A clinical and research 3T MRI protocol under 30 minutes

(Yes, it's possible!)

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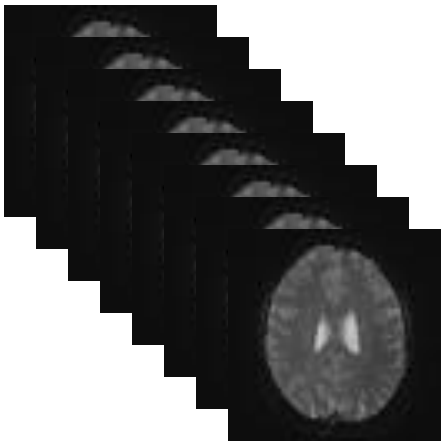
github.com/LRQ3000/mri_protocol

V1.0.2

Coma Science Group
GIGA Consciousness
University & Hospital of Liège, Belgium

CME 2019
Dortmund, September 23th 2019

What we do: MRI analyses

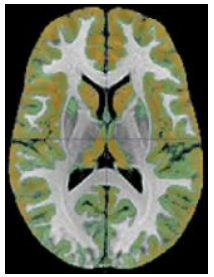


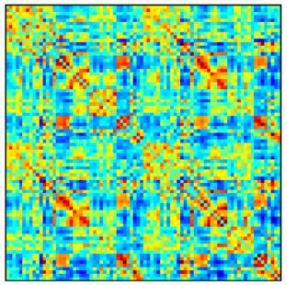
fMRI timeseries
(one per subject)

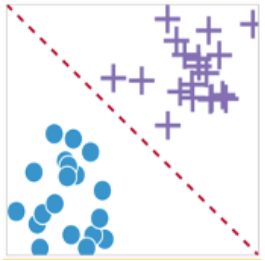
Preprocessing
(SPM12)

Analysis
(CONN)

Machine
learning
(SVM)

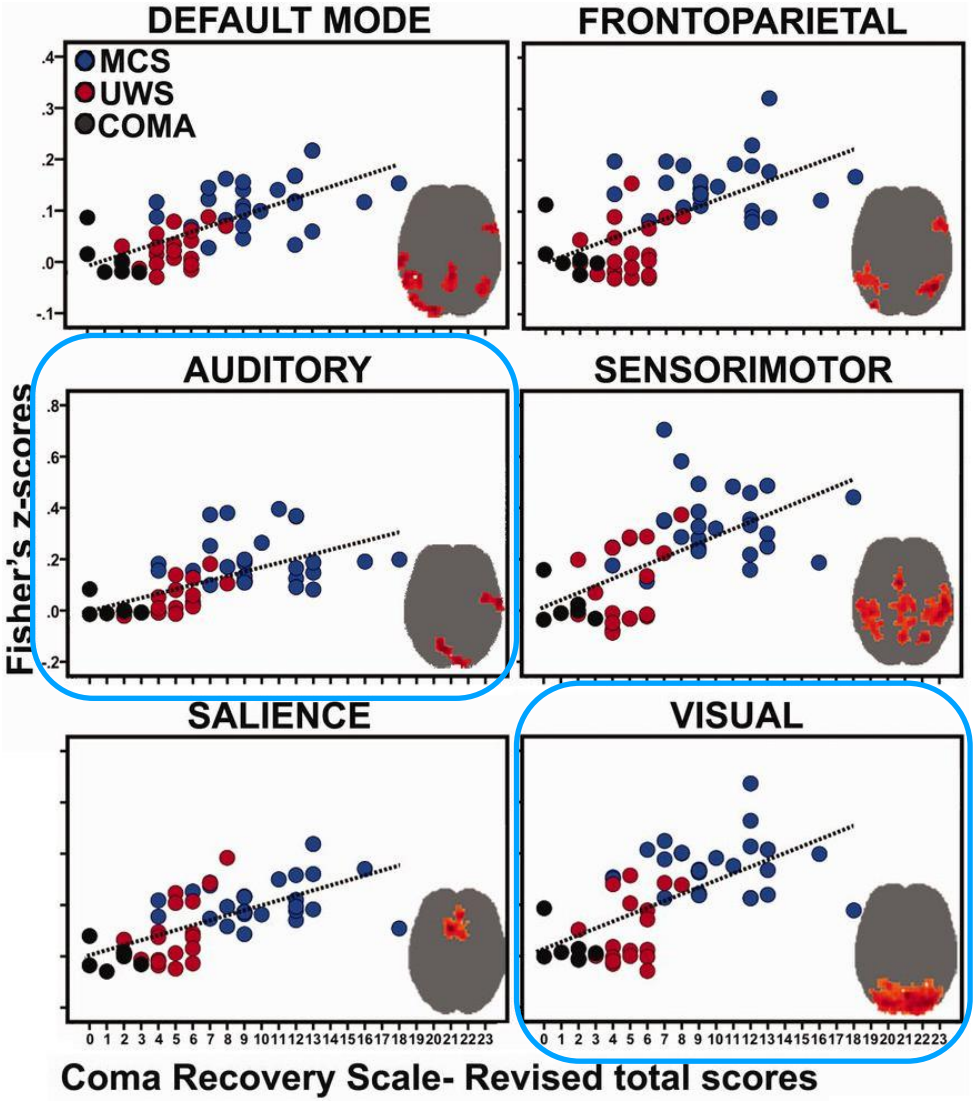


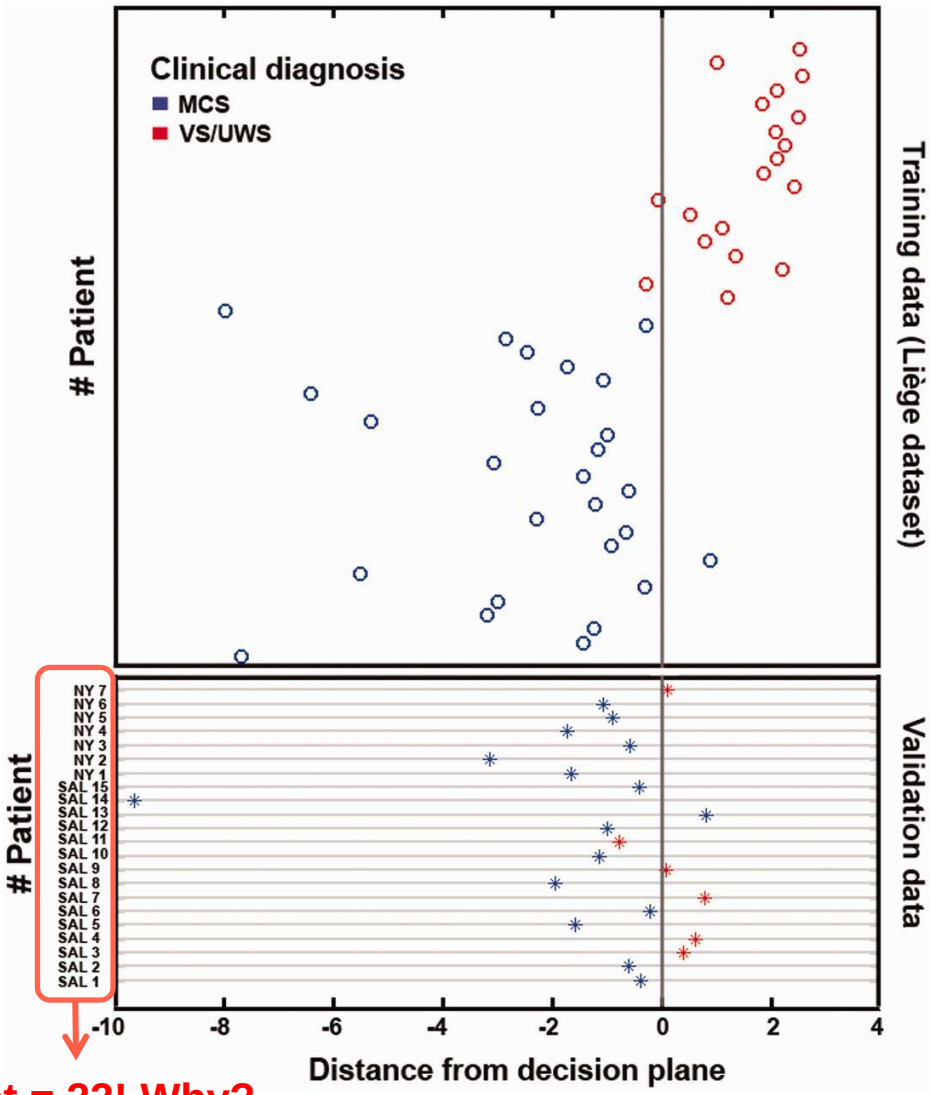




[1] Demertzi, Antonopoulos et al, Brain, 2015

What we do: MRI analyses



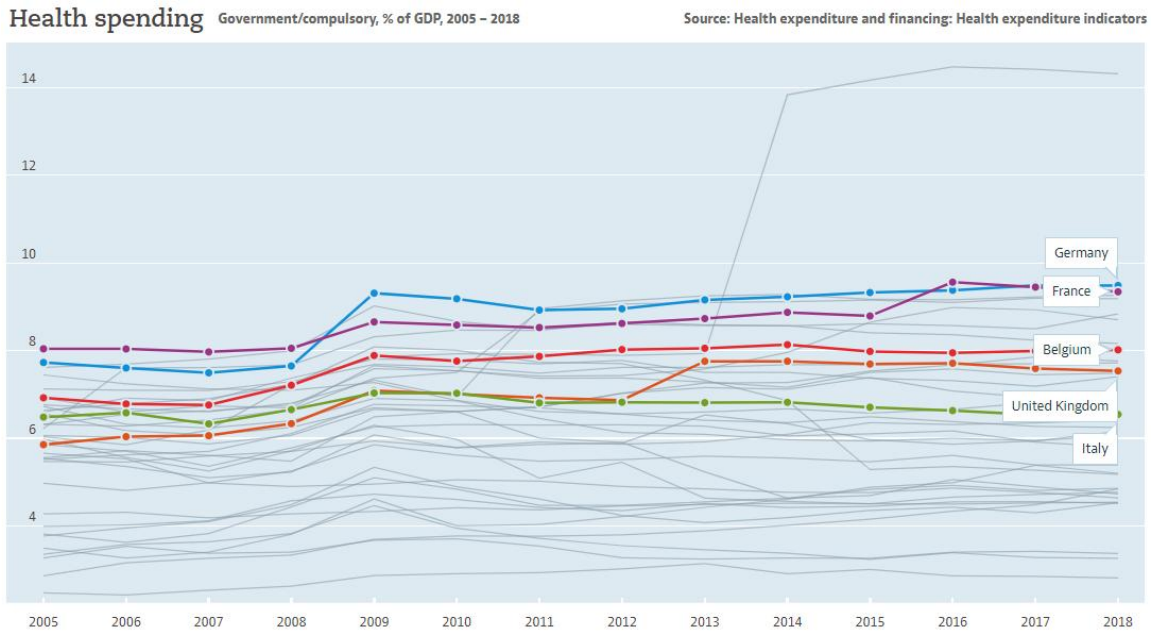


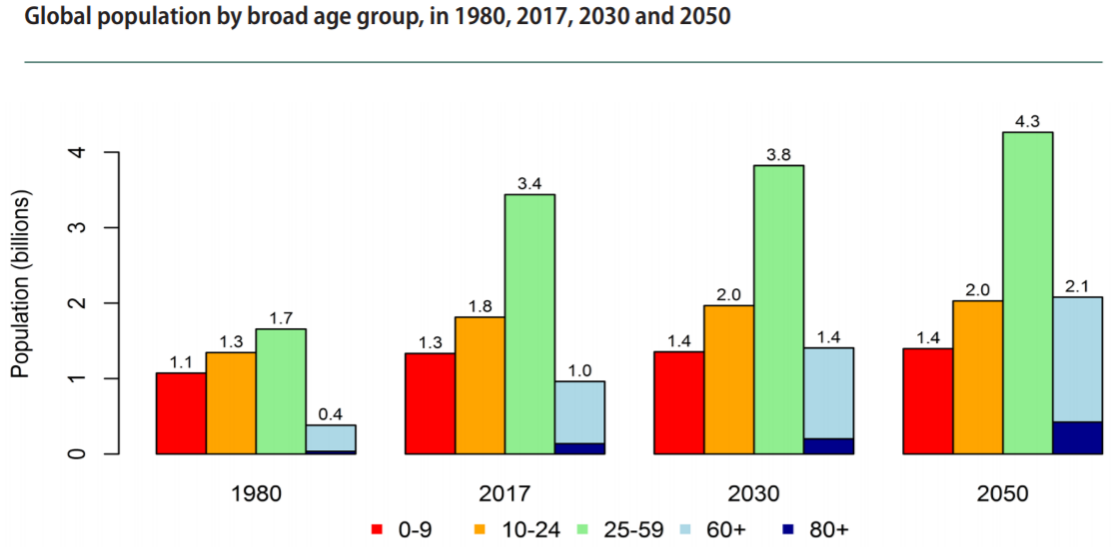
N-test = 22! Why?

[1] Demertzi, Antonopoulos et al, Brain, 2015

Limitations to sample size

1. Time & Cost





Fee-for-service, Diagnosis-related-group payment[4]

[1] OECD Data 2019 [2] UN - World Population Ageing 2017 highlights [3] Luke Allen, Conversation, 2015 [4] KCE Report 302Cs

Limitations to sample size

1. Time & Cost

Healthy volunteers: compliant, cognitively autonomous

2. Motion & Sedation

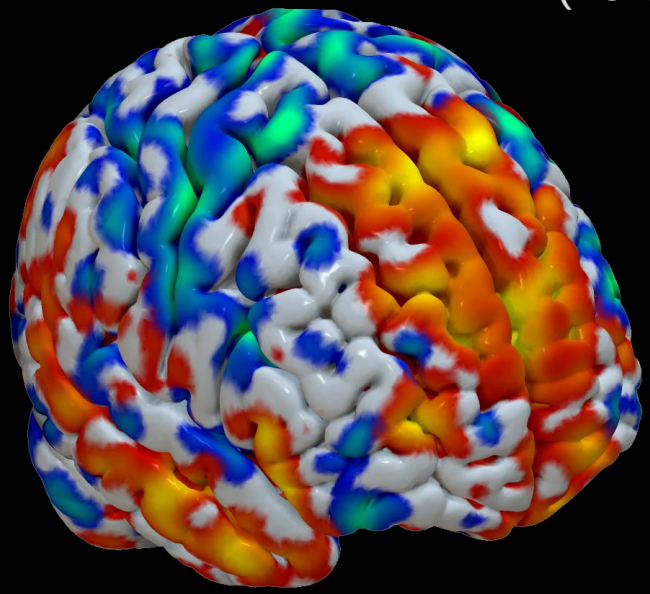
Patients: uncontrolling or non-compliant, discomfort, monitoring vital parameters

	Admitted	With MRI	**Analyzable**	**Non-sedated**
Over 10 years (%):	676 (100%)	465 (69%)	**256 (38%)**	**~110 (16%)**

→ Overcome limitations by optimizing acquisition?

A 30 min cutting-edge, motion-resilient MRI protocol

(20-channel coil, 3T Siemens Vida)



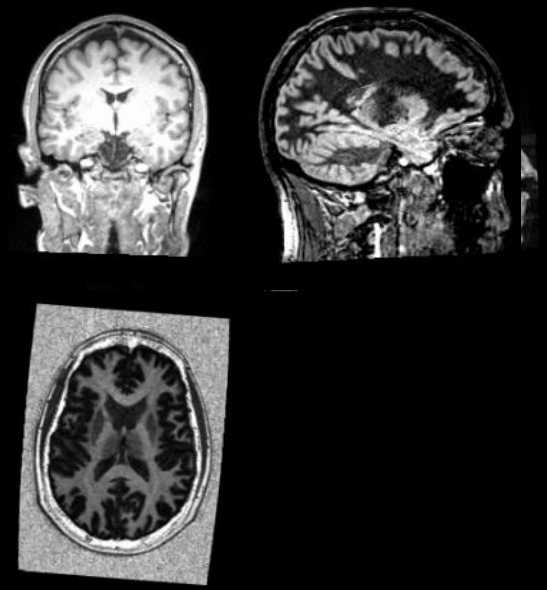
Sub-second BOLD

TR 728ms

500 vols in 6:13

T1 FLAWS

5:02

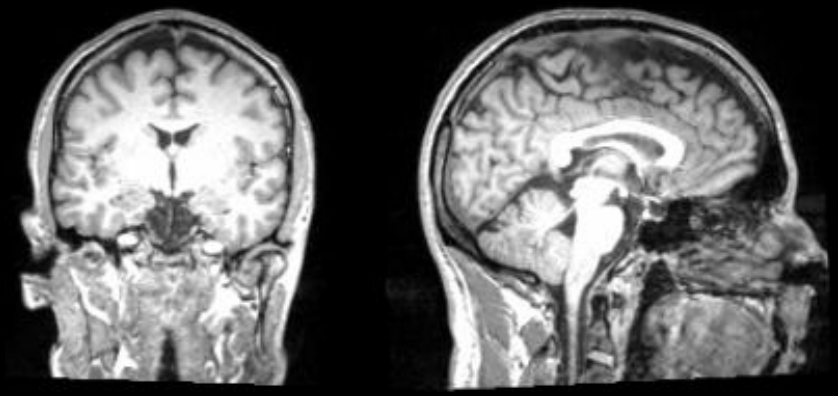


3-shells DWI

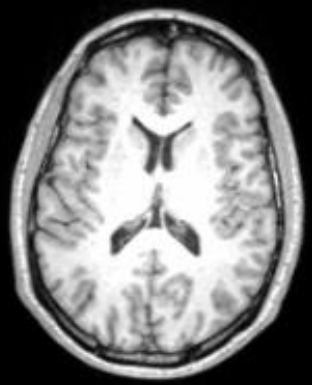
13:25

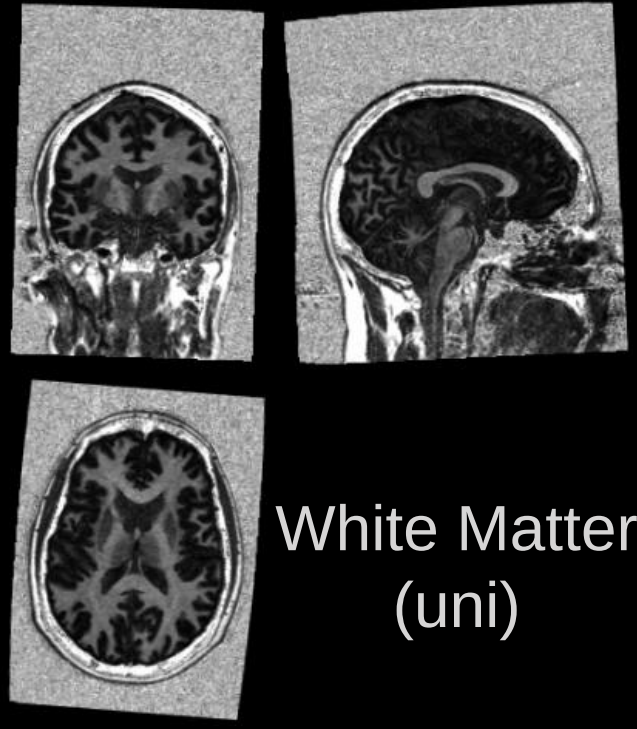
N=35 (8 test controls, 10 stable controls, 17 patients)

T1 FLAWS[1] produces simultaneously:

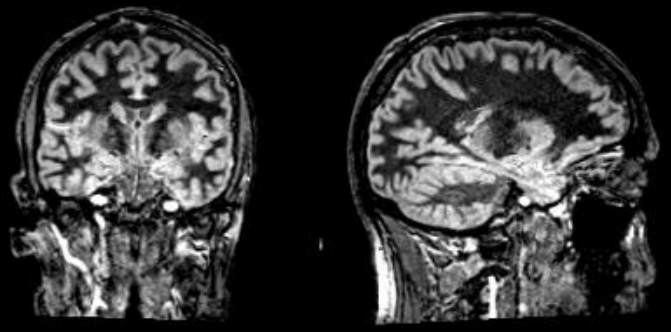


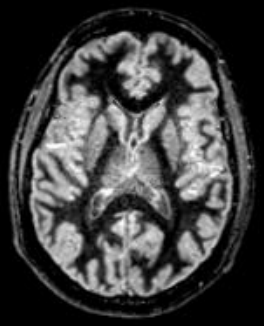
MPRAGE
(inv2)
(structural, 1mm³ iso)





White Matter
(uni)





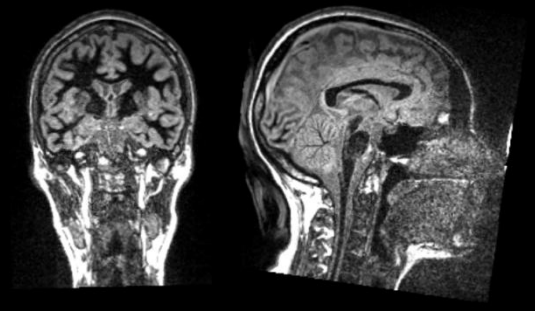
Grey Matter
(inv1)

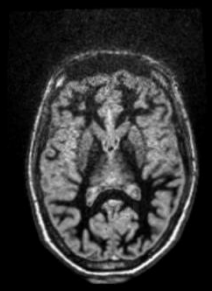
→Physiological segmentation:

- No approximation (not computational!)
- In subject-space
- Always coregistered (even with motion)
- All in 5 min (on 3T), voxel size: 1mm iso
- More clinical infos (complement FLAIR)

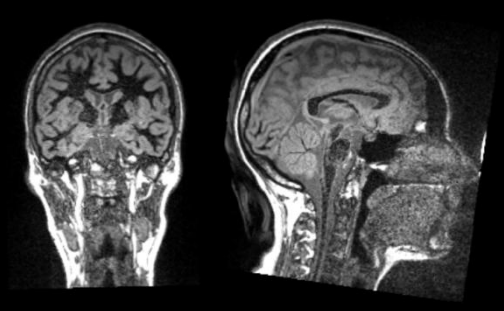
[1] Tanner et al, 2012

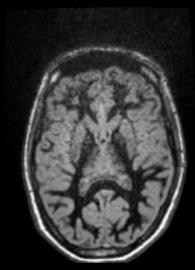
Our T1 FLAWS enhancements: (see also alternatives in [1])



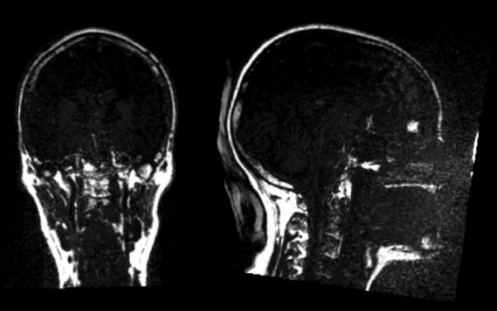


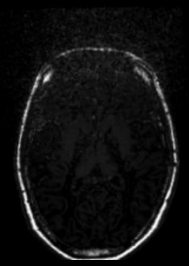
GM
min(inv1, inv2)



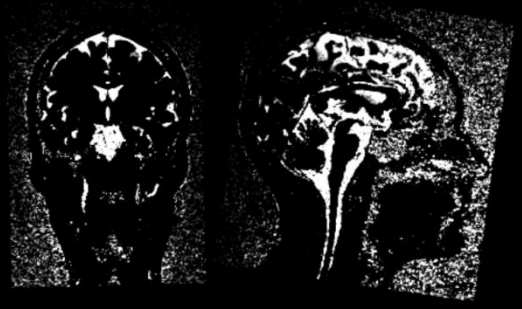


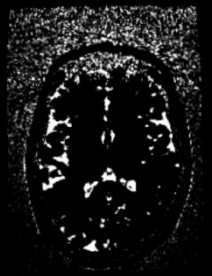
GM mIP
(inv1 .* inv2)
./ (inv1 + inv2)



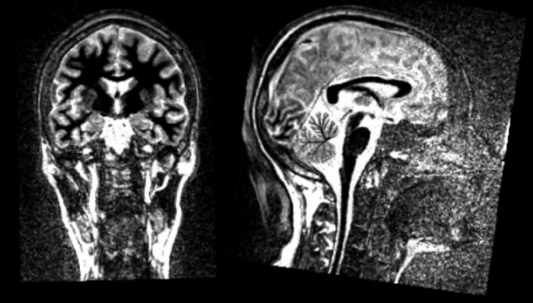


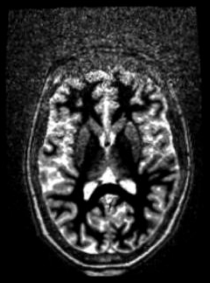
Skull
inv1 .* uni



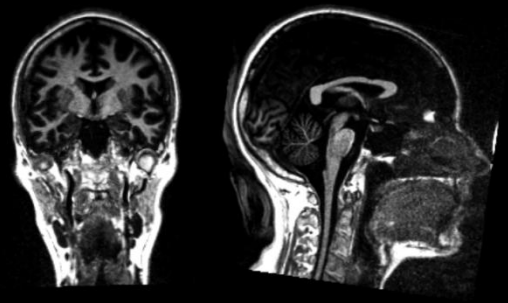


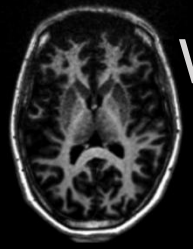
CSF
inv1 - GM





CSF mIP
inv1 - GM mIP

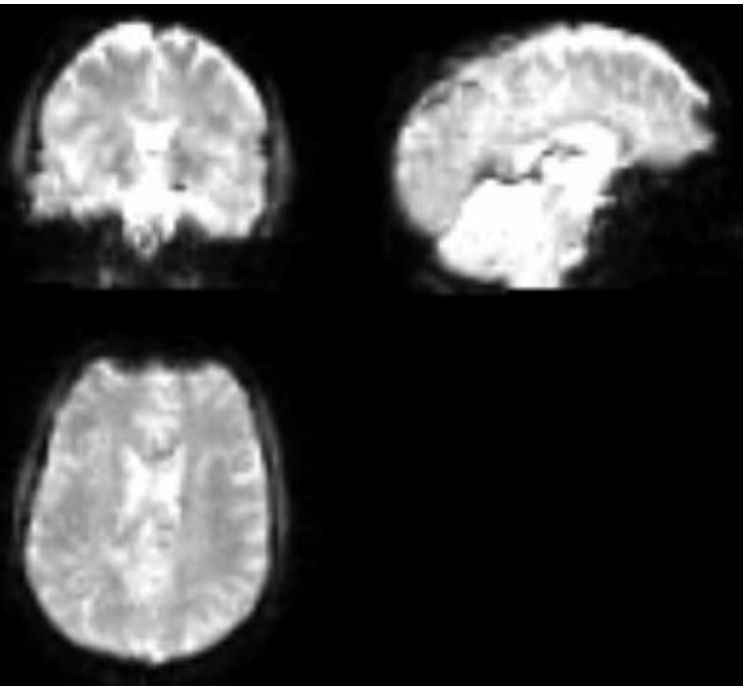




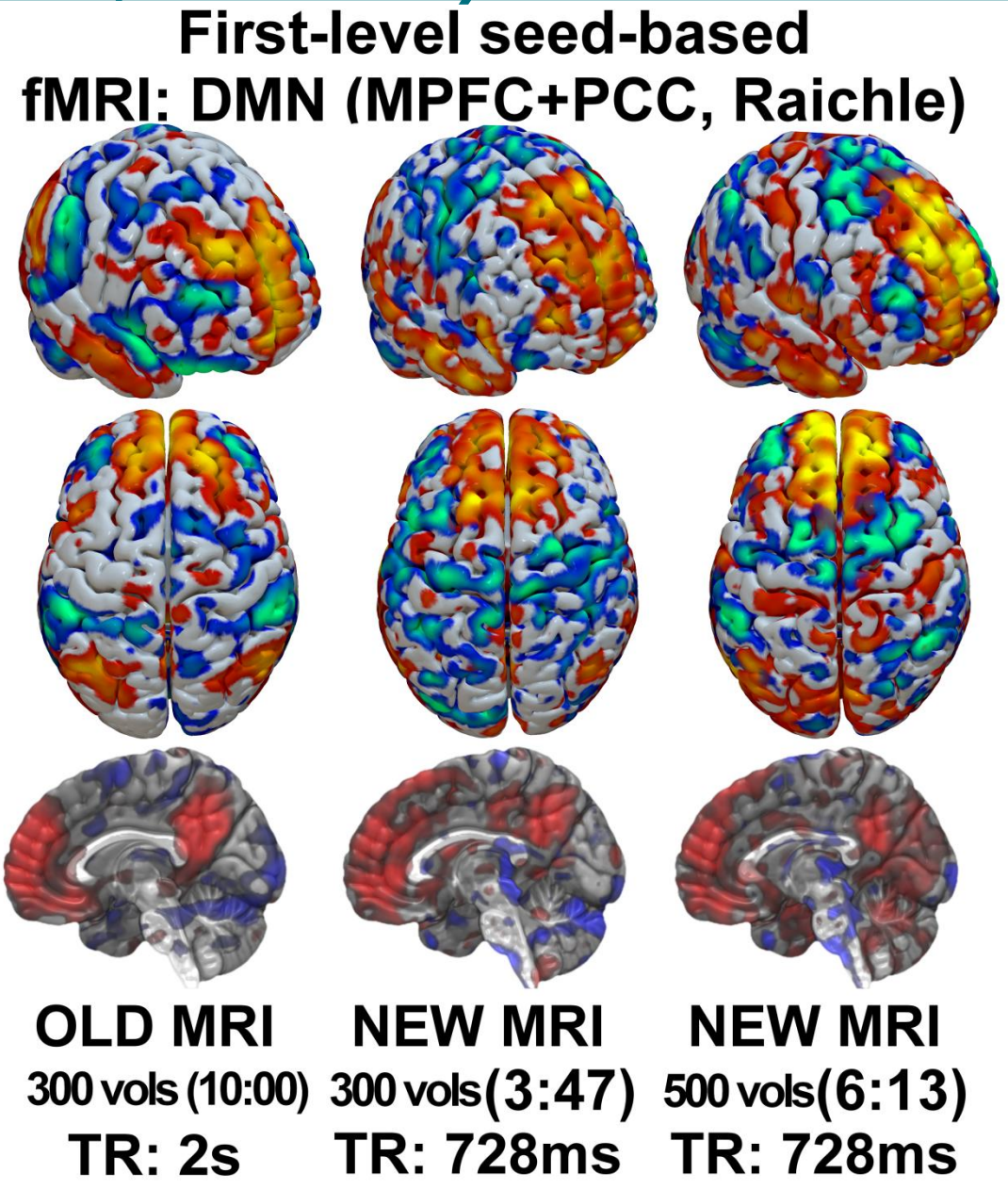
WM denoised
inv2 .* uni

[1] Wang, Y., Wang, Y., Zhang, Z., Xiong, Y., Zhang, Q., Yuan, C., & Guo, H. (2018). *Segmentation of gray matter, white matter, and CSF with fluid and white matter suppression using MP2RAGE. Journal of Magnetic Resonance Imaging.*

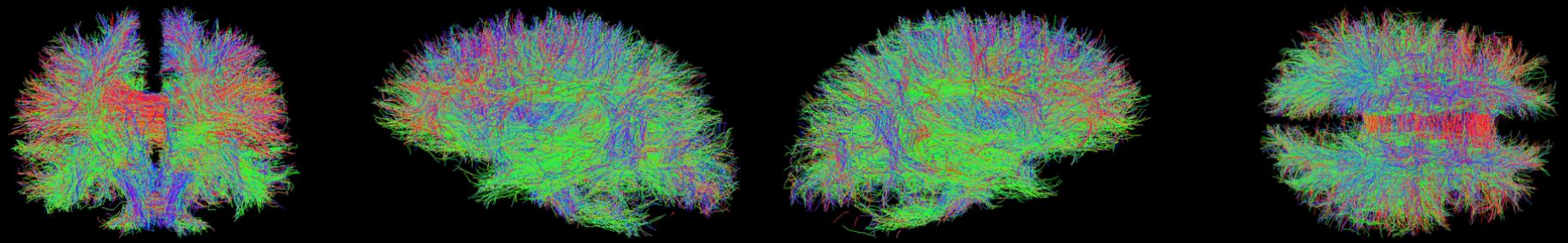
Sub-second EPI Bold fMRI
(728 ms, SMS x3, PI x2, 3mm³ iso)



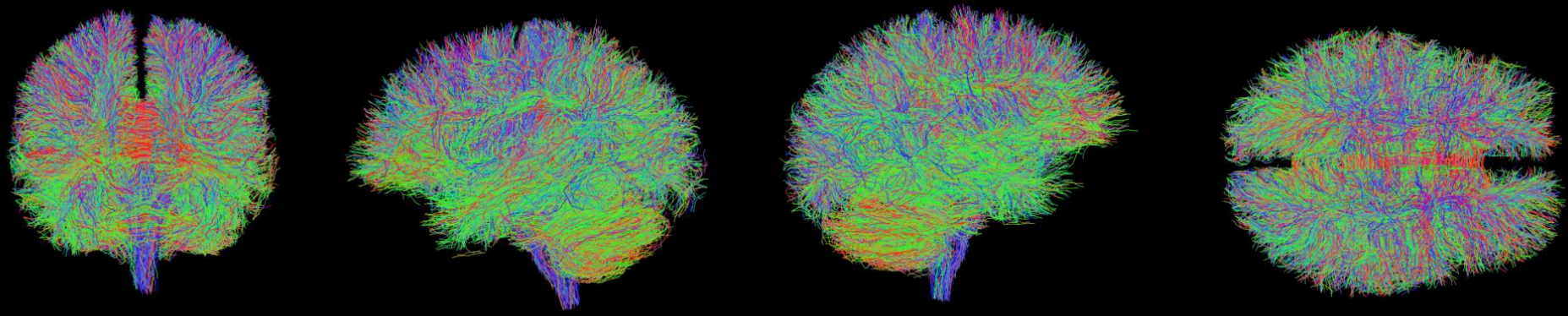
- Dynamic connectivity
- Bypass HRF (<1.5s)
- Motion resilient



OLD MACHINE DTI (SINGLE-SHELL B1000, WITH ACT)



NEW MACHINE DTI (MULTI-SHELL 3-SHELLS, NO ACT) [1]



Optimizations:

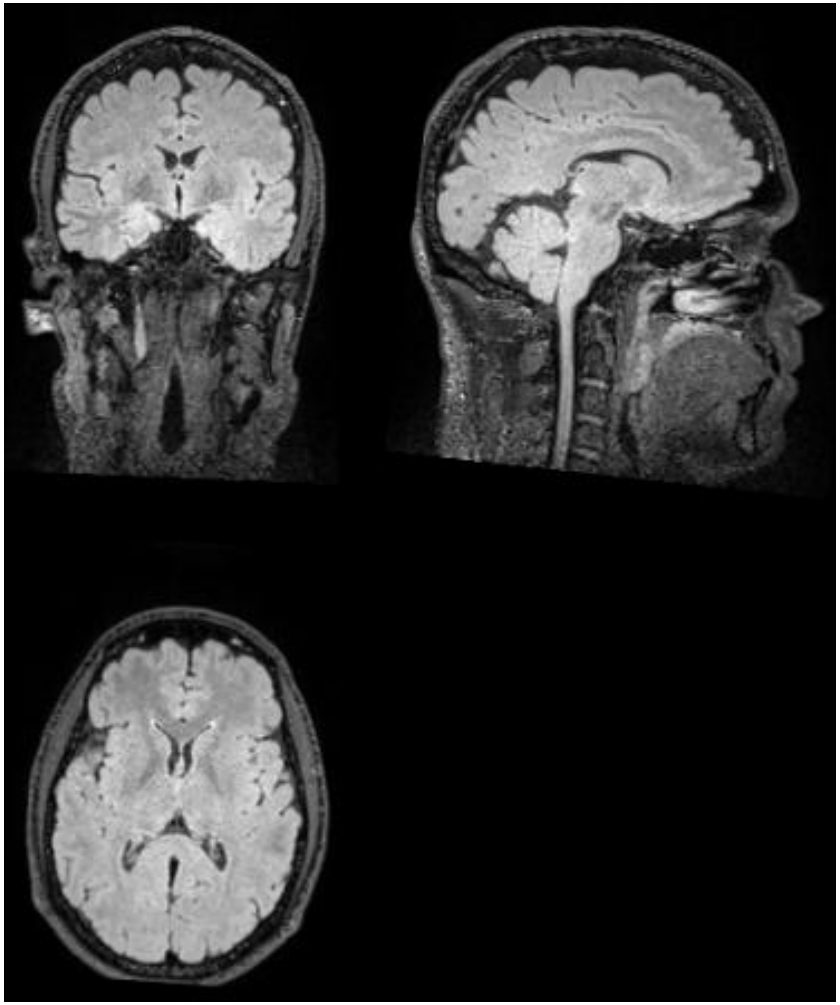
- 3 shells: b700 30dir, b1000 64dir, b2000 64dir.
- b1000 is high quality (small TE), others: higher TE → faster TR.
- SMS x4.
- Partial fourier 7/8 (warning: prevents mrdegibbs!)

Great for:

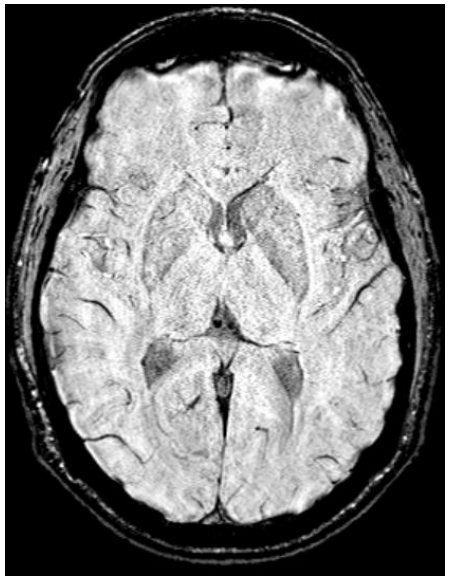
- Clinical tissue assessment under varying diffusion bvals
- Worst case: degrades to single-shell
- Standalone (structural unnecessary)

[1] Dhollander et al, 2016

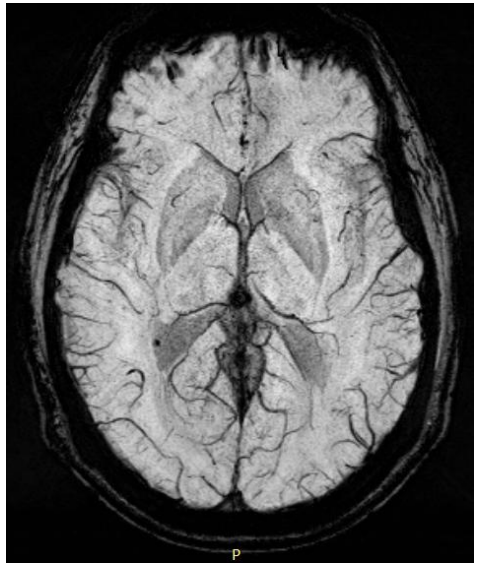
Clinical sequences: FLAIR, SWI, T2, ASL



FLAIR
3:12, 1mm³

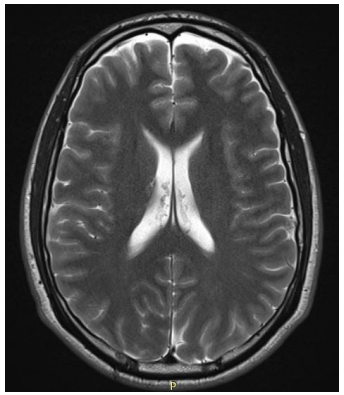


SWI

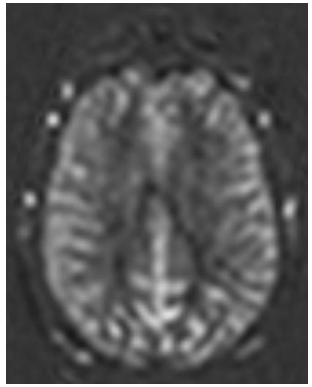


SWI/mIP

3:57, 0.6x0.6x2mm³



T2-TSE
1:21, 0.4x0.4x4.0mm³

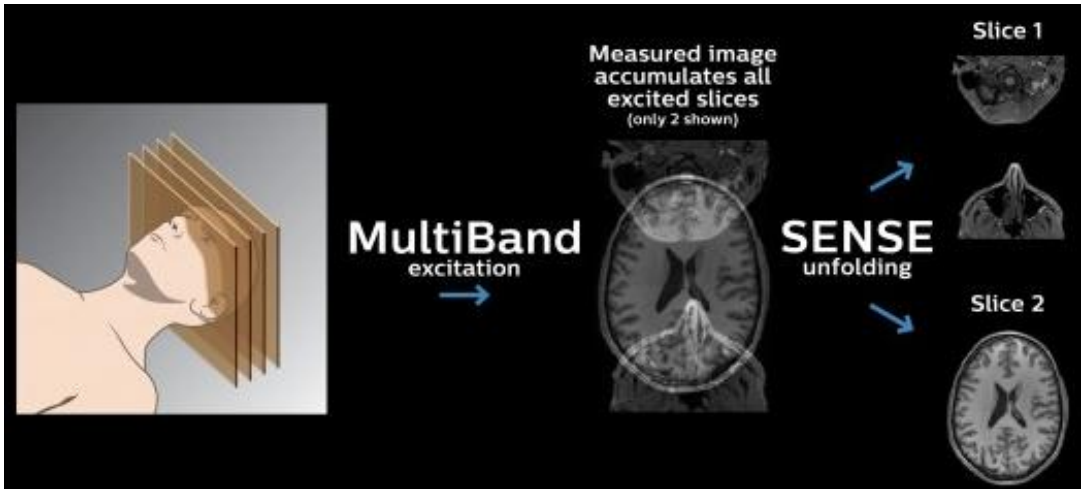


PC-ASL
2:17, 3mm³

How did we make it?

1) Technological optimizations:

- Modern **acceleration**:
  GRAPPA x multiband (SMS)[1] = max x6 no loss, x8 with loss [2,3,4]



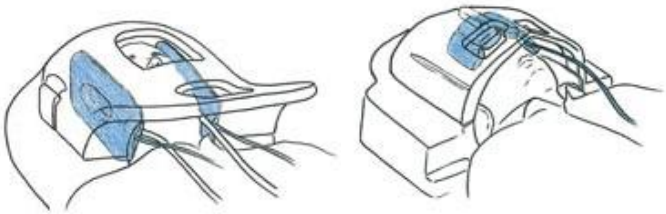
- Literature
  MP2RAGE FLAWS, multi-shell DTI, multi-band BOLD
- Fine-tuning: calculations + trial-and-error
  BOLD flip angle, time of inversion, bandwidth, filters, …

[1] practicalfmri.blogspot.com **[2]** Preibisch, Plos One, 2015 **[3]** Todd, NeuroImage, 2016 **[4]** Smith, 2018, 10.1016/j.mri.2018.06.013

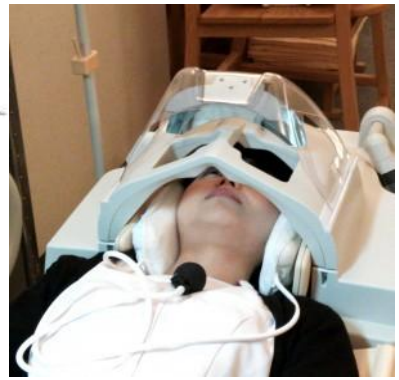
How did we make it? - 2

2) Meta-protocol optimizations:

- Protocol programming:
  - **Maximize speed** (motion resilience, avoids sedation & reacquisitions)
  - Acquire BOLD first (unlikely sedated)
  - Conditional naming
- Physical devices:
  - **3D Head immobilizer**



(here: Pearltec MultiPad)



  - Comfort pillows (reduces back pain), blanket, etc.

[1] Yamamura & Inatomi et al, 2018

Take home message

- Cutting-edge research MRI under clinical constraints possible
- Quality-speed trade-off can be an opportunity
- **New analyses opportunities** in clinical populations
  (dynamic connectivity, multi-tissues unconstrained DTI, …)
- **Reduce risks** & ethical issues by **avoiding sedation**
- Future: compressed sensing, quantitative MRI, thermoplastic mask[1], AI reconstruction

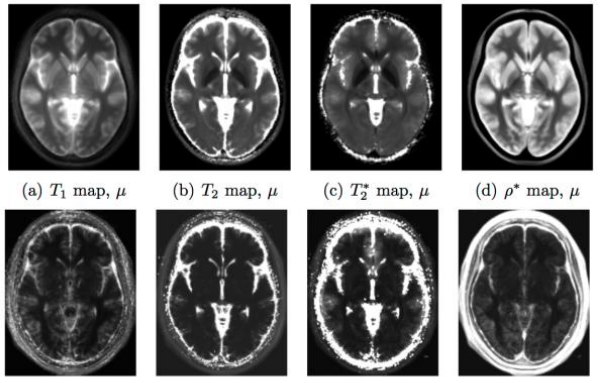


Figure: Mean and standard deviation templates of the T_1, T_2, T_2^* and ρ^* maps.

→ Full protocol for Siemens Vida (need SMS license) & bibliography: **github.com/LRQ3000/mri_protocol**
& analysis scripts: github.com/LRQ3000/csg_mri_pipelines

[1] Mandija, Agata et al 2019

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Thank you for your attention!

github.com/LRQ3000/mri_protocol

Basic analysis scripts: github.com/LRQ3000/csg_mri_pipelines

Huge thanks to Jean-Marc Léonard at Siemens Healthineers, Nathalie Maquet and the Liège Hospital's radiology department team and Pearltec for their support!

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Bonus slides

MRI: the time-quality conundrum

- Great polyvalence, for both research and clinical purposes
- Wide array of imaging contrasts: structural/function anatomy/connectivity, blood flow, lesions, etc.
- But clinical vs research needs are different:
  - Limited acquisition time (30 to 60 min) vs virtually unlimited (2h+)
  - Clinical pertinence (eg, lesions) vs cutting-edge (multi-shell DTI)
  - Uncooperative/uncontrolling patients (motion, discomfort, panic!) vs healthy volunteers (instruction compliance, no motion, calm)
- Usually results in a compromise: most sequences are clinical, some are for research with sub-optimal outdated (but faster) parameters

→ Can we make a MRI protocol both with cutting-edge research sequences and under clinical constraints?

How did we make it?

1) Technological optimization:

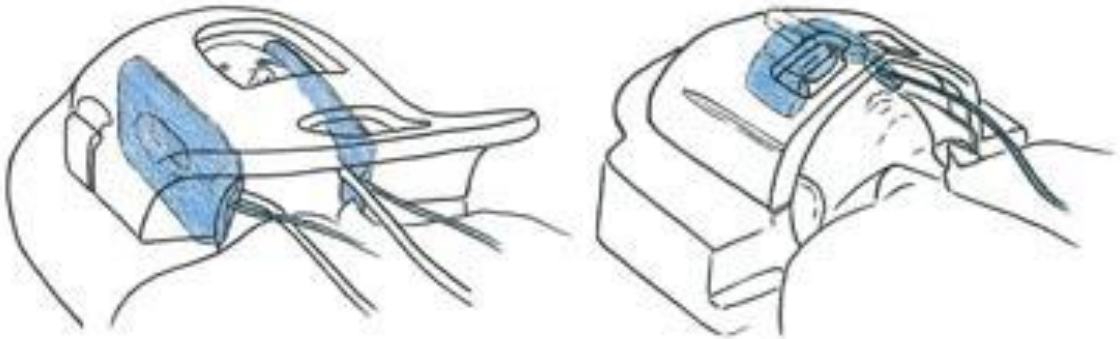
- Modern acceleration technologies:
  GRAPPA parallel imaging + simultaneous multi-slice (SMS aka multi-band).
  Beware of speed-quality trade-off!
- Literature for base sequences (MP2RAGE FLAWS, multi-shell DTI, multi-band BOLD)
- Calculations + trial-and-error to fine-tune parameters (BOLD flip angle, time of inversion, bandwidth)

How did we make it? - 2

2) Meta-protocol optimization:

- Careful protocol programming:
  - Maximize speed of sequence acquisition (reduces risk of motion and need for sedation)
  - Place BOLD first, structural/rest after (ensures patient is awake, less distressed, always guarantees a non-sedated BOLD)
  - Sequence renaming depending on choices (eg, sedated or not?) for automatic documentation stored in DICOMs *(bypass lack of conditional custom data storage in MRI software)*
- Physical devices:
  - Head immobilizer
  - Comfort knee pillow (reduces back pain), blanket, etc.

Inflatable 3D head immobilizer

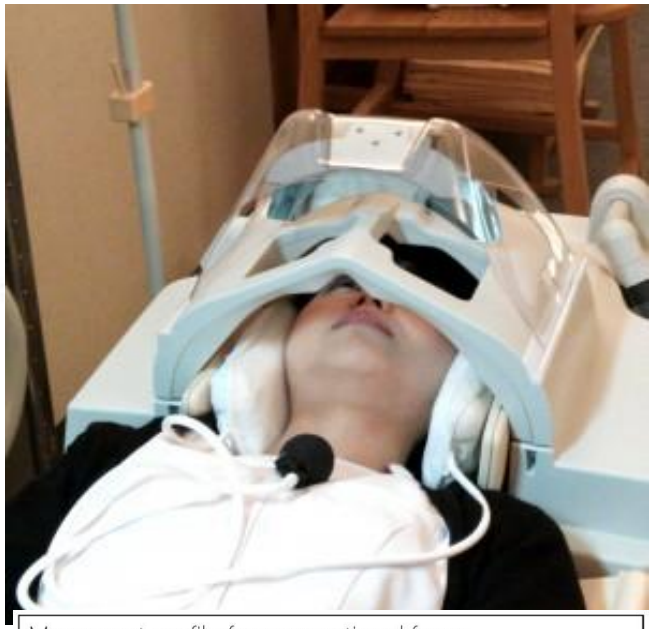


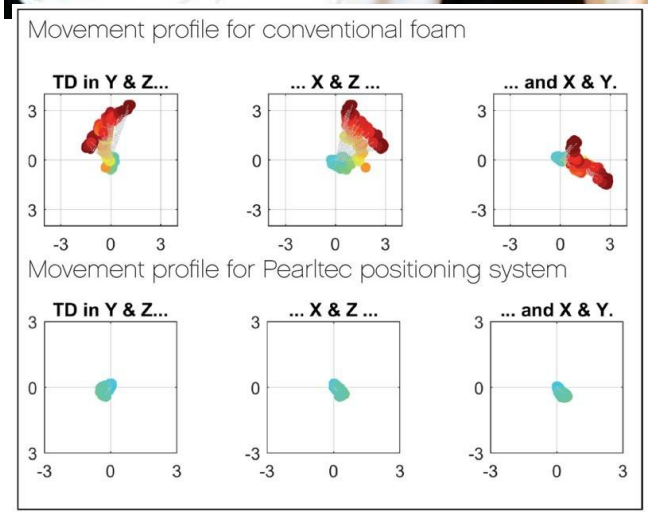
(here: Pearltec MultiPad)

Reduces:

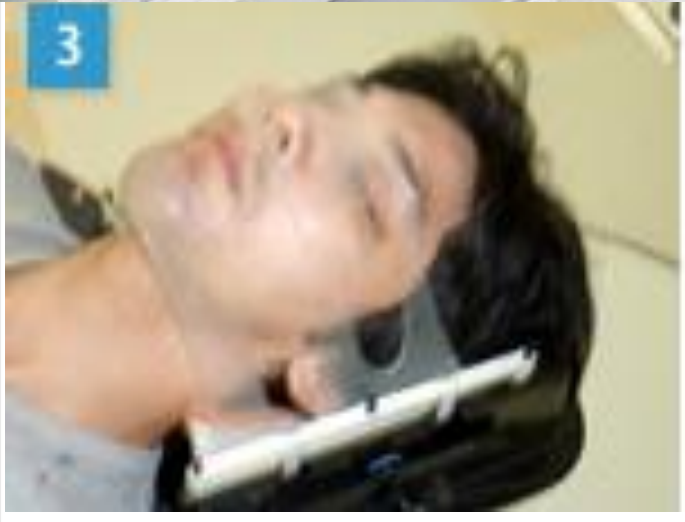
- **motion** artifacts
- need for **sedation**

(see infants studies, eg, Yamamura & Inatomi et al, 2018)





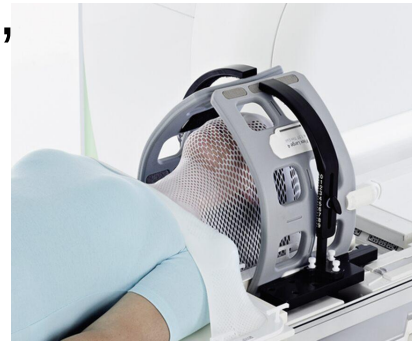
Future: Thermoplastic masks?



(Mandija, Agata et al 2019)

Take home message

- Possible to have a cutting-edge research MRI protocol under clinical constraints, through careful optimization
- Don't need perfection, just something that works with sufficient quality (speed-quality trade-off always applies)
- **New analyses opportunities** in clinical populations (dynamic connectivity, multi-tissues unconstrained DTI, accurate subject-level segmentation)
- **Reduce risks** & ethical issues by avoiding sedation
- Future: compressed sensing, quantitative MRI, thermoplastic mask[1]



→ Full protocol for Siemens Vida (req SMS):
github.com/lrq3000/neuro_slides/cme2019

[1] Mandija, Agata et al 2019

Additional advices

- Enable 3D distortion correction, for all!
- Use alternate streams, allows to save uncorrected versions at no cost! Eg, distortion correction + motion can mess FLAWS, nice to have the original!

TODO Add example FLAWS messed

- Enable Prescan Normalize for subcortical analysis (all sequences), disable other filters (Hamming etc)
- Disable PACE (prospective motion correction), as this prevents retrospective motion correction (ie, with external softwares such as ART)
- If lots of Gibbs noise (eg, in FLAWS or MP2RAGE), lower GRAPPA acceleration!
- For multi-shell DTI, acquire 3 different DTI sequences and bundle together with a Copy Reference to copy the acquisition parameters automatically (necessary for the multi-shell DTI to be valid)

Additional advices

- With uncooperative/uncontrollable populations, the speed-quality trade-off might be simpler: better to speed up and have a more stable (but lower resolution) image, than have a high-resolution image that fails most of the time to be acquired because of motion!
- Acquire with interpolation and rescale, eg: acquire at 0.5x0.5x1.0mm and rescale to 1.0mm³, slight increase in SNR
- Increasing bandwidth reduces susceptibility to metal and chemical artifacts, useful for patients with potentially blood or metal infarcts

About free experimentation

- Feel free to experiment with your protocol, often the sequences are not optimized for your machine and/or needs.
- How to proceed: no necessary need for calculations, trial and error is still the best approach (use bisection approach), but where available, calculations can save you some time instead.
- Try on a dummy or a healthy volunteer, under supervision from radiologists or MRI brand engineer to ensure no risks notably of tissue over-heating. Normally most modern machines implement safeguards that should in any case prevent these issues by warning the operator and change adequately the protocol.

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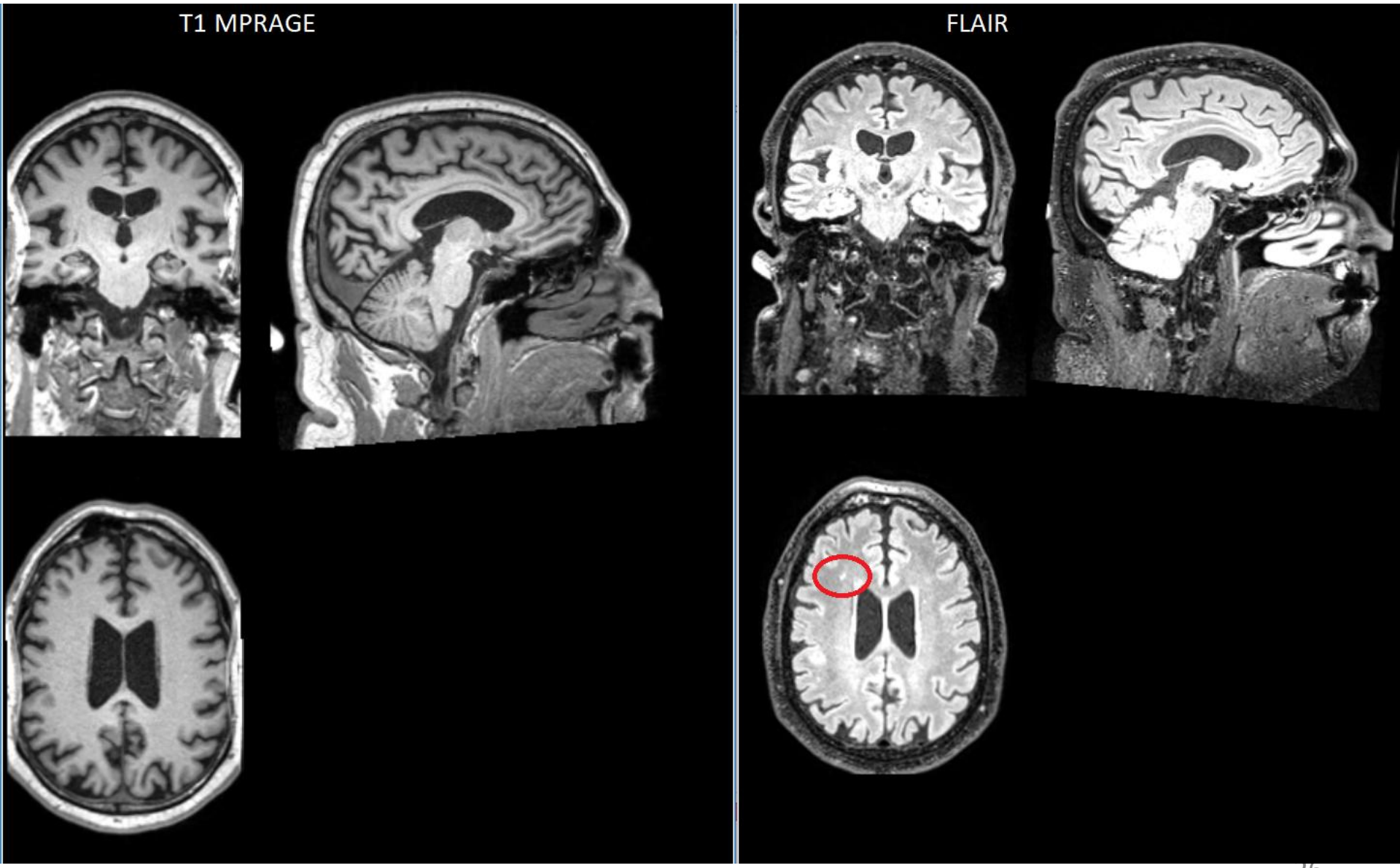
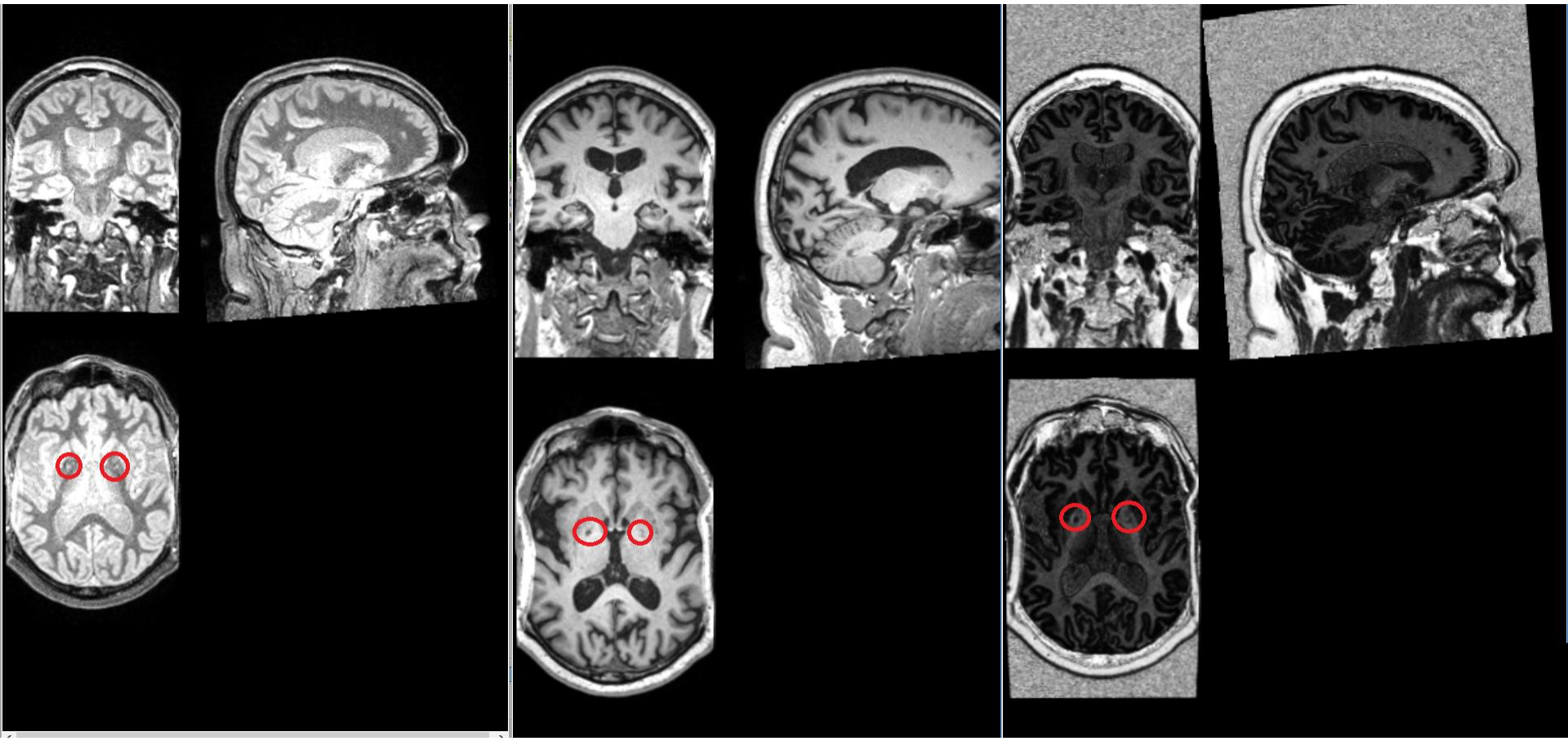
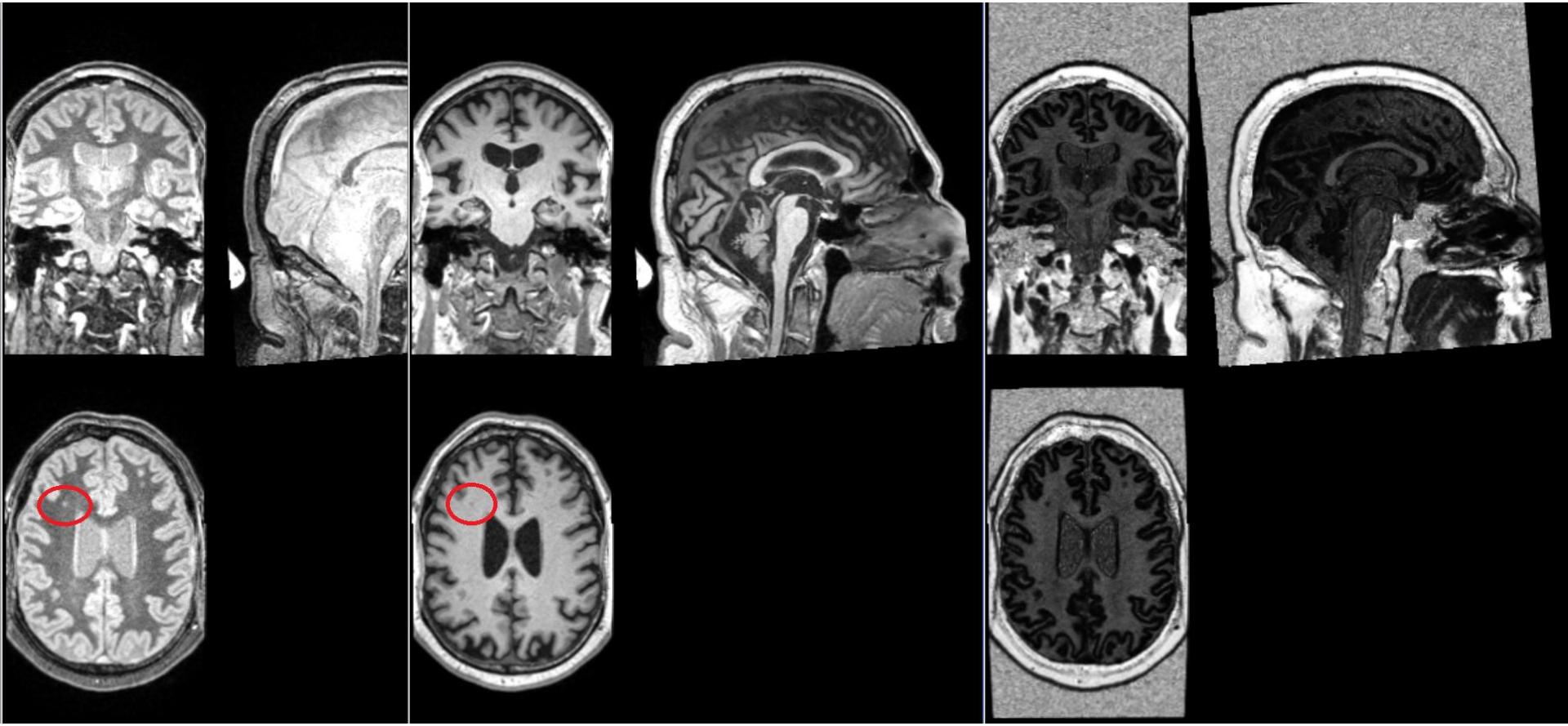
Clinical T1 FLAWS vs FLAIR



Clinical T1 FLAWS vs FLAIR



Clinical T1 FLAWS vs FLAIR



MRI protocol sequences list

1. AAhead_scout

2. Decision: Patient anesthetized?

Yes:

ep2d_bold_repos_moco_s3_p2_short_avec_AG

No:

ep2d_bold_repos_moco_s3_p2_short_sans_AG

3. Decision: Patient anesthetized?

Yes:

- AAhead_scout
- ep2d_bold_repos_moco_s3_p2_long_avec_AG

No:

- ep2d_bold_repos_moco_s3_p2_long_sans_AG

4. gre_field_mapping
5. t1_mp2rage_sag_p3_iso
6. t1_mp2rage_sag_p2_iso_FLAWS_fast
7. ep2d_diff_mddw_30_p2_s3_b700
8. ep2d_diff_mddw_64_p2_s3_b1000
9. ep2d_diff_mddw_64_p2_s3_b2000
10. t2_space_FLAIR_sag_p3_iso
11. t2_swi_tra_p3_1.5mm
12. t2_tse_tra_512_p2
13. asl_3d_tra_fast

→ 20 channels coil but also possible with 64 channels!

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Slice order: check in the machine's printout!

SIEMENS MAGNETOM TrioTim syngo MR B15

\\USER\Head Lg\Study Neuro Lg\MyGroup Lg\ep2d_bold_rest

TA: 10:06 PAT: Off Voxel size: 3.0×3.0×3.0 mm Rel. SNR: 1.00 SIEMENS: ep2d_bold

Properties	
Prio Recon	Off
Before measurement	
After measurement	
Load to viewer	On
Inline movie	Off
Auto store images	On
Load to stamp segments	Off
Load images to graphic segments	Off
Auto open inline display	Off
AutoAlign Spine	Off
Start measurement without further preparation	On
Wait for user to start	On
Start measurements	single

Routine	
Slice group 1	
Slices	32
Dist. factor	25 %
Position	Isocenter
Orientation	Transversal
Phase enc. dir.	A >> P
Rotation	0.00 deg
Phase oversampling	0 %
FoV read	192 mm
FoV phase	100.0 %
Slice thickness	3.0 mm
TR	2000 ms
TE	30 ms
Averages	1
Concatenations	1
Filter	Prescan Normalize
Coil elements	HEA;HEP

Contrast	
MTC	Off
Flip angle	78 deg
Fat suppr.	Fat sat.
Averaging mode	Long term
Reconstruction	Magnitude
Measurements	300
Delay in TR	0 ms
Multiple series	Off

Resolution	
Base resolution	64
Phase resolution	100 %
Phase partial Fourier	Off
Interpolation	Off
PAT mode	None
Matrix Coil Mode	Auto (CP)
Distortion Corr.	Off
Unfiltered images	Off
Prescan Normalize	On
Raw filter	On
Elliptical filter	Off
Hamming	Off

Geometry	
Multi-slice mode	Interleaved
Series	Ascending

Special sat.	None

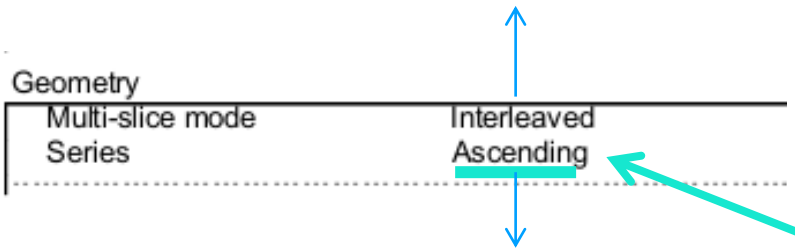
System	
Body	Off
HEP	On
HEA	On
Positioning mode	REF
Table position	H
Table position	0 mm
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P
Transversal	F >> H
Coil Combine Mode	Adaptive Combine
Auto Coil Select	Default
Shim mode	Standard
Adjust with body coil	Off
Confirm freq. adjustment	Off
Assume Silicone	Off
! Ref. amplitude 1H	353.882 V
Adjustment Tolerance	Auto
Adjust volume	
Position	Isocenter
Orientation	Transversal
Rotation	0.00 deg
R >> L	192 mm
A >> P	192 mm
F >> H	120 mm

Physio	
1st Signal/Mode	None

BOLD	
GLM Statistics	Off
Dynamic t-maps	On
Starting ignore meas	0
Ignore after transition	0
Model transition states	On
Temp. highpass filter	On
Threshold	4.00
Paradigm size	30
Meas[1]	Baseline
Meas[2]	Baseline
Meas[3]	Baseline
Meas[4]	Baseline
Meas[5]	Baseline
Meas[6]	Baseline
Meas[7]	Baseline
Meas[8]	Baseline
Meas[9]	Baseline
Meas[10]	Baseline
Meas[11]	Baseline
Meas[12]	Baseline
Meas[13]	Baseline
Meas[14]	Baseline
Meas[15]	Baseline
Meas[16]	Active
Meas[17]	Active
Meas[18]	Active
Meas[19]	Active
Meas[20]	Active
Meas[21]	Active
Meas[22]	Active
Meas[23]	Active

5/+

This « interleaved » means nothing!



Ascending = sequential ascending. Else it would be «interleaved » here for interleaved ascending.

Typical fMRI processing steps

Manual

- Select subjects, prepare demographics (age, gender, etiology, sedation, etc)
- Convert from DICOM to NIfTI
- Exclude bad subjects (too much motion, artifacts, brain surgery, metallic prosthesis, etc)
- T1 reorient
- EPI/DTI manual coregistration

Takes > 90% of the analysis time!

Automatic (mostly)

- Slice timing correction
- Realignment (motion correction)
- Auto coregistration
- Segmentation + Normalization (MNI 152)
- Smoothing
- Movement correction/rejection
- Denoising (PCA aCompCorr, ICA, etc.)

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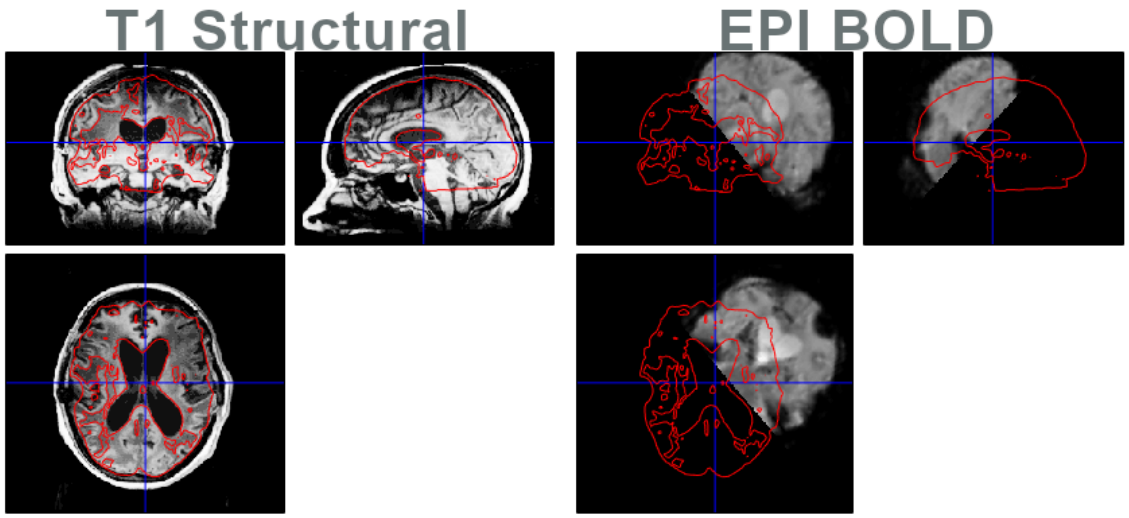
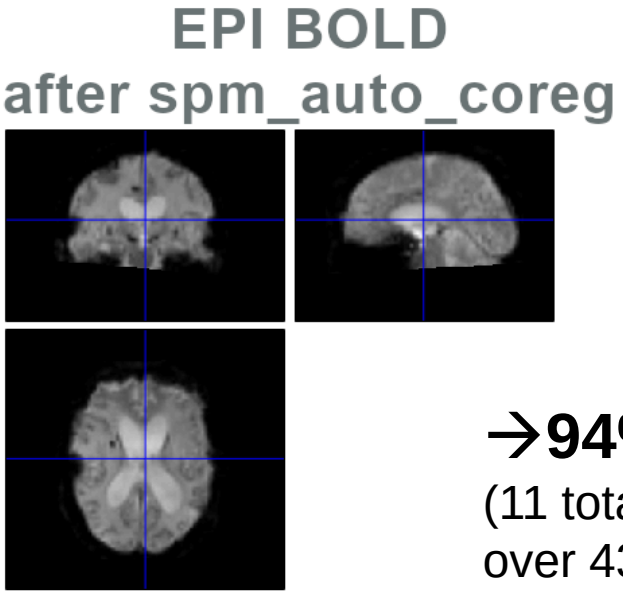
spm_auto_reorient_coregister: Enhanced automatic reorientation and coregistration on brain damaged patients with SPM12

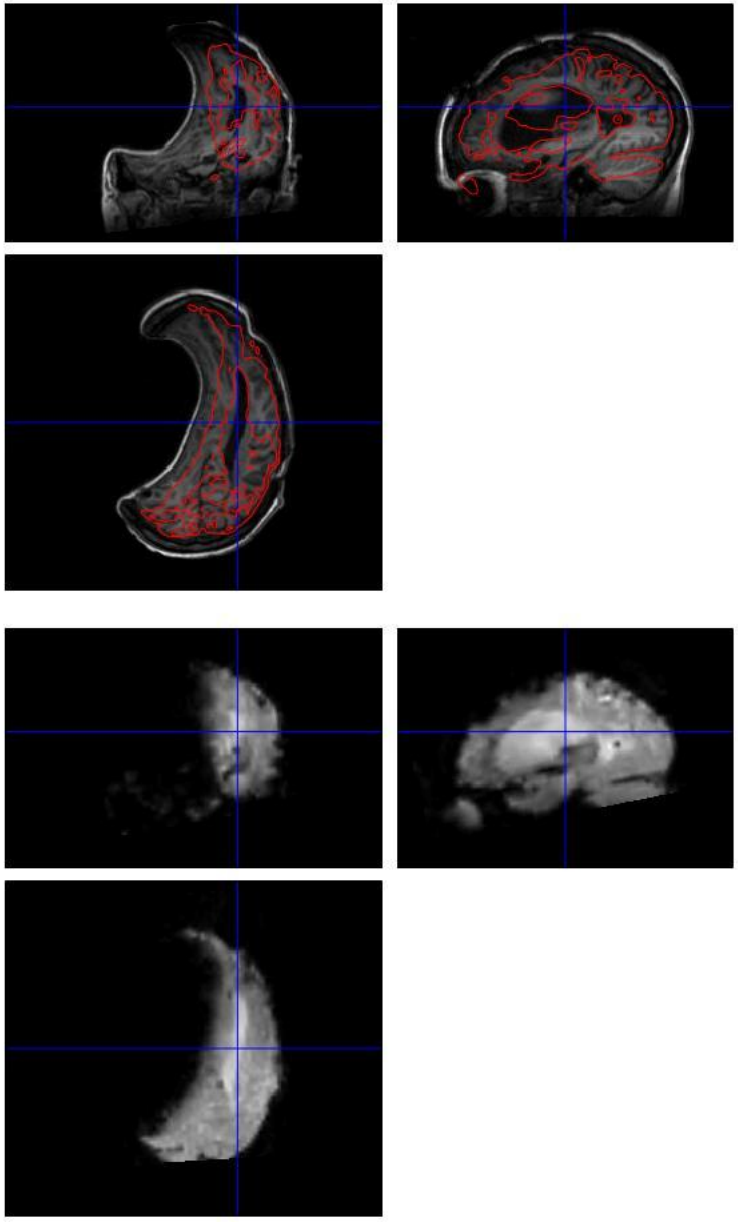




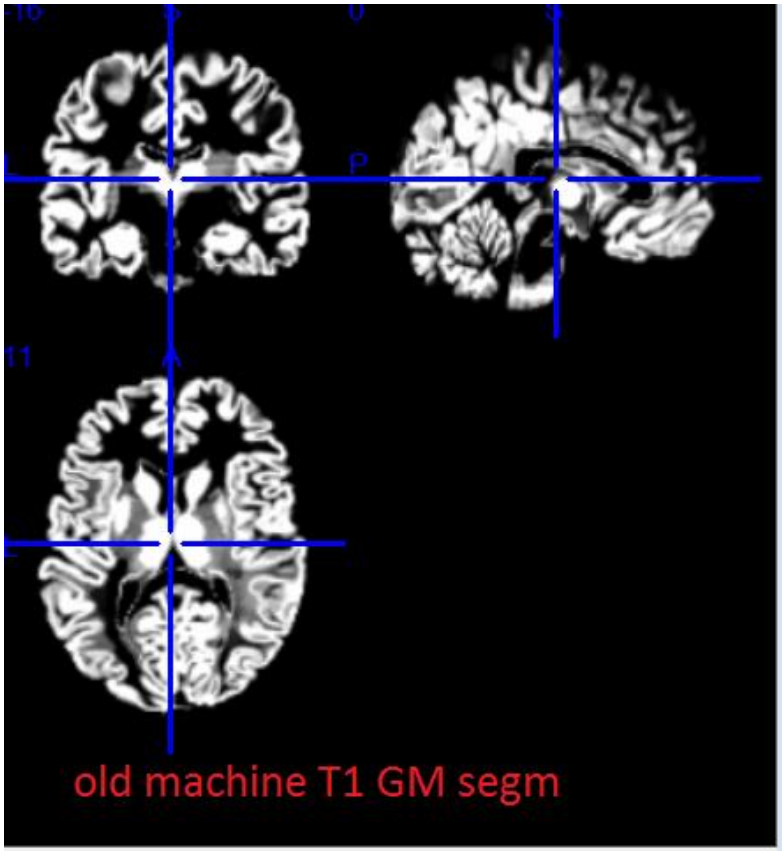
→94% success rate

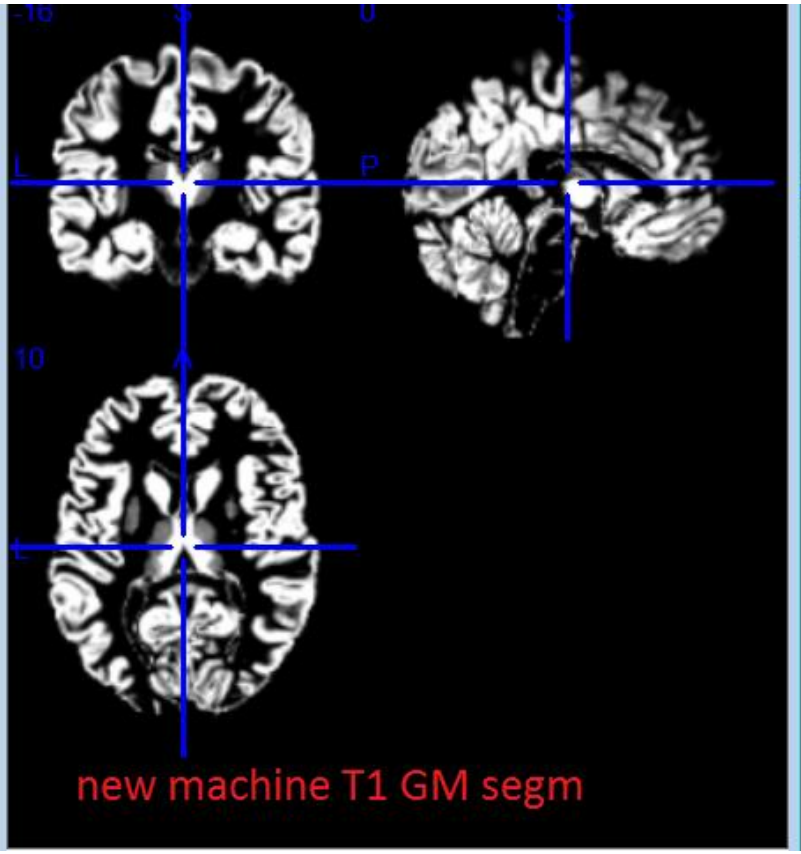
(11 totally off, 17 slightly over 434 sessions, 410 subjects)

https://github.com/lrq3000/spm_auto_reorient_coregister



QA image example (same subject)





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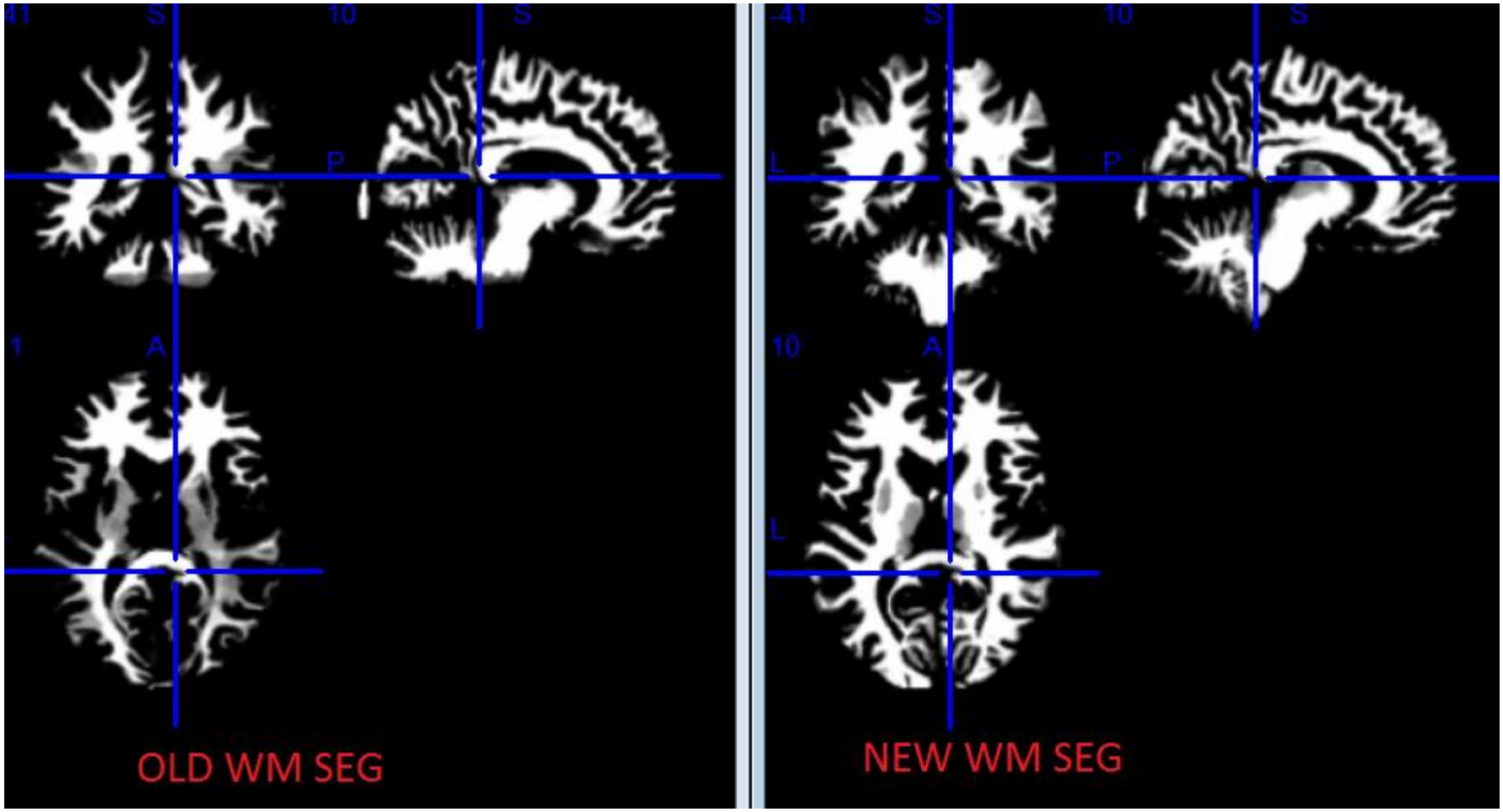
QA image example (same subject)



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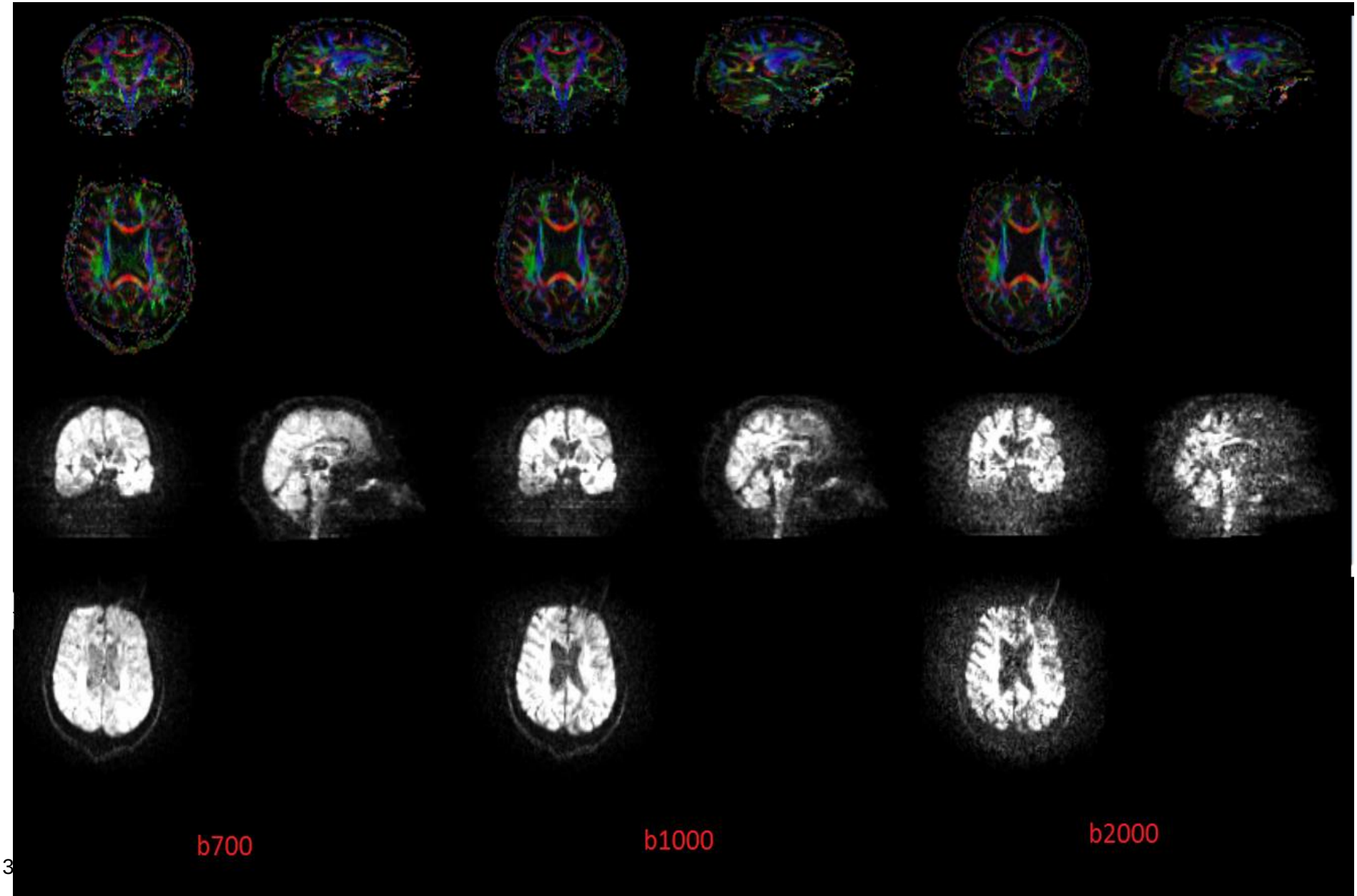
Multi-shell DTI



A 30 min cutting-edge MRI protocol

(20-channel coil)

Short BOLD 3min47: Non-sedated! (except if really problematic patient)
Better have motion than sedation! (we can correct motion, but not sedation!

Might be sedated if necessary, but please avoid

Structural: Sedation OK!

Note: If sedated, please choose « yes » in the boxes highlighted here in red.
Please do not delete or replace any sequence!
(Sequence name will change according to sedation decision set here)

Note2: 3 DTI sequences go together ALWAYS!
If you need to redo DTI, please redo them all!

All sequences can be implemented on any 3T Siemens with multiband and MP2RAGE (multi-echo T1) support (here Vida)

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