Extracting myelin and iron maps of the brain using biophysical modelling - some of the many roles of an MRI physicist

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Zé Pedro

U C

FÍSICA

FISICA.UC.PT

1995-99

undergrad studies

IBEB

Instituto de Biofísica e Engenharia Biomédica

FACULDADE DE CIÊNCIAS

UNIVERSIDADE DE LISBOA

2000-01

doctoral program

Joesei

The University of Nottingham

Sir Peter Mansfield Magnetic Resonance Centre

the home of epi and slice selection

2001-04

PhD

- Long Range Dipolar Fields
- ΔB_0 due to air tissue interfaces
- GE &SE BOLD sim.

Dr. José Marques

2005-06

postdoc

EEG-fMRI in epilepsy:

ICA-based construction of the fMRI regressor

Joesé / Jôse Rebelo

UNIL | Université de Lausanne

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

2007-14

Postdoc, MA

senior scientist

Quantitative MRI

Fast Imaging

Motion correction

Jôse

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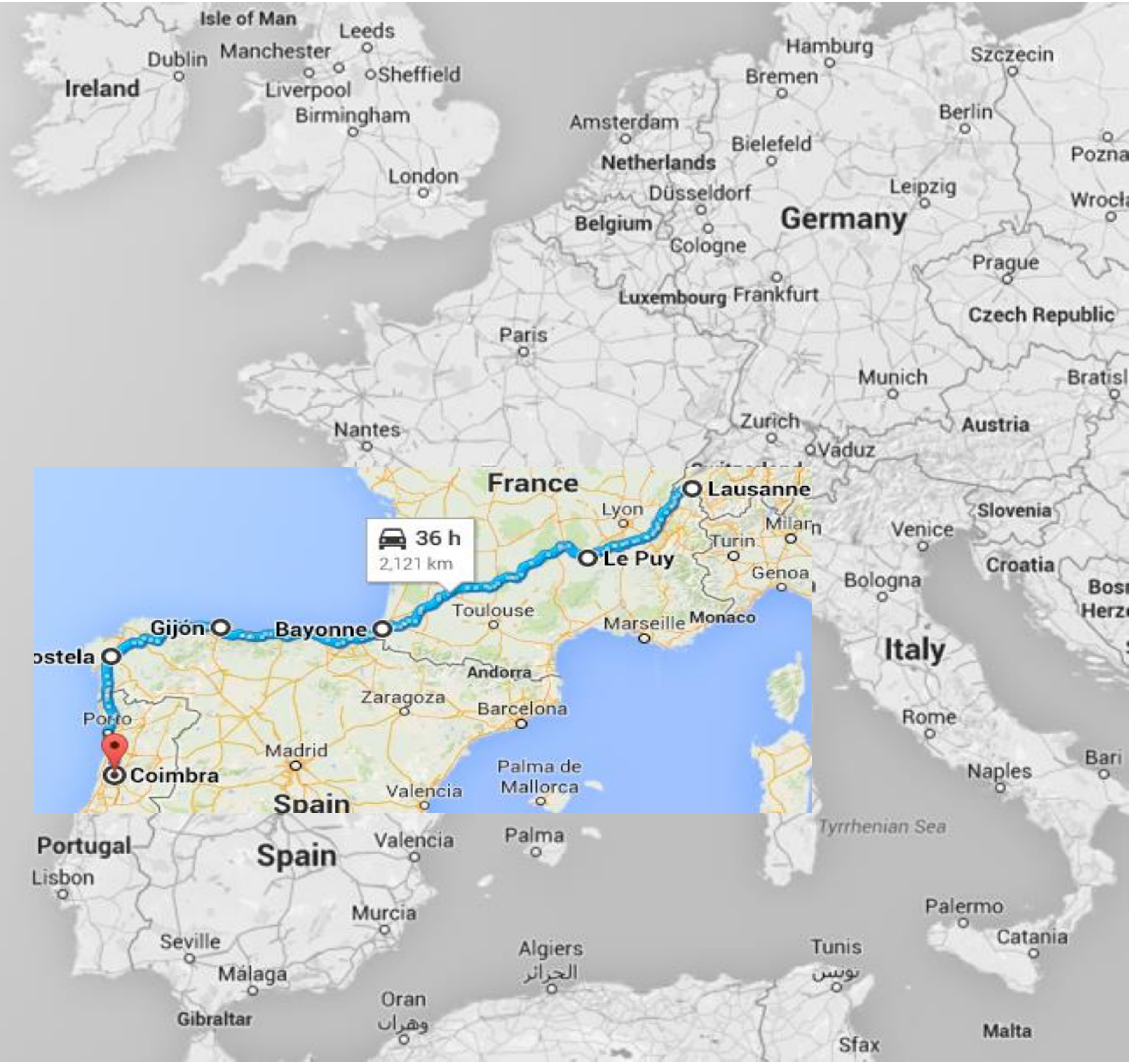
UNIL | Université de Lausanne

2007-14

Postdoc, MA

senior scientist



Radboud University

DONDERS WONDERS

2015- Senior scientist

Associate PI

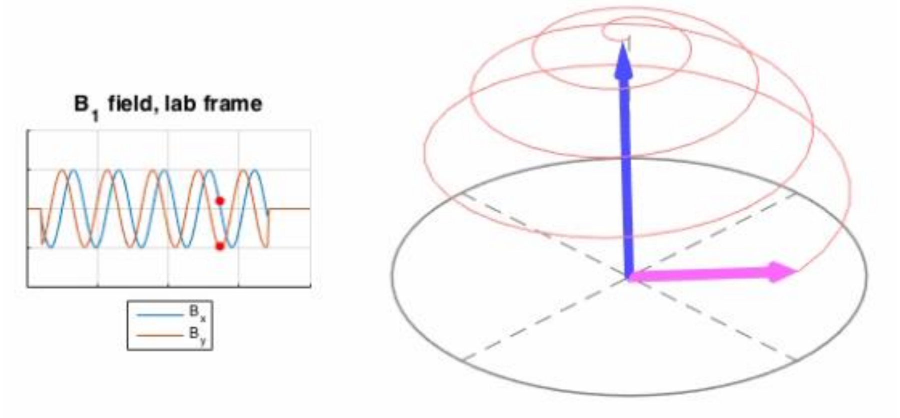
Quantitative MRI

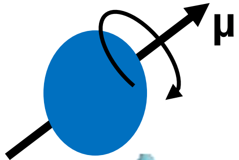
Myelin Imaging

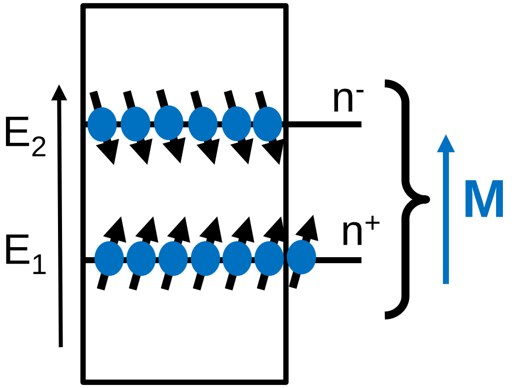
Overview

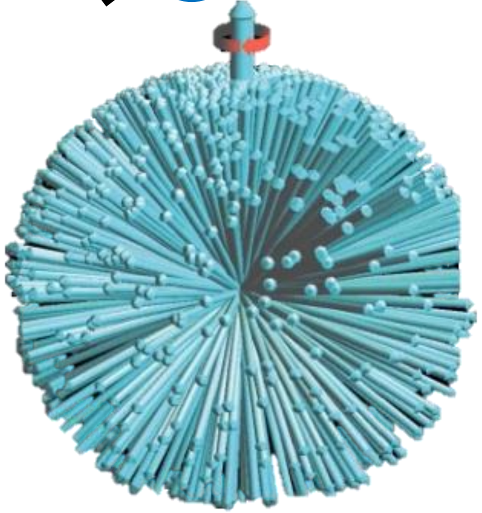
- ❑ Quick recap on how MRI works
- ❑ What can MRI do (almost) out of the box
- ❑ How can an MR physicist contribute to MRI?
  - ❑ Improving image reconstruction
  - ❑ Making imaging quantitative
  - ❑ Decoding microstructure

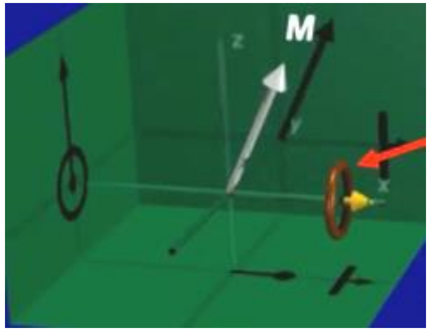
How does MRI work?











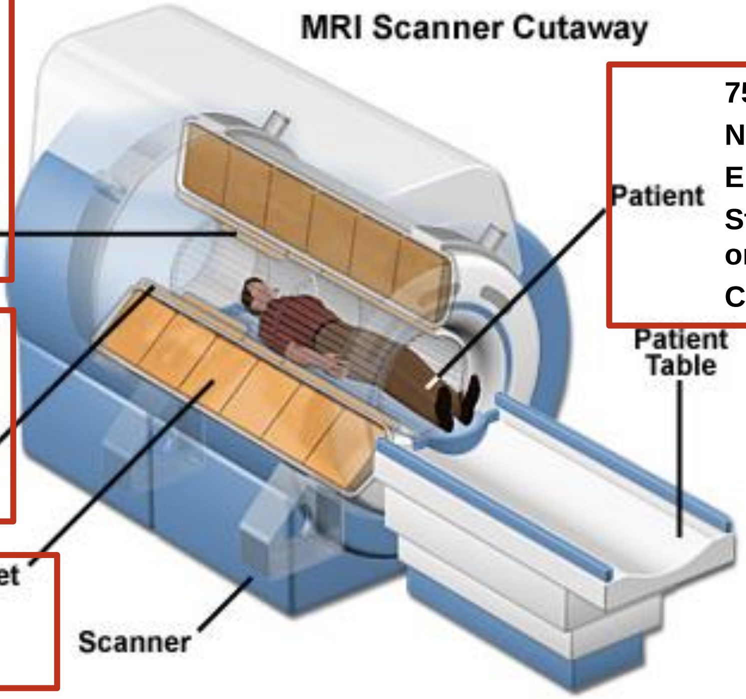
Generates RF wave to change spins state

The precession of this spins can be detected by induction of an antena

Allows to ask the question of: which spins are precessing where

B_0

Makes sure there are two energy states for spins



75 % water

Nuclear spins (are sort of a magnet)

Energy difference between states

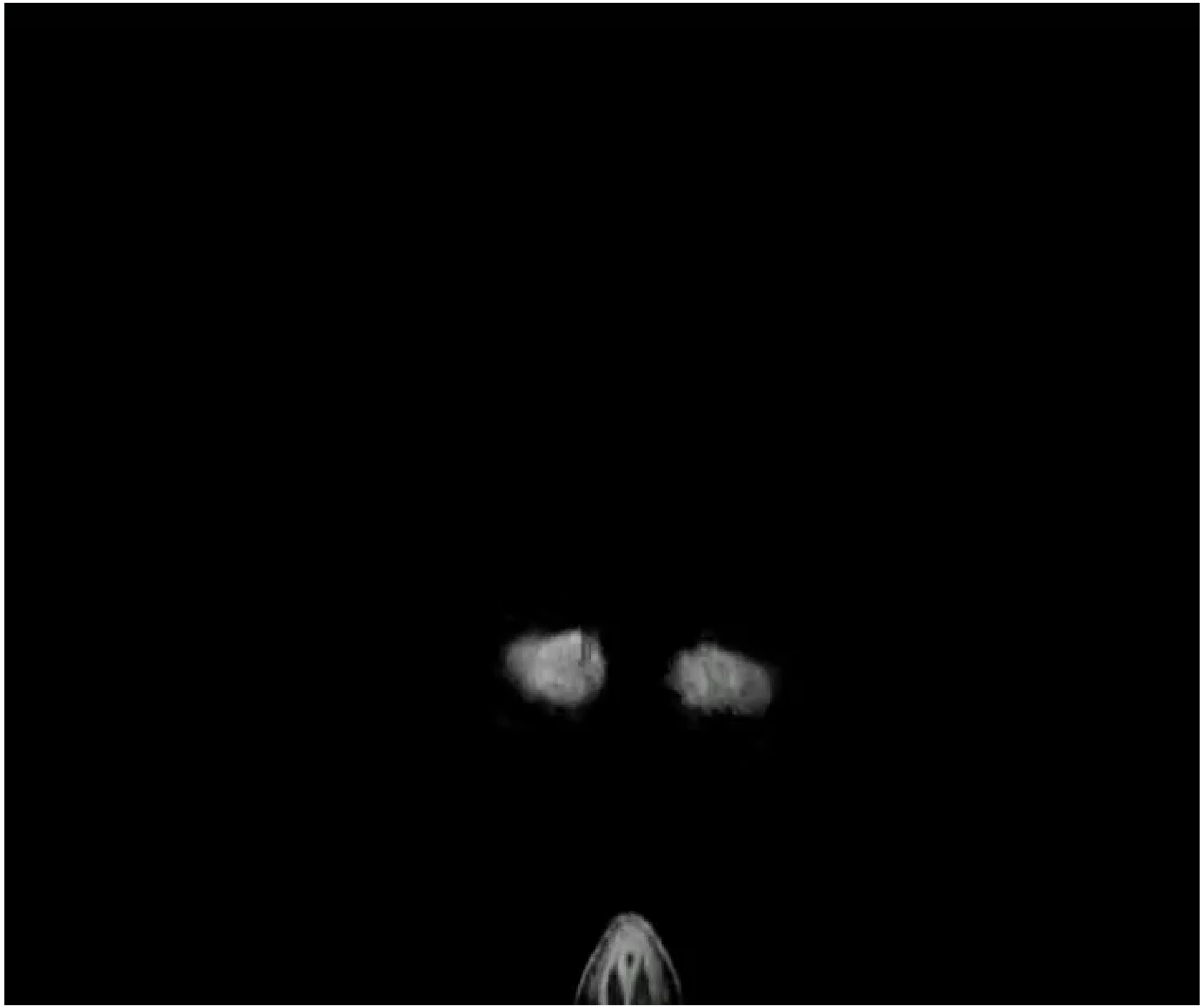
States transitions can be induced using a on resonance RF pulse

Coherent spins will precess and relax

What can MRI see?

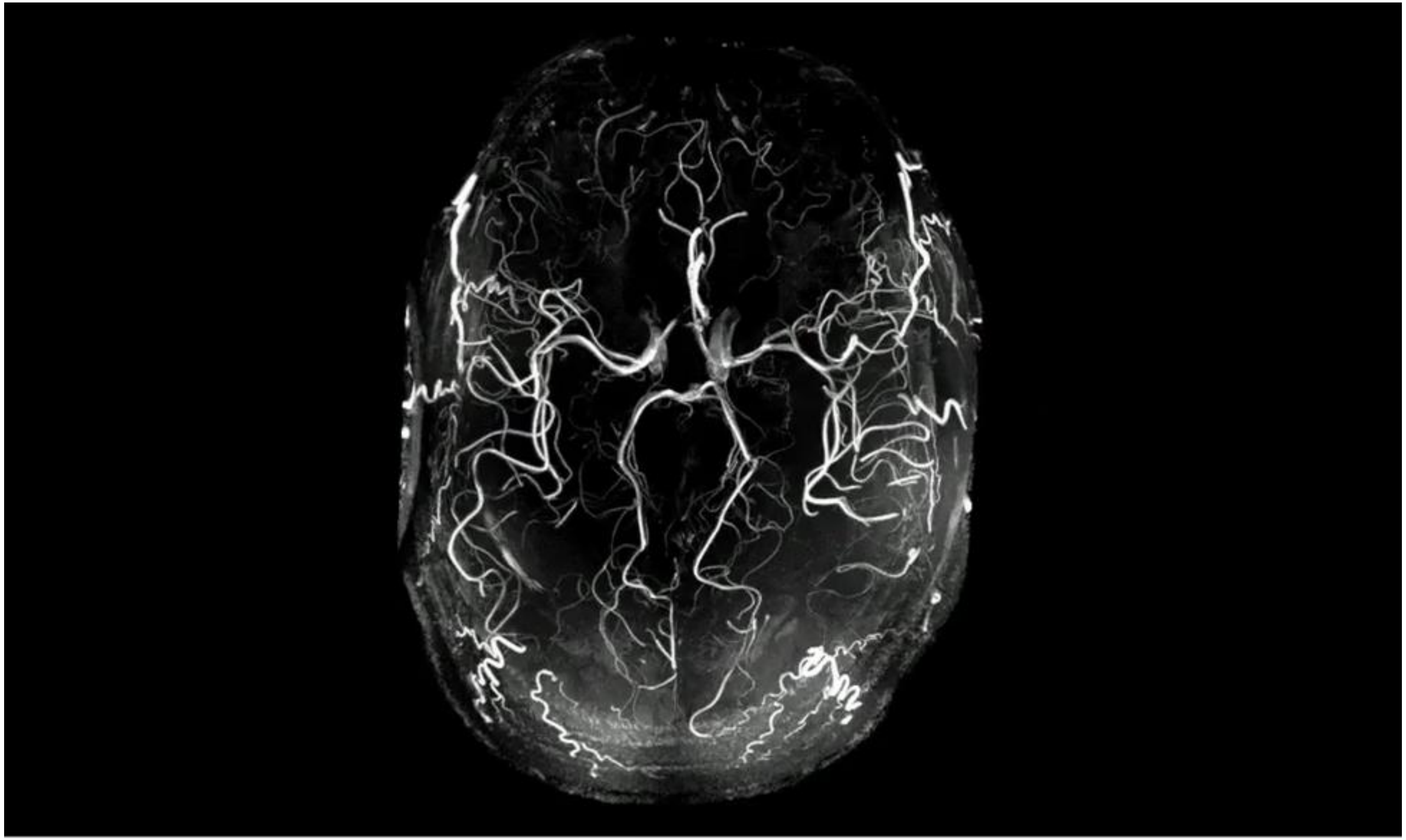
- ❑ Hidrogen proton spins in large quantities – Water or Fat
- ❑ Water in different environments (magnetic, macromolecular...)
- ❑ Water moving in macroscopically
- ❑ Water moving microscopically

MRI allows looking at brain structure

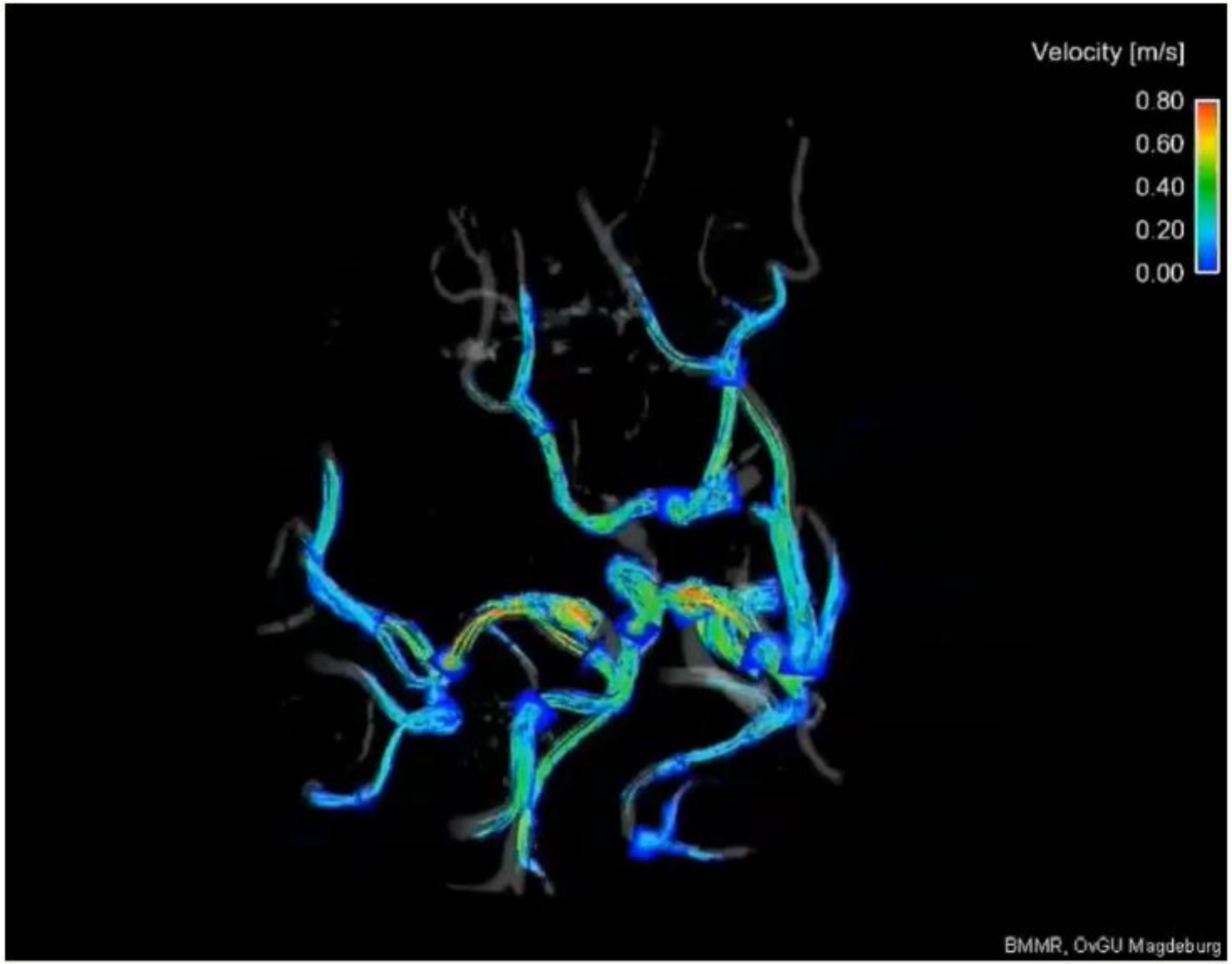


Courtesy of Oliver Speck, Magderburg

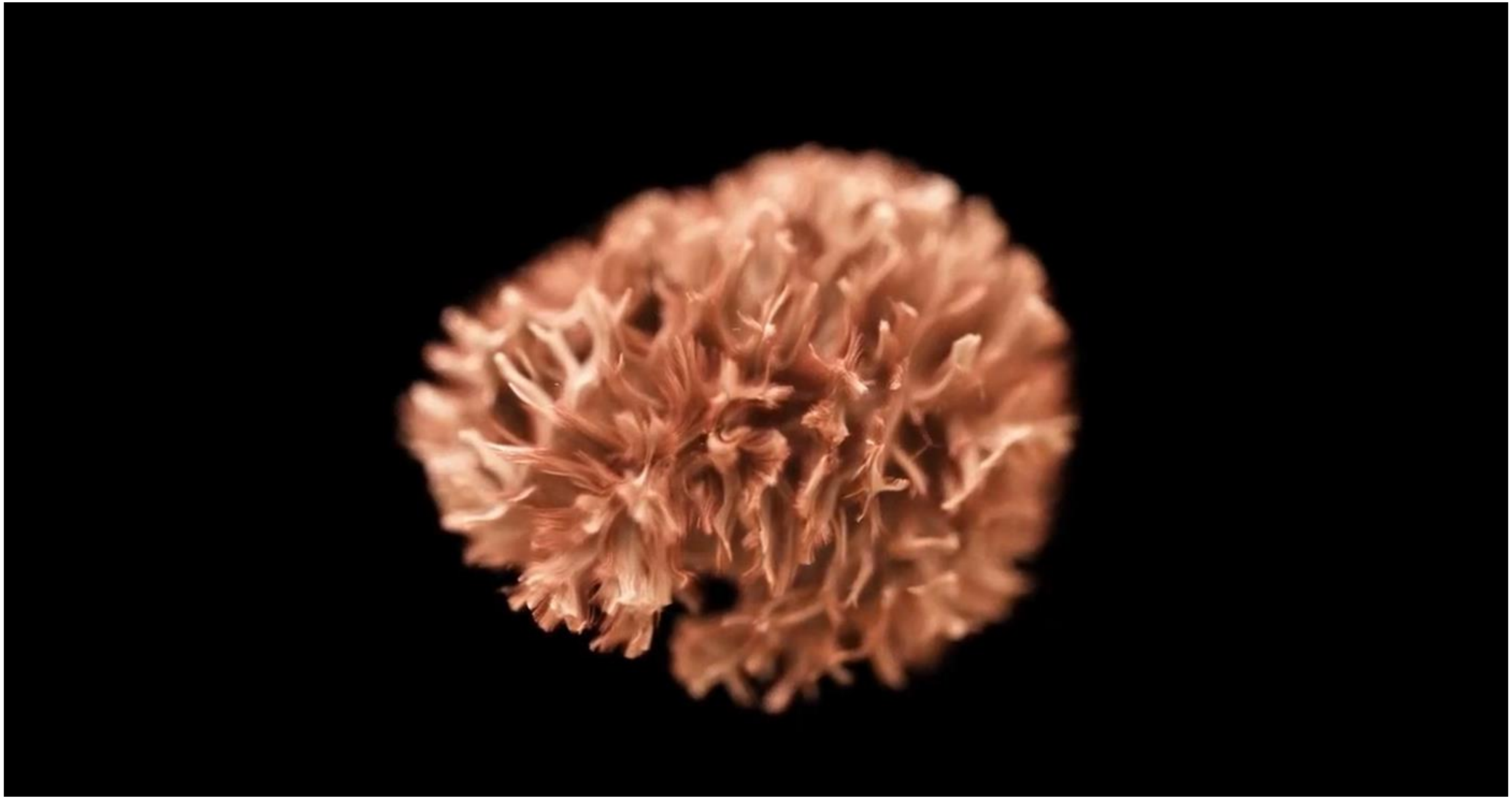
Allows looking at arteries



Allows looking at flow in arteries



MRI allows looking at brain microstructure

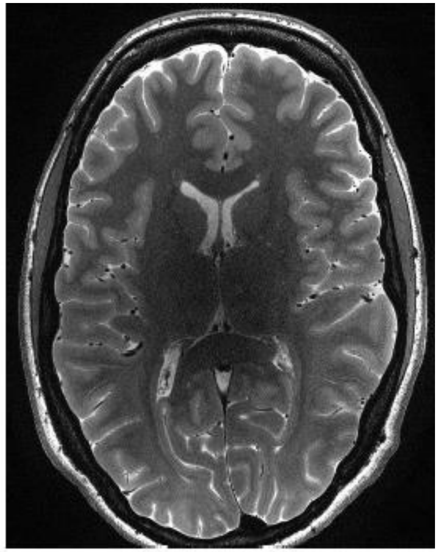


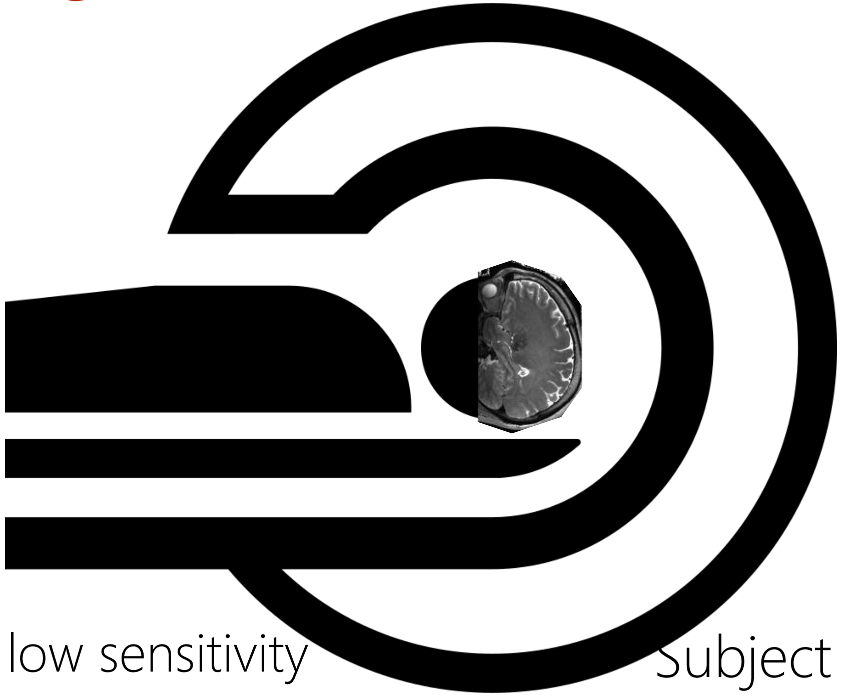
Courtesy of CUBRIC, Cardiff

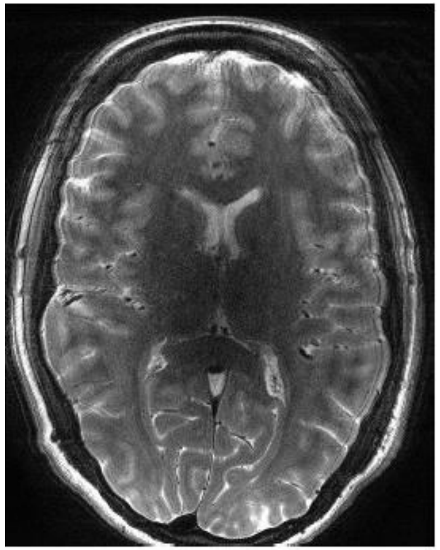
MR Physicist contribution to MRI

- ❑ Hardware design
- ❑ Image encoding and improving image reconstruction
- ❑ Fast and robust contrast encoding strategies
- ❑ Decoding the MR signal – extracting tissue properties

Improving image reconstruction







MRI has inherently a low sensitivity

Anatomical MRI

- high-res data requires long acquisitions
- Subjects are alive…

Subject movement results in:

- ❑ Aliasing, Blurring, ghosting and ringing…
- ❑ Need of rescan in 8 – 30% of subject

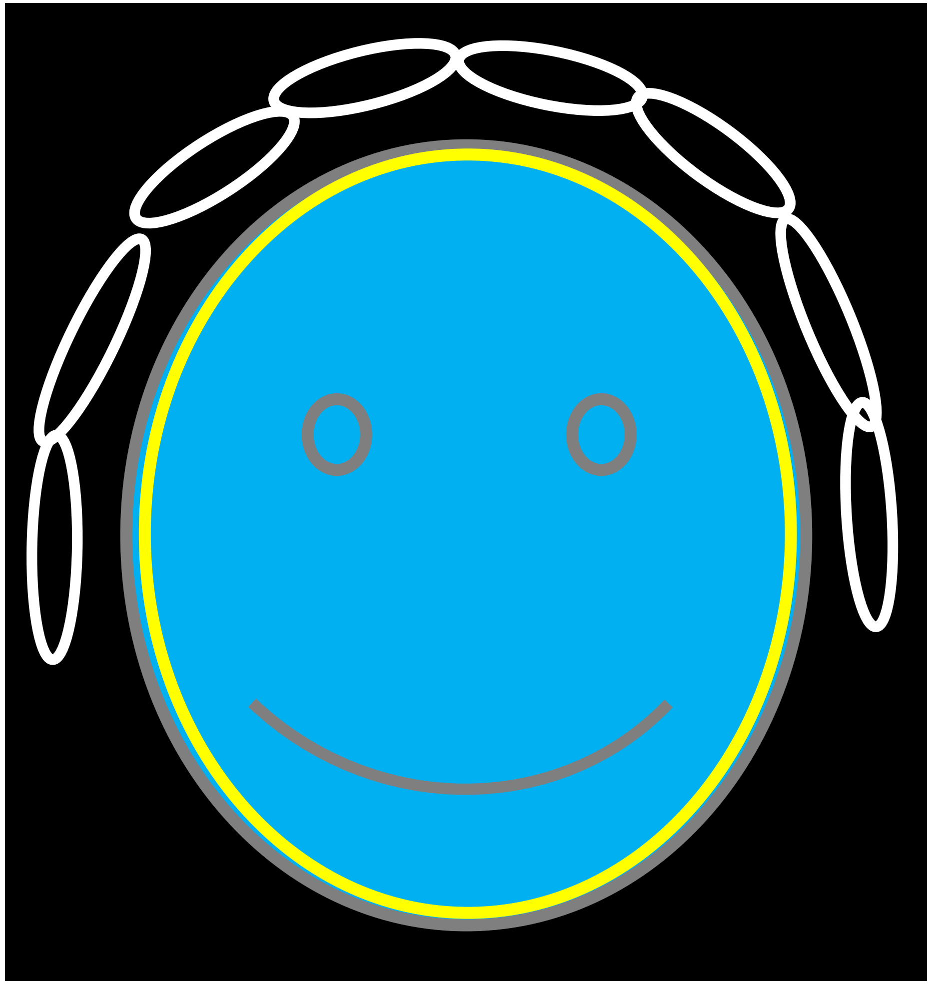
Motion causes inconsistency of encoding

$S(k) = \iiint Im(r,t)e^{ik(t)\cdot r} \quad Im(r) = FFT_{3D}(S(\boldsymbol{k}))\mathrm{dr}$

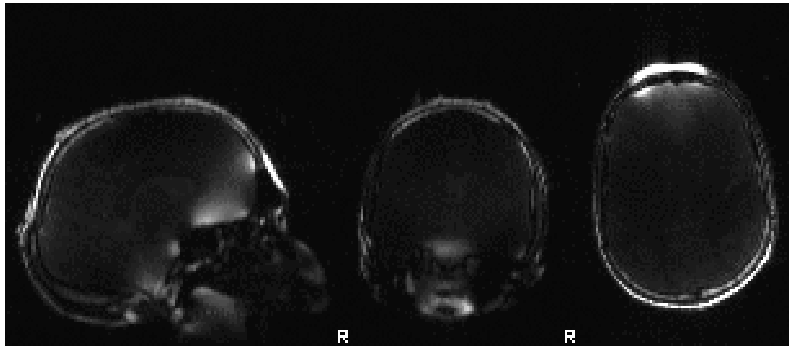
- ❑ Signal changes $Im(r,t) \neq Im(r)$
- ❑ Encoding the objects in the expected way
  $k_{actual}(t) \neq k_{designed}(t)$

Andre et al. (J Am CollRadiol2015)

The whole head takes some time to encode…

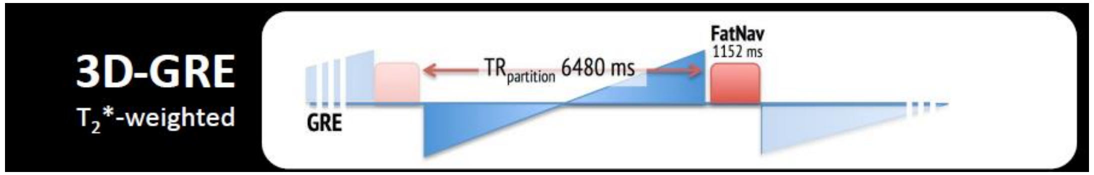


fat is sparse and fast to image ~16-64x



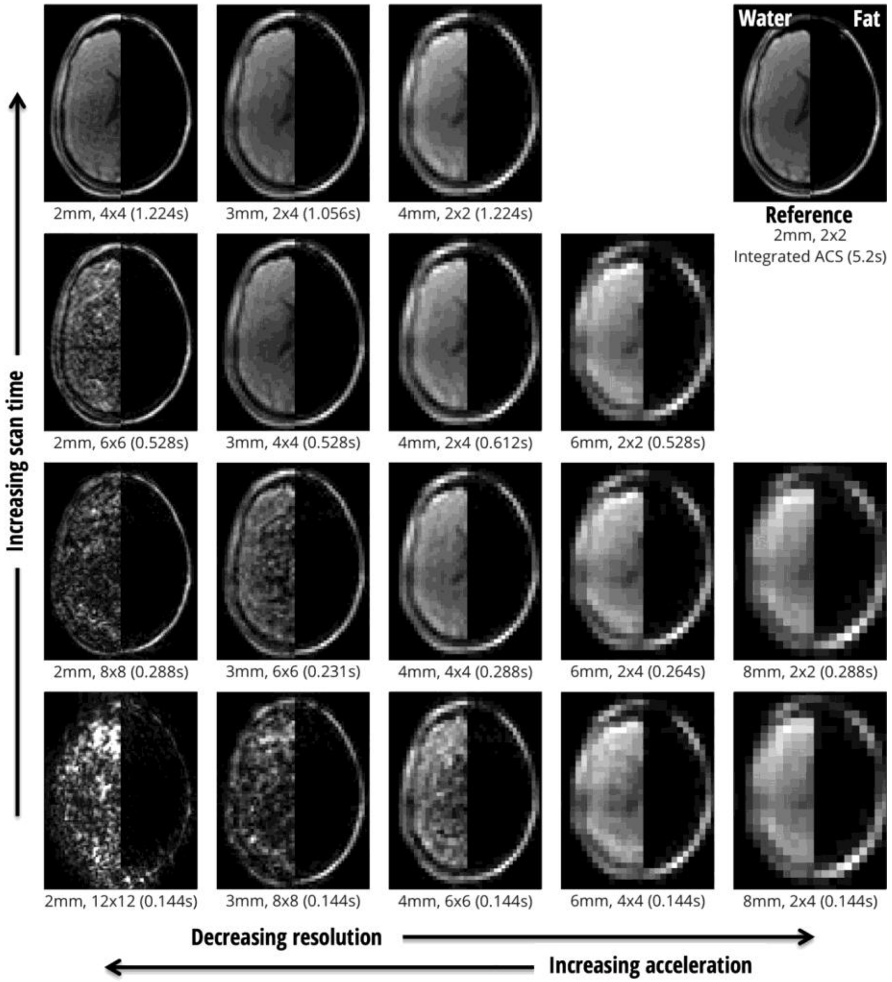
It does not «cost» water signal

Most high field anatomical sequences have a dead time for a 3D nav



1. Gallichan et al. (Proc ISMRM 2013); 2. Skare et al. (MRM 2015)

Motion estimation accuracy of Water and Fat Navigators



Gallichan & Marques, MRM, 2017

Examples of motion (un)corrected data

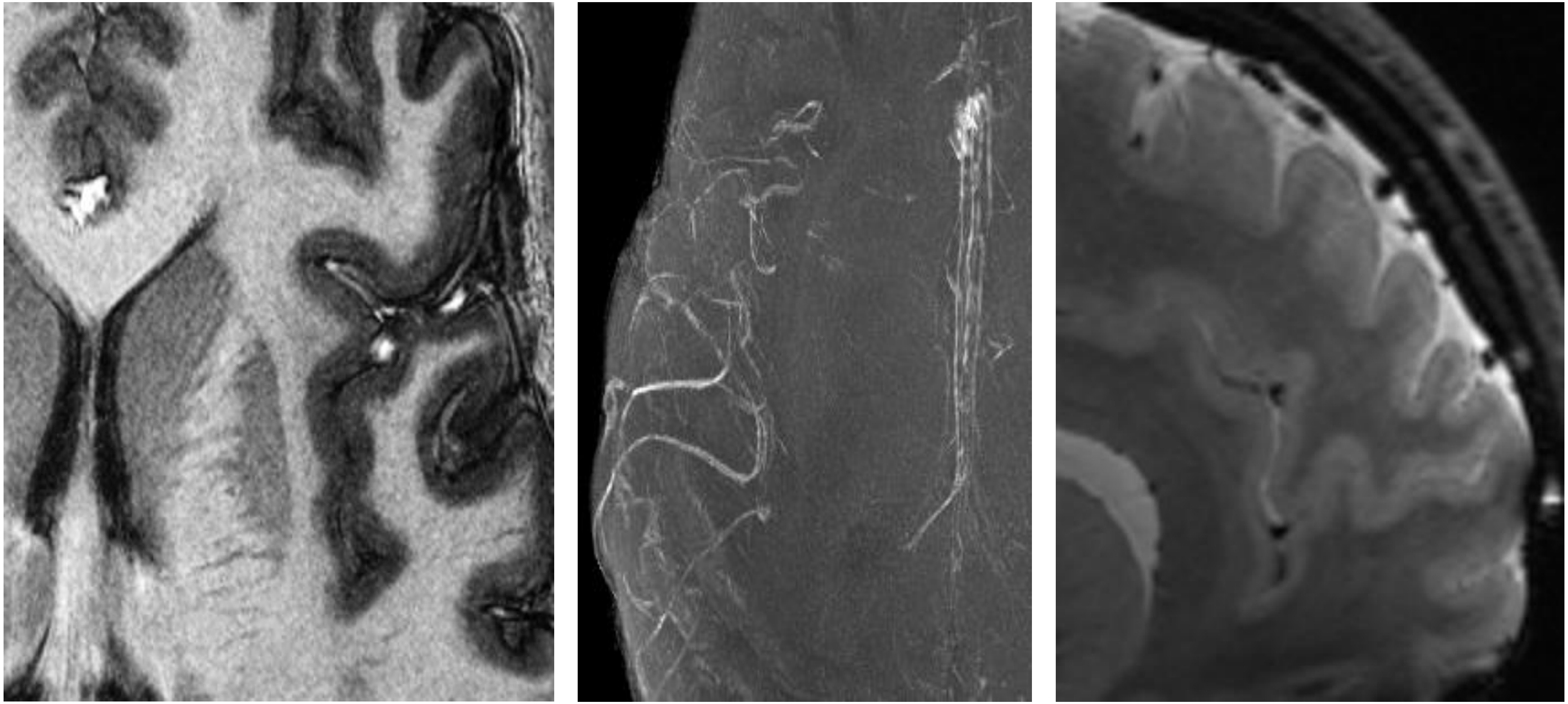
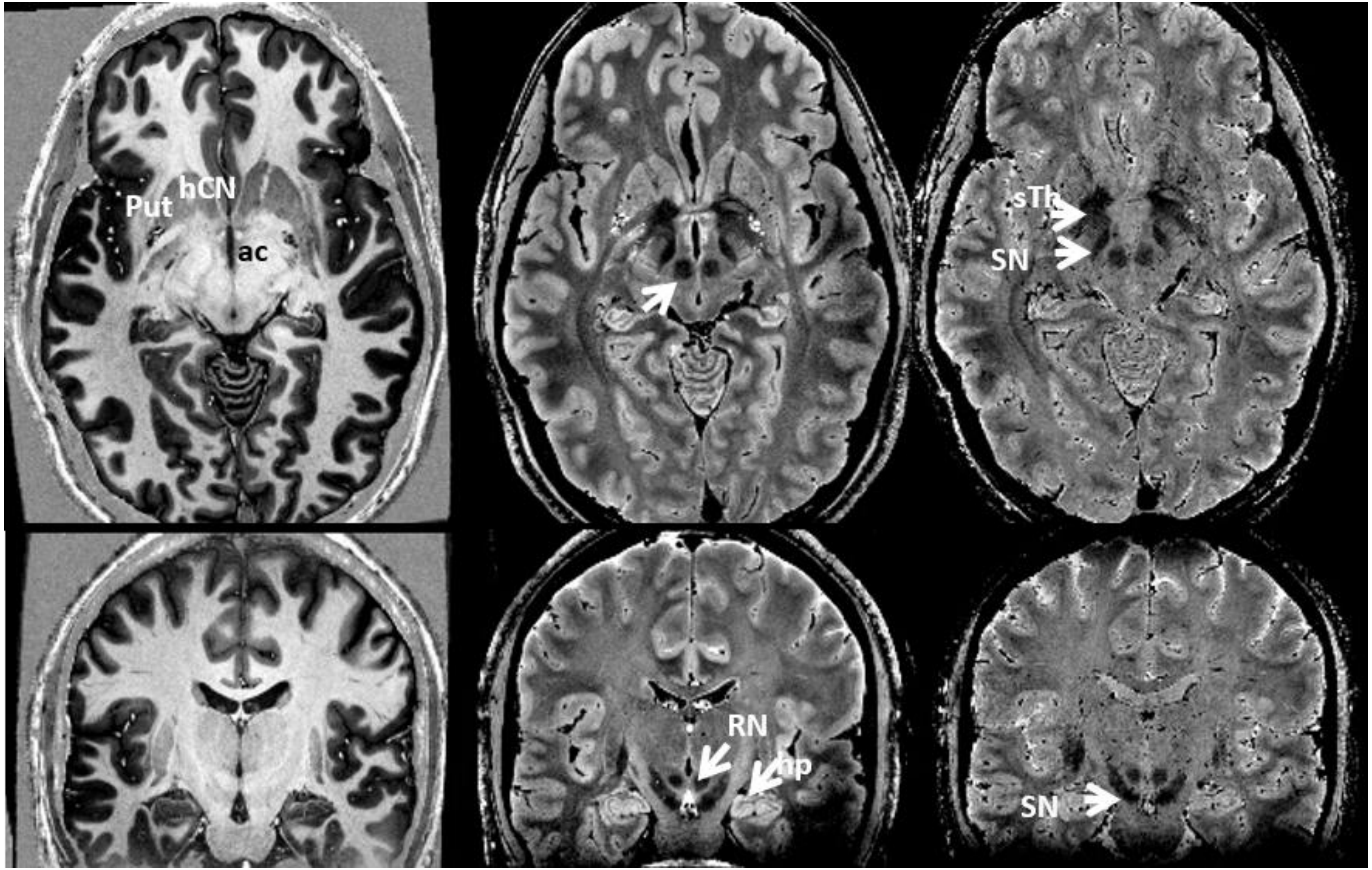


Image Quality Fixed

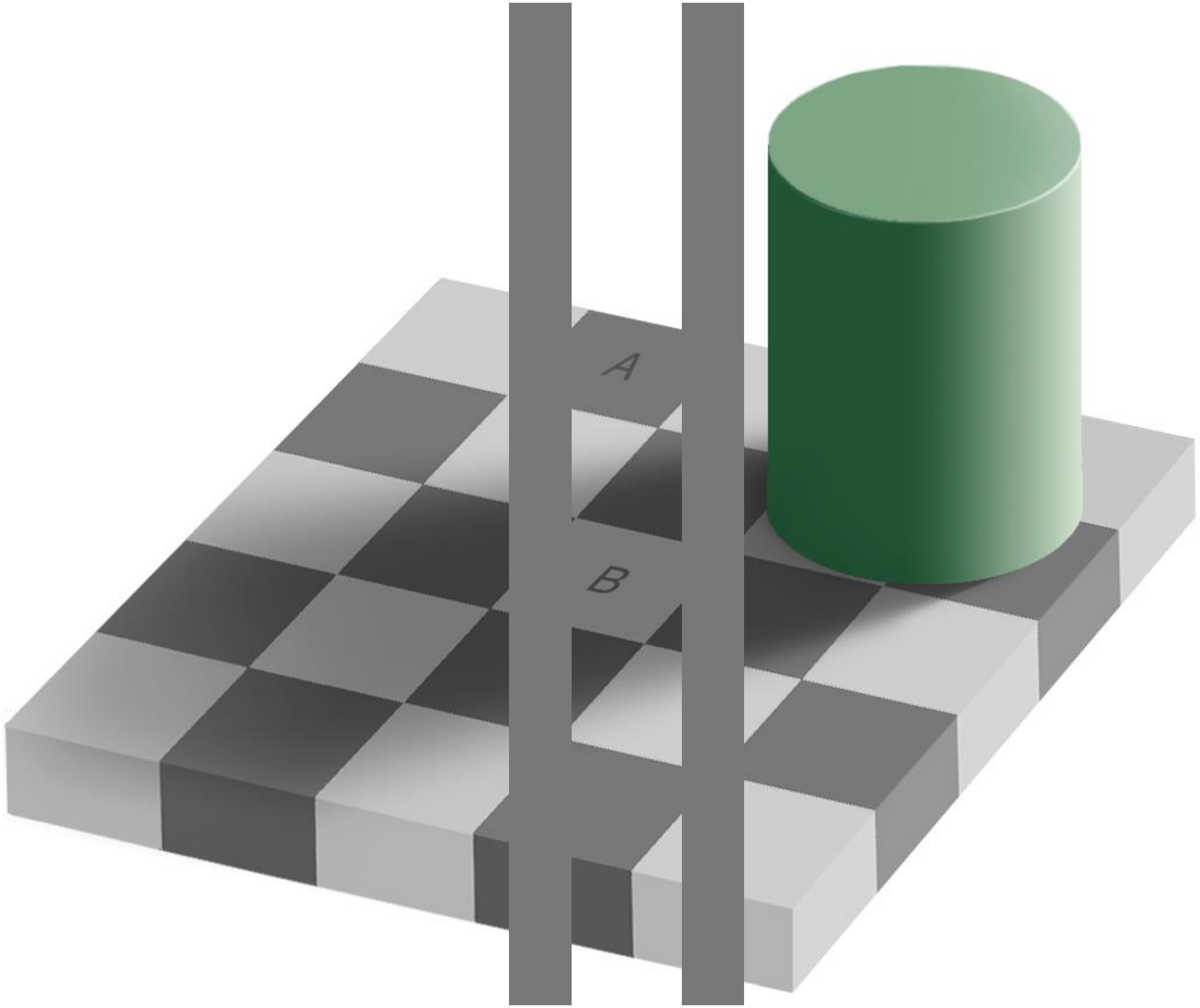
MRI comes with many flavours – "weightings"



C. Federau and D. Gallichan, PLOSone, 2016

The problem

- How does it relate to MRI images?

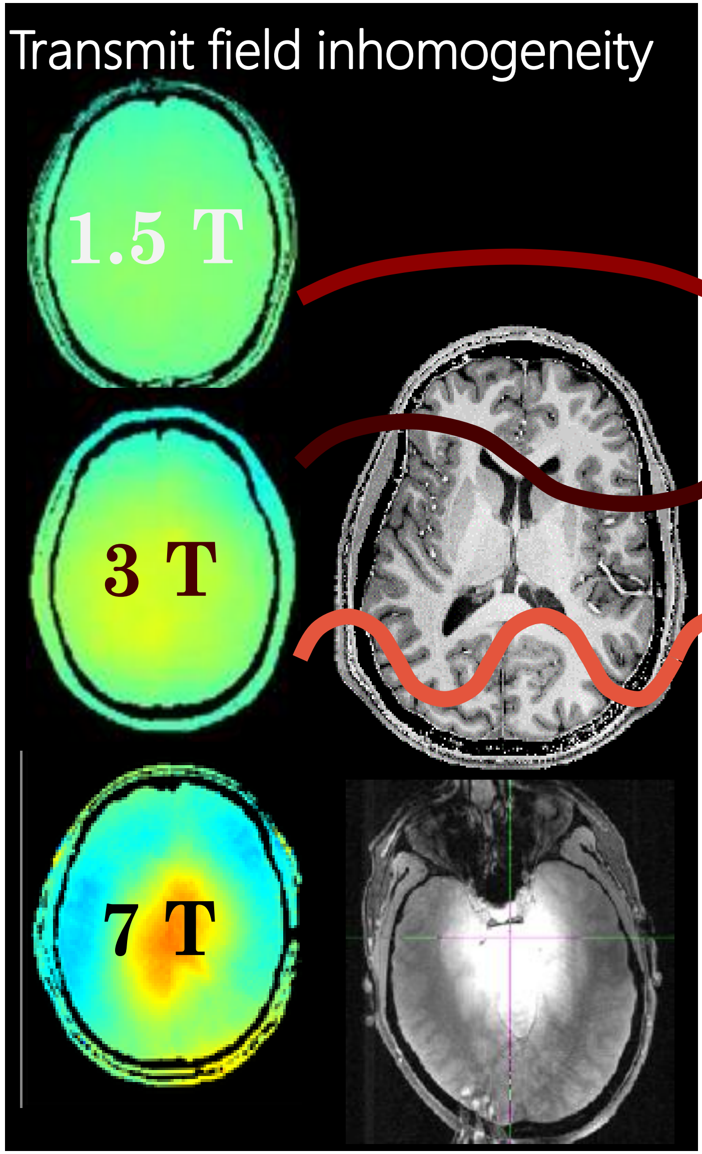


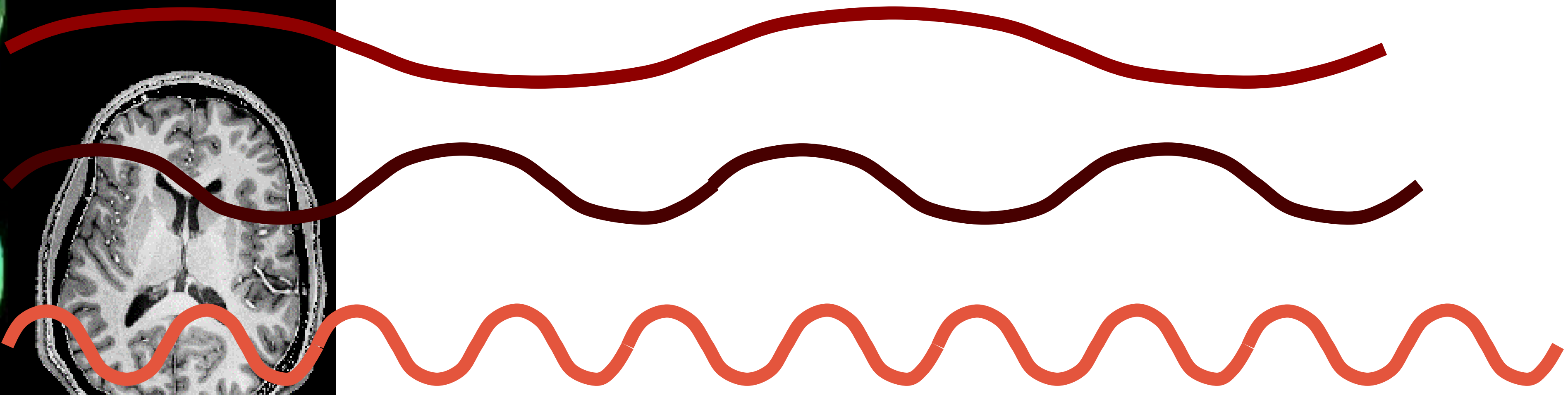
RF inhomogeneity

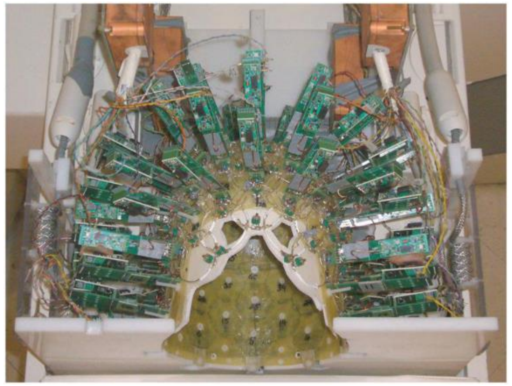
– We all want more signal, the "easy way": higher B_0

$$\omega \propto B_0$$

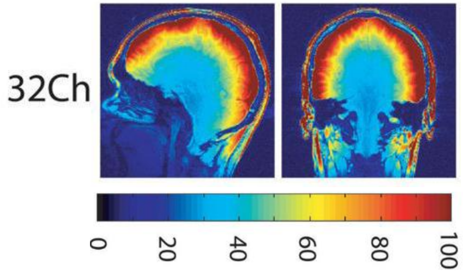
$$\lambda \propto \frac{1}{B_0}$$





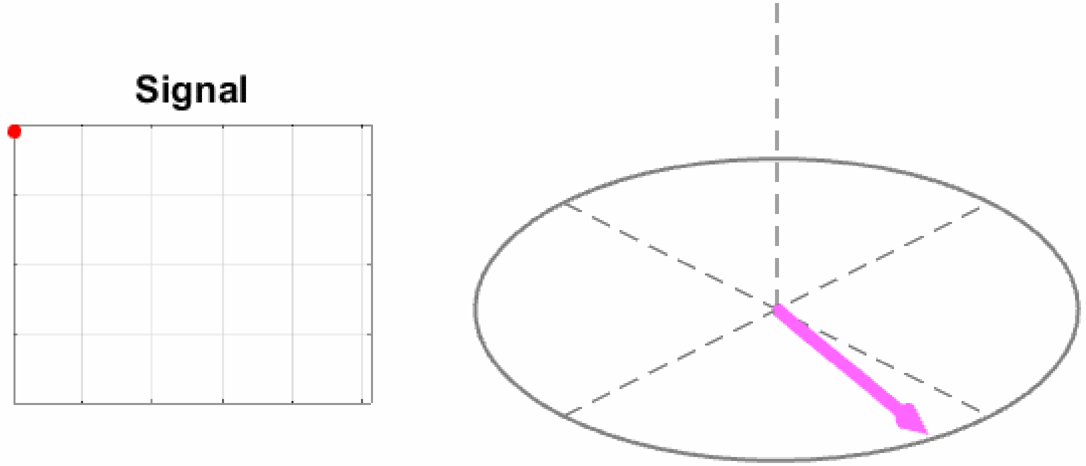


Receive field inhomogeneity



But there is hope…

Quantitative Imaging and Relaxation…



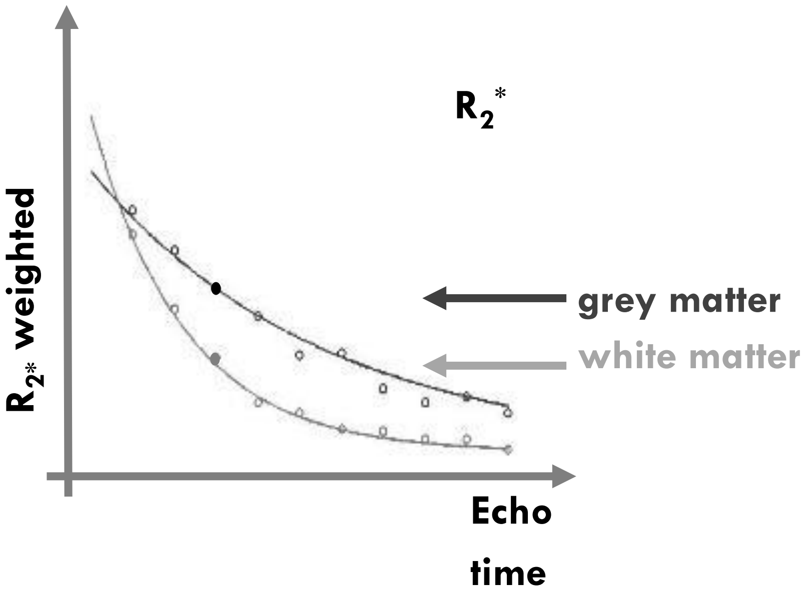
Relaxation restores the thermal **equilibrium** distribution of spins and builds up equilibrium magnetization

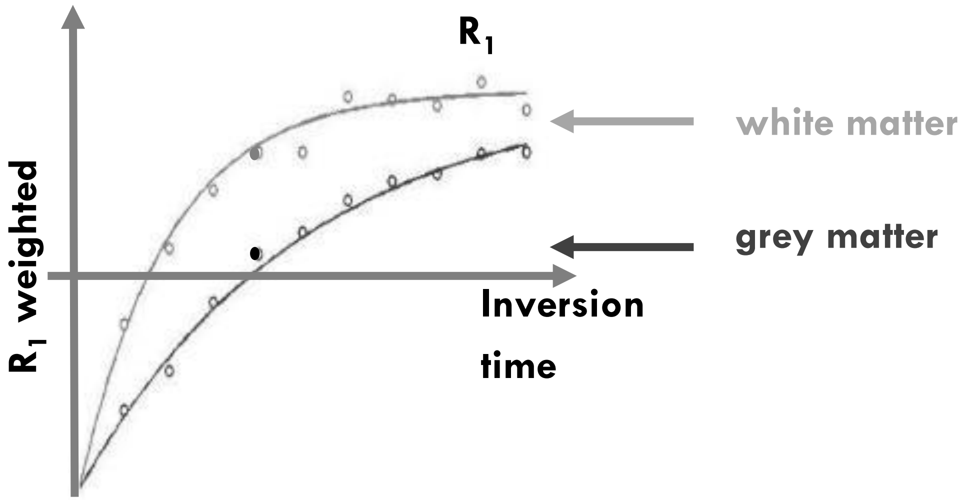
$R_2^{(*)}$ *(apparent) transverse relaxation rate* $[s^{-1}]$

$-\ \{M_x, M_y, M_z\} \equiv \{0, 0, M_0\}.$

R_1 *longitudinal relaxation rate* $[s^{-1}]$

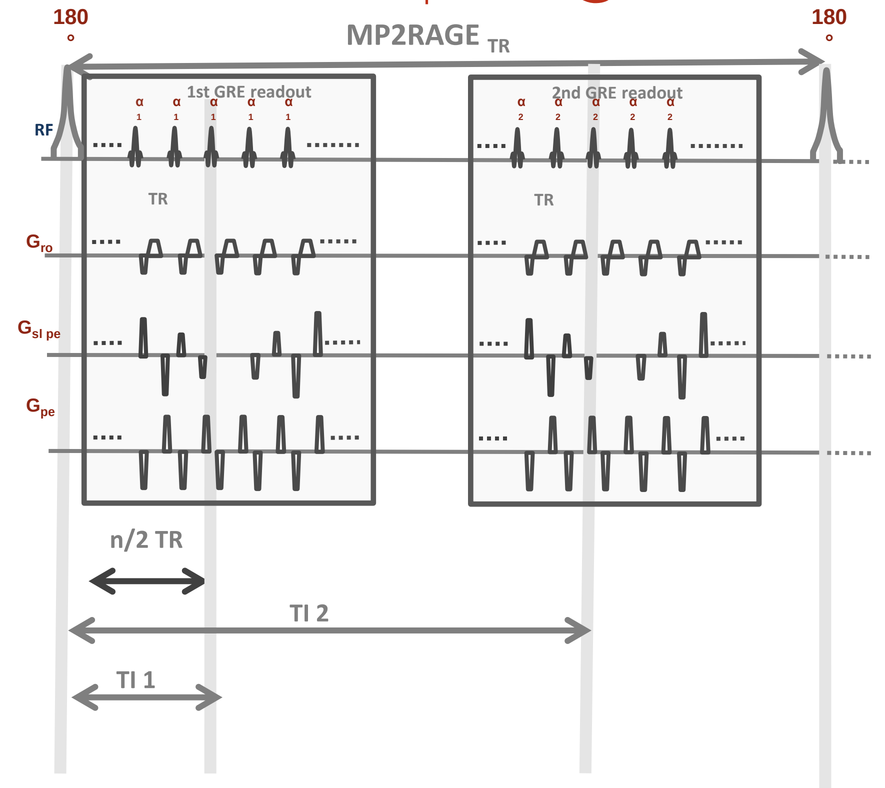
Weighted imaging vs relaxometry





The price:
- More data points - > more acquisition time
- If one parameter is to be measured, you have to ensure that the signal does not depend on the remaining relaxation properties -> less efficient
- Non-linear fitting - > can be computationally expensive particularly as multiple parameters are obtained in one acquisition

From T_1 weighted to MP2RAGE and T1 mapping



After the combination of the two images:

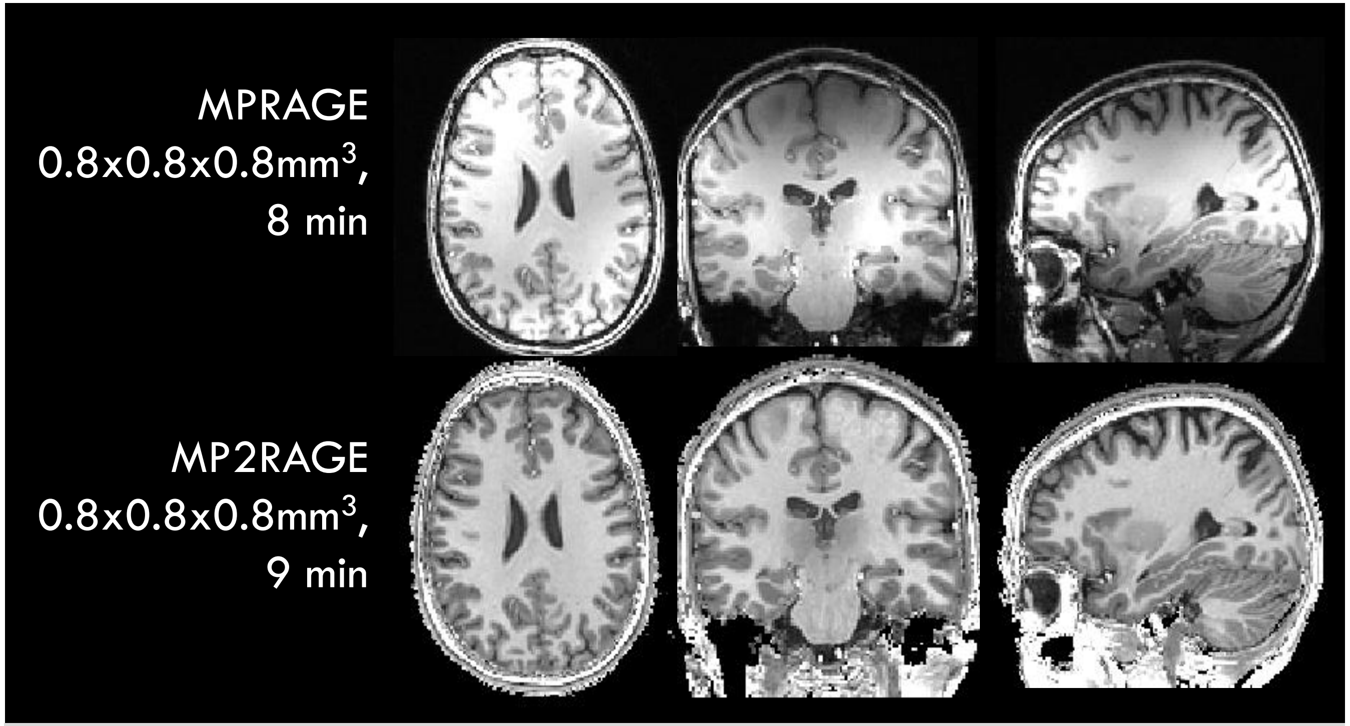
~~M_0 effects;~~

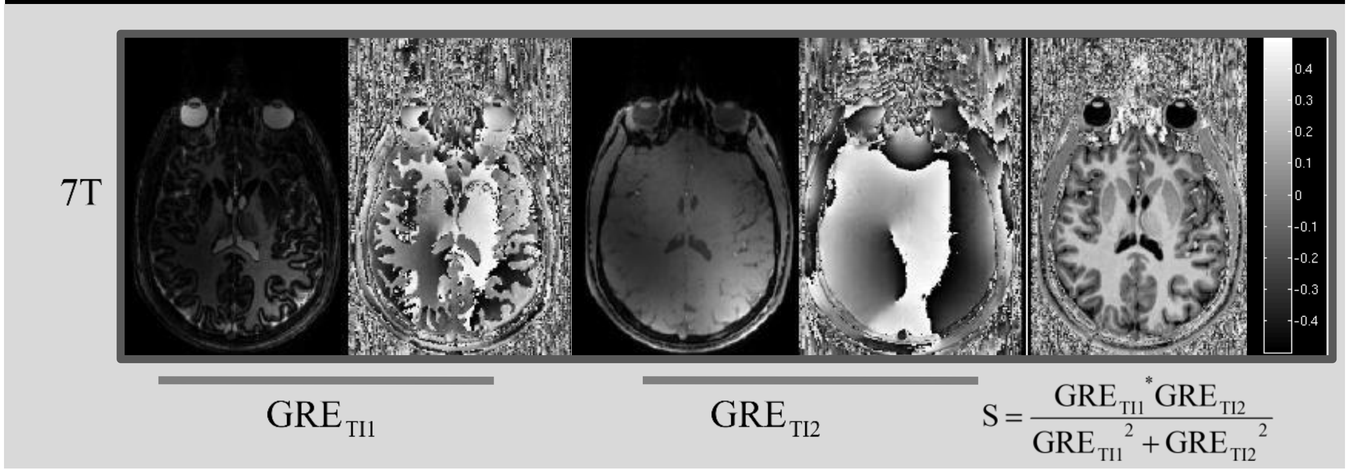
~~T_2^* effects;~~

~~reception B_1^- effects;~~

~~transmission B_1^+ effects (not really);~~

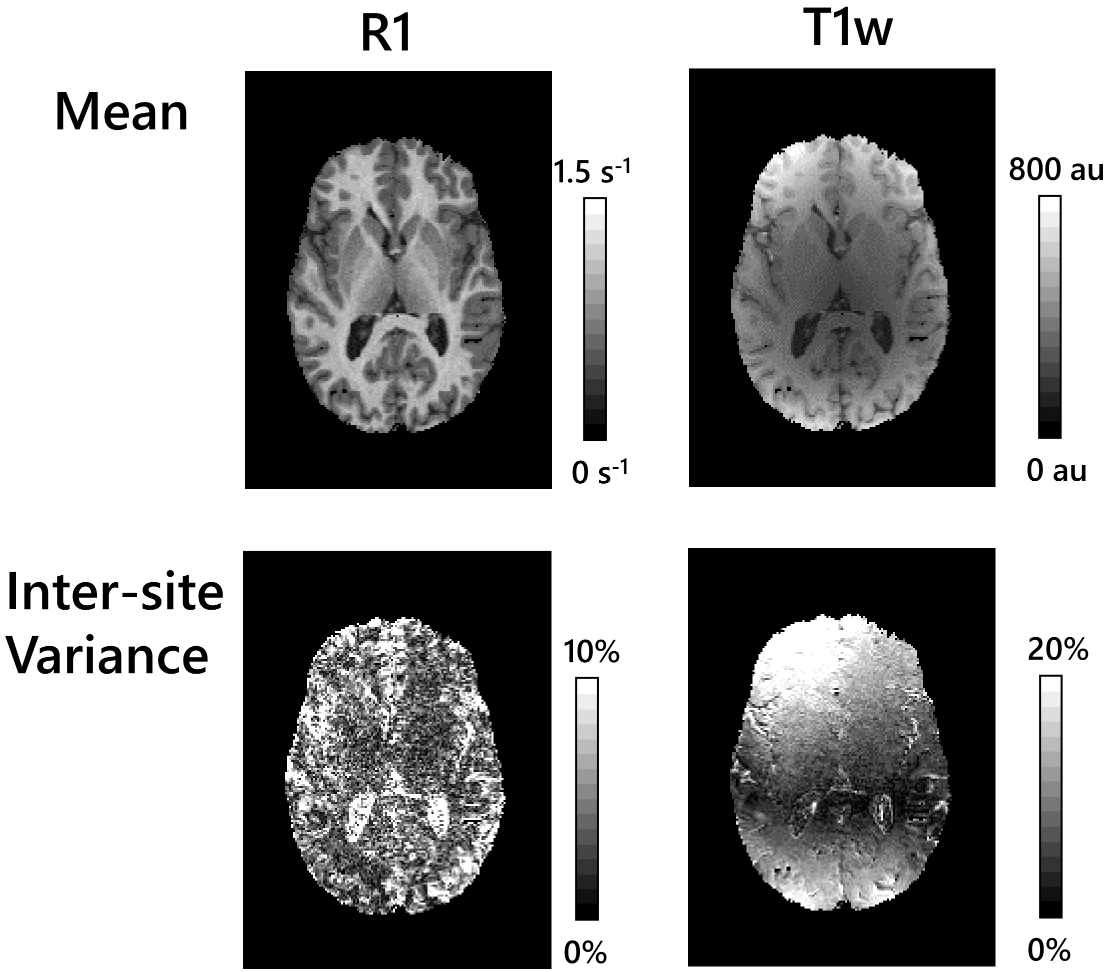
All we are left is mostly a T_1 dependence… T_1 estimation





Marques JP, Kober T et al, Neuroimage, 2010

Quantitative imaging facilitates multi-center studies / comparing data



Weiskopf et al., FIBIM 2013

Relaxation rates

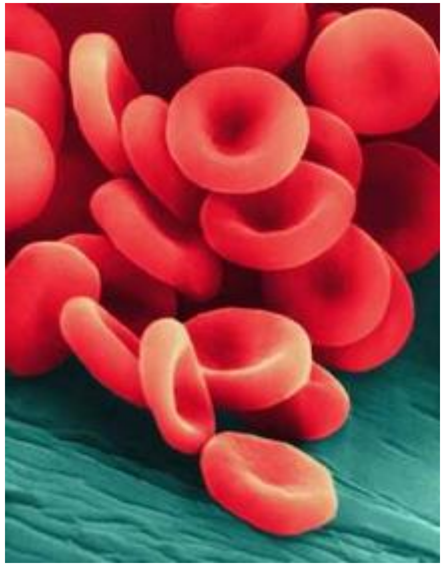
$$R_{1/2} = R_{1/2base} + \quad r_{1/2stuff}[stuff]$$

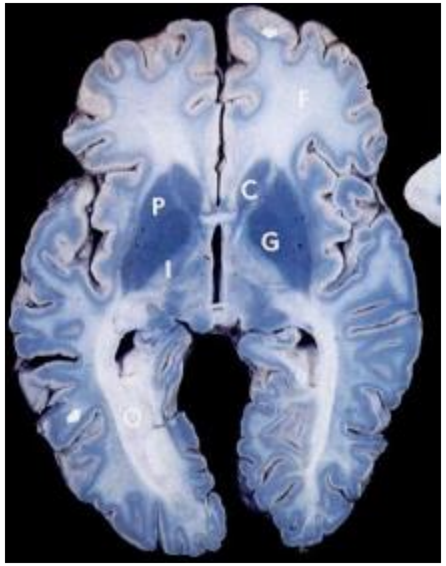
$$R_{1/2} = \frac{1}{T_{1/2}}$$

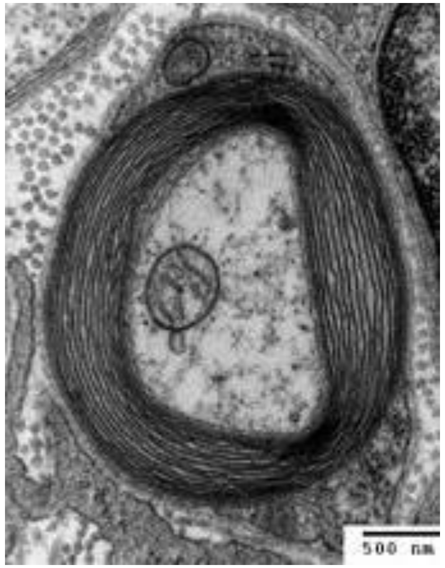
What is stuff in the brain?

The usual suspects

Deoxygenated Blood	Iron (non-heme)	Myelin density



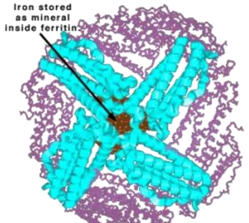


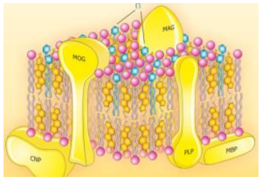


Paramagnetic	*Paramagnetic*	*Diamagnetic*
$\chi = +$	$\chi = +$	$\chi = -$

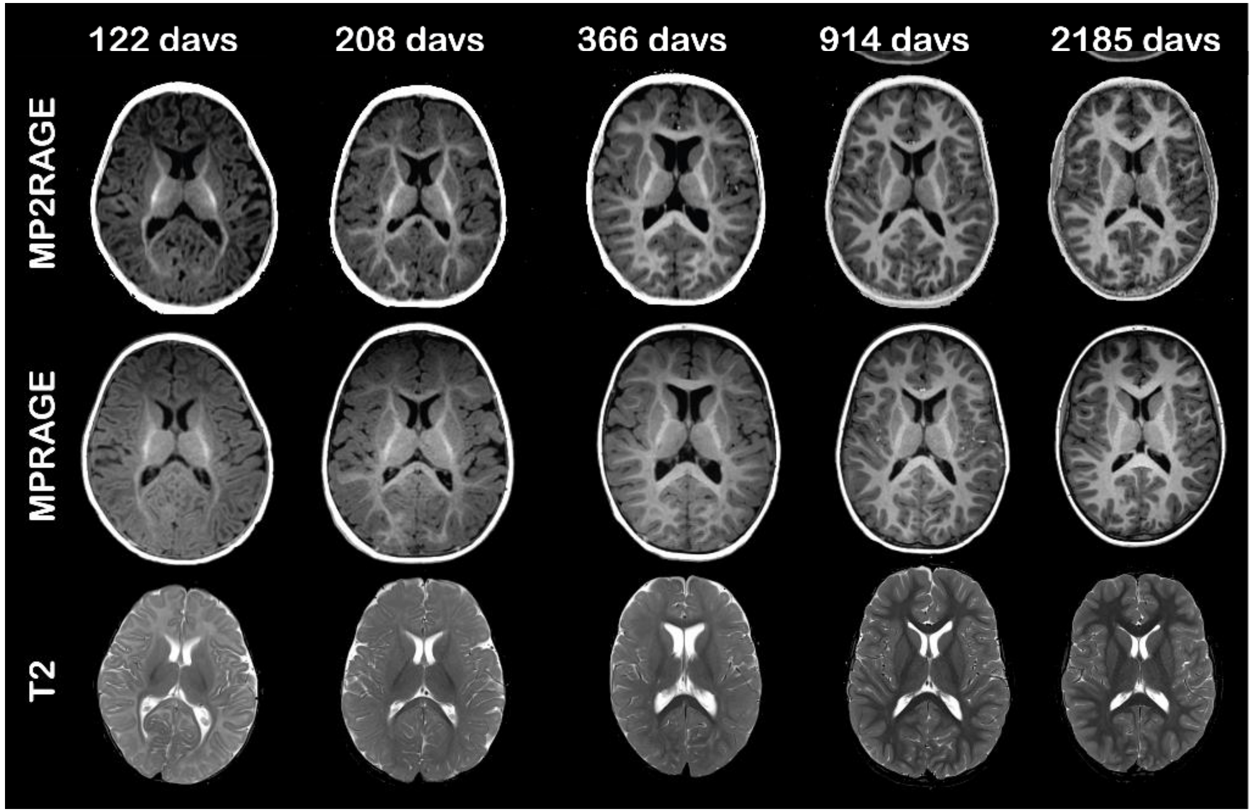
Fe^{2+}

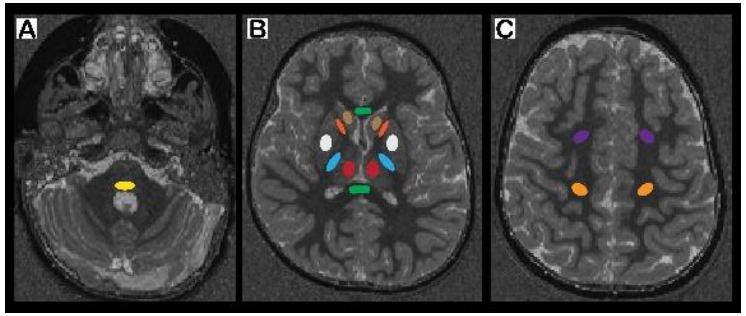
Fe^{3+}

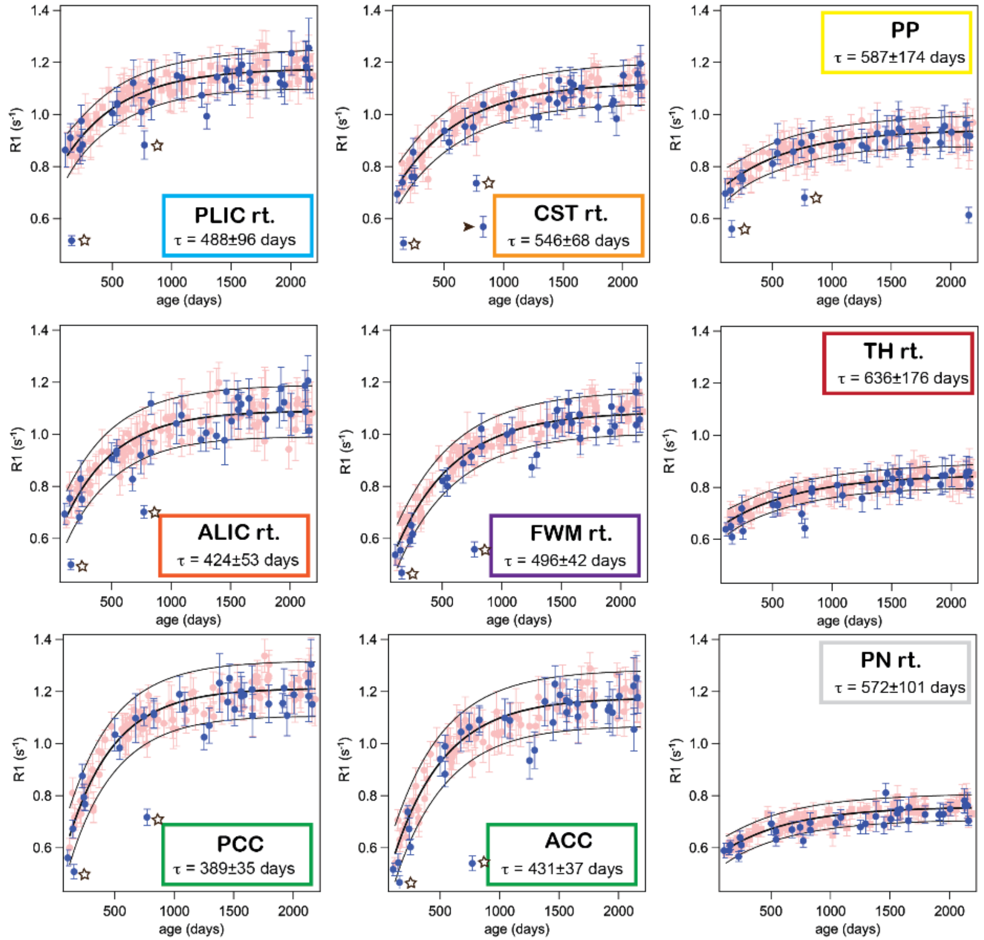




R1 mapping to study brain myelination



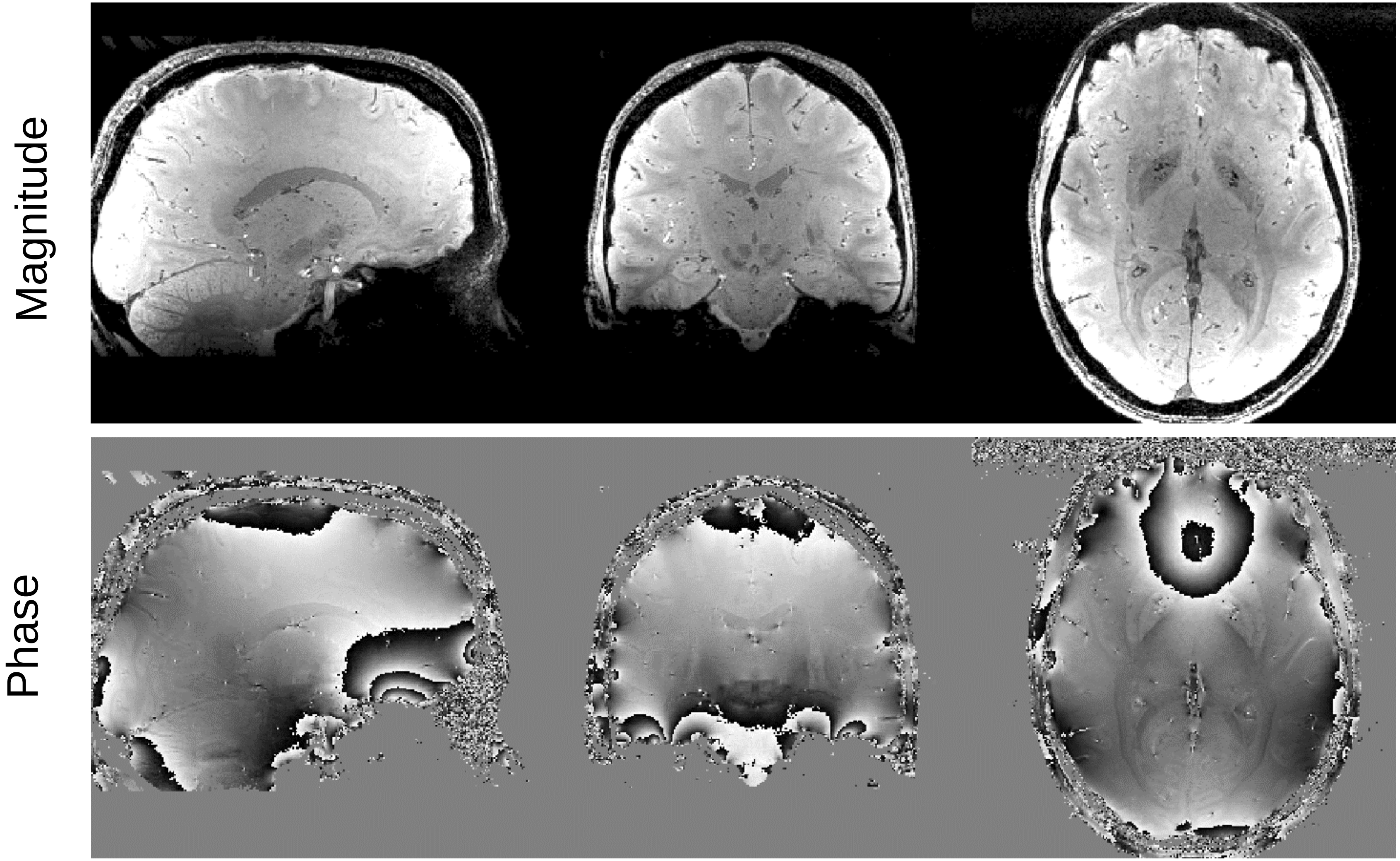




Kuhne et al, Ped. Radiology, 2021

There is more to quantitative imaging than just relaxation

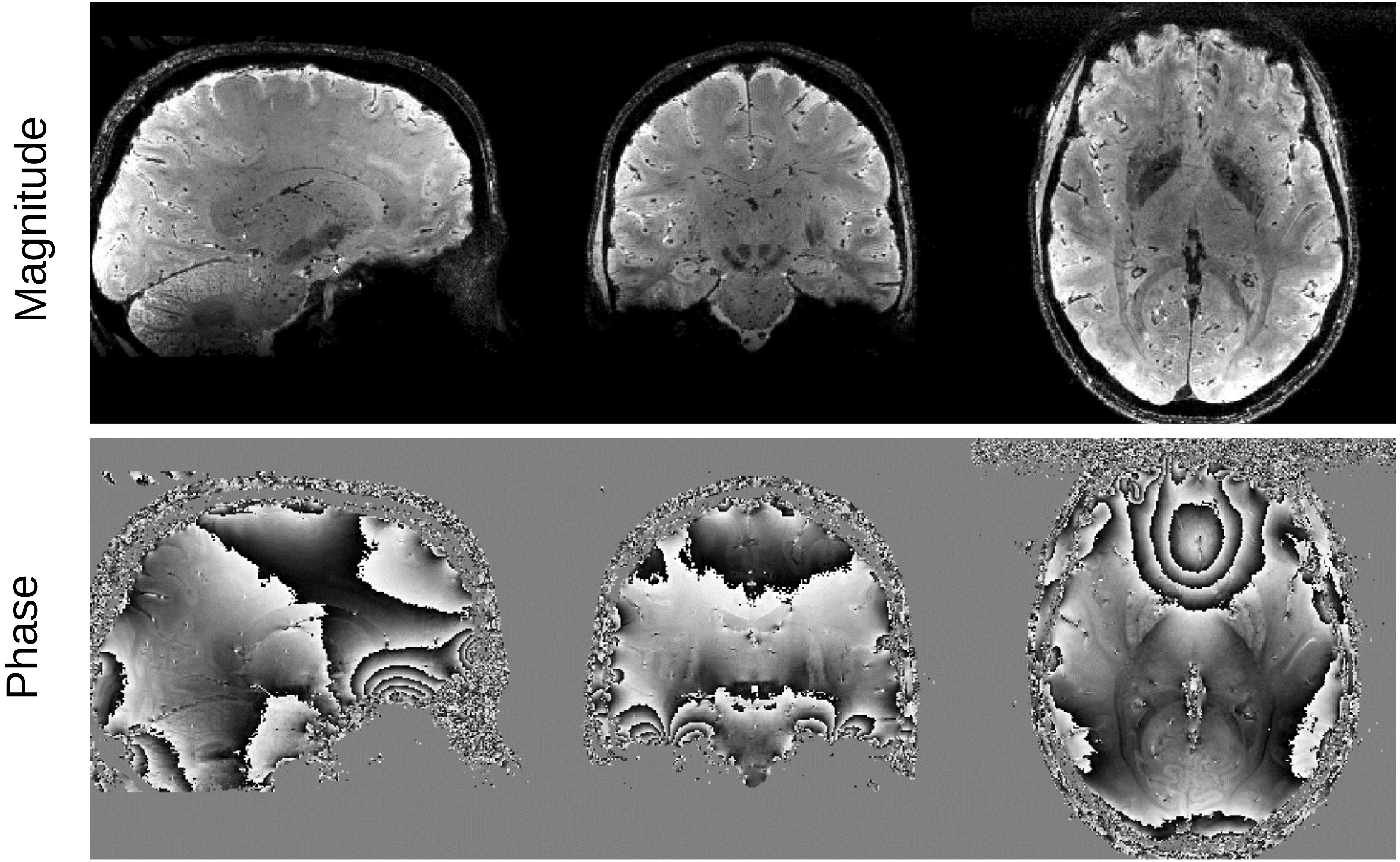
Gradient echo images TE1



$$S = S_0 \exp\left(\frac{-TE}{T_2^*}\right)$$

$$\phi = \Delta B \gamma TE B_0$$

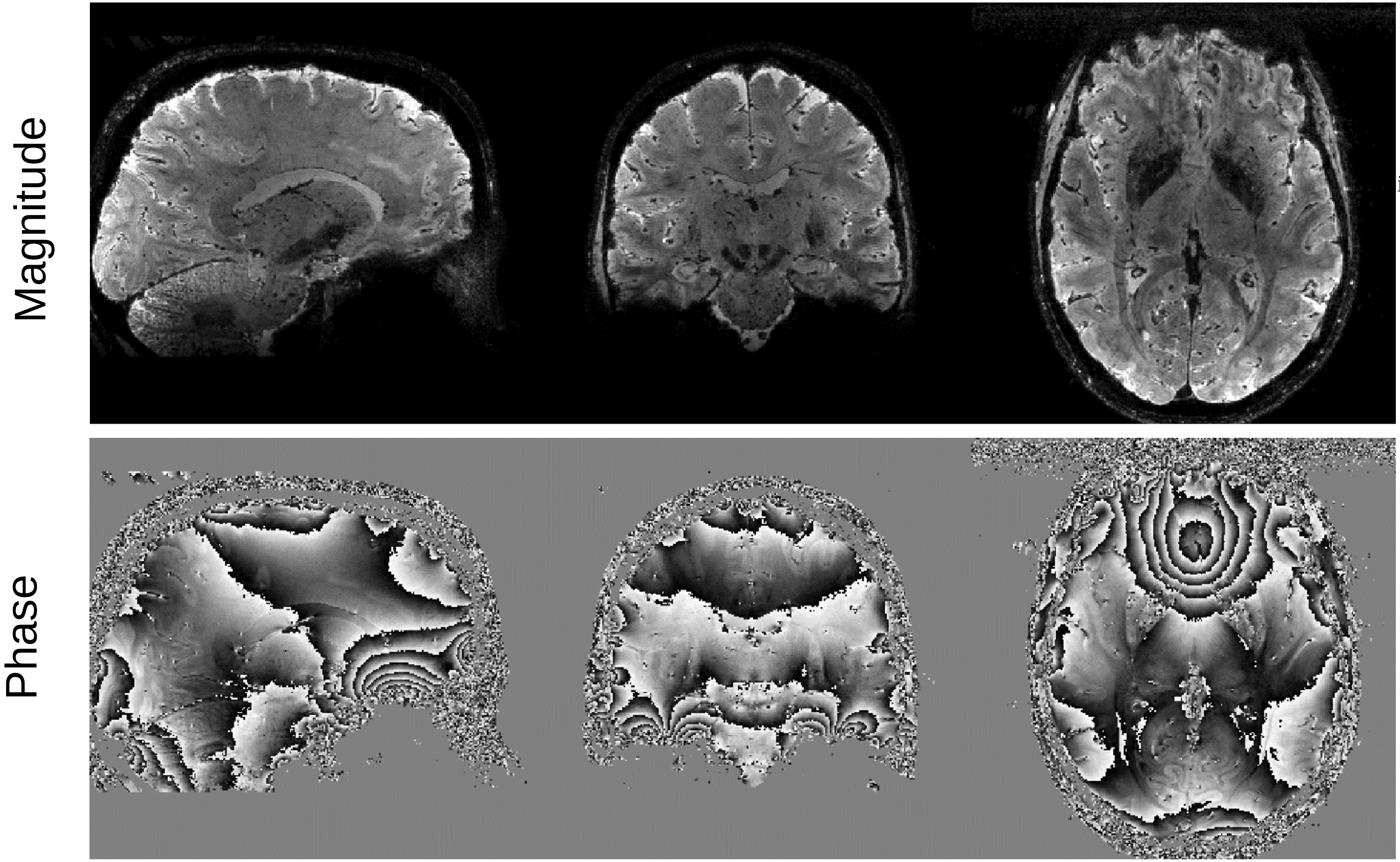
Gradient echo images TE2



$$S = S_0 \exp\left(\frac{-TE}{T_2^*}\right)$$

$$\phi = \Delta B \gamma TE B_0$$

Gradient echo images TE3

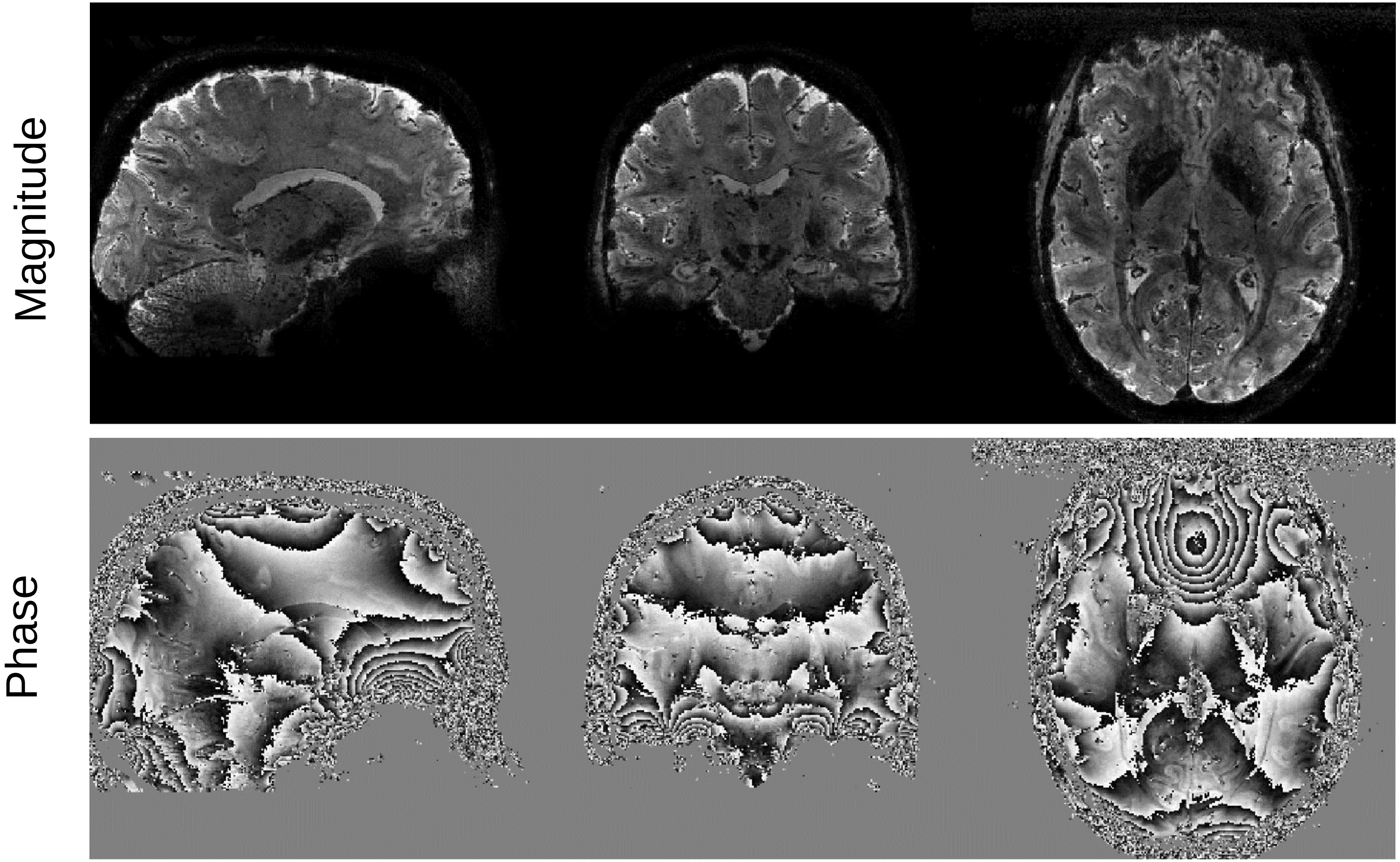


iγΔB$_0$TE

$$S = S_0 \exp\left(\frac{-TE}{T_2^*}\right)$$

$$\phi = \Delta B \gamma TE B_0$$

Gradient echo images TE5

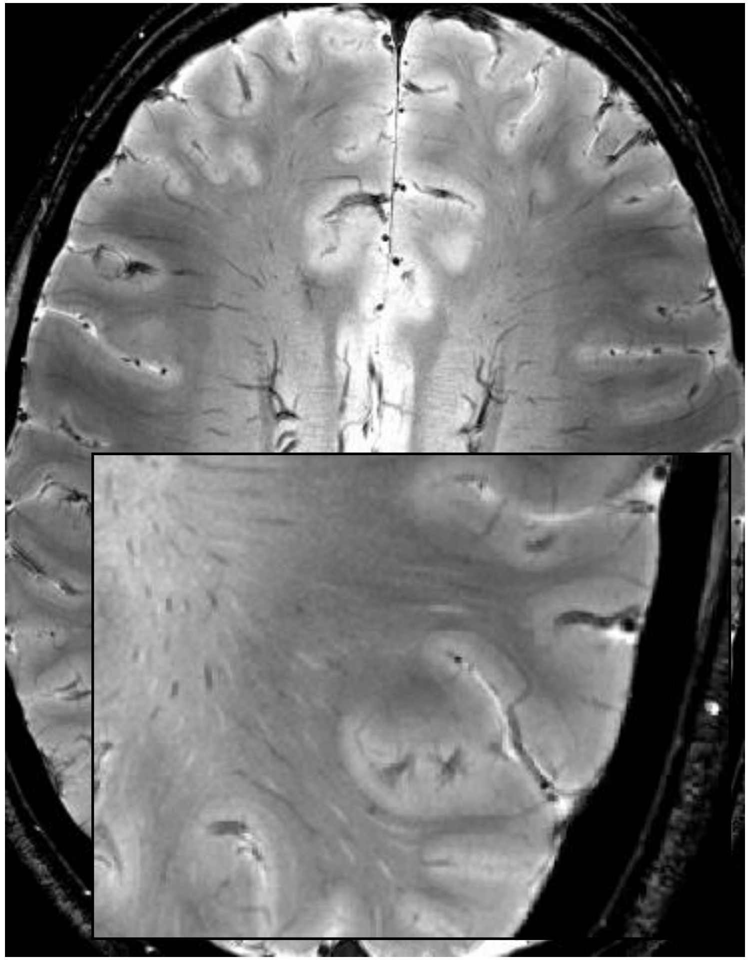


$$S = S_0 \exp\left(\frac{-TE}{T_2^*}\right)$$

$$\phi = \Delta B \gamma TE B_0$$

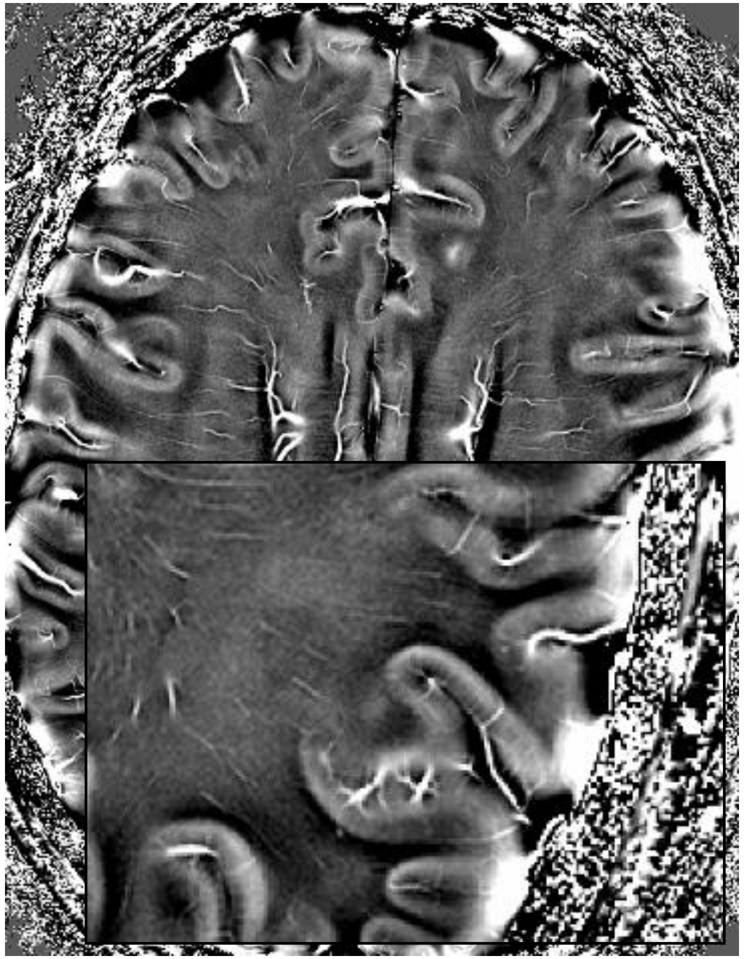
… after background field removal

Magnitude



$$S = S_0 \exp\left(\frac{-TE}{T_2^*}\right)$$

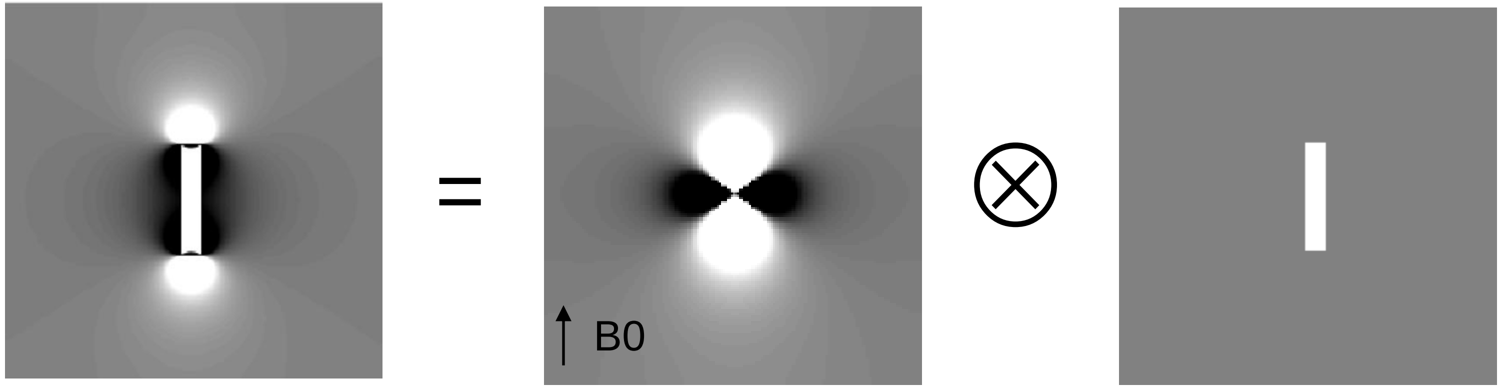
Phase

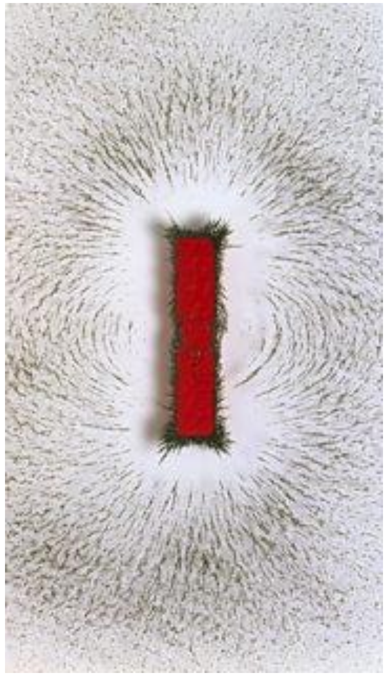


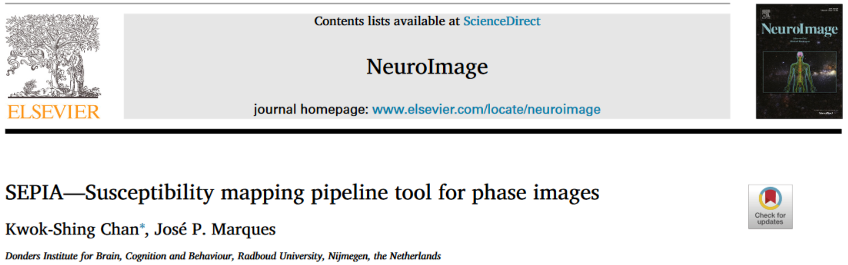
$$\phi = \Delta B \gamma TE B_0$$

Quantitative Susceptibility Map

$\Delta B_z \qquad = \qquad D \qquad \otimes \qquad \chi$






Contents lists available at ScienceDirect

NeuroImage

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

ELSEVIER

SEPIA—Susceptibility mapping pipeline tool for phase images

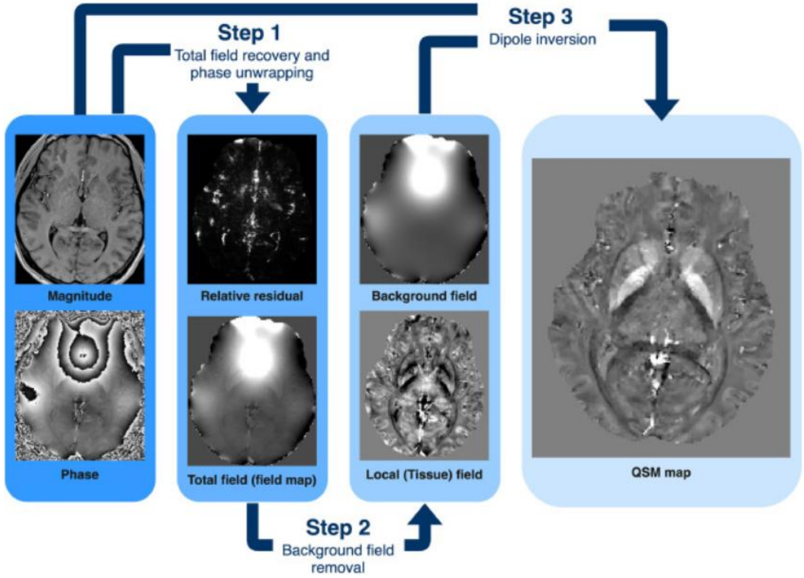
Kwok-Shing Chan*, José P. Marques

Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, the Netherlands

MRI can measure the field perturbation

Quantitative Susceptibility Mapping (QSM) finds χ that could have generated ΔB

$$\min_{\chi} \|\Delta B - D * \chi\| + \lambda R(\chi)$$



Salomir R et al Conc. In MRb , 2004, Marques et al. Conc in MR pB. 2005., Liu et al 2011, Chan and Marques, Neuroimage, 2021

QSM Challenges & open science

Magnetic Resonance in Medicine 79:1661–1673 (2018)

Quantitative Susceptibility Mapping: Report From the 2016 Reconstruction Challenge

Christian Langkammer,[1] Ferdinand Schweser,[2,3]* Karin Shmueli,[4] Christian Kames,[5] Xu Li,[6,7] Li Guo,[8] Carlos Milovic,[9,10] Jinsuh Kim,[11] Hongjiang Wei,[12] Kristian Bredies,[13] Sagar Buch,[14] Yihao Guo,[6] Zhe Liu,[15] Jakob Meineke,[16] Alexander Rauscher,[5] José P. Marques,[17] and Berkin Bilgic[18]

FULL PAPER
Magnetic Resonance in Medicine

QSM reconstruction challenge 2.0: A realistic in silico head phantom for MRI data simulation and evaluation of susceptibility mapping procedures

José P. Marques[1] | Jakob Meineke[2] | Carlos Milovic[3,4,5] | Berkin Bilgic[6,7,8] | Kwok-Shing Chan[1] | Renaud Hedouin[1,9] | Wietske van der Zwaag[10] | Christian Langkammer[11] | Ferdinand Schweser[12,13]

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FULL PAPER
Magnetic Resonance in Medicine

QSM reconstruction challenge 2.0: Design and report of results

QSM Challenge 2.0 Organization Committee | Berkin Bilgic[1,2,3] | Christian Langkammer[4] | José P. Marques[5] | Jakob Meineke[6] | Carlos Milovic[7,8,9] | Ferdinand Schweser[10,11]

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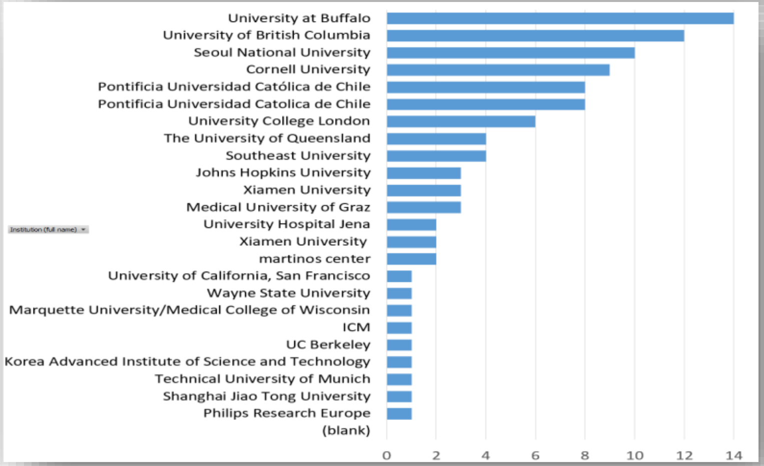

Make your code and data available…

Data Sharing Collection @ Donders Repository

Quantitative Susceptibility Mapping (QSM) Challenge 2.0

di.dccn.DSC_3015069.02_542

Here we present the creation of a modular and realistic digital brain phantom to serve as a ground-truth to assess the quality of different reconstruction algorithms for Quantitative Susceptibility Mapping (QSM). The phantom is derived from high-resolution, quantitative MRI data of a healthy volunteer, features a realistic morphology including a non piece-wise constant susceptibility distribution.

Files | Metadata | Manifest | History

The files in this collection can be downloaded from https://webdav.data.donders.ru.nl/dccn/DSC_3015069.02_542_v1. To download several files or the entire collection at once, you can use a WebDAV client.

dccn / DSC_3015069.02_542_v1

Name	Size	Modified
ManuscriptFigures		19 January 2021 10:58:01
Simdata		19 January 2021 10:59:26
data		19 January 2021 10:56:32
func		19 January 2021 10:57:36
DirectoryTree.docx	19.5 KiB	19 January 2021 11:01:17
LICENSE.txt	2.4 KiB	19 January 2021 09:36:11
MANIFEST.txt	27.7 KiB	19 January 2021 11:01:18
MacroAddingMicrostructure.m	3.2 KiB	19 January 2021 11:01:17
MacroCreateQSMpipelineAndCompareHighResLowRes.m	22.2 KiB	19 January 2021 11:01:17
MacroCreateSimulationData.m	5.9 KiB	19 January 2021 11:01:18
MacroCreateSusceptibiltyPhantom.m	2.6 KiB	19 January 2021 11:01:18
MacroLoopReconstructionsOfPhantoms.m	8.1 KiB	19 January 2021 11:01:18
MacroProcessInvivoData.m	2.4 KiB	19 January 2021 11:01:18
README.txt	2.2 KiB	19 January 2021 09:36:10

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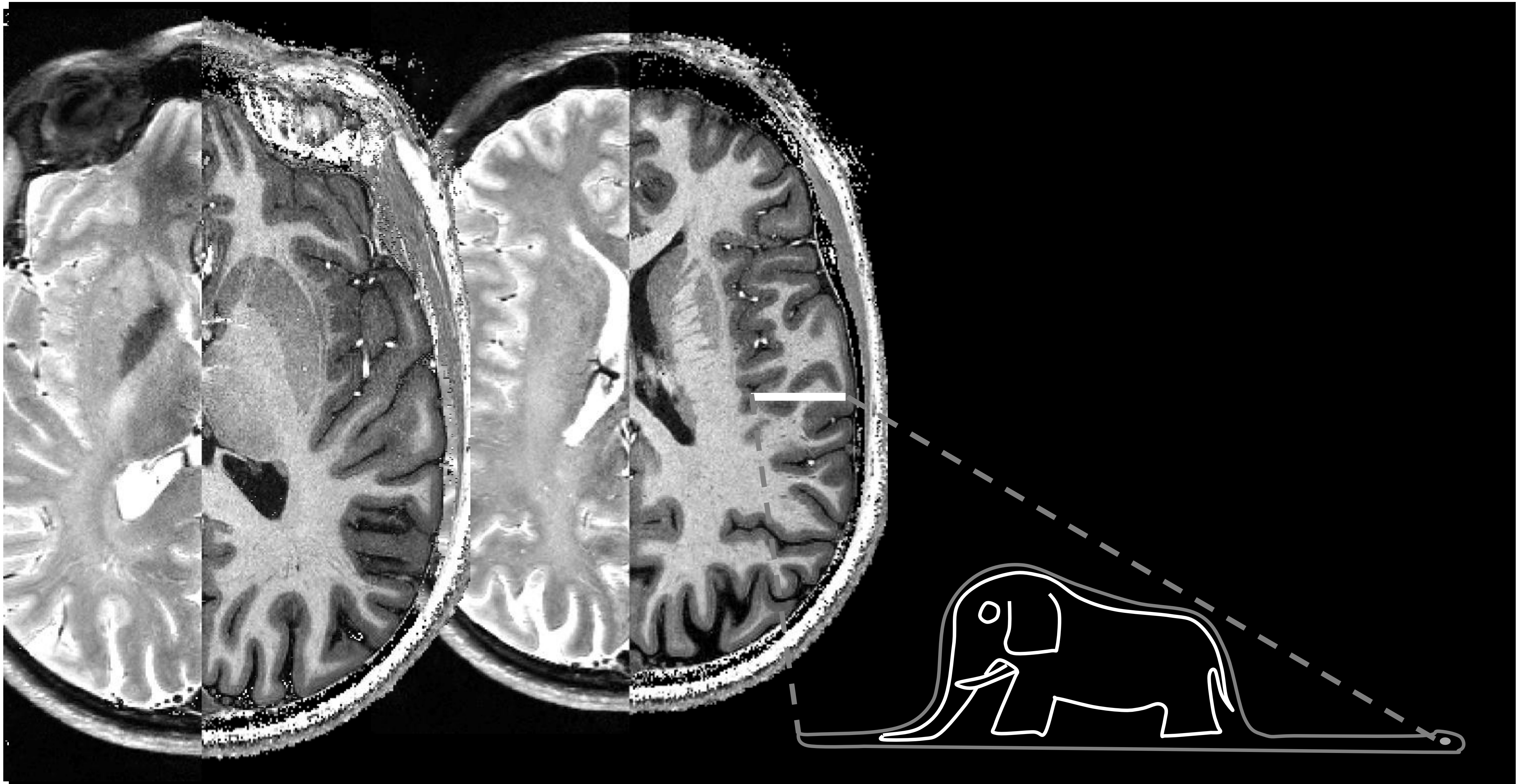
Overview of dataset structure

Collection contains potentially Recognizable Human Data

Scripts used to generate suceptibility phantom (allowing you to modify it)

Scripts to reproduce the paper

unveiling what is beneath?

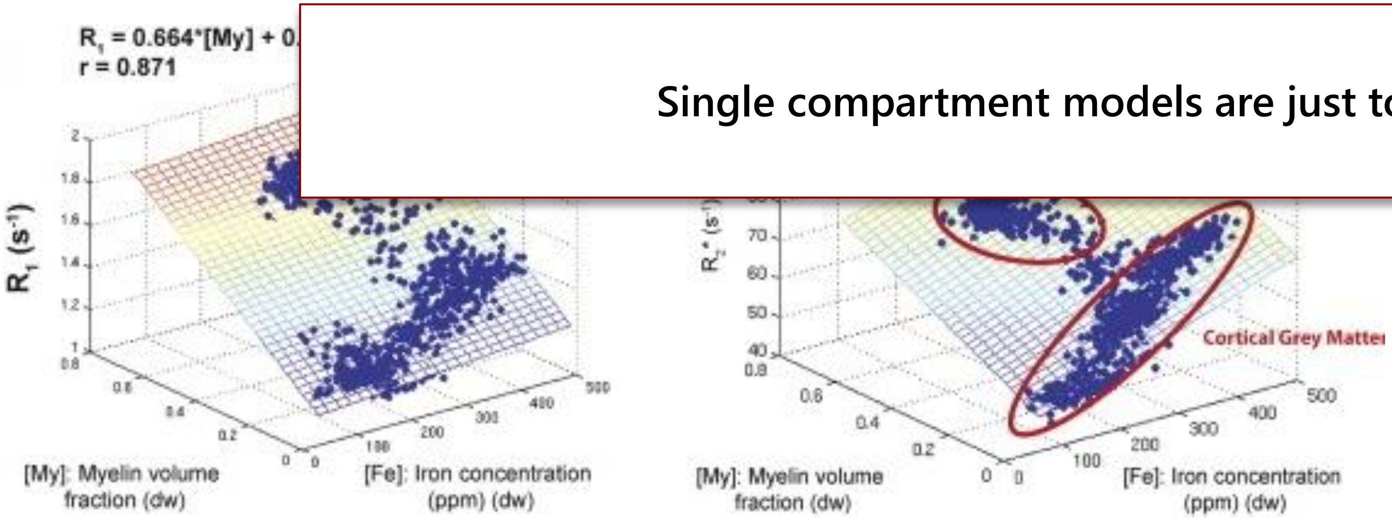


Are relaxation rates / times a specific measure of myelin?

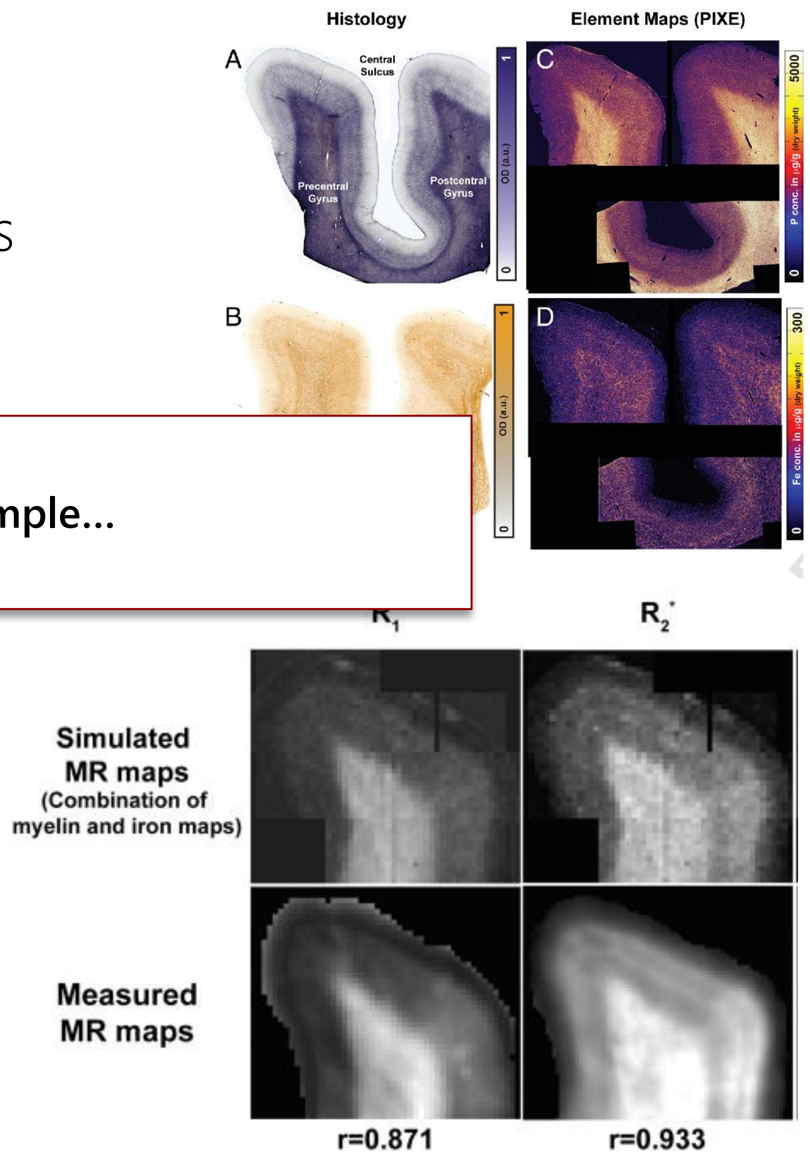
- Myelin affects all relaxation parameters…

  but other "stuff" also does

R_1 $\qquad R_2^*$



Single compartment models are just too simple…



Stuber et al. Neuroimage, 2014

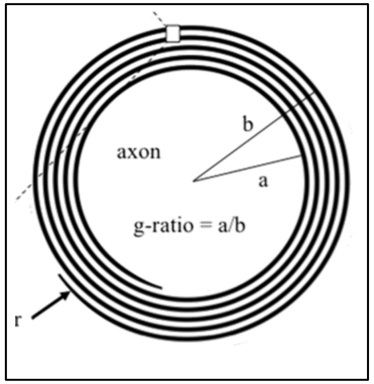
if we want to be more specific
we need to get a better understanding of
how myelin affects the MR signal!

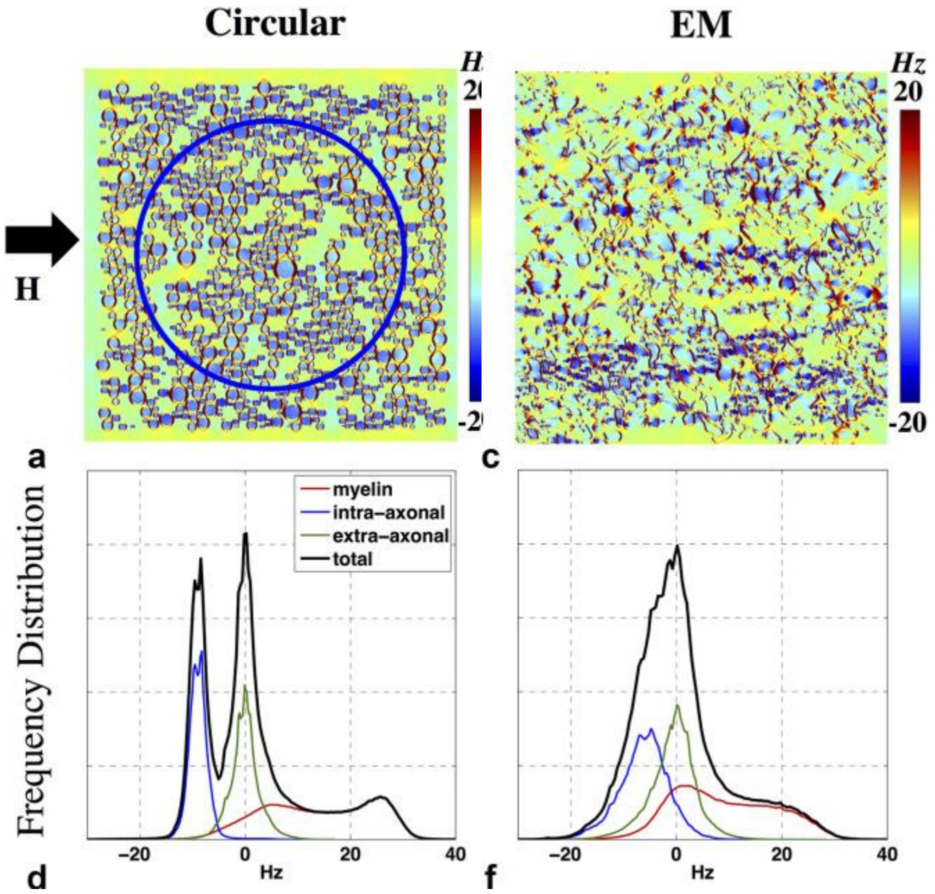
White matter microstructure

Relaxation properties are a too indirect measure of WM microstructure…

What we really want to measure is:

- ❑ Fiber volume fraction
- ❑ g-ratio – conductivity of WM
- ❑ How much myelin there is





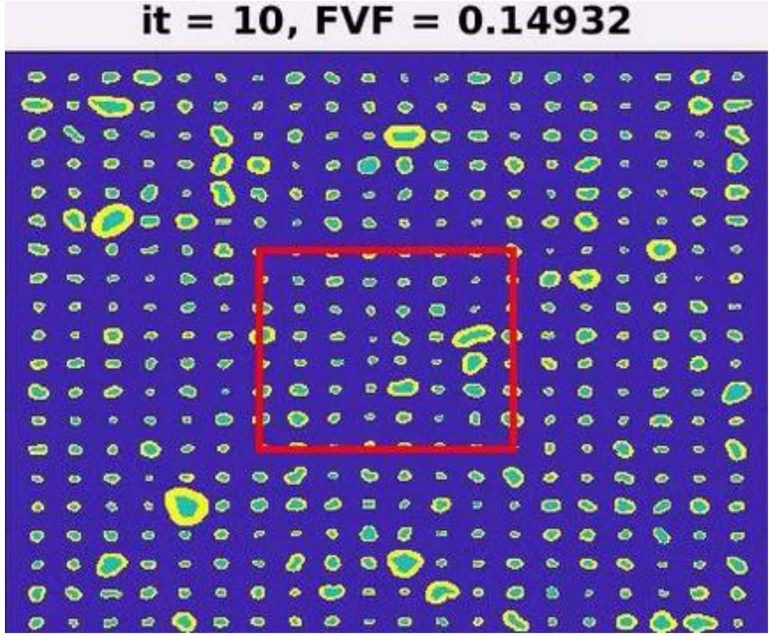
These metrics have an impact in the GRE signal,
And cylinders are not sufficient to describe it..

,Xu et al, MRM, 2017

Creating realistic White Matter models

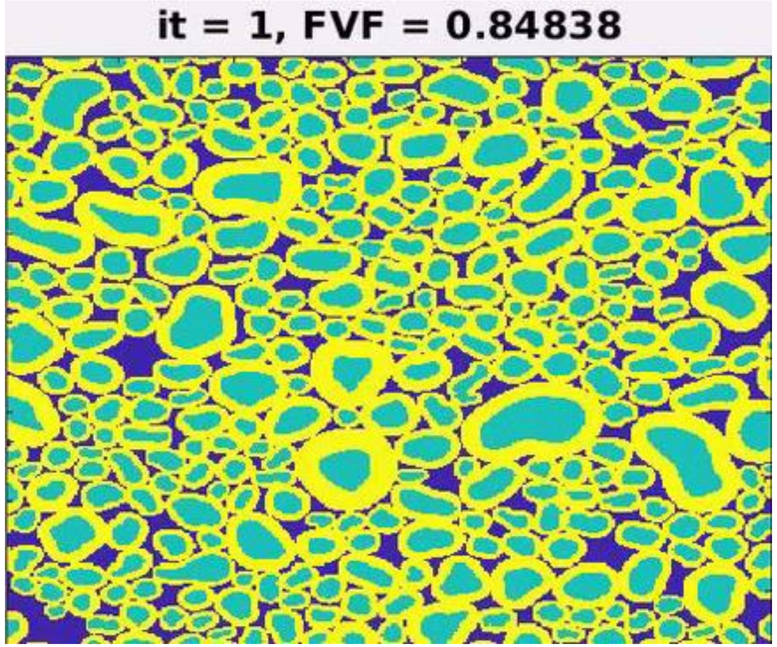
Axon packing

To create realistic WM models

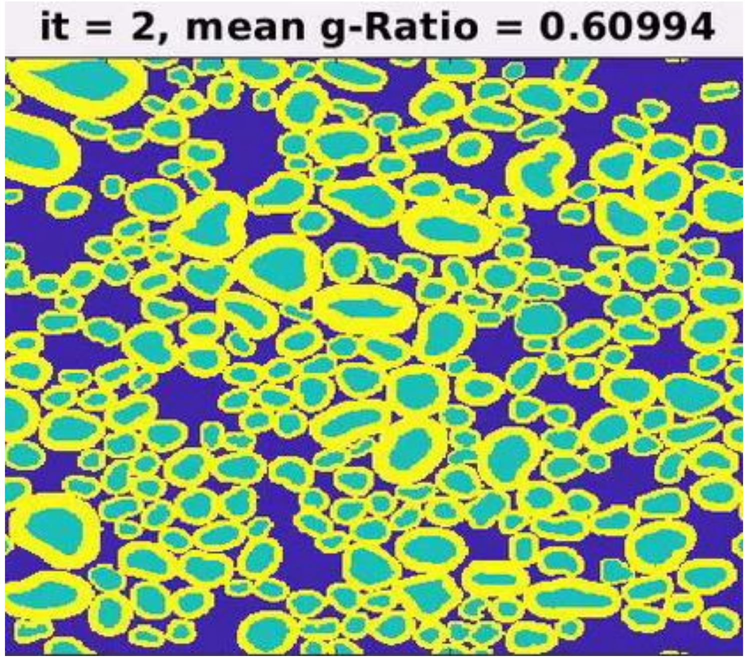


Axon removal

To be able to realistically modulate the FVF



g-factor modulation



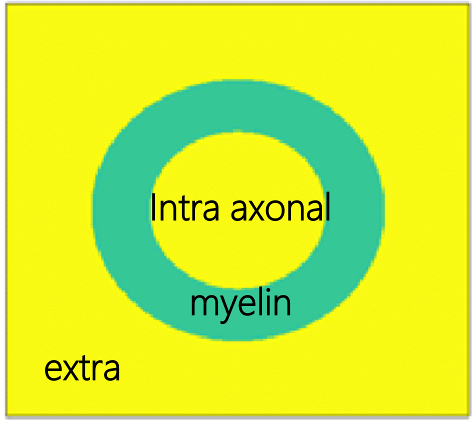
Hedouin, et al Neuroimage, 2021

Getting the model rigtht... (enough)

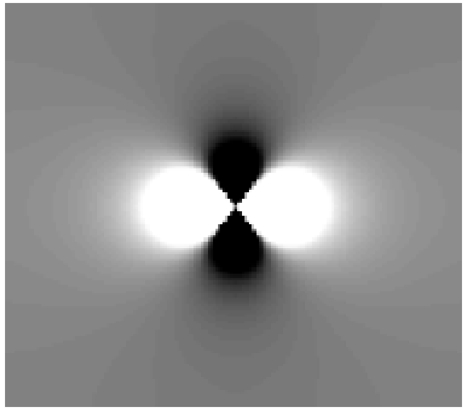
$\bar{\bar{\chi}}\,(r)$ $\quad D \quad$ $\Delta B_0(r)$

The Hollow cylinder model

Is "very" easy to compute

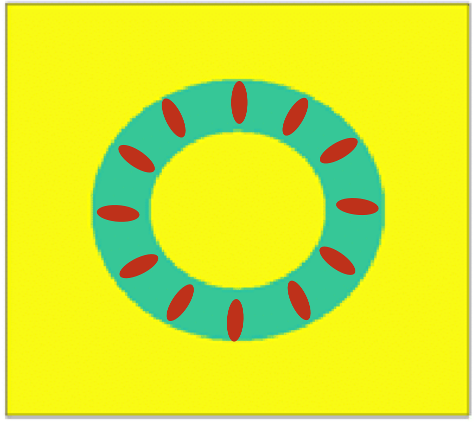


$\otimes$

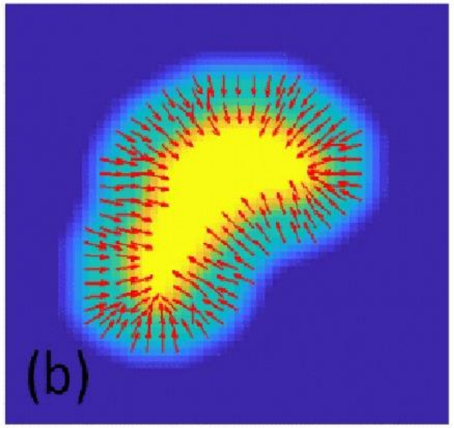


$=$

Yet water is not everywhere, not in the regions of susceptibility



Analytical Lorentzian correction



Axons are not cylinders...

Signal Simulation & Dictionary creation

Different

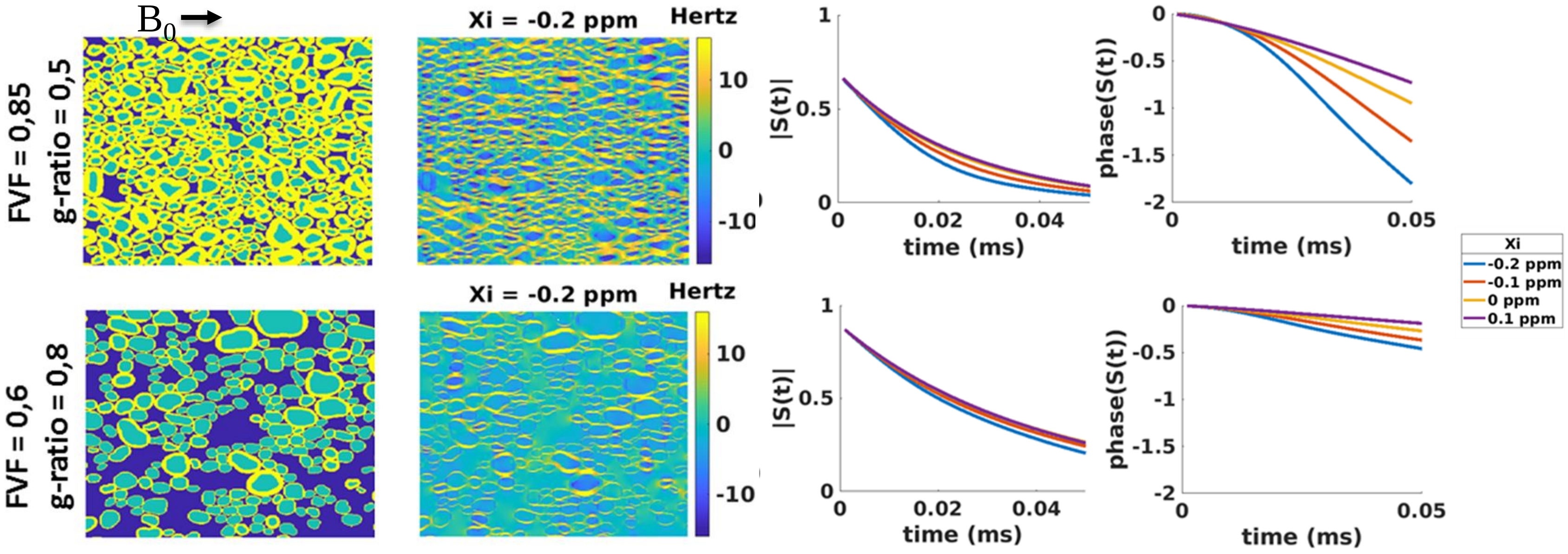
Microstructure

Parameters

different

Field perturbation

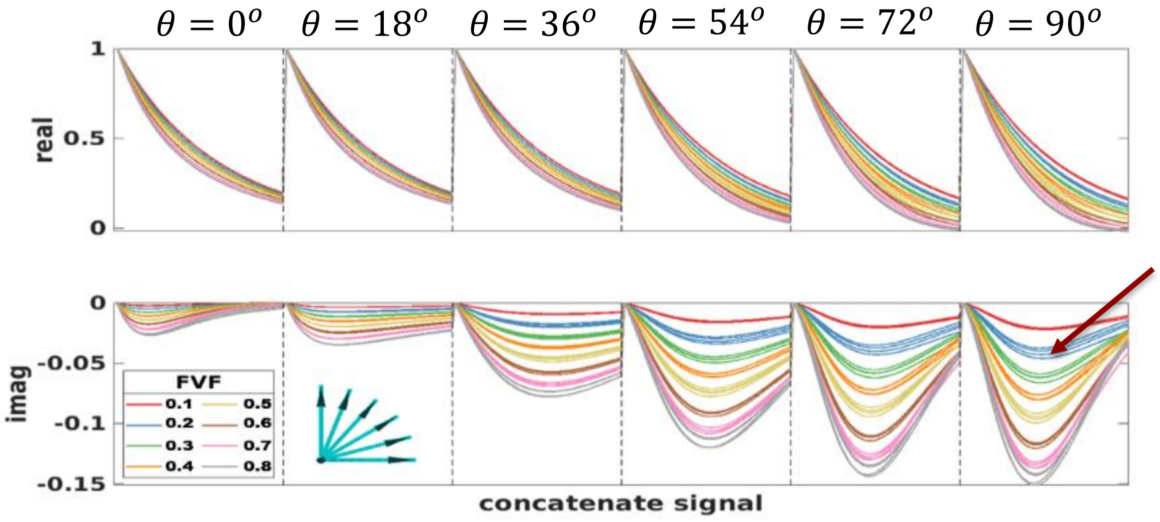
& GRE signal



Different white matter models

with same microstructural parameters

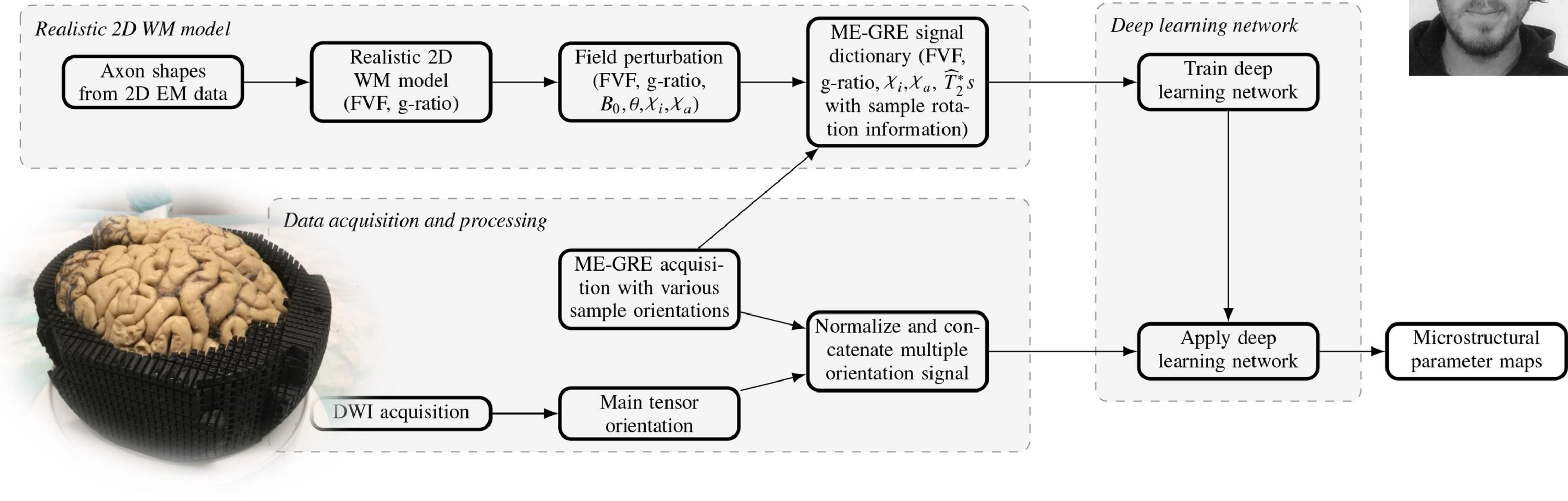
Result in similar signals



Different
Realistic
WM models

Neuroimage, 2021

Using Realistic White matter models for decoding microstructure

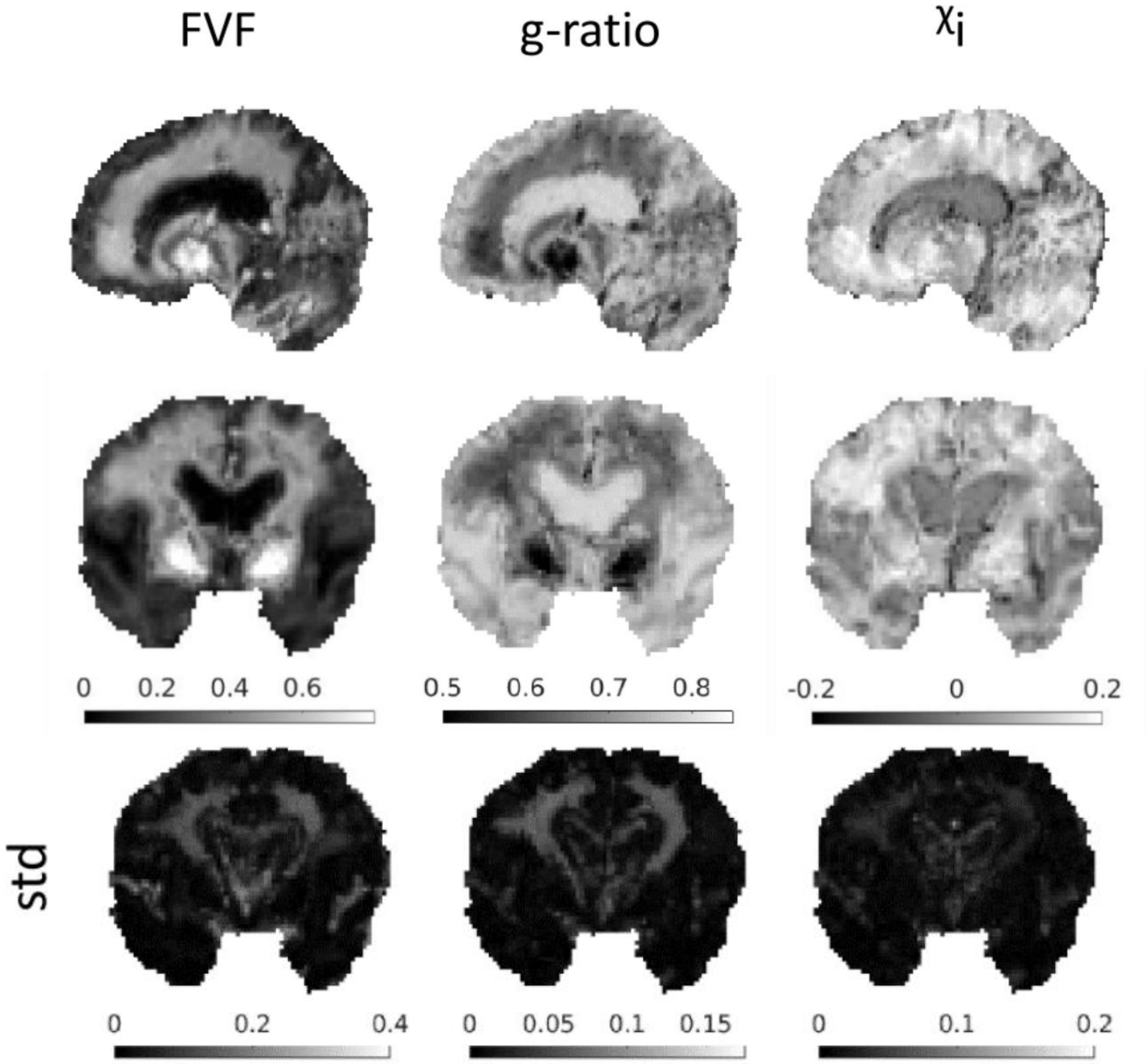


Microstrucutre property mapping

Whole brain maps decoded from 9 head positions

Whole brain maps decoded from 9 head positions

With different T1w



What can an MR Physicist do?

- Understanding how MRI works and the physical interactions in place can take you a long way

- Image reconstruction, motion correction, segmentation and quantitative imaging are being taken over by AI… But AI is better when it knows the right physics!

- Quantitative imaging and biophysical modelling – finding the right complexity balance:

- Share your code, it could help someone else!

Acknowledgements

Co-workers

- Kwok-Shing Chan
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- …

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FOM

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Thank you ☺

Radboud University Radboudumc