Methods

Data Sources

Toronto Western Hospital Neurosurgical Clinic:
64 MS-TN patients
64 healthy controls

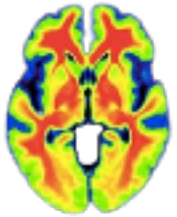
Cam-CAN:
64 healthy controls

Data Processing

Myelin Map (MM) computation

Analysis Plan

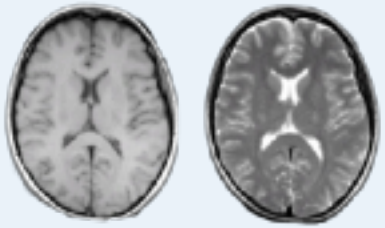
Two-one-sided t-tests & univariate region-based statistical testing (python)



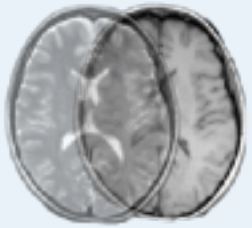
Li CMF et al. Neuroimage Clin. 2021.
Li CMF et al. Mult Scler. 2020.

T1-w MRI (FSPGR) and **T2-w MRI** (B0 average of DWI)

1. **Skull stripping** (BET2)



2. **Bias correction** (FSL)
3. **Image resampling** (3D Slicer)
4. **Image registration & transformation** (ANTs)



T2 → T1

5. **Standardization & computation of myelin map** (FSL)

Figure 1: Construction of myelin map through calculation of ratio co-registered T1-w/T2-w images. FSPGR: fast spoiled gradient echo, DWI: diffusion weighted imaging, BET2: brain extraction tool 2, FSL: FMRIB Software Library, ANTs: Advanced Normalization Tools

Results

MS-TN Cohort Demographics

Age (years, mean ± SD)	54 ± 10
Sex (M : F)	28 : 36
Duration of MS (years, mean ± SD)	16 ± 9
Duration of TN pain (years, mean ± SD)	5 ± 4

Healthy controls were age and sex matched.

Chi-square test demonstrated no significant differences in handedness distribution between MS-TN and healthy controls.
A region-based univariate analysis demonstrated a significant difference of handedness related myelination asymmetry in the tapetum in MS-TN patients compared to healthy controls.

Myelin Map External Validity

Two-one-sided t-tests demonstrated equivalence between MMs of local and external HCs (all regions $p<0.05$), confirming cross-scanner generalizability

Myelin Map Internal Validity

MM differences between MS-TN patients and healthy controls ($p<0.0001$) in the following regions:

- Superior fronto-occipital fasciculus (ipsi + contra)
- Superior longitudinal fasciculus (ipsi + contra)
- Cingulum-hippocampus (ipsi + contra)
- Cingulum-cingulate gyrus (ipsi + contra)
- Sagittal stratum (ipsi + contra)
- Posterior thalamic radiation (ipsi + contra)
- Posterior corona radiata (ipsi + contra)
- Superior corona radiata (ipsi + contra)
- Anterior corona radiata (ipsi + contra)
- Retrolenticular part of internal capsule (ipsi + contra)
- Corticospinal tract (ipsi + contra)
- Corpus callosum (splenium, genu, body)
- Pontine crossing tract part of MCP
- Middle cerebellar peduncle

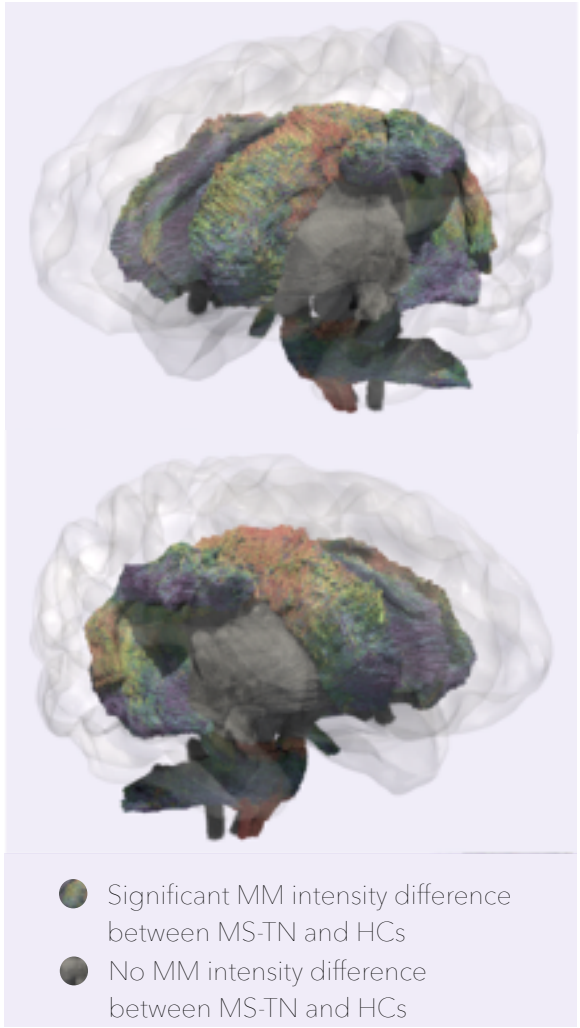
- Medial lemniscus (ipsi/contra)

Decreased MM intensity (myelin content) in MS-TN

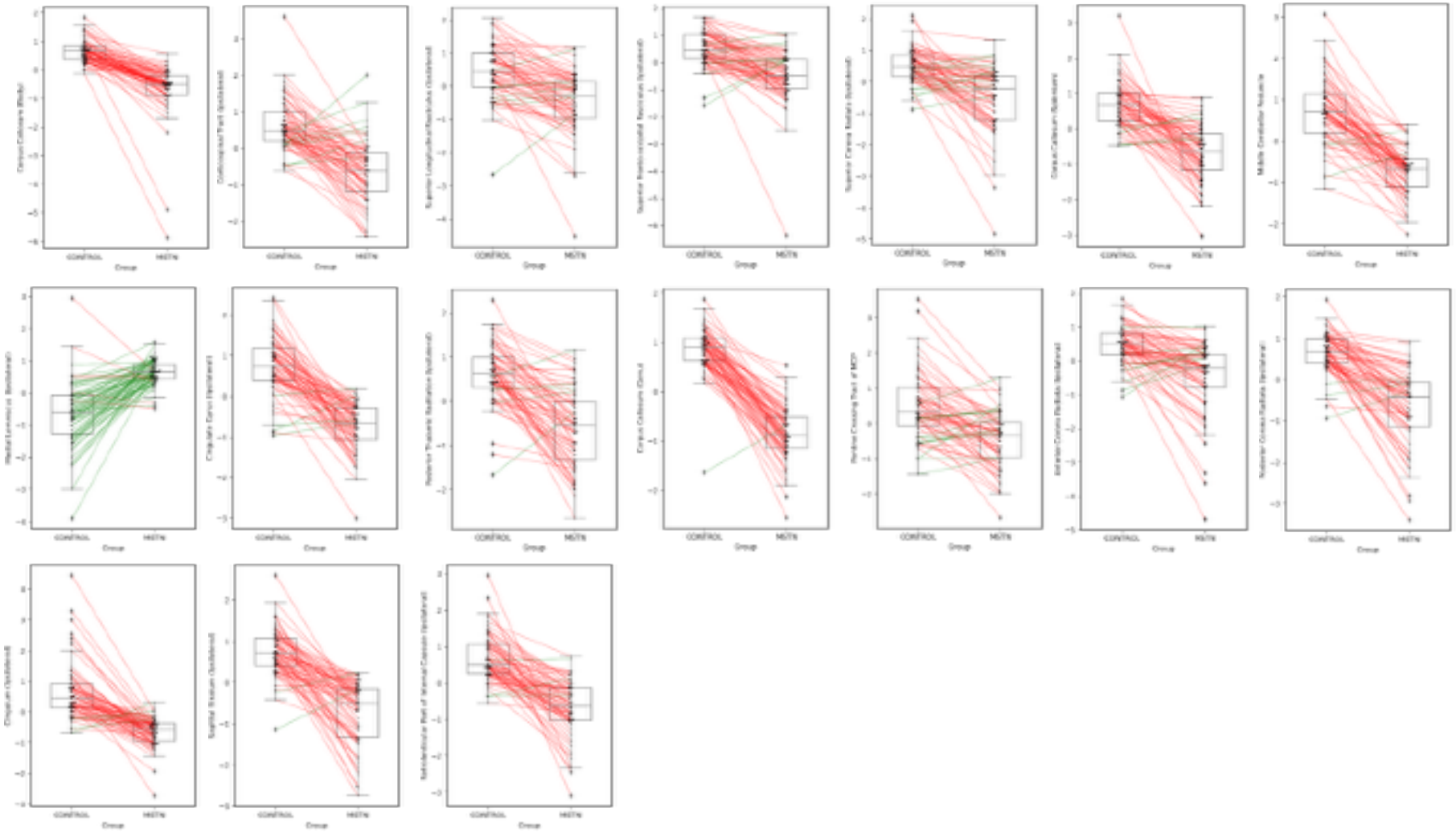
Increased MM intensity (myelin content) in MS-TN

29/48 JHU regions demonstrated significant differences ($p<0.0001$).

Figure 2:
Univariate analysis identified regional white matter differences between MS-TN and HCs in 29/48 JHU regions (p<0.0001).



a. Proportion of JHU regions demonstrating significant MM intensity differences between MS-TN and HCs



b. Region based univariate analysis of myelin maps. Vertical axis displays intensity of MM (higher intensity represents higher myelin content). Lines connect each MS-TN patient to the corresponding age and sex matched HC (only ipsilateral and bilateral regions shown).