

Cortex pathology in MS patients

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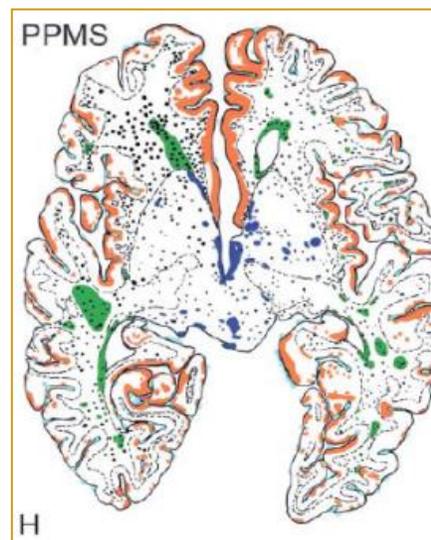
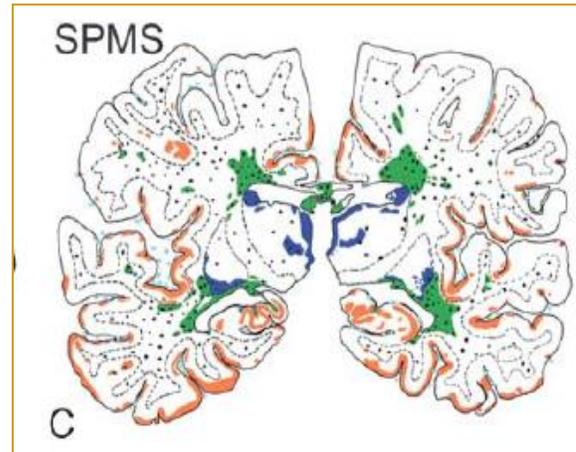
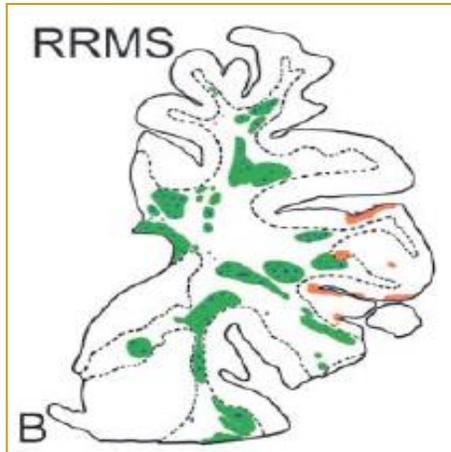
Cortex pathology in MS patients

- MS physiopathology and cortical damage
- Clinic of cortical damage
- Imaging cortical damage
- Implications

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MS: focal & diffuse pathological processes



● **FOCAL DEMYELINATED PLAQUES IN WM**

● **LESIONS in CORTEX and DEEP GM**

Dark dots: diffuse inflammation in WM

Multiple Sclerosis damage

WM

GM

Focal ● "plaques"

Focal cortical ● and deep ● GM lesions

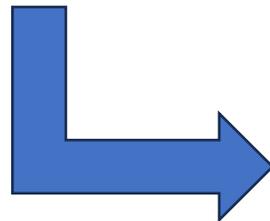
NAWM
Normal appearing WM = Non focal lesional WM (NFLWM)

NFLGM
Non focal lesional grey matter

What happens inside the MS cortex?

Compared to
WML
physiopathology

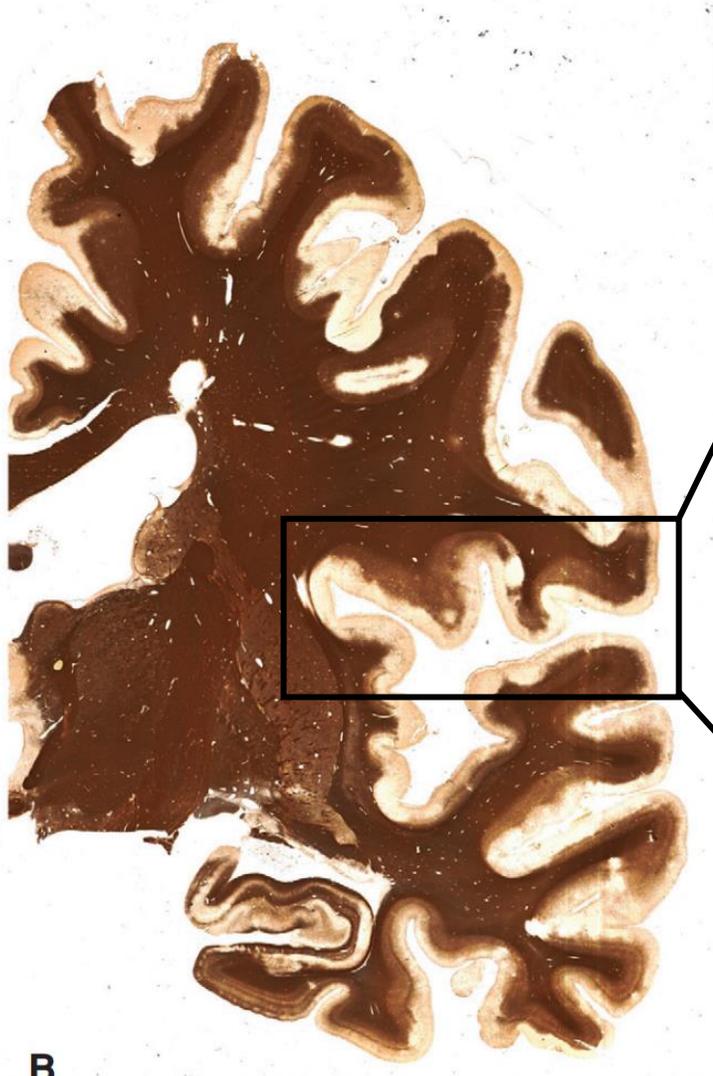
- Less BBB alterations
- Less lymphocytes recruitment
 - *BUT increased immune cell infiltration into overlying meninges (TYPE III CL)*
- Less complement deposition
- Less activated microglia



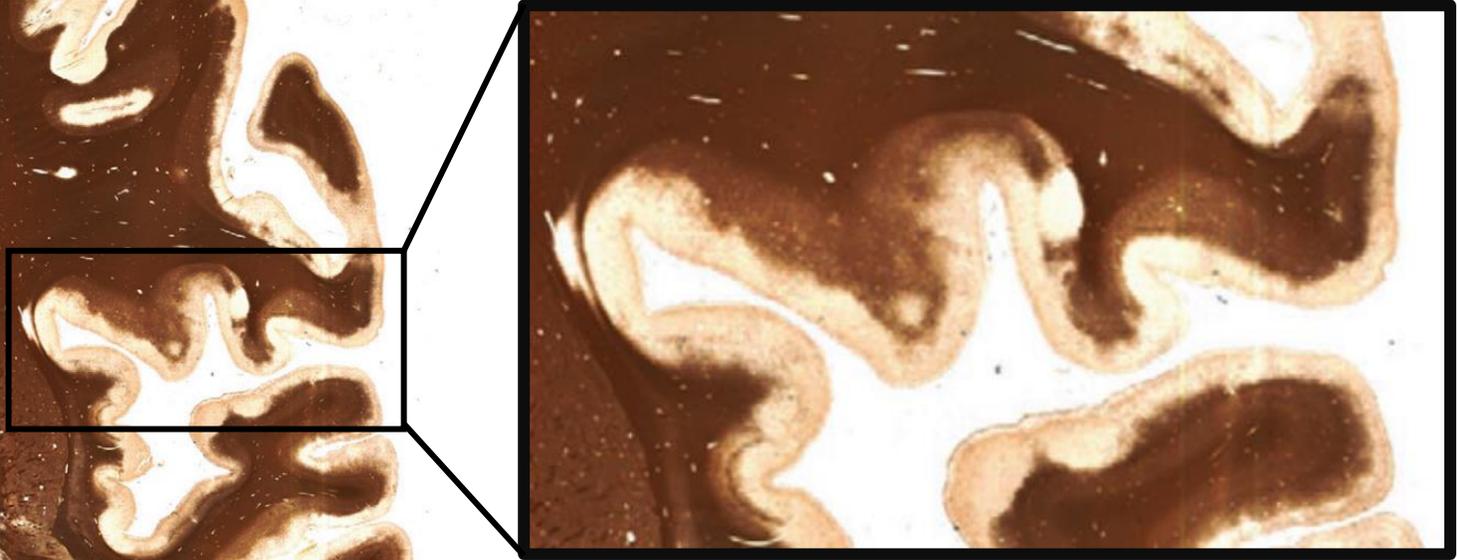
- Cortical demyelination
- Synaptic loss
- Neuro-axonal damage
- Iron loss



A

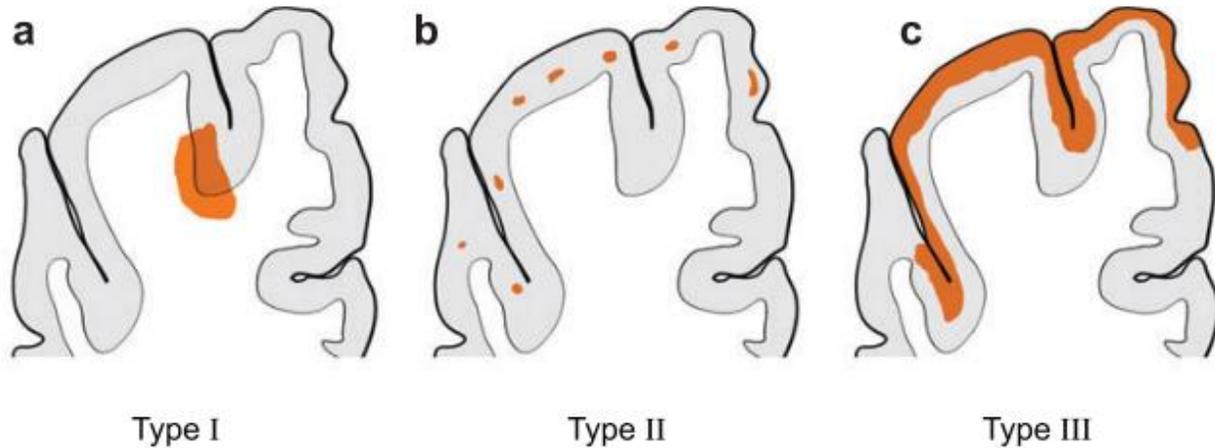


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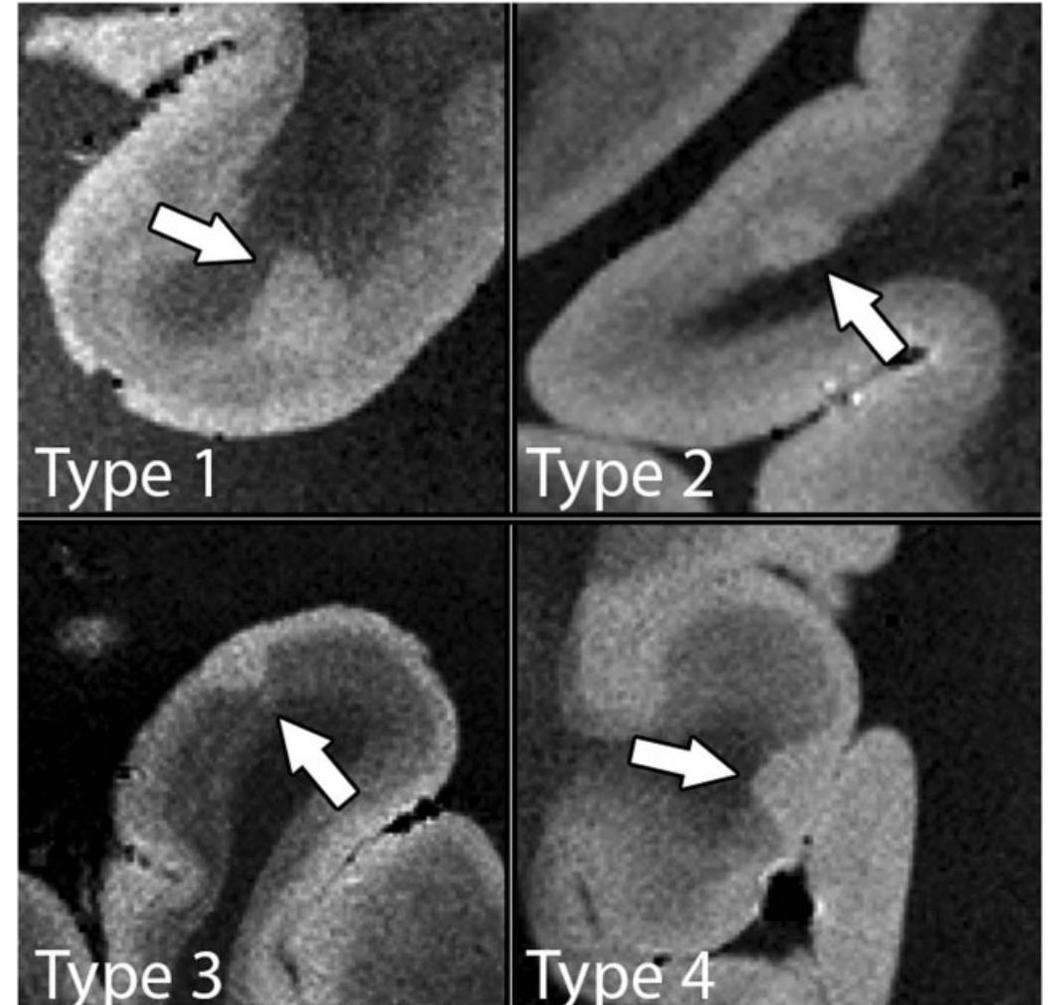


Focal cortical lesions sub-classes

Trapp et al. 2008



- *Type I : leuco-cortical/juxta-cortical*
- *Type II : intra-cortical*
- *Type III : subpial*
- *Type IV : all cortex deep*



7T-T2* (post-mortem)

Kilsdonk et al. 2016

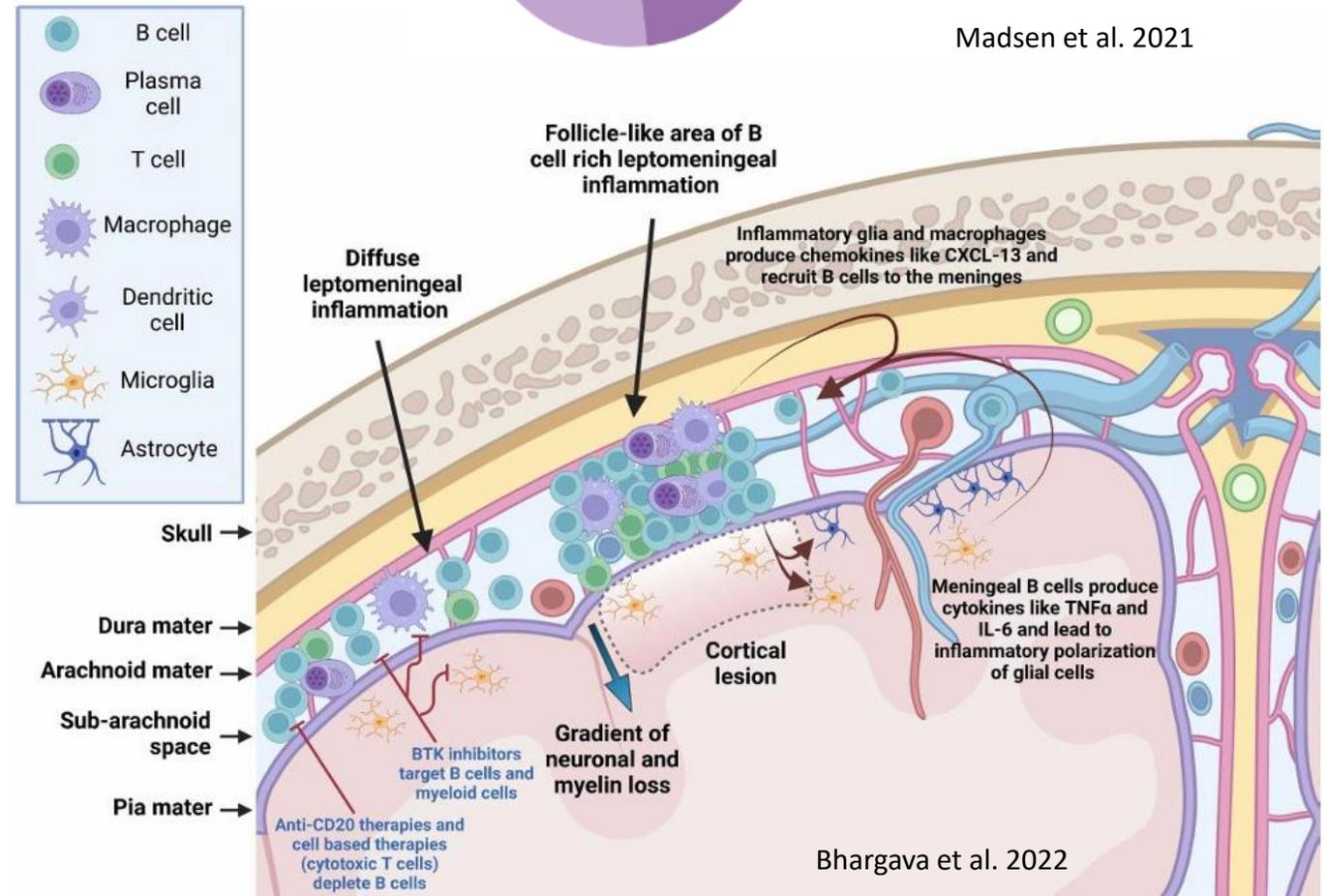
➤ *Type I : leuco-cortical/juxta-cortical*

➤ *Type II : intra-cortical*

➤ ***Type III : subpial***

➤ *Type VI : all cortex deep*

Lepto-meningeal inflammation



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Clinical manifestations of cortex damage



- Progression
- Cognitive impairment
- Epilepsy
- Mood change, psychiatric symptoms
- Fatigue?

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Conventional MRI

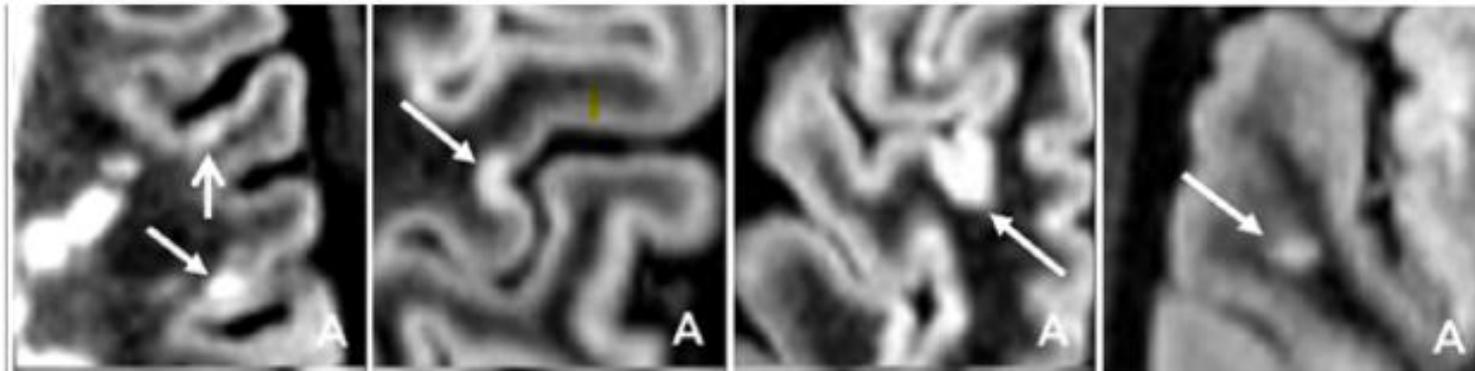
- **1,5T – 3T MRI** best sequences for CL detection
 - DIR
 - PSIR

POST-MORTEM
histological/MRI
confrontation

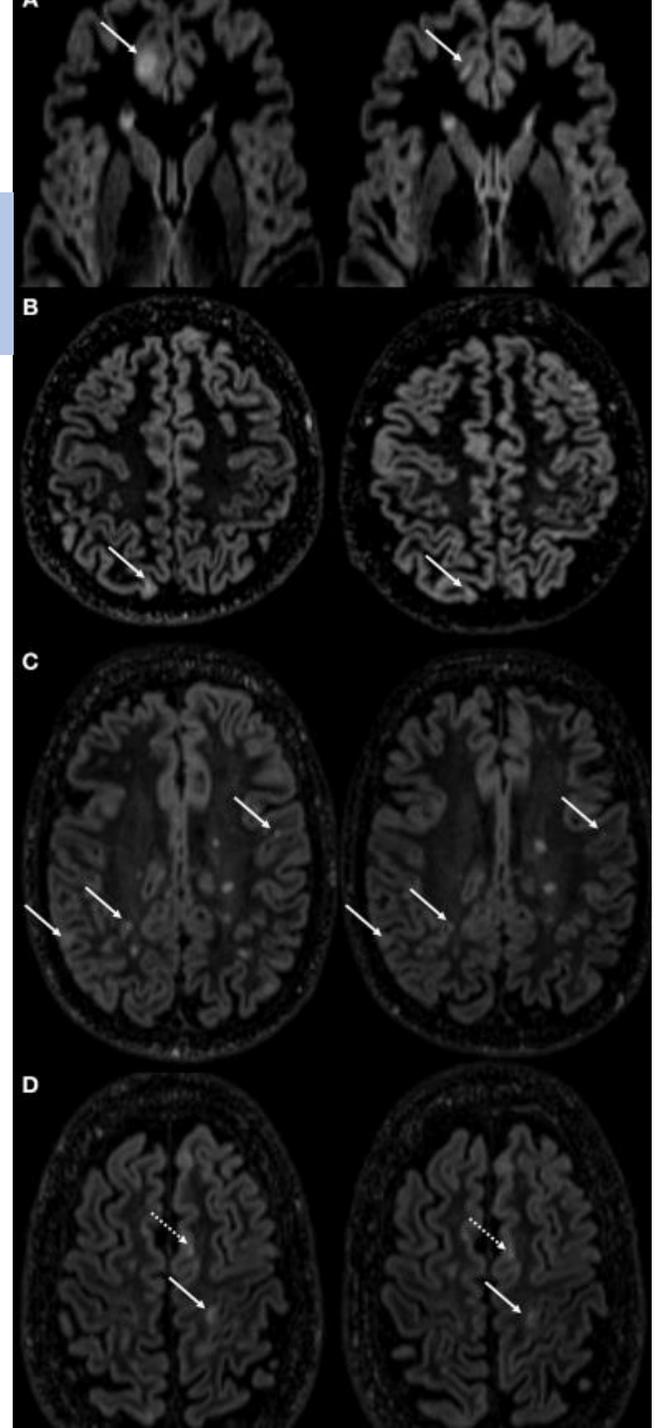


+ - 20% CL

Conventional MRI – 3T DIR



Nelson et al. 2011



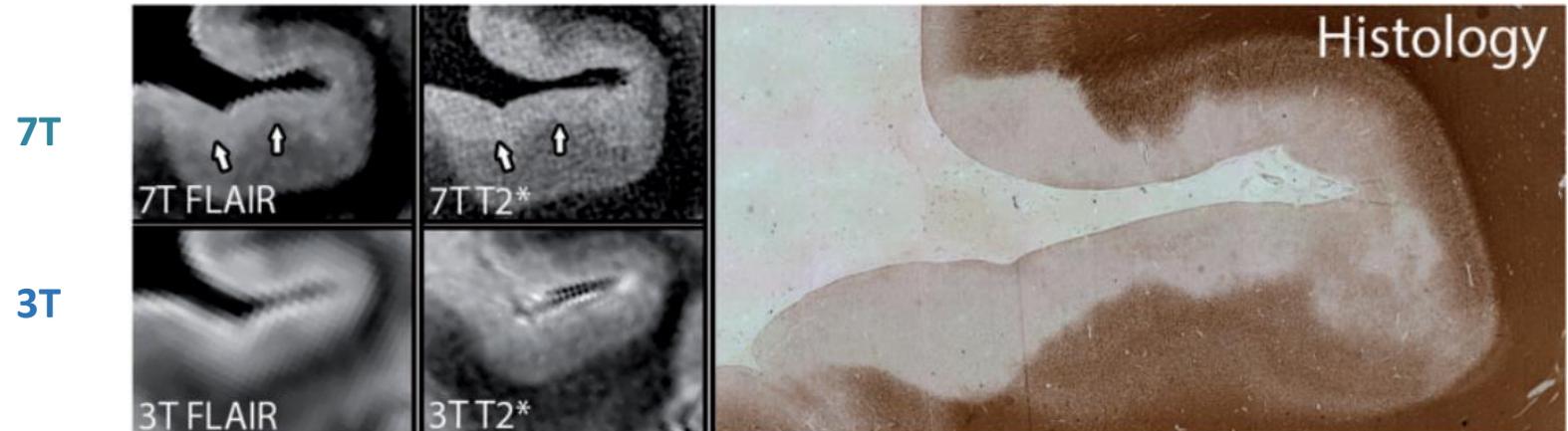
Faizy et al. 2019

Non-Conventional MRI

- **UHF 7T MRI**

for CL detection

- FLAIR
- T2*
- MPRAGE/
MP2RAGE

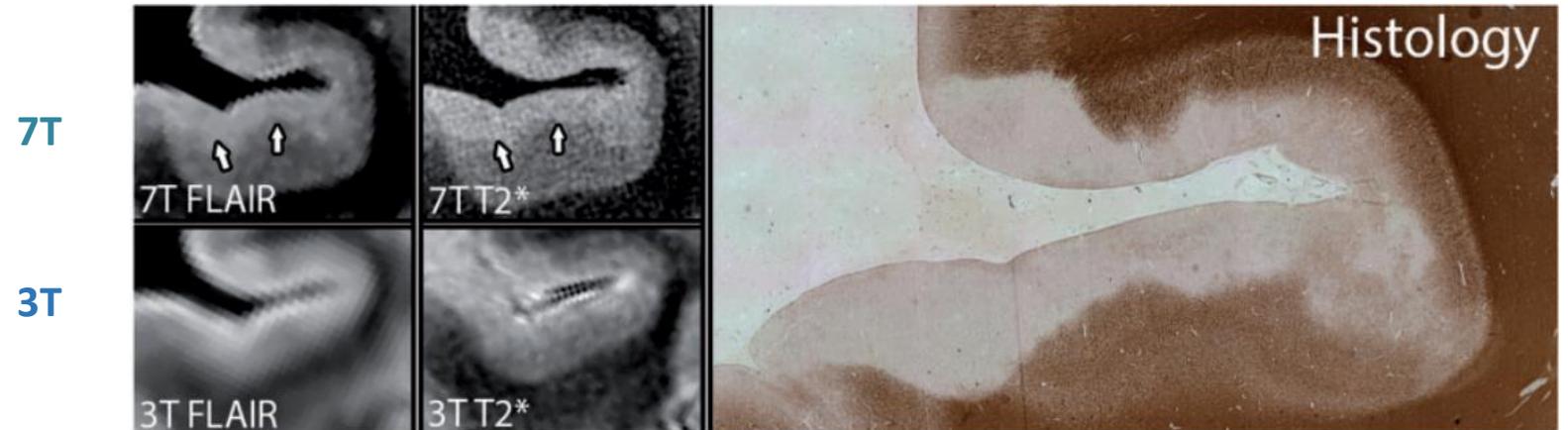


Non-Conventional MRI

- **UHF 7T MRI**

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Kilsdonk et al 2016

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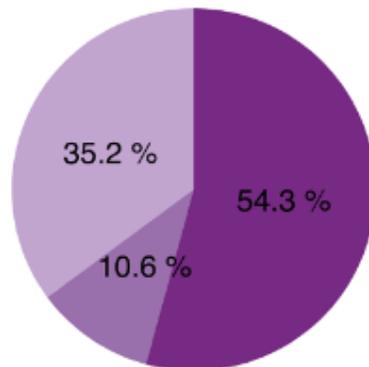
+ - 35-40 % CL

Non-Conventional UHF MRI

- Imaging of **cortical demyelinated lesions**
 - Type I (leucocortical) more easily detected

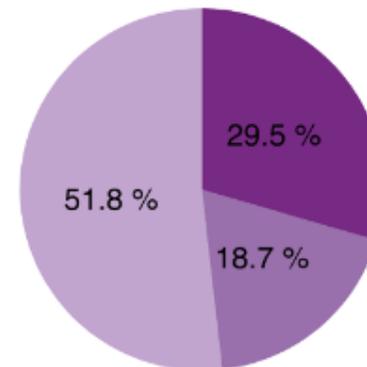
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MRI



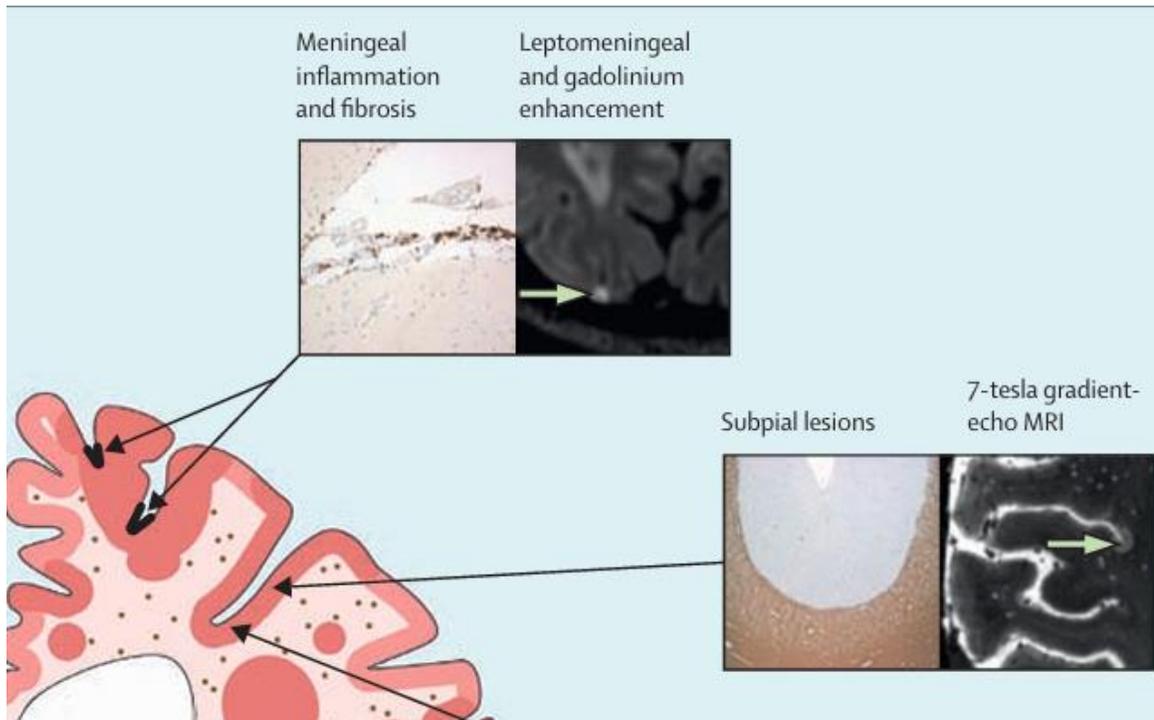
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Histology

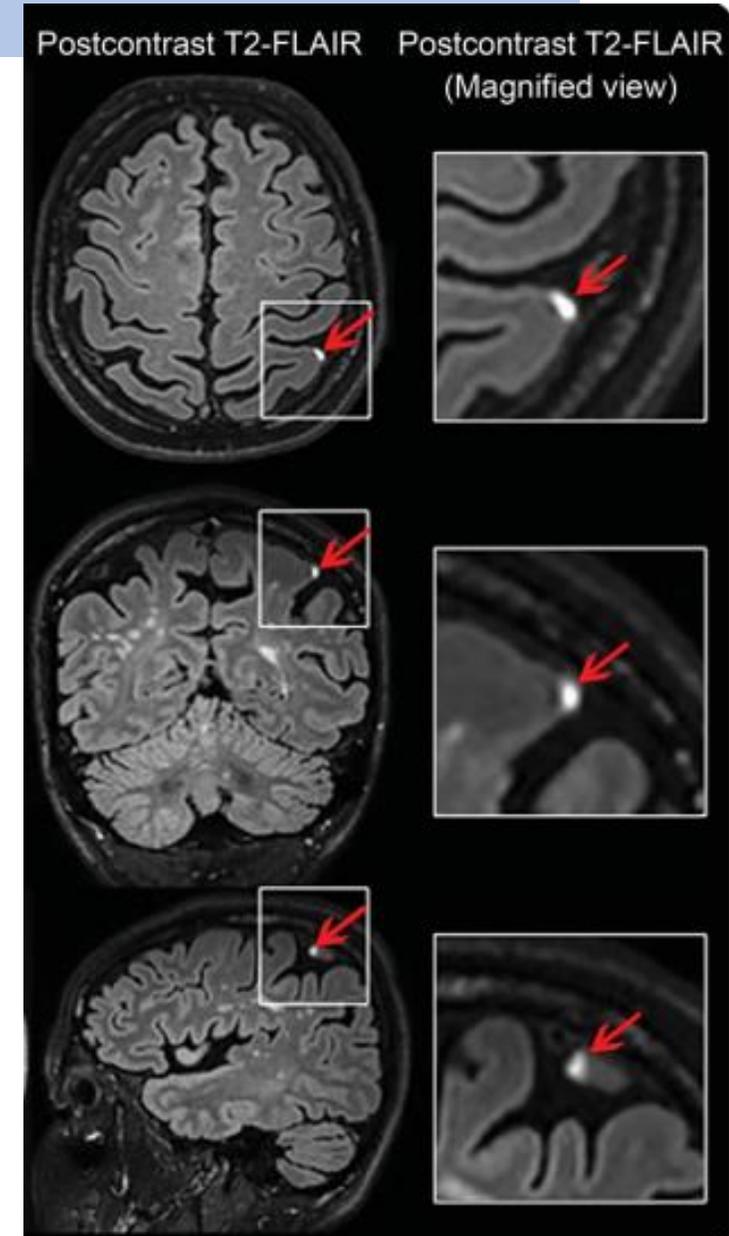


Non-Conventional MRI

- Imaging of **meningeal inflammation** → post-gado FLAIR
 - Highly unspecific!
 - LME in MS: +- 30% (> 80% at 7T) (*Ineichen, Absinta et al. 2022*)
 - Pronostic factor (EDSS, cortical volume,...)



Kuhlmann et al. 2023

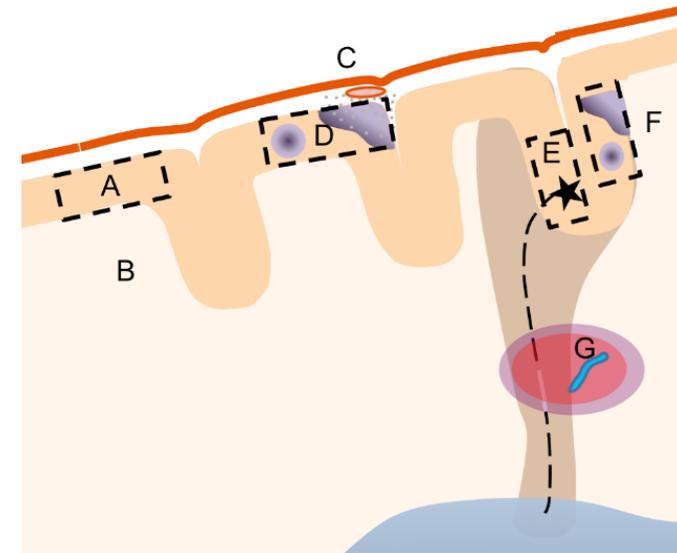


Absinta et al. 2017

Non-Conventional imaging @ Liège CRC

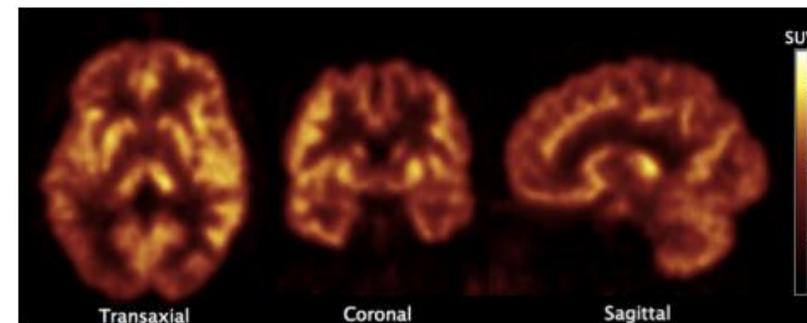
- **7T MRI**

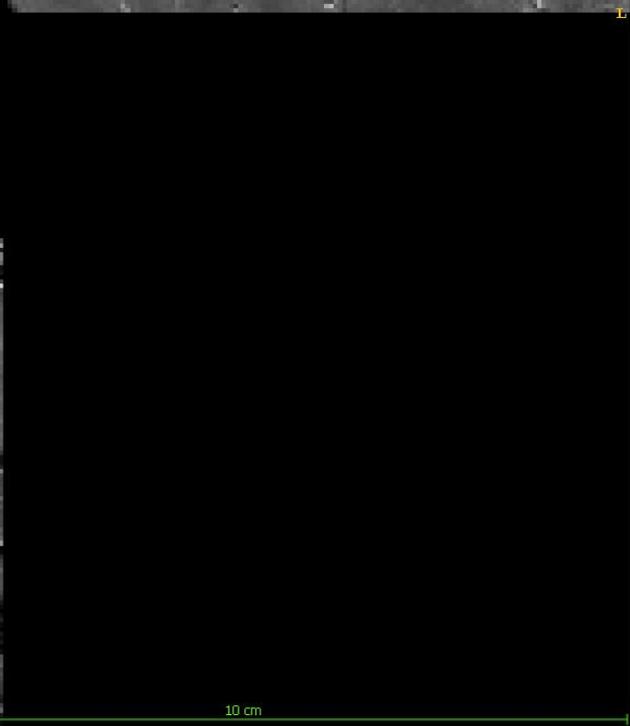
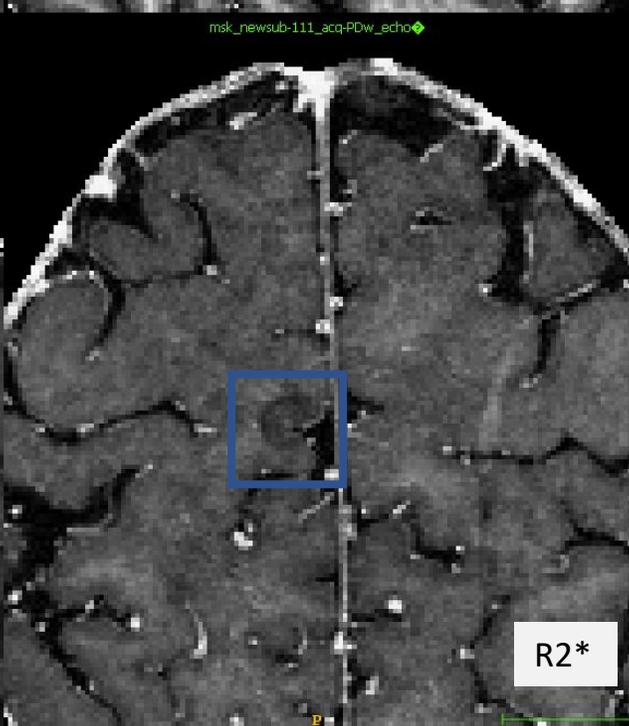
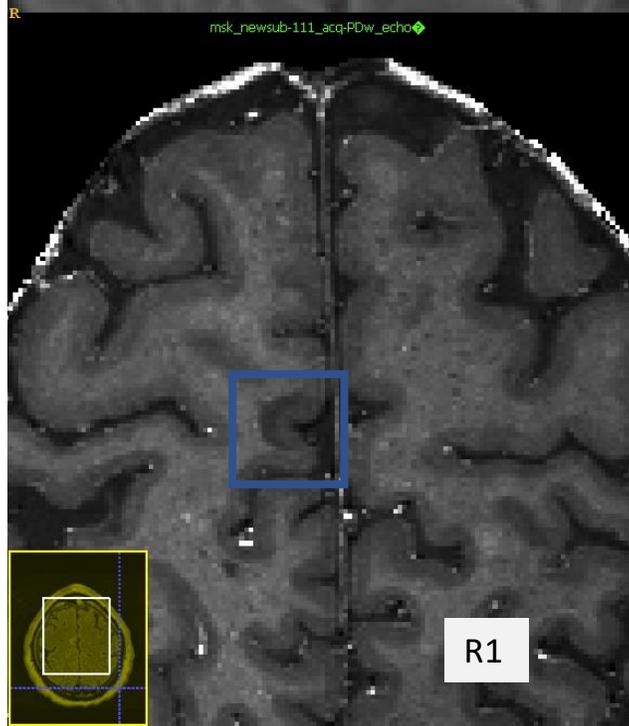
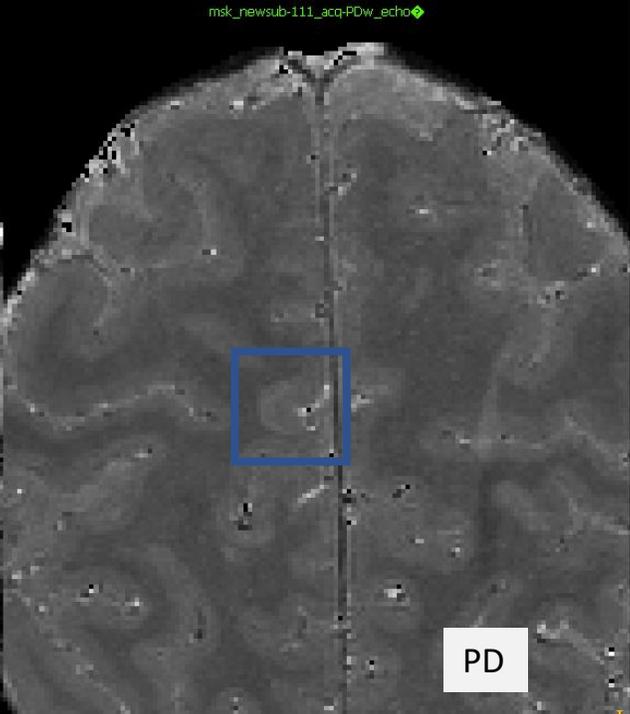
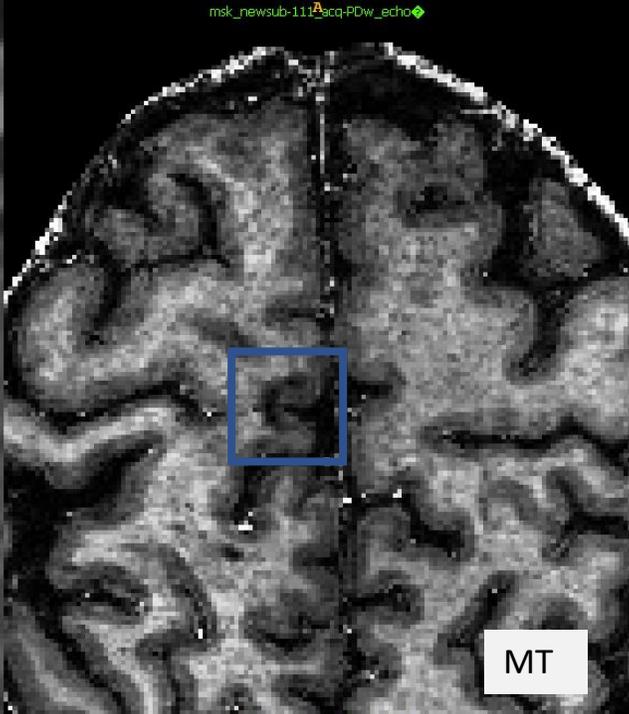
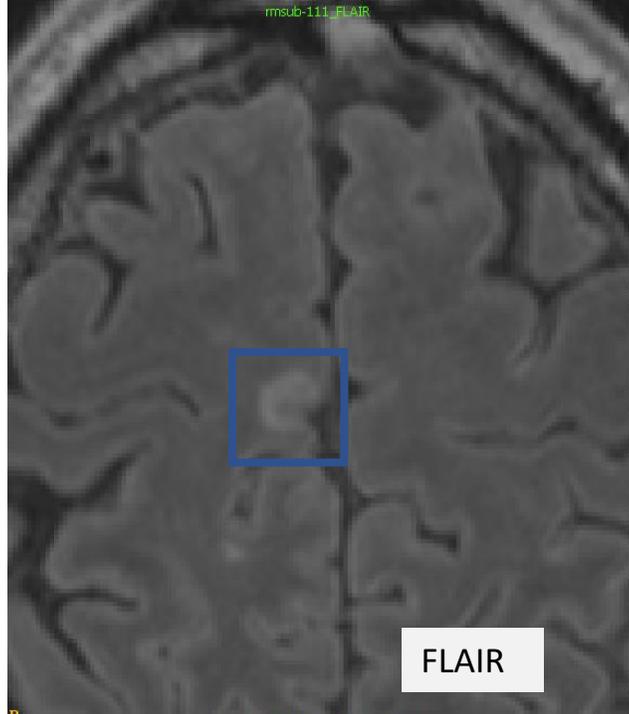
- FLAIR
- MP2RAGE
- Quantitative protocole: « MPM »
- NODDI
 - ➔ Microstructural changes

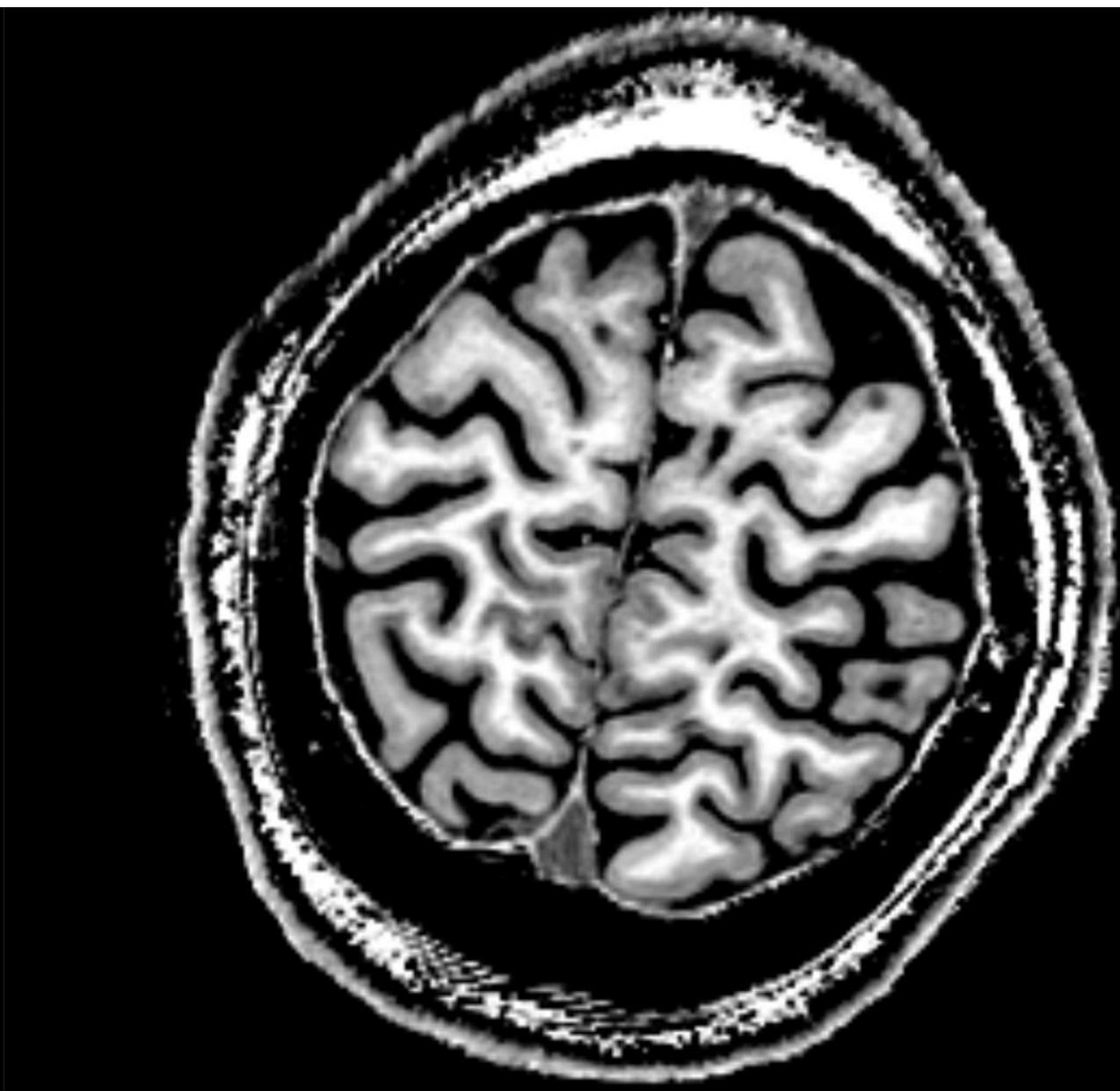
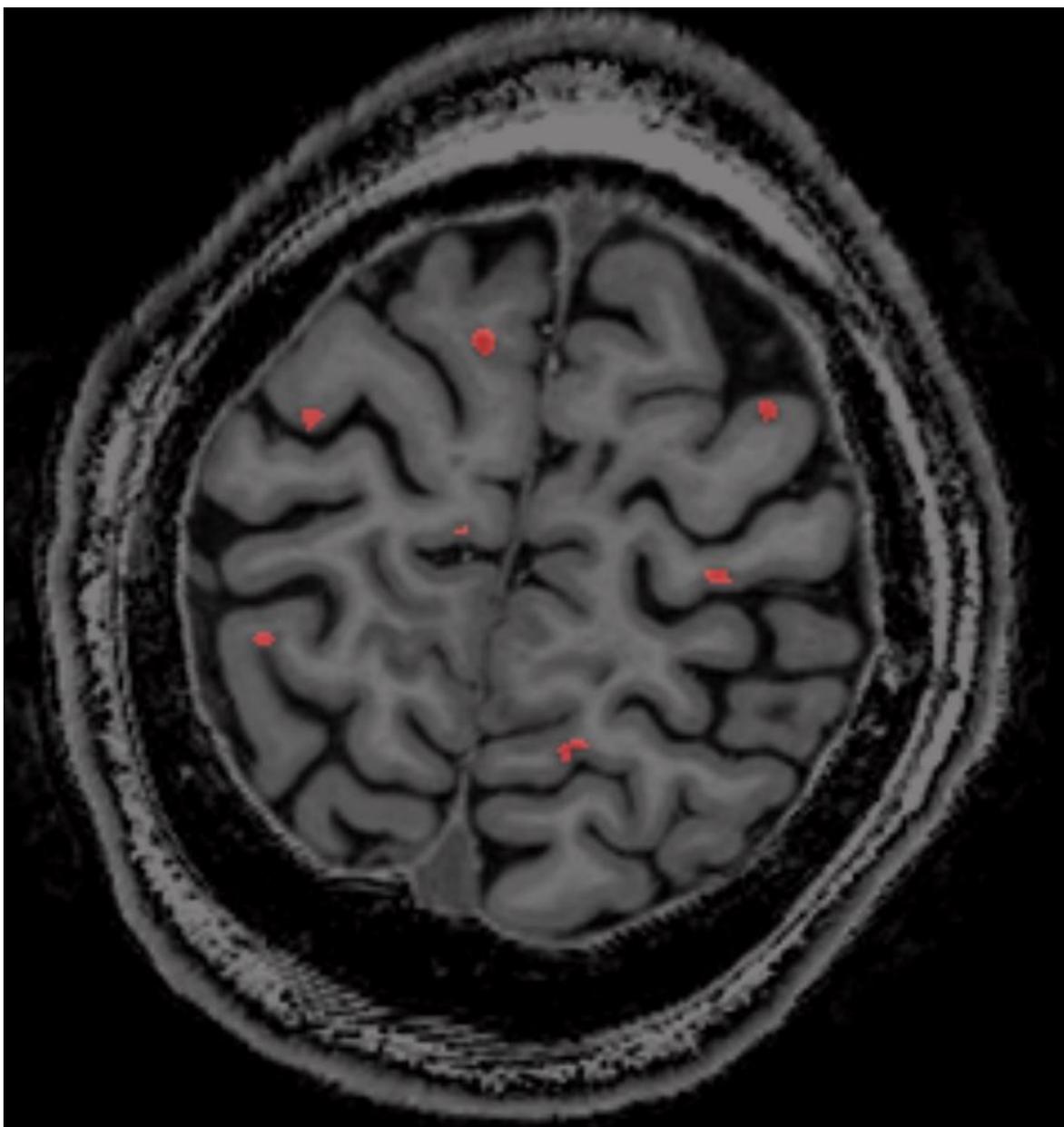


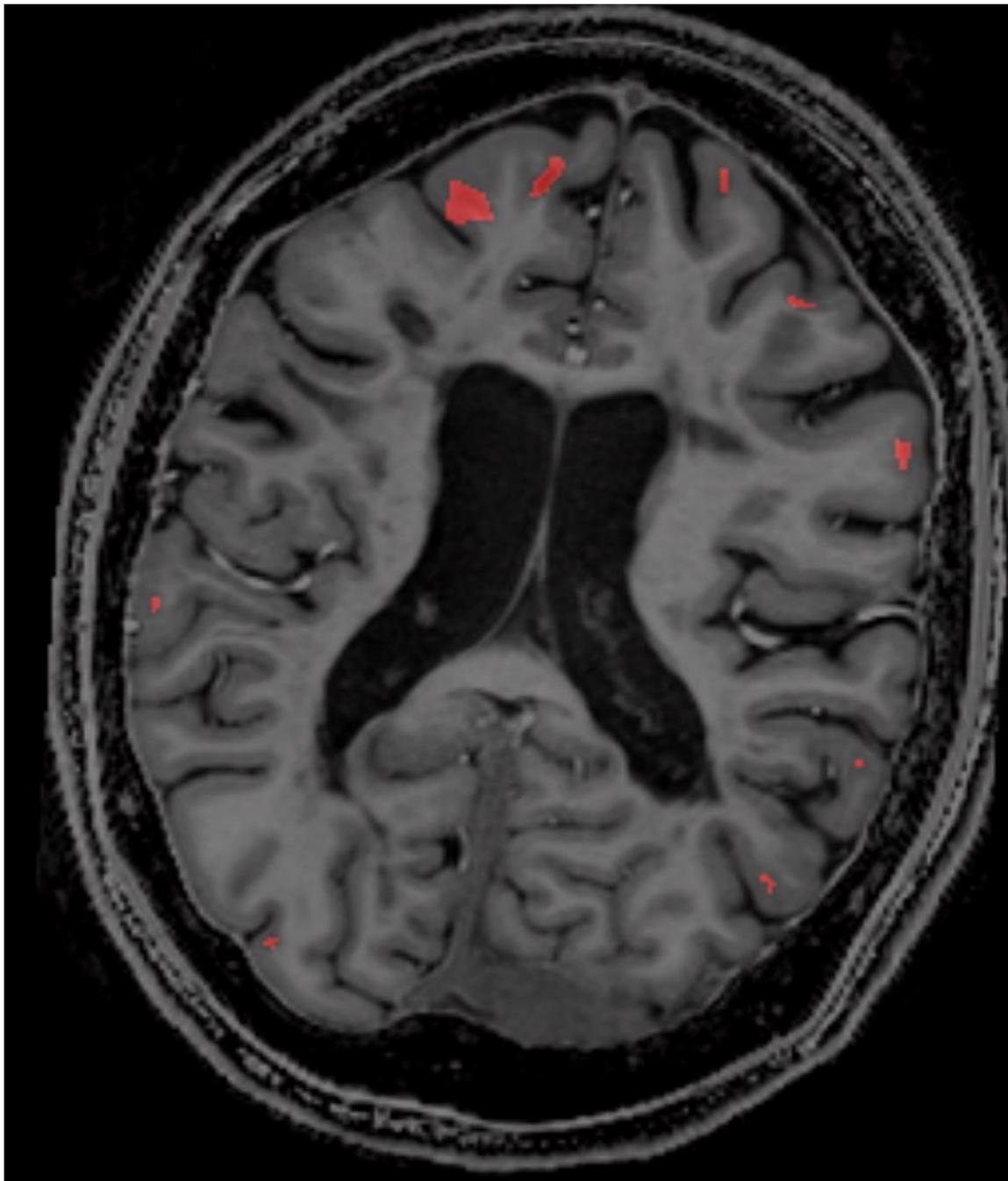
- **PET scanner**

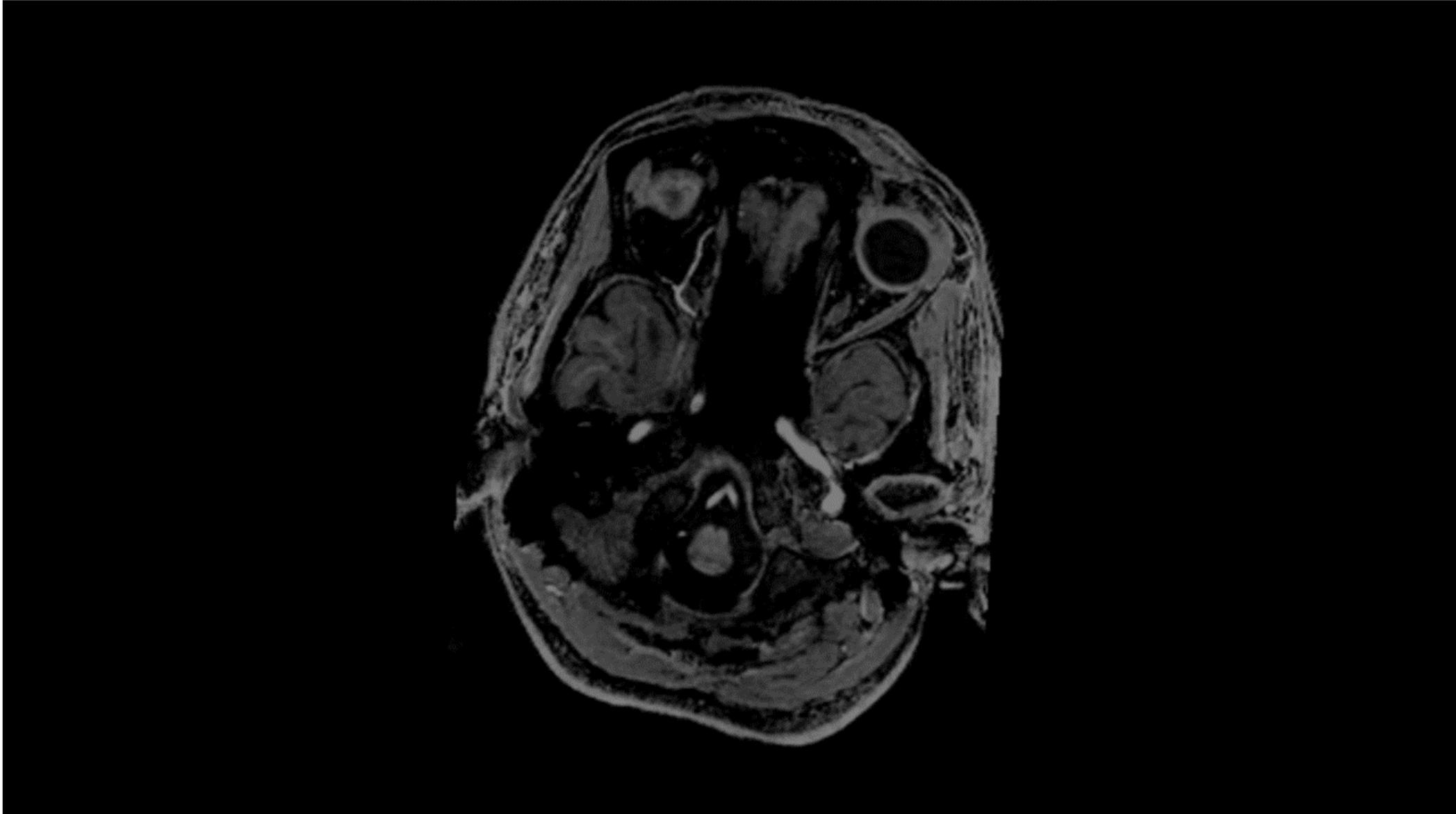
- UCBH tracer (target=SV2A)
 - ➔ Synaptic density











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Implications of CL on diagnosis and prognosis

- Diagnosis

- Mc Donald 2017: DIS

• Cortical and juxtacortical lesions can be used in fulfilling MRI criteria for dissemination in space. Cortical lesions could not be used in fulfilling MRI criteria for dissemination in space in the 2010 McDonald criteria.

Thompson et al. 2018

- Differential diagnosis: rule out MS mimiks because

« **Cortical lesions are specific of MS** »

- !! MOGAD

- Prognosis

- Correlation between CL load and
 - Cognitives impairment
 - Disability progression
 - ...

Take home messages

- Important place of cortex pathology in MS with real but sometimes subtle clinical manifestations
- 3 (4) types of focal cortical demyelinated lesions
 - **Type III** being most frequent / represented on pathological studies and linked to meningeal inflammation
 - **Type I** being most depicted on available MRI imaging
- Interest of cortical lesion detection (and LME): (differential) diagnosis, prognosis, treatment → DIR + post-gado FLAIR
- Conventional (and even unconventional) MRI: Still very insufficient comparing to histology!

Thank you for your attention !