

# A convolutional neural network-based framework for imaging biomarkers in multiple sclerosis: white matter hyperintensity and brain region volumes



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## Introduction

- White matter (WM) lesions are a hallmark of multiple sclerosis (MS) and reflect the inflammatory activity.
- Automatic detection of WM hyperintensities (WMH) from magnetic resonance imaging (MRI) T2-fluid attenuated inversion recovery (FLAIR) scans can support MS diagnosis and help to monitor treatment effectiveness in clinical trials.
- Brain volumetric measures can be used to study the neurodegenerative component of MS, to predict disability progression, and to evaluate potential anti-inflammatory, remyelinating or neuroprotective therapies.<sup>1-3</sup>
- IXICO's IXIQ.Ai is a framework for MRI segmentation workflows.<sup>4-6</sup>

## Objectives/Aims

To validate convolutional neural networks (CNNs) for:

- segmentation of WMH from 3D FLAIR scans
- segmentation of MS-relevant brain regions from 3D T1-weighted (T1W) scans
- volumetric analysis

## Methods

- CNNs trained to segment WMH from 3D FLAIR scans and brain regions, incl. whole-brain (WB) and thalamus, from 3D T1W scans
- Jacobian integration used to estimate WB volume change
- Dataset for WMH workflow validation: a publicly available MS dataset<sup>7</sup> with 3D FLAIR scans, manual segmentations by seven expert raters, and a rater majority voting consensus
- Datasets for brain region workflow validation: ADNI (<https://adni.loni.usc.edu/>), OASIS (<https://www.oasis-brains.org/>), Huntington's disease (two, internal), multiple system atrophy (internal), healthy controls aged 75-86 and 19-25 (<https://brain-development.org/ixi-dataset/>)
- WMH ground truth = majority voting consensus
- Brain region ground truth = semi-automated segmentations (with manual edits)
- Accuracy/robustness from dice score coefficient (DSC), visual assessment, volume correlation/volume error, group separation
- Test-retest performance (ADNI BTB and OASIS datasets)

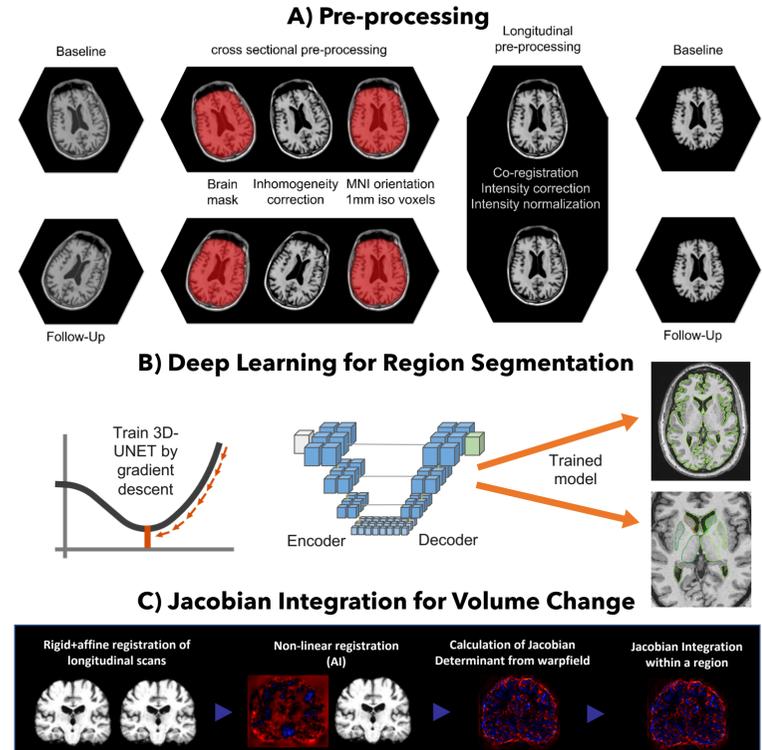


Figure 1: IXIQ.Ai workflows for A) pre-processing for cross-sectional and longitudinal analyses, B) region segmentation, and C) Jacobian Integration for volume change analysis

## Results

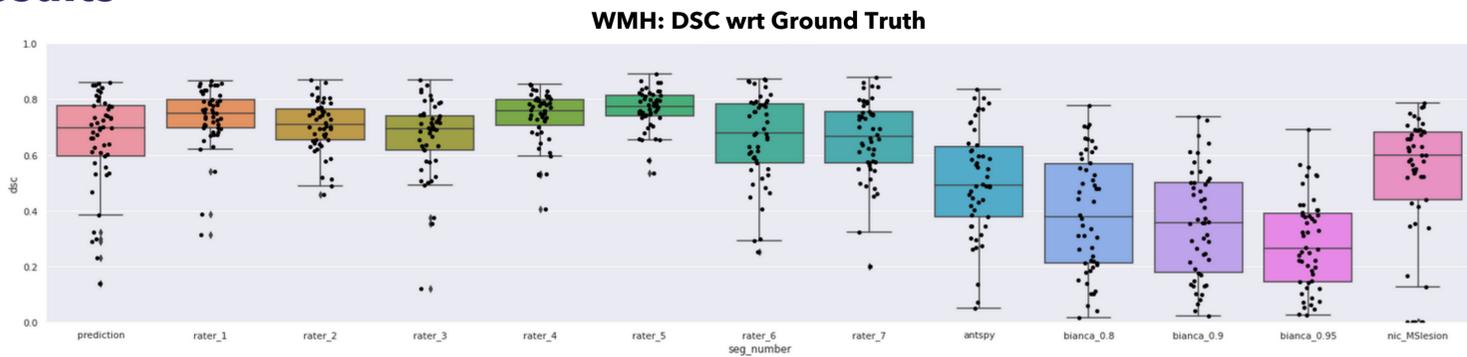


Figure 2: Boxplots showing the distribution of DSCs: IXIQ.Ai WMH workflow (prediction), each individual expert rater (raters 1-7) and other WMH segmentation methods compared to the WMH ground truth (consensus). (antspsy, <https://github.com/ANTsX/ANTs/wiki>; BIANCA, <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/BIANCA/Userguide-lesion-probability-maps-thresholded-at-0.8/0.9/0.95>; nic\_MSlesion, <https://github.com/sergivalverde/nicMSlesions>)

The WMH workflow's ground-truth overlap (mean±SD DSC = 0.65±0.17) was comparable to the individual raters' and higher than for other automated methods (antspsy 0.51±0.19; bianca\_0.9 0.35±0.19; nic\_MSlesion 0.52±0.23) (also see Figure 2). Its average volume correlation with the ground truth ( $r = 0.96$ ) was higher than for the other methods (antspsy  $r = 0.85$ ; bianca\_0.9  $r = 0.69$ ; nic\_MSlesion  $r = 0.87$ ) and its average volume error (AVE) relative to the ground truth (mean±SD AVE, mL = 3.1±3.3) was the lowest (antspsy 6.5±9.1; bianca\_0.9 8.3±11.0; nic\_MSlesion 5.1±6.9).

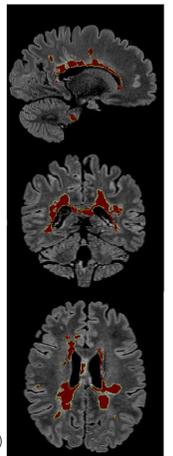


Figure 3: WMH segmentation from 3D FLAIR (yellow = ground truth; red = prediction)

### Region Segmentation: WB and Thalamus

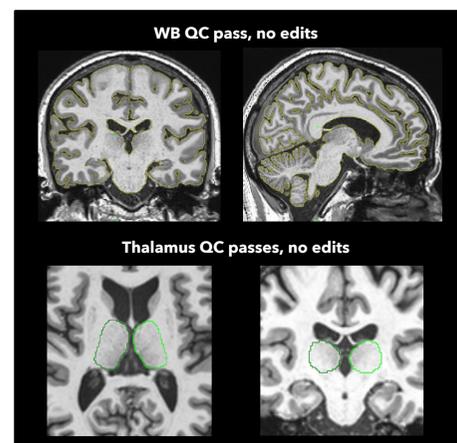


Figure 4: Examples of WB and thalamus segmentations from IXIQ.Ai brain region workflow (CNN) that passed QC without manual edits.

### Volume Change: WB

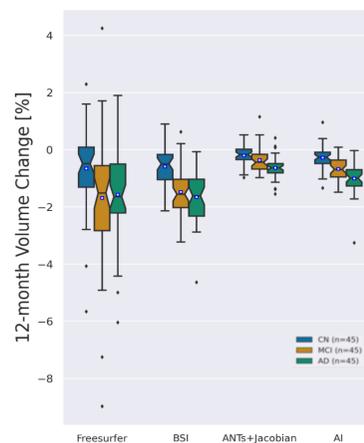


Figure 5: WB volume change (negative change = loss) estimated by IXIQ.Ai (CNN + Jacobian), compared to FreeSurfer<sup>8</sup>, BSI<sup>9</sup>, and ANTS (<https://github.com/ANTsX/ANTs/wiki>) + Jacobian. p-value: Mann-Whitney U-test. CLES: Common Language Effect Size.

CN vs MCI				
	Freesurfer	BSI	ANTs+J	IXIQ.Ai
p-value	0.004	5e-7	0.007	8e-6
CLES	0.67	0.81	0.67	0.78
Median (SD) group difference [%]	1.02 (0.16)	1.06 (0.02)	0.27 (0.01)	0.43 (0.01)
CN vs AD				
	Freesurfer	BSI	ANTs+J	IXIQ.Ai
p-value	0.005	1e-7	6e-8	2e-10
CLES	0.67	0.83	0.84	0.89
Median (SD) group difference [%]	1.16 (0.11)	1.12 (0.03)	0.46 (0.01)	0.73 (0.01)
MCI vs AD				
	Freesurfer	BSI	ANTs+J	IXIQ.Ai
p-value	0.86	0.41	0.009	0.001
CLES	0.48	0.55	0.66	0.70
Median (SD) group difference [%]	0.13 (0.18)	0.05 (0.03)	0.18 (0.01)	0.30 (0.01)

The IXIQ.Ai segmentations (CNN) had high ground-truth overlaps (mean DSC>97). Visual QC found consistently high segmentation quality (see Figure 4): 98% of the whole-brain and 100% of the thalamus segmentations passed QC.

The IXIQ.Ai volume change method (CNN + Jacobian), applied to the WB, detected significant group differences in changes over 12 months, with similar or higher CLES and similar or lower SD of group differences (%) than other methods (Figure 5).

The WB and thalamus volume differences were normally distributed and the distributions zero-centred.

## Conclusions

- The WMH workflow shows higher overlap and volume correlation with the ground truth than comparable automated methods.
- The brain region workflow produces high-quality and reliable whole-brain and thalamus regions for volumetric analysis.
- The IXIQ.Ai framework provides a scalable and robust automatic solution for volumetric analysis of brain WMH and regions of interest in MS.

## References

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