Brain Structural MRI Introduction

Louvain-la-Neuve - Neuroimaging Workshop 2019

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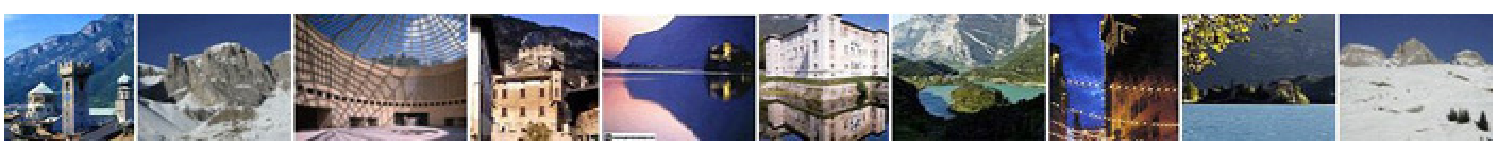


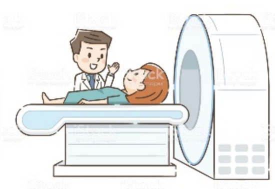
Concept map for lectures

Lecture 1

NMR Signal origin
- Powerful magnet
- Radio frequency
- Magnetic field gradients

MR Image & Contrast
- Spatial encoding
- Magnetic gradients
- Pulse sequences

MR Safety
- Powerful magnet
- Radio frequency
- Magnetic field gradients



Lecture 2

Structural MRI
- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications

Lecture 3

Diffusion MRI
- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications

Lecture 4

Functional MRI
- Contrast, important parameters
- Sequences & artifacts
- Pre-processing

Lecture 2 outline

Brain structure MRI

- What is a structural MRI?
- What is image contrast?
- How can image contrast be manipulated?
- What image analyses are common from brain structural MRI?
- What are some structural MRI applications?
- What are some structural MRI challenges?

Structural versus Functional MRI

- **Structural MRI:**
  - **Contrast sensitive to macro- or micro-structural anatomy in space**
  - **Examples**
    - **Gray matter, white matter, cerebral spinal fluid (CSF)**
    - **Iron content**
    - **Myelin content**
    - **Fat tissue**
    - **Etc.**

- **Functional MRI:**
  - **Contrast sensitive to blood oxygenation, or perfusion or metabolism in time**
  - **Examples**
    - **Hemodynamic changes in time (during task or rest)**
    - **Blood perfusion changes**
    - **Blood volume changes**
    - **Concentration of metabolite changes**
    - **Etc.**

The key thing is contrast. What is it?

Lecture 2 outline

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Image contrast definition

- **Structural contrast: difference in MR signals between different tissues**
- **Goal: maximize the contrast of interest (USEFUL IMAGES!)**

Tissue 1 | **Tissue 2**

Water protons' mobility/environment:

T_1, T_2, T_2^*, ρ, Diffusion, Flow, … | **T_1, T_2, T_2^*, ρ, Diffusion, Flow, …**

MR signal: S_1 | S_2

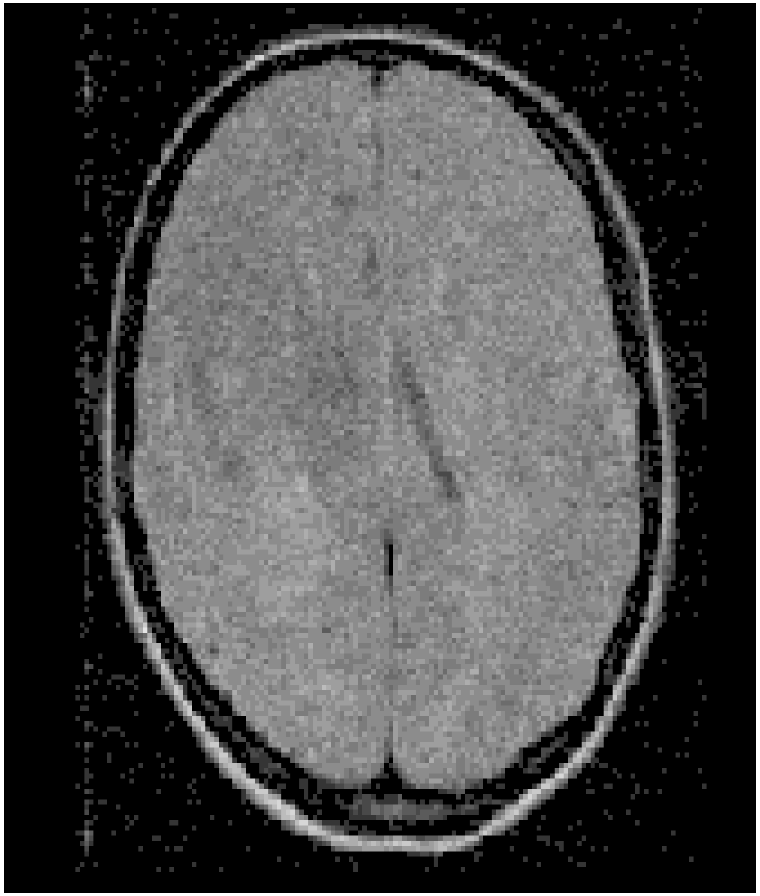
Contrast to Noise ratio (CNR):

$$CNR = \frac{S_1 - S_2}{\sqrt{\sigma_1^2 + \sigma_2^2}}$$

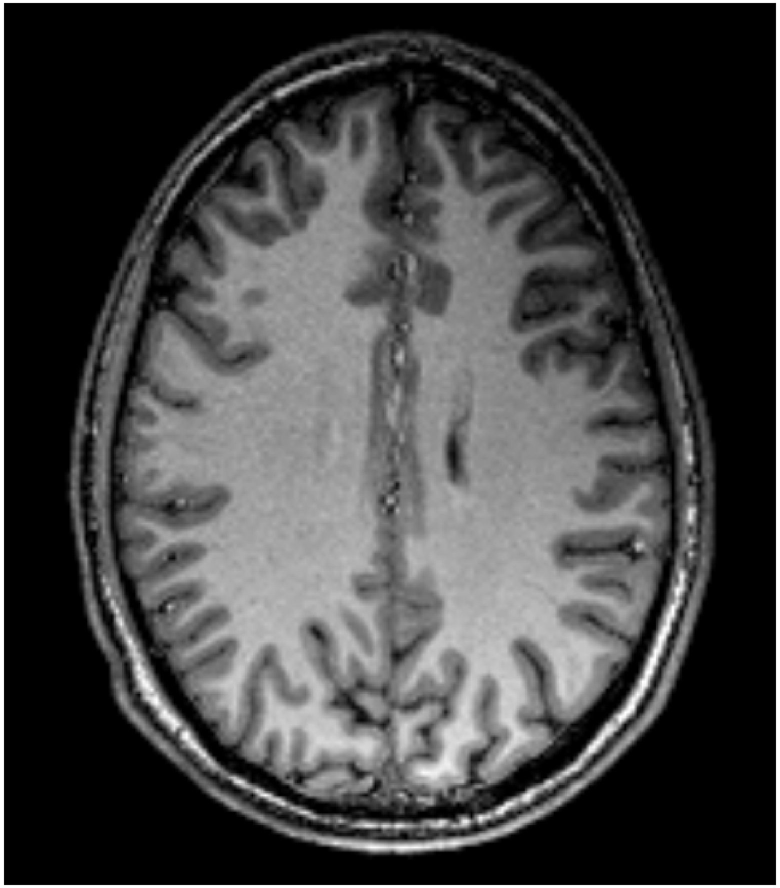
Focus: structural contrast
Examples?

Structural image example

Poor gray/white matter contrast



Good gray/white matter contrast
(T1 contrast)



MRI contrast: what can be manipulated?

Tissue Properties: fixed

Tissue	T_1^+ (ms)	T_2 (ms)	ρ^*
Fat	260	84	0.90
White Matter	780	90	0.72
Gray Matter	920	100	0.84
CSF	3000	300	1.00

T1 values for B_0 = 1.5T

ρ^*: % H_2O relative to CSF

Experimental Variables

- **Magnetic field**
- **Pulse sequence**
- **Pulse sequence parameters**
  - **- Repetition time: TR**
  - **- Echo time: TE**
  - **- Inversion time: TI**
  - **- RF flip angle: α**
- **Contrast agent**

What's the effect of these variables?

Contrast weight on the MRI signal

- **<u>General MRI pulse sequence</u>: combination of contrasts**

Signal Intensity:

$$S(x,y) = k \times \rho \times T_1 \times T_2 \times \ldots$$

- **<u>Contrast Weighting</u>: maximize one term, minimize the others**

Example: T_1-weighting

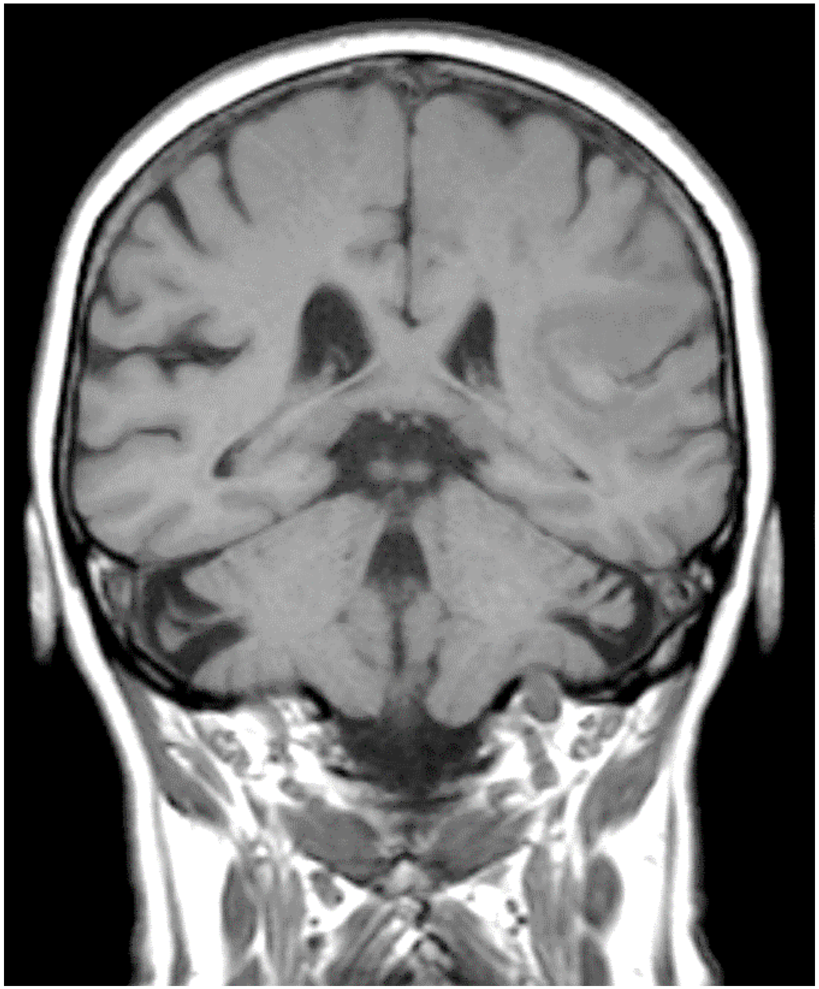
$$S(x,y) = k \times \rho \times T_1 \times T_2 \times \ldots$$

by choosing adequate sequence & sequence parameters

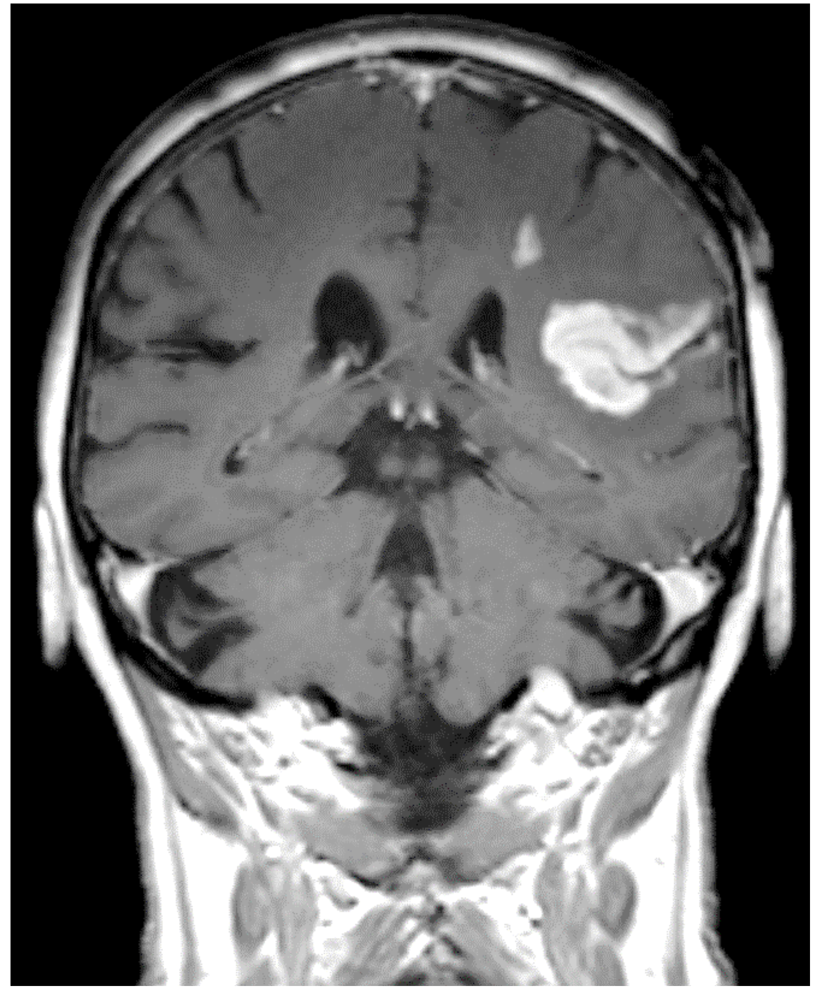
Examples?

Using image contrast agents in clinics

Without contrast agent



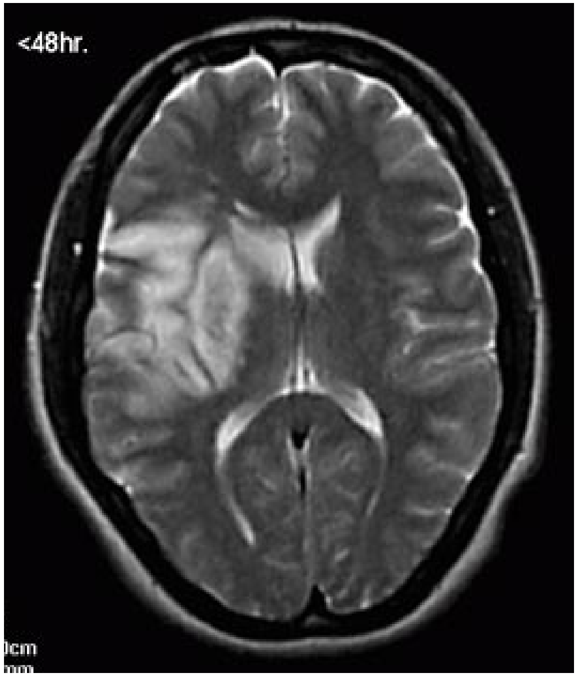
With contrast agent



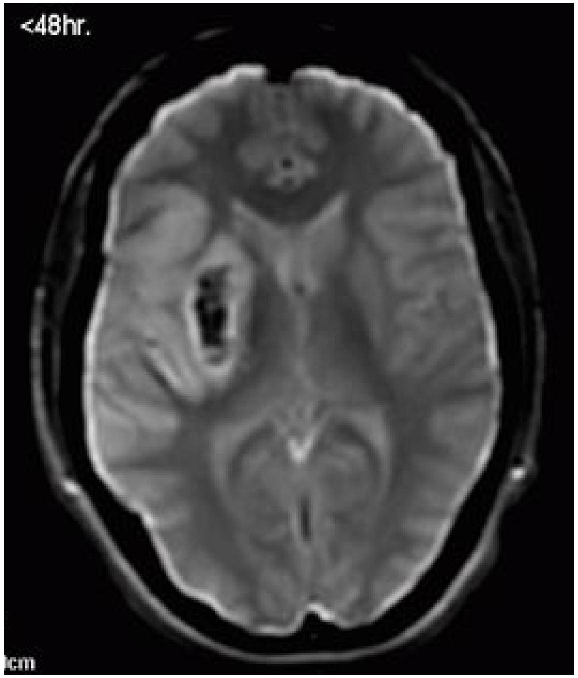
Defect of the blood-brain barrier after stroke
shown in MRI T1-weighted images.

Multiple contrasts are used for diagnosis

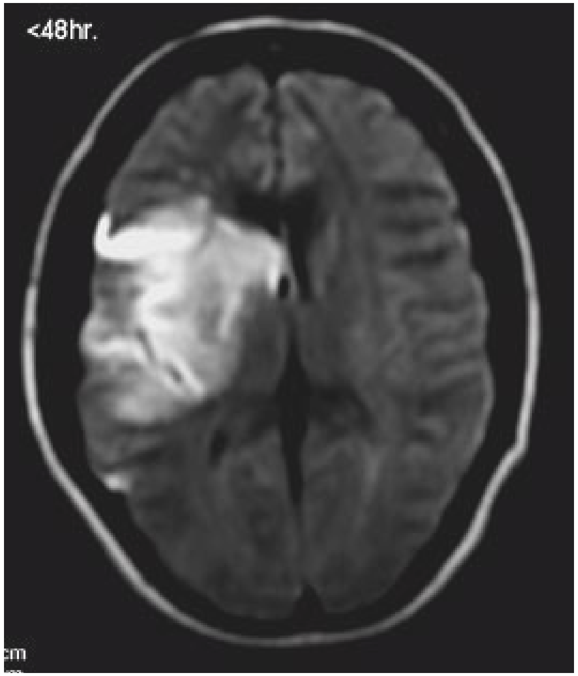
< 48 hours postictal acute infarct in right hemisphere



T_2-weighted



T_2*-weighted
(presence of blood)

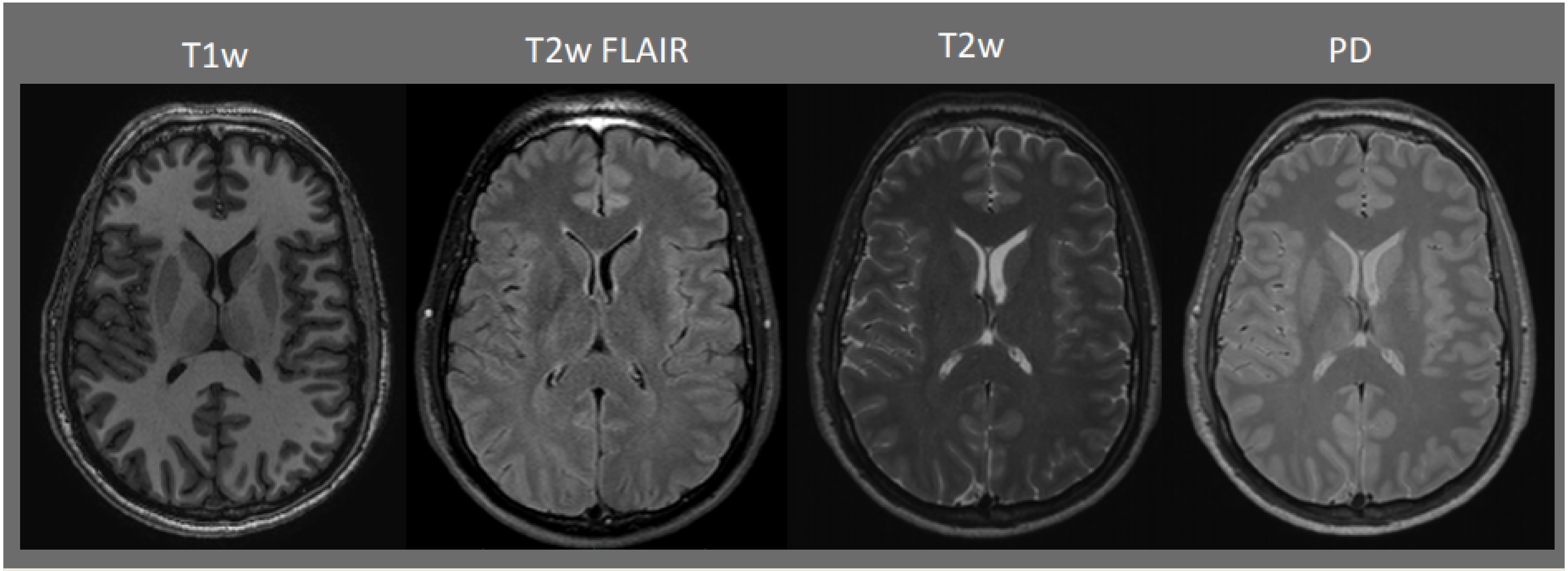


Diffusion-weighted
(full infarct extent)

Images from Toshiba Image gallery

Multiple contrasts in healthy tissue

Research with healthy volunteers: endogenous natural tissue contrast



http://www.mc.vanderbilt.edu/documents/fmri/files/2013_Phys352A_StructuralMRI.pdf

T1w: T1-weighted MRI
T2w: T2-weighted MRI
T2w FLAIR: T2-weighted Fluid Attenuation Inversion Recovery
PD: Proton Density weighted MRI

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Multiple options to manipulate MRI contrast

Magnetic Field strength → ***MRI Sequences*** → ***MRI Sequence Parameters***

1.5 T
3.0 T
4.0 T
7.0 T
9.4 T
…

Gradient Echo sequences:
- Proton Density weighting
- T1 weighting
- T2* weighting

Spin Echo sequences:
- Proton Density weighting
- T1 weighting
- T2 weighting
- Double echo: PD & T2 weighting

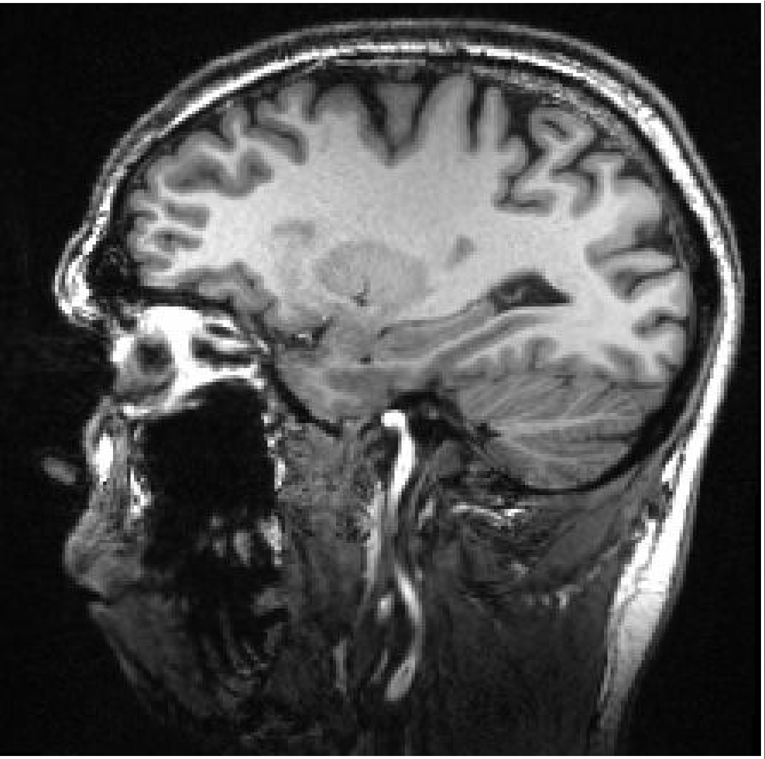
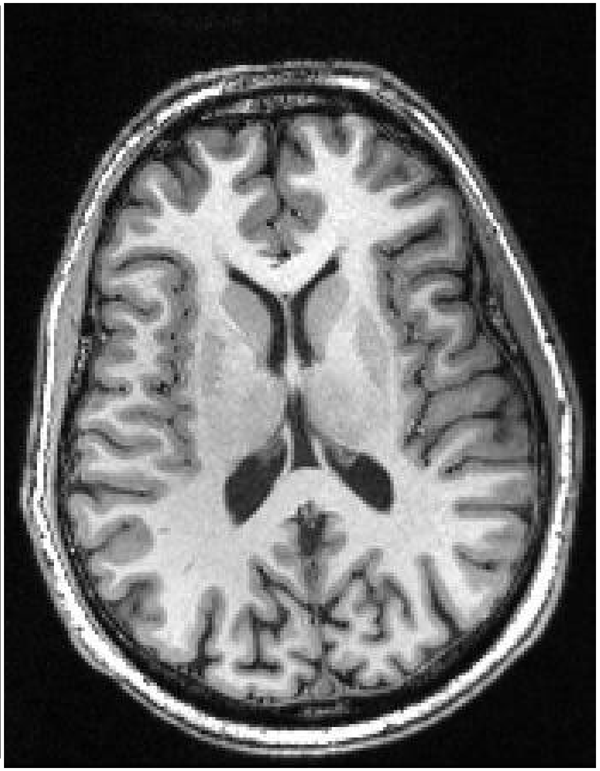
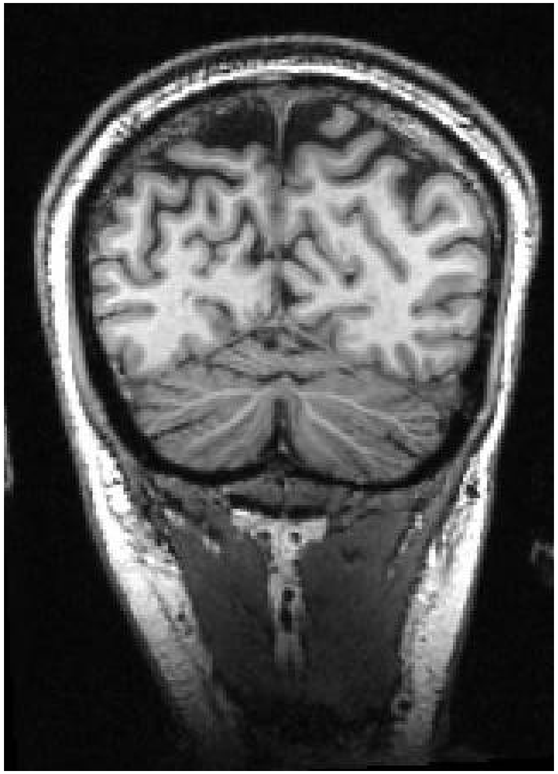
Inversion Recovery sequences:
- MP-RAGE: for high T1 contrast
- FLAIR: for PD or T2 weighting without CSF signal

Voxel size
Repetition time: TR
Echo time: TE
Inversion time: TI
Flip angle: α
Fat suppression: yes/no
Averaging: yes/no
Acceleration: no/how much
Slice orientation
Brain coverage
…

The choice of a particular sequence & parameters depends on the metrics you want to derive and analyze from the images

Example: T1-weighted MRI

Most common brain structural MRI contrast used
in cognitive neuroscience studies

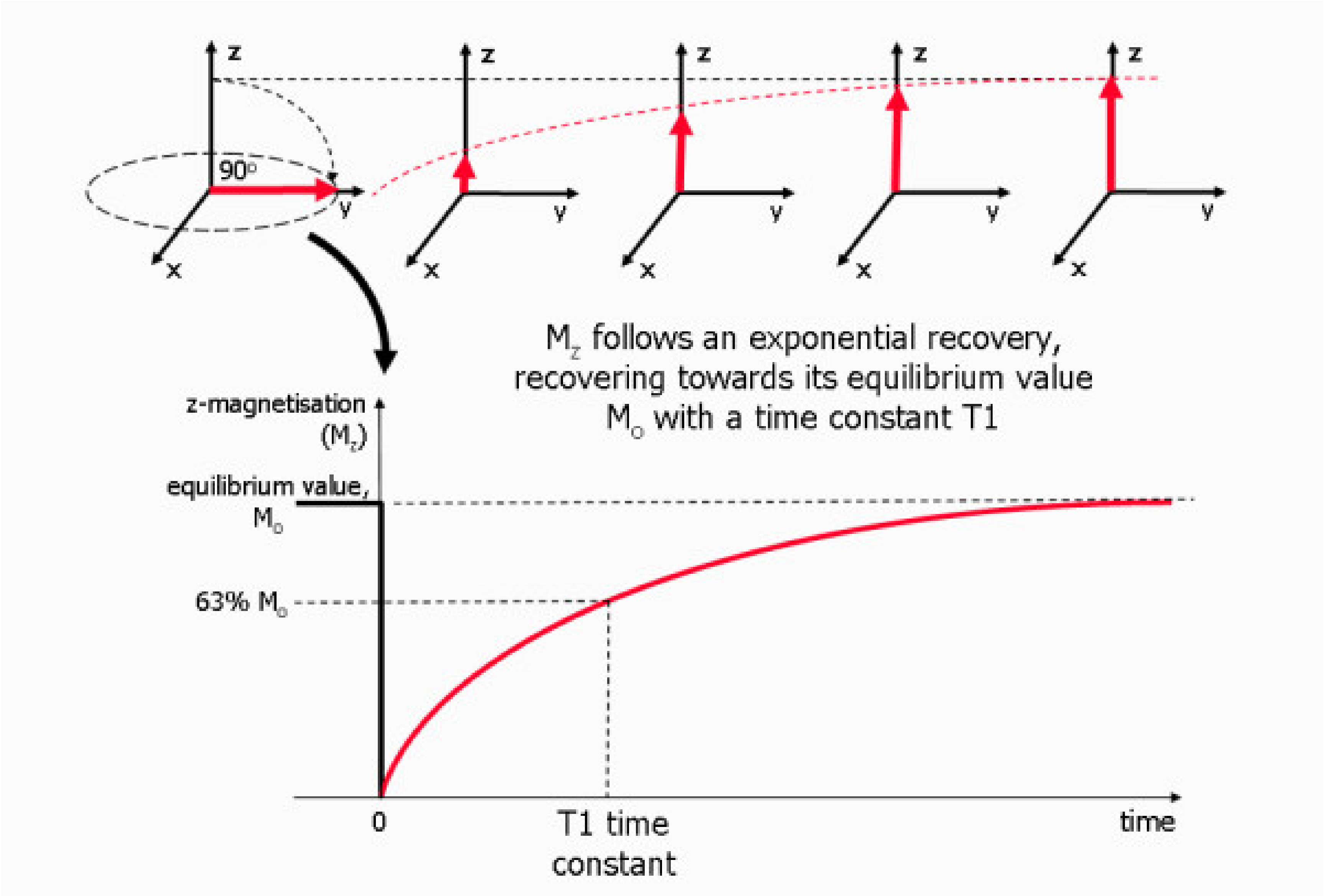




3D MP-RAGE (T1 contrast, 4T)

Spatial Resolution: 1 x 1 x 1 mm^3
Acquisition time: 5 minutes

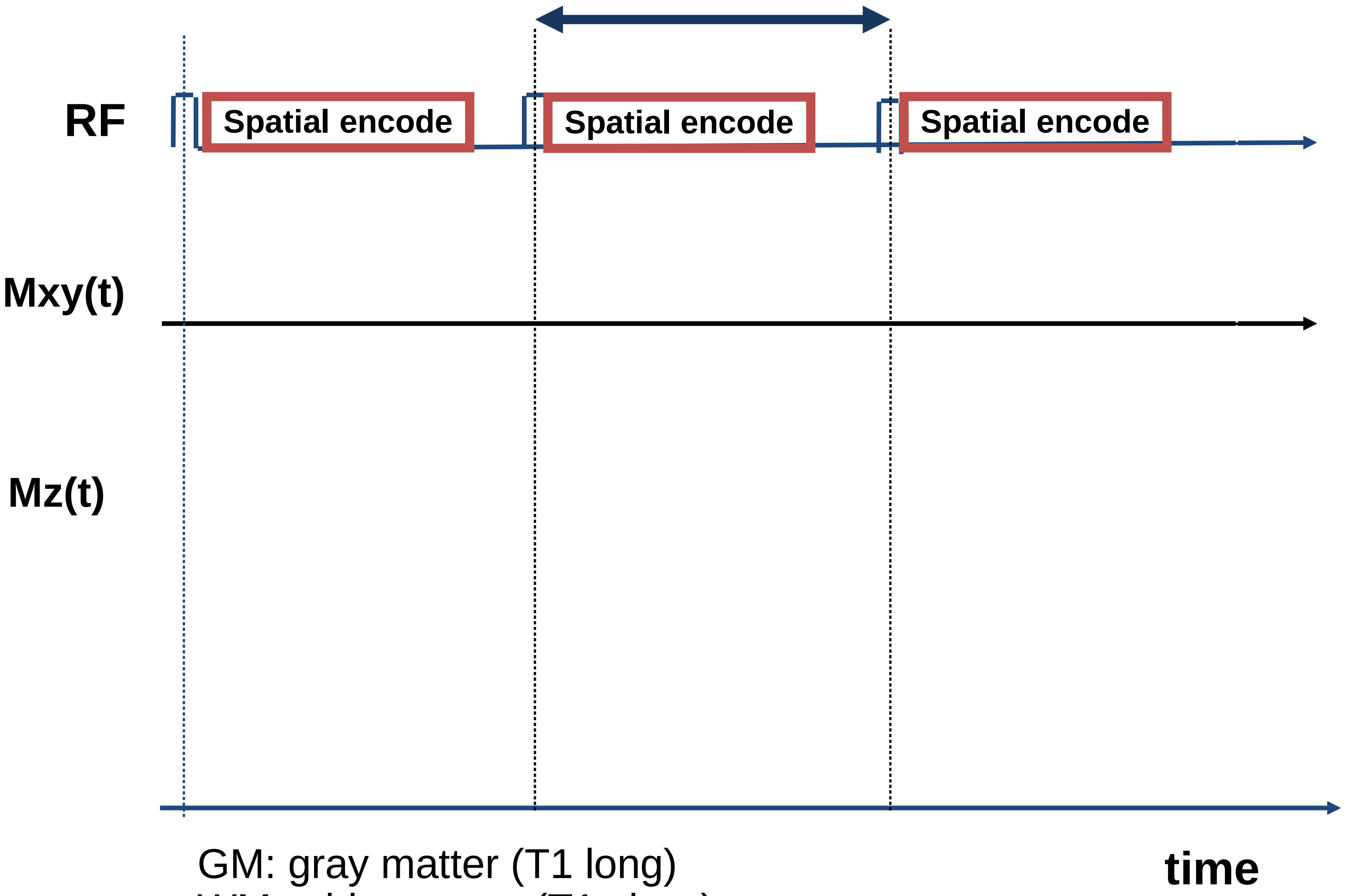
How is this contrast obtained?

Reminder of T1 relaxation



Example: changing contrast with TR

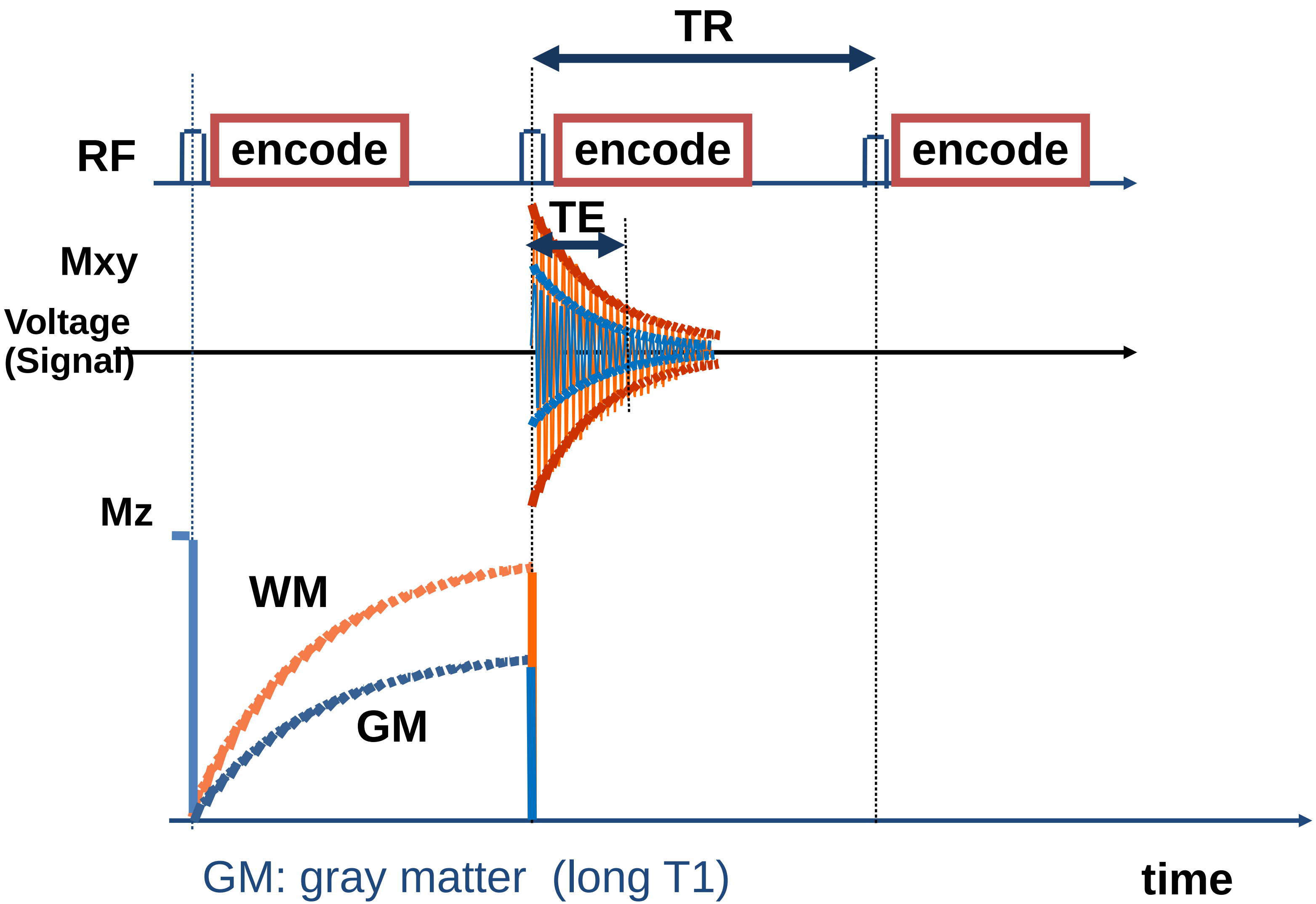
TR: Repetition Time (time between RF excitations of the magnetization)



GM: gray matter (T1 long)
WM: white matter (T1 short)
Assume T2* similar and very short in both GM & WM

Example: changing contrast with TR

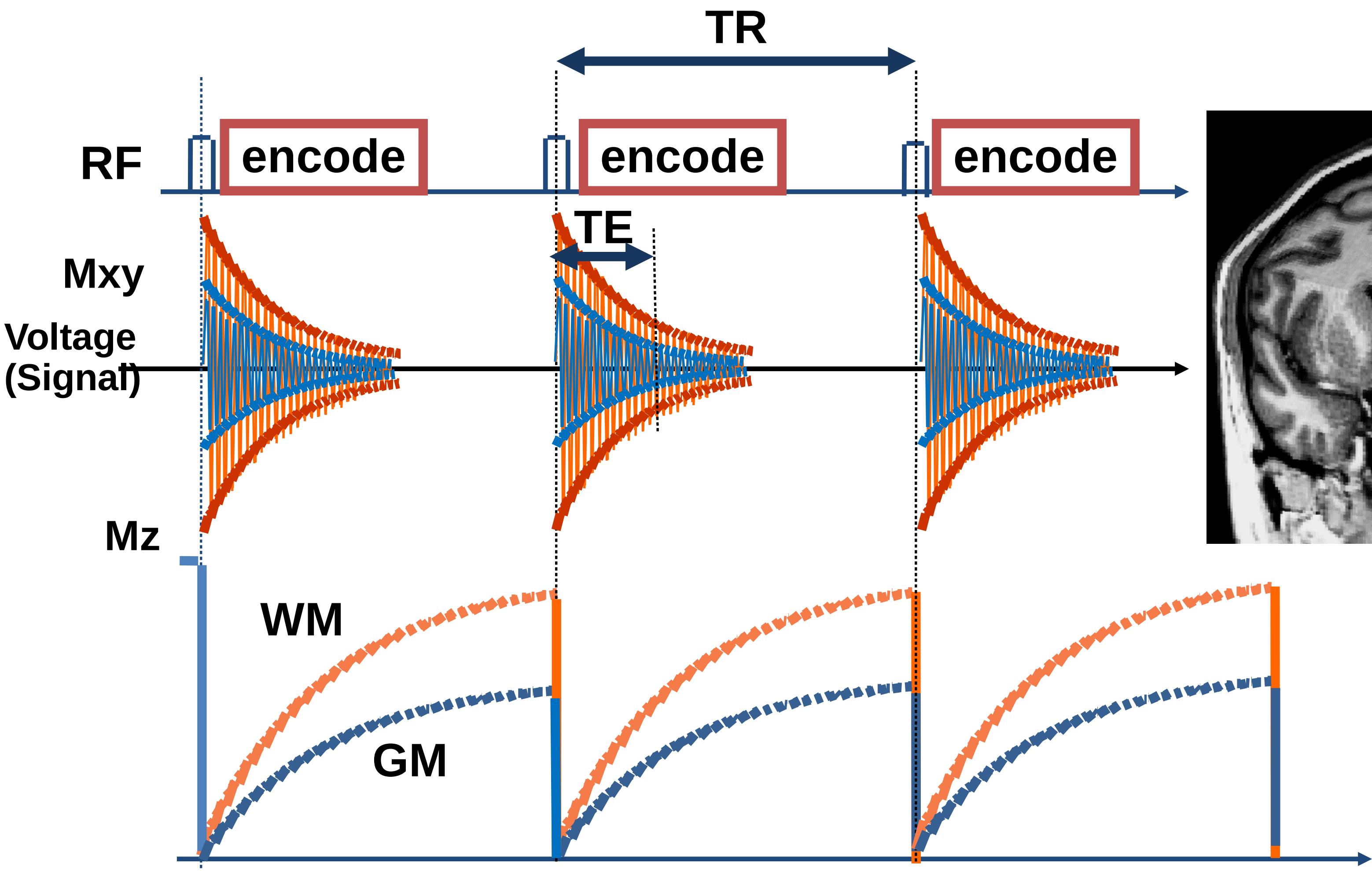
TR: Repetition Time (time between RF excitations of the magnetization)



GM: gray matter (long T1)
WM: white matter (short T1)

Example: changing contrast with TR

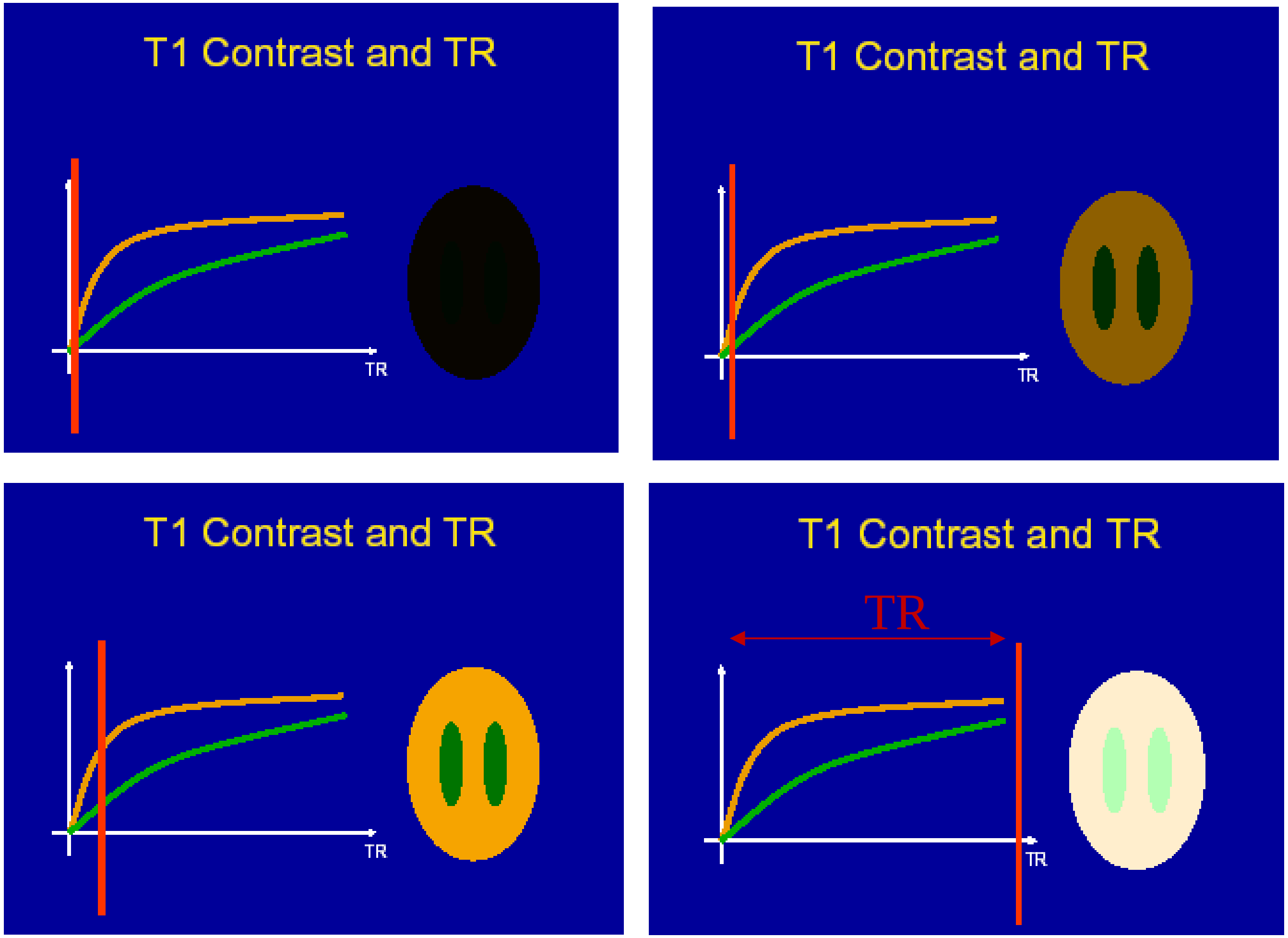
TR: Repetition Time (time between RF excitations of the magnetization)

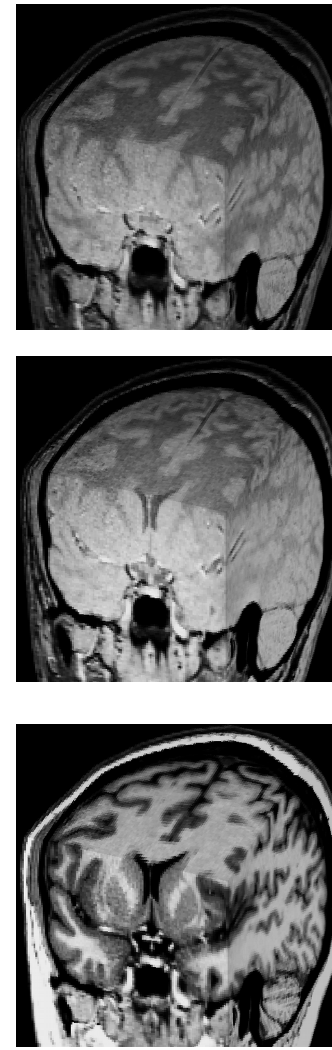


GM: gray matter (long T1)
WM: white matter (short T1)

time

Example: changing contrast with TR

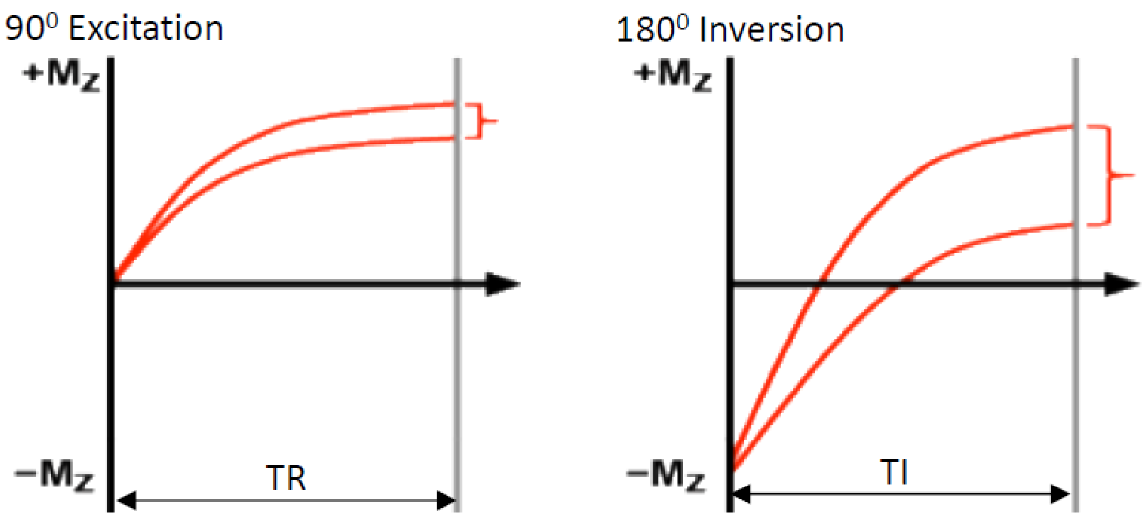




To optimize the contrast-to-noise ratio between tissues
we need to know T1 of the tissues of interest

Better T1 contrast with «inversion pulse»

Behavior of Magnetization during T1 Relaxation



Modified from: http://mriquestions.com/why-use-ir.html

Saturation with a short TR

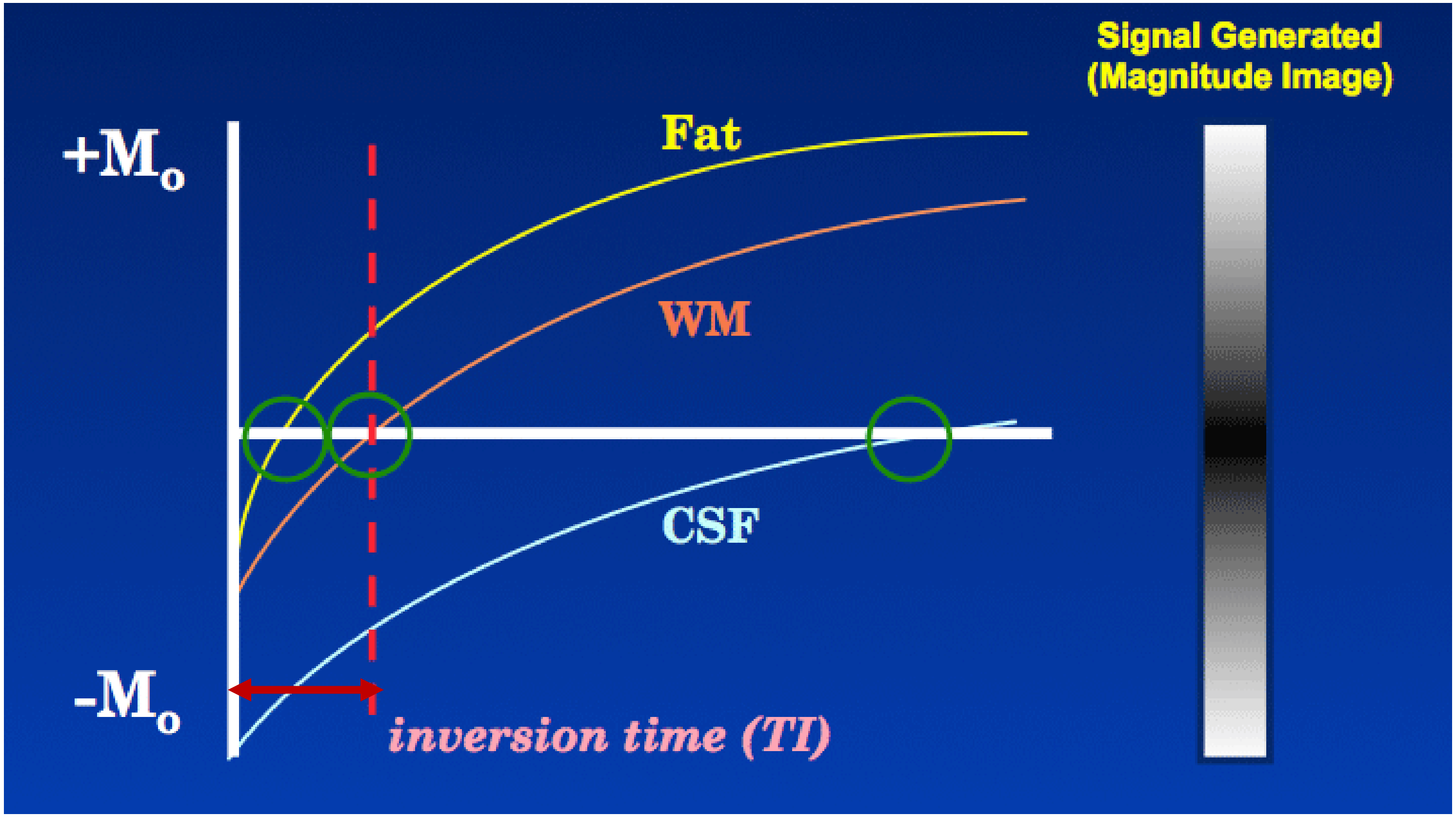
- TSE with TR = 400 – 700 ms
- GRE with TR = 3 – 200 ms

Preparation with IR

- T1 FLAIR
- IR-SPGR / MP-RAGE

Better T1 contrast with «inversion pulse»

Inversion time choice: selects tissue to «eliminate» from image

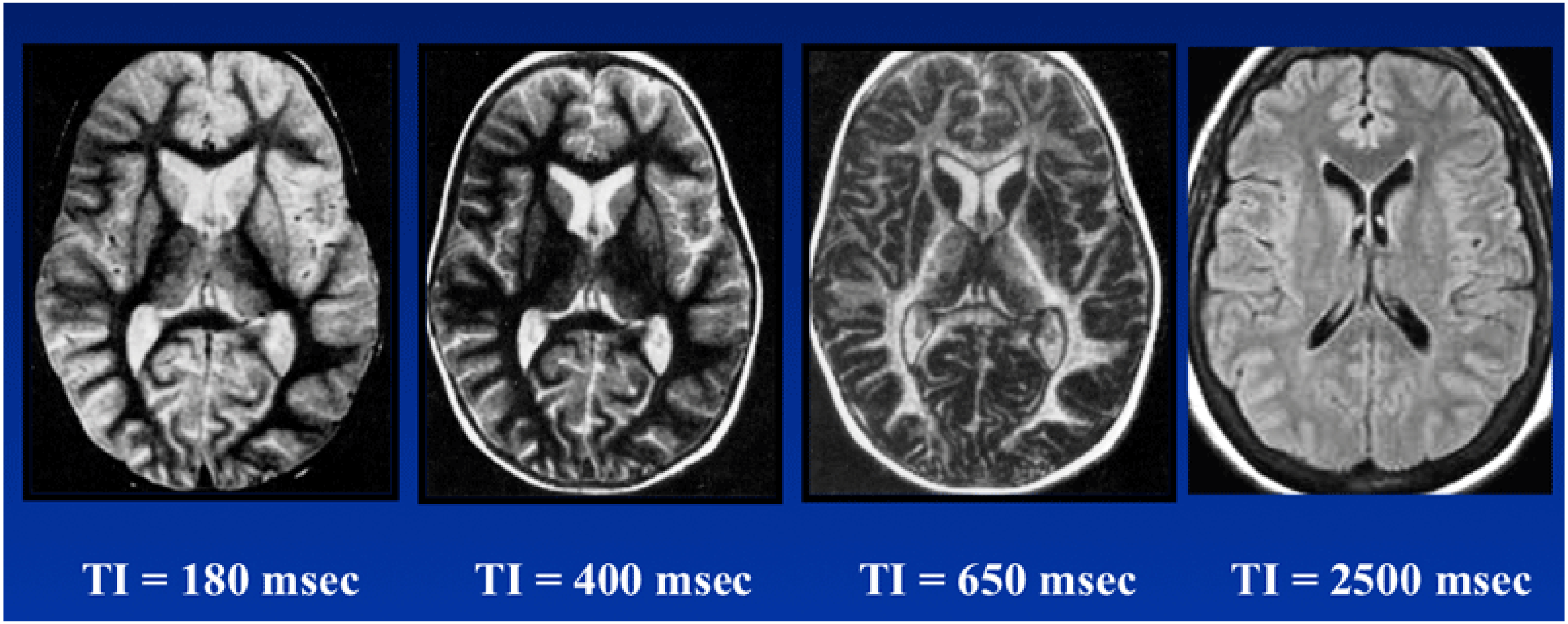


Longitudinal magnetization recovery aftern a
180° inversion pulse (WM: white matter, CSF: cerebral spinal fluid)

Source: http://mriquestions.com/ti-to-null-a-tissue.html

Better T1 contrast with «inversion pulse»

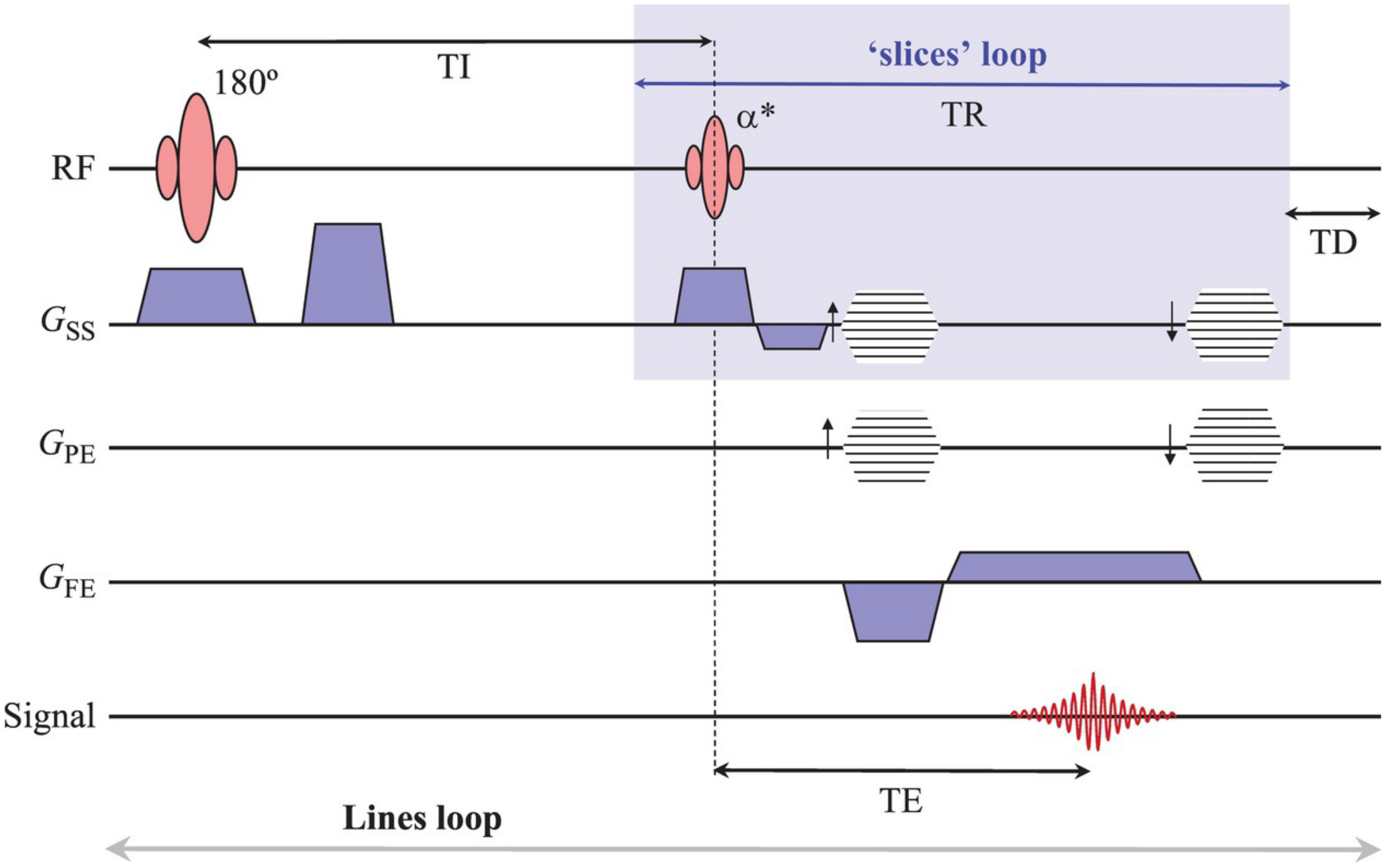
Choice of TI: selective suppression of tissue MRI signal



Fat suppression (STIR sequence)	White matter suppression	Gray matter suppression	CSF suppression (FLAIR sequence)

Source: http://mriquestions.com/choice-of-ir-parameters.html

Magnetization Prepared Rapid Gradient Echo (MPRAGE)



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Before MRI data acquisition

0) Define what metrics do you need

Define your hypothesis testing criteria

This defines:

- acquisition protocol
- analyses strategies

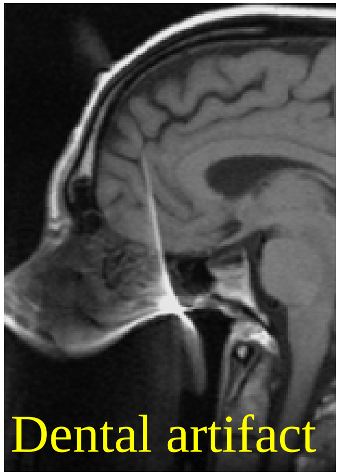
Structural analysis: first step

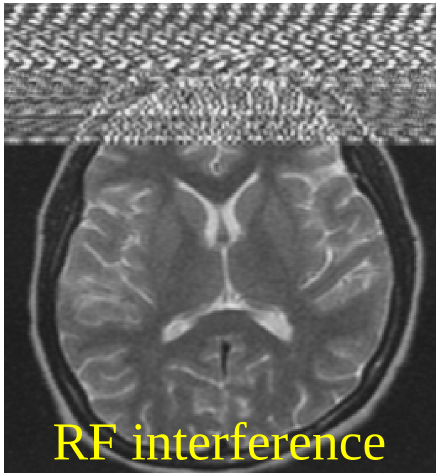
0) Define what metrics do you need

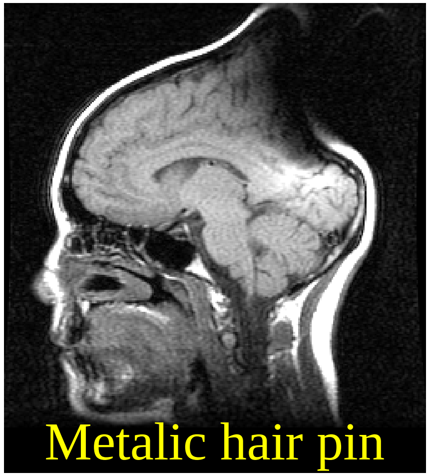
1) MRI quality control

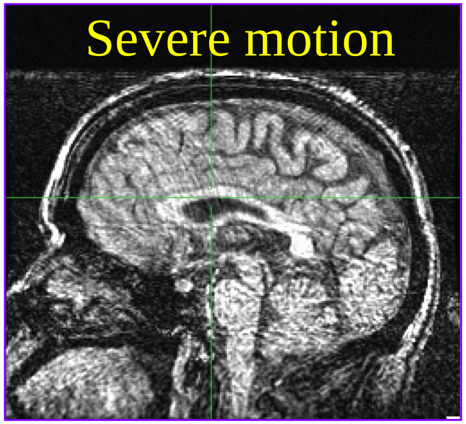
- Problems with subject
  - Movement?
  - Inplants?
  - Lesions?
  - Position inside coil?
- Problems with sequence-parameters
  - Contrast good?
- Problems with MRI system
  - Inhomogeneities B0
  - Inhomogeneities B1
  - Inestabilities
- Problems in laboratory
  - Interference with other equipment
- Etc.

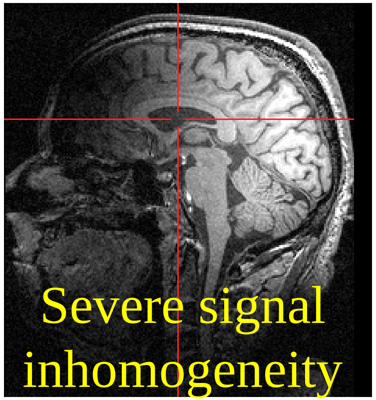
LOOK at images, LOOK for problems

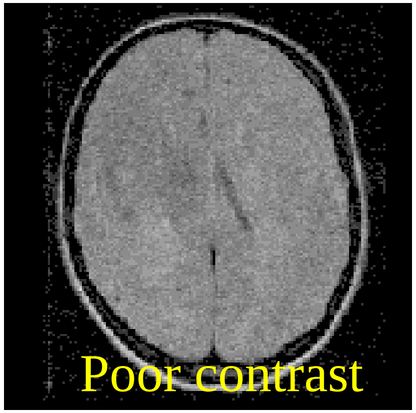


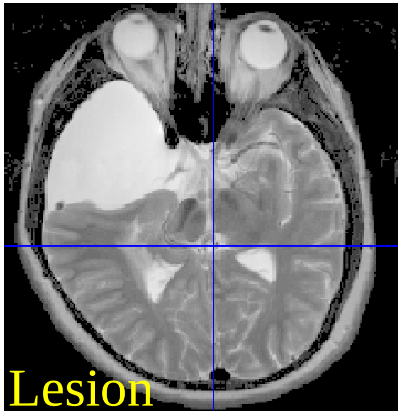


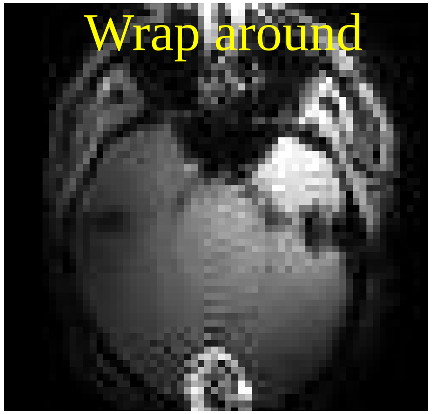




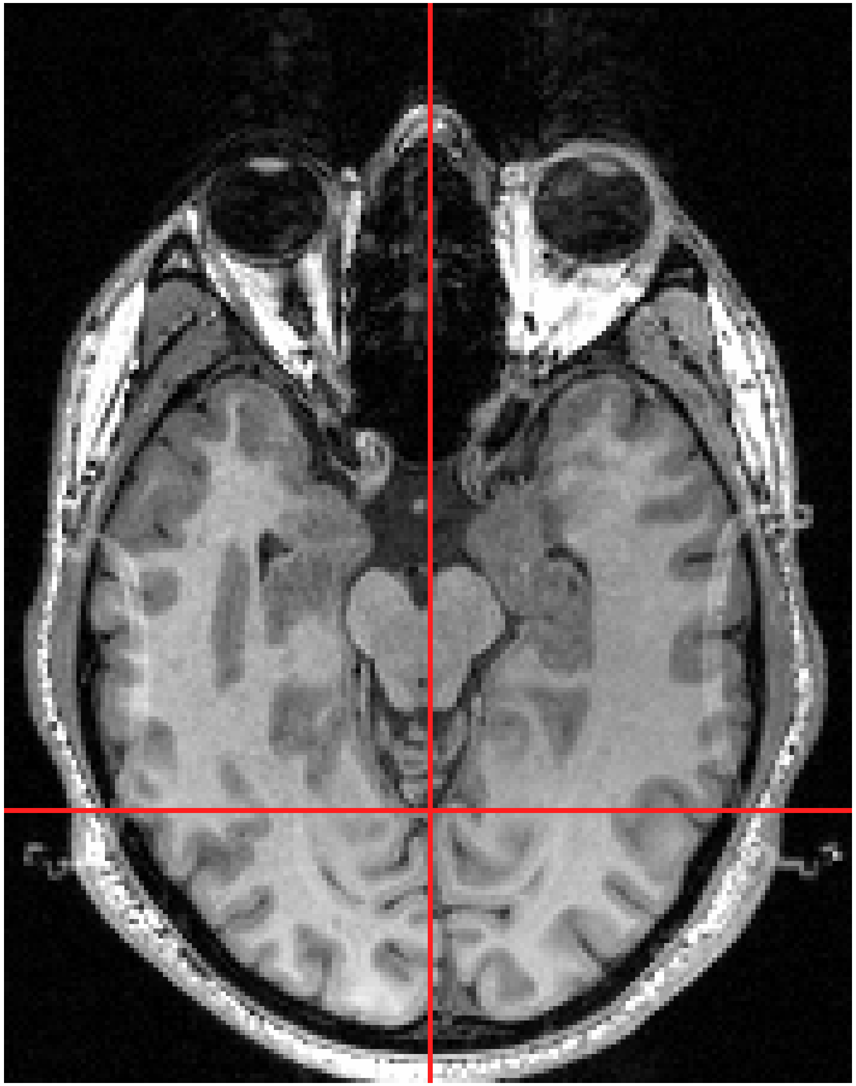








Is this OK?



Structural MRI analysis

0. **Define target metrics needed**

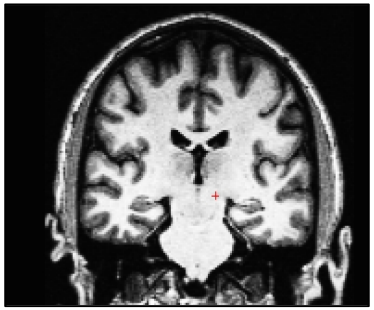
1. **MRI quality control**

2. **Metrics extraction will depend on experimental details**
   Examples:
   - **Segmentation of cortex, subcortical structures, ventricles**
     Acquire T1 (+ T2 for improved segmentation)
     Brain morphometry (volumes, thickness, curvature, etc.)

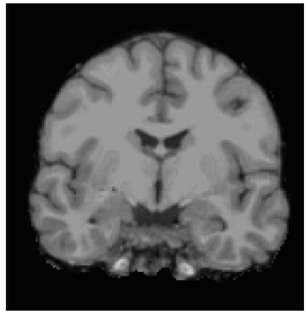
   - **Lesion segmentation**
     Acquire T2* sequence for microvascular bleeding
     Acquire FLAIR sequence for deep white matter lesions

Example: Freesurfer segmentation

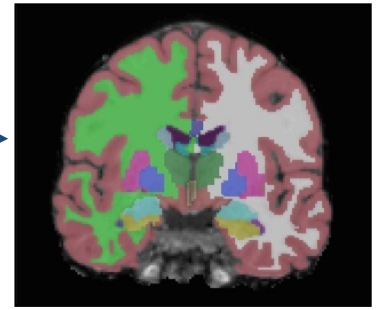
Fully automated segmentation of cortex, ventricles, subcortical structures



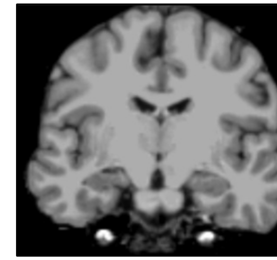
T1 Weighted Input



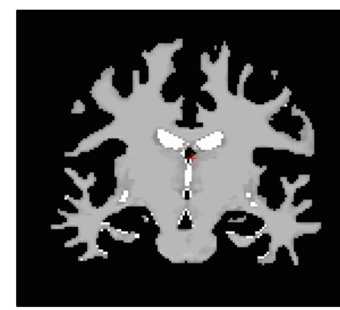
Skull Stripping



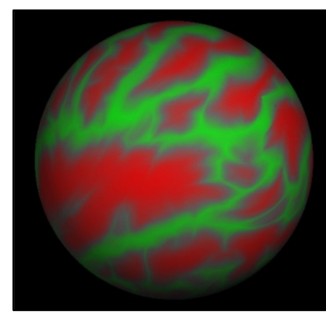
Volumetric Labeling



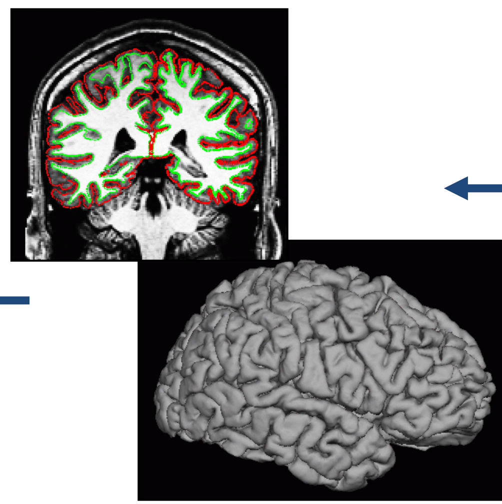
Intensity Normalization



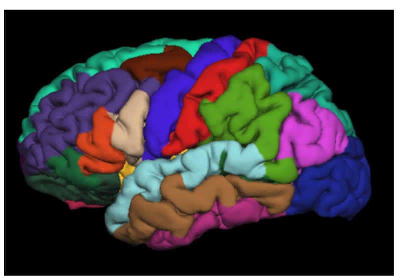
White Matter Segmentation



Surface Atlas Registration



Surface Extraction

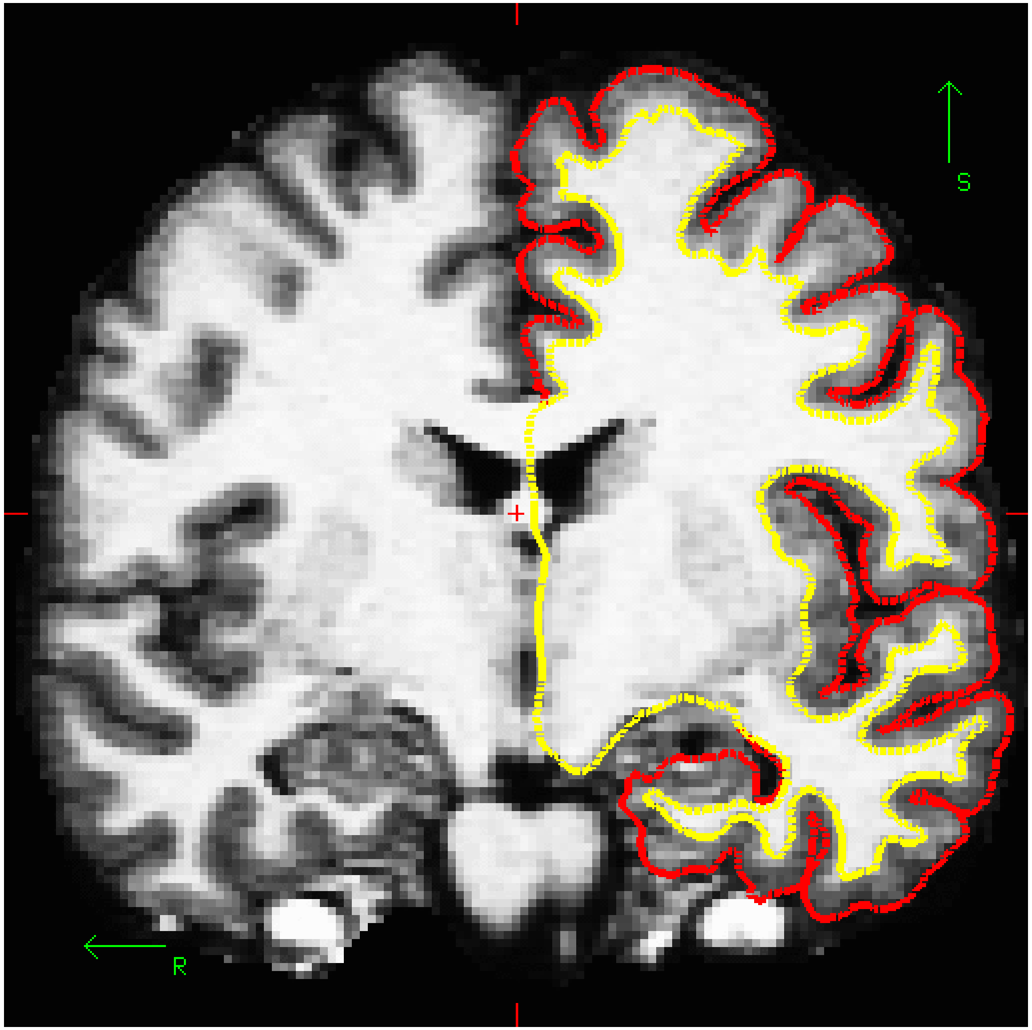


Gyral Labeling

Stats!

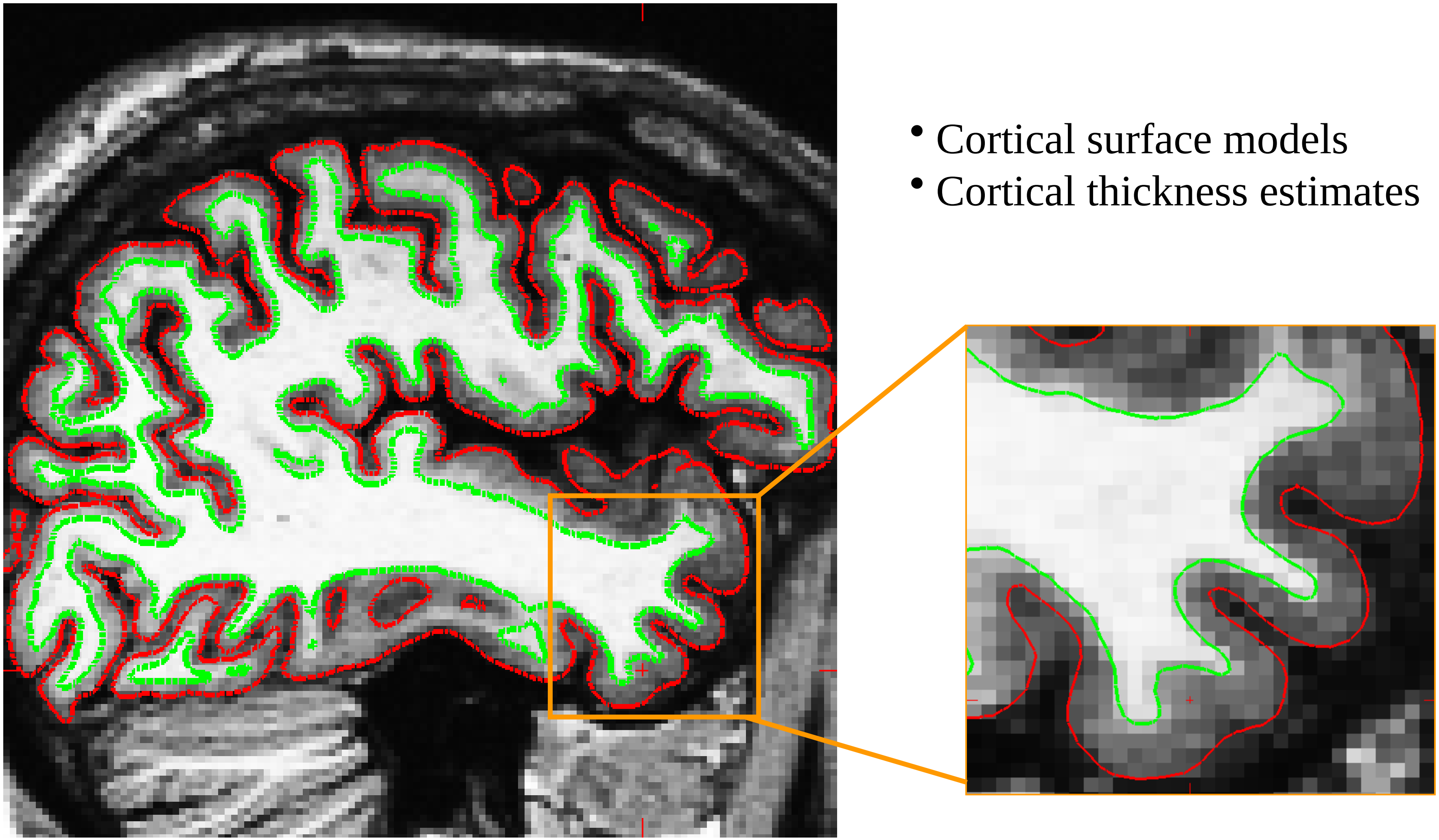
https://surfer.nmr.mgh.harvard.edu/fswiki

Freesurfer: WM/GM surface grows to pial surface



GM: gray matter
WM: white matter

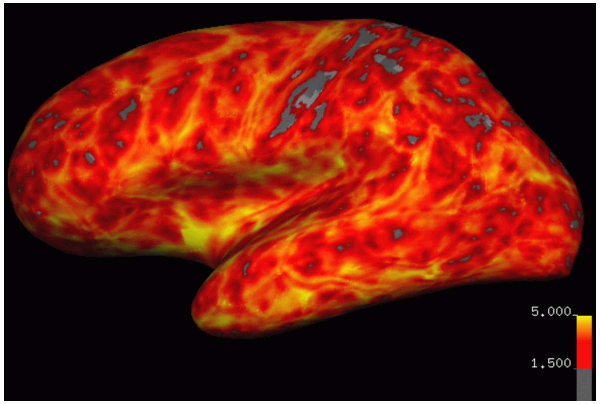
Cortical segmentation needs good T1 contrast



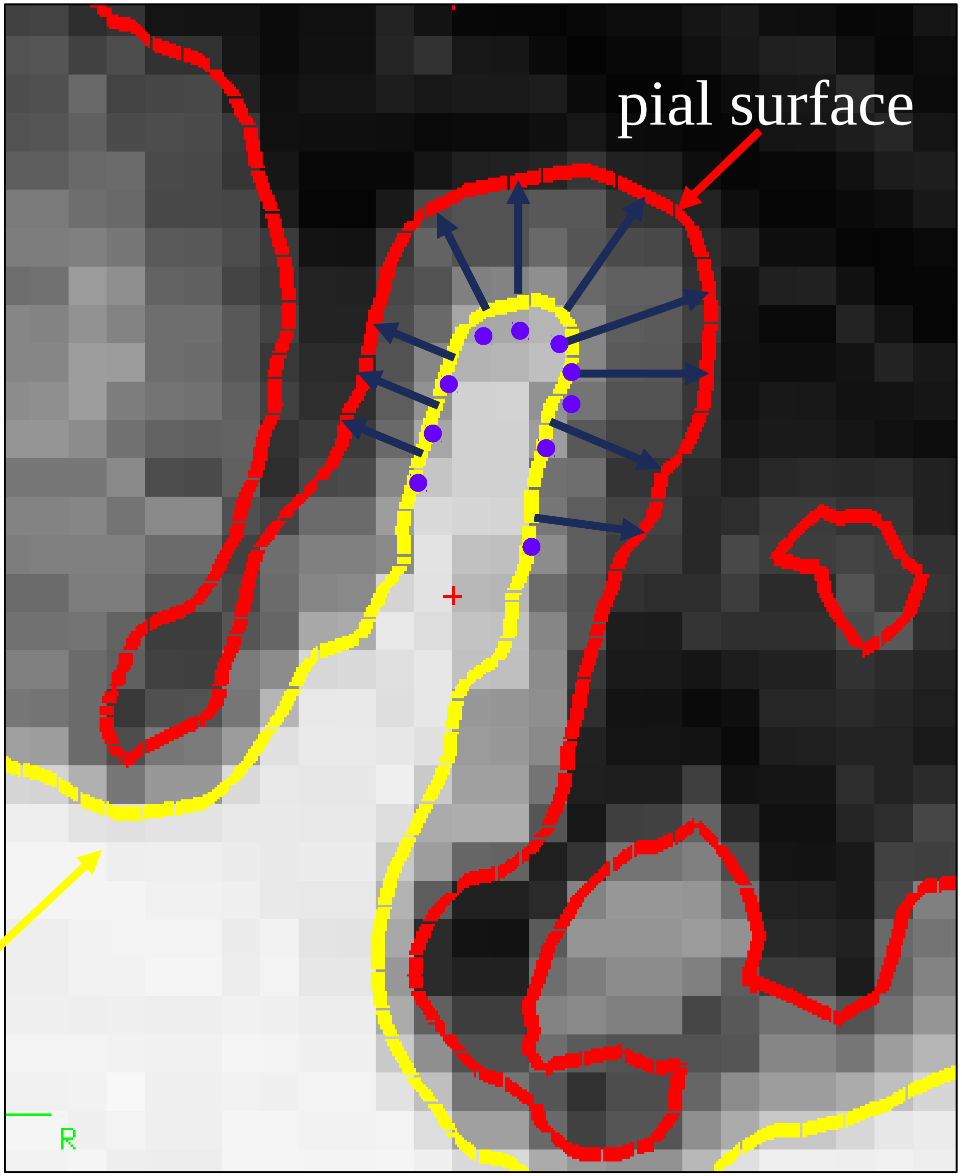
- Cortical surface models
- Cortical thickness estimates

Cortical thickness estimations

- Distance between white and pial surfaces
- One value per vertex
- Surface-based more accurate than volume-based



mm

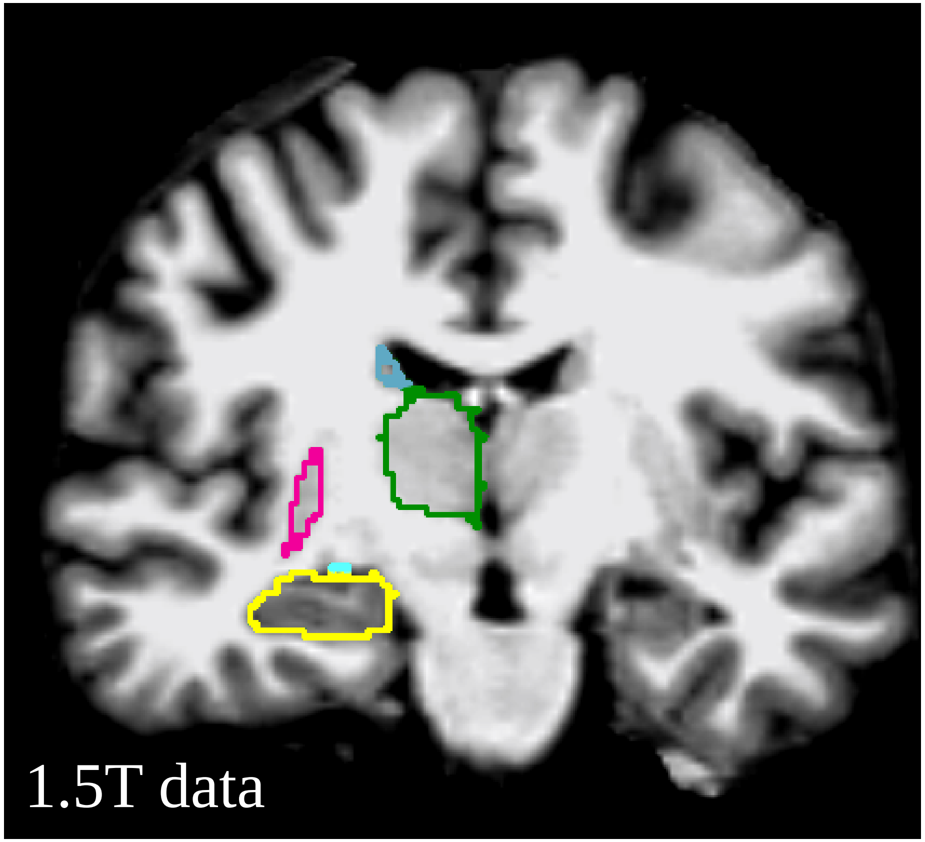


white/gray surface

lh.thickness, rh.thickness

Segmentation of subcortical structures

- Good gray/white contrast: subcortical structures segmentation
- Subcortical structures: ROIs for fMRI analyses
- Subcortical structures: Shape and volume characterization



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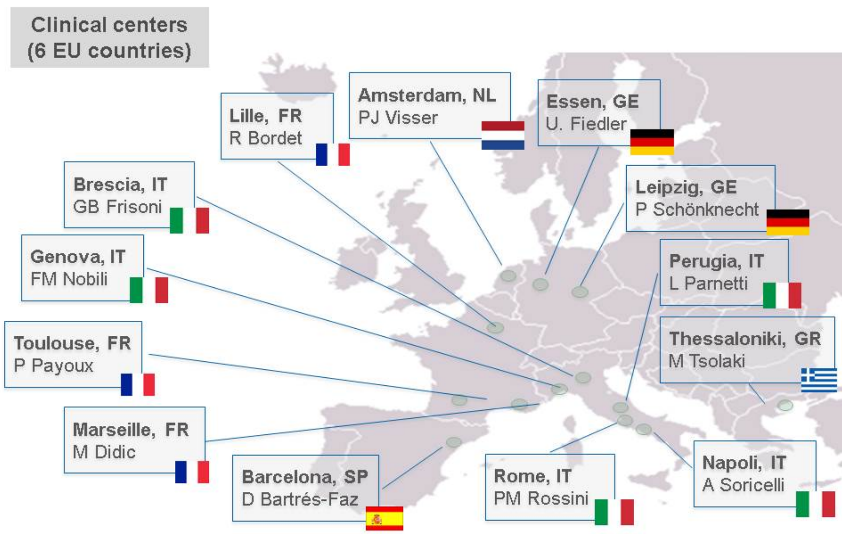
Structural MRI: Application examples

- Medical anatomical information
- Anatomical information for functional studies
  - Registration with other MRI data
    - Same subject: other images, other acquisition sessions
    - Different subjects: group analyses
  - Registration with data from other modalities (PET, EEG, MEG)
  - Development of tissue models (dipoles for EEG, MEG)
- Morphometry analyses
  - Comparisons across populations (healthy or not)
  - Correlation with behavioural or demagraphics measures
  - Treatment effects (e.g., learning, therapeutical, etc.)
- Anatomical covariance (network analyses)
- Tissue mapping (T1, T2, T2*, myelin, etc.)

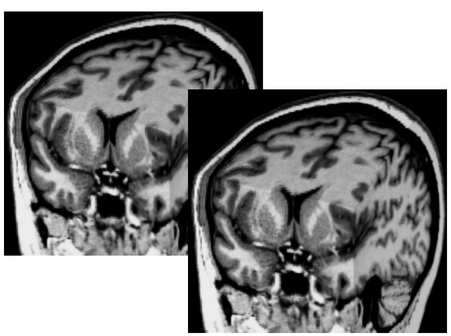
Structural MRI: multisite hippocampal segmentation to study Alzheimer's disease progression

Pharmacog Human MRI Consortium

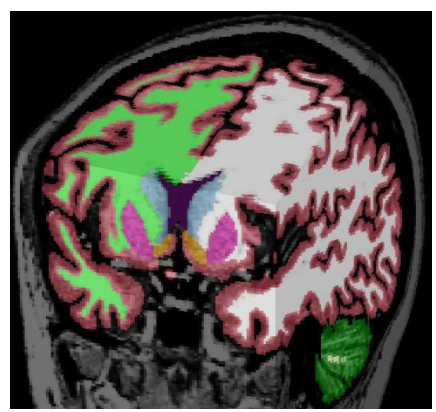


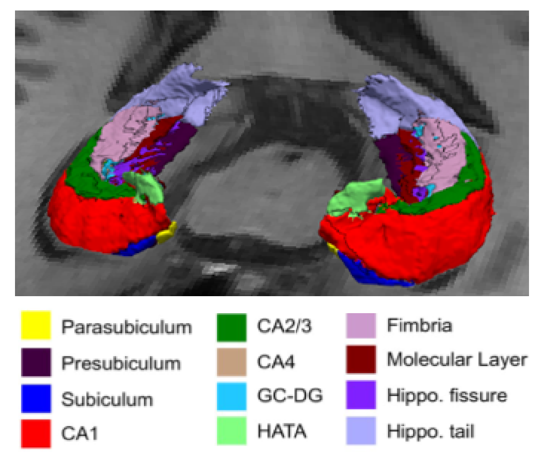
MR Vendor	Models	Sites (n=13)	Head RF Coils	Acceleration
Siemens (n=6)	Allegra	Verona	Birdcage	None
	TrioTim	Barcelona, Leipzig	8-ch	GRAPPA
	Skyra	Essen	20-ch	GRAPPA
	Verio	Marseille	12-ch	GRAPPA
	Biograph mMR	Napoli	12-ch	GRAPPA
Philips (n=4)	Achieva	Chieti, Peugia, Lille, Toulouse	8-ch	SENSE
GE (n=3)	HDxt	Genova, Amsterdam, Thessaloniki	8-ch	ASSET

Vendor T1-weighted 3D MRI



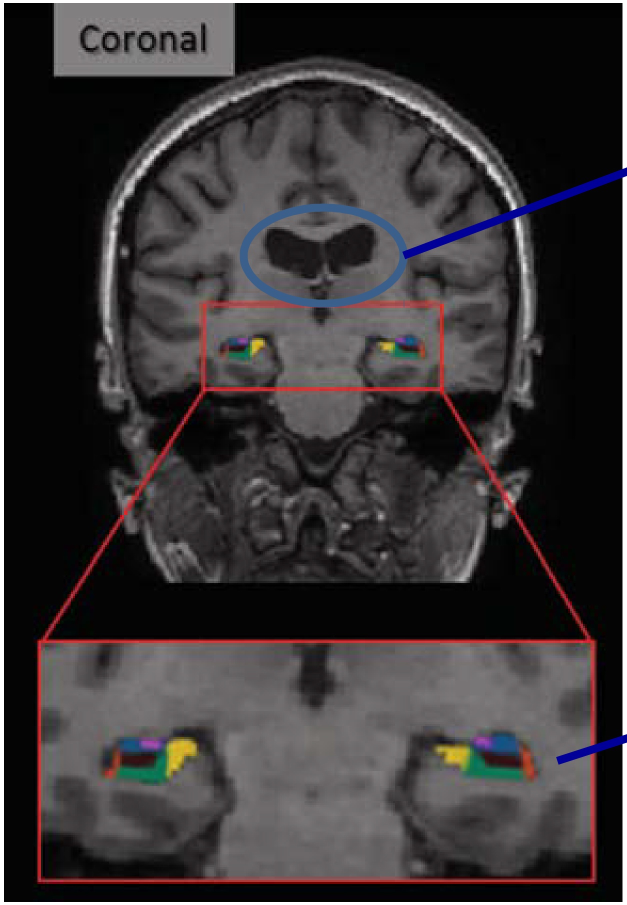
MPRAGE, 1x1x1 mm^3
Two acquisitions (~5 min each)

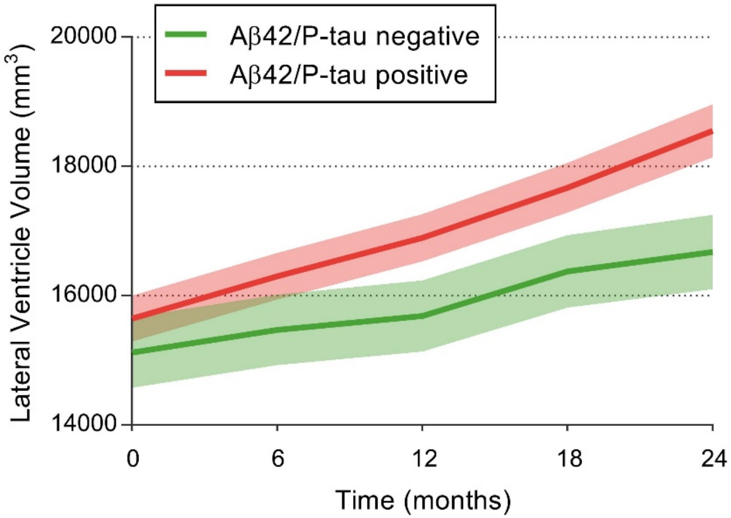


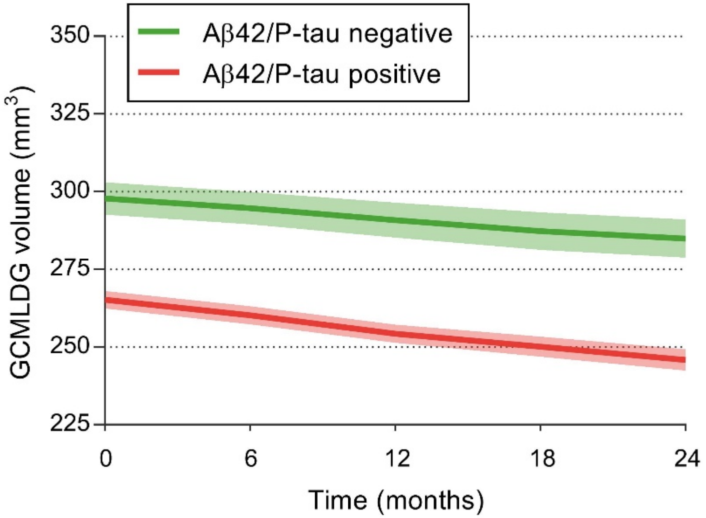


Structural biomarkers with differential disease progression

- 150 amnestic Mild Cognitive Impaired patients
- Followed longitudinally: T0, T6, T12, T18, T24
- Separated in low risk (negative) and high risk (positive) based on CSF amyloid/p-tau levels







Marizzoni et al., JAD 2018

Lecture 2 outline

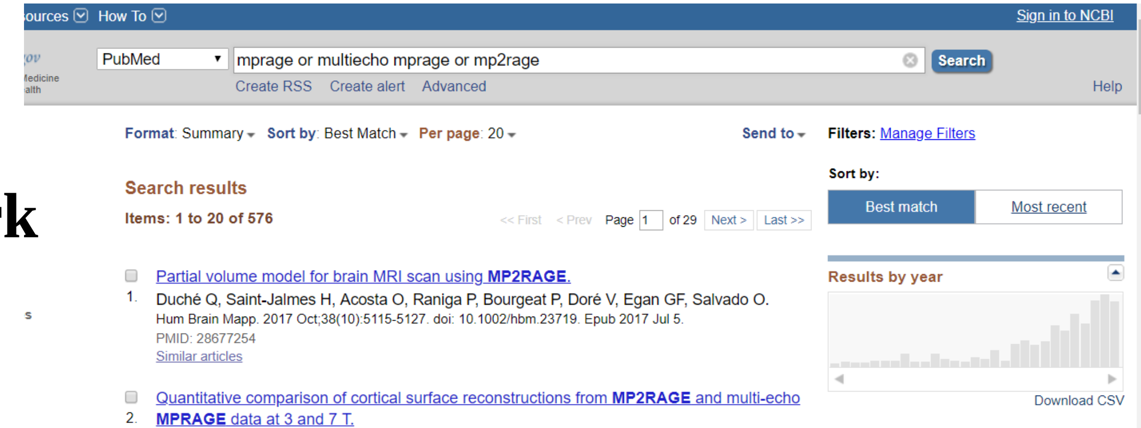
Brain structure MRI

- What is a structural MRI?
- What is image contrast?
- How can image contrast be manipulated?
- What image analyses are common from brain structural MRI?
- What are some structural MRI applications?
- What are some structural MRI challenges?

3D MPRAGE: Most common brain T1

https://www.ncbi.nlm.nih.gov/pubmed/?term=mprage+or+multiecho+mprage+or+mp2rage

- **Lots of interest**
- **Lots of optimization work**

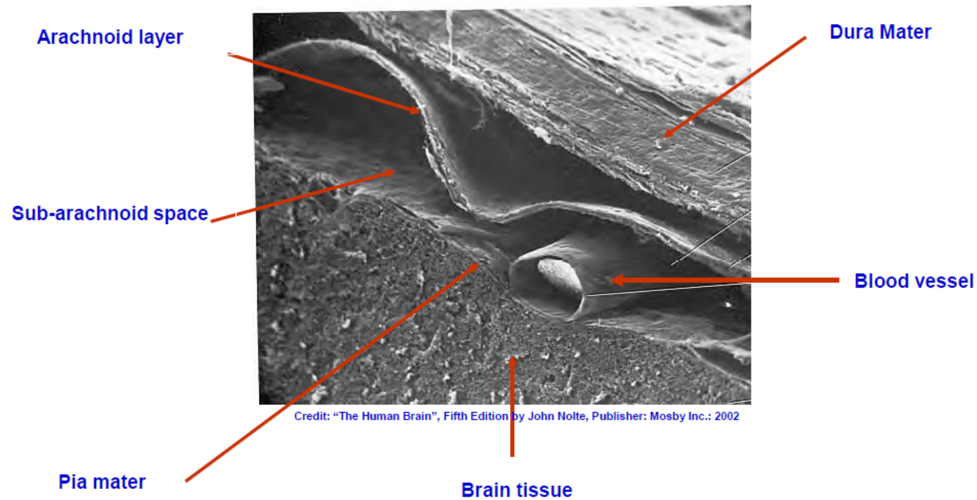


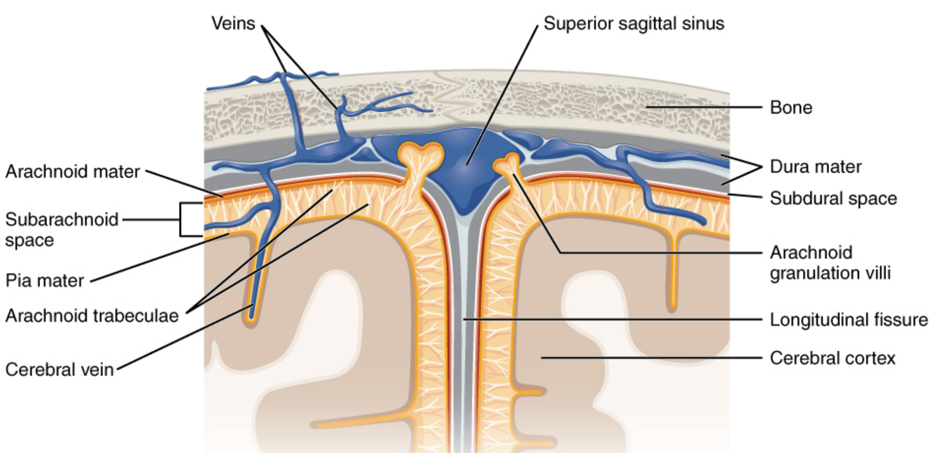
- Optimization criteria reflect challenges, and include:
  - Tissue contrast-to-noise ratio
  - Intensity non-uniformities
  - Image distortions
  - Spatial and temporal resolution
  - Strategies for motion correction
  - Reproducibility and accuracy of segmentations

Structural MRI: Challenges

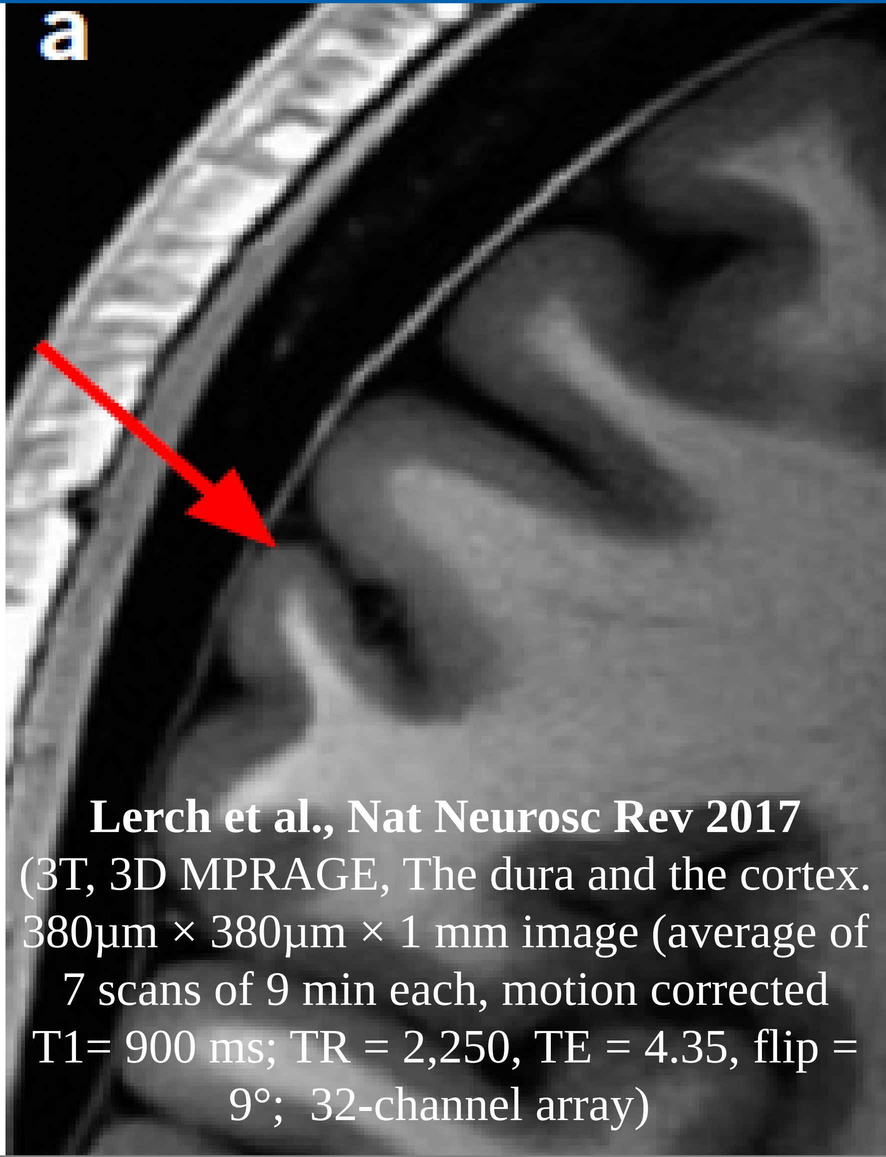
- **Optimization of image contrast**
- Head movement correction (retrospective, prospective)
- Optimization of spatial-temporal resolution
- Optimization of automated segmentations
- Validation of segmentations (histology)
- Multi-vendor protocol harmonization
- …

Anatomical challenge: differentiate gray matter border (pial surface) from dura



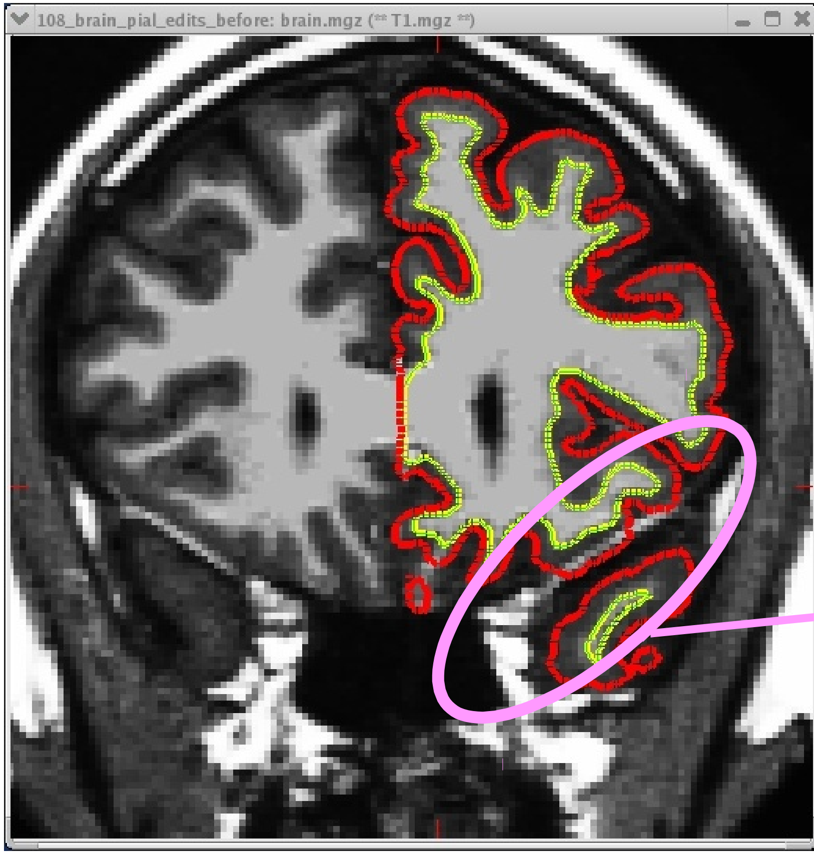


https://en.wikipedia.org/wiki/Meninges



Lerch et al., Nat Neurosc Rev 2017
(3T, 3D MPRAGE, The dura and the cortex. 380µm × 380µm × 1 mm image (average of 7 scans of 9 min each, motion corrected T1= 900 ms; TR = 2,250, TE = 4.35, flip = 9°; 32-channel array)

Pial misplacement



Segmentation errors:
Tissue that is neither white nor gray matter (like blood vessels, dura or pial), get wrongly classified as one of the two just because of similar image intensity values

Dura or Blood Vessel
White/Gray OK, but
Pial Inaccurate

Dura and GM have extremely similar intensity characteristics on most T1-weighted sequences (but different T2*!).

https://surfer.nmr.mgh.harvard.edu/

Gray matter segmentation errors

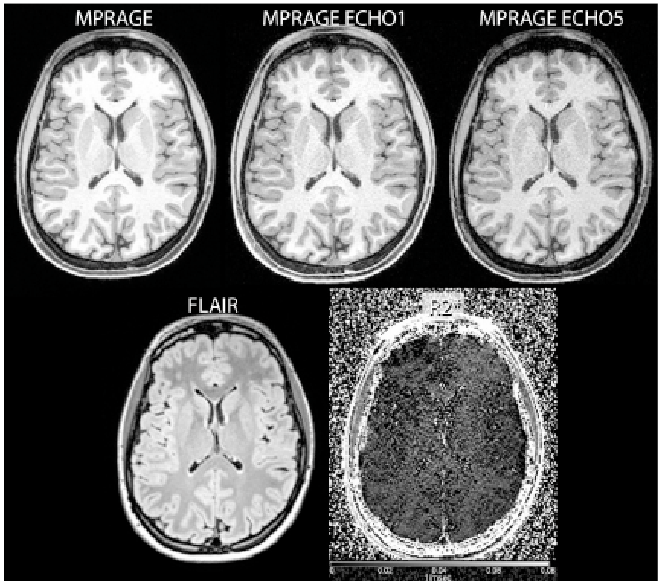
frontiers in Neuroscience

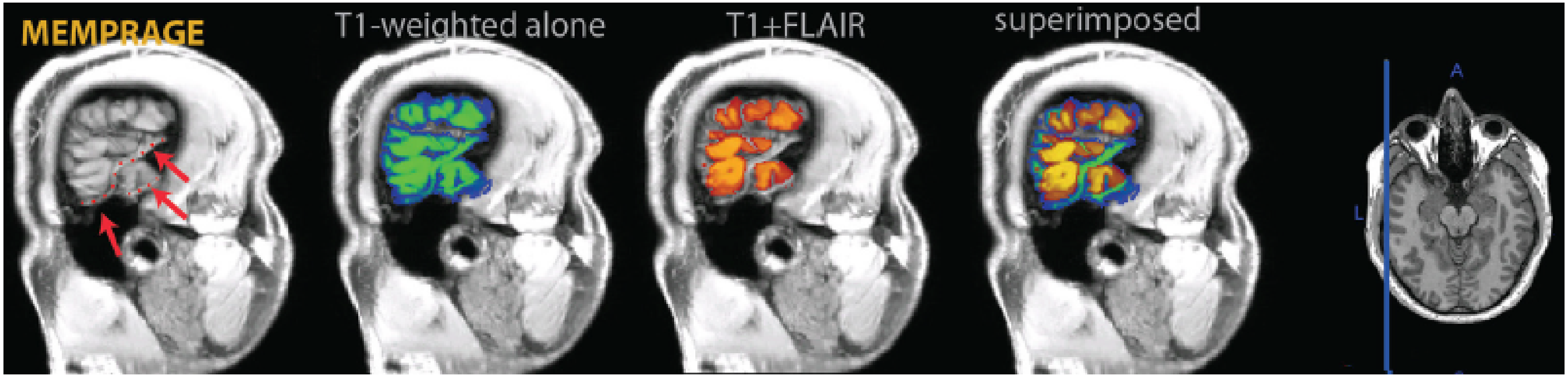
ORIGINAL RESEARCH
published: 09 May 2017
doi: 10.3389/fnins.2017.00258

Multimodal MEMPRAGE, FLAIR, and R_2^* Segmentation to Resolve Dura and Vessels from Cortical Gray Matter

Roberto Viviani[1,2], Eberhard D. Pracht[3], Daniel Brenner[3], Petra Beschoner[4], Julia C. Stingl[5,6] and Tony Stöcker[3,7]*

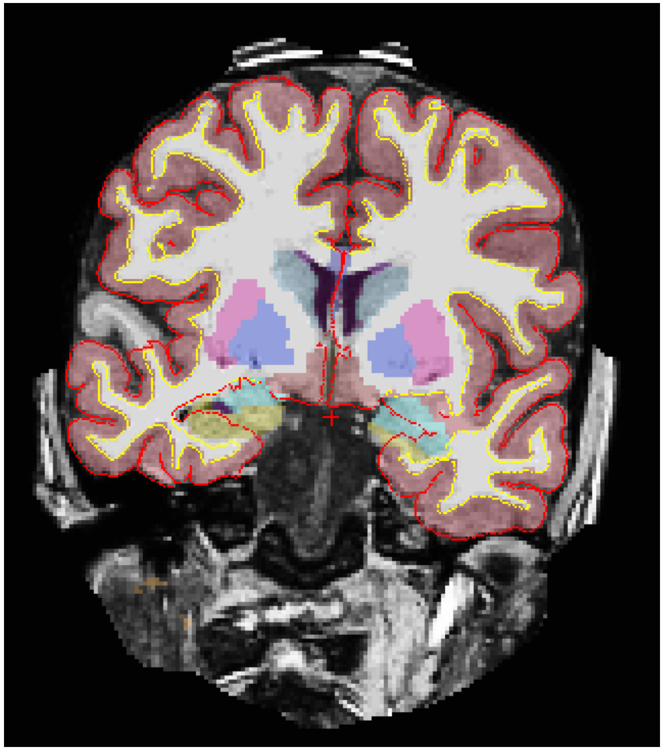
[1] Institute of Psychology, University of Innsbruck, Innsbruck, Austria, [2] Psychiatry and Psychotherapy Clinic III, University of Ulm, Ulm, Germany, [3] German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany, [4] Clinic for Psychosomatic Medicine and Psychotherapy, University of Ulm, Ulm, Germany, [5] Research Division, Federal Institute for Drugs and Medical Devices, Bonn, Germany, [6] Center for Translational Medicine, University of Bonn Medical School, Bonn, Germany, [7] Department of Physics and Astronomy, University of Bonn, Bonn, Germany

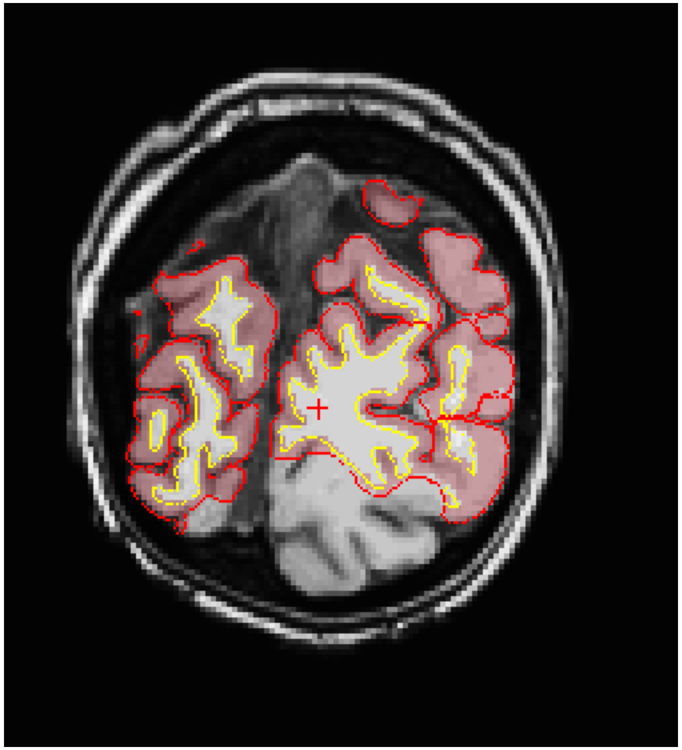




Missclassification of sulcal vessels as GM

Skull stripping errors





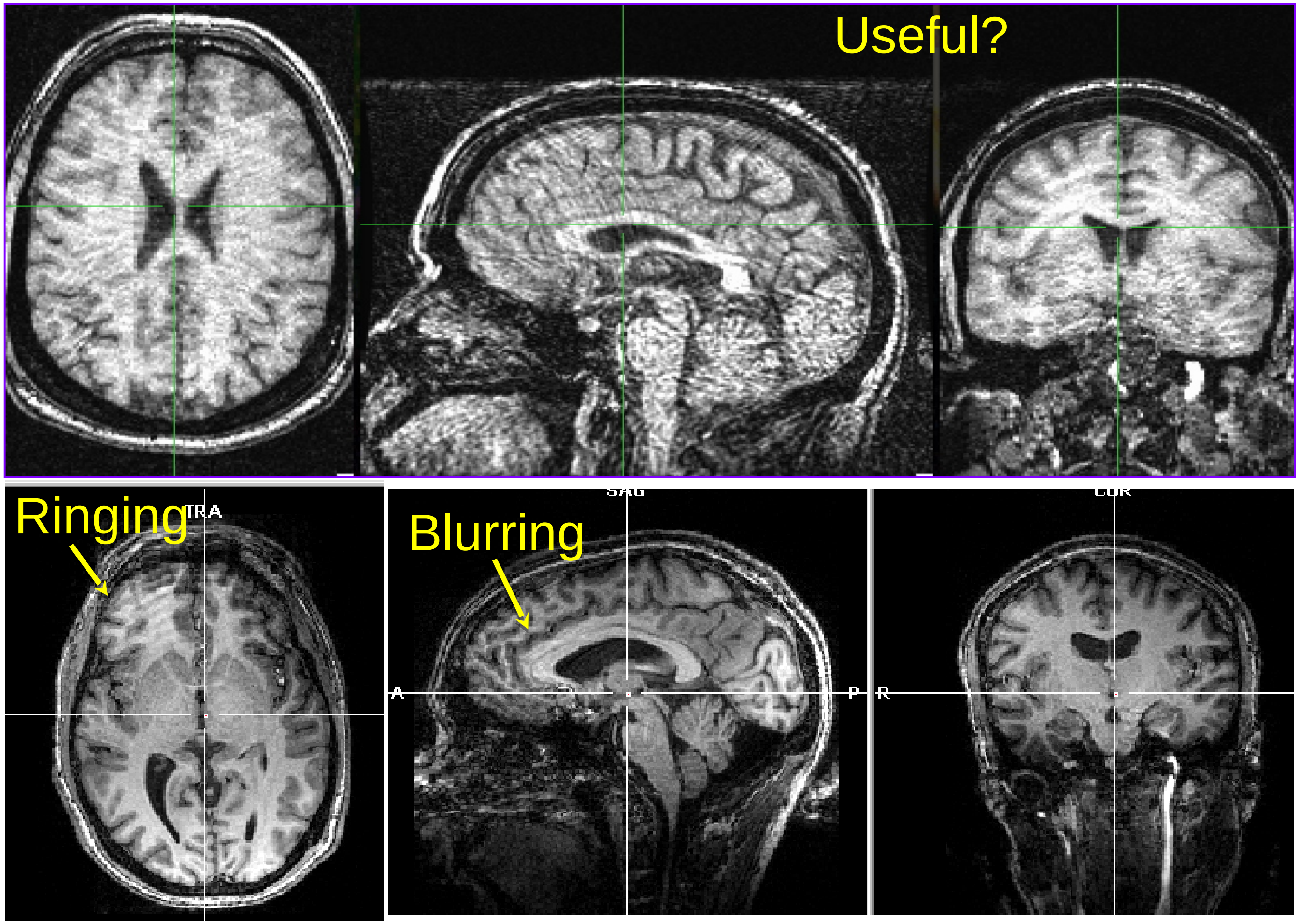
Parts of brain tissue removed
Such errors are ONLY detected by VISUAL quality assurance
<u>YOU</u> NEED TO LOOK AT THE DATA AND RESULTS

Structural MRI: Challenges

- Optimization of image contrast
- **Head movement correction (retrospective, prospective)**
- Optimization of spatial-temporal resolution
- Optimization of automated segmentations
- Validation of segmentations (histology)
- Multi-vendor protocol harmonization
- …

Head motion in structural MRI

- Brain morphometry estimates are useful biomarkers
- Problem: head motion



Head motion biases morphometry data

NeuroImage 107 (2015) 107–115

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

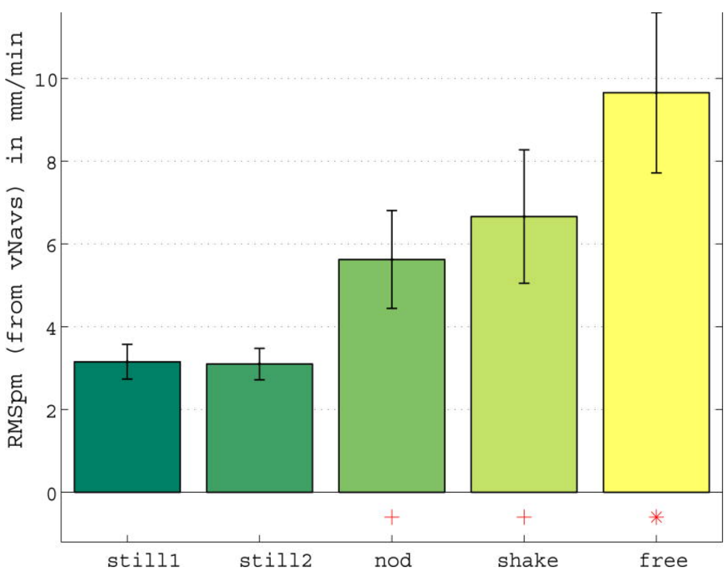
Head motion during MRI acquisition reduces gray matter volume and thickness estimates

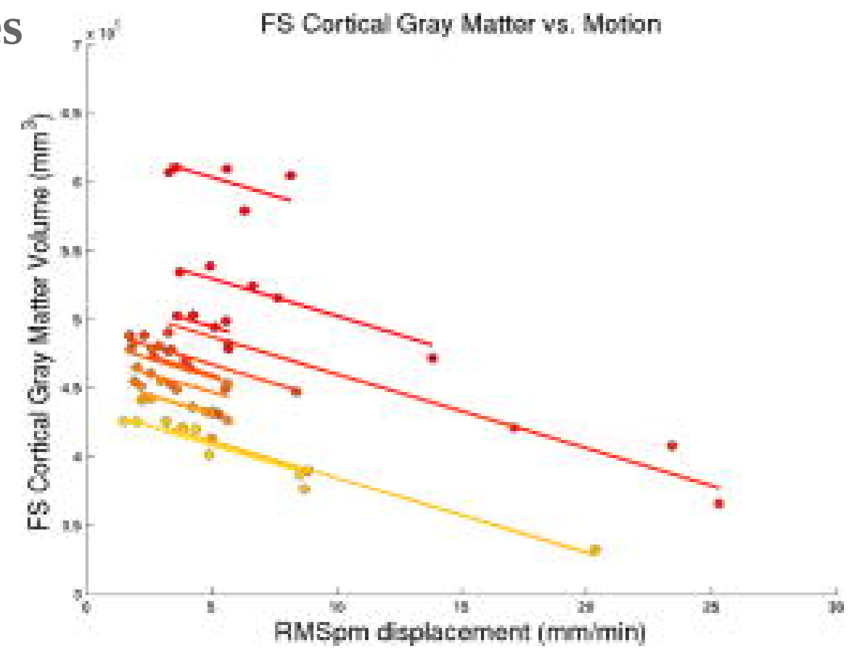
Martin Reuter [a,b,c,d,*,1], M. Dylan Tisdall [b,d,1], Abid Qureshi [a,d], Randy L. Buckner [b,d], André J.W. van der Kouwe [b,d], Bruce Fischl [b,c,d]

Experiment design:

- 12 healthy adults, 3T MRI
- For each subject:
    - Scan still
    - Scan during 3 motion conditions
- Segment both scans
- Quantify morpohmetry changes

ifferent Motion Levels across Motion Types





Prospective motion correction reduces biases

NeuroImage 127 (2016) 11–22

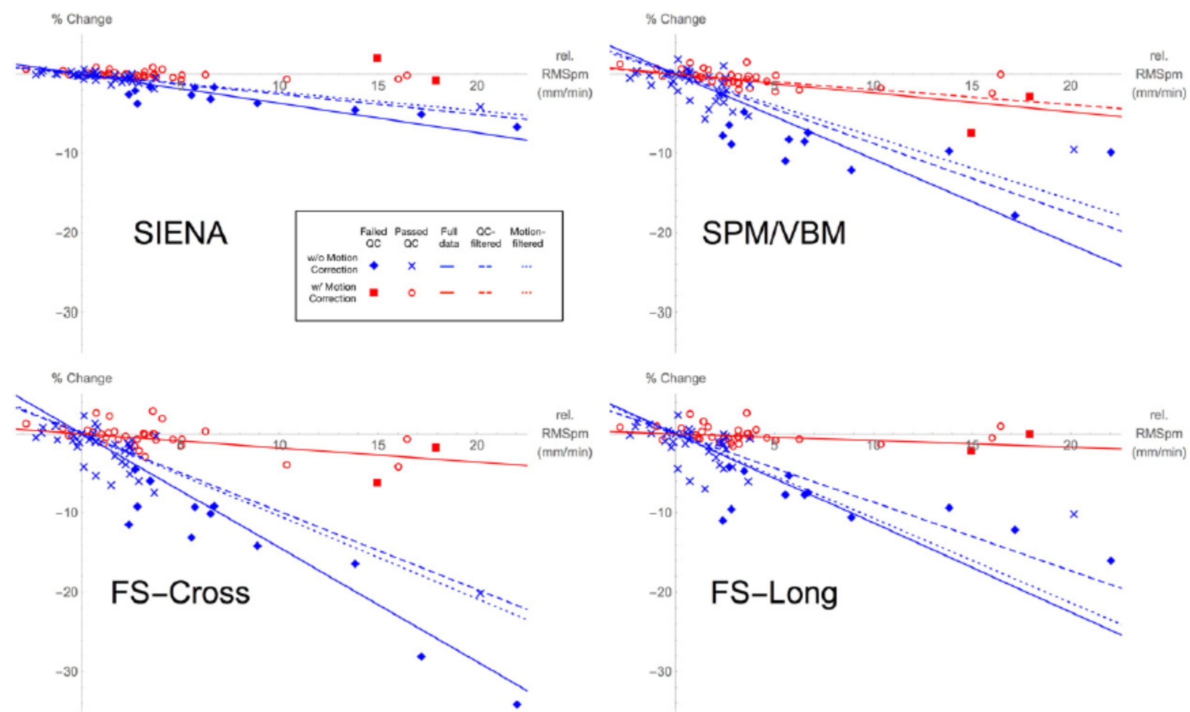
Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

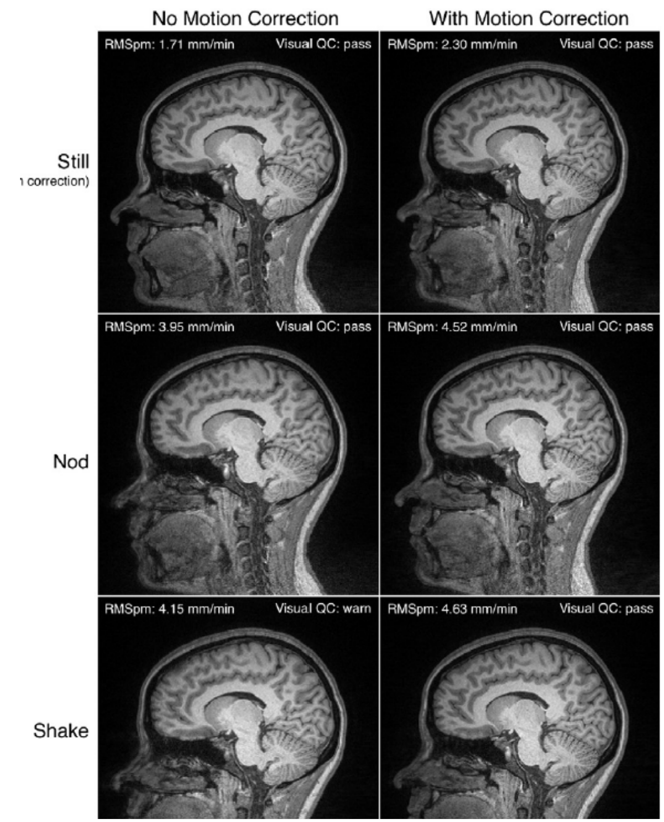
Prospective motion correction with volumetric navigators (vNavs) reduces the bias and variance in brain morphometry induced by subject motion

M. Dylan Tisdall [a,b,*,1], Martin Reuter [a,c,g,1], Abid Qureshi [c], Randy L. Buckner [a,d,e,f], Bruce Fischl [a,b,g], André J.W. van der Kouwe [a,b]



Experiment design:

- 12 healthy adults, 3T MRI
- For each subject:
  - Scan still
  - Scan during 3 motion conditions (no mc)
  - Scan during 3 motion conditions (mc)
- Segment both scans
- Quantify morpohmetry changes

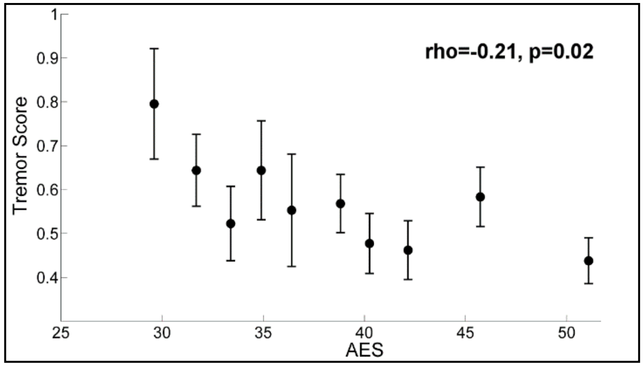


Estimation motion degree from MPRAGE

Method for Retrospective Estimation of Natural Head Movement During Structural MRI

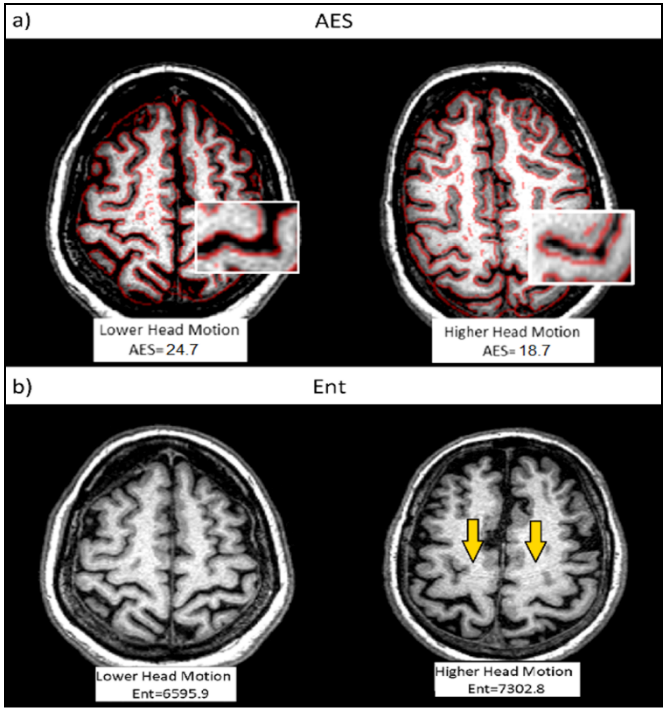
Domenico Zacà, PhD,* Uri Hasson, PhD, Ludovico Minati, PhD, and Jorge Jovicich, PhD

J. MAGN. RESON. IMAGING 2018;00:000–000.



3D MPRAGE: Parkinson's Progression Markers Initiative

Groups	Age (years)	Gender
HC: n=84	59.6 ± 10.9	M 54/ F 30
PD: n=124	60.4 ± 9.8	M 77/F 47
Group differences	T=-0.44, p=0.66	X^2=0.10, p=0.75



Motion Metrics evaluated:

- Average Edge Strength (AES)
- Image entropy

$$AES = \frac{\sqrt{\sum_{i,j} E(I_{i,j}^k)\left[\left(G_x(I_{i,j}^k)\right)^2 + \left(G_y(I_{i,j}^k)\right)^2\right]}}{\sum_{i,j} E(I_{i,j}^k)}$$

$$Ent = -\sum_{p=1}^{n} \frac{I_p}{I_{tot}} ln\left(\frac{I_p}{I_{tot}}\right) \qquad I_{tot} = \sqrt{\sum_{p=1}^{n} I_p^2}$$

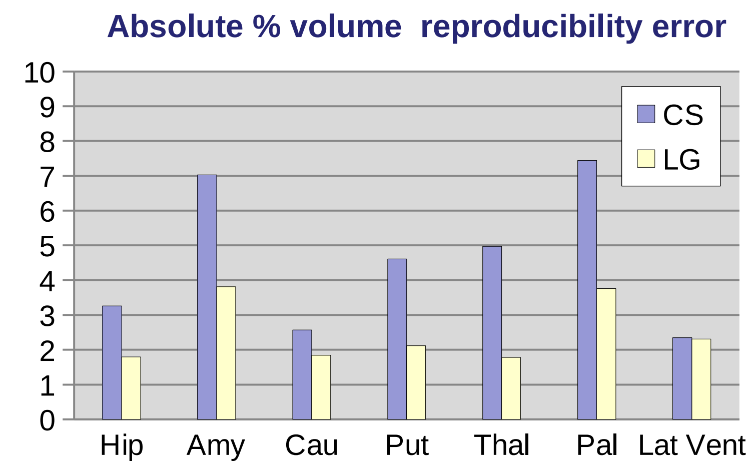
Structural MRI: Challenges

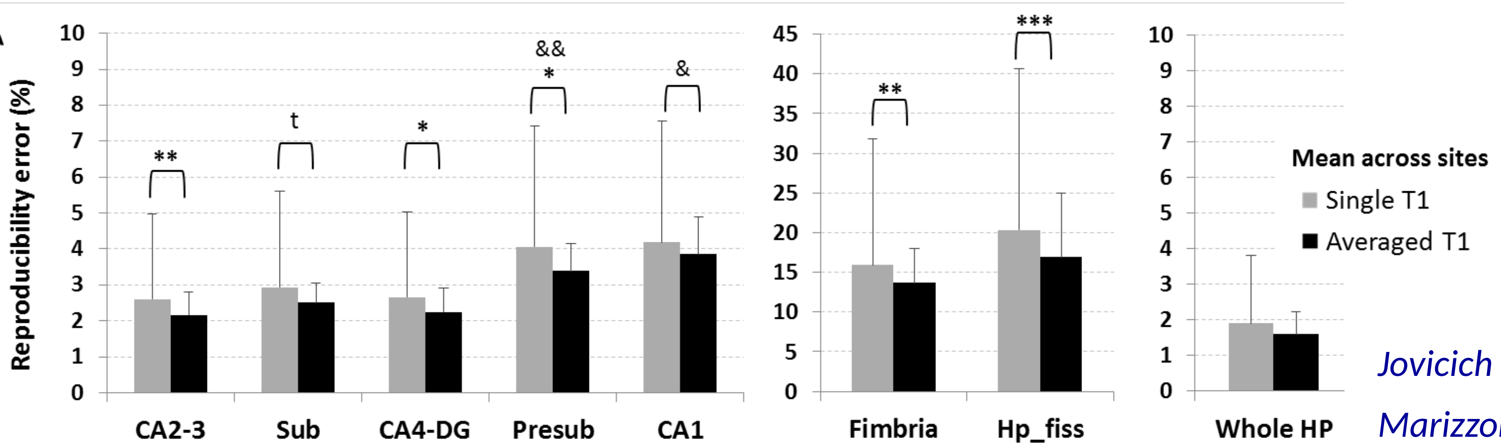
- Optimization of image contrast
- Head movement correction (retrospective, prospective)
- Optimization of spatial-temporal resolution
- Optimization of automated segmentations
- Validation of segmentations (hystology)
- **Multi-vendor protocol harmonization**
- …

Multicentric morphometry optimizations

Pharmacog study findings for structural T1 harmonization:

- Despite MR site variability, vendor sequences + harmonized protocol give good quality automated segmentations
- Accelerated MPRAGE ~ non-accelerated
  - Time efficient, lower head motion sensitivity
- Longitudinal Freesurfer (LG) more reliable than cross-sectional Freesurfer (CS)
- Averaging 2 MPRAGE improves hippo. subfields



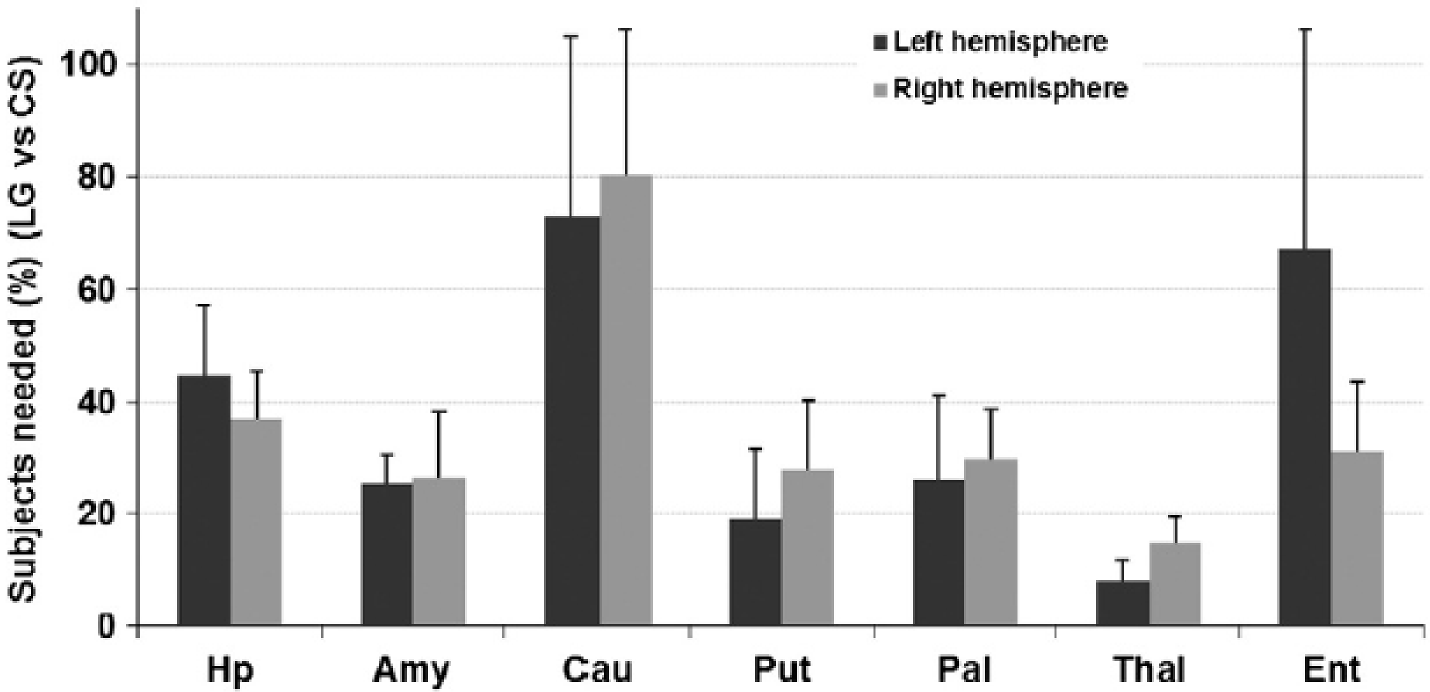


Jovicich et al., Neuroimage 2013

Marizzoni et al., Neuroimage 2015

Multicentric morphometry optimizations

Practical consecuences of reproducibility improvements



Sample size ratio needed to have the same power analysis using LG instead of CS stream. The percentage of subjects needed is less than 50% for most of the structures considered.

Left and right hemispheric structure labels are: Hp = hippocampus, Amy = amygdala, Cau = caudate, Put = putamen, Pal = pallidum, Thal = thalamus and Ent = entorhinal cortex.

Lecture 2 outline

Brain structure MRI

- What is a structural MRI?
- What is image contrast?
- How can image contrast be manipulated?
- What image analyses are common from brain structural MRI?
- What are some structural MRI applications?
- What are some structural MRI challenges?

Complementary reading

REVIEW FOCUS ON HUMAN BRAIN MAPPING

nature neuroscience

Studying neuroanatomy using MRI

Jason P Lerch[1,2], André J W van der Kouwe[3,4], Armin Raznahan[5], Tomáš Paus[6–8], Heidi Johansen-Berg[9], Karla L Miller[9], Stephen M Smith[9], Bruce Fischl[3,4,10] & Stamatios N Sotiropoulos[9,11]

The study of neuroanatomy using imaging enables key insights into how our brains function, are shaped by genes and environment, and change with development, aging and disease. Developments in MRI acquisition, image processing and data modeling have been key to these advances. However, MRI provides an indirect measurement of the biological signals we aim to investigate. Thus, artifacts and key questions of correct interpretation can confound the readouts provided by anatomical MRI. In this review we provide an overview of the methods for measuring macro- and mesoscopic structure and for inferring microstructural properties; we also describe key artifacts and confounds that can lead to incorrect conclusions. Ultimately, we believe that, although methods need to improve and caution is required in interpretation, structural MRI continues to have great promise in furthering our understanding of how the brain works.

314 VOLUME 20 | NUMBER 3 | MARCH 2017 NATURE NEUROSCIENCE

NeuroImage

SUPPORTS OPEN ACCESS

Articles in press Latest issue Sp

Segmenting the Brain

Edited by Cameron Craddock, Pierre Bellec, Saad Jbabdi

Volume 170, Pages 1-494 (15 April 2018)

https://www.sciencedirect.com/journal/neuroimage/vol/170/suppl/C

Free brain segmentation software tools include:

Freesurfer: https://surfer.nmr.mgh.harvard.edu/fswiki

SPM: https://www.fil.ion.ucl.ac.uk/spm/

ANTS: http://stnava.github.io/ANTs/

FSL: https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FAST

- Functional connectivity parcellation (9)
- Segmentation of different structures (9)
- Atlas of (sub)cortical cytoarchitectonics areas (3)
- White matter bundles (4)
- Quality of cortical models (3)
- Multi-modality (task) areal parcellation (5)
- Automated segmentation of structural MRI data (5)

Concept map for lectures

Lecture 1

NMR Signal origin

- Powerful magnet
- Radio frequency
- Magnetic field gradients

MR Image & Contrast

- Spatial encoding
- Magnetic gradients
- Pulse sequences

MR Safety

- Powerful magnet
- Radio frequency
- Magnetic field gradients

Lecture 2

Structural MRI

- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications

Lecture 3

Diffusion MRI

- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications

Lecture 4

Functional MRI

- Contrast, important parameters
- Sequences & artifacts
- Pre-processing