A MACHINE LEARNING MODEL TO PREDICT PROGRESSION OF CORTICAL THICKNESS IN MULTIPLE SCLEROSIS

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INTRODUCTION:

Multiple sclerosis (MS) is one of the most common causes of neurological disability in young adults in the Western world.

Several MRI studies have demonstrated the presence of cortical grey matter atrophy, which strongly correlates with the progression of neurological impairment in MS patients [1].

The substrate of this atrophy, is, however, still largely unknown: It is not clear whether cortical atrophy is mainly the result of local pathological processes or disconnection from distant white matter (WM) lesions [2].

In addition, MS lesions have different degrees of destructiveness, that appears greater when a susceptibility hypointense rim is present [3].

OBJECTIVES:

The aim of this study was to investigate the interplay between cortical atrophy and different types of lesions at Ultra-High Field (UHF) 7 T MRI, including cortical lesions and lesions with a susceptibility rim (a feature which pathological studies have associated with impaired remyelination and progressive tissue destruction)

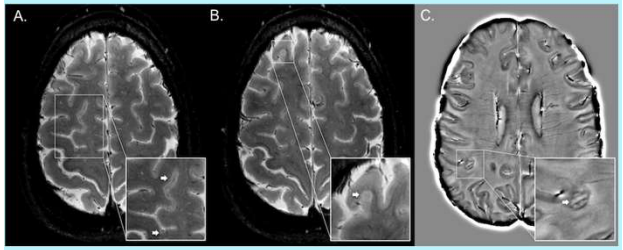


Figure 1. *Examples of intracortical (A) and leukocortical (B) lesions on the 7T magnitude T2* images in a MS patient. One of the white matter lesions from the same patient is surrounded by a peripheral paramagnetic rim that is easily identifiable on the 7T phase image (C)*

METHODS:

Study participants: 100 MS patients [relapsing remitting (RRMS) N=74, secondary progressive (SPMS) N=26].

MRI Protocol and Image Analysis:

7-Tesla 2D T2*-weighted images (magnitude and phase images for lesion segmentation) (Figure 1).

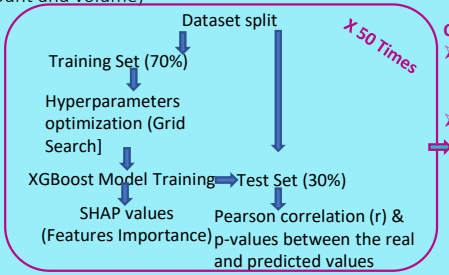
3-Tesla 3D T1-weighted scans (Freesurfer reconstruction, cortical and regional cortical thickness evaluation in 150 brain regions determined by a predefined parcellation (Desikan atlas)]. Mean thickness in single hemispheres and in the whole brain has been calculated by averaging local thickness values)

Predictive model Development:

We used the **XGBoost method** to:

- generate prediction models for cortical thickness
- to illustrate the importance of each feature included in the models.

13 demographic and lesional features (gender, patients age, age at onset, rim lesions presence [binary variable, rim lesions/no rim lesions] rim lesions load [binary variable, <4 rim lesions/≥4 rim lesions], rim lesions count and volume, leukortical lesions count and volume, intracortical lesions count and volume, rimless WM lesions count and volume)



TAKE HOME MESSAGES:

- A small subset of features [WM lesion volume (not considering rim lesions), patient age and WM lesion count (not considering rim lesions), intracortical lesion volume] carried most of the prediction power.
- WM lesion load is most important when it is small, whereas cortical lesion load behaves in the opposite way.
- **Our results suggest that disconnection and axonal degeneration due to WM lesions and local cortical demyelination are the main factors determining cortical thinning.**
- **These findings further elucidate the complexity of MS pathology across the whole brain and the need for both statistical and mechanistic approaches to understanding the etiopathogenesis of lesions.**

REFERENCES:

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MODELS PERFORMANCES

Mean Thickness	r-value	p-value
Right Hemisphere	0.47 (0.15)	0.009 (0.0013)
Left Hemisphere	0.44 (0.18)	0.016 (0.020)
Whole Brain	0.48 (0.17)	0.008 (0.011)

Table I: *Mean (across 50 repetitions) Pearson correlation (r) as well as related p-values between the real and predicted values evaluated in a 70.30 test/train split. Standard deviations across 50 repetitions are shown in brackets.*

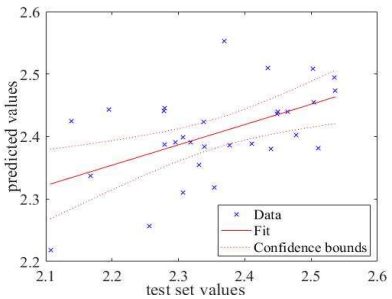

Figure 2. *Example of correlation (in one single test set) between real and predicted whole brain cortical atrophy values (r=0.51, p=0,007).*

RESULTS:

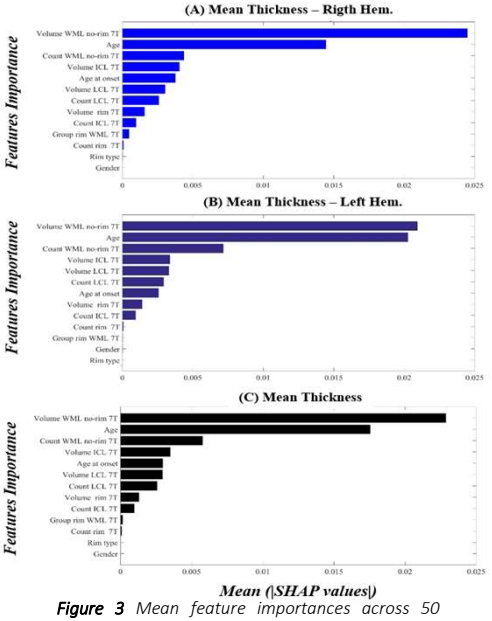

Figure 3 *Mean feature importances across 50 repetitions for thickness prediction in the two hemispheres (A,B) and in the whole brain (C)*

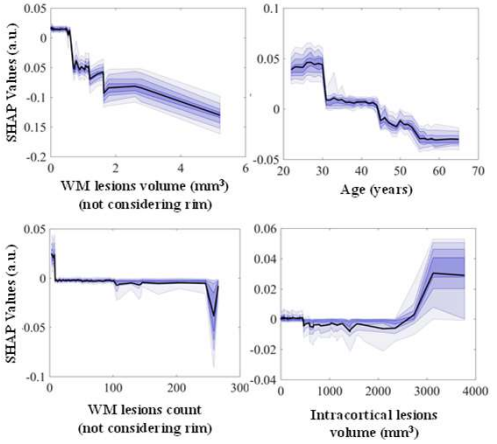

Figure 4. *SHAP dependence plots of the four most important features in the prediction of globally averaged mean thickness (in order of importance: WM lesions volume, not considering rim lesions; patient age; WM lesions counts, not considering rim lesions and intracortical lesions volume.*