

Quantitative MRI, practical considerations & applications

Agenda

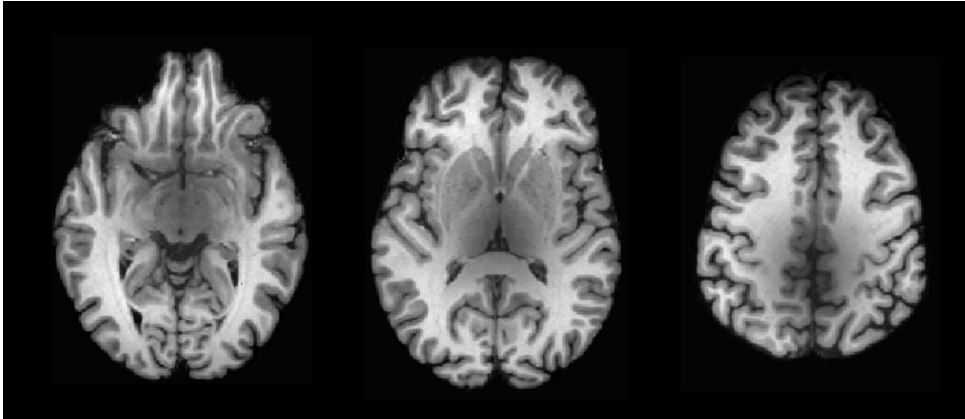


- ▶ Quantitative MRI
- ▶ qMRI application in
 - Multiple sclerosis
 - Alzheimer disease
- ▶ Conclusions

Classical vs quantitative MR imaging



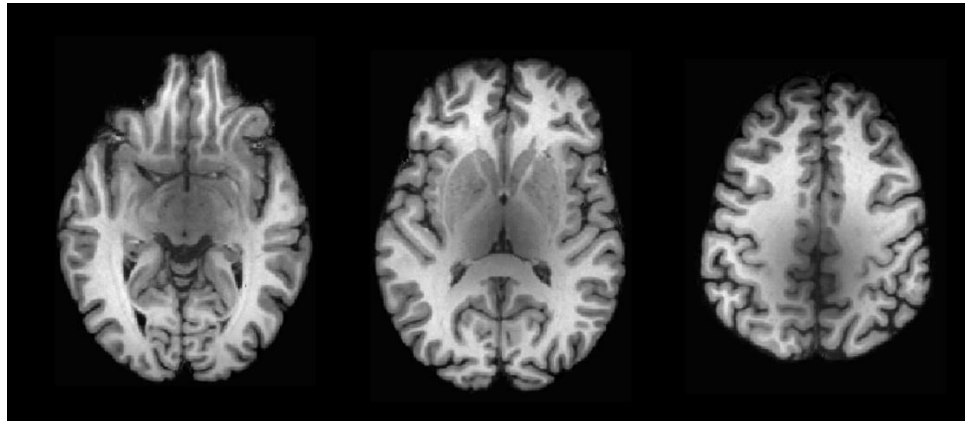
$$SI_{\text{MPRAGE}} = f(\text{sequence parameters, scanner hardware, physical MRI parameters})$$



Classical vs quantitative MR imaging

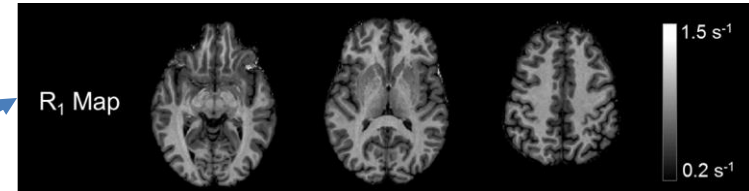


$$SI_{\text{MPRAGE}} = f(\text{sequence parameters, scanner hardware, physical MRI parameters})$$

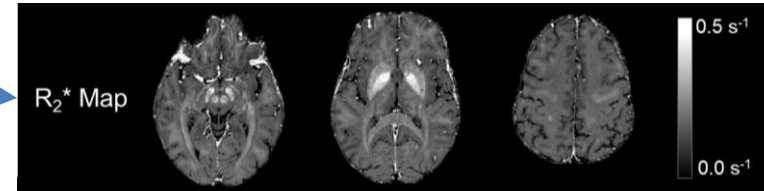


⇒ Quantitative MRI & “Voxel-Based Quantification”

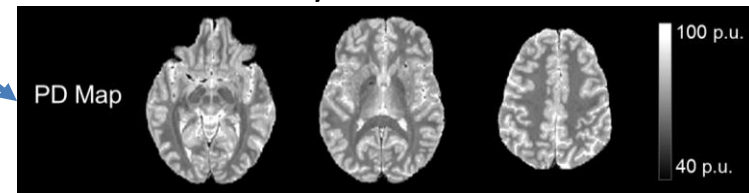
Longitudinal Relaxation Rate



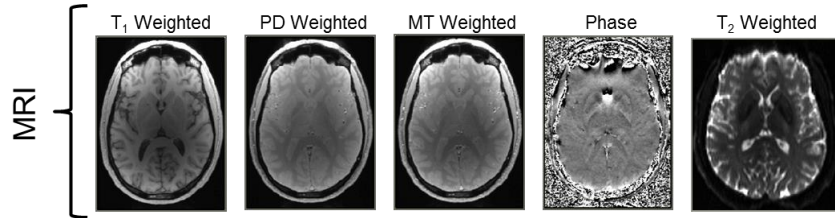
Effective Transverse Relaxation Rate



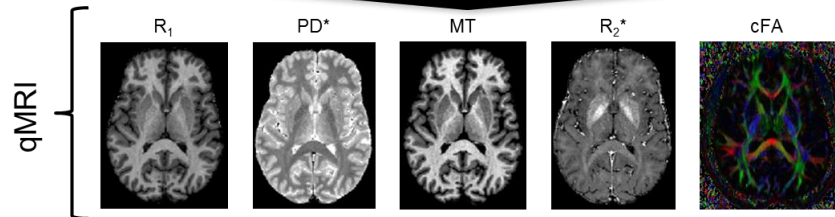
Proton Density



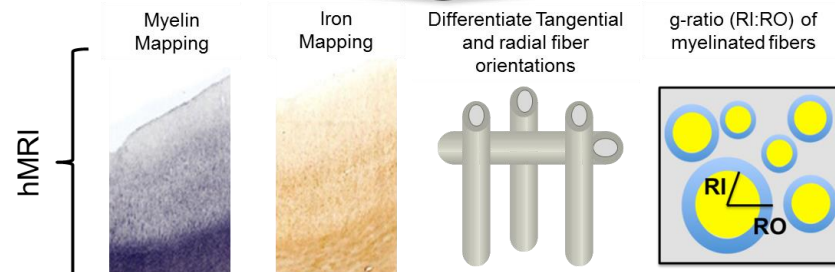
In vivo histology using MRI (hMRI)



Physical Models



Biophysical Models



Begin by getting quantitative maps of specific parameters

The ultimate target is biological mapping

qMRI interpretation as hMRI



Water
Content

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

Macromolecules
e.g. myelin

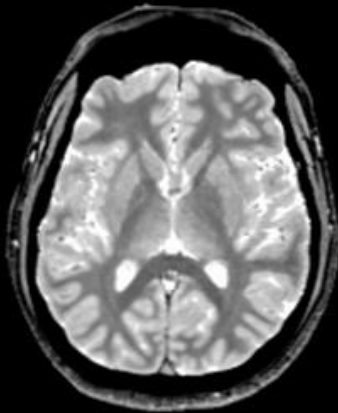
Iron

40p.u. 100p.u.

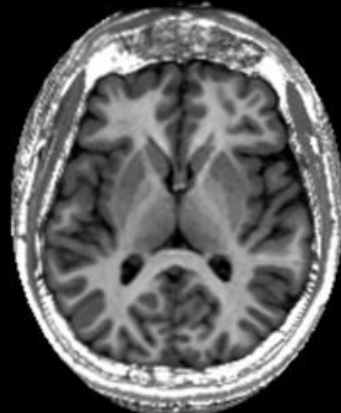
0.2s⁻¹ 1.5s⁻¹

0.2p.u. 2.2p.u.

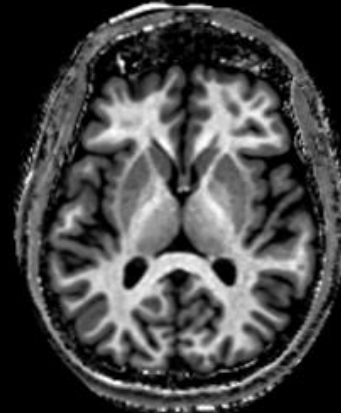
0s⁻¹ 50s⁻¹



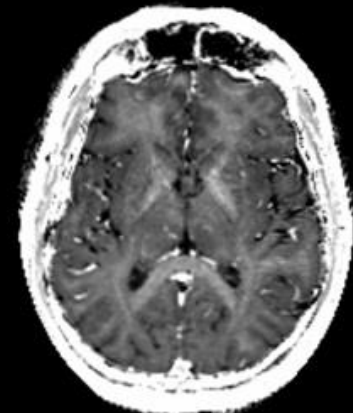
PD*



R1



MT



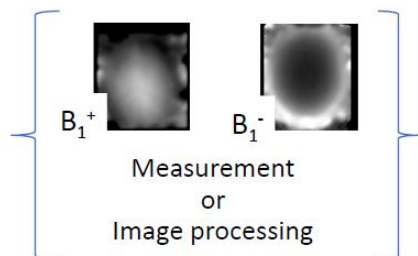
R2*

hMRI toolbox: MPM to quantitative maps

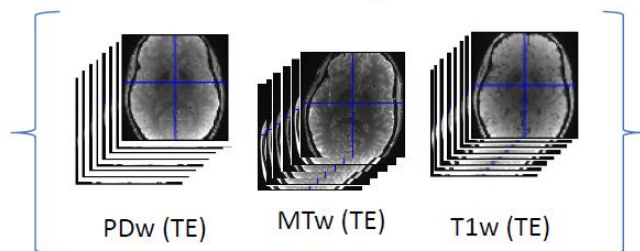


Map Creation

Bias field correction

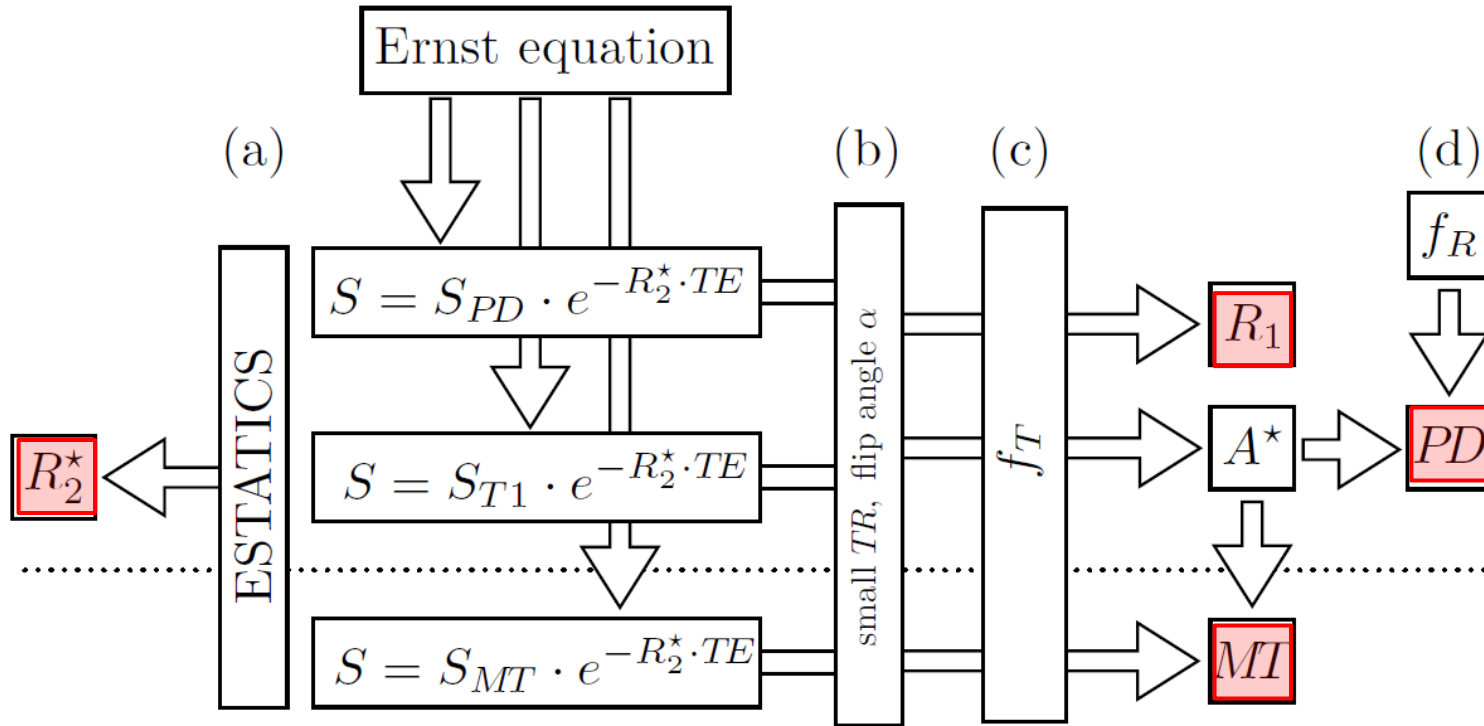


Raw images



NIfTI images and JSON metadata (acquisition parameters: flip angle, TE, TR, MT on/off, ...)

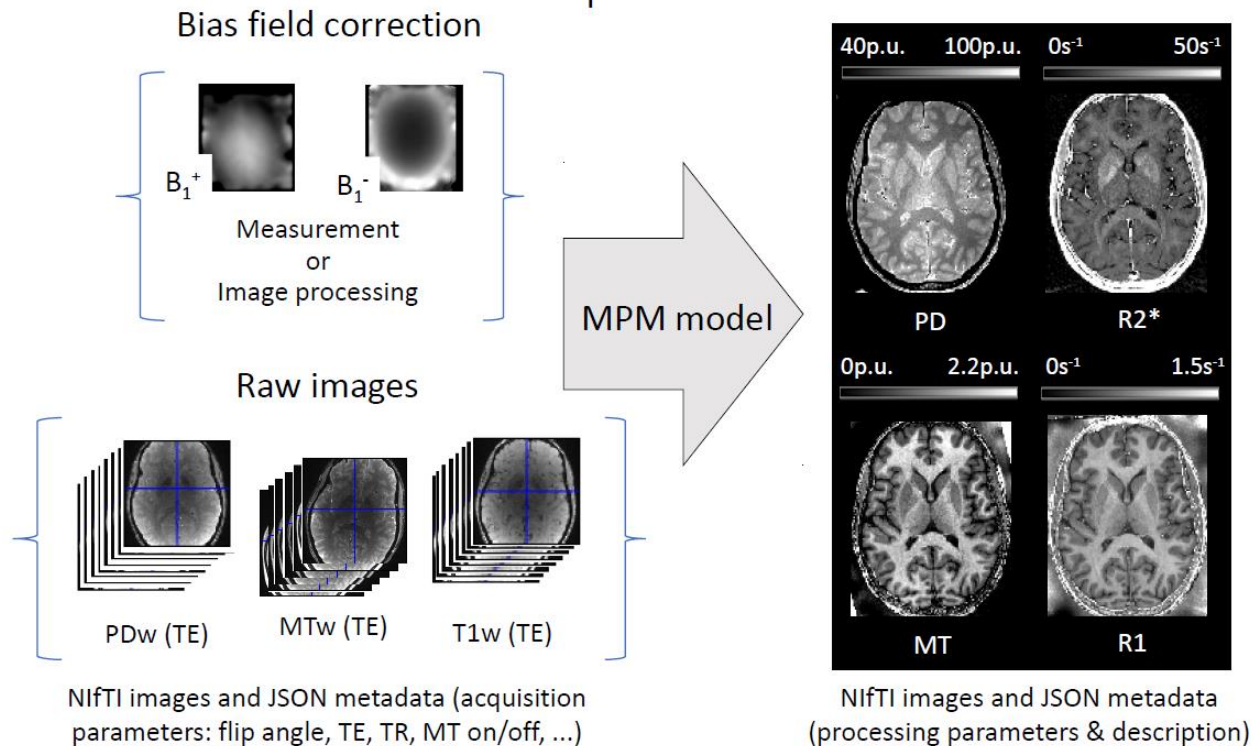
Multi-Parameter Mapping (MPM) Protocol



hMRI toolbox: MPM to quantitative maps



Map Creation





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
<i>Participant moved to new position via primary rotation about z</i>		
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
<i>Participant returned to approximate alignment with the original position</i>		
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

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
<i>Participant moved to new position via primary rotation about z</i>		
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
<i>Participant returned to approximate alignment with the original position</i>		
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

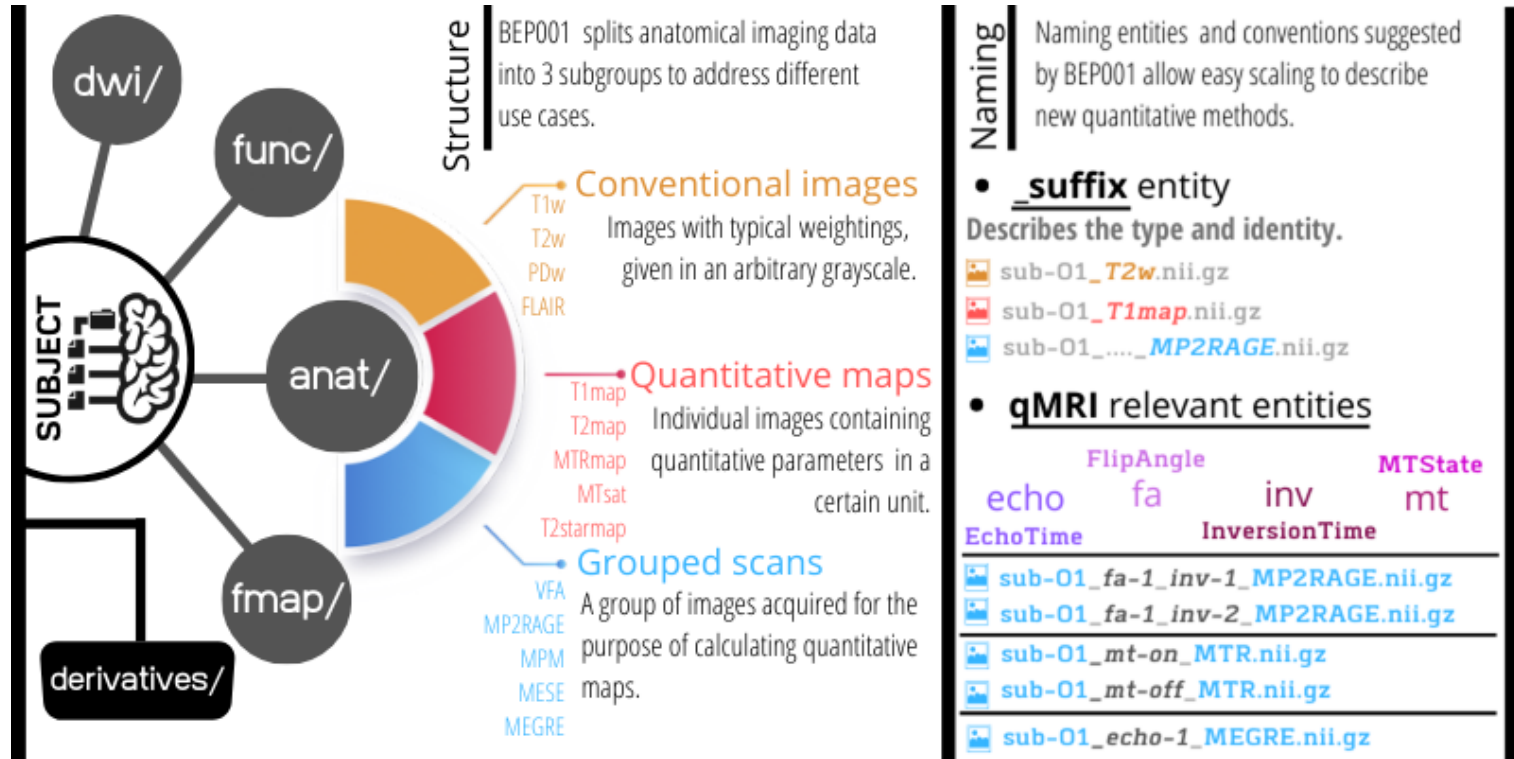
- hmri_sample_dataset_with_maps
- gre_field_mapping_1acq_rl_0005
- gre_field_mapping_1acq_rl_0006
- mfc_seste_b1map_v1e_0004
- mfc_smaps_v1a_Array_0007
- mfc_smaps_v1a_Array_0010
- mfc_smaps_v1a_Array_0013
- mfc_smaps_v1a_QBC_0008
- mfc_smaps_v1a_QBC_0011
- mfc_smaps_v1a_QBC_0014
- mtw_mfc_3dflash_v1i_R4_0012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

BIDS, with qMRI extension...



Brain Imaging Data Structure



Raw data sorted...

```
{
  "Manufacturer": "SIEMENS ",
  "ManufacturersModelName": "Prisma_fit",
  "DeviceSerialNumber": "167025",
  "StationName": "MRC35437",
  "MagneticFieldStrength": 3,
  "ScanningSequence": "RM",
  "SequenceName": "fl3d_i13d6",
  "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."
    }
  }
}
```

“BIDSme” tool

Beliy *et al.*, <https://doi.org/10.21105/joss.05575> &
<https://github.com/CyclotronResearchCentre/bidsme>

- 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

qMRI application in multiple sclerosis (MS)

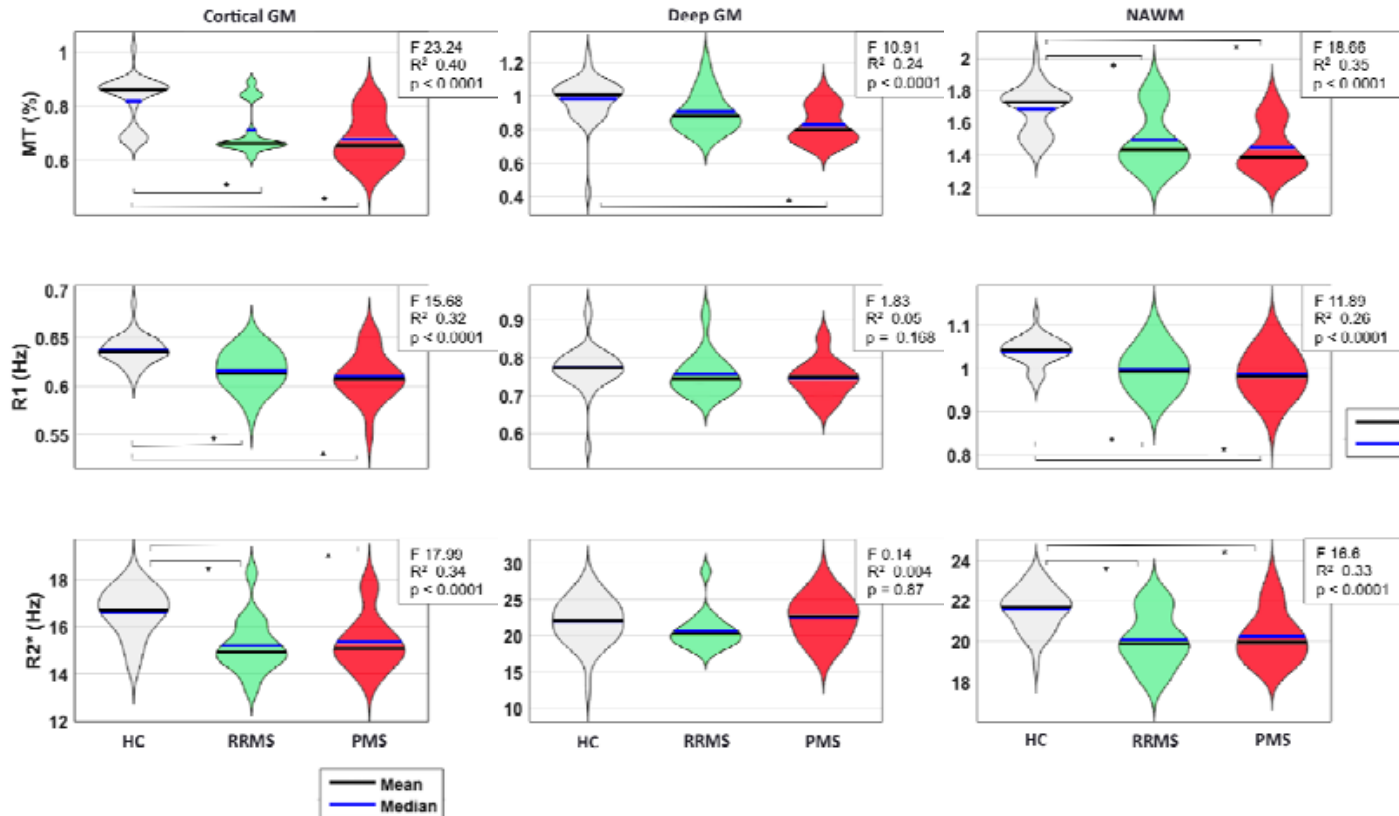


- ▶ 35 MS patients (14 RRMS, 21 PMS) & 36 matched controls
- ▶ qMRI data + FLAIR
- ▶ Processing:
 - “unified segmentation with lesion”
 - tissue-weighted smoothing
 - population GM mask

Application in MS: healthy tissues global changes

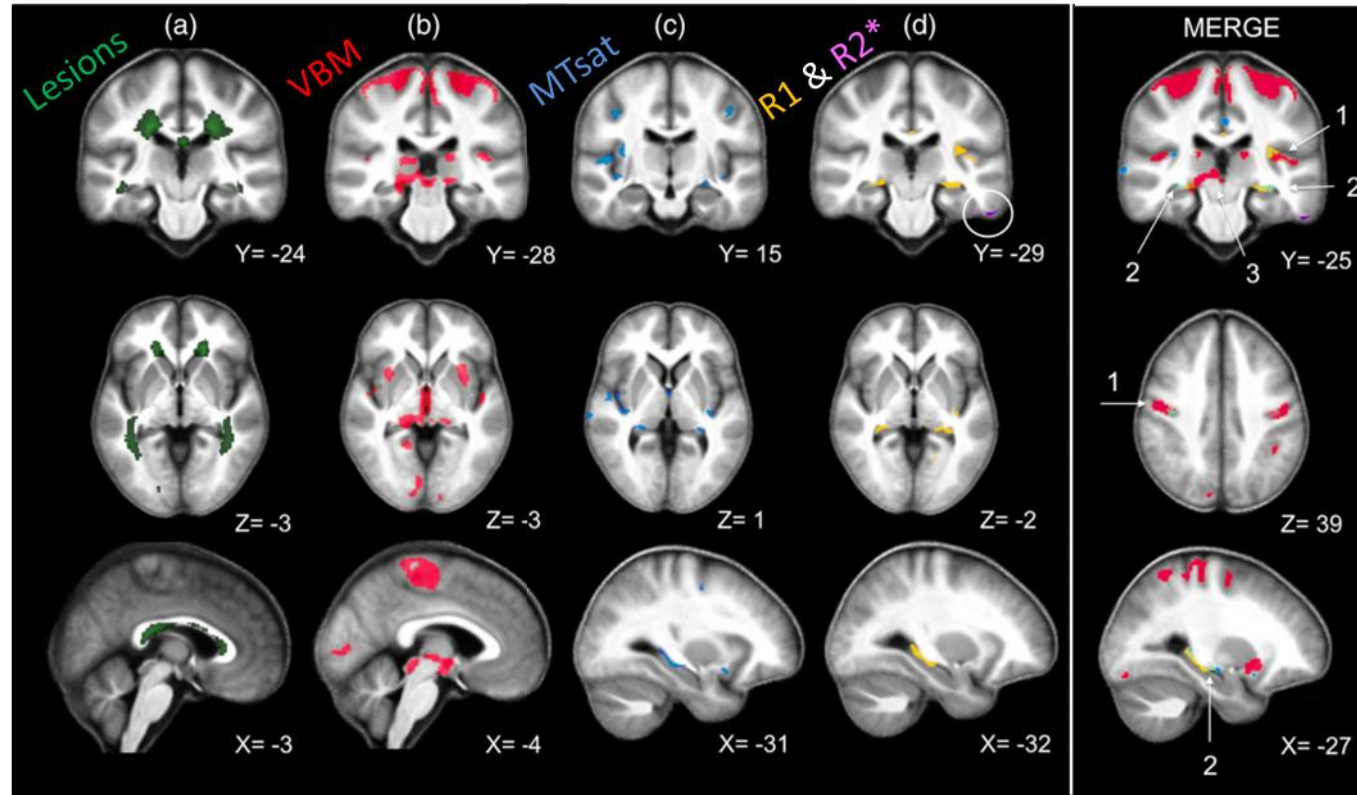


- ▶ 35 MS patients (14 RRMS, 21 PMS) & 36 matched controls
- ▶ qMRI data + FLAIR
- ▶ Processing:
 - “unified segmentation with lesion”
 - tissue-weighted smoothing
 - population GM mask
- ▶ GM-specific global comparison of
 - MTsat, R1 & R2*
 - Across HC vs. RRMS vs. PMS



Application in MS: healthy tissue 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)
 - HC > MS



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

Longitudinal qMRI analysis in MS



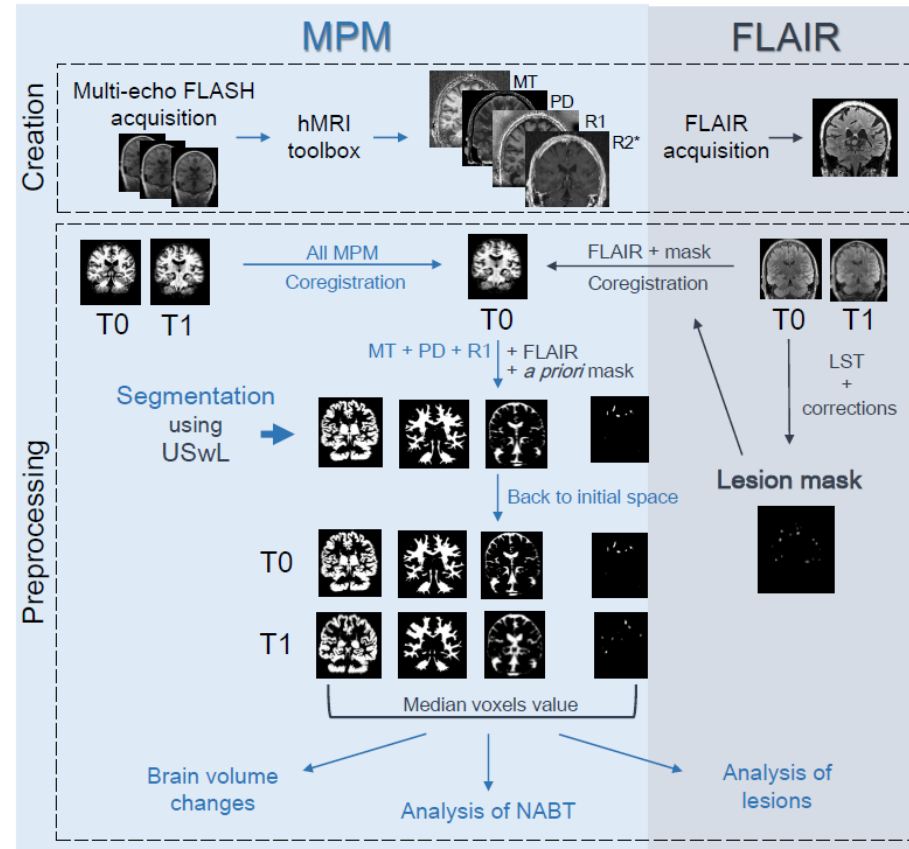
Data

- ▶ 17 MS patients (11 RRMS, 6 PMS),
 - scanned twice over 1-5 years (T0 & T1), on 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 properties



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

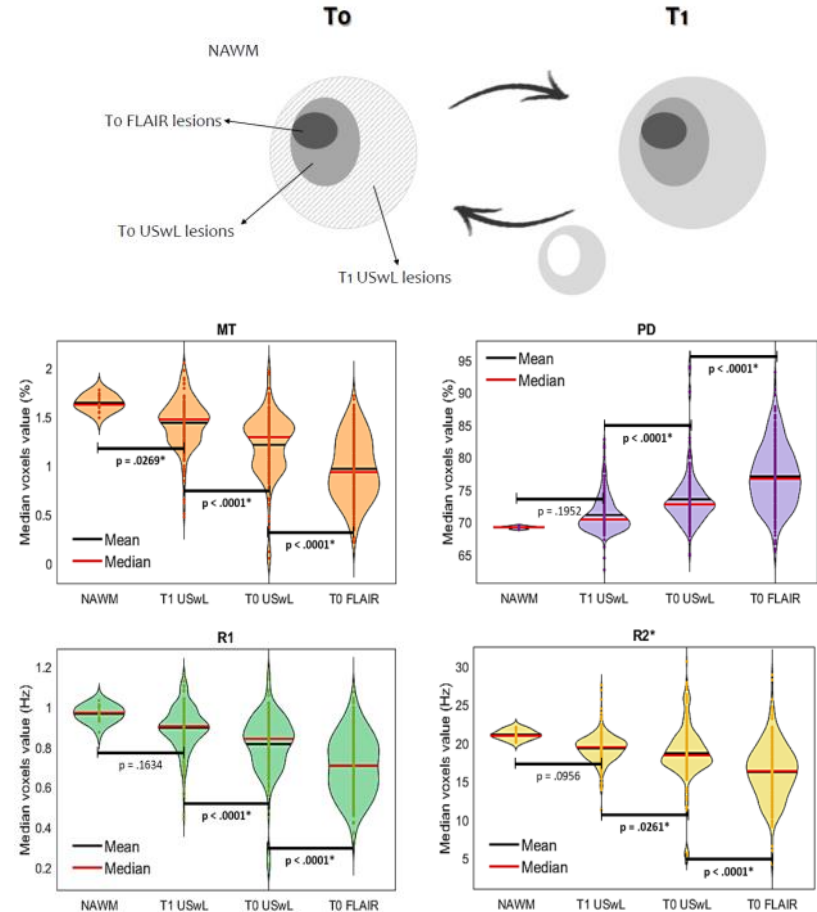
► FLAIR hyper-intensity lesions

< 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

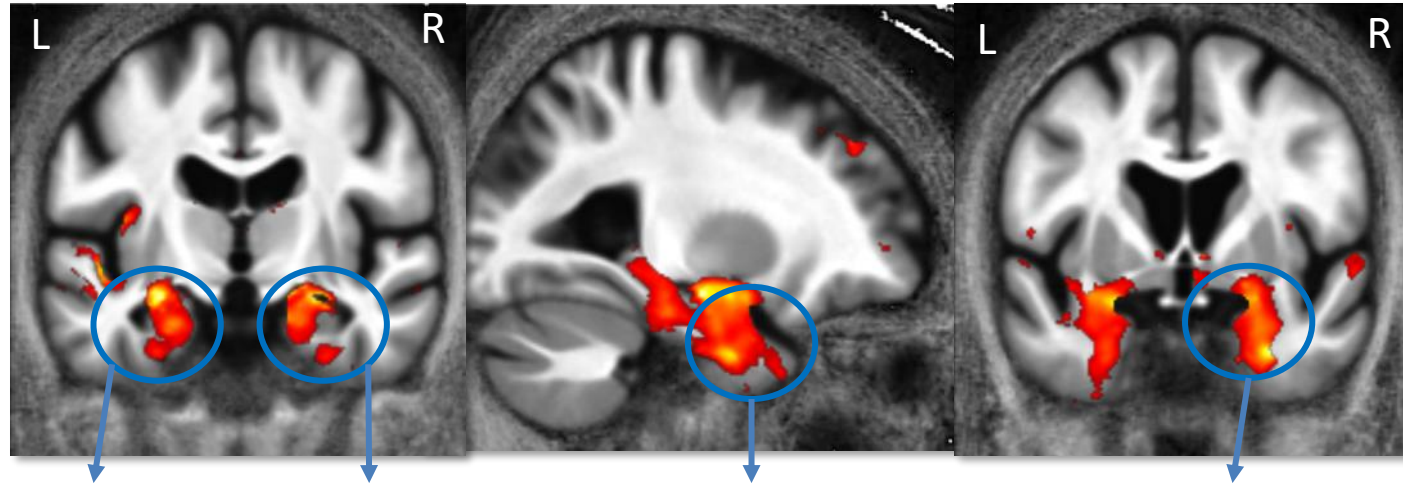
+ Normal appearing WM



Application in Alzheimer disease



- ▶ 24 AD patients & 19 matched controls
- ▶ Data
 - qMRI : Mtsat and R2*
 - SV2A PET images
 - Grey matter density
- ▶ Multivariate GLM for voxel wise analysis, i.e. 1 mGLM for 4 modalities!

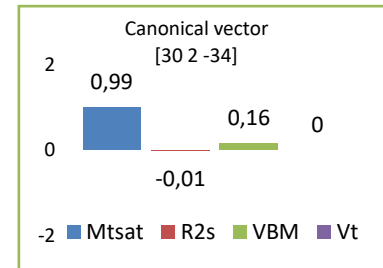
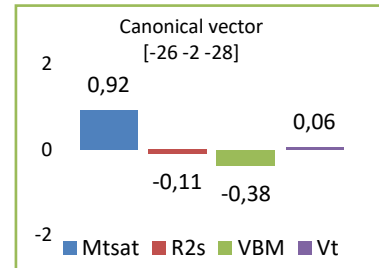
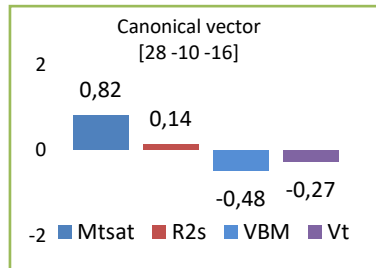
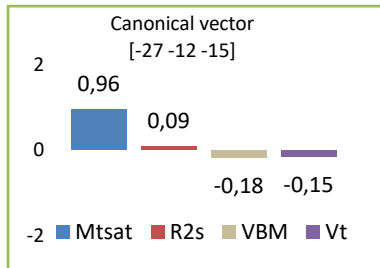


L-hippocampus

R-hippocampus

L-fusiform

R-parahippocampal



Conclusions



- ▶ Morphometry still useful but...
- ▶ qMRI biomarkers
 - enhance specificity
 - disentangle effects via multi-modal quantification
 - reproducible across scanner
- ▶ getting closer to *in vivo* histology using MRI
 - follow tissue changes w/o (or before...) volume changes
 - (explore structure/function relationships)
- ▶ hMRI toolbox (SPM12 add-on) to create & process maps

Perspectives



- ▶ Improve MRI acquisition sequence:
speed, SNR, resolution, different scanners, 3T & 7T,...
- ▶ Improve image reconstruction & processing:
noisy voxels, automatization, data & meta-data organization (BIDS),...
- ▶ Linking to neuro-biological tissue properties:
combining with PET, clinical applications,...

CRC references



- ▶ N. Belyi 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> & 2023, <https://doi.org/10.21105/joss.05575>
- ▶ E. Lommers et al., *Multiparameter MRI quantification of microstructural tissue alterations in multiple sclerosis*. 2019, <https://doi.org/10.1016/j.nicl.2019.101879>
- ▶ 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., *Using quantitative MRI to characterize cerebral damage in multiple sclerosis: a longitudinal study*. 2023, <https://doi.org/10.1002/brb3.2923>
- ▶ S. Moallemian et al., *Multimodal imaging of microstructural cerebral alterations and loss of synaptic density in Alzheimer's disease*. 2023, <https://doi.org/10.1016/j.neurobiolaging.2023.08.001>



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, <https://doi.org/10.1038/s41597-022-01571-4>

Thank you for your attention!

Acknowledgments:

C. Bastin , E. Lommers, P. Maquet, S. Moallemian,
N. Vandeleene, S. Sheriff
+ the GIGA CRC human imaging &
the international hMRI teams

