

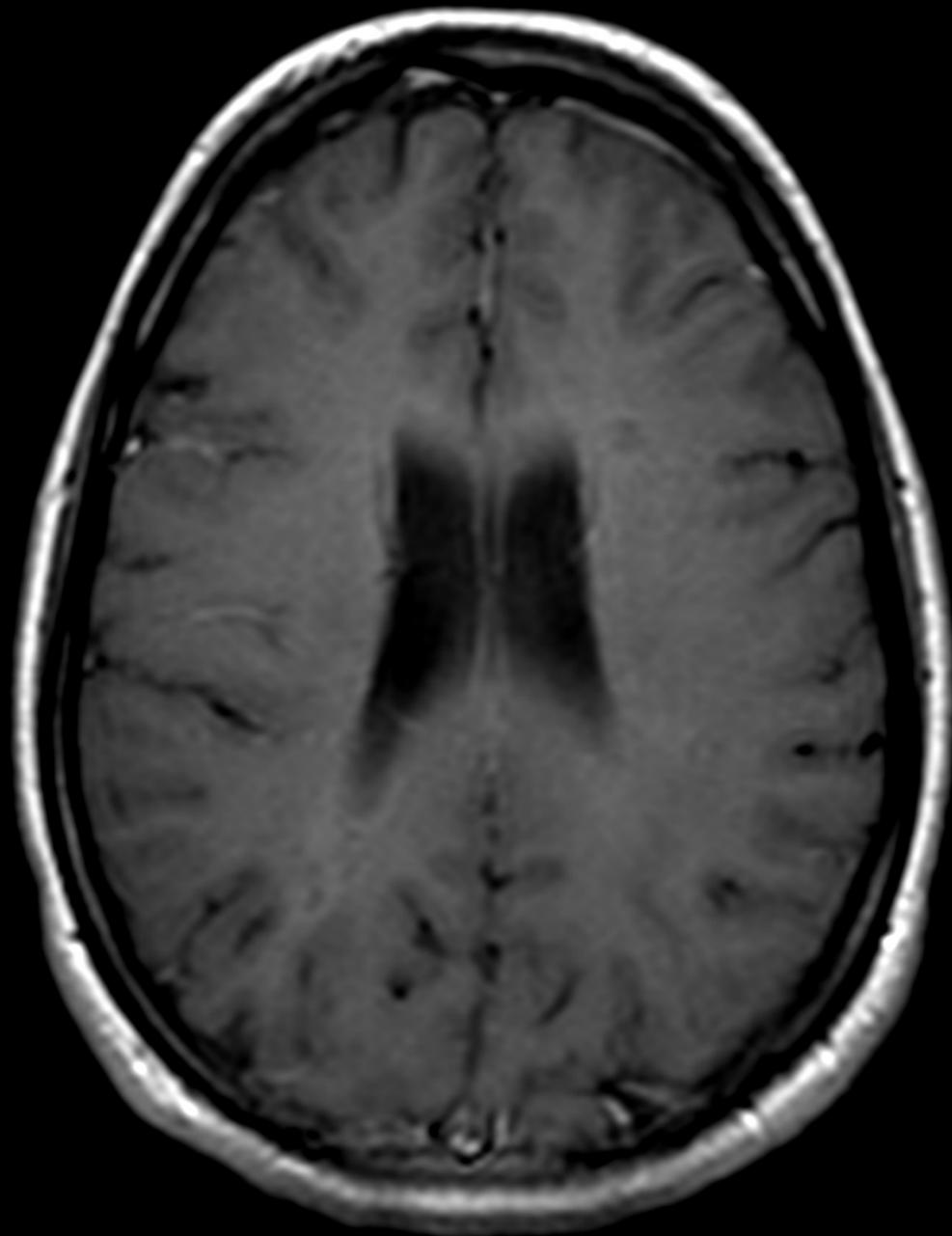
# MR imaging of chronic inflammation in multiple sclerosis

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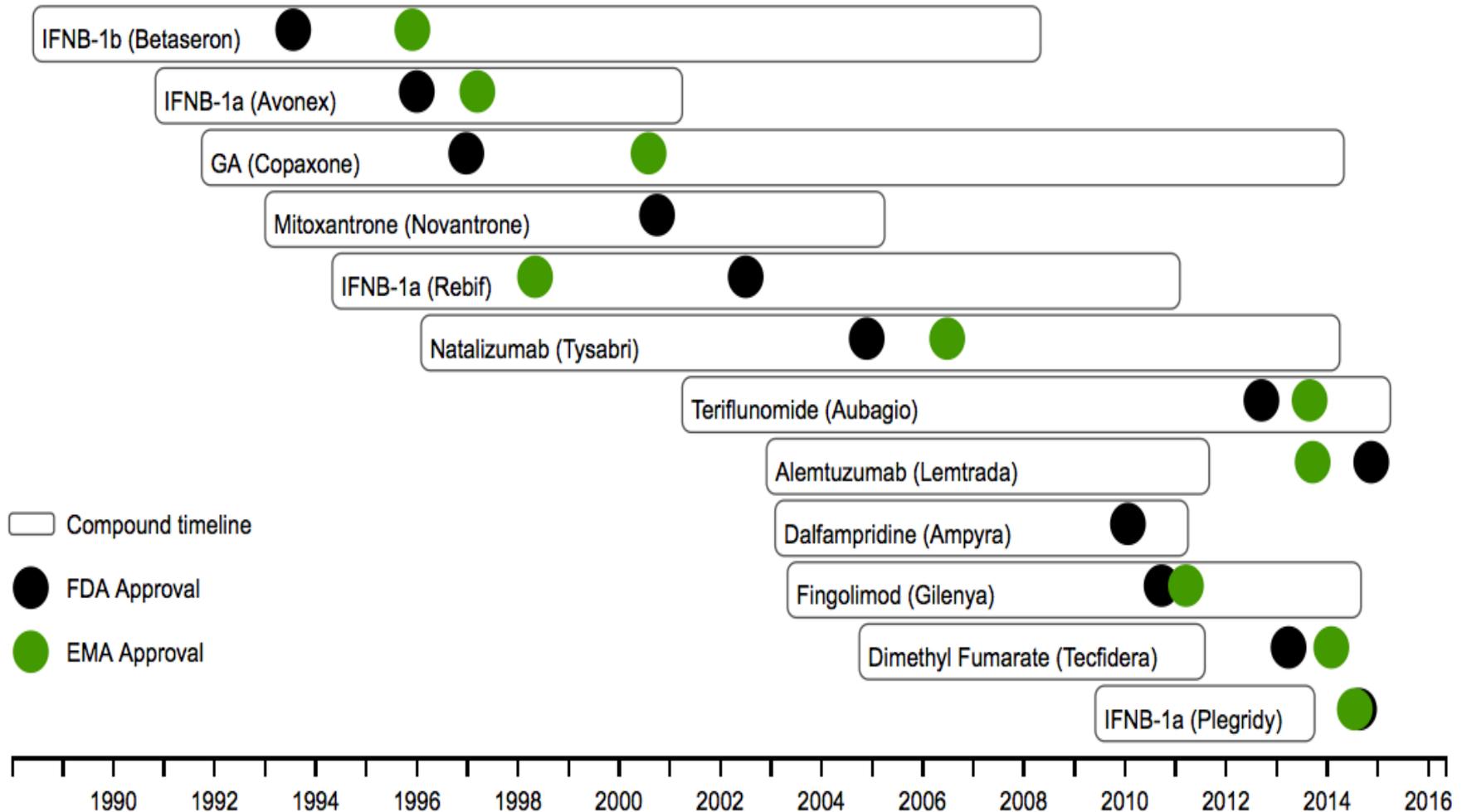


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NMSS grant award #FG 2093-A-1



*Time-lapse MRI - 24 years of MS*

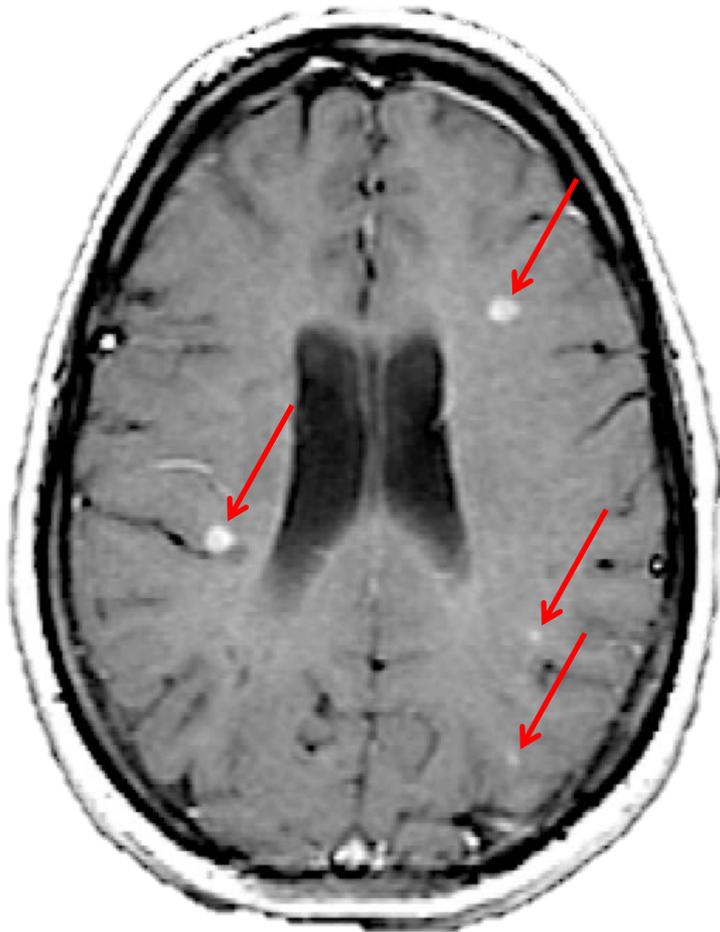
# MS treatments reduce the number of new enhancing lesions



# MR imaging biomarkers of inflammation

Acute inflammation  
BBB opening

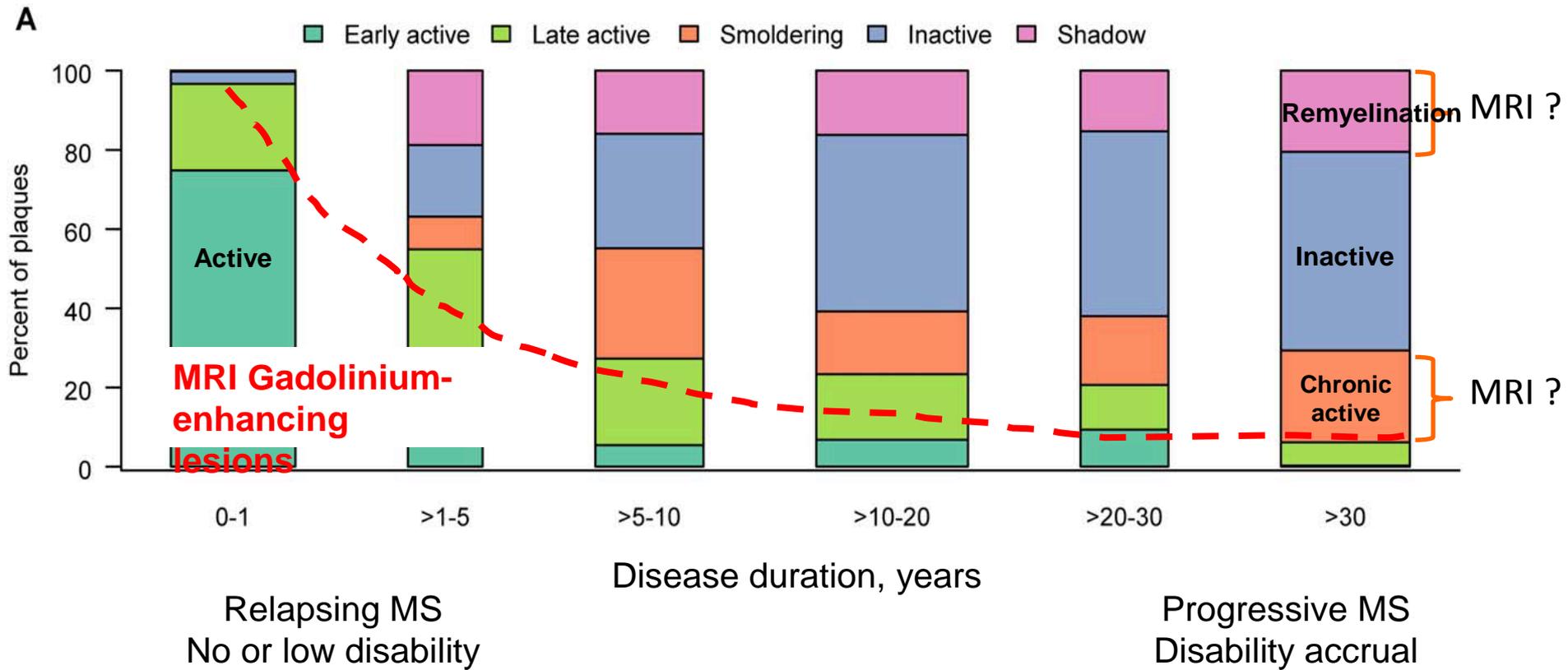
Chronic inflammation  
BBB closed



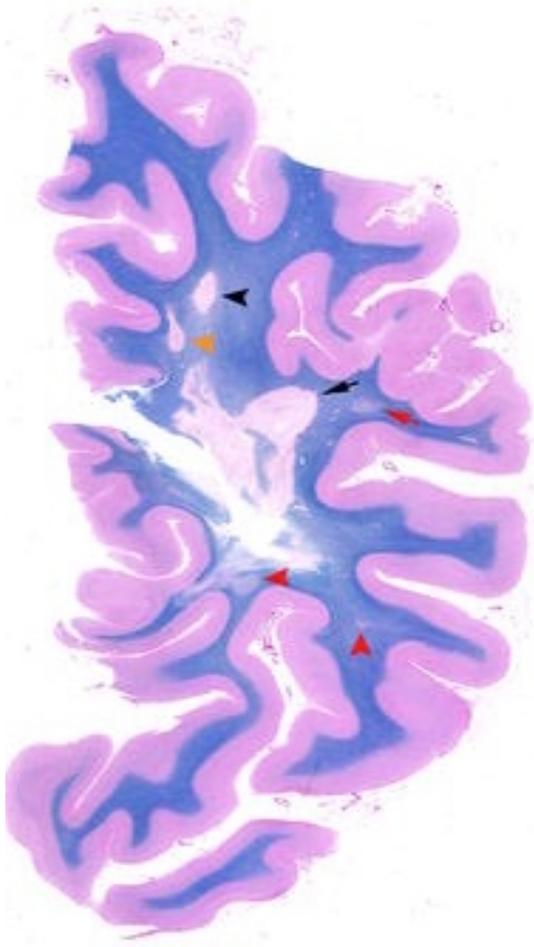
?

- ✧ Plaque-level
- ✧ Leptomeninges

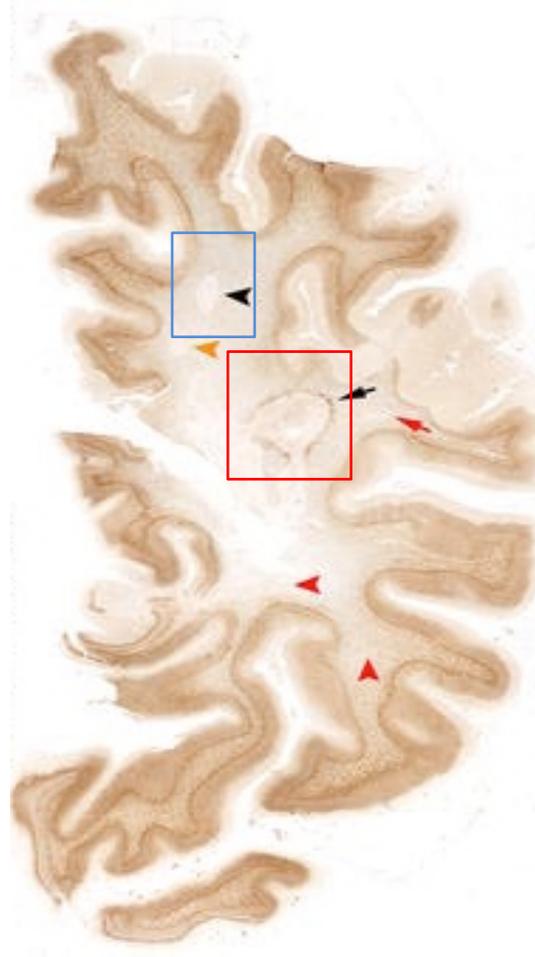
# Pathological staging of MS lesions



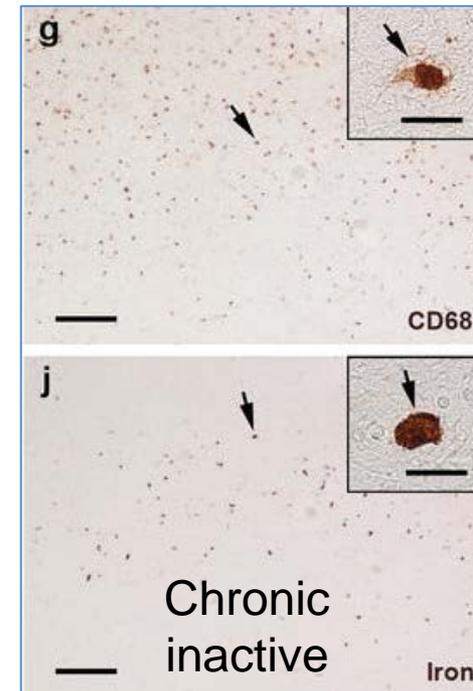
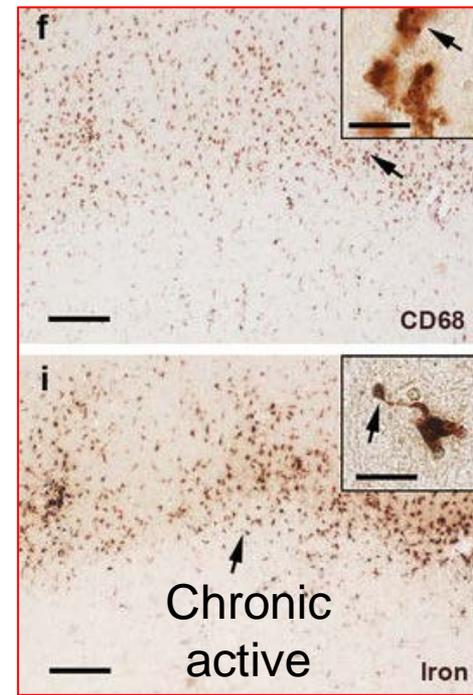
LFB-PAS  
Myelin



DAB-Turnbull  
Iron

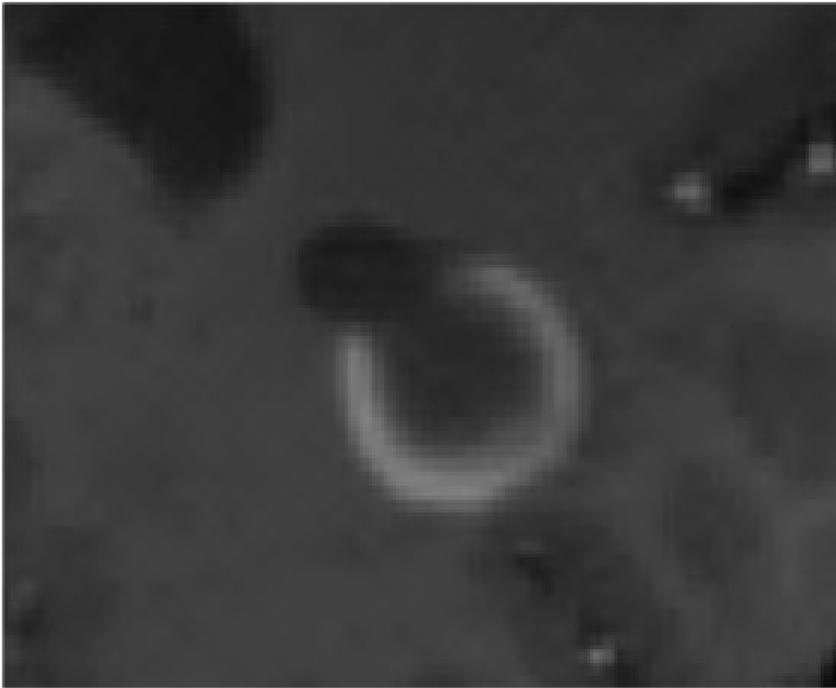


Susceptibility-based 7T MRI

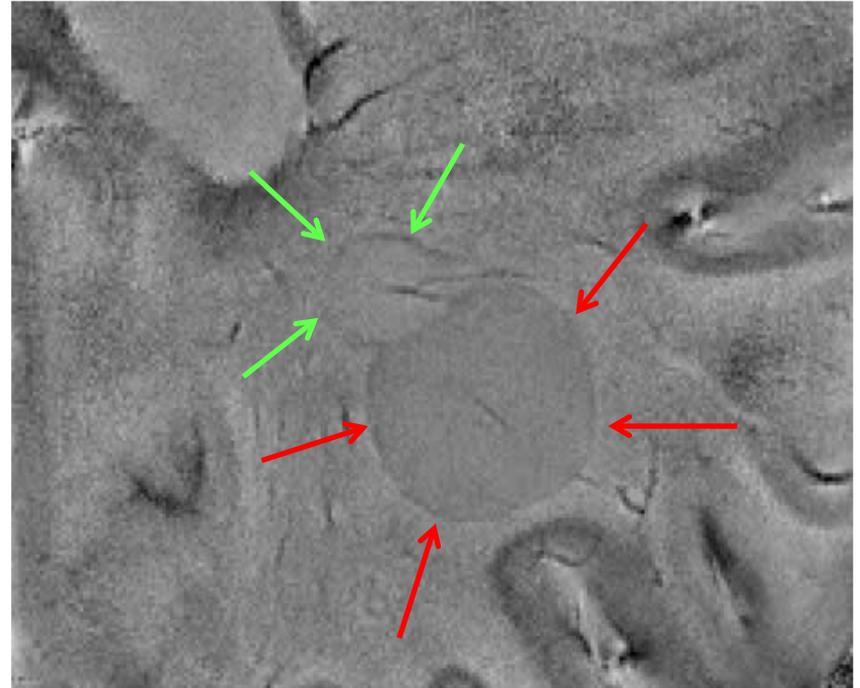


# Paramagnetic rim on susceptibility-based 7T MRI

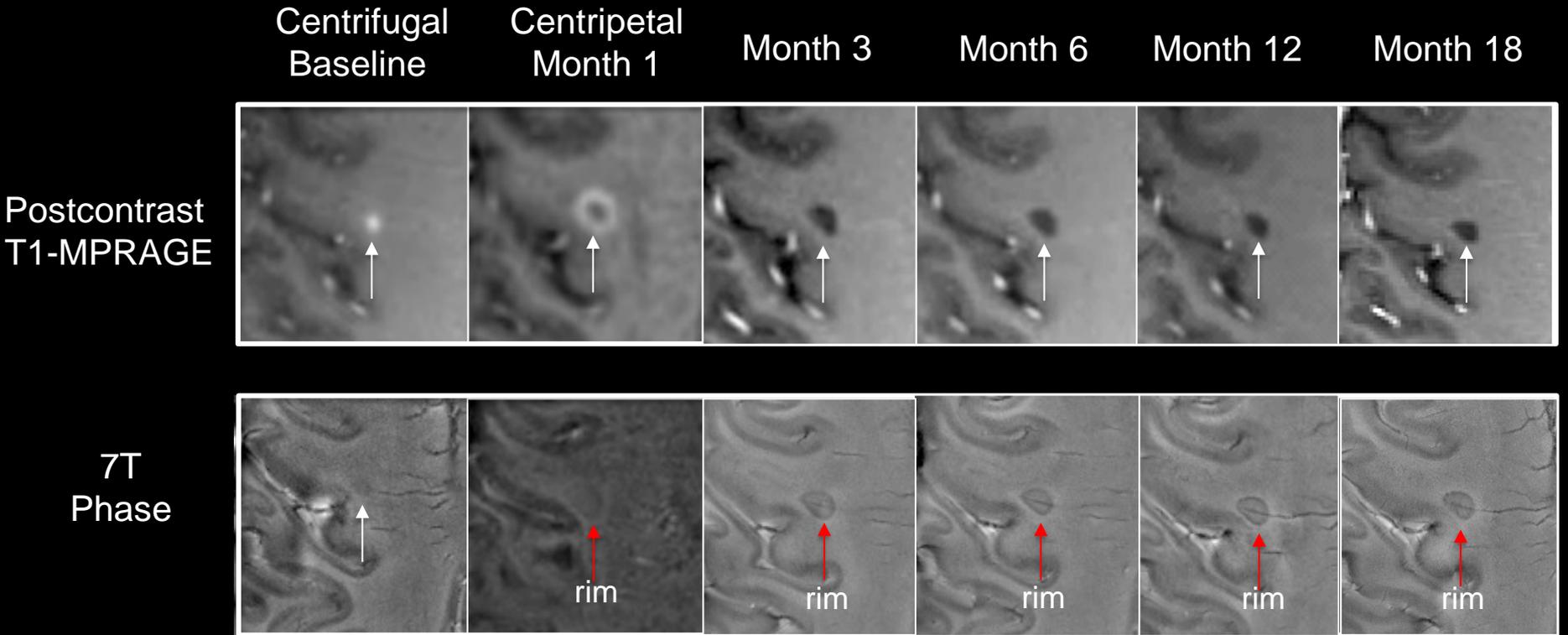
Postcontrast T1-MPRAGE



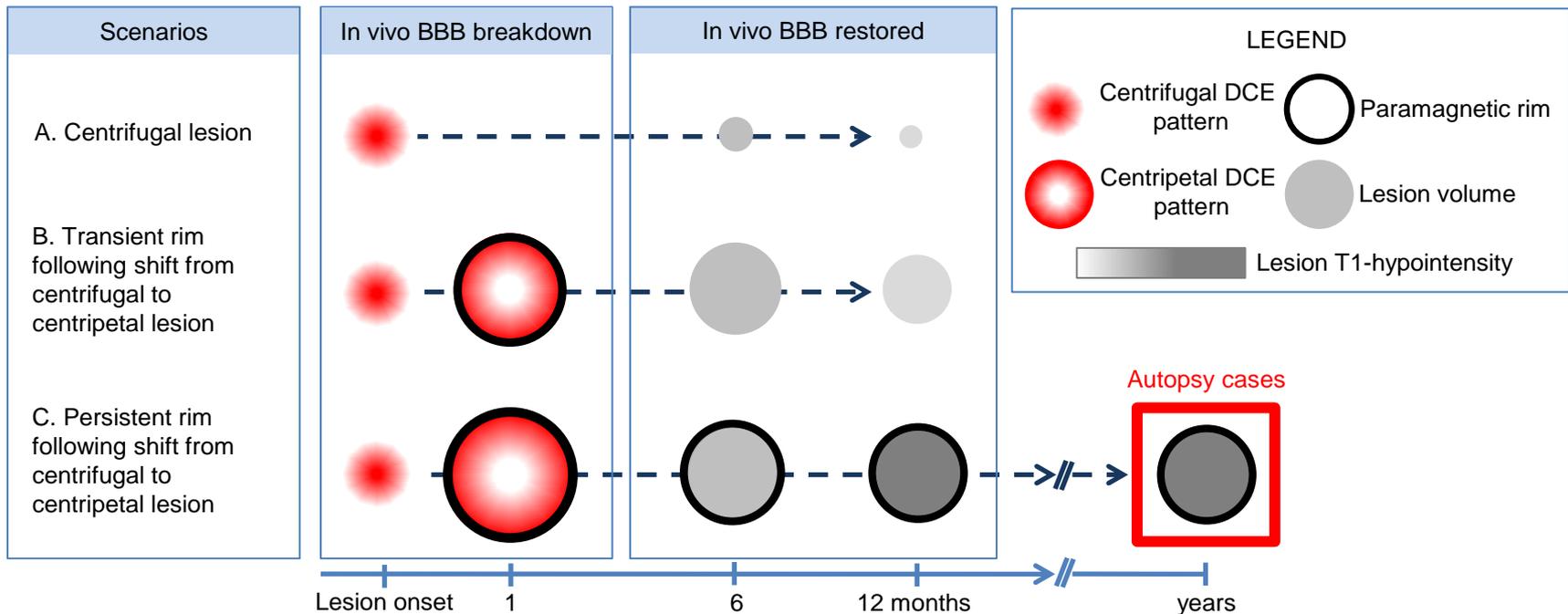
7T Phase 200  $\mu$ m resolution



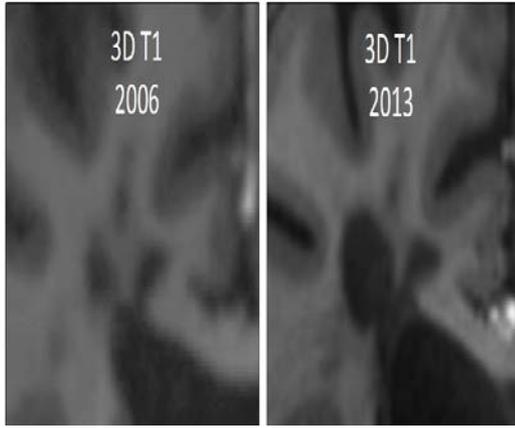
# Transition to persistent chronic inflammation



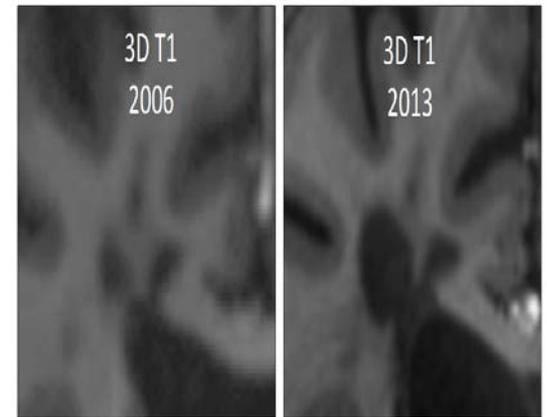
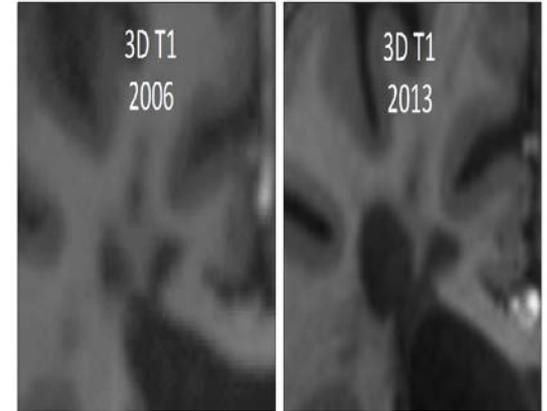
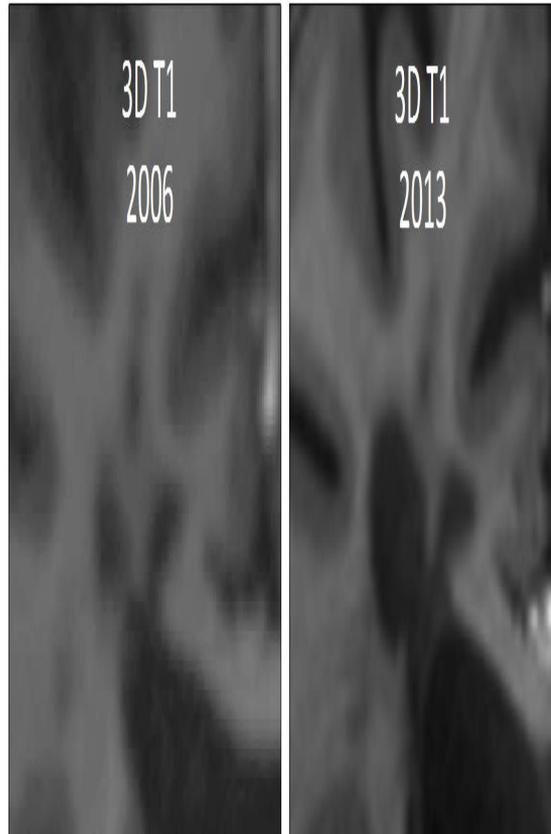
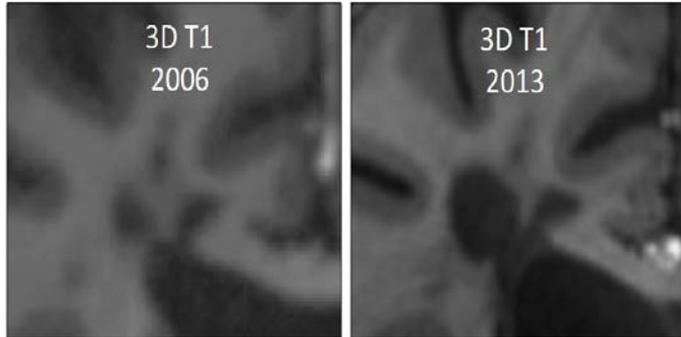
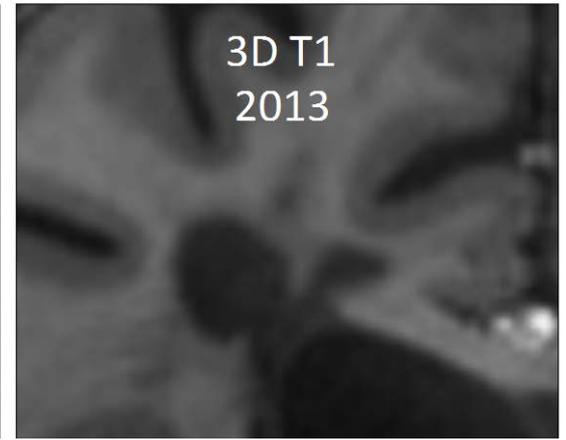
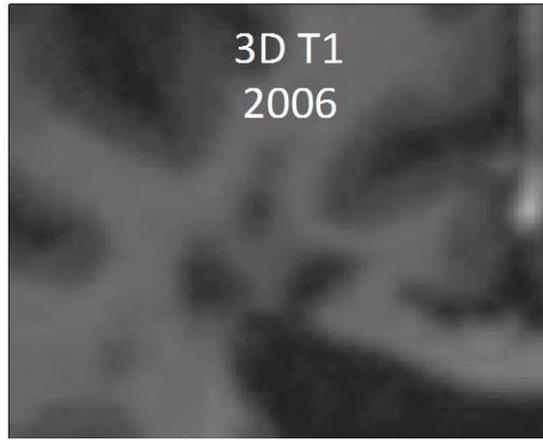
# Different scenarios of lesion evolution and propensity to repair @ 7T MRI



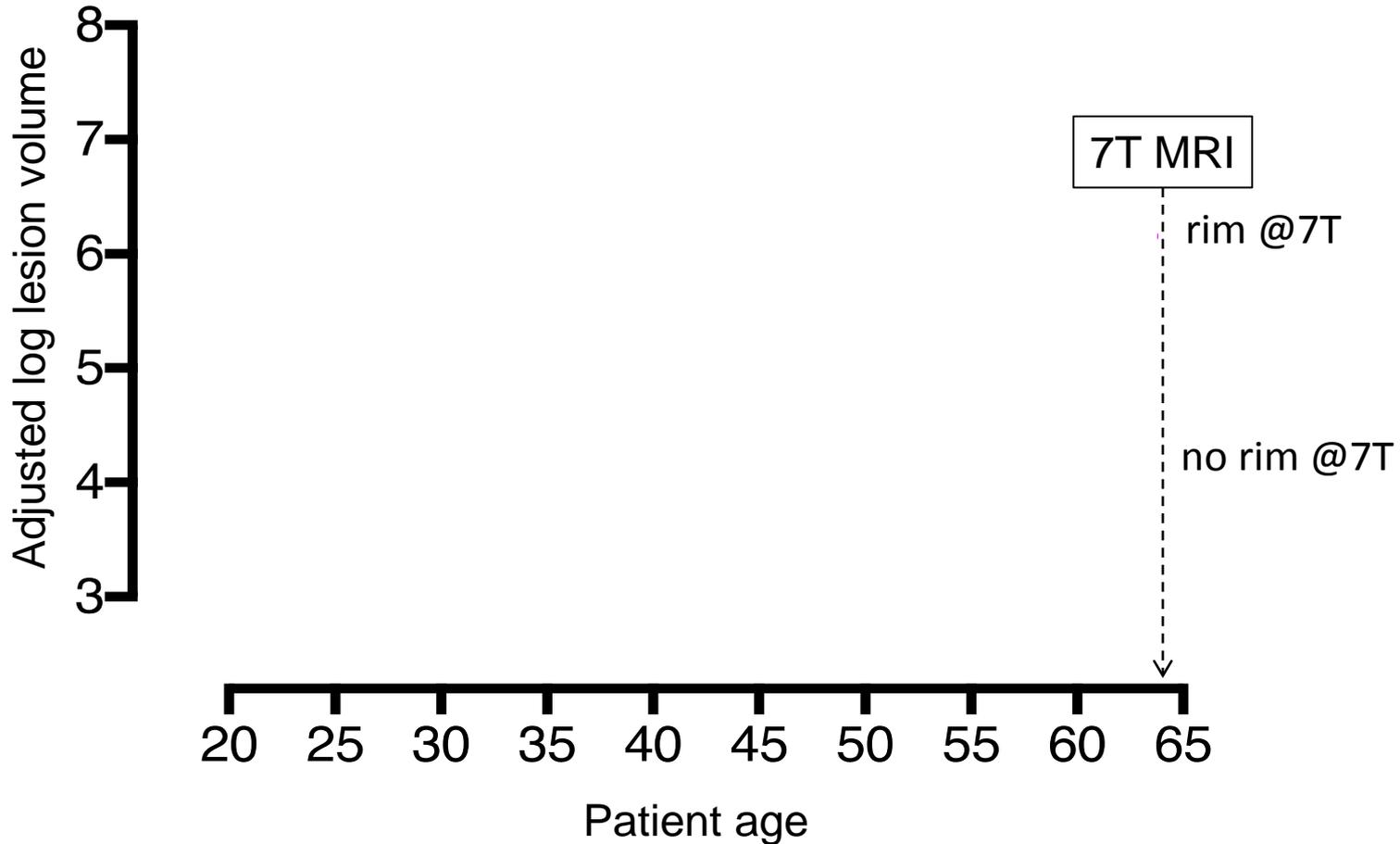
# Postmortem 7T MRI



# Longitudinal in vivo MRI



# MS lesions with vs. without rim: dichotomy in longitudinal evolution



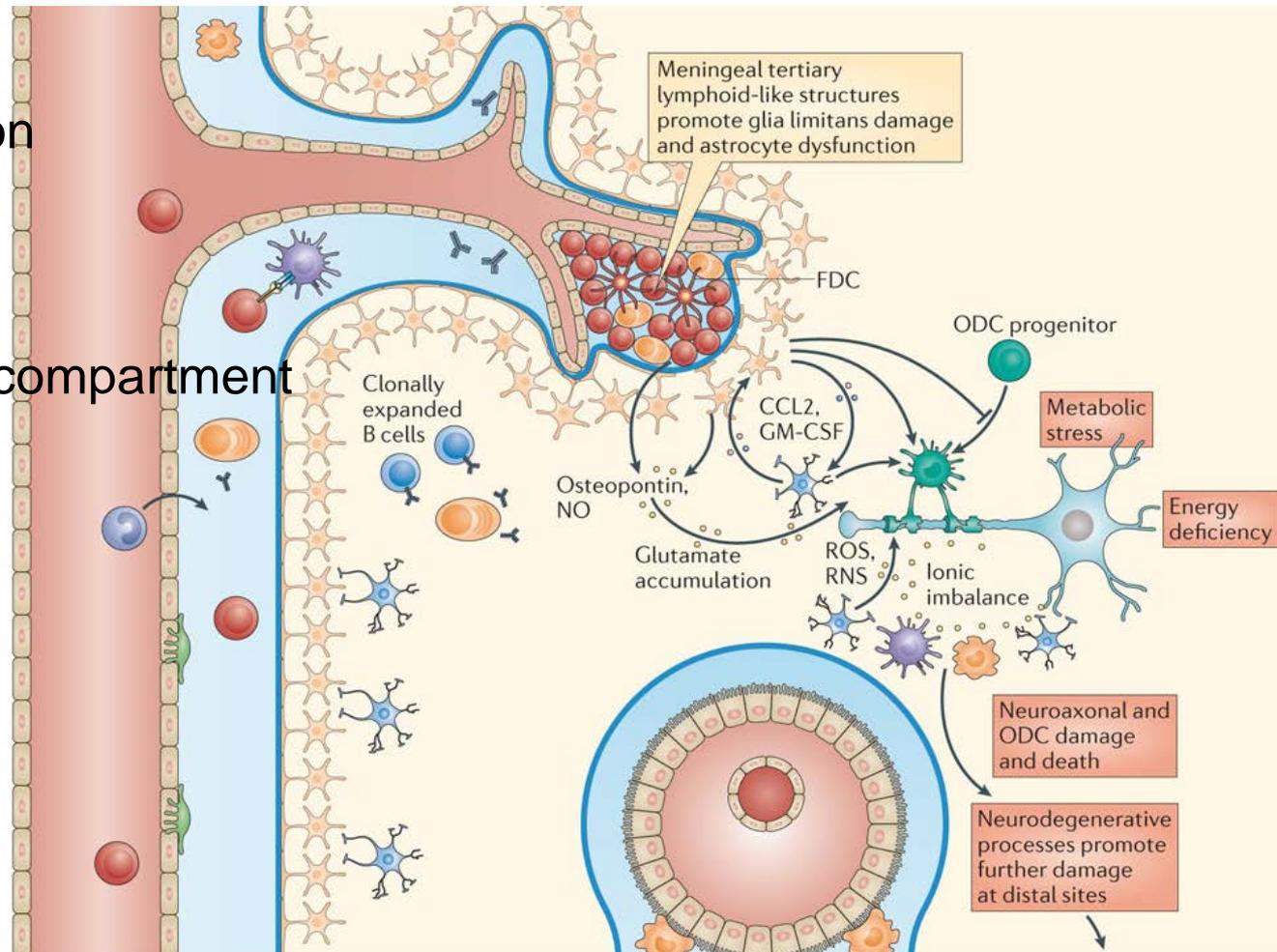
## Take-home messages

- ✧ Chronic active lesions can be seen on high-resolution MRI
- ✧ In newly forming MS lesions, chronic inflammation develops within the first 3 months and marks the failure of early lesion repair.

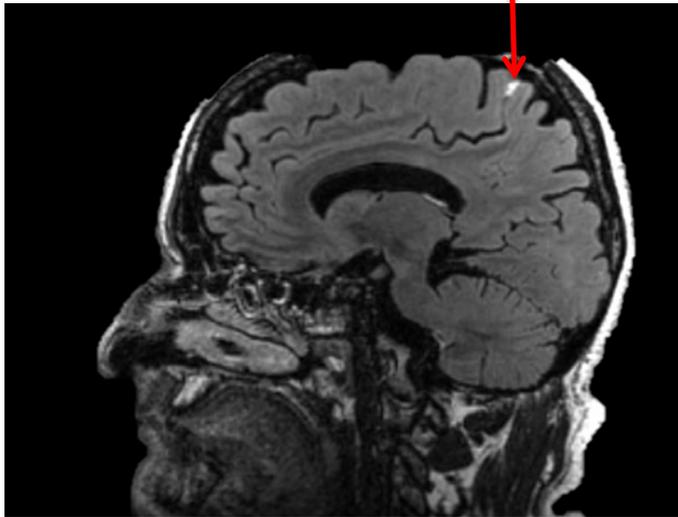
# MR imaging of chronic inflammation in multiple sclerosis

## Chronic inflammation

- Plaque-level
- Leptomeningeal compartment



# Focal leptomeningeal enhancement (LME) on postcontrast 3D T2-FLAIR



299 MS patients

>> progressive MS cases

MS cases with vs. without LME:

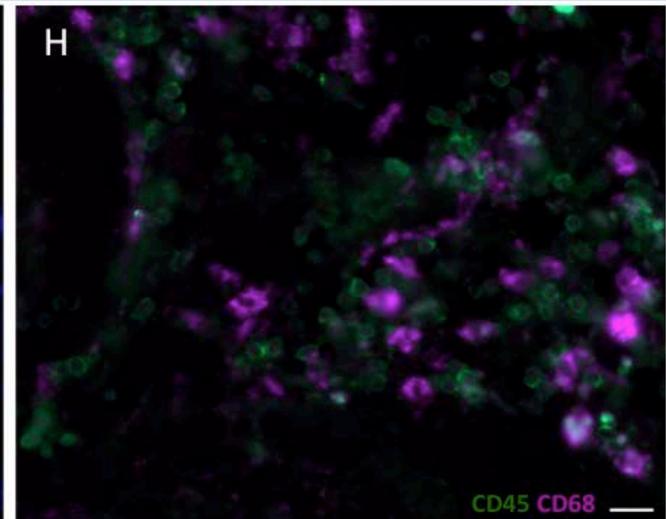
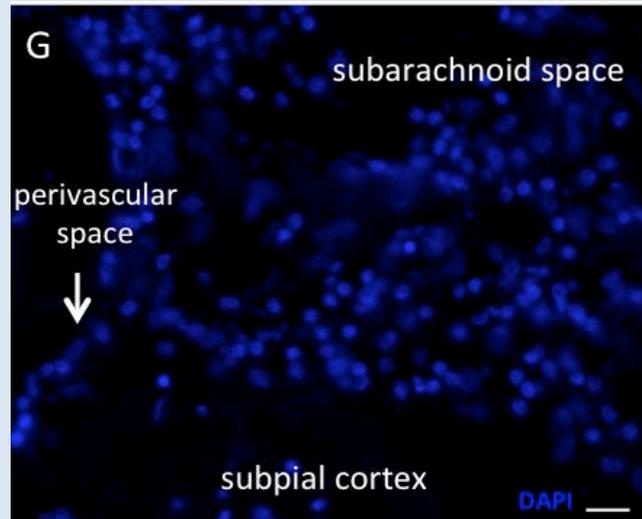
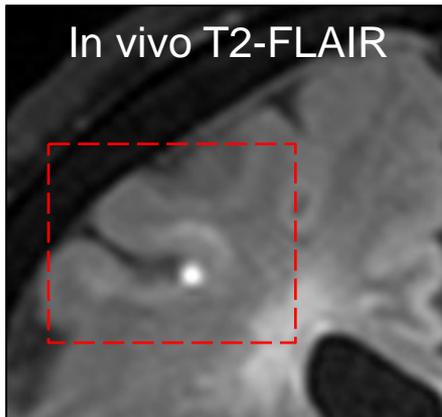
- ↑ disability, age, disease duration
- ↓ brain and cortical volumes

No association of LME with:

- enhancing WM lesions
- total WM lesion volume
- disease-modifying treatments

# LME discloses leptomeningeal inflammation

- ✧ Leptomeningeal inflammatory infiltrate (lymphocytes and monocytes)

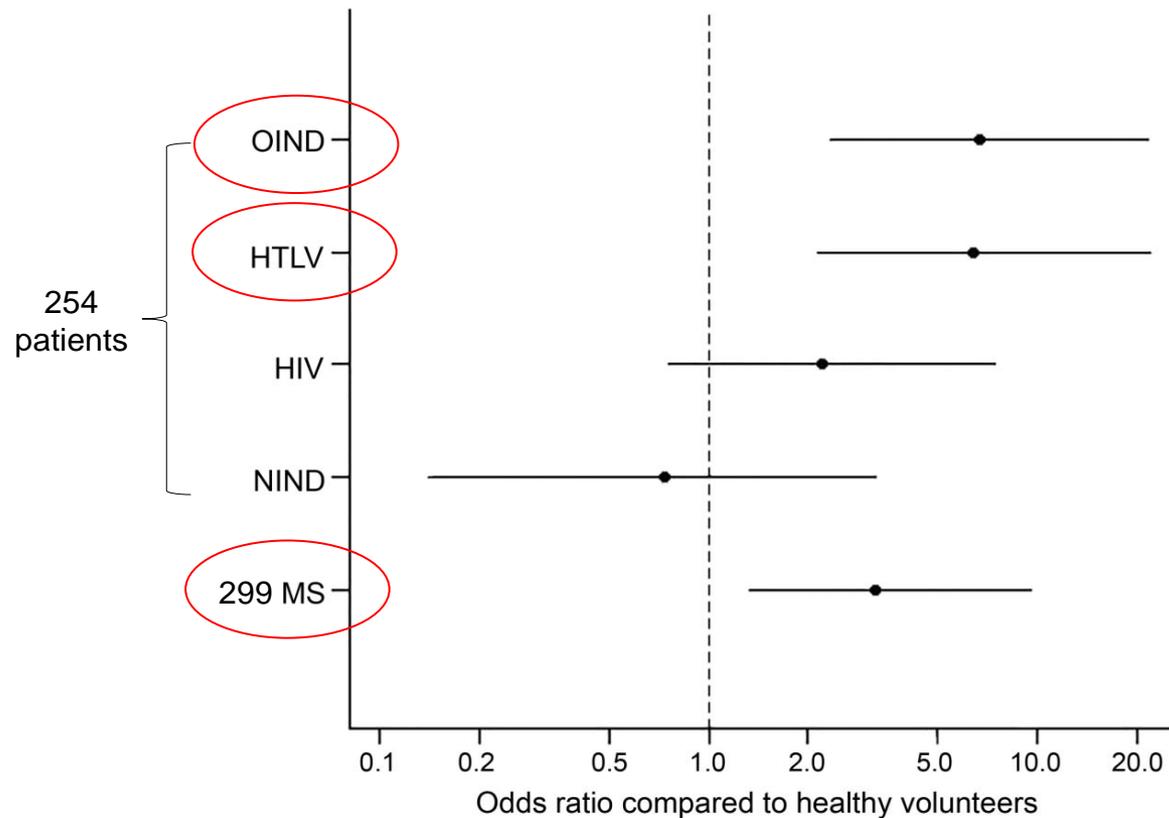


- ✧ Subpial cortical demyelination



# LME in other chronic neuroinflammatory conditions

**Figure 3** Odds ratios of leptomenigeal enhancement in disease groups compared to healthy controls



HTLV = human T-lymphotropic virus; MS = multiple sclerosis; NIND = noninflammatory/infectious neurologic diseases; OIND = other inflammatory/infectious neurologic diseases.

## Take-home messages

- ✧ Blood-meningeal barrier impairment due to meningeal inflammation can be visualized on high-res MRI
- ✧ LME and susceptibility rim are novel imaging biomarkers for chronic inflammation and might help patient selection and stratification
- ✧ Current disease-modifying treatments are not completely effective on chronic inflammation-> new therapeutic targets

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## **7T FMRIF staff, NIH**

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