

## T2/T1 ratio z-scores as a quantitative metric for Multiple Sclerosis

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### Target Audience

This research is intended for clinicians and researchers interested in Multiple Sclerosis.

### Purpose

Multiple sclerosis is a neurodegenerative disease that affects over 2.3 million people around the world. This disease is characterized by inflammatory demyelination, which occurs when the body's immune system attacks the protective myelin sheath that covers the nerves and aids in sending electrical signals. To demonstrate correlations between lesions and clinical symptoms, it is important to be able to characterize the lesions of a patient in a quantitative and objective measure. Many studies use a lesion load metric; however, lesion segmentation is a subjective and time-consuming task. The ratio of T2 and T1 is sensitive to demyelination in the brain and the degree of damage from multiple sclerosis lesion and therefore can potentially be used as a quantitative marker of tissue injury.<sup>1</sup>

### Methods

T2/T1 ratio maps were generated for the 20 controls from the Expression, Proteomics, Imaging, Clinical (EPIC) study. By registering these maps to the 2mm resolution MNI standard, an average control atlas of expected values was created. A T2/T1 ratio map was generated for each of 521 MS patients (16% clinically isolated syndromes, 70% relapsing-remitting, 10% secondary progressive, and 4% primary progressive) and compared to the control map distribution, in order to generate a voxel-wise z-score map indicating how different the diseased brain is compared to a normal brain.

Both univariate and multivariate regression methods were used to determine whether this metric has a strong correlation for the existing T2 lesion volume measurements as well as the relative role in correlations with clinical metrics, such as the Expanded Disability Status Scale (EDSS) score. In addition, we used univariate regression methods to compute spearman coefficients for each voxel and generate correlation maps for various clinical measures. The resulting maps were multiplied by a white matter mask, thresholded, and then morphologically opened with a 2mm Gaussian kernel to eliminate noisy voxels.

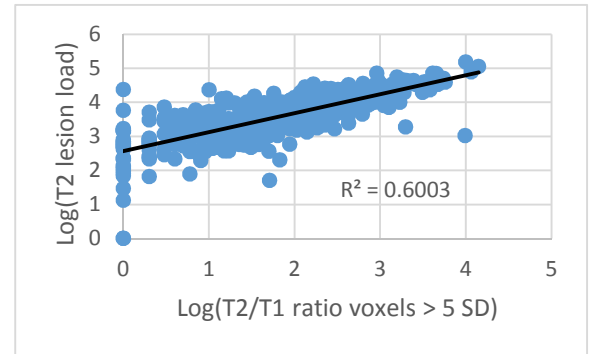


Figure 1. The log was taken of the normalized T2 lesion load and the voxel count of T2/T1 z-scores with minimum threshold of 5 SD. Plotted against each other, the linear regression (black) yielded a RSQ value of 0.6003.

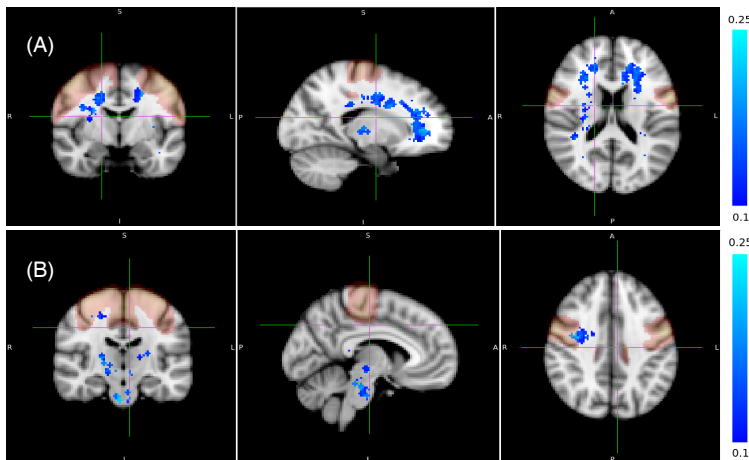


Figure 2. Correlations are shown in blue, while red is the probabilistic representation of the precentral gyrus ROI from the Harvard-Oxford Cortical Structural Atlas. (A) Analysis of T2/T1 z-score and EDSS score show diffuse frontal white matter correlations, primarily located around the ventricles. (B) Voxel-wise analysis between T2/T1 z-score and clinical brainstem scores shows correlated clusters in both brainstem and the motor pathway.

### Results

The log voxel count of white matter z-scores thresholded at 5 and 10 standard deviations (SDs) were significantly correlated ( $p < 0.001$ ) to T2 lesion volume with 0.60 and 0.48 RSQ values, respectively. Stepwise multivariate regression including volume above T2/T1 ratio of 5 SDs, T2 lesion volumes, and whole brain volume selected only brain volume and T2/T1 ratio volume to be important in predicting EDSS score, and not T2 lesion volume. Voxel-wise correlation maps with EDSS versus T2/T1 ratio z-score showed notable regionality with higher spearman correlations around the ventricles and frontal white matter while correlations with the clinical brainstem scores indicated clusters in the brainstem and motor pathways.

### Conclusion

The T2/T1 ratio z-score shows itself to be a new metric comparable to T2 lesion load with the additional benefit of superior prediction of clinical disability, ease of computation, and in principle a richer description of tissue injury. With further validation, it can allow for better tracking of white matter disease burden and prediction of patients' disease progression and will allow for retrospective studies since T2 and T1 scans are generally available for all MS patients.

### References

1. Khan O, Bao F, Hreha S, et al. A novel approach to classifying MS phenotype: brain MRI T1/T2 lesion ratio correlates with clinical phenotype and disability. ECTRIMS. September 9-12, 2009, Düsseldorf, Germany.