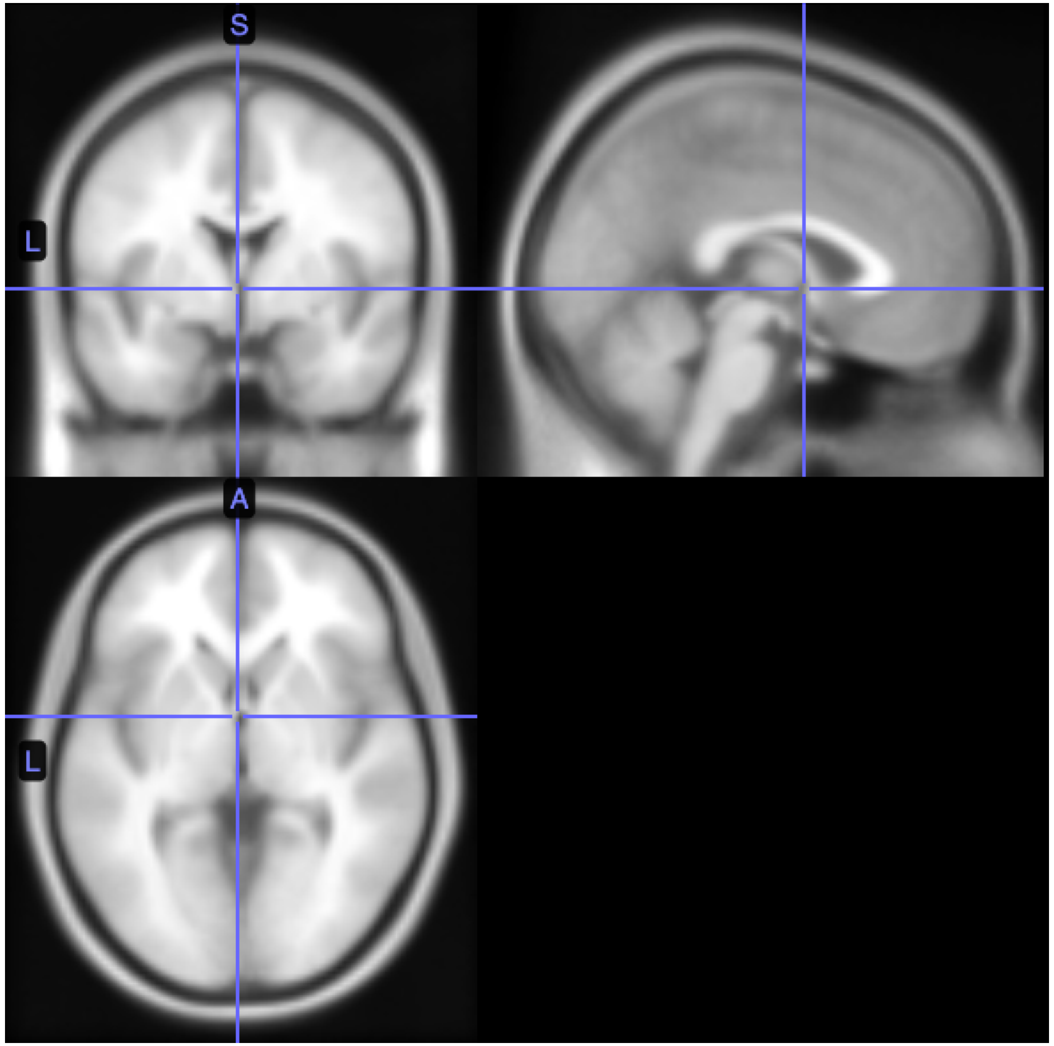
- Montreal Neurological Institute (MNI) coordinate system
  [https://www.fieldtriptoolbox.org/faq/coordsys/]
  - Origin in the anterior commissure
  - *X*-axis from left to right
  - *Y*-axis from posterior to anterior
  - *Z*-axis points from inferior to superior
  - Used if the geometry is spatially warped to the MNI152 template brain (average of 152 T1-weighted MRI scans from young adults)





[https://carpentries-incubator.github.io/SDC-BIDS-sMRI/03-Image_Spatial_Normalization/index.html]

MNI coordinate system



MNI152 template brain

- Transformation matrix
  - Links array indices to 3D coordinates

$$\begin{bmatrix} 2 & 0 & 0 & -90 \\ 0 & 2 & 0 & -126 \\ 0 & 0 & 2 & -72 \end{bmatrix} \begin{bmatrix} i \\ j \\ k \end{bmatrix} \rightarrow \begin{bmatrix} x \\ y \\ z \end{bmatrix}$$

Voxel indices

3D coordinates

MRI File Format

- Provides a standardized way to store the information describing an image in a computer file [Larobina and Murino, 2014]
  - How image data are organized inside an image file
  - How image data should be interpreted by software for the correct loading and visualization

- Basic concepts common to all image file formats
  - Voxel depth: number of bits used to encode the information of each voxel
    - Integer, real number, or complex number in different bits
  - Photometric interpretation: how image data should be interpreted for the correct image display as a monochrome or color image
    - Samples per voxel: number of channels
    - Grey scale photometric interpretation for MRI data

- Metadata: information that describe an image
  - Typically stored at the beginning of the file as a header
  - Contains at least image matrix dimensions, spatial resolution, voxel depth, and photometric interpretation
  - Enables software to recognize and correctly open an image in a supported file format
  - Tool to annotate and exploit image-related information for clinical and research purposes
- Image data: section where numerical values of voxels are stored
  - Usually stored as integers or floating-point numbers using the minimum number of bytes required to represent values according to a designated data type

- Image file size = header size + image data size
  - Metadata and image data in a single file or in separate files
- Major file formats currently used in brain imaging
  - Intended to standardize images generated by diagnostic modalities
    - Digital Imaging and Communications in Medicine (DICOM)
  - Aimed to facilitate and strengthen post-processing analysis
    - Analyze
    - Neuroimaging Informatics Technology Initiative (NIfTI)

Format	Header	Extension	Data types
Analyze	Fixed-length: 348 byte binary format	.img and .hdr	Unsigned integer (8-bit), signed integer (16-, 32-bit), float (32-, 64-bit), complex (64-bit)
Nifti	Fixed-length: 352 byte binary format[a] (348 byte in the case of data stored as .img and .hdr)	.nii	Signed and unsigned integer (from 8- to 64-bit), float (from 32- to 128-bit), complex (from 64- to 256-bit)
Minc	Extensible binary format	.mnc	Signed and unsigned integer (from 8- to 32-bit), float (32-, 64-bit), complex (32-, 64-bit)
Dicom	Variable length binary format	.dcm	Signed and unsigned integer, (8-, 16-bit; 32-bit only allowed for radiotherapy dose), float not supported

[Larobina and Murino, 2014]

Characteristics of image file formats

- DICOM
  - Not only a file format but also a network communication protocol
  - Established by the American College of Radiology and the National Electric Manufacturers Association
  - Introduced to imaging departments at the end of 1990s
  - Today, backbone of every medical imaging department
  - Contains the most complete description of the entire procedure used to generate an image, such as acquisition protocol, scanning parameters, and patient information, in the header
  - Can only store voxel values as integers

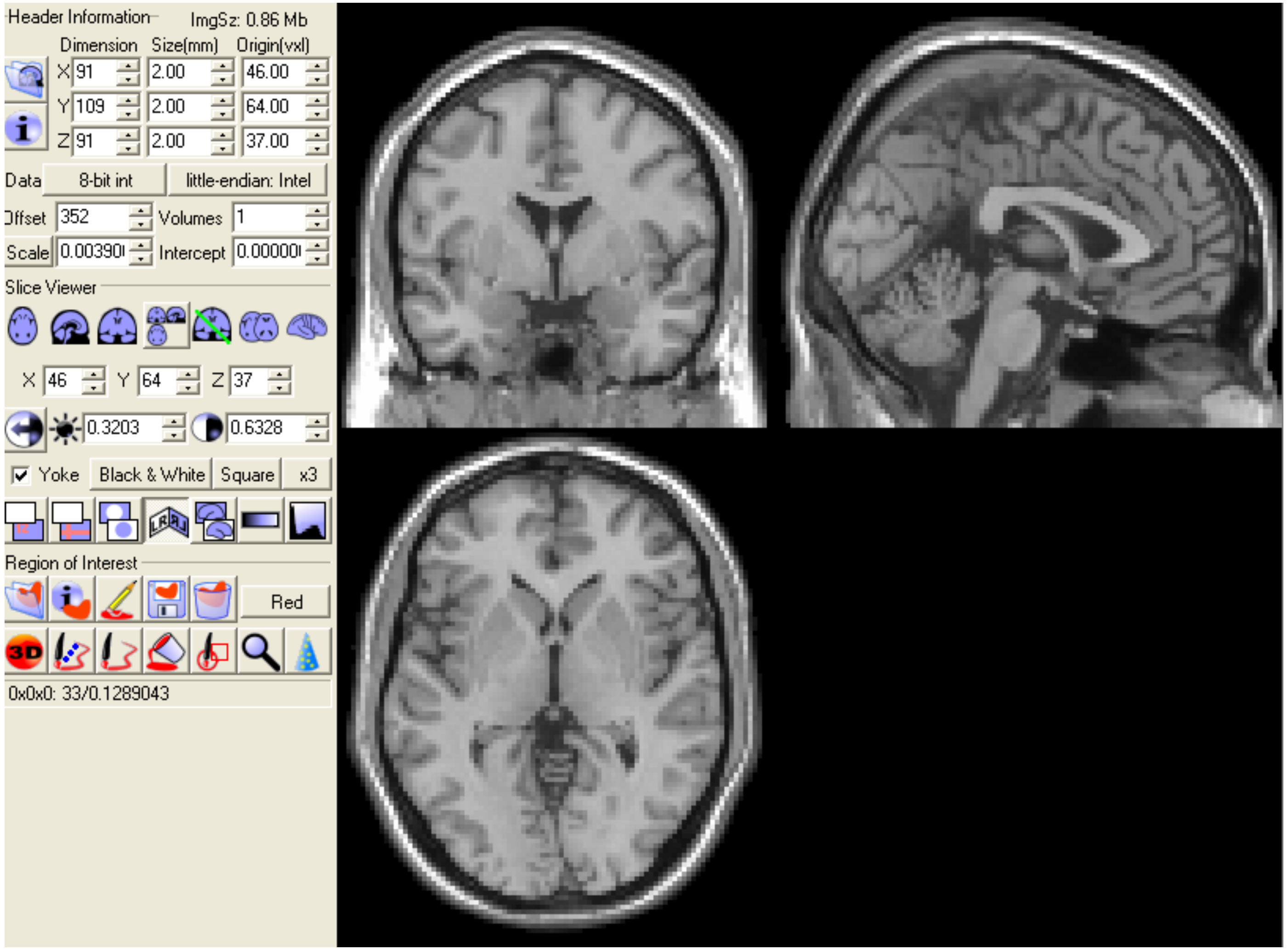
- NIfTI
  - Created at the beginning of 2000s by a committee based at the National Institutes of Health
  - Revised Analyze format
    - Can store new information like image orientation with the intent to avoid the left–right ambiguity
  - Typically saved as a single .nii or .nii.gz file in which the header and image data are merged
    - In the case of a single file, header with a size of 352 bytes
  - Adopted as the default format by the most widespread public domain software packages

[Practice 1]

- Open the DICOM files (MRI/DICOM/brain_*.dcm) and check the metadata and image data
  - In MATLAB, `dicominfo` and `dicomread` functions in the Image Processing Toolbox
  - In Python, `pydicom` and `simpleITK` modules

[Practice 2]

- Open the NIfTI file (MRI/NIfTI/single_subj_T1.nii) and check the metadata and image data
  - In MATLAB, `niftiinfo` and `niftiread` functions in the Image Processing Toolbox
  - In Python, `nibabel` and `simpleITK` modules



Dimensions: 91 × 109 × 91
Voxel depth: 8-bit integer
Voxel size: 2 mm × 2 mm × 2 mm
Origin: [46, 64, 37]

File size:
Header = 352 B
Image data = 91 × 109 × 91 × 8 bits
Total = 352 B + 902,629 B
= 902,981 B
= 0.86 MB

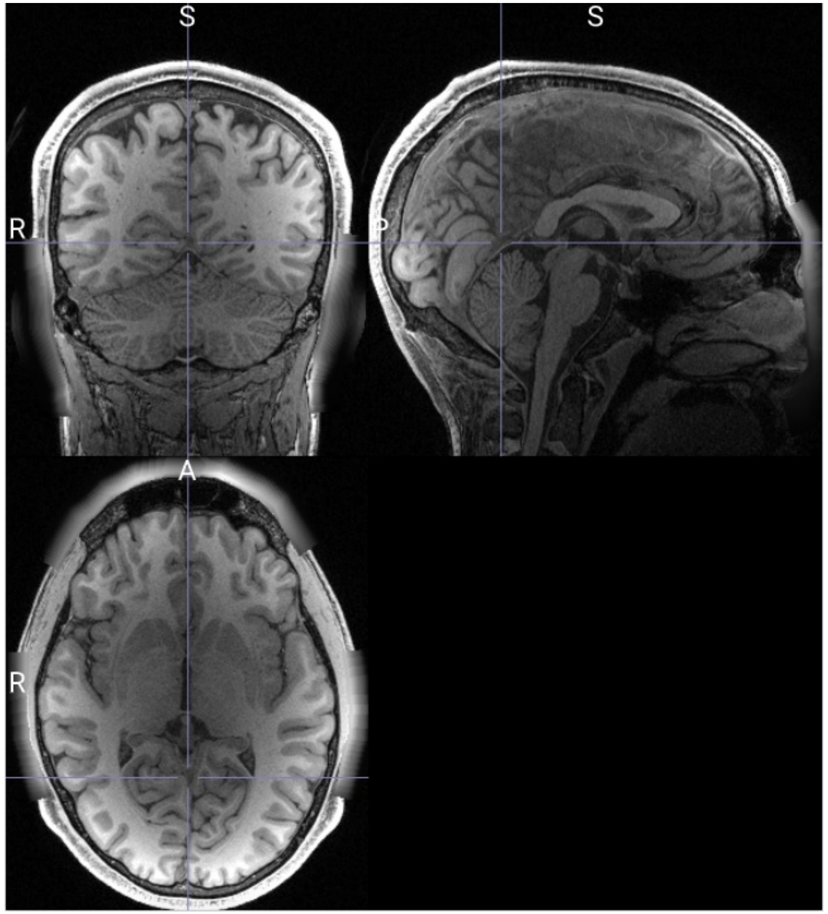
Example NIfTI file

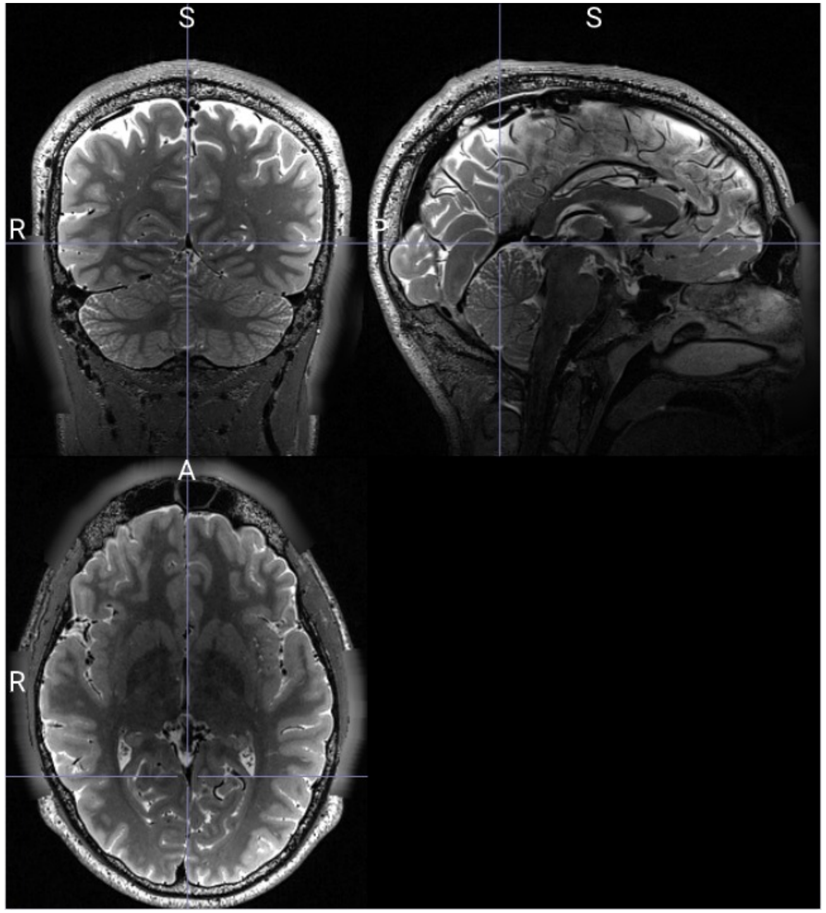
[Practice 3]

- Open the NIfTI files of structural MRI (MRI/sMRI/3T_T1w_MPR1.nii.gz, MRI/sMRI/3T_T2w_SPC1.nii.gz) and check the metadata and image data by using GUI software
  - MRIcro
  - MRIcron
  - MRIcroGL

Structural MRI (sMRI)

- MRI technique primarily for examining the anatomy and pathology of the brain
  - As opposed to using functional MRI to measure brain activity
- Usability of sMRI
  - Abnormality detection
  - Brain morphometry
  - Spatial reference of other modalities

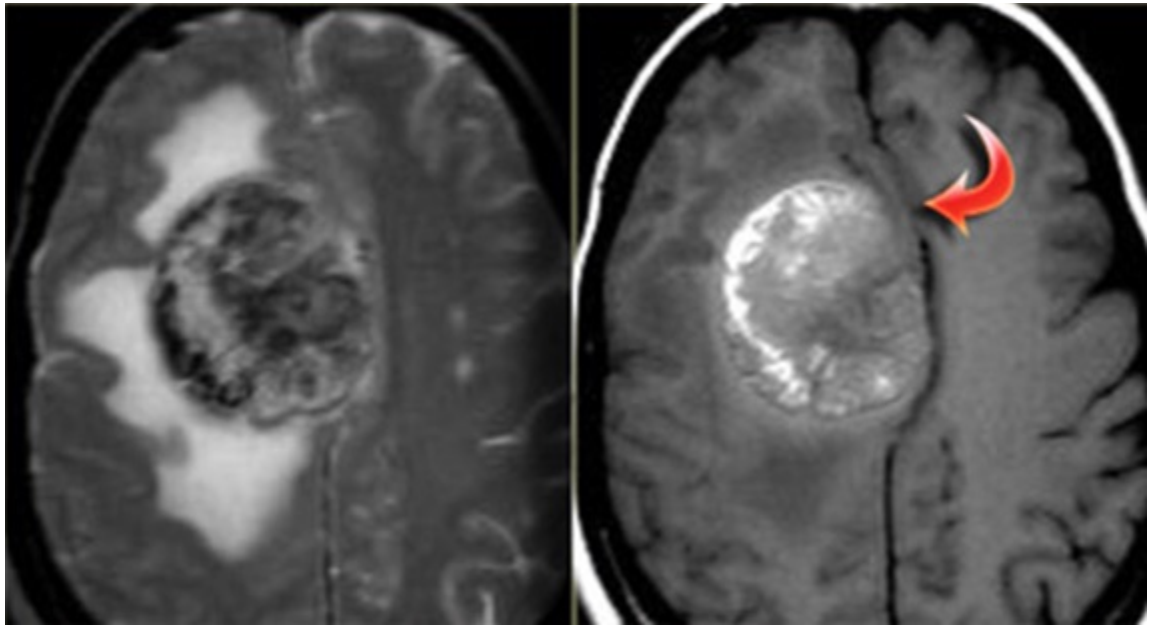




T1-weighted and T2-weighted sMRI

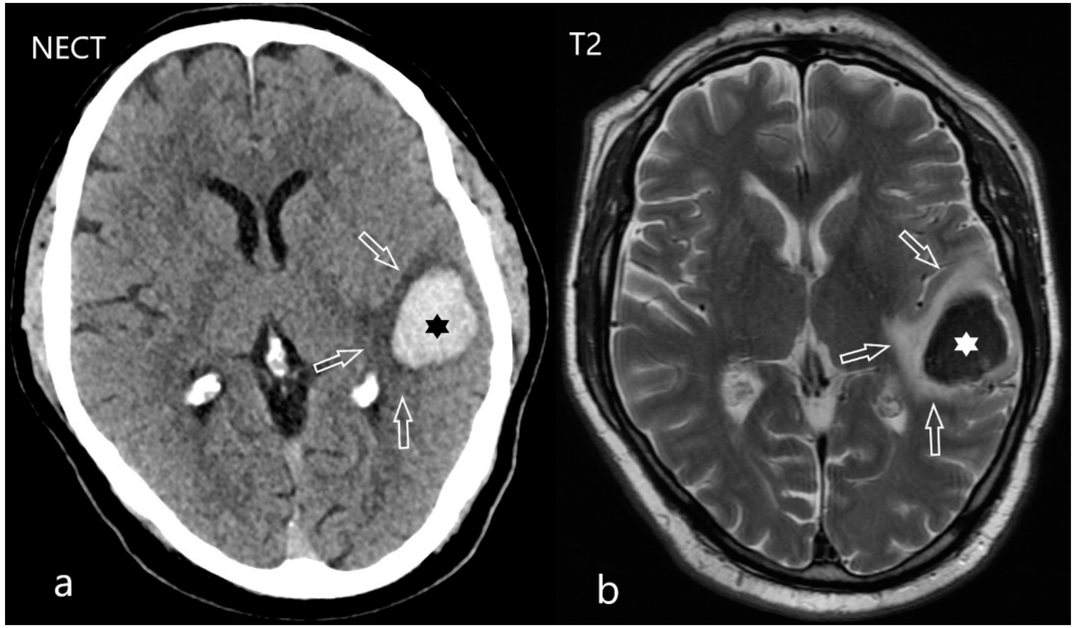
Abnormality Detection with sMRI

- Brain lesion
  - Region that has been damaged by an injury or a disease
  - Disrupts the way the brain works, causing a wide range of symptoms



[https://radiologyassistant.nl/neuroradiology/brain-tumor/systematic-approach]

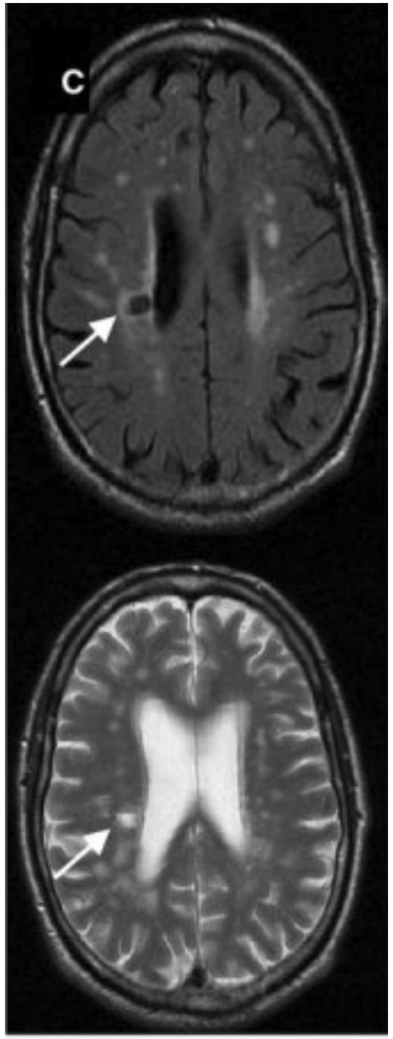
Brain tumour (melanoma metastasis) on T2-weighted and T1-weighted images



[Malikova and Weichet, 2022]

Stroke lesion (acute intracerebral hemorrhage) on CT and T2-weighted images

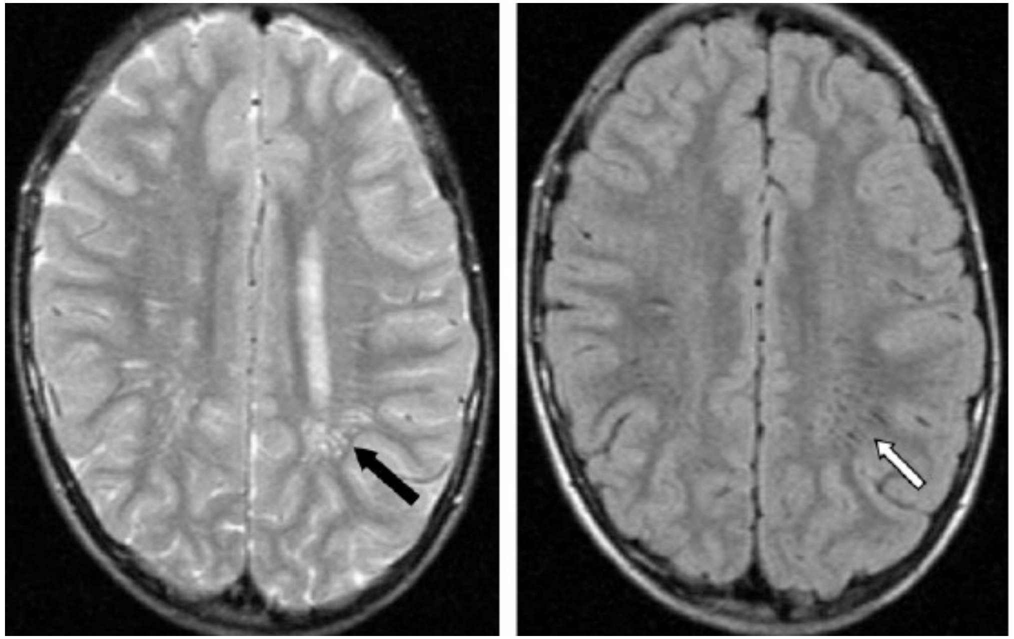
- White matter hyperintensity
  - Region of high intensity (increased brightness) within the cerebral white matter on a T2-weighted image
  - Reflects a lesion produced largely by demyelination and axonal loss
  - Frequently seen in older people and possibly associated with increased risk for some brain diseases



[Wardlaw et al., 2015]

White matter hyperintensity on FLAIR and T2-weighted images

- Perivascular space (Virchow–Robin space)
  - Fluid-filled space surrounding certain blood vessels
  - Typically located in the basal ganglia and white matter of the brain
  - Can become enlarged or dilated, in a close association with ageing or signaling abnormalities



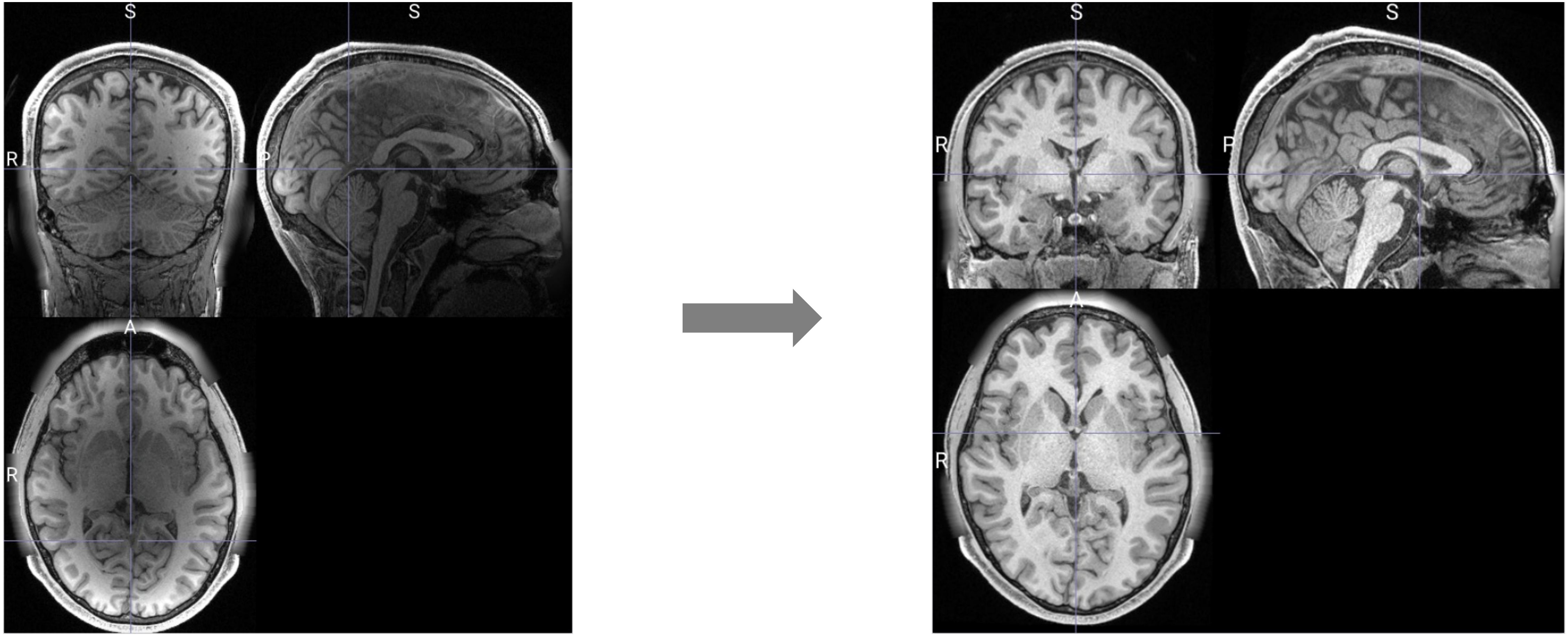
[Kwee and Kwee, 2007]

Perivascular space on T2-weighted and FLAIR images

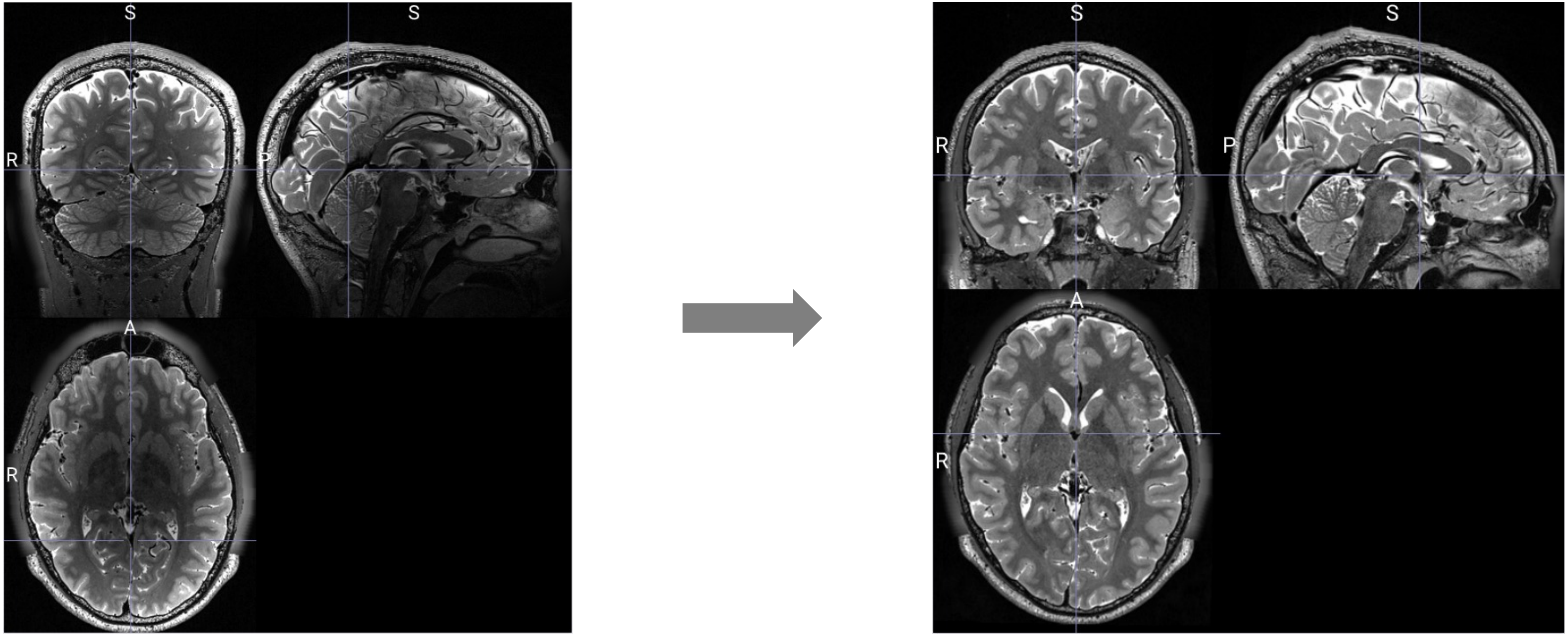
Brain Morphometry with sMRI

- Brain morphometry
  - Measurement of brain structures
    - Size
    - Shape
  - Based on the notion that variations in macroscopic brain anatomy are sufficiently conserved to allow for comparative analyses, yet diverse enough to reflect variations within and between individuals

- Processing before quantifying anatomical features of the brain
  - Correction for unwanted variation
    - Intensity non-uniformity
  - Segmentation
    - Classifies an image into the non-brain and brain and, furthermore, the brain into different tissues usually including grey matter, white matter, and cerebrospinal fluid
  - Normalisation
    - Transforms an image from a native space to the standard space

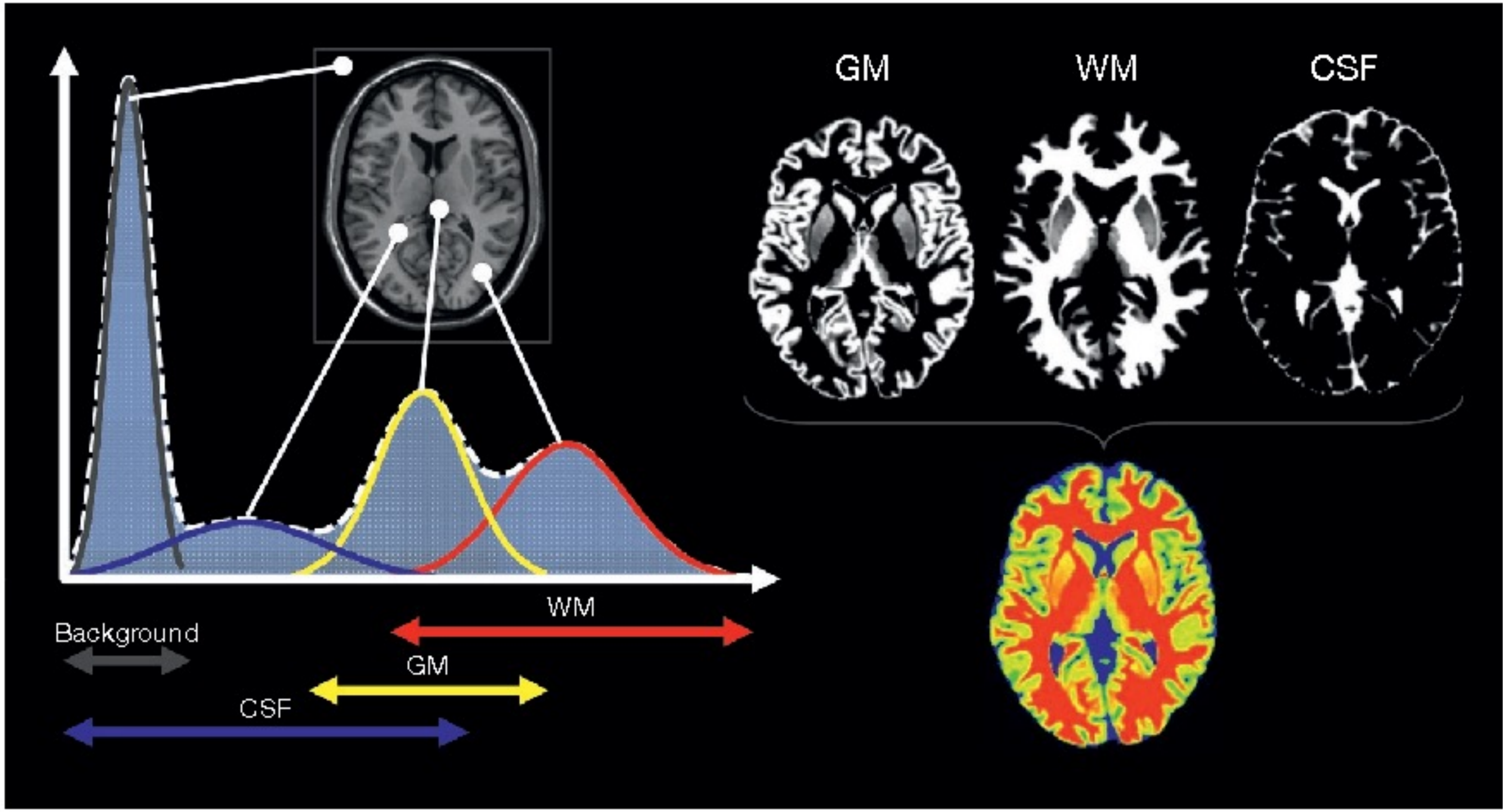


Processing of T1-weighted sMRI



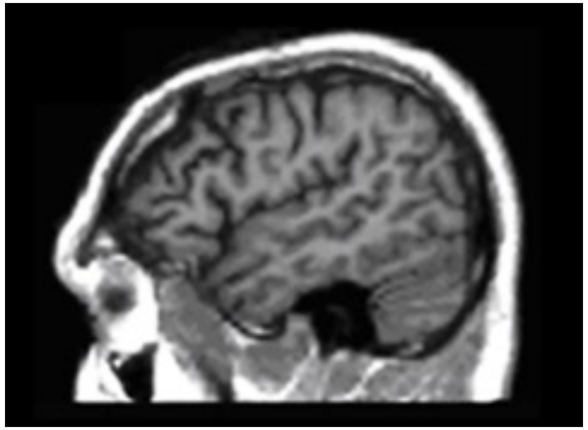
Processing of T2-weighted sMRI

- Voxel-based morphometry (VBM)
  - Local differences in density or volume
  - Given that, after the segmentation of an image, each voxel contains a measure of the probability according to which it belongs to a specific segmentation class
- Surface-based morphometry (SBM)
  - Local differences in thickness or gyrification
  - Given that, after the segmentation of an image, the boundary between different segmentation classes can be reconstructed as a surface

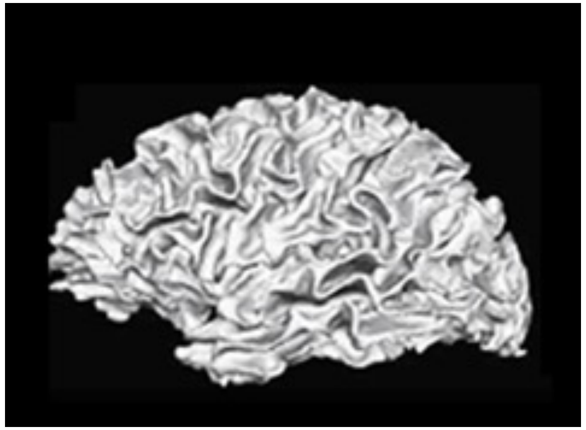


[Kurth et al., 2015]

Segmentation of the brain into different tissues



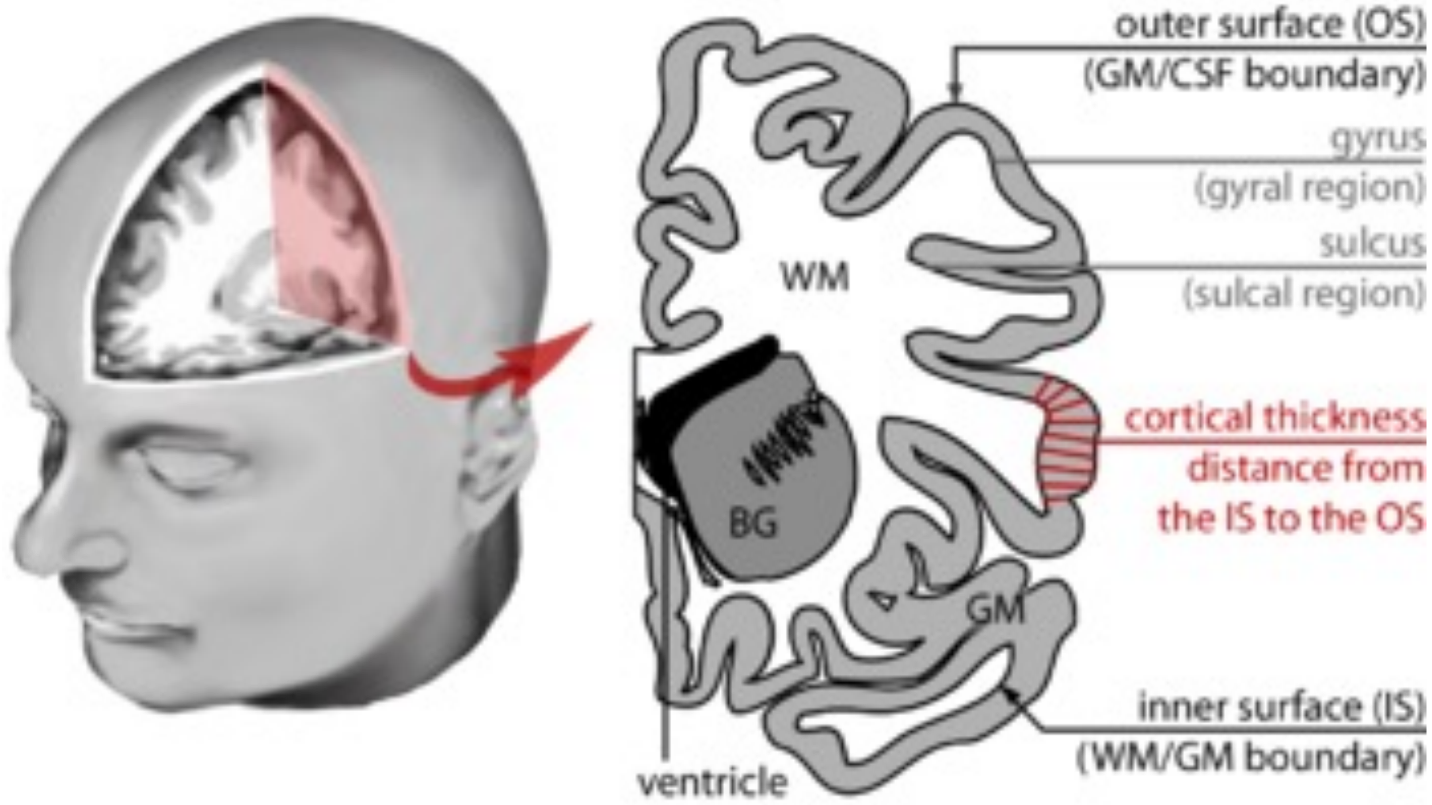
T1-weighted sMRI



Reconstructed brain surfaces

[https://en.citizendium.org/wiki/Surface-based_morphometry]

Reconstruction of brain surfaces from T1-weighted sMRI



[https://en.citizendium.org/wiki/Brain_morphometry]

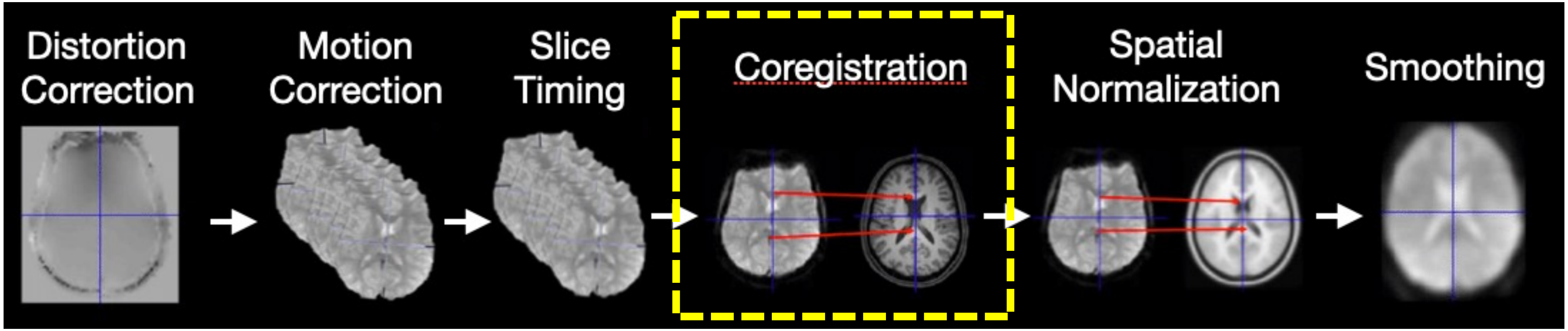
Measurement of cortical thickness based on a surface representation of the cerebral cortex

sMRI as an Individual’s Spatial Reference

- Brain imaging data processing pipeline
  - Optimised procedure for processing brain imaging data by using a wide variety of software tools
  - Relies heavily on having usable sMRI, specifically a T1-weighted image

- Aligning modalities by coregistering between sMRI and functional/diffusion-weighted MRI
  - Enables to make full use of data from the other modalities
  - For the anatomical localization of an individual’s brain activity or diffusion properties

Within-subject sMRI-functional MRI registration



[https://dartbrains.org/content/Preprocessing.html]

Coregistration as a step of the functional MRI data processing pipeline