

# **CIBM Annual Symposium 2024**

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# **Towards Longitudinal Characterization of Multiple Sclerosis Atrophy Employing SynthSeg Framework and Normative Modeling**

Pedro M. Gordaliza<sup>1,2,3</sup>, Nataliia Molchanova<sup>2,3,4,</sup> Maxence Wynen<sup>5,6</sup>, Pietro Maggi<sup>6,7</sup>, Jaume Banus<sup>2</sup>, Joost Janssen<sup>8</sup>, Alessandro Cagol<sup>9</sup>, Cristina Granziera<sup>9</sup>, Meritxell Bach Cuadra<sup>1,2,3</sup>

<sup>1</sup>CIBM Center for Biomedical Imaging, Switzerland, <sup>2</sup>Radiology Department, Lausanne University and University Hospital, Switzerland, <sup>3</sup>University of Lausanne, Switzerland, <sup>4</sup> University of Applied Sciences of Western Switzerland, <sup>5</sup>ICTeam, UCLouvain, Louvain-la-Neuve, Belgium, <sup>6</sup>Louvain Inflammation Imaging Lab (NIL), Institute of Neuroscience (IoNS), UCLouvain, Brussels, Belgium,<sup>7</sup>Department of Neurology, Cliniques universitaires Saint-Luc, Université catholique de Louvain, Brussels, Belgium, <sup>8</sup>Department of Child and Adolescent Psychiatry, Institute of Psychiatry (HGUGM-IiSGM) and CIBERSAM, Instituto de Salud Carlos III, Madrid, Spain,<sup>9</sup>Translational Imaging in Neurology (ThINk) Basel, Department of Biomedical Engineering, University Hospital Basel and University of Basel, Switzerland

## BACKGROUND

- Multiple Sclerosis (MS) is an autoimmune disease with unknown cause<sup>G</sup>.
- MS is always progressive beyond MRI & clinical measures<sup>L,F</sup>.
- MRI essential for Disease Progression Modeling (DPM).
- Lesion quantification alone misses MS progression.
- MS-accelerated subcortical atrophy enables continuous DPM

# CHALLENGES & AIMS

- Challenge 1: Need for robust clinical segmentation of T1w and FLAIR in MS.
  - SynthSeg+ and SynthSeg-WMH provide DL-based subcortical segmentation.
- Challenge 2: Small samples fail to capture MS evolution heterogeneity.
  - $\circ$  Normative modeling<sup>M</sup> on large healthy populations enables comparison



[F] Filippi et al. Nature. 2018. [G]Granziera et al. Brain. 2021. [L]Lublin et al. Brain. 2022 [B] Bermel et al. Lancet. 2010, [M] Marquand et al. Nature Molecular Psychiatry. 2019

#### **METHODS**

• Processing workflow for heterogeneous dataset: 326 MS patients, 460



## FLAIR/T1w scans from 5 sources



[B]Billiot et al. PNAS 2023. [L] Laso et al. ISBI. 2024, [F] Fortin et al. Neurolm. 2017. [P] Pomponio et al. Neurolm. 2021, [Ge] Ge et al. Lancet 2024.

- 1. To obtain the estimations of counterfactual healthy subcortical volumes from CentileBrain Model<sup>G</sup>
- 2. To obtain surrogate truth volumes by employing SynthSeg<sup>+</sup> and SynthSeg-WMH on T1w and FLAIR



#### RESULTS

- Experiment 1: Reliability of Subcortical Segmentations:
  - Comparing (K-S) literature-reported<sup>P</sup> subcortical volumes with SynthSeg.
  - SynthSeg-WMH closer to reference values.
  - Modality independence. Except for the thalamus



- Experiment 2: Volumetric Deviations from Normative Trajectories:
  - Consistent trend of increasing deviation with age.
  - SynthSeg<sup>+</sup> showing more extreme values  $\bigcirc$



#### CONCLUSIONS

- Methodological Advances:
  - Novel DL integration with normative modeling.
  - Multi-modal analysis framework.
- Key Implications:
  - FLAIR sequences highly relevant.
  - Reliable lesion-aware processing.
- Future Directions:
  - Lesion load analysis integration.
  - Confirm findings and establish clinical relevance.













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