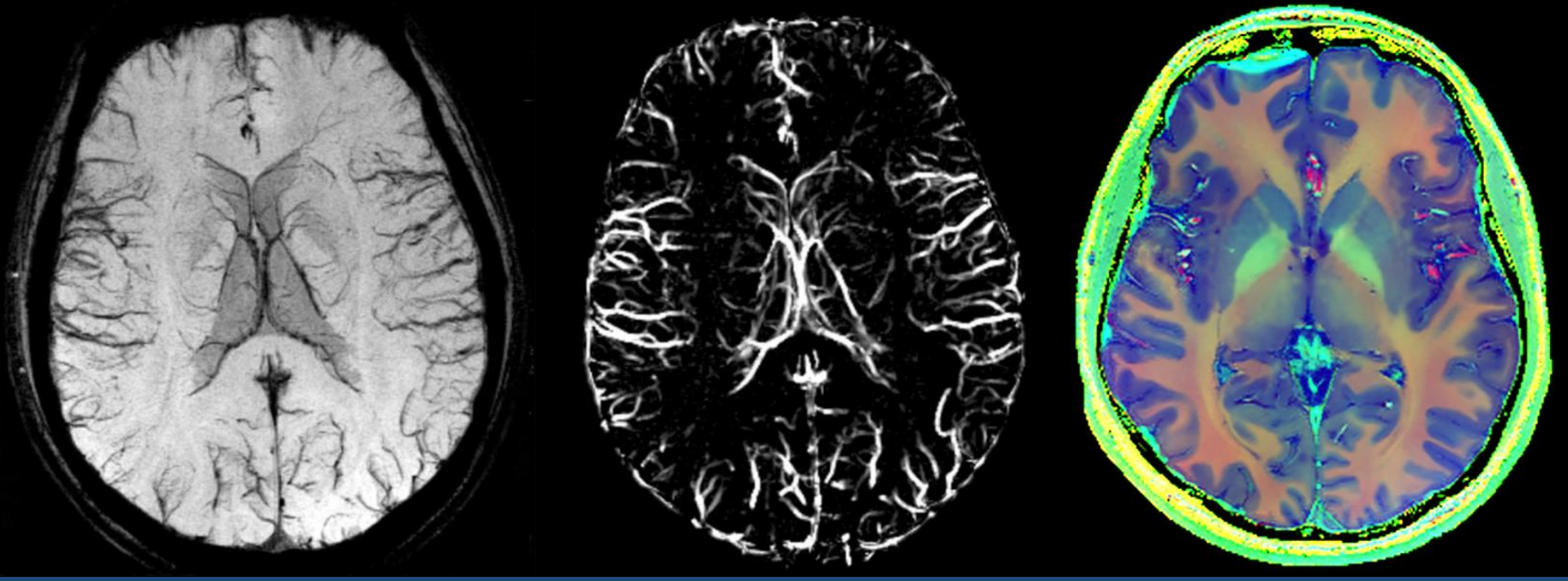

Relaxometry and QSM
The RESUME strategy for clinical qMRI

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ISMRM Italian Chapter

Per quanto concerne i moderatori, relatori, formatori, tutor, docenti è richiesta dall'Accordo Stato-Regioni vigente apposita dichiarazione esplicita dell'interessato, di trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali relativi agli ultimi due anni dalla data dell'evento. La documentazione deve essere disponibile presso il Provider e conservata per almeno 5 anni.

Dichiarazione sul Conflitto di Interessi

Il sottoscritto___Giuseppe Palma_____ in qualità di:

□ responsabile scientifico □ moderatore □ docente **X relatore** □ tutor

dell'evento "X CONGRESSO AIRMM - RISONANZA MAGNETICA IN MEDICINA 2019: DALLA RICERCA TECNOLOGICA AVANZATA ALLA PRATICA CLINICA"
Milano, 28-29 marzo 2019

da tenersi per conto di **Biomedia srl Provider n. 148,**

ai sensi dell'Accordo Stato-Regione in materia di formazione continua nel settore "Salute" (Formazione ECM) vigente,

Dichiara

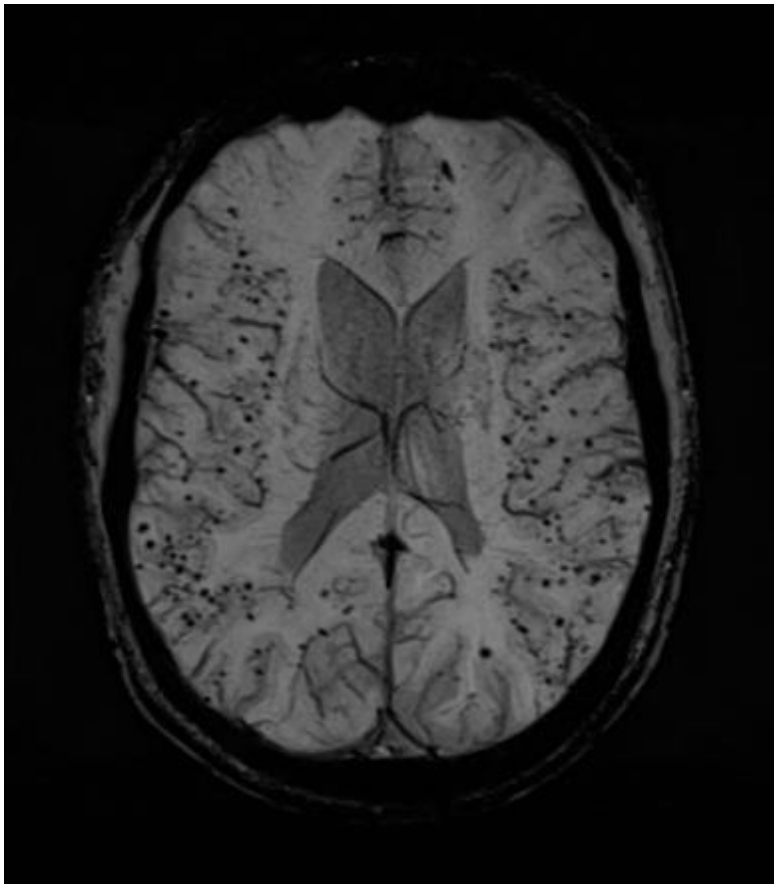
X che negli ultimi due anni NON ha avuto rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

□ che negli ultimi due anni ha avuto rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario (indicare quali):

_____ _____
_____ _____
_____ _____
_____ _____

SWI in the clinical practice

- In the last decade, SWI gained considerably increasing momentum in neuroimaging:
  - Low oxygen saturation or increased venous blood volume following stroke
  - Microbleeds from diffuse axonal injury in TBI
  - "Central vein sign" in MS lesions
  - Tumor characterization by evaluation of angiogenesis and venous drainage
  - …



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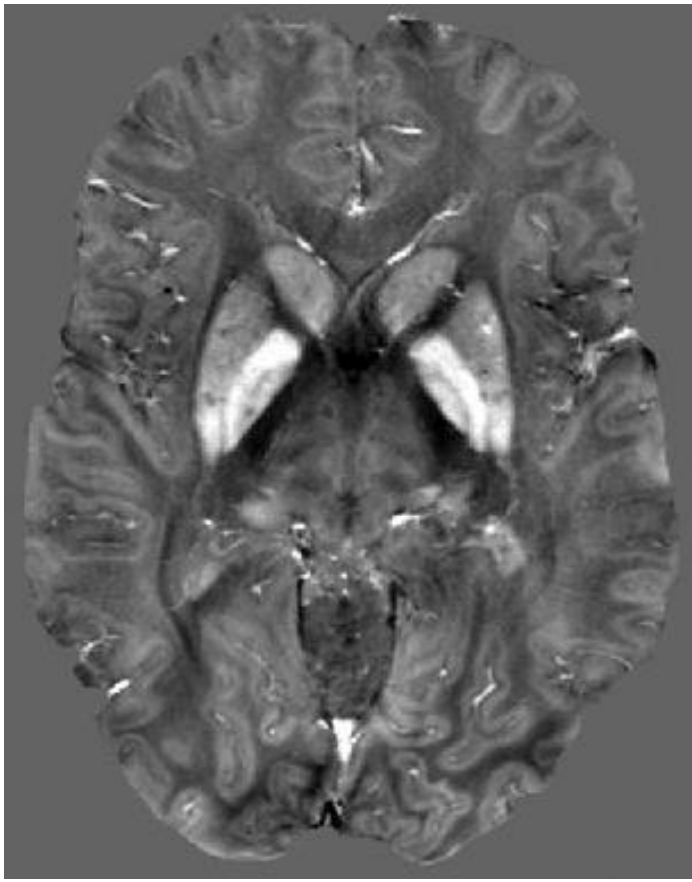
Mapping is better than weighting: QSM

- Phase images reflect the Larmor frequency variations resulting from the magnetization induced by B0, and some *other stuff*…
- Once we get rid of the *other stuff* by some pre-processing, and we assume a *fair behavior* of the tissue, we can enjoy a deconvolution to derive a susceptibility map:
  - Differentiation of paramagnetic (deoxyhaemoglobin, heamosiderin, iron deposits, …) from diamagnetic compounds (oxyhaemoglobin, apatite-like minerals, calcium deposits, …)
  - Absolute evaluation of tissue properties



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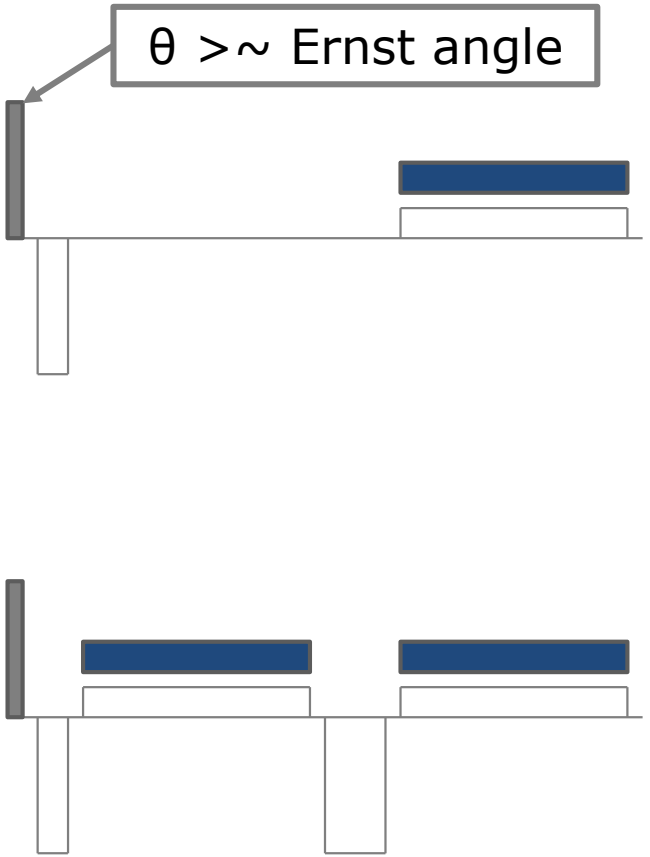
The sequence timing or: How to turn an SWI into a thorough susceptibility probe

- SWI (and to some extent QSM) commonly relies on a single echo spoiled GRE acquired at long T_E ~ 60 ms*T/B_0
- Except for few specific indications (mainly FC), it is a poor choice even at low acquisition BW
- Two (or more) monopolar echoes allow for:
  - A more accurate estimation of QSM
  - Mapping the free-induction decay rate (R_2^*)
- Same acquisition time!



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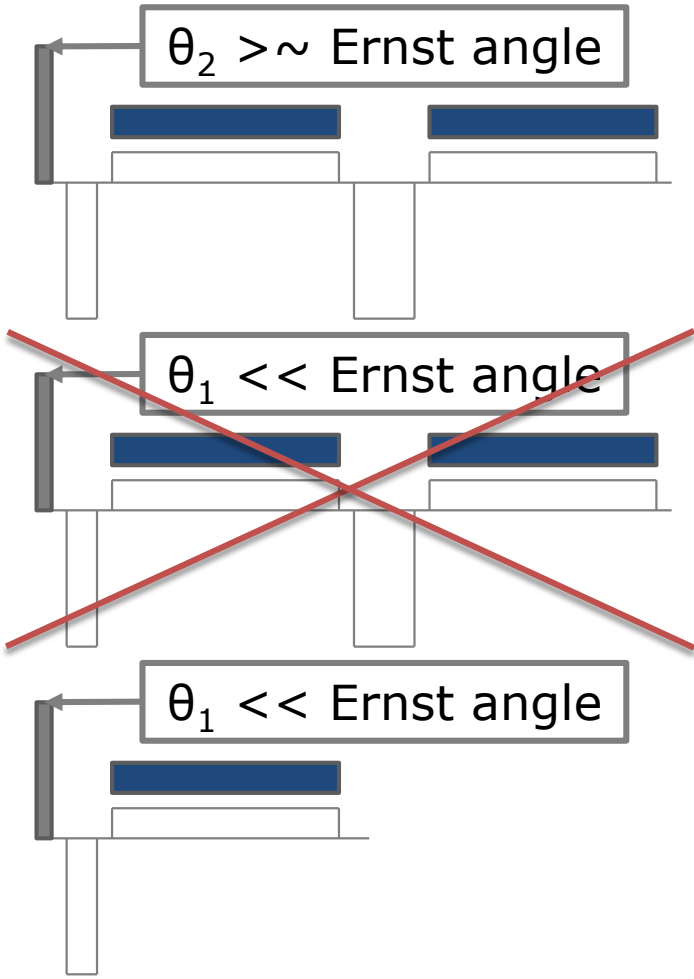
The cost of a comprehensive qMRI experiment

- In the classical **variable FA** scheme, R1 and PD maps would require a **doubled acquisition time**
- **RESUME** aims at turning an acquisition intended for SWI into a qMRI protocol providing full-resolution
  - QSM
  - R_2^* map
  - R_1 map
  - PD map
- The cost is an extra 50% acquisition time of the original SWI sequence



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R_2^*: the easy part

- A **general solution** for arbitrarily many echoes and variable acquisition BWs can be easily derived:

$$R_2^* = -\frac{\sum_{i=1}^{n} w_i (T_{E,i} - \overline{T}_E)(\log s_i - \overline{L})}{\sum_{i=1}^{n} w_i (T_{E,i} - \overline{T}_E)^2}$$

$$\overline{T}_E = \frac{\sum_{i=1}^{n} w_i T_{E,i}}{\sum_{i=1}^{n} w_i}, \qquad \overline{L} = \frac{\sum_{i=1}^{n} w_i \log s_i}{\sum_{i=1}^{n} w_i}, \quad \text{and} \quad w_i = \frac{1}{\mathrm{BW}_i \cdot s_i^2}$$

- In case of **double echo** acquisition, it reduces to the well-known solution

$$R_2^* = \frac{\log (s_1/s_2)}{T_{E,2} - T_{E,1}}$$

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R_1: dealing with $T_R/2$

- We can find an analytical solution, or rather two:

$$E_{1,0}^{\pm} = \frac{R \pm \sqrt{R^2 + 4C(q-k)}}{2C}$$

$$q = S_1/S_2$$

$$k = \frac{\sin\theta_1}{\sin\theta_2} \qquad C = q\cos\theta_1 - k\cos\theta_2 \qquad R = q(1-\cos\theta_1)$$

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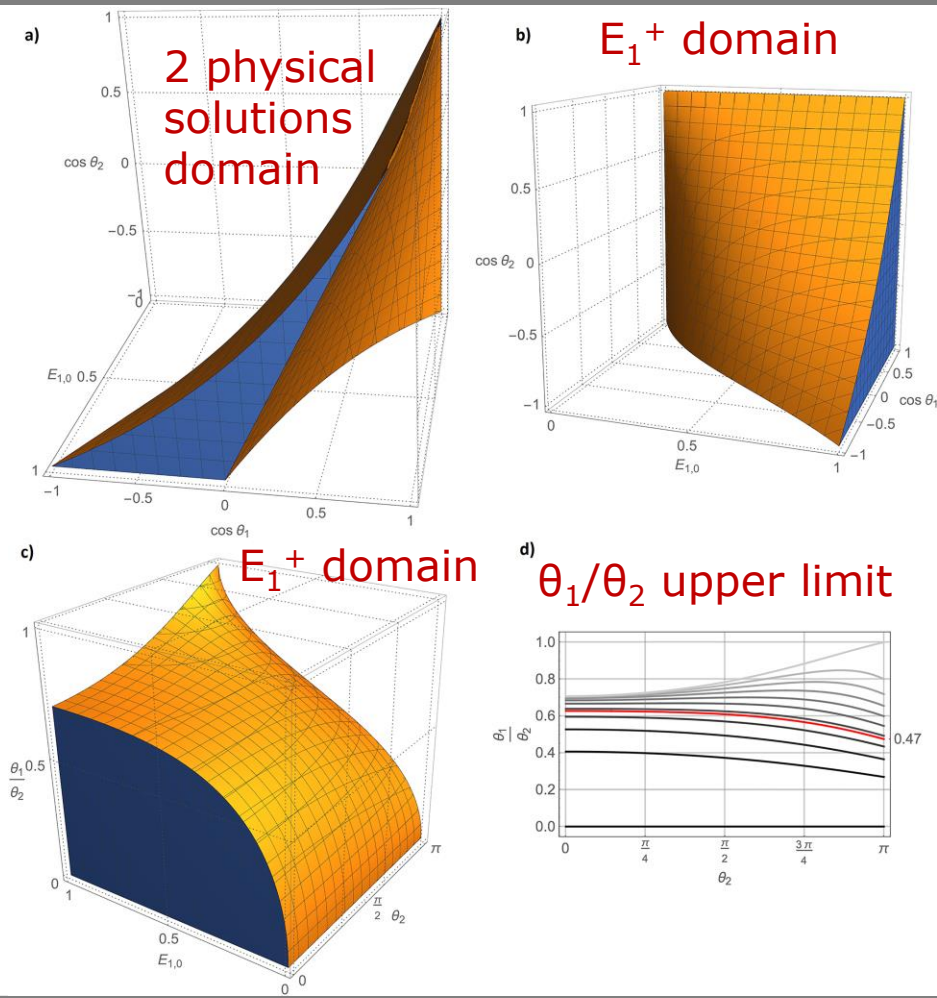
Houston…

- For some pairs (θ_1, θ_2) **both solutions** satisfy **$0 < E_1 < 1$**
- Typical 3D SWI T_R (< 50 ms) << T_1 (> 100 ms)
- The parameter space favorable to **E_1^+ is predominant**
- As long as $T_R < T_1$, θ_1 can be safely as high as $\theta_2/2$



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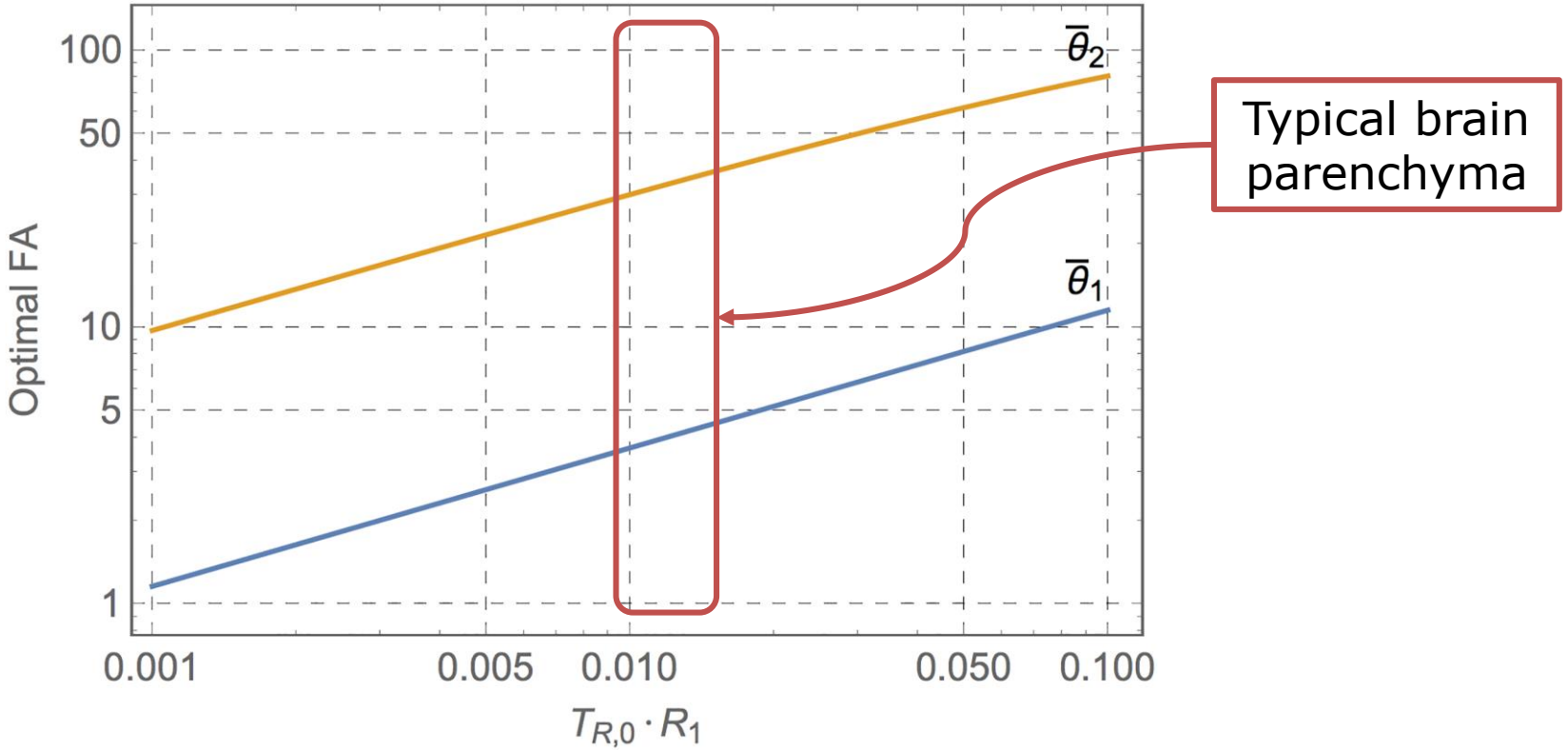
Optimal FAs for R_1 map

- The **optimal** pair **(θ_1, θ_2)** for a common RESUME protocol (single-GRE + **dual-GRE**) at constant acquisition BW is:



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PD map and QSM

- Once R_1 and R_2^* are known, **PD map** is trivial:

$$|K|M_0 = S_2 \cdot \frac{1 - E_{1,0}^2 \cos\theta_2}{\sin\theta_2 \cdot (1 - E_{1,0}^2)}$$

- There are plenty of techniques to derive **QSM**

NeuroImage 108 (2015) 111–122

Contents lists available at ScienceDirect

NeuroImage

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

A method for estimating and removing streaking artifacts in quantitative susceptibility mapping

Wei Li [*,a,b,c], Nian Wang [a], Fang Yu [d], Hui Han [a], Wei Cao [a,e], Rebecca Romero [f], Bundhit Tantiwongkosi [d], Timothy Q. Duong [b], Chunlei Liu [**,a,g]

Actual RESUME protocol

- **3D flow-compensated** sequences;
- Axial orientation (GRAPPA factor = 2);
- FOV: 230 (AP) x 194 (LR) x 166 (HF) mm^3;
- **Voxel**: **0.65** (AP) x **0.65** (LR) x **1.3** (HF) mm^3;
- Acquisition BW: 190 Hz/pixel;

Sequence	Acquisition Time	Provided Maps
Dual FC FLASH FA: 20°; T_R: 28 ms; T_E: [7 22] ms	4’ 46”	(SWI,) R_2^*, QSM
FC FLASH FA: 2°; T_R: 14 ms; T_E: 7 ms	2’ 23”	R_1, PD

- **Acquisition time** of complete protocol: **7’ 09”**.

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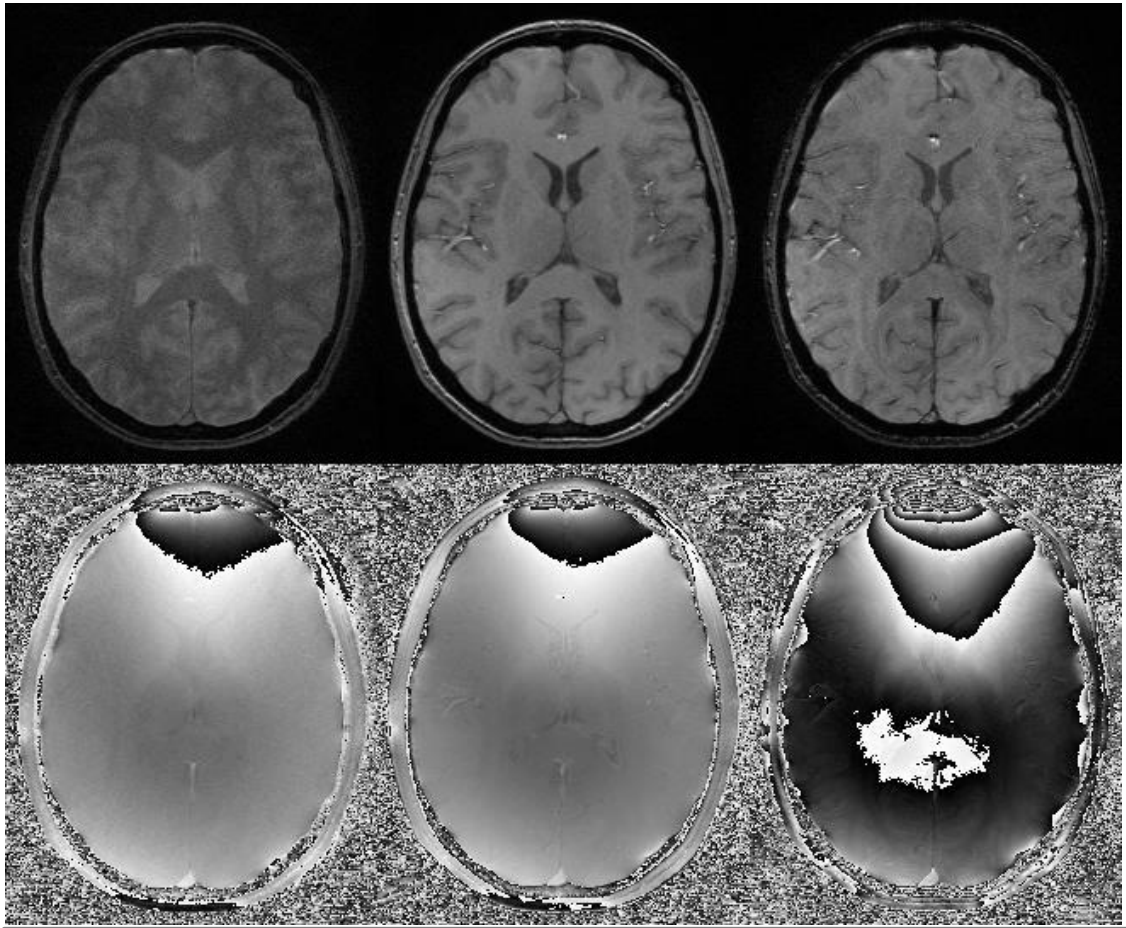
RESUME acquired datasets

FA=2; T_E=7 FA=20; T_E=7 FA=20; T_E=22

MAGNITUDE

PHASE



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Denoising: Self-tuning Multi-spectral Non-Local Means for parallel MRI

- A **self-tuning NLM** filter is designed to provide a homogeneous SNR improvement throughout the images:

$$\left[\mathrm{MNLM}_{\kappa,\rho,\varsigma}(X)\right]_m(\vec{x}) = Y_m(\vec{x}) = \frac{\int_{B_r[\vec{x}]} W_m(\vec{x},\vec{y}) X_m(\vec{y}) d\vec{y}}{\int_{B_r[\vec{x}]} W_m(\vec{x},\vec{y}) d\vec{y}}$$

$$W_m(\vec{x},\vec{y}) \equiv \exp\left[-\frac{d_\rho^2(\vec{x},\vec{y})}{\varsigma^2} \cdot \frac{Q_m(\vec{x})}{\sum_{l=1}^{M} Q_l(\vec{x})}\right] \qquad Q_m(\vec{x}) \equiv \frac{\int_\Omega X_m^2(\vec{y}) d\vec{y}}{\int_\Omega \sigma_m^2(\vec{x}) d\vec{y}}$$

Filter strength

$$d_\rho^2(\vec{x},\vec{y}) \equiv \sum_{m=1}^{M} \left\{ \int_{\mathbb{R}^N} \frac{\left|X_m(\vec{x}+\vec{t}) - X_m(\vec{y}+\vec{t})\right|^2}{\sigma_m^2(\vec{x}) + \sigma_m^2(\vec{y})} \cdot \frac{\exp -\frac{\|\vec{t}\|^2}{2\rho^2}}{\left(\sqrt{2\pi}\cdot\rho\right)^N} d\vec{t} \right\}$$

Similarity radius

Noise power maps

$$\int_{B_r[\vec{x}]} W_m(\vec{x},\vec{y}) d\vec{y} = \kappa$$

Search criterion

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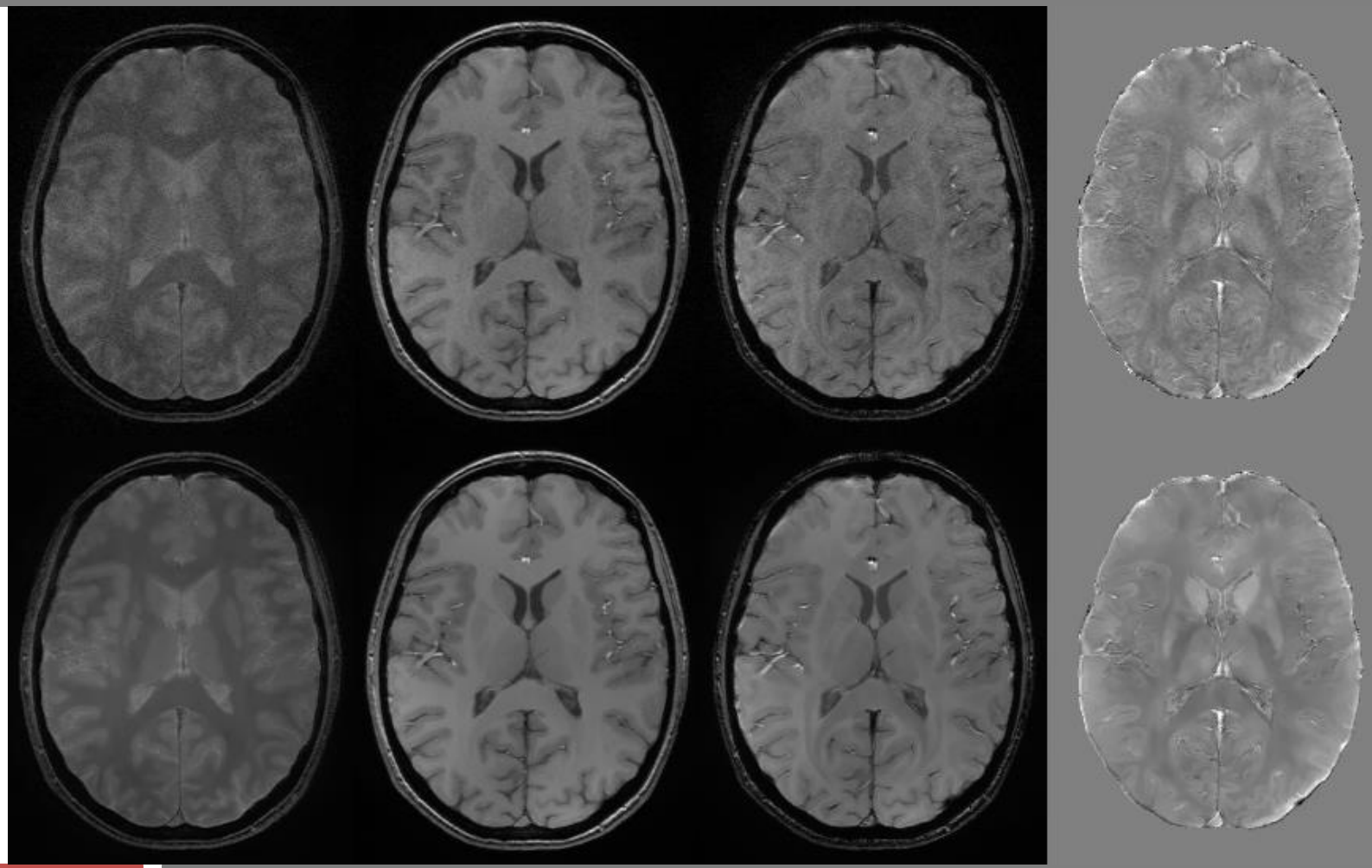
Do we really need denoising?

ORIGINAL

DENOISED



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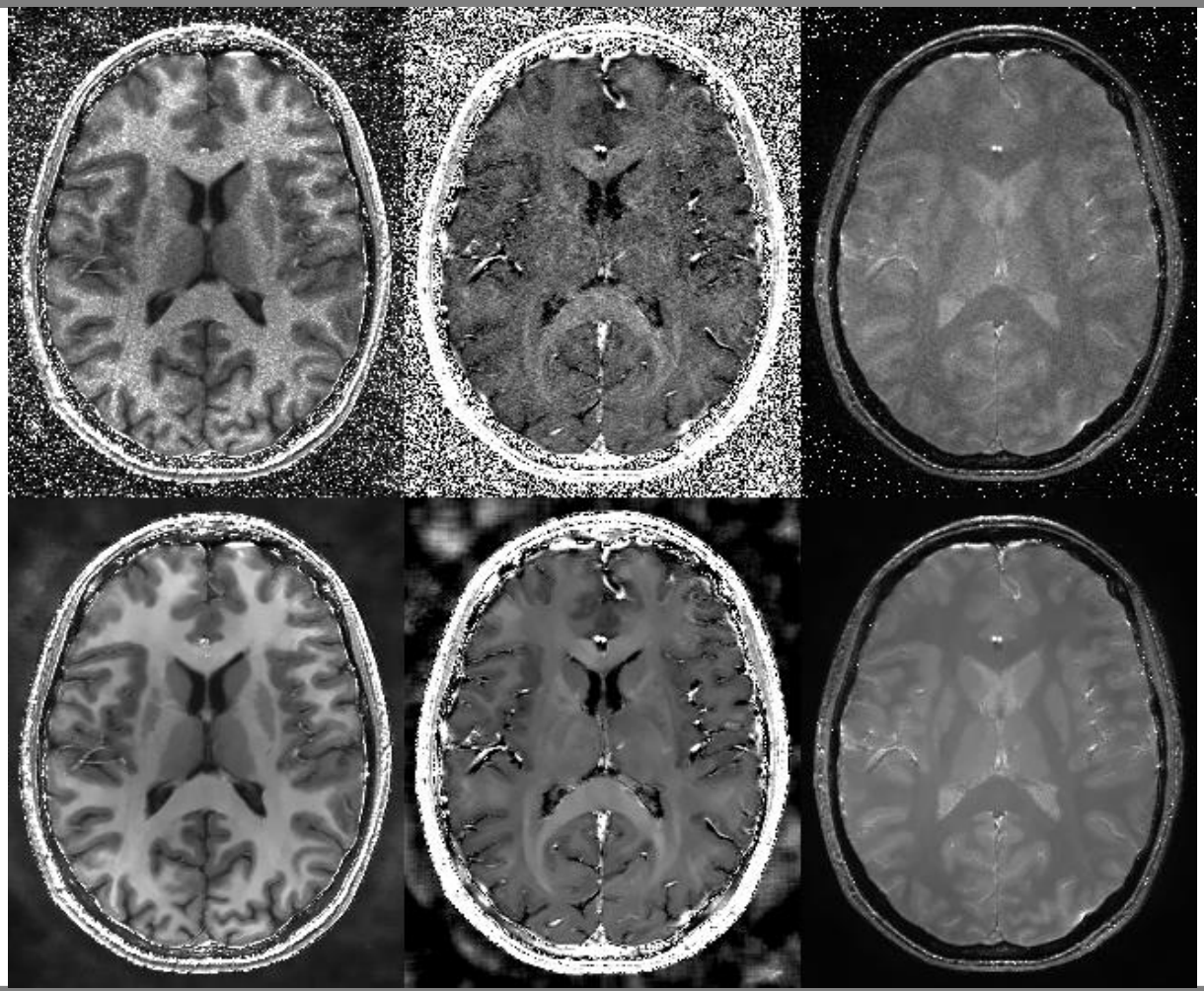
Yes, we probably do

RESUME(ORIGINAL)

RESUME(DENOISED)



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FA and B_1^- correction

- Both **R_1 and PD** estimation locally **depend on FA**:
  - B_1^+ inhomogeneity
  - RF pulse design
- **PD** estimation is also influenced by **B_1^-** profile
- Two scenarios:
  1. Analytical correction based on **FA/B_1^- mapping protocol**
     - Pro: Accurate map estimation
     - Cons: Additional scan time; potential ill-conditioned problem
  2. Iterative correction based on the **minimization of the entropy** of the joint histogram
     - Pro: No special protocols/sequences required
     - Con: Potential underfitting or removal of actual low frequency variations

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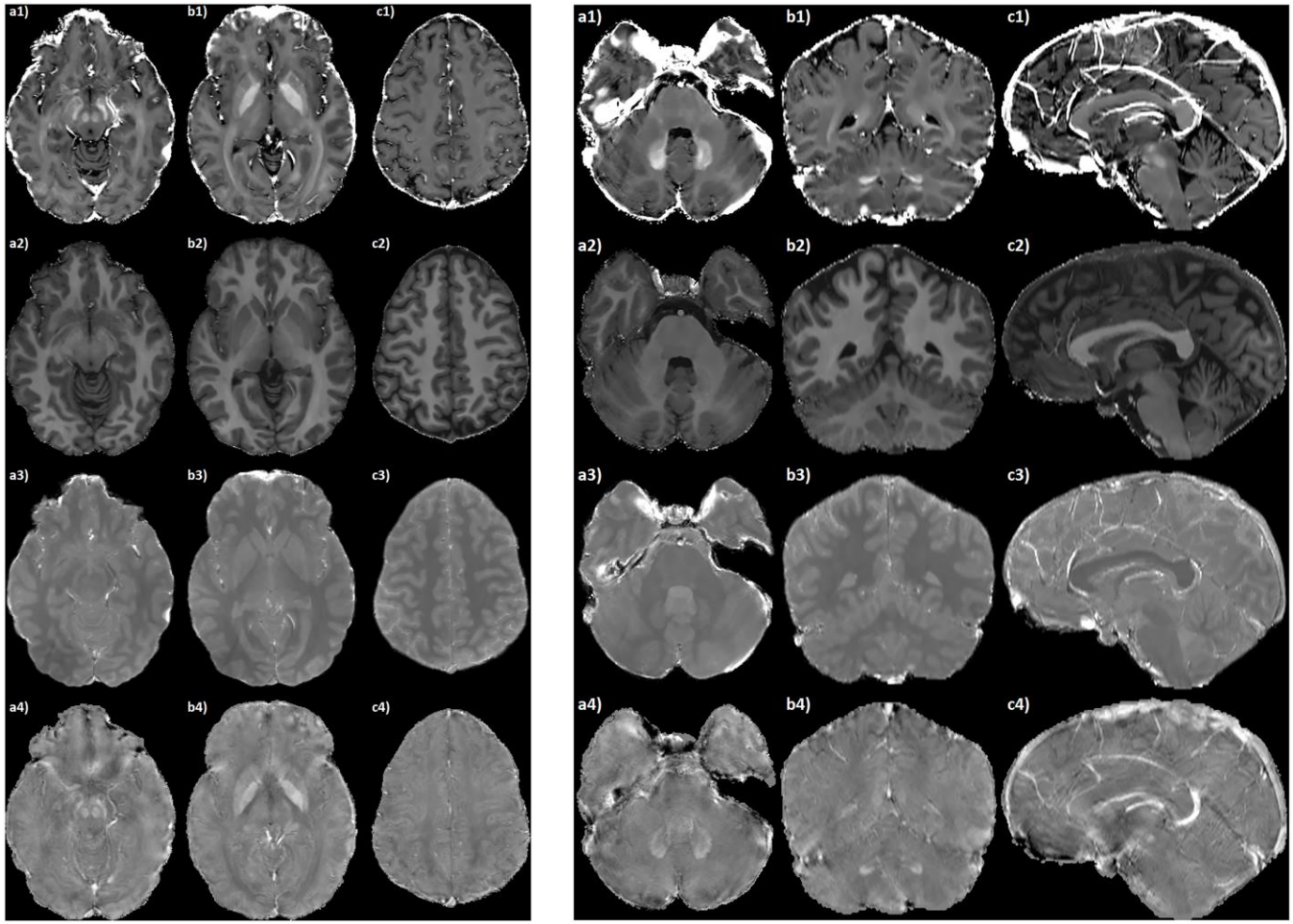
The maps @ 3T, 8-Channel Coil

R_2^*

R_1

PD

QSM



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Comparison with other methods

	R_1 (s^{-1})	R_2^* (s^{-1})	PD (CSF)	QSM · 10^9
White matter	1.08 ± 0.10	21.1 ± 1.1	0.718 ± 0.015	−5 ± 10
	1.07 ± 0.11 (Ref)	21.2 ± 1.2 (Ref)	0.699 ± 0.016 (Ref)	−2 ± 13 (Ref)
	1.036 ± 0.036 [39]	21.0 ± 0.8 [39]	0.742 ± 0.070 [39]	−18 ± 9 [40]
	1.190 ± 0.071 [41]		0.683 ± 0.006 [42]	
Cortical grey matter	0.624 ± 0.032	15.1 ± 1.6	0.852 ± 0.037	23 ± 30
	0.603 ± 0.045 (Ref)	14.6 ± 1.9 (Ref)	0.840 ± 0.043 (Ref)	21 ± 27 (Ref)
	0.609 ± 0.008 [39]	15.2 ± 0.4 [39]	0.796 ± 0.078 [39]	16 ± 10 [40]
	0.622 ± 0.043 [41]		0.844 ± 0.019 [42]	
Head of caudate nucleus	0.625 ± 0.054	20.2 ± 1.6	0.883 ± 0.019	68 ± 31
	0.615 ± 0.046 (Ref)	19.5 ± 1.4 (Ref)	0.860 ± 0.039 (Ref)	66 ± 29 (Ref)
	0.683 ± 0.022 [39]	18.2 ± 1.2 [39]	0.851 ± 0.084 [39]	60 ± 30 [43]
	0.719 ± 0.025 [41]		0.827 ± 0.016 [42]	78 ± 32 [44]
Putamen	0.663 ± 0.052	23.0 ± 2.0	0.886 ± 0.013	29 ± 16
	0.656 ± 0.051 (Ref)	22.8 ± 1.2 (Ref)	0.865 ± 0.018 (Ref)	30 ± 15 (Ref)
	0.752 ± 0.040 [41]	30.6 ± 4.7 [45]		70 ± 20 [40]
	0.70 ± 0.05 [46]			40 ± 20 [43]

https://doi.org/10.1371/journal.pone.0189933.t001

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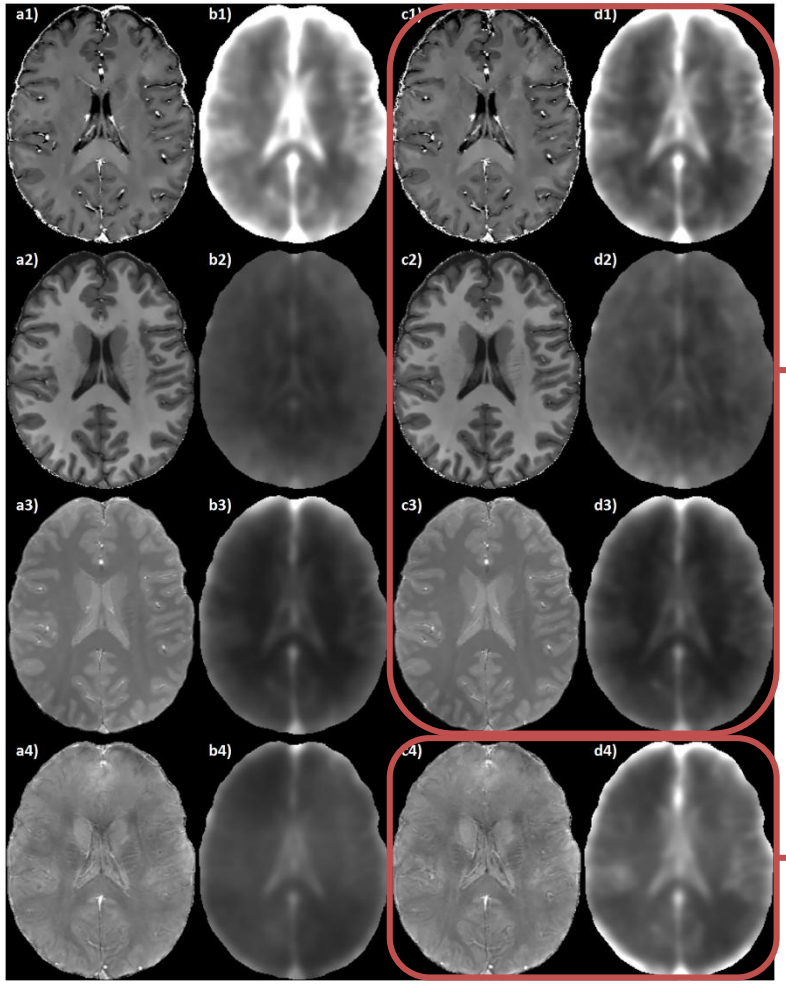
Test-retest variability and accuracy

RESUME 20*σ Ref 20*δ



R_2^*

R_1

PD

QSM

Variable FAs

8 echoes

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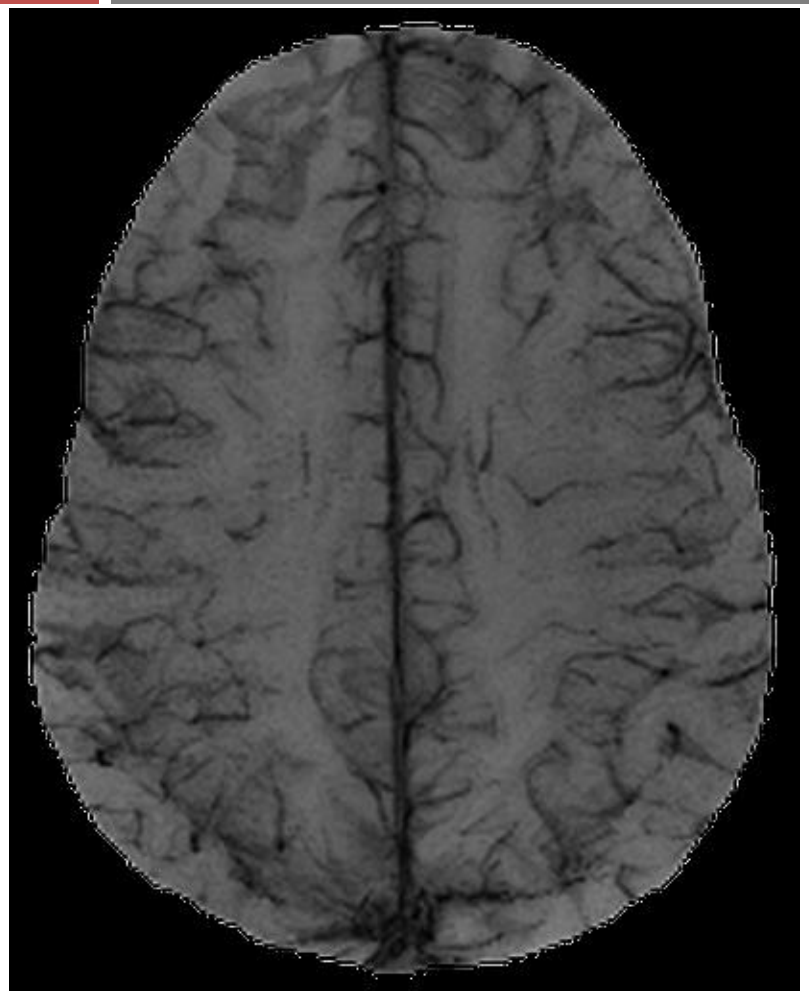
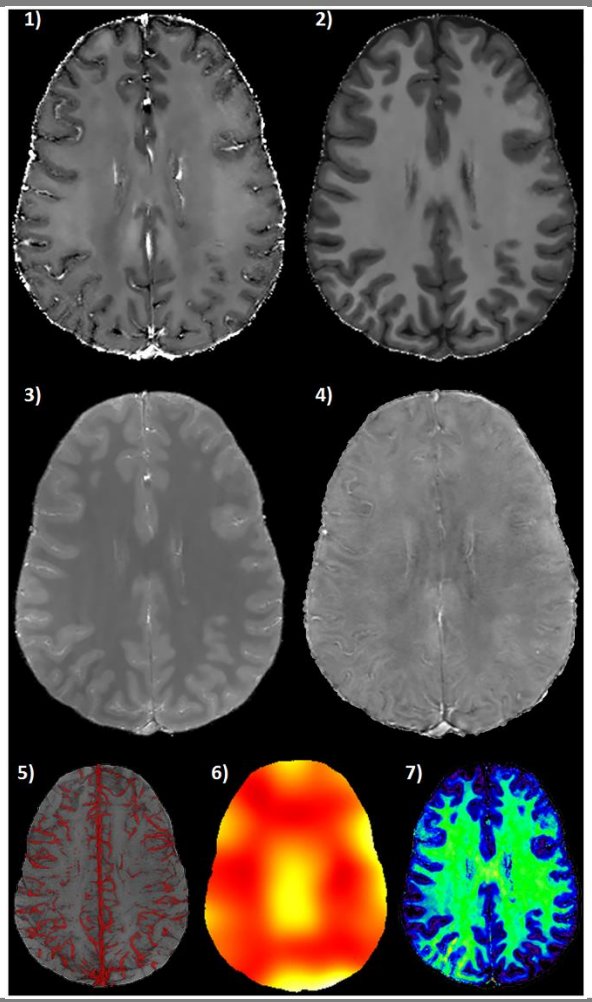
We have a choice

4’ 46”



OR

7’ 09”



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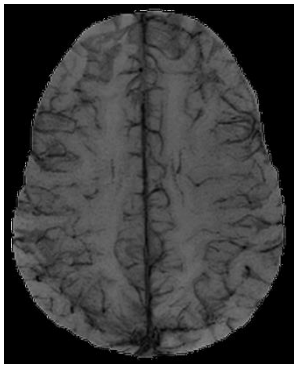

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Clinical and research opportunities: present and future

- Mineral metabolism
  - Iron build up in the DGM of patients with neurodegenerative disorders (*e.g.*, Parkinson's disease, Huntington's disease, Friedreich ataxia, …)
  - Iron build up in the DGM of patients with neuroinflammatory disorders (*i.e.*, MS)
  - Calcium accumulation (Fahr's disease, Fabry's disease, …)
- Vein segmentation (*e.g.*, central vein sign)
- Absolute estimates of contrast agent (*e.g.*, Gd) within tissues
- Lipid accumulation in metabolic disorders (*e.g.*, Gaucher's disease)

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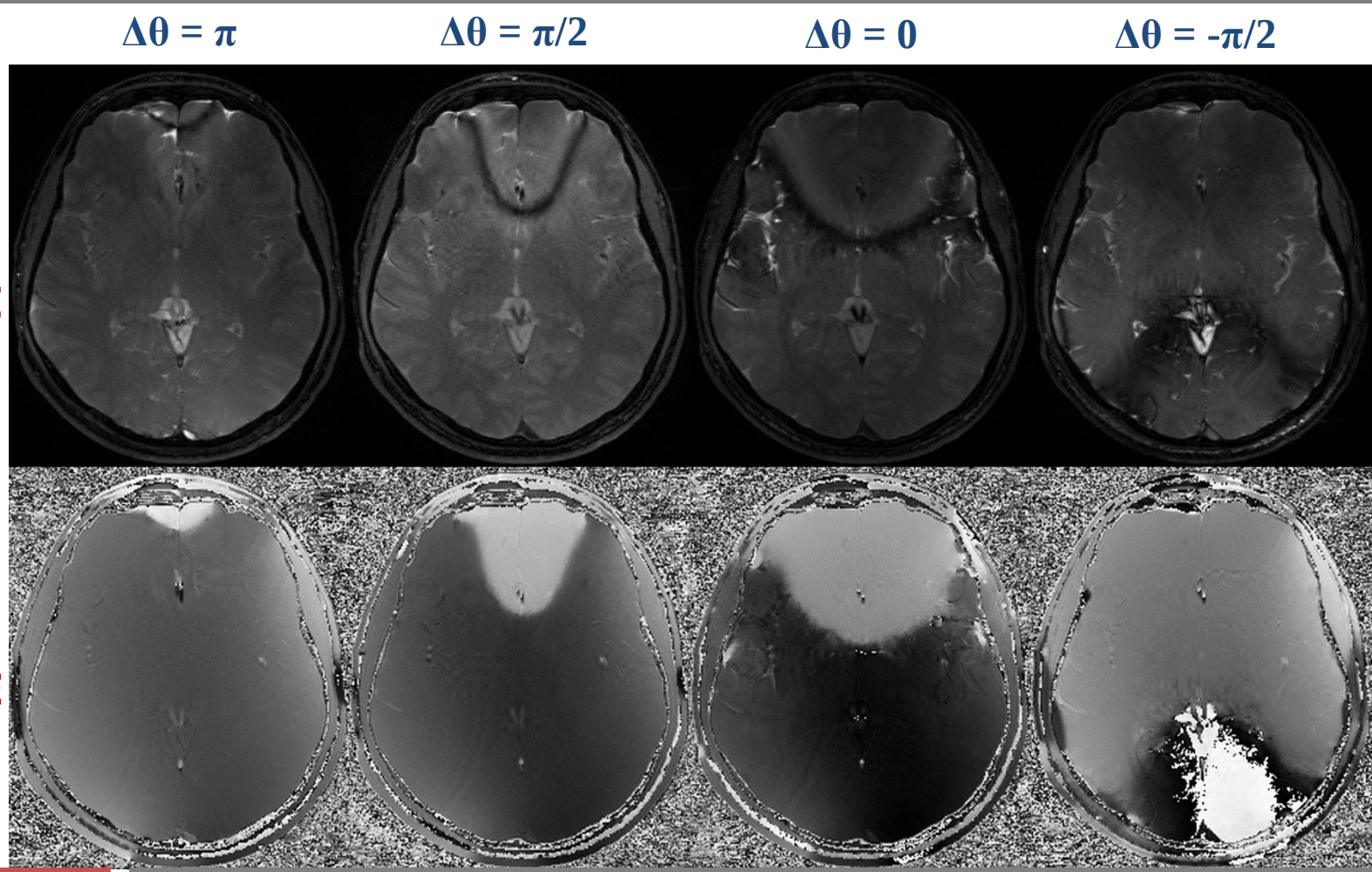
An optional R_2 module: 3D bSSFPs



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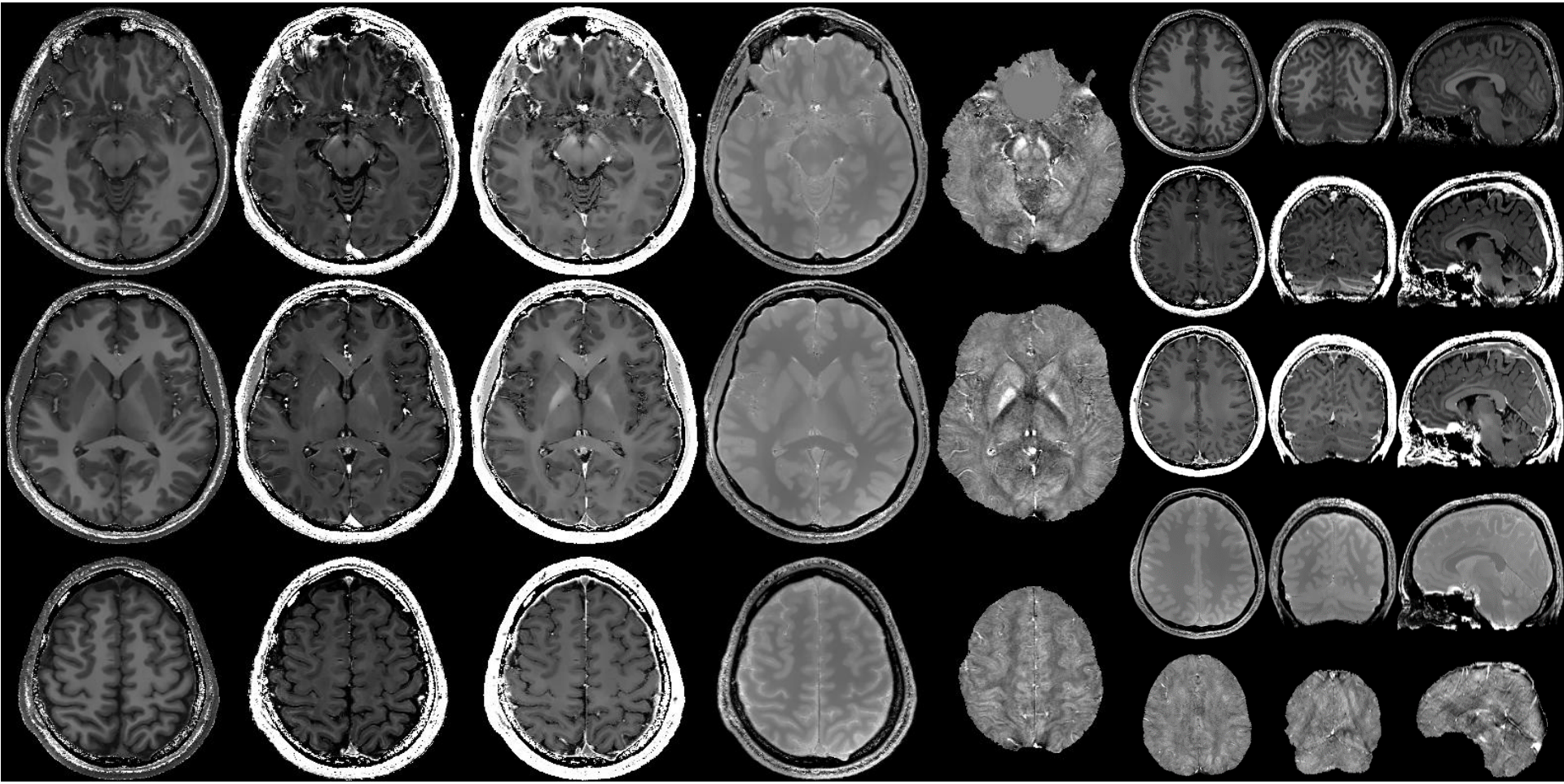
Extended RESUME



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Take home messages

- Low cost **extension of an SWI** protocol
- R_1, (R_2,) R_2^*, proton density and susceptibility quantitation
- **3D** full brain mapping with voxels of **0.6 mm³** in **7'** (10' extended RESUME)
- **No bias** due to intra-voxel FA variation (**imperfect 2D RF-pulses**)
- **Compared to** unbalanced SSFP relaxometry (**TESS**):
  - No Flow Sensitivity (CSF, blood) → Brain imaging
- **Compared to DESPO** methods:
  - Fully **analytical solution** of the relaxometry equations
  - **No** need to acquire **high-FA bSSFP**:
    - **No SAR** issues
    - **No periventricular** flow artifacts (**ghosts**) that mimic demyelinating lesions

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Thanks for your attention

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  - **Serena Monti**, PhD

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