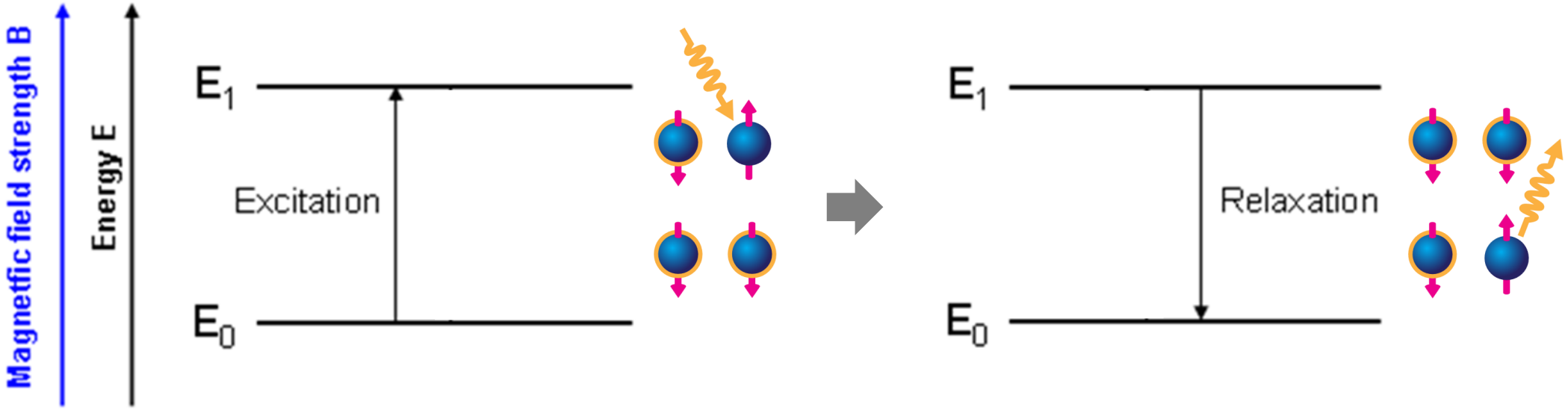
Medical/Bio Research Topics Ⅱ: Week 02 (12.09.2025)

Structural MRI: Basic Principles and Data Processing Methods

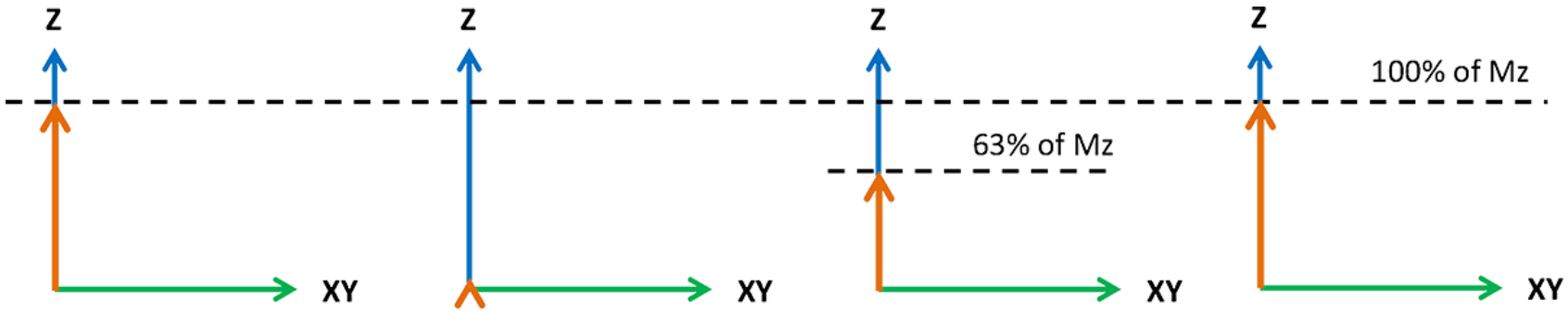
구조 자기공명영상: 기본 원리 및 데이터 처리 방법

MRI Principles

- Medical application of nuclear magnetic resonance (NMR)
  - Generates different contrasts between tissues based on the relaxation properties of hydrogen nuclei therein



Longitudinal or spin-lattice relaxation



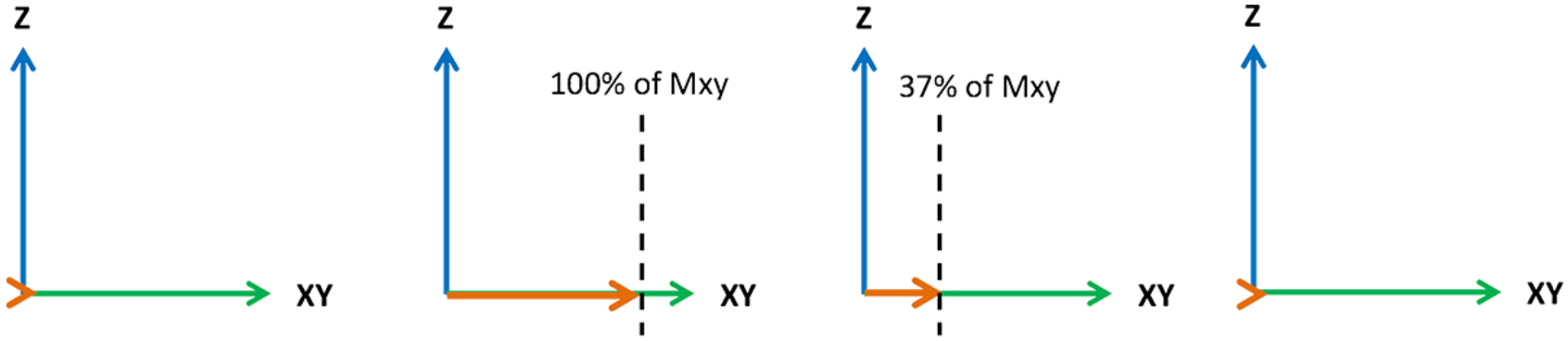
1. Before 90° pulse Mz is 100%

2. After the 90° pulse the Mz is 0

3. The Mz slowly recovers. The time it takes to recover to 63% is the time constant T1

4. The Mz continues to recover until it reaches its starting value of 100%

Transverse or spin-spin relaxation



1. Before 90° pulse Mxy is 0%

2. After the 90° pulse the Mxy is 100%

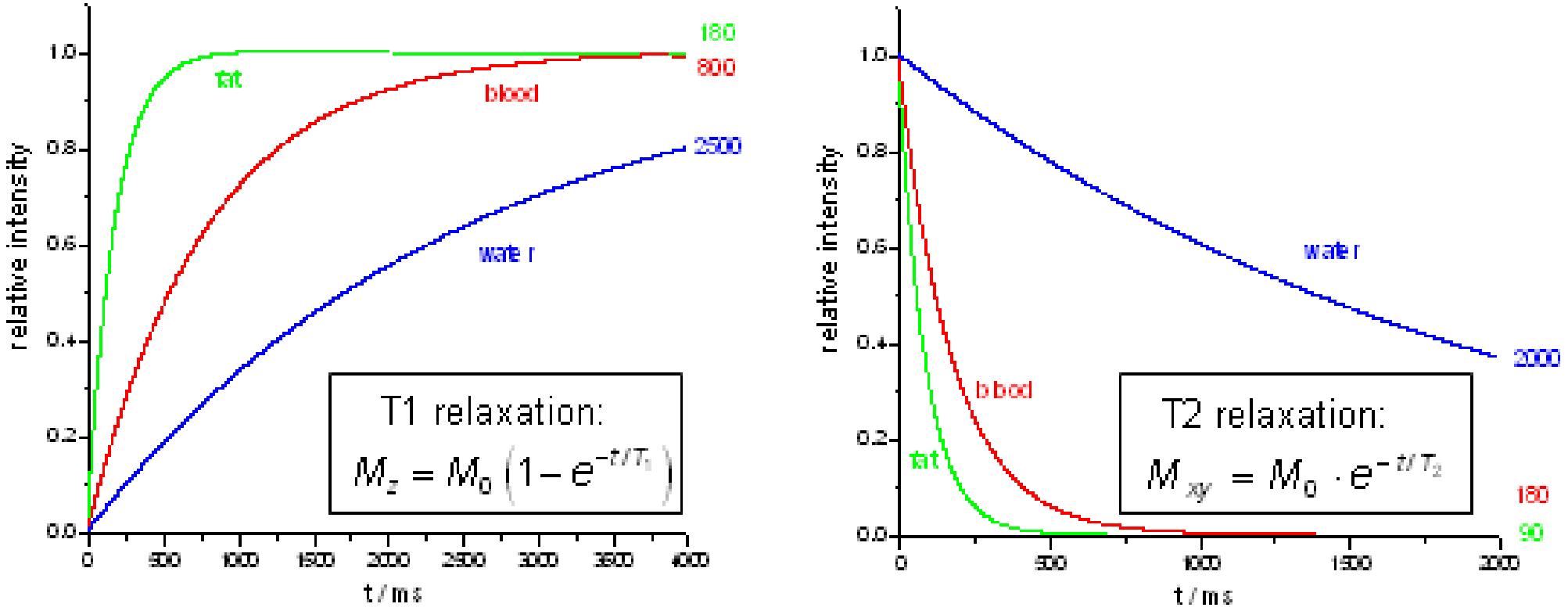
3. The Mxy slowly decays. The time it takes to decay to 37% is the time constant T2

4. The Mxy continues to decay until it reaches its starting value of 0%

[https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/t1-and-t2-signal/]

Two Relaxation Processes Occurring at the Same Time But Completely Independently

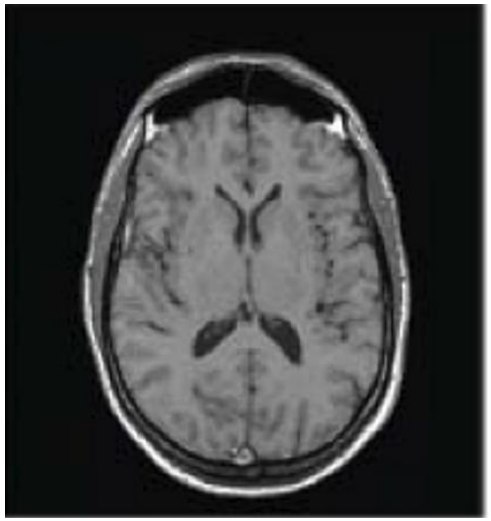
- Two different relaxation times
  - T1 (longitudinal relaxation time or spin-lattice relaxation time)
    - Time taken for hydrogen nuclei to realign with the external magnetic field
    - Time taken for the longitudinal magnetization to recover 63% (1-(1/*e*)) of its initial value
    - Water-based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

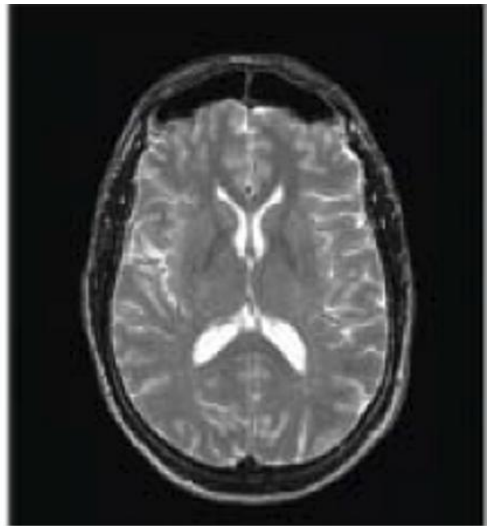


[Pollacco, 2016]

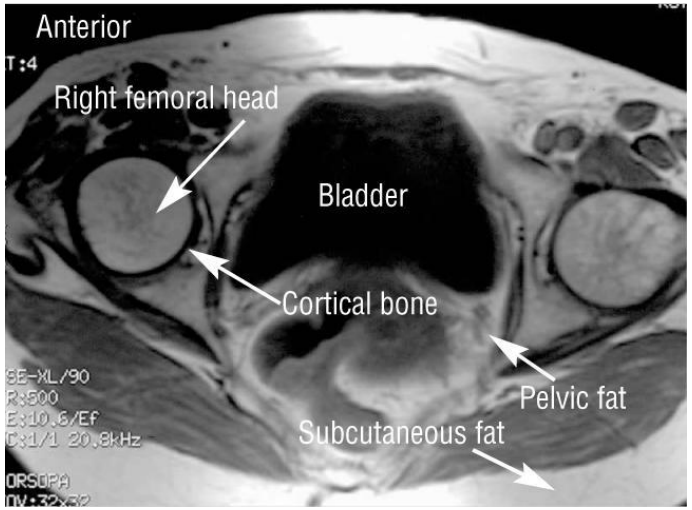
Differences in T1 and T2 Relaxation Times between Tissues

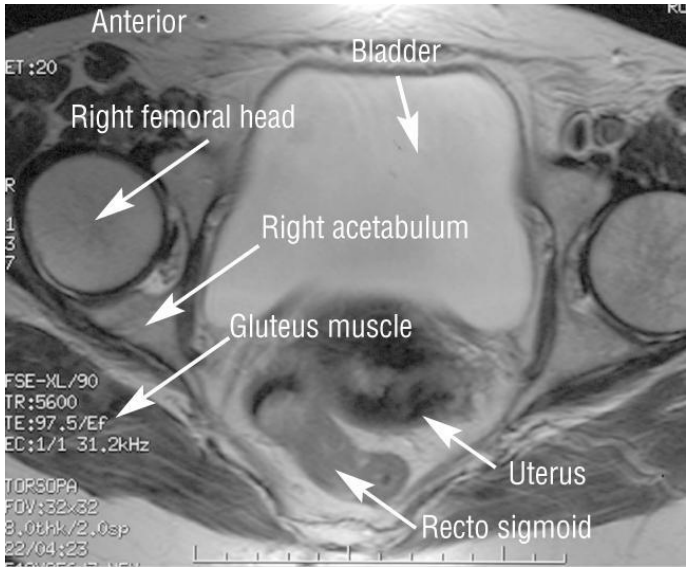
Brain





Pelvis

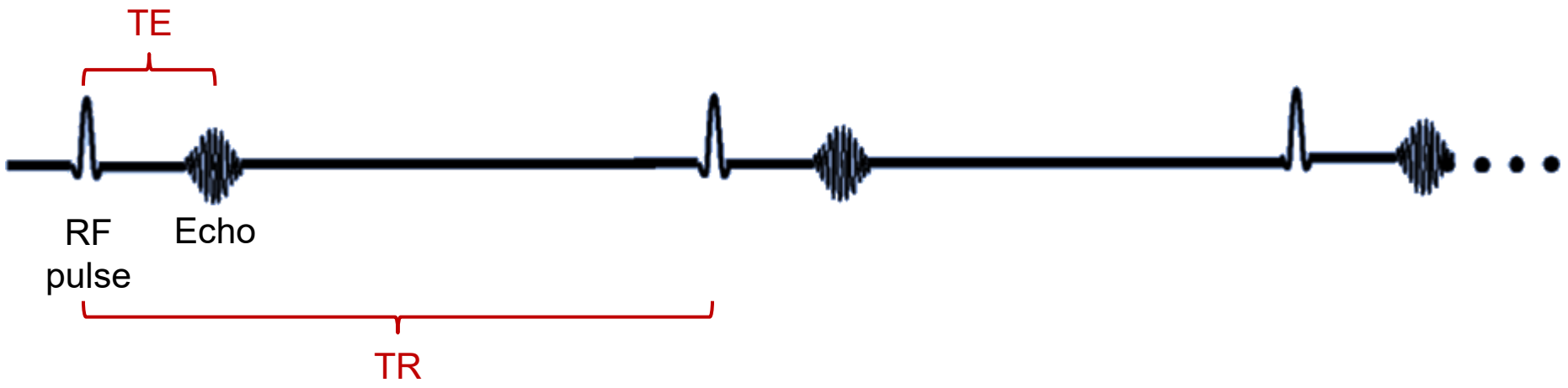




[https://radiologykey.com/mr-relaxation-theory-and-exchange-processes-in-the-presence-of-contrast-agents/; Berger, 2002]

T1-weighted vs. T2-weighted MRI

- By varying the sequence of radio frequency (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



[https://mriquestions.com/tr-and-te.html]

MRI Contrast Types

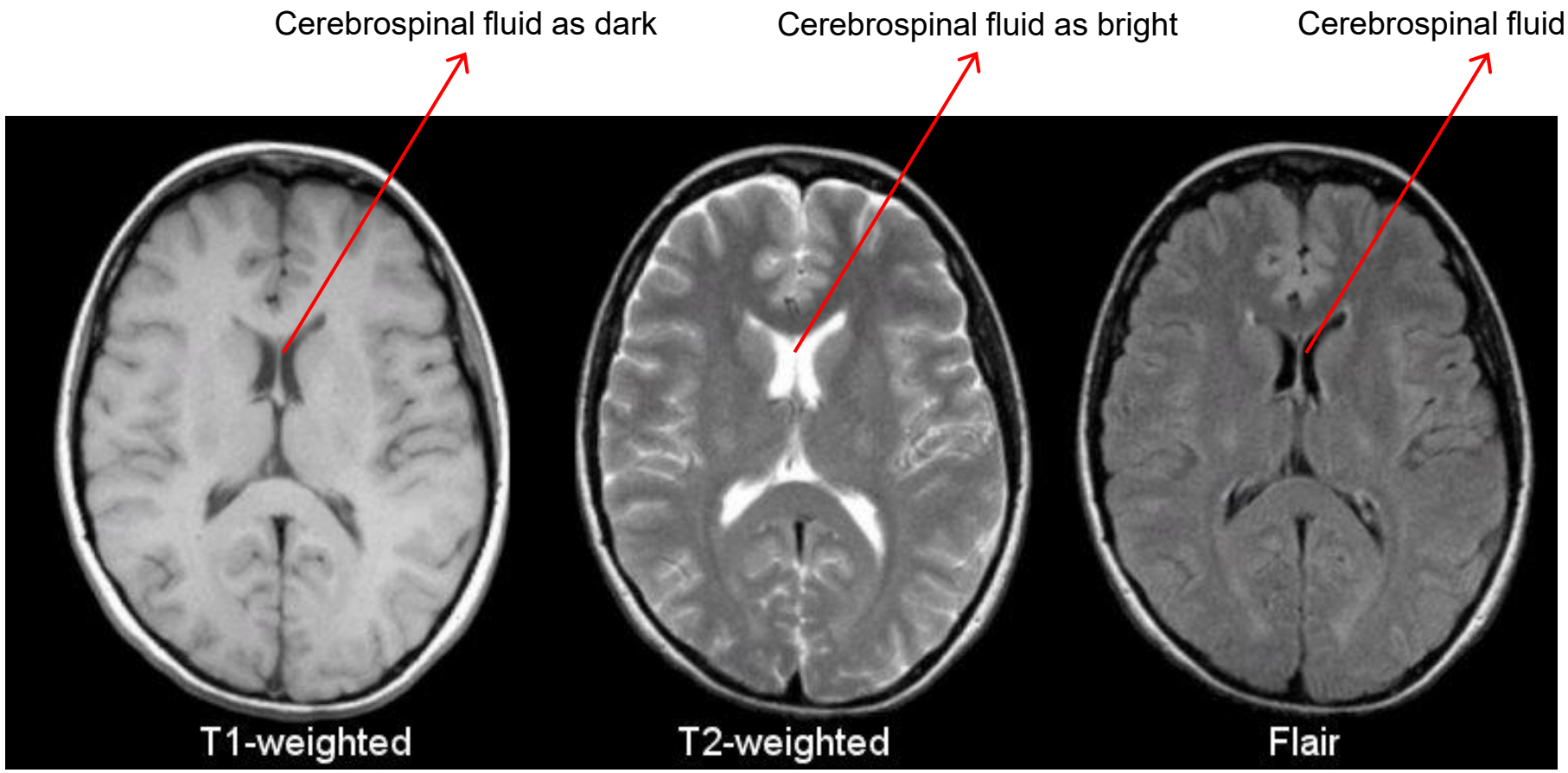
- T1-weighted
  - Contrast predominately determined by T1 differences between tissues
  - Produced by using shorter TE (decreasing the T2 effect) and shorter TR (enhancing the T1 effect by rapidly exposing hydrogen nuclei to RF pulses)
  - Tissues that return to alignment faster than other tissues are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

	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**

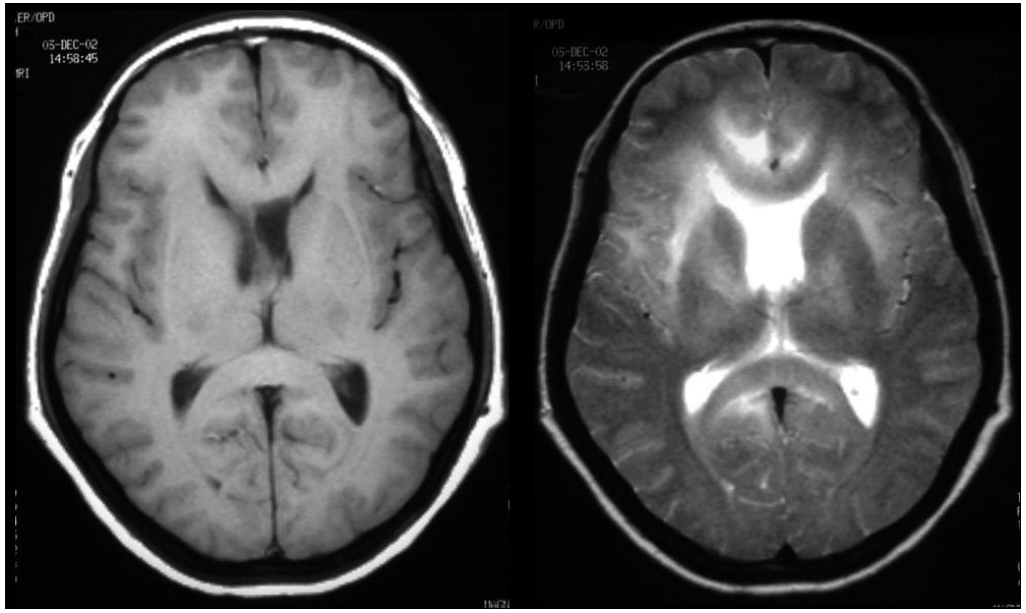
[https://case.edu/med/neurology/NR/MRI Basics.htm]



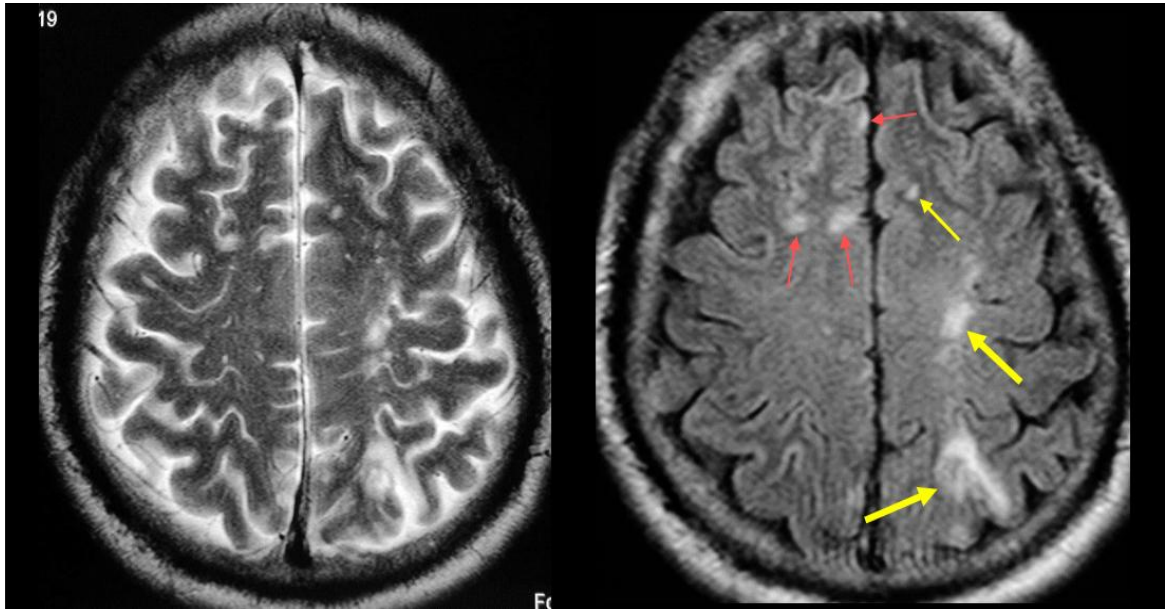
[https://case.edu/med/neurology/NR/MRI Basics.htm]

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

T1-weighted vs. T2-weighted

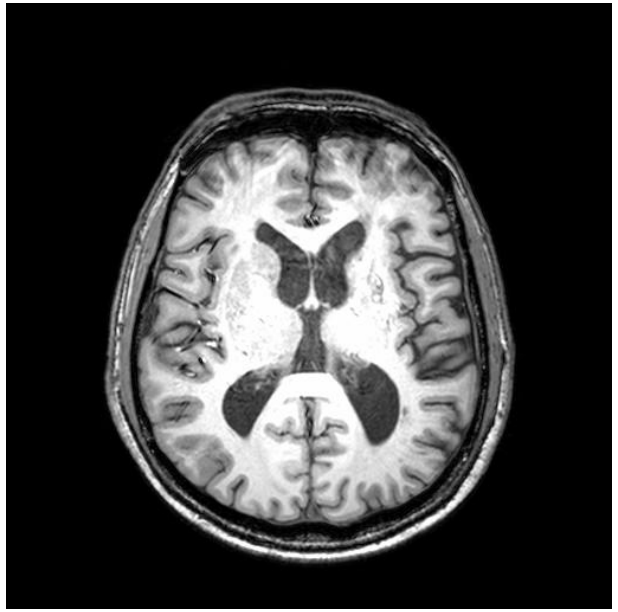


T2-weighted vs. FLAIR



Contrasts of the Brain

- White matter (nerve fibers) 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

T1-weighted contrast of the brain

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]

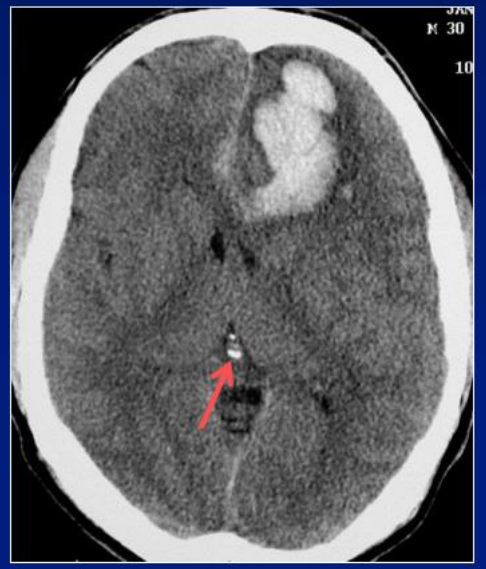
Different Contrasts of the Brain

Structural MRI (sMRI)

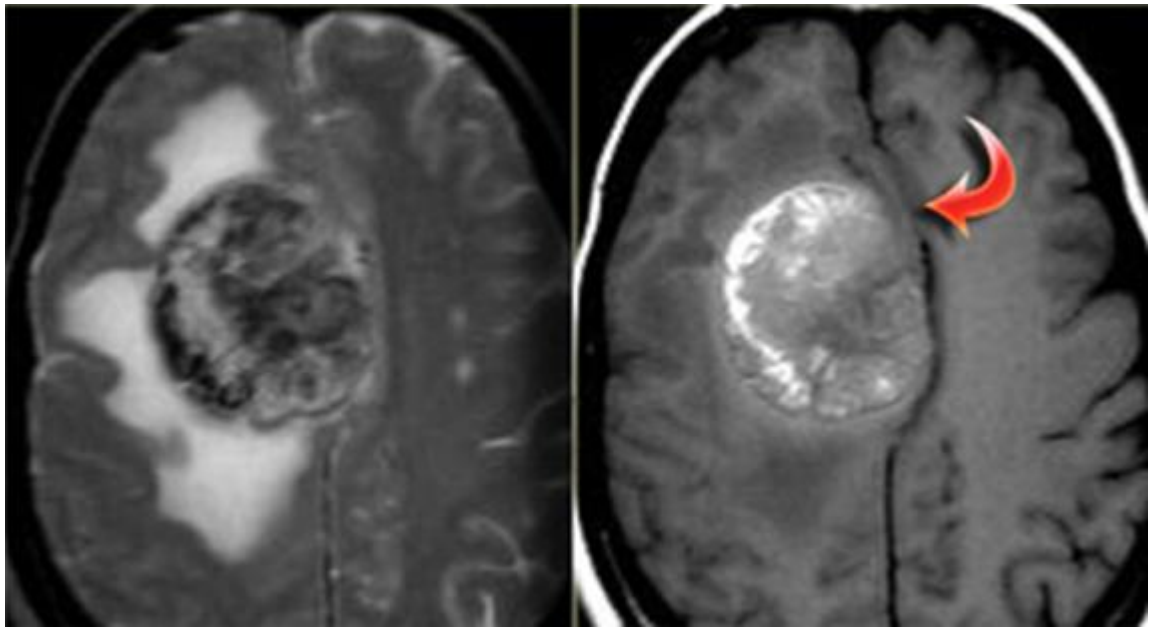
- MRI technique primarily for examining the macroscopic anatomy and tissue composition (grey matter, white matter, and cerebrospinal fluid) of the brain
- Applications of sMRI
  - Clinical diagnosis and abnormality detection
  - Quantitative brain morphometry
  - Anatomical reference for co-registration

Abnormality Analysis with sMRI

- MRI > CT
  (almost all disease)
  - infarct, tumor, inflammation, infection
  - degeneration, atrophy
  - hemorrhage, trauma
- CT = MRI
  - acute hemorrhage
- CT > MRI
  - calcification

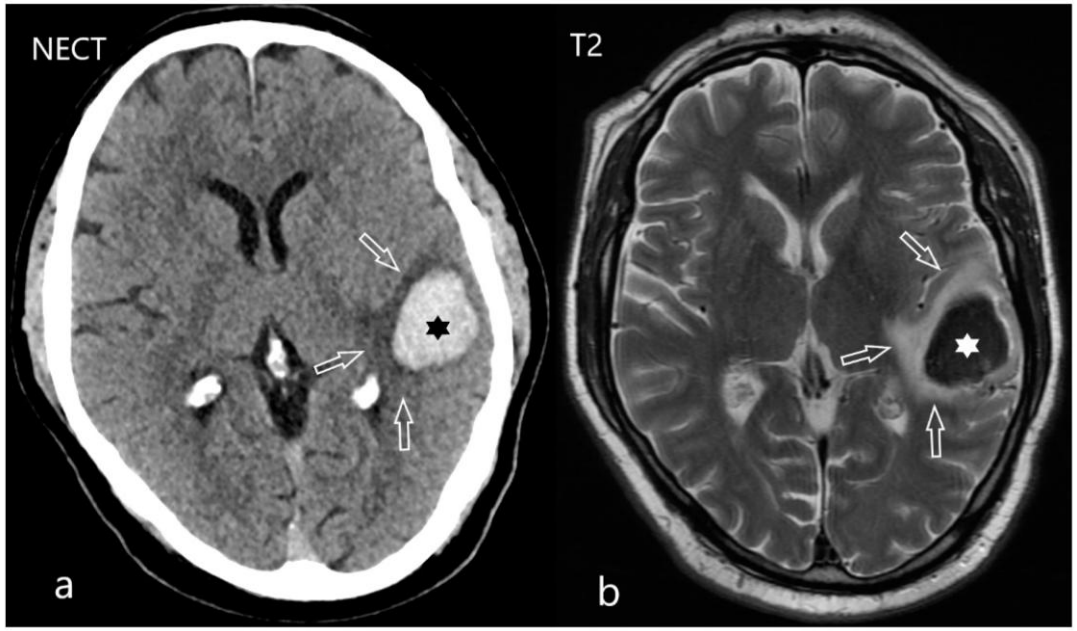


- Brain lesion
  - Damaged brain tissue caused by injury, disease, or developmental abnormality
    - Brain tumor
    - Stroke
    - Epilepsy
    - Multiple sclerosis
  - Disrupts the way the brain works, causing a wide range of symptoms



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

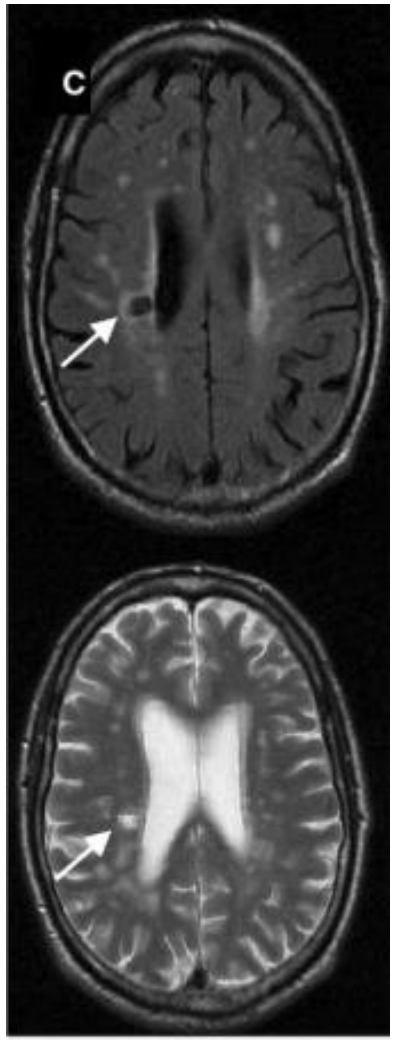
Brain Tumor (Melanoma Metastasis) on T2-weighted and T1-weighted Images



[Malikova and Weichet, 2022]

Stroke Lesion (Acute Intracerebral Hemorrhage) on CT and T2-weighted Images

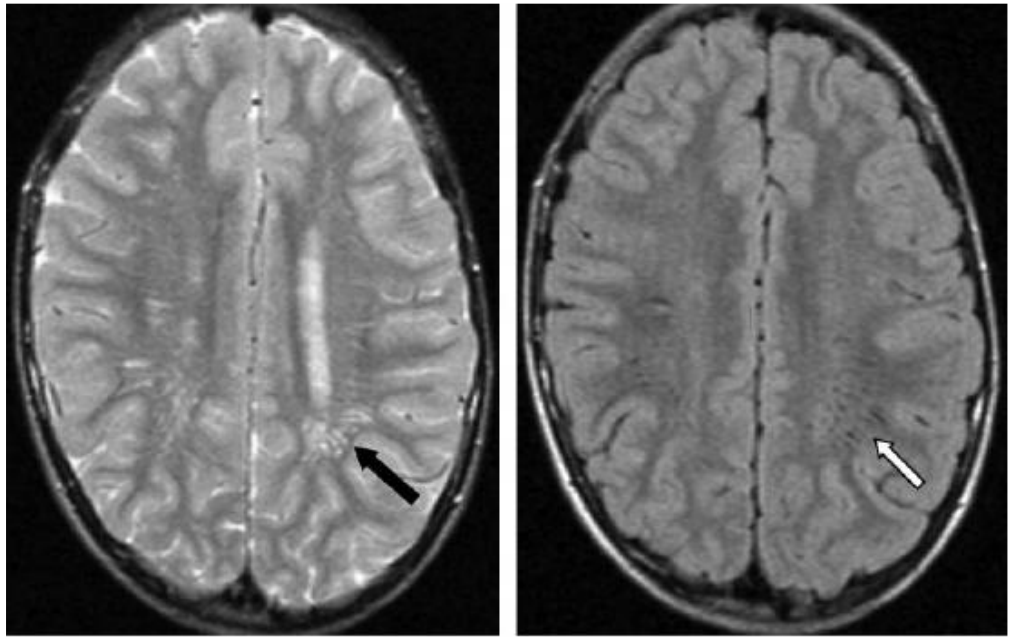
- White matter hyperintensity
  - Hyperintense signal within the cerebral white matter on a T2-weighted image
  - Reflects a lesion produced largely by demyelination and axonal loss
  - Frequently seen in older people and possibly associated with increased risk for some brain diseases



[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 aging or signaling abnormalities

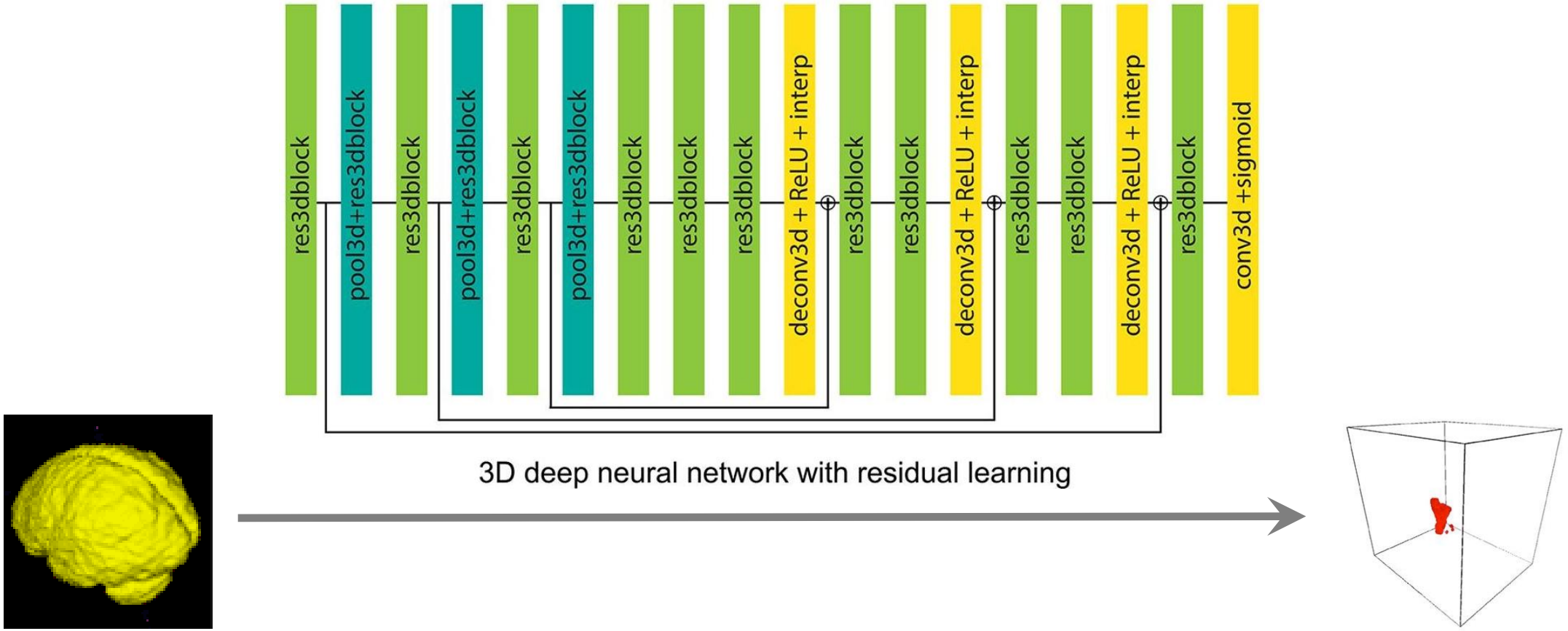


[Kwee and Kwee, 2007]

Perivascular Space on T2-weighted and FLAIR Images

Automated Abnormality Detection

- Leverages deep learning algorithms to detect pathological changes in brain tissue
  - Identifies subtle abnormalities that may be overlooked in visual assessment
- Segmentation: Automated delineation of lesion boundaries with voxel-level precision
- Grading: Standardized classification of abnormality severity using predefined scales



[Tomita et al., 2020]

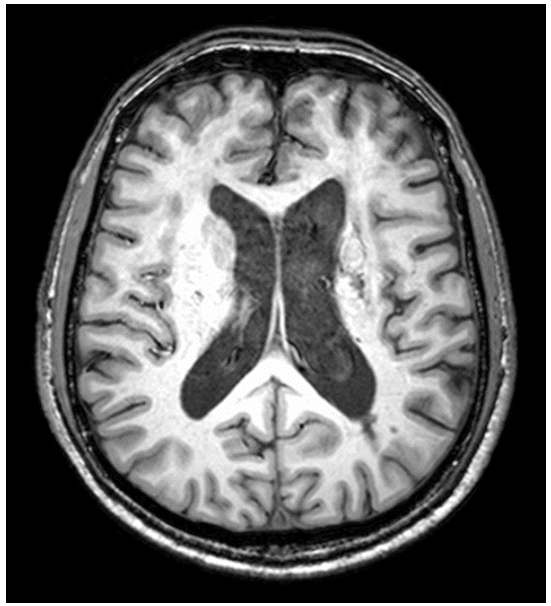
3D Convolutional Neural Network for Stroke Lesion Segmentation

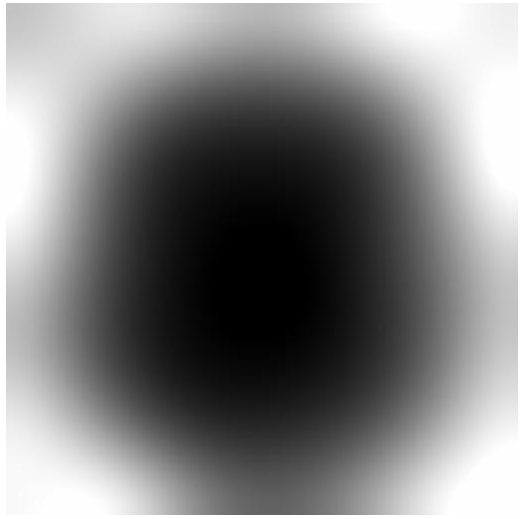
Brain Morphometry with sMRI

- Brain structure
  - Preserved macroscopic organization with individual variability
    - Consistent anatomical landmarks
    - Bilateral organization
    - Hierarchical arrangement

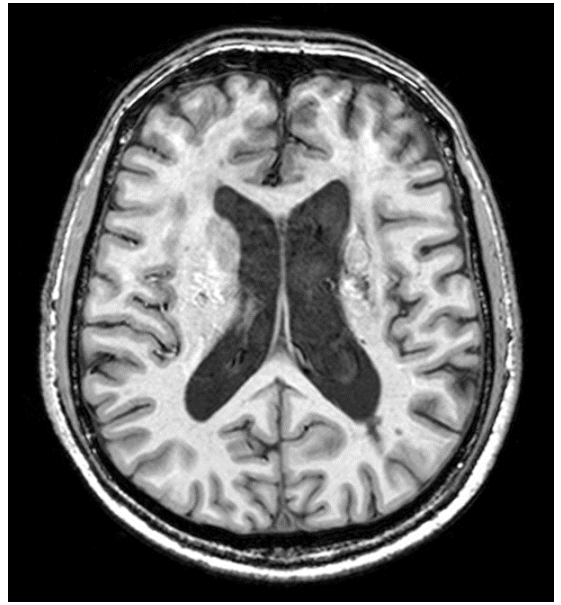
- Brain morphometry: Quantitative analysis of brain structure
  - Volume and density measurements
    - Global brain volume
    - Regional tissue volumes
  - Size and shape analysis
    - Cortical thickness
    - Surface area
    - Regional shape variations
  - Gyrification and folding patterns
    - Gyrification index
    - Sulcal depth and length
    - Folding complexity

- Preprocessing before quantifying anatomical features of the brain
  - Correction for intensity non-uniformity (bias field)
    - From a broader range of sources, including imperfections in the MRI scanner's main magnetic field, inhomogeneities in the radiofrequency coil performance, and magnetic susceptibility-induced field inhomogeneities
    - Often characterized by a smooth variation in image brightness
  - Segmentation
    - Classifies an image into the non-brain and brain and, furthermore, the brain into different tissues including grey matter, white matter, and cerebrospinal fluid
  - Normalization
    - Transforms an image from native space to standard space

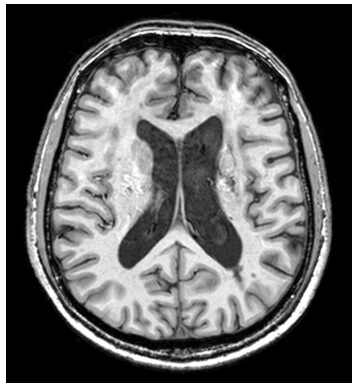




Intensity non-uniformity



Correction for Intensity Non-uniformity



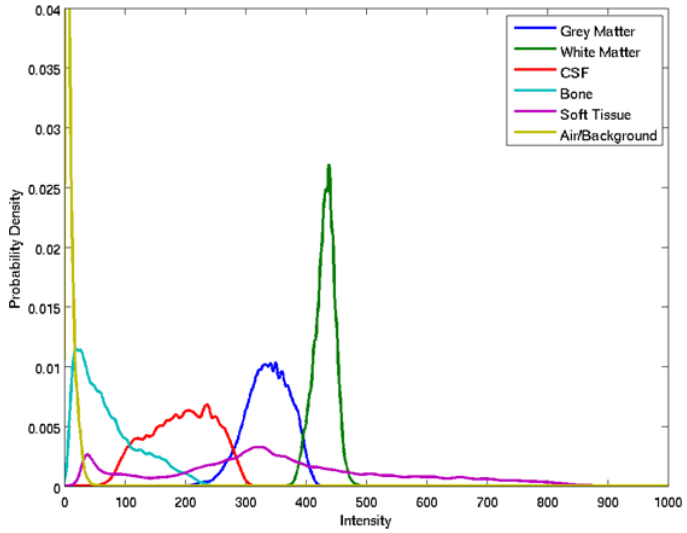
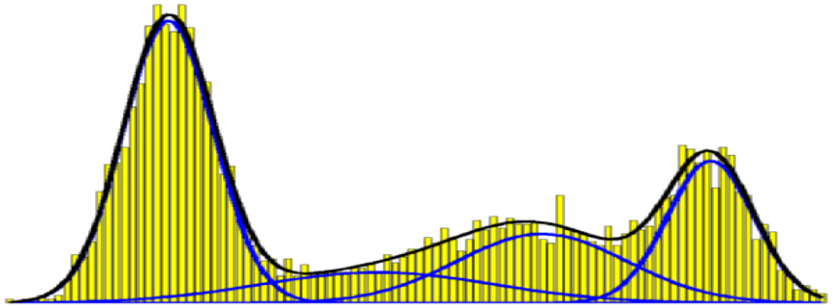


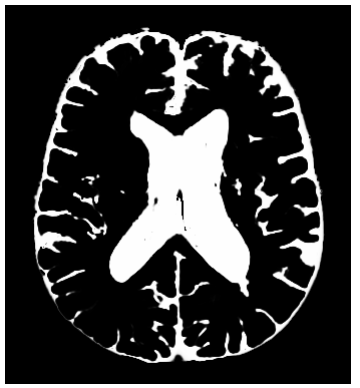
Image intensity distribution



Mixture of Gaussians model

Grey matter

White matter



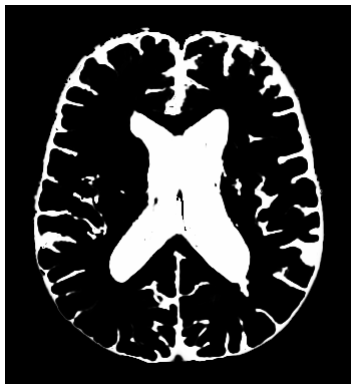
Cerebrospinal fluid

Segmentation into Different Tissues

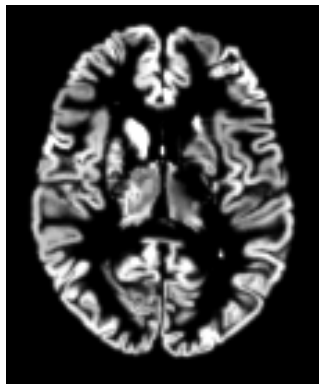
Grey matter

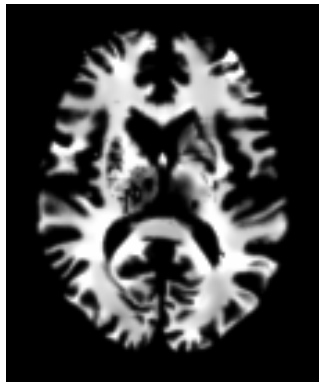
White matter

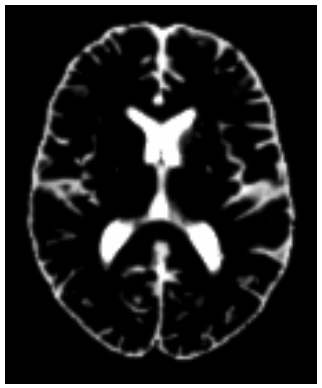
Cerebrospinal fluid



Template tissue probability maps

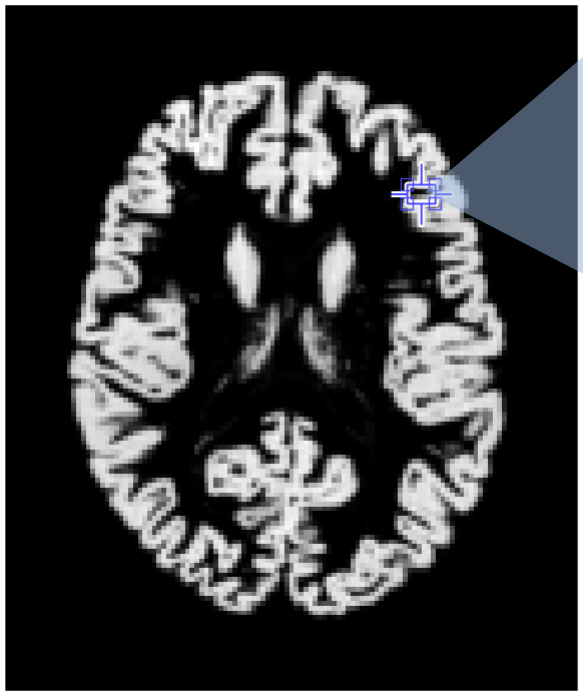


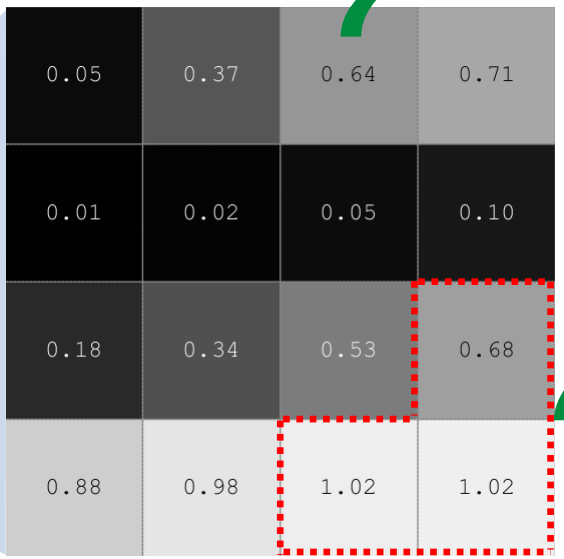




Normalization

- 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
    - For a tissue probability map in the native space or its modulated one in the standard space





Voxel

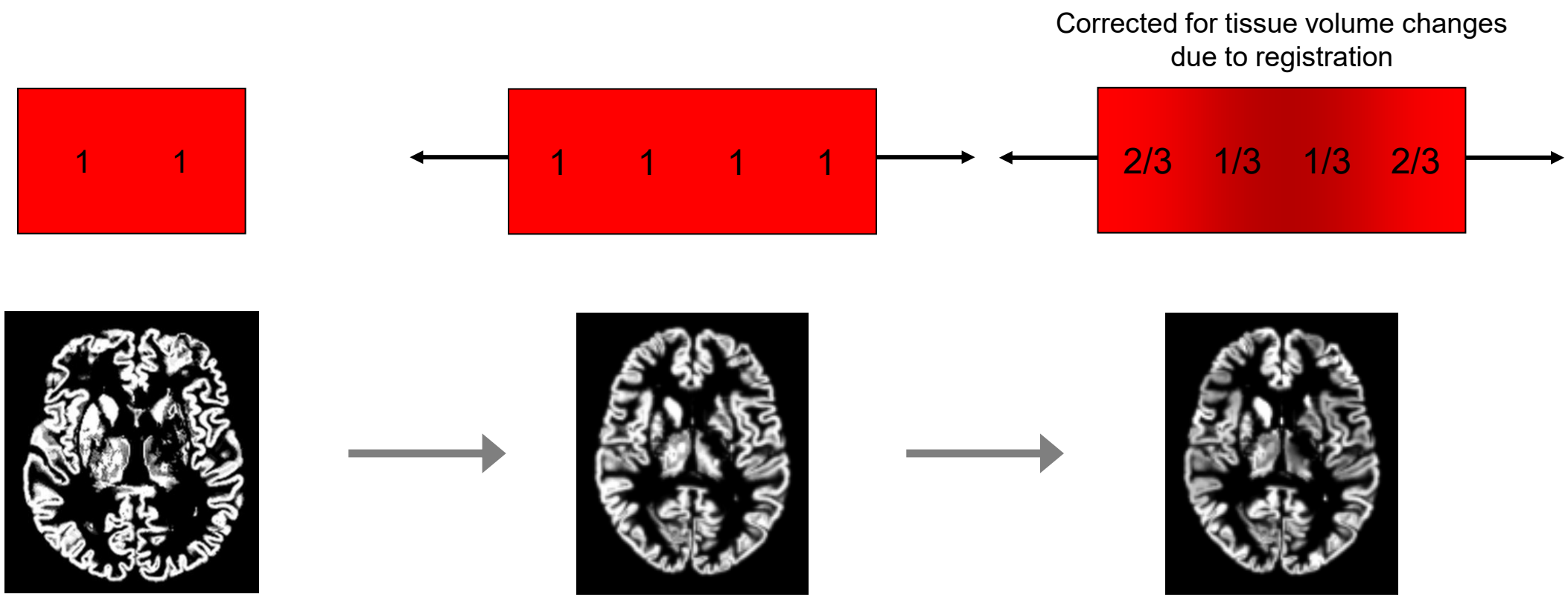
Grey matter volume = 0.64 × 3.375 mm^3
= 2.16 mm^3

Voxel cluster

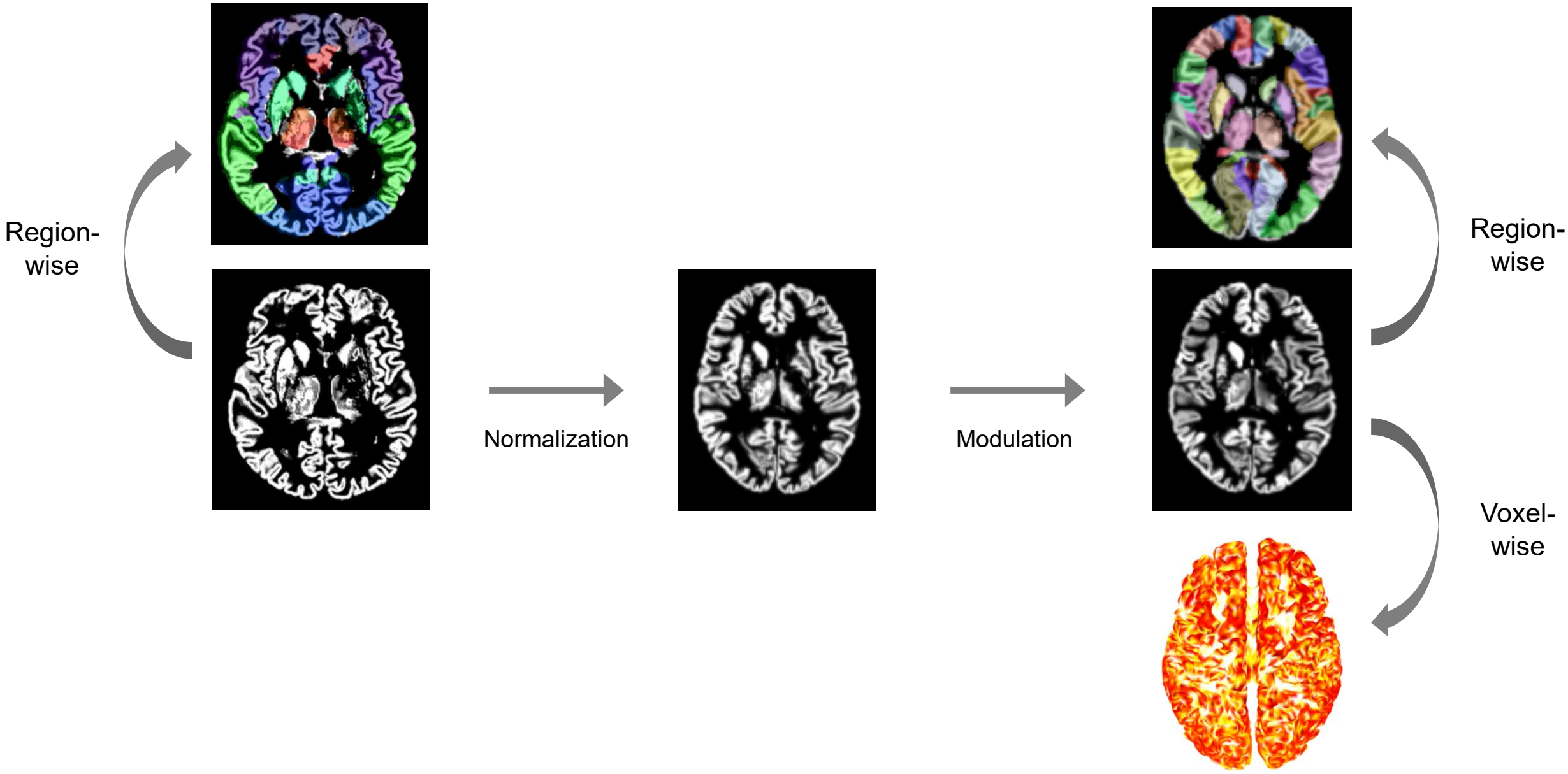
Grey matter volume = 9.18 mm^3

Voxel size: 1.5 mm × 1.5 mm × 1.5 mm
Voxel volume: 3.375 mm^3

Computation of Grey Matter Volume for a Voxel or a Voxel Cluster



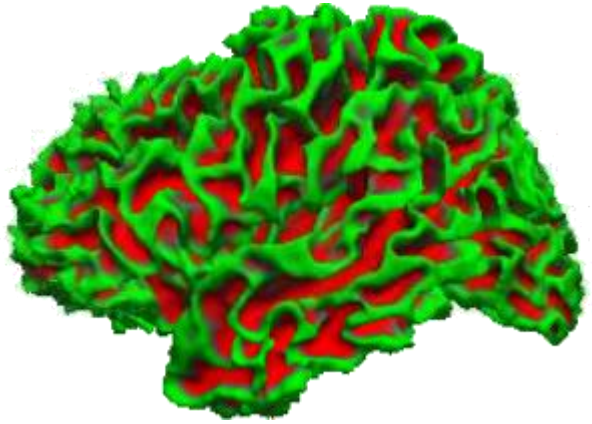
Normalization and Modulation



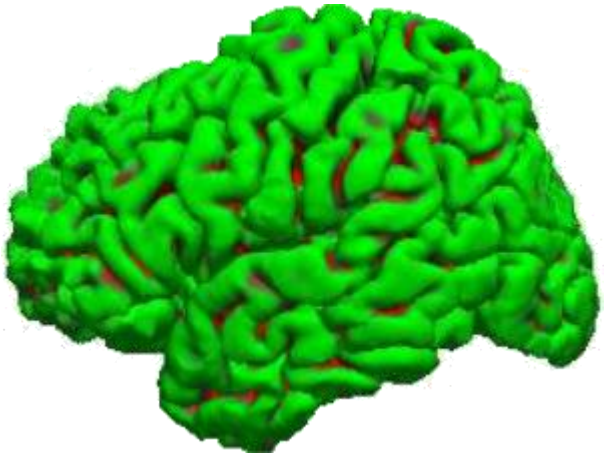
Features of Grey Matter Volume

- 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
    - White matter surface (inner cortical surface): inner cortical boundary between grey matter and white matter
    - Pial surface (outer cortical surface): outer cortical boundary between pia mater and subarachnoid space containing corticospinal fluid

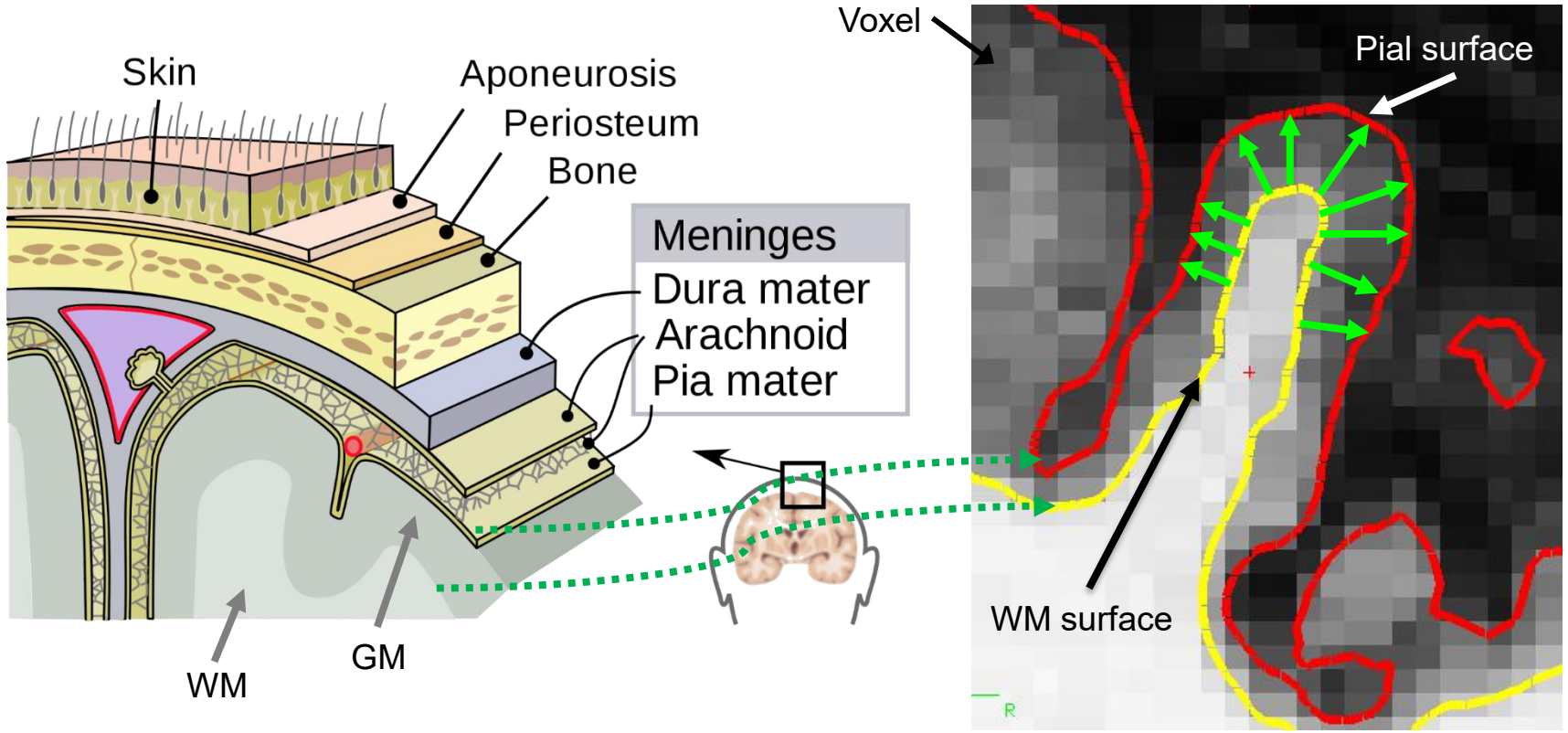
White matter surface



Pial surface

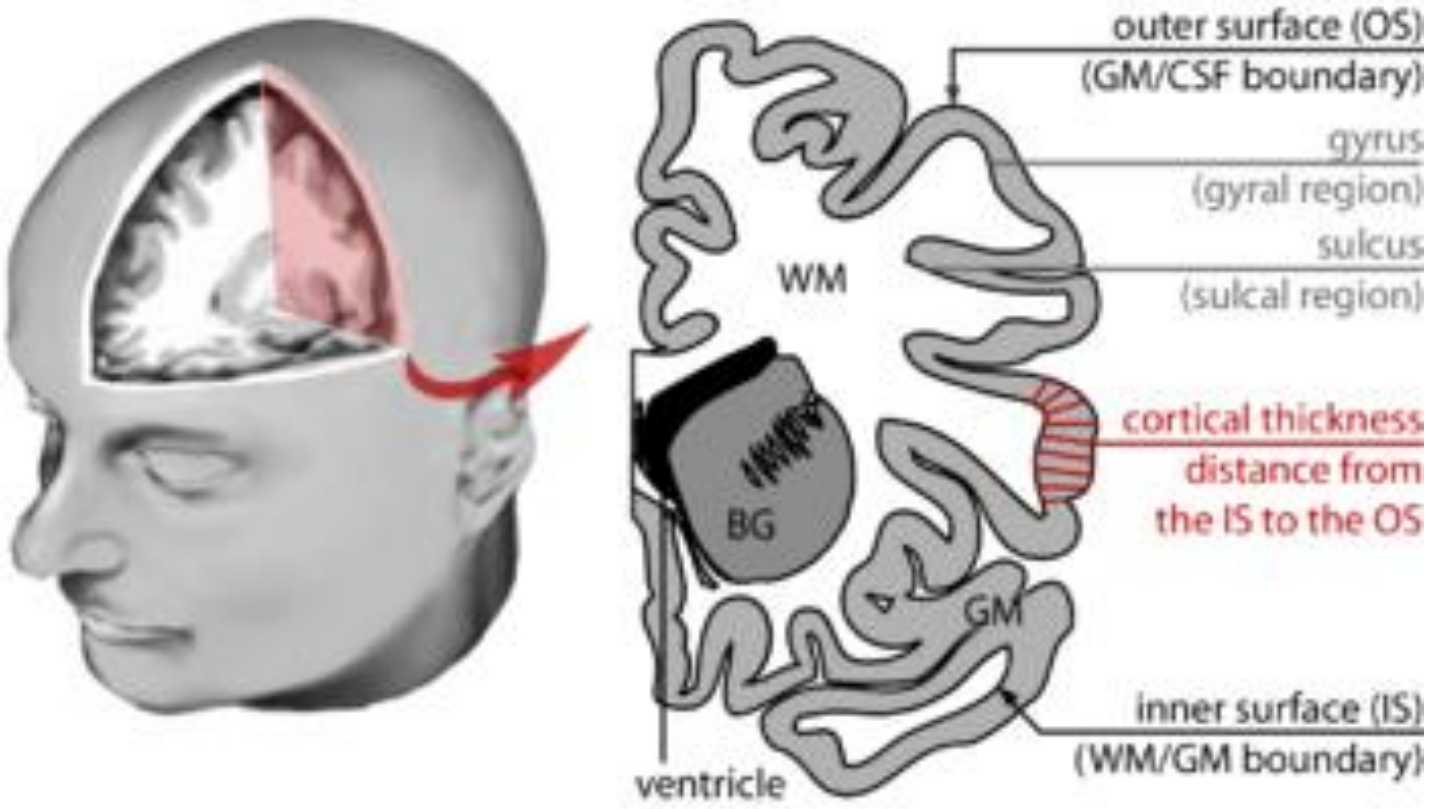


Reconstructed Inner and Outer Cortical Surfaces



[https://www.physio-pedia.com/Meninges]

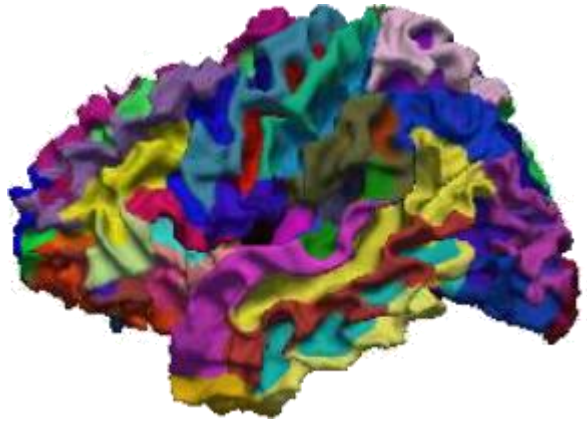
Grey Matter Boundary Surfaces: White Matter and Pial Boundaries



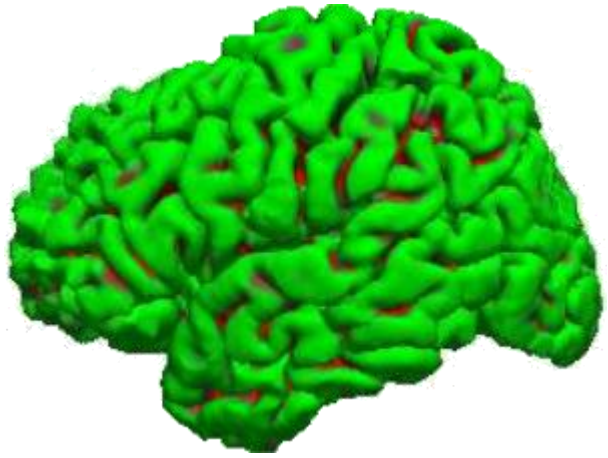
[https://en.citizendium.org/wiki/Brain_morphometry]

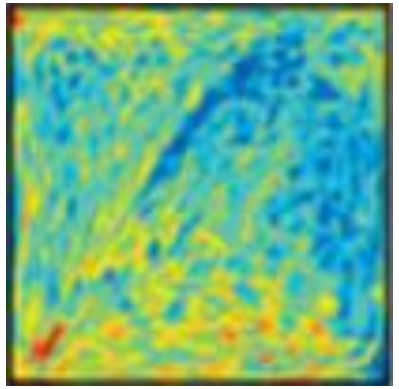
Cortical Thickness Estimation from Surface Reconstruction

Region-wise



Vertex-wise



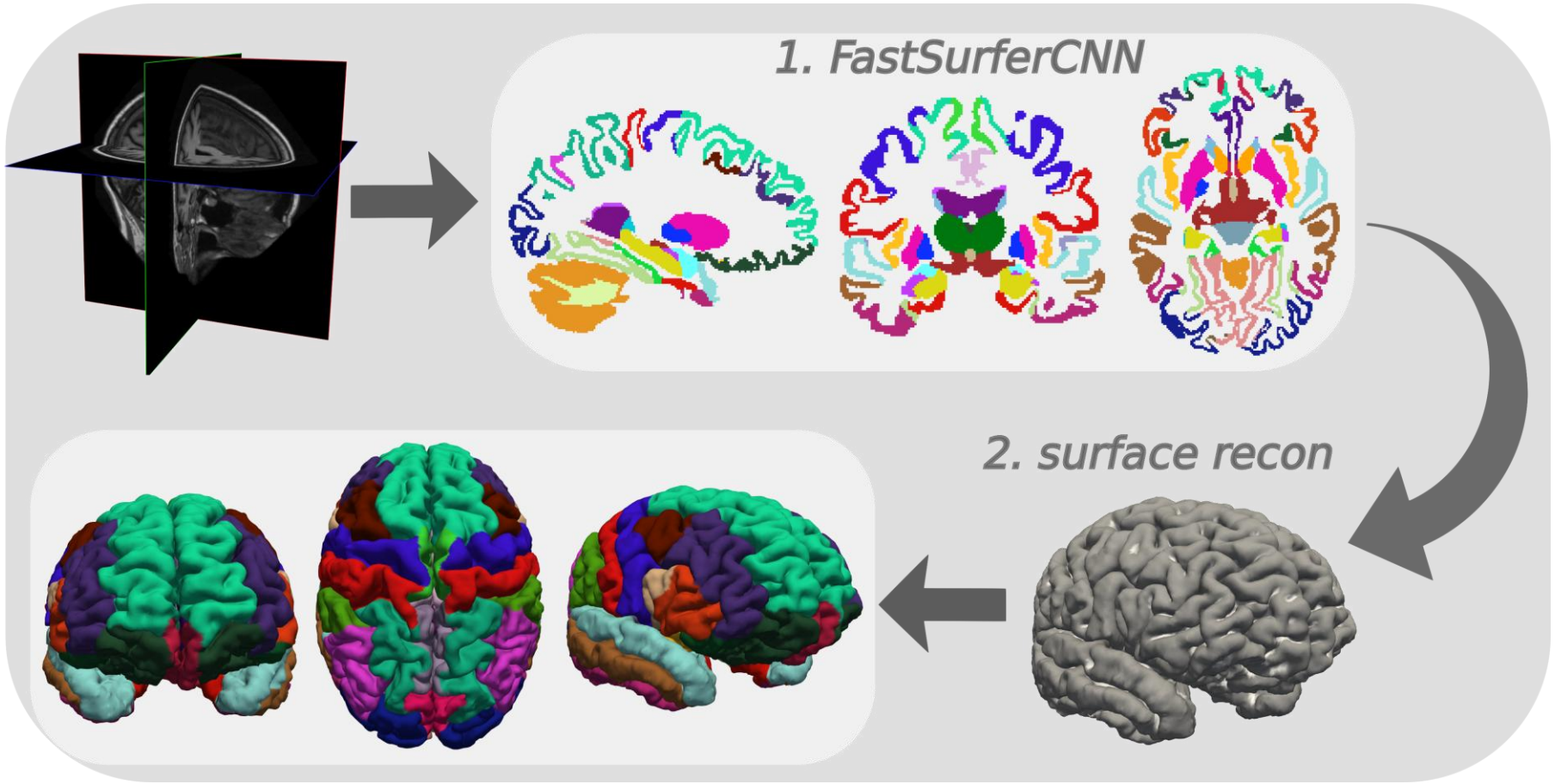


2D planar image

Features of Cortical Thickness

Automated Brain Morphometry

- Employs deep learning algorithms to provide objective measurements of brain structures and their relationships
- Cortical metrics: Automated measurement of cortical thickness, surface area, and volume
- Subcortical segmentation: Precise delineation and volumetric analysis of deep brain structures



[Henschel et al., 2020; https://github.com/Deep-MI/FastSurfer]

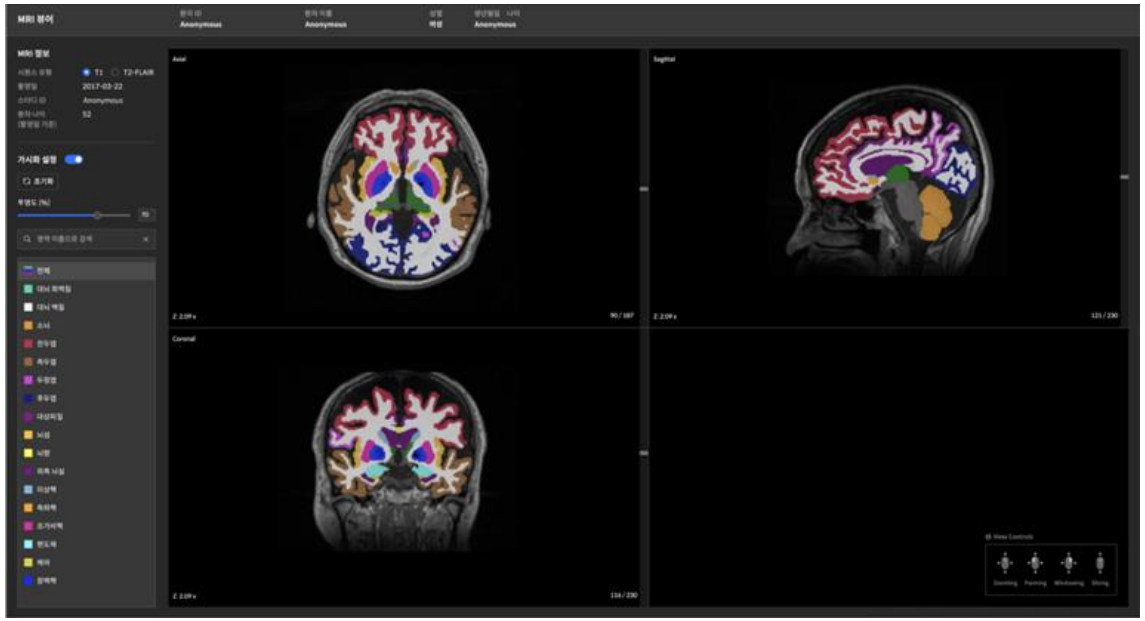
FastSurfer: Volumetric and Surface-based Cortical Thickness Analysis

Software	FDA Approved	MFDS Approved	EU CE Marked	URL	Country	Company	Character
NeuroQuant®	FDA approved	NA	CE marked	https://cortechs.ai/	USA	Cortechs Lab	NeuroQuant, LesionQuant*
Neuroreader®	FDA approved	NA	CE marked	https://brainreader.net/	USA	Brainreader	
Icobrain	FDA approved	NA	CE marked	https://icometrix.com/	EU	Icometrix	Icobrain MS, Icobrain DM, Icobrain TBI, Icobrain ep
Quantib® Brain	FDA approved	NA	CE marked	https://www.quantib.com/	Netherlands	Quantib	
syMRI® Neuro	FDA approved	NA	CE marked	https://syntheticmr.com/	Sweden		Multicontrast† Volumetry (GM, WM, CSF volume)
InBRAIN®	NA	MFDS approved	NA	https://www.inbrain.co.kr/	South Korea	Midas IT	
Neurol	NA	MFDS approved	NA	http://www.infomeditech.com/ https://neurozen.ai/	South Korea	Infomeditech	
mdbrain	NA	NA	CE marked	https://www.qmenta.com	EU	Qmenta Inc	
DeepBrain®	NA	MFDS approved	CE marked	https://www.vuno.co/	South Korea	Vuno	
Atroscan	NA	MFDS approved	NA	http://jlkgroup.com	South Korea	JLK	

*LesionQuant: measurement of WM lesion volume.
†Multicontrast: acquisition of multiple pre-defined contrast weighted images such as T1W, T2W and T2W FLAIR, as well as double inversion recovery and phase sensitive inversion recovery using synthetic MRI.
CSF = cerebrospinal fluid, EU CE Marked = conformite Europeenne marked, FDA = Food and Drug Administration, FLAIR = fluid attenuated inversion recovery, GM = grey matter, MFDS = Ministry of Food and Drug Safety, NA = not applicable, T1W = T1-weighted, T2W = T2-weighted, WM = white matter

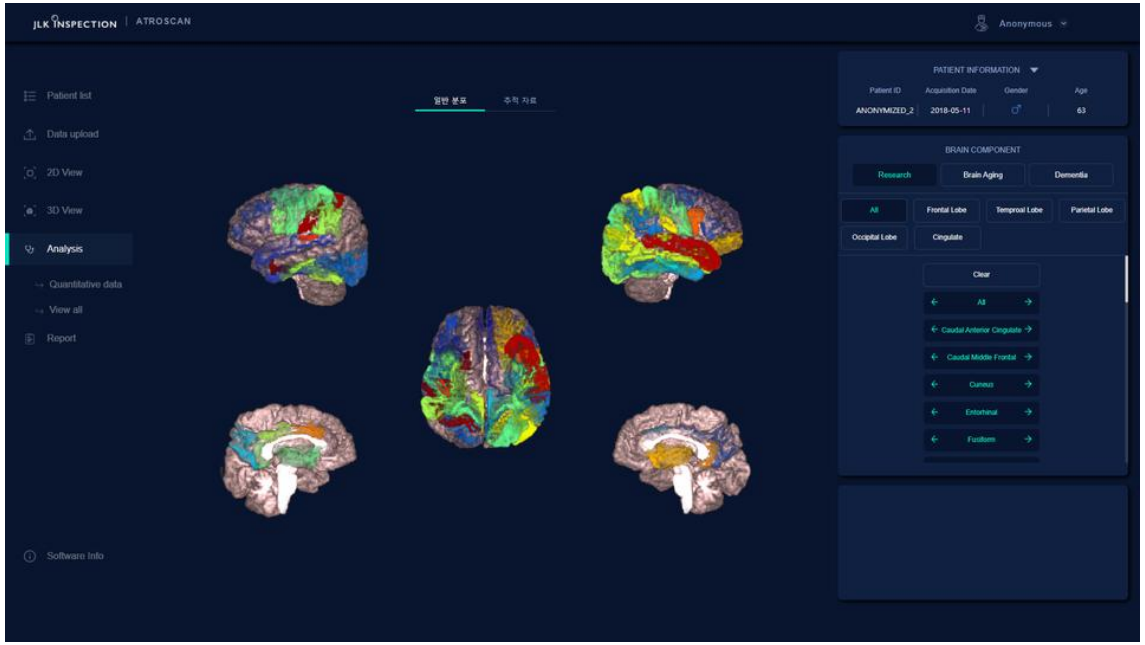
[Lee et al., 2021]

Commercially Available Brain Morphometry Software

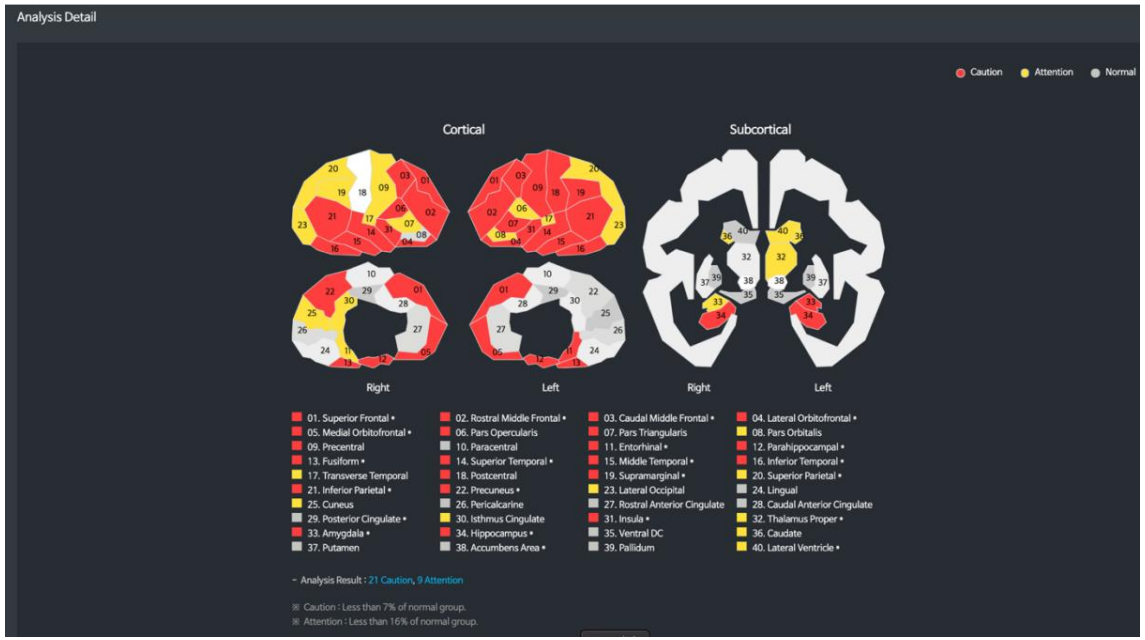


neurophet **AQUA**

VUNO **Med-DeepBrain**



JLK **ATROSCAN**



NEUROZEN **Neuro I**

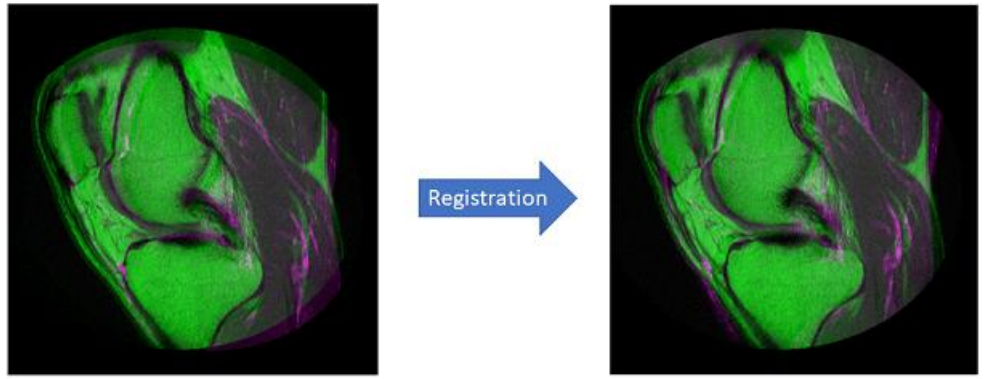
sMRI as Anatomical Reference

- Anatomical alignment of other modalities of MRI
  - Within-subject between-modality registration

Rigid registration
(global shift and rotation)

Within-subject within-modality

Affine registration
(global shift, rotation, scale, and shear)



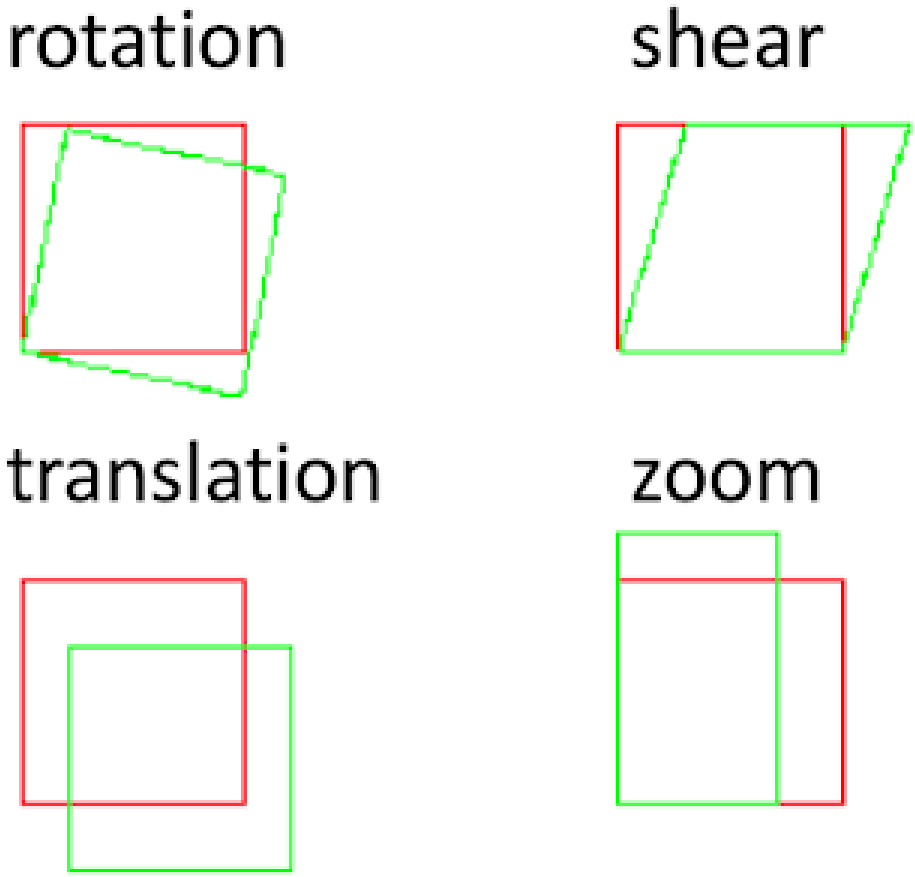
Within-subject between-modality

Deformable registration
(local transformations)

Between-subject

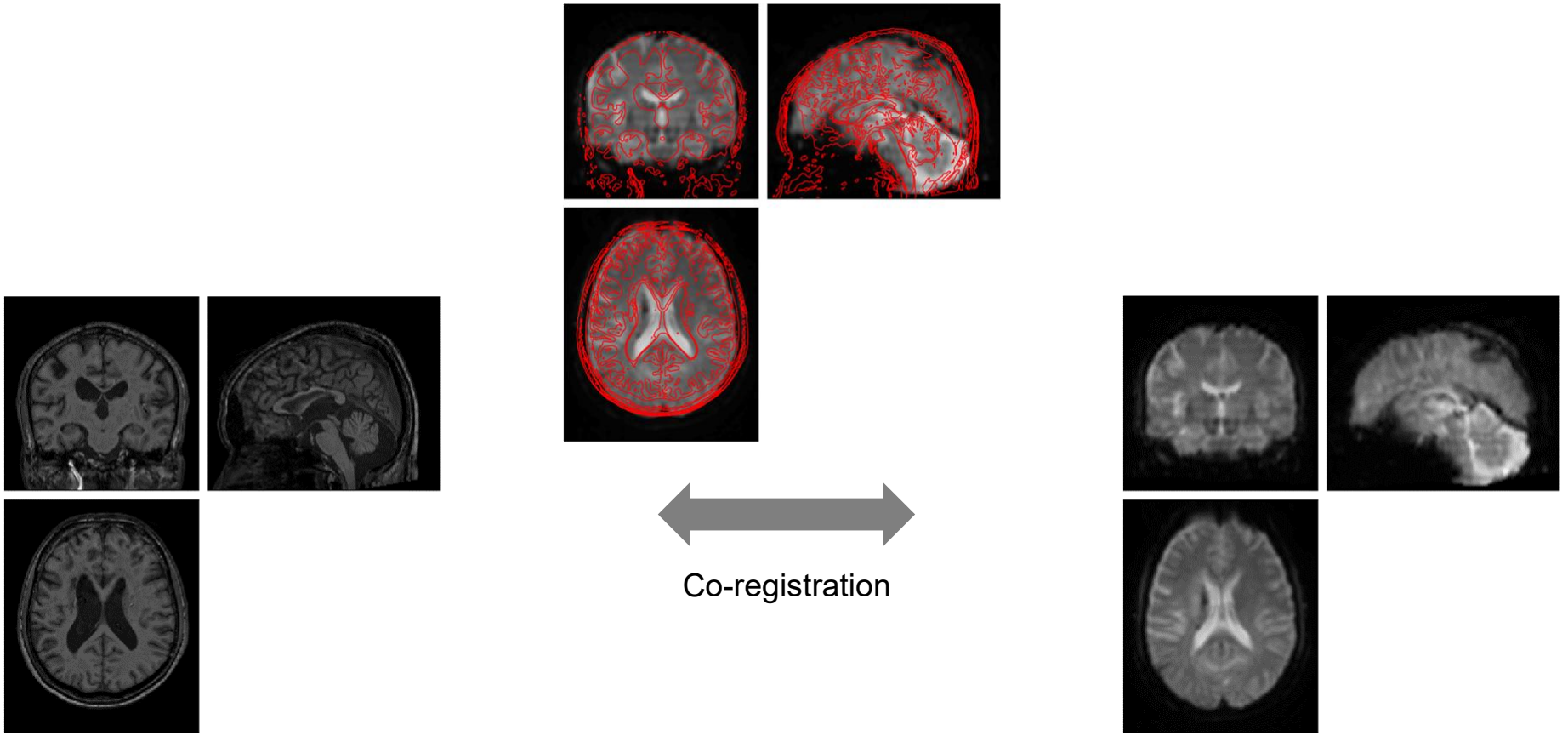
[https://kr.mathworks.com/help/medical-imaging/ug/medical-image-registration.html]

Image Registration

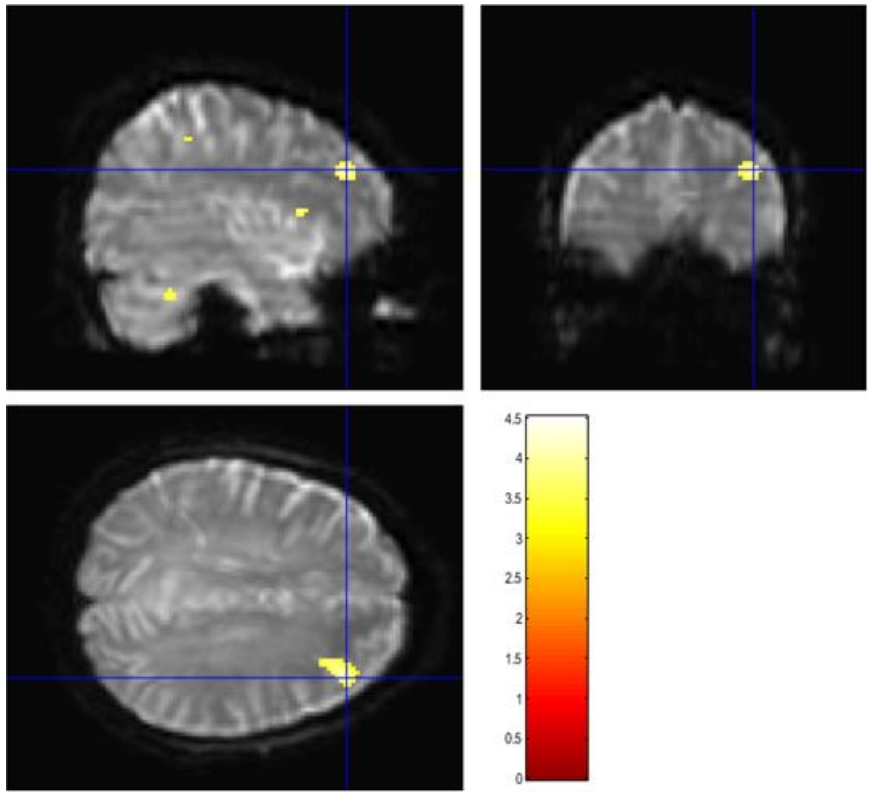


[https://www.diffusion-imaging.com/2015/10/dti-tutorial-2-normalization-and.html]

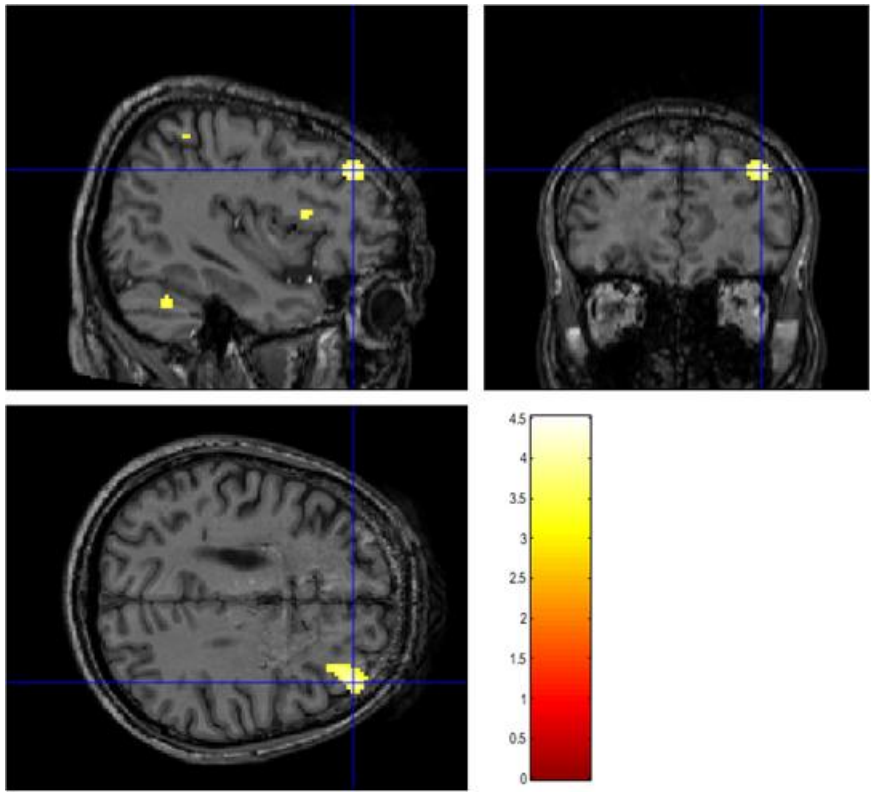
Affine Registration Based on 12 Parameter Transformation



Co-registration between sMRI and Functional MRI

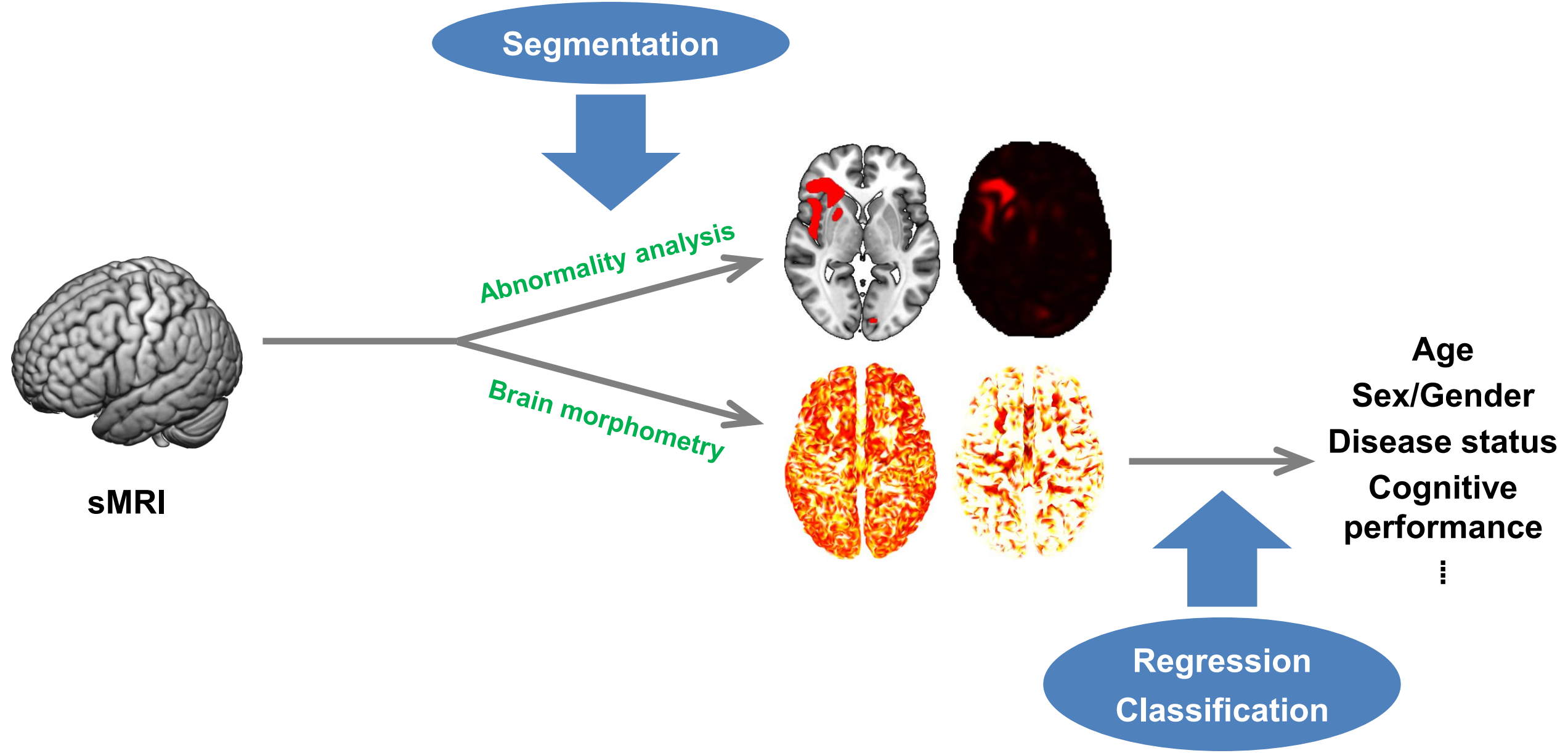


Brain activity map overlaid on a functional image



Brain activity map overlaid on a structural image

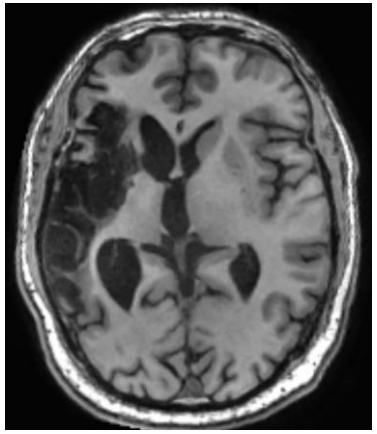
Anatomical Localization of Brain Activity


Segmentation
Abnormality analysis
Brain morphometry
sMRI
Age
Sex/Gender
Disease status
Cognitive performance
...
Regression
Classification

Lesion Segmentation

$P(Y|X) = P(\text{lesion\_mask} \mid \text{T1\_native})$
where X = raw T1-weighted image in native space
and Y = lesion mask in native space

Raw T1-weighted image

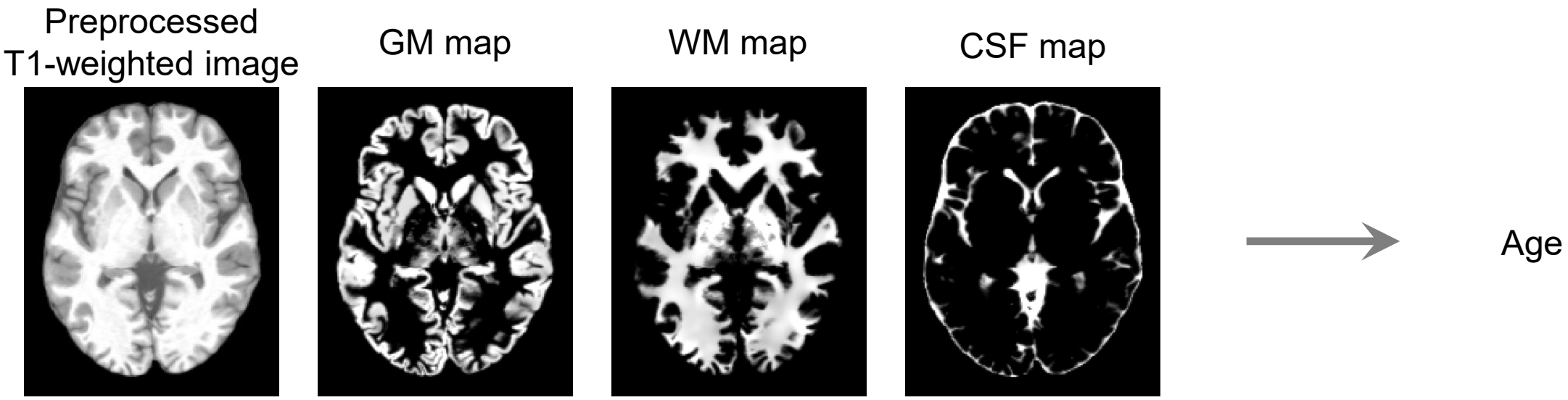


Lesion mask

Single-channel Input for Lesion Segmentation

Age Prediction

$P(Y|\mathbf{X}) = P(\text{age} \mid [\text{T1\_prep, GM, WM, CSF}])$
where **X** = [preprocessed T1-weighted image and derived maps in standard space]
and Y = age



Multi-channel Input for Age Prediction

Native vs. Standard Space: Lesion Segmentation vs. Age Prediction

- Lesion segmentation
  - Input: Raw T1-weighted image in native space
  - Goal: Accurate lesion boundary detection
  - Output: Lesion mask
- Age prediction
  - Preprocessed T1 + tissue maps in standard space
  - Goal: Population-level aging pattern recognition
  - Output: Age

Rationale for Different Preprocessing Strategies

- Native space for lesion segmentation
  - Preserves critical information
    - Lesion morphology: Original shape and boundaries
    - Tissue contrast: Hyperintense/hypointense characteristics
    - Spatial precision: Exact anatomical location
  - Avoids information loss
    - Registration artifacts → boundary blurring
    - Intensity normalization → contrast reduction
    - Template warping → lesion distortion

- Standard space for age prediction
  - Enables cross-subject comparison
    - Anatomical alignment: Consistent brain regions
    - Population patterns: Age-related atrophy signatures
    - Feature standardization: Comparable measurements
  - Removes confounding factors
    - Individual brain size/shape variations
    - Scanner-specific intensity differences
    - Anatomical landmark misalignment

- Matches preprocessing strategy to task objectives
  - Lesion segmentation prioritizes individual precision
    - Raw T1-weighted image in native space ← To preserve individual characteristics
  - Age prediction prioritizes population generalizability
    - Preprocessed T1-weighted image in standard space ← To enable population comparison

Aspect	Native space (Lesion segmentation)	Standard space (Age prediction)
Spatial accuracy	Precise boundaries	Registration errors
Cross-subject comparison	High variability	Standardized features
Tissue contrast	Preserved	May be altered
Population analysis	Difficult	Enabled
Clinical translation	Subject-specific	Generalizable

Native vs. Standard Space