LIÈGE université
GIGA
CRC In vivo Imaging

Quantitative MRI,
EM head modelling and more,
practical considerations and applications

Christophe Phillips, Ir Ph.D.
c.phillips@uliege.be

fnrs
LA LIBERTÉ DE CHERCHER

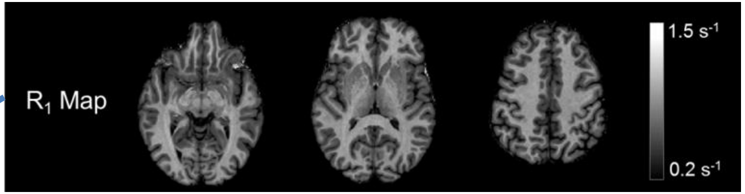
Program

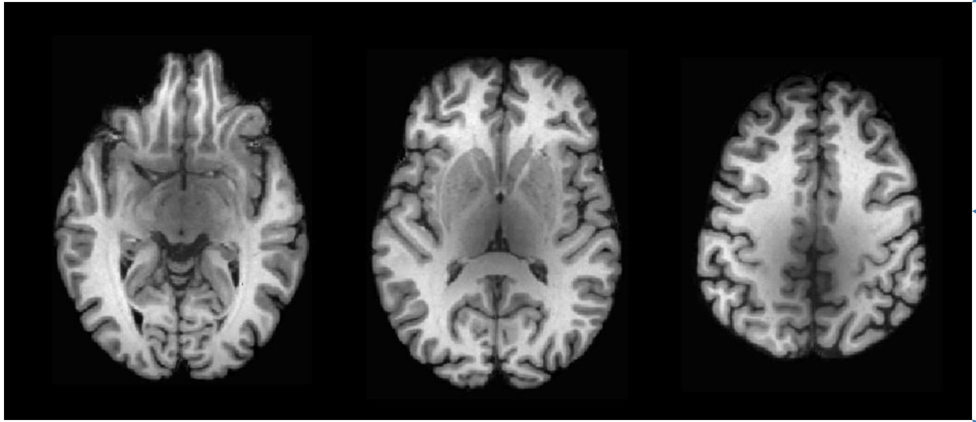
- Quantitative MRI
  - Introduction
  - Multiple sclerosis application
- EM head modelling… and more

Anatomical vs quantitative MR imaging

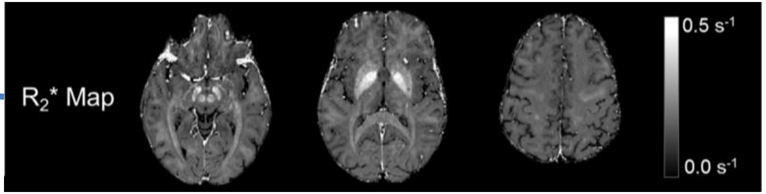
SI_{MPRAGE} = f (sequence parameters,
scanner hardware,
physical MRI parameters)

Longitudinal Relaxation Rate

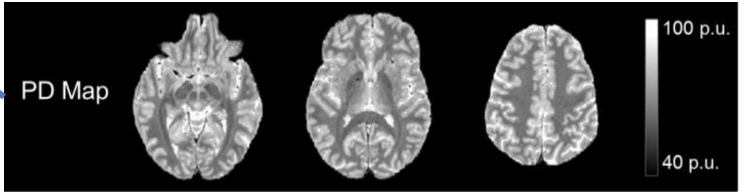




Effective Transverse Relaxation Rate

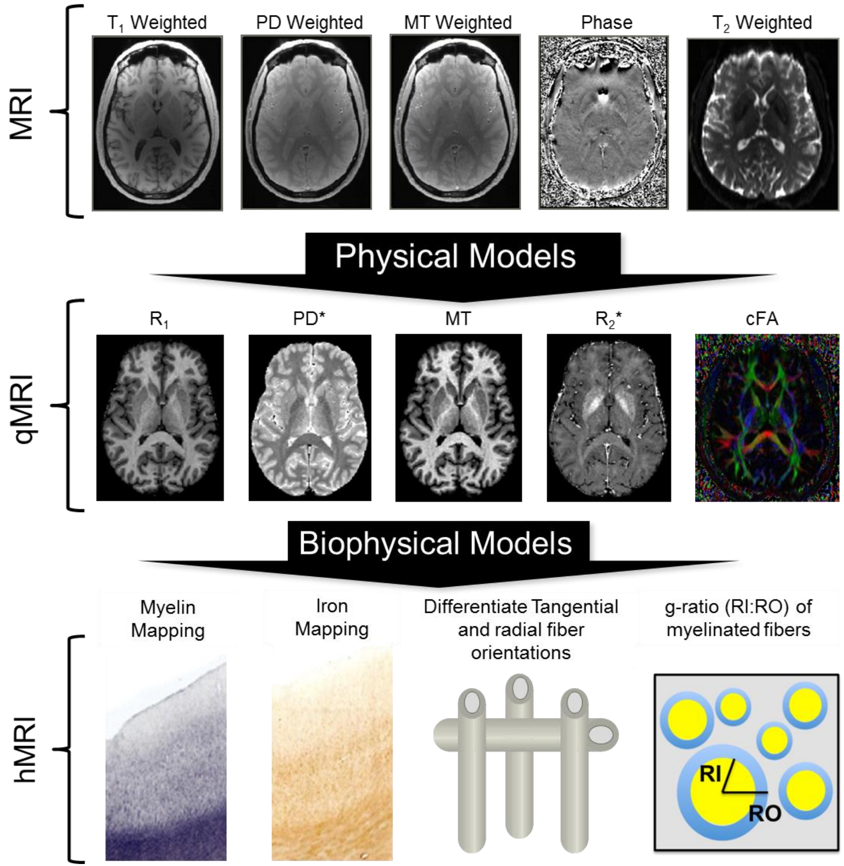


Proton Density



⇒ Quantitative MRI &
Voxel-Based Quantification

In vivo histology using MRI (hMRI)

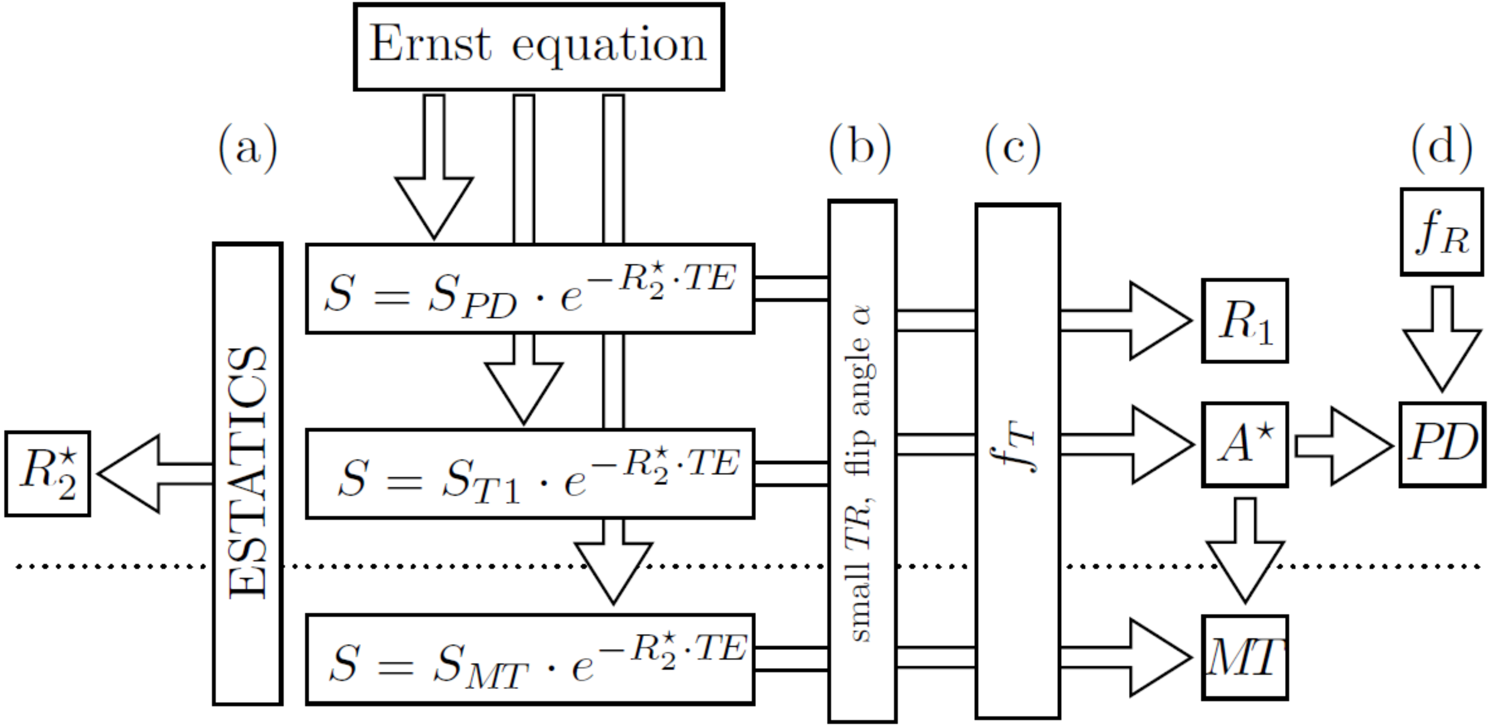


Begin by getting quantitative maps of specific parameters

The ultimate target is biological mapping

Weiskopf *et al.*, https://doi.org/10.1097/WCO.0000000000000222

Multi-Parameter Mapping (MPM) Protocol



Weiskopf *et al.*, https://dx.doi.org/10.3389%2Ffnins.2013.00095

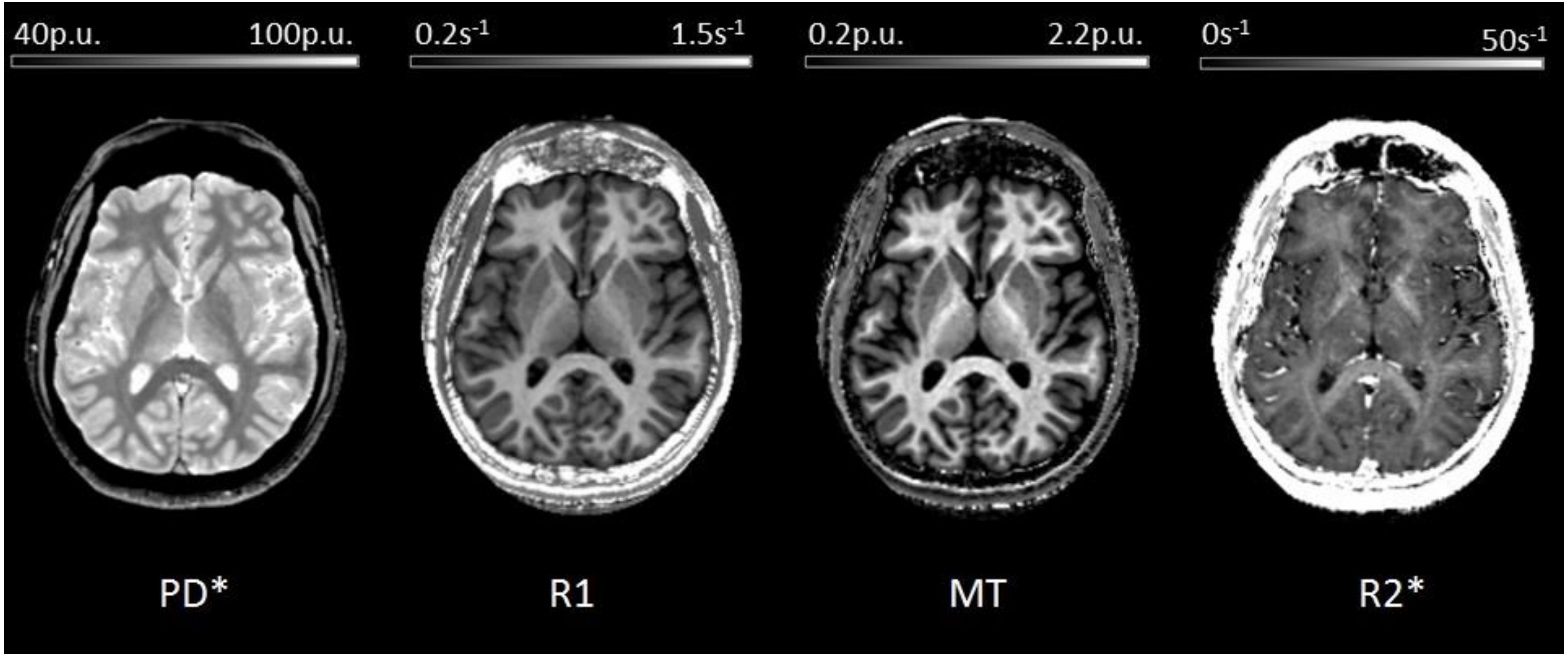
qMRI interpretation

Water Content

Water Content; Macromolecules, e.g. myelin; Iron

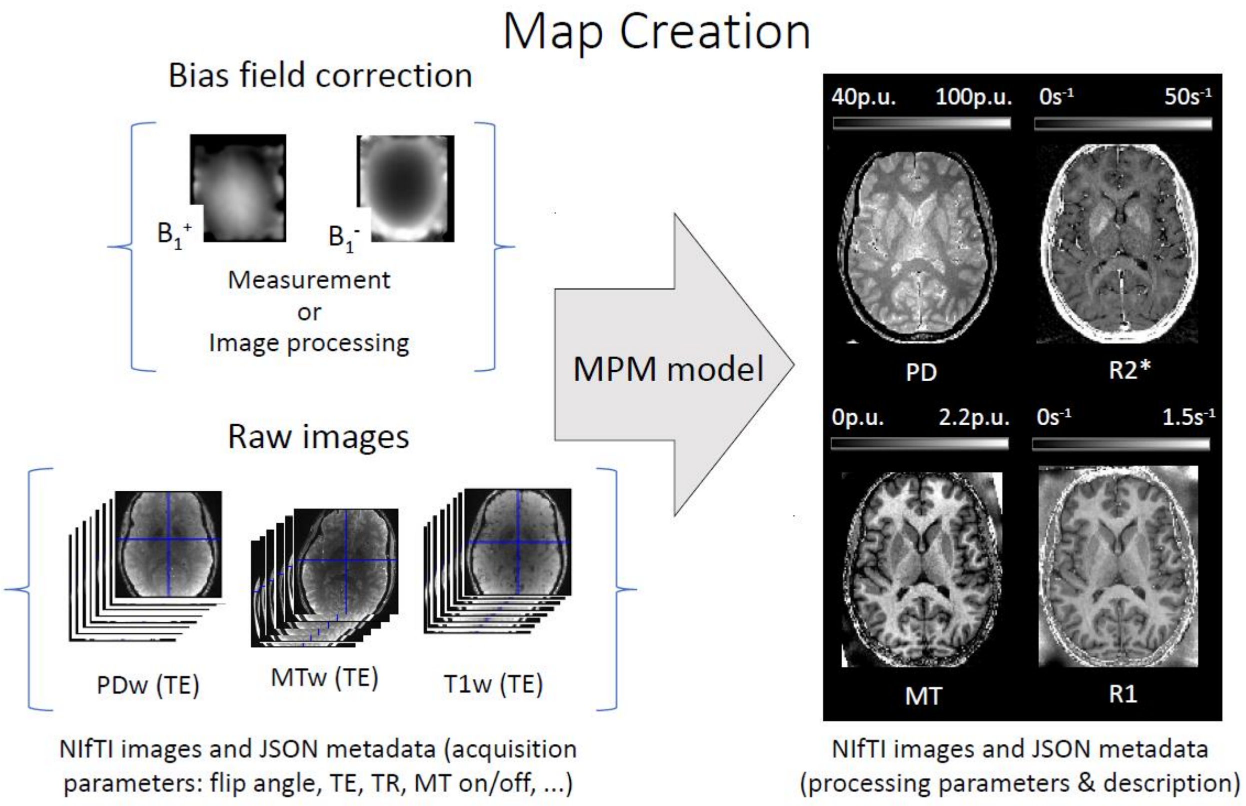
Macromolecules e.g. myelin

Iron



Weiskopf *et al.*, https://doi.org/10.1038/s42254-021-00326-1

Multi-Parameter Mapping (MPM) Protocol



Weiskopf *et al.*, https://dx.doi.org/10.3389%2Ffnins.2013.00095

Raw data are messy…

qMRI relies on

- multiple series of images (different weighting & field maps)
- specific acquisition parameters (echo times, flip angles,…)

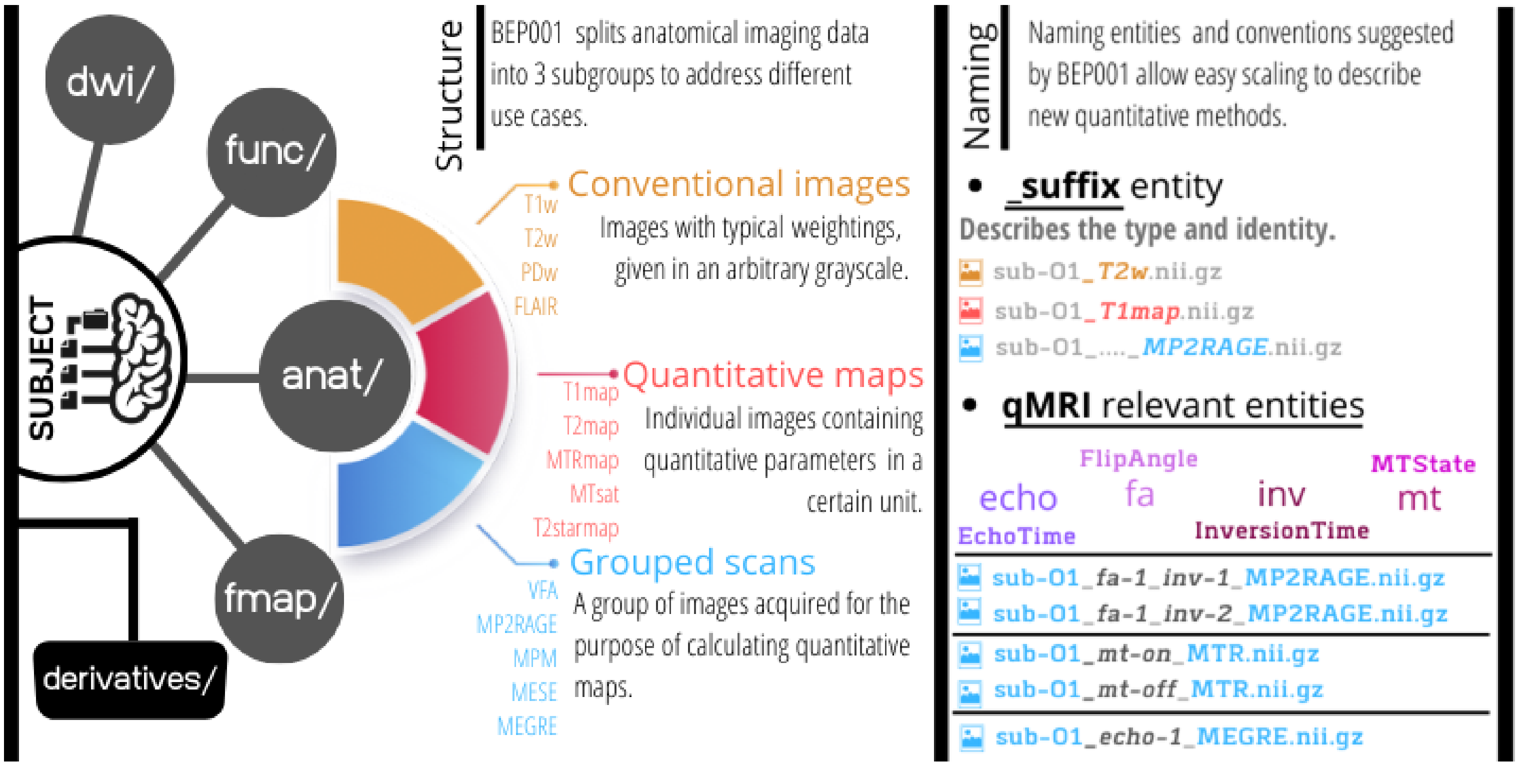
Image Series No.	Sequence Name	Description
4	mfc_seste_b1map_v1e	B_1^+ Mapping Data
5	gre_field_mapping_1acq_rl	B_0 Mapping Magnitude
6	gre_field_mapping_1acq_rl	B_0 Mapping Phase Difference
7	mfc_smaps_v1a_Array	Net Receive Sensitivity Mapping of Array
8	mfc_smaps_v1a_QBC	Net Receive Sensitivity Mapping of Body Coil
9	pdw_mfc_3dflash_v1i_R4	Lower flip angle multi-echo FLASH
Participant moved to new position via primary rotation about z		
10	mfc_smaps_v1a_Array	Net Receive Sensitivity Mapping of Array
11	mfc_smaps_v1a_QBC	Net Receive Sensitivity Mapping of Body Coil
12	mtw_mfc_3dflash_v1i_R4	FLASH acquisition with MT pre-pulse
Participant returned to approximate alignment with the original position		
13	mfc_smaps_v1a_Array	Net Receive Sensitivity Mapping of Array
14	mfc_smaps_v1a_QBC	Net Receive Sensitivity Mapping of Body Coil
15	t1w_mfc_3dflash_v1i_R4	Higher flip angle multi-echo FLASH

- hmri_sample_dataset_with_maps
  - gre_field_mapping_1acq_rl_0005
  - gre_field_mapping_1acq_rl_0006
  - mfc_seste_b1map_v1e_0004
  - mfc_smaps_v1a_Array_0007
  - mfc_smaps_v1a_Array_0010
  - mfc_smaps_v1a_Array_0013
  - mfc_smaps_v1a_QBC_0008
  - mfc_smaps_v1a_QBC_0011
  - mfc_smaps_v1a_QBC_0014
  - mtw_mfc_3dflash_v1i_R4_0012
  - pdw_mfc_3dflash_v1i_R4_0009
  - t1w_mfc_3dflash_v1i_R4_0015

Name	Type	Size
anon_s2018-02-28_18-26-190921-00001-00224-1.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-00224-1.nii	NII File	39.201 KB
anon_s2018-02-28_18-26-190921-00001-00448-2.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-00448-2.nii	NII File	39.201 KB
anon_s2018-02-28_18-26-190921-00001-00672-3.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-00672-3.nii	NII File	39.201 KB
anon_s2018-02-28_18-26-190921-00001-00896-4.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-00896-4.nii	NII File	39.201 KB
anon_s2018-02-28_18-26-190921-00001-01120-5.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-01120-5.nii	NII File	39.201 KB
anon_s2018-02-28_18-26-190921-00001-01344-6.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-01344-6.nii	NII File	39.201 KB
anon_s2018-02-28_18-26-190921-00001-01568-7.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-01568-7.nii	NII File	39.201 KB
anon_s2018-02-28_18-26-190921-00001-01792-8.json	JSON File	101 KB
anon_s2018-02-28_18-26-190921-00001-01792-8.nii	NII File	39.201 KB

Callaghan *et al.*, https://doi.org/10.1016/j.dib.2019.104132

BIDS, with qMRI extension…



Karakuzu *et al.*, https://doi.org/10.1101/2021.10.22.21265382

Raw data sorted…


```
{
  "Manufacturer": "SIEMENS ",
  "ManufacturersModelName": "Prisma_fit",
  "DeviceSerialNumber": "167025",
  "StationName": "MRC35437",
  "MagneticFieldStrength": 3,
  "ScanningSequence": "RM",
  "SequenceName": "fl3d_1i3d6",
  "PulseSequenceDetails": "mtw_mfc_3dflash_v1i_R4",
  "RepetitionTimeExcitation": 0.025,
  "EchoTime": 0.0092,
  "FlipAngle": 6,
  "MTState": 1,
  "NumberShots": 1,
  "PhaseEncodingDirectionSign": 1,
  "history": {
    "procstep": {
      "descrip": "dicom to nifti import",
      "version": "spm_dicom_convert.m - version 6899 - SPM12 (12.3)",
      "procpar": []
    },
    "input": {
      "filename": "AnonymousFileName",
      "history": []
    },
    "output": {
      "imtype": "ORIGINAL\\PRIMARY\\M\\ND ",
      "units": "a.u."
    }
  }
}
```


- sub-01
  - anat

sub-01_acq-MTw_echo-1_flip-1_mt-on_MPM.json	804 B
sub-01_acq-MTw_echo-1_flip-1_mt-on_MPM.nii	40.1 MB
sub-01_acq-MTw_echo-2_flip-1_mt-on_MPM.json	804 B
sub-01_acq-MTw_echo-2_flip-1_mt-on_MPM.nii	40.1 MB
sub-01_acq-MTw_echo-3_flip-1_mt-on_MPM.json	818 B
sub-01_acq-MTw_echo-3_flip-1_mt-on_MPM.nii	40.1 MB
sub-01_acq-MTw_echo-4_flip-1_mt-on_MPM.json	804 B
sub-01_acq-MTw_echo-4_flip-1_mt-on_MPM.nii	40.1 MB
sub-01_acq-MTw_echo-5_flip-1_mt-on_MPM.json	804 B
sub-01_acq-MTw_echo-5_flip-1_mt-on_MPM.nii	40.1 MB
sub-01_acq-MTw_echo-6_flip-1_mt-on_MPM.json	804 B
sub-01_acq-MTw_echo-6_flip-1_mt-on_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-1_flip-1_mt-off_MPM.json	804 B
sub-01_acq-PDw_echo-1_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-2_flip-1_mt-off_MPM.json	804 B
sub-01_acq-PDw_echo-2_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-3_flip-1_mt-off_MPM.json	818 B
sub-01_acq-PDw_echo-3_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-4_flip-1_mt-off_MPM.json	804 B
sub-01_acq-PDw_echo-4_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-5_flip-1_mt-off_MPM.json	804 B
sub-01_acq-PDw_echo-5_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-6_flip-1_mt-off_MPM.json	804 B
sub-01_acq-PDw_echo-6_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-7_flip-1_mt-off_MPM.json	804 B
sub-01_acq-PDw_echo-7_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-PDw_echo-8_flip-1_mt-off_MPM.json	804 B
sub-01_acq-PDw_echo-8_flip-1_mt-off_MPM.nii	40.1 MB
sub-01_acq-T1w_echo-1_flip-2_mt-off_MPM.json	805 B
sub-01_acq-T1w_echo-1_flip-2_mt-off_MPM.nii	40.1 MB

- sub-01
  - anat
  - fmap

sub-01_acq-bodyMTw_RB1COR.json	1.2 kB
sub-01_acq-bodyMTw_RB1COR.nii	39.8 kB
sub-01_acq-bodyPDw_RB1COR.json	1.3 kB
sub-01_acq-bodyPDw_RB1COR.nii	39.8 kB
sub-01_acq-bodyT1w_RB1COR.json	1.3 kB
sub-01_acq-bodyT1w_RB1COR.nii	39.8 kB
sub-01_acq-headMTw_RB1COR.json	1.2 kB
sub-01_acq-headMTw_RB1COR.nii	39.8 kB
sub-01_acq-headPDw_RB1COR.json	1.3 kB
sub-01_acq-headPDw_RB1COR.nii	39.8 kB
sub-01_acq-headT1w_RB1COR.json	1.3 kB
sub-01_acq-headT1w_RB1COR.nii	39.8 kB
sub-01_echo-1_flip-01_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-01_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-02_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-02_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-03_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-03_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-04_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-04_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-05_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-05_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-06_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-06_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-07_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-07_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-08_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-08_TB1EPI.nii	295.3 kB
sub-01_echo-1_flip-09_TB1EPI.json	2.2 kB
sub-01_echo-1_flip-09_TB1EPI.nii	295.3 kB

BIDSme to rule them all…

- Python package to BIDSify “any” data type
- Fully parameterized through config/schema files
- Supports plugin for data conversion or metadata extraction

0. **map** (once):
   - creates a bidsification schema
1. **prepare**:
   - Put source dataset into standardized folder structure
   - Identifies subjects, sessions, modalities and series
   - (Plugin) Retrieve metadata from exterior sources
2. **process** (optional):
   - Test for various errors and inconsistencies
   - (Plugin) Transform prepared dataset (e.g. 3D to 4D merging)
3. **bidsify**:
   - Bidsifies prepared dataset
   - Manages *participants.tsv* and *scans.tsv*
   - (Plugin) Creates behavioural and derived data

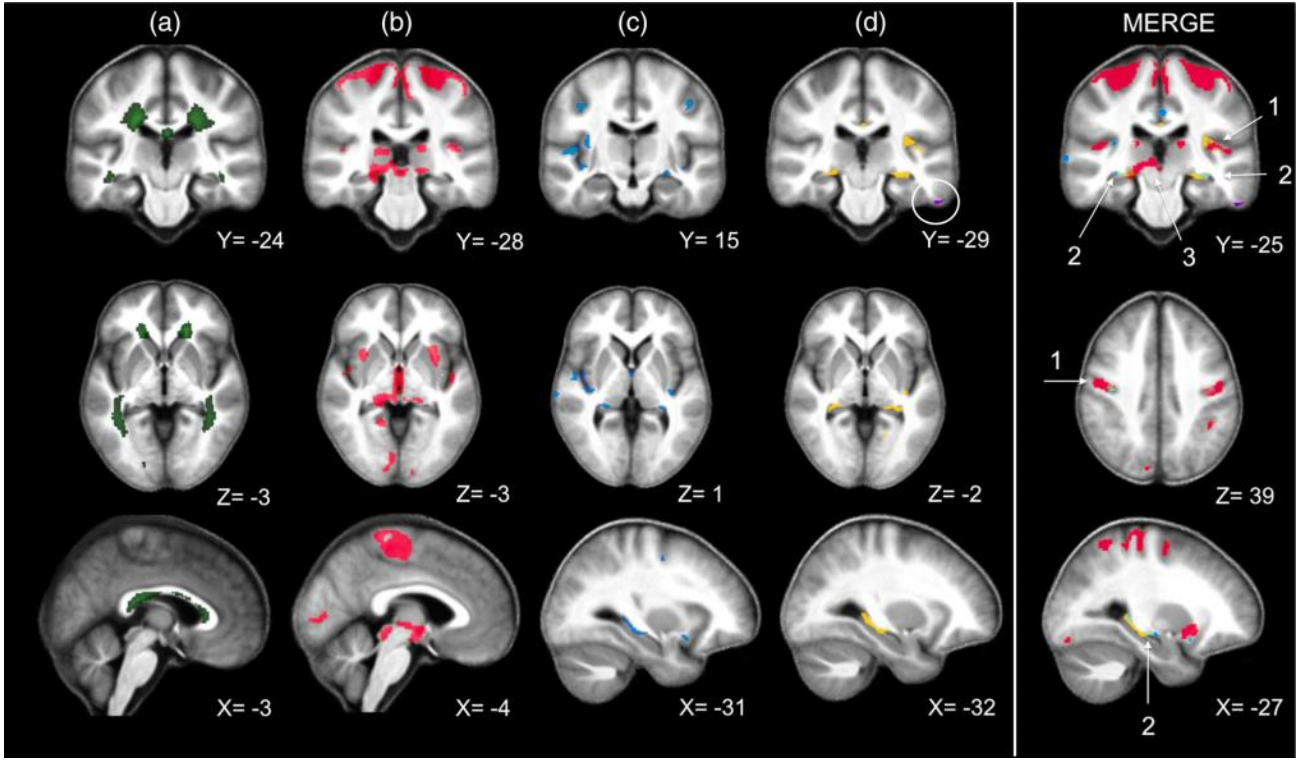
Beliy *et al.*, https://github.com/CyclotronResearchCentre/bidsme

Program

- Quantitative MRI
  - Introduction
  - Multiple sclerosis application
- EM head modelling… and more

qMRI application in MS: voxel-wise analysis

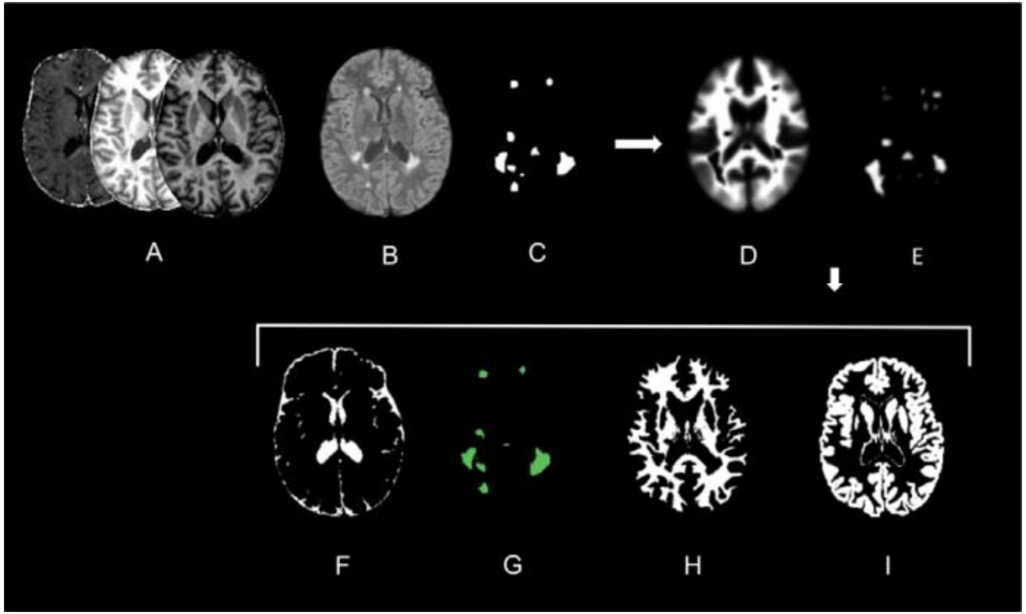
- 35 MS patients (14 RRMS, 21 PMS) & 36 matched controls
- qMRI data + FLAIR
- Processing:
  - "unified segmentation with lesion"
  - tissue-weighted smoothing
  - population GM mask
- GM-specific voxel-wise comparison of
  - MTsat, R1 & R2* (VBQ)
  - GM density (VBM)

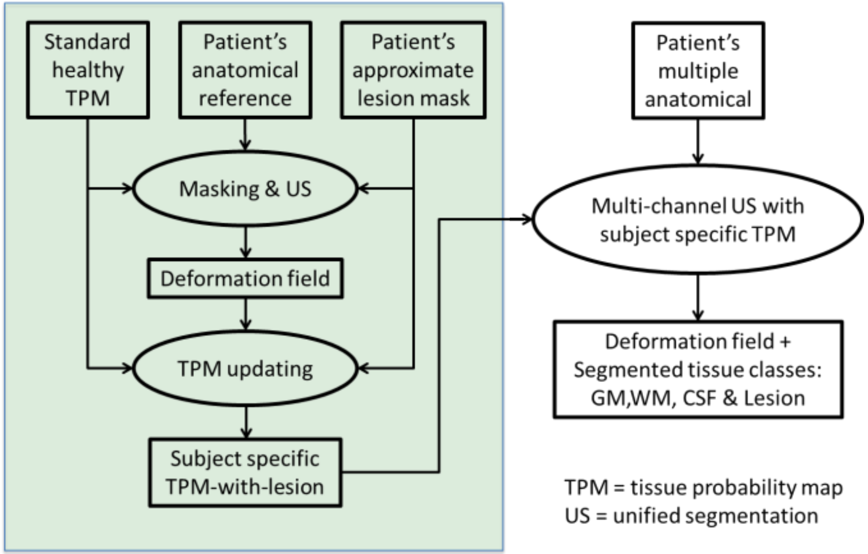


⇒ 3 different patterns: Primary Neocortical Regions (1), Hippocampus (2), Deep Gray Matter Nuclei (3)

Lommers *et al.*, http://dx.doi.org/10.1002/hbm.25274

MS image segmentation & warping





Key features of "Unified Segmentation with Lesion"

1. More principled segmentation and normalisation approach for lesioned brain
2. Increased sensitivity, from multichannel qMRI segmentation, wrt. FLAIR hyper-intensity lesion detection

Phillips *et al.*, https://github.com/CyclotronResearchCentre/USwLesion

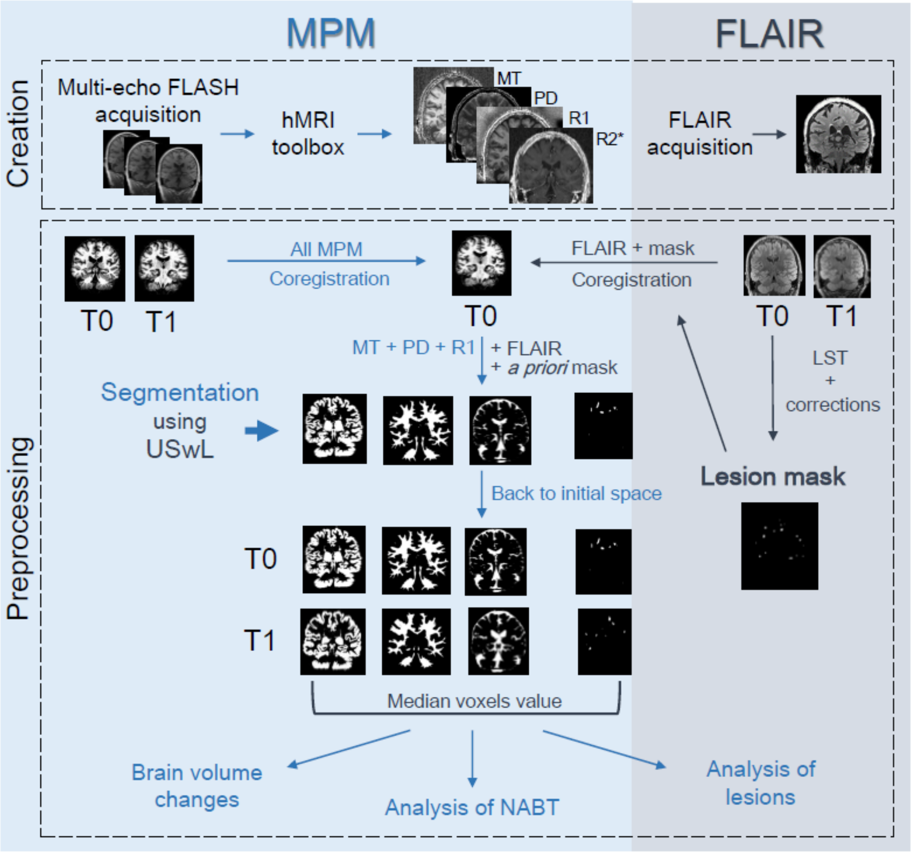
Longitudinal qMRI analysis in MS

Data

- 17 MS patients (11 RRMS, 6 PMS),
  - scanned twice over 1-5 years (T0 & T1), o average 2.5 years
  - 13 patients with disease-modifying treatments (11 RRMS, 6 PMS)
- qMRI & FLAIR images

Processing

- FLAIR derived mask + qMRI-USwL multichannel segmentation
  → normal appearing tissues (NAWM, NACGM, NADGM) & lesion
- Spatial alignment to T0
- Extract volumes & tissue preperties



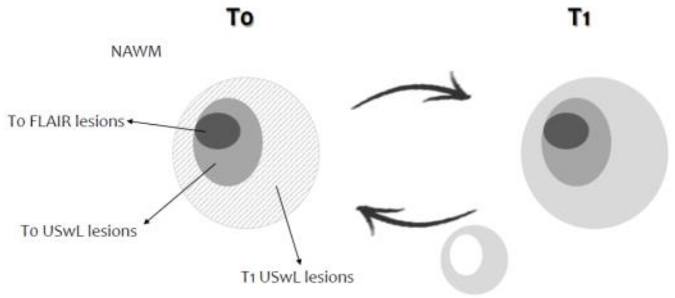
Vandeleene *et al.*, in preparation

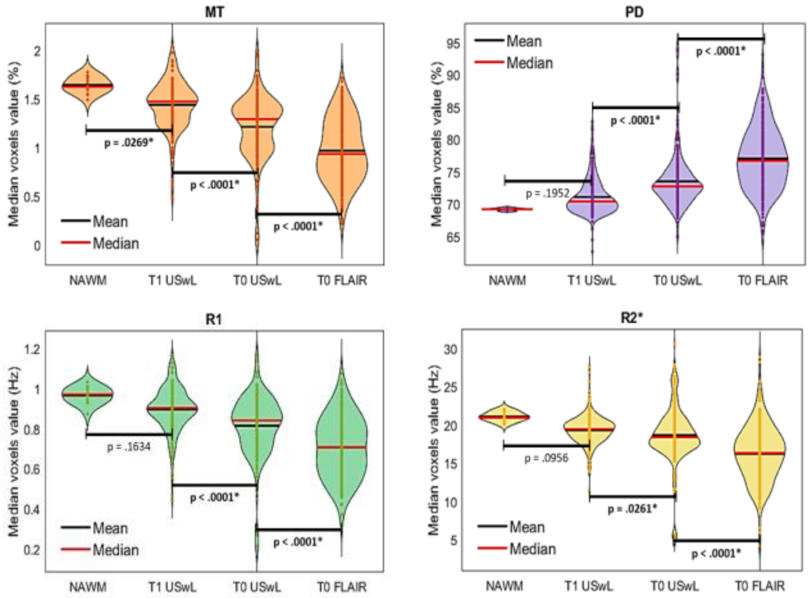
Longitudinal qMRI analysis in MS

- Significant longitudinal effects
  - (Relative) lesion volume increase
  - Rate of change for some qMRI values in NA tissues, associated to clinical status

- FLAIR hyper-intensity lesions
  < US-w-Lesion qMRI detected lesions
  ⇒ 3 “lesional tissue” types in WM
  - Clinical lesion (FLAIR hyp-int) at T0
  - Peripheral lesion (qMRI USwL) at T0
  - Peripheral lesion (qMRI USwL) at T1

  \+ Normal appearing WM

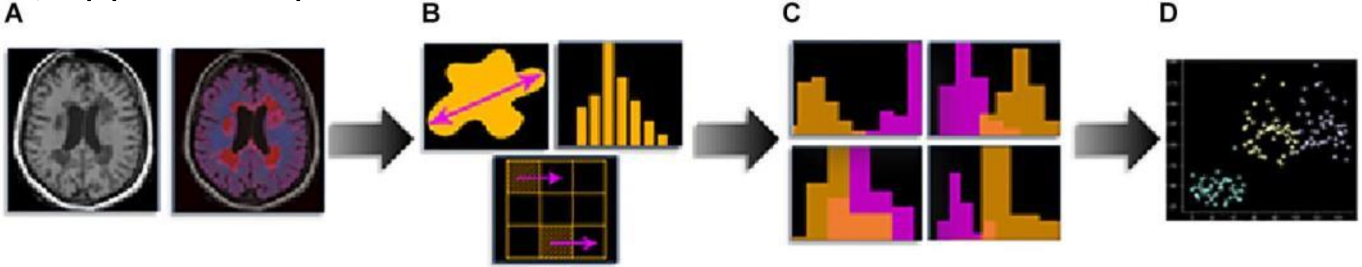




Vandeleene *et al.*, in preparation

Early diagnosis of multiple sclerosis?

Radiomics approach, applied on qMRI and standard T1w MRI



- Image segmentation (A), GM/WM or GM/NAWM/lesion
- Radiomics features extraction (B), for each (image and) tissue type, then selection (C)
- Classification through supervised learning (D), with RF, SVM or LR
- Validation, with cross-validation (CRC data set) & on open data set (healthy or MS T1w)

Results:

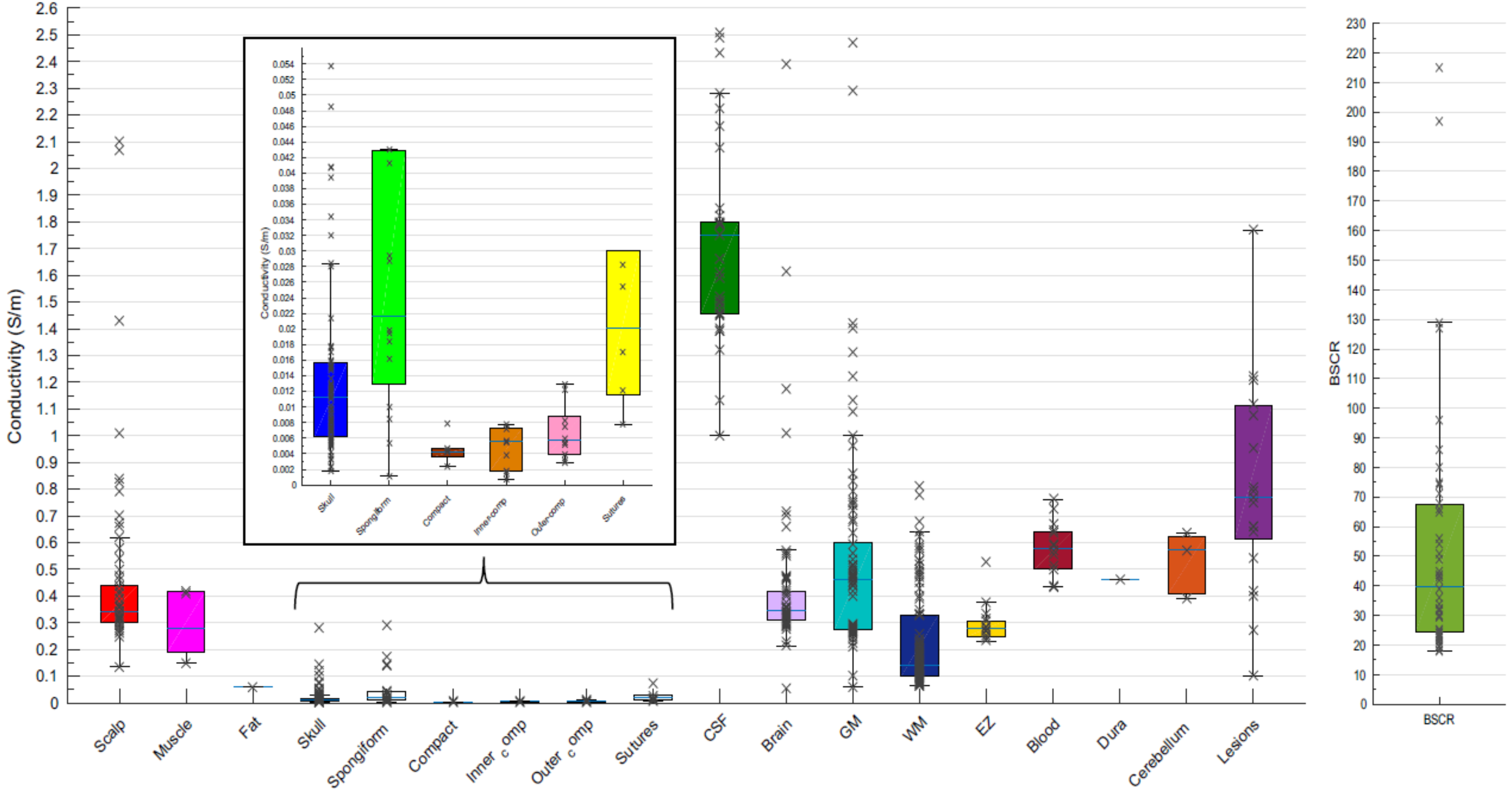
- WM-4-qMRIs features give best results for cross-validation (CRC data set only)
- WM-T1w features could be useful (CRC data set only) for routine check
- WM-T1w features performance on external data set was poor but…

Lavrova *et al.*, http://dx.doi.org/10.3389/fnins.2021.679941

Program

- Quantitative MRI
  - Introduction
  - Multiple sclerosis application
- EM head modelling… and more

Head tissue conductivity…

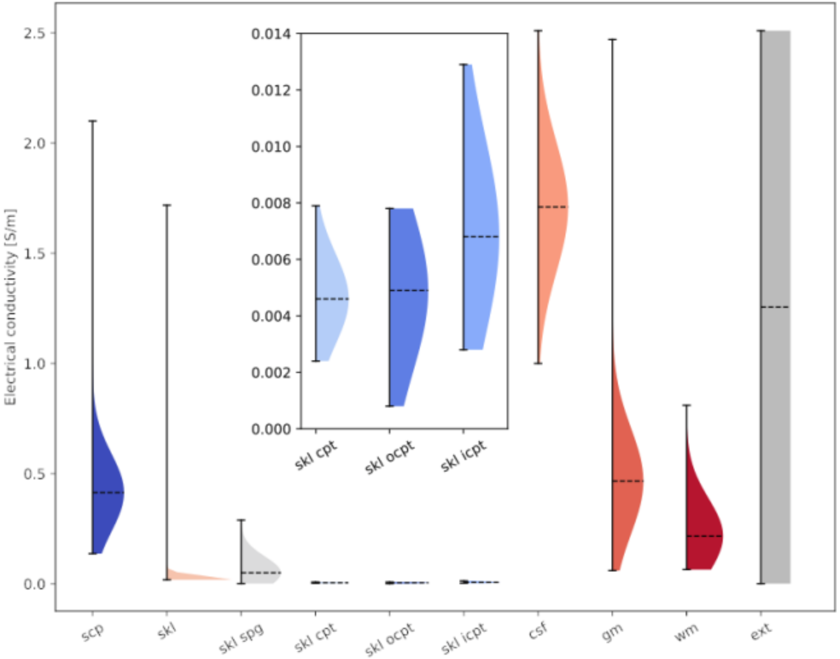


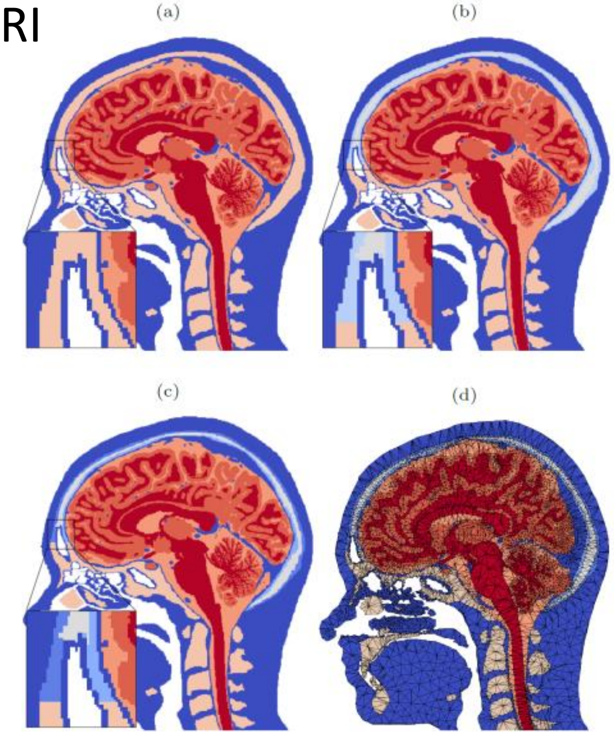
from McCann *et al.*, https://doi.org/10.1007/s10548-019-00710-2

shamo, Stochastic HeAd MOdelling

Calculate forward problem solution for **EEG** , as $V = L(\sigma) \cdot J$, and **tDCS**

- build FEM head model(s), based on segmented MRI
- consider stochastic variable for conductivity σ





Grignard *et al.*, https://github.com/CyclotronResearchCentre/shamo

shamo, Stochastic HeAd MOdelling

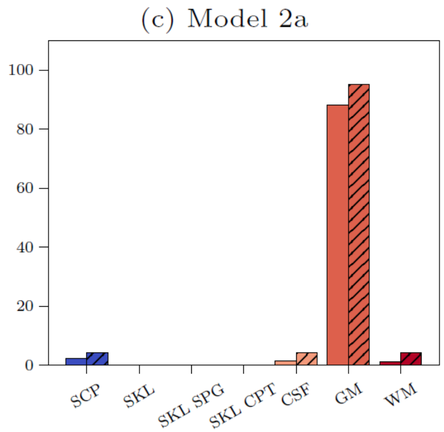
- Use *getDP* to solve the FEM problem, given conductivity values σ
- Build surrogate model to explore the N-D conductivity space.
- Sensitivity analysis with Sobol indices based on scalar $m(\sigma)$

EEG forward solution, sensitivity of the whole leadfield

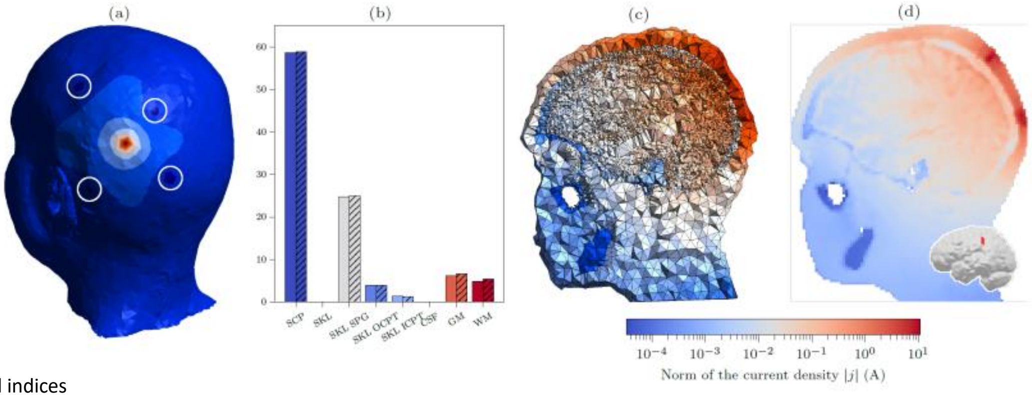
$$m(\sigma) = \left\| L(\sigma) - L_{\text{ref}} \right\|_F$$

tDCS current density, sensitivity in target region of interest

$$m(\sigma) = \text{mean}(\|j\|_2)_{\text{ROI}}$$



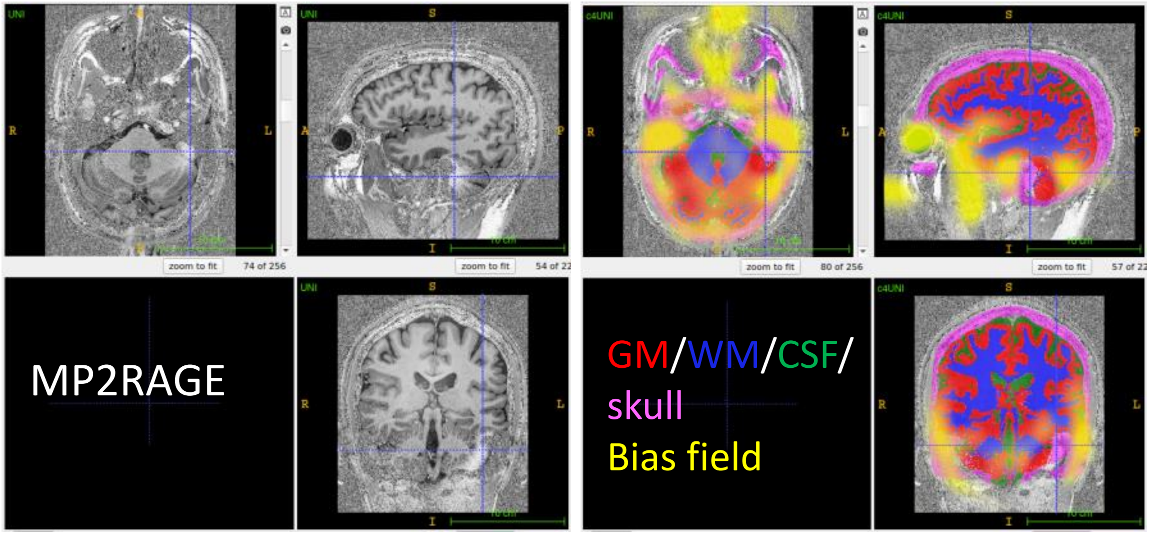
First order Sobol indices
Total order Sobol indices



Grignard *et al.*, https://arxiv.org/abs/2103.08164v1

Other topics of interest

- 7T MRI:
  - Sequence & protocol development for QSM, CEST
  - B1 & intensity inhomogeneities issues (MP2RAGE & qMRI)
  - qMRI reproducibility within/across different centres

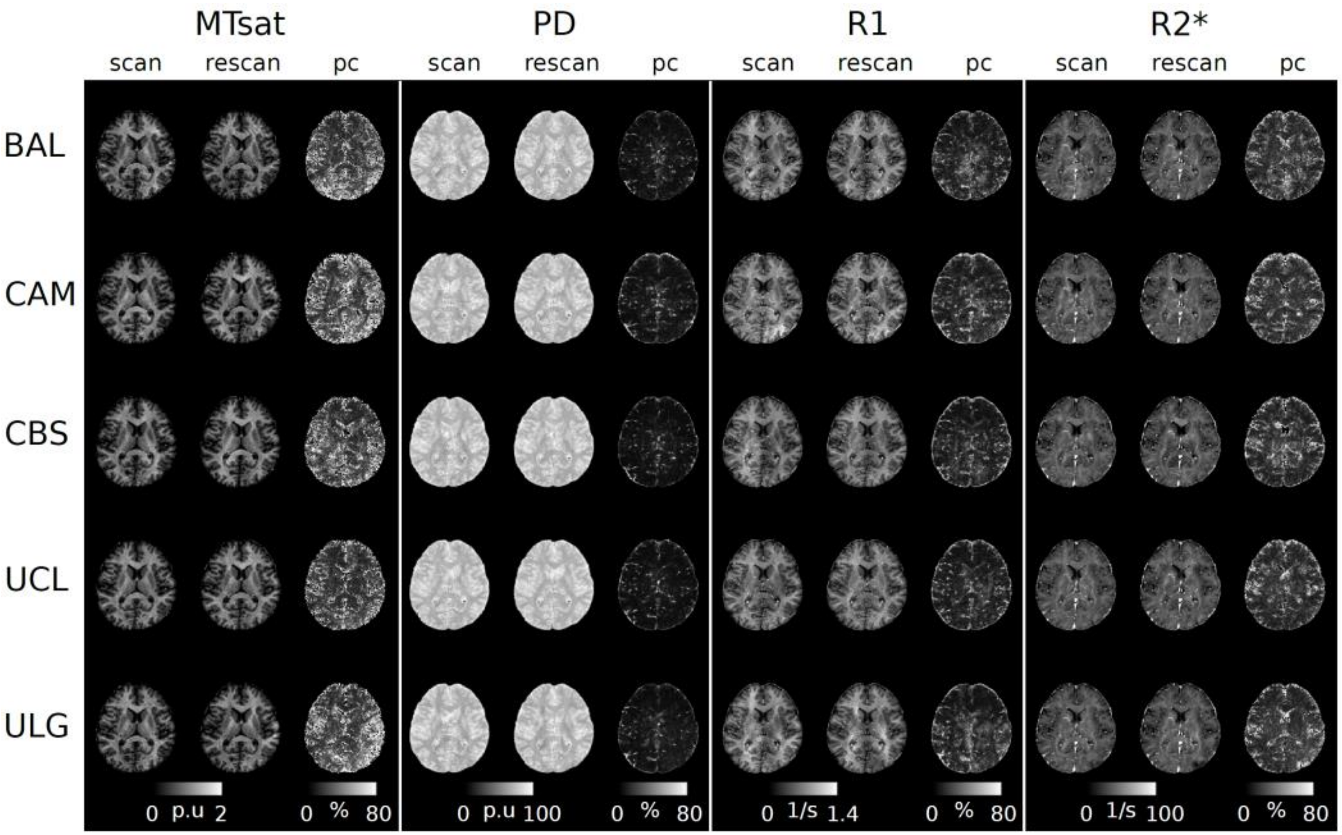


7T MRI, repeatability and replicability

"Travelling head"

- Single subject
- 5 centres (BE, DE, CH, UK)
- (Different field mapping techniques)

⇒ within centre, scan/rescan signal CoV



(later across centre analysis)

Sherif *et al.*, in preparation

Other topics of interest

- 7T MRI:
  - Sequence & protocol development for QSM, CEST
  - B1 & intensity inhomogeneities issues (MP2RAGE & qMRI)
  - qMRI reproducibility within/across different centres
- PET imaging
  - Modeling of tau & amyloid tracers + synaptic density, cf. C. Bastin's paper
  - PET + qMRI, multimodal integration
- Electrophysiology & actigraphy
  - cf. G. Hammad's pyActigraphy toolbox
- Applications for heathy ageing, AD, PD, stroke, glioblastome,…

Team at CRC & elsewhere

- Camille Guillemin
- Christine Bastin
- Christina Schmidt
- Christian Degueldre
- Christophe Geuzaine
- Elizaveta Lavrova
- Emilie Lommers
- Eric Salmon
- Evelyne Balteau
- Fabienne Collette
- Frederique Depierreux
- Gilles Reuter
- Gilles Vandewalle
- Gregory Hammad
- Martin Grignard
- Mohamed Bahri
- Nikita Beliy
- Nora Vandeleene
- Pierre Maquet
- Siya Sherif
- Solène Dauby
- Soodeh Moallemian
- Steve Majerus

- The international hMRI team
- P. Lambin's team at UMaastricht (NL)

(and apologies to those I forgot…)

CRC references

- N. Beliy et al., *BIDSme, a user friendly open-source python toolkit to "bidsify" source-level neuroimaging data-sets to BIDS-conformed*. 2019. https://github.com/CyclotronResearchCentre/bidsme
- E. Lommers et al., *Voxel-Based quantitative MRI reveals spatial patterns of grey matter alteration in multiple sclerosis*. 2021. http://dx.doi.org/10.1002/hbm.25274
- N. Vandeleene et al., *Unifying lesion masking and tissue probability maps for improved segmentation and normalization*. In preparation & https://github.com/CyclotronResearchCentre/USwLesion
- N. Vandeleene et al., *Using quantitative MRI to characterize cerebral damage in multiple sclerosis: a longitudinal study.* In preparation.
- E. Lavrova et al., *Exploratory radiomic analysis of conventional versus quantitative brain MRI: Towards automatic diagnosis of early multiple sclerosis.* 2021. http://dx.doi.org/10.3389/fnins.2021.679941
- M. Grignard et al., *shamo: A tool for electromagnetic modelling, simulation and sensitivity analysis of the head.* 2021. https://arxiv.org/abs/2103.08164v1 & https://github.com/CyclotronResearchCentre/shamo
- C. Bastin et al., *In vivo imaging of synaptic loss in Alzheimer's disease with [18F]UCB-H positron emission tomography*. 2020. https://doi.org/10.1007/s00259-019-04461-x
- G. Hammad et al., *pyActigraphy: Open-source python package for actigraphy data visualization and analysis*. 2021. https://doi.org/10.1371/journal.pcbi.1009514 & https://github.com/ghammad/pyActigraphy
- S. Sherif et al., *Harmonization of 7T Multi-Parameter Mapping protocol across multiple sites*. In preparation.

Some qMRI/hMRI references

- Toolbox, http://hmri.info & https://doi.org/10.1016/j.neuroimage.2019.01.029
- MPM protocol, https://dx.doi.org/10.3389%2Ffnins.2013.00095
- hMRI review, https://doi.org/10.1097/WCO.0000000000000222
- Multi-centre study, https://doi.org/10.3389/fnins.2013.00095
- Ageing studies, https://doi.org/10.1016/j.neuroimage.2011.01.052 and https://doi.org/10.1016/j.neurobiolaging.2014.02.008
- Example dataset, https://doi.org/10.1016/j.dib.2019.104132
- qMRI-BIDS, http://dx.doi.org/10.1101/2021.10.22.21265382

Thank you for your attention!

LIÈGE université
GIGA