Atrophied T2 Hyperintense Lesion Volume is Highly Predictive of Disability Progression. A 2-year Longitudinal Study Using Voxel-Wise Dynamic Classification

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Introduction: Changes in hyperintense T2 lesion volume (LV) have shown weak to modest predictive value for sustained progression of disability in the mid- to long-term.

Objective: To develop and validate a fully automated voxel-wise based dynamic method of T2-LV classification into new, stable, resolving and atrophied T2-LVs.

Methods: We studied 208 MS patients (age 43.5+/-9.8 years, disease duration 10.8 +/-6.7years and EDSS 3 +/-1.8), of which 173 ha relapsing-remitting and 35 secondary-progressive MS at baseline. LV masks and follow-up cerebrospinal fluid (CSF) masks were create via semi-automated methods, and were then co-registered into a common space via their source images. Voxel-wise analysis was the performed on the longitudinally paired LV masks to classify all voxels within the union of masks as new, resolving, stable, or atrophie (Figure 1). Patients received full clinical and quantitative MRI evaluation at baseline and after 2 years.

Results. At follow-up, 46 (22.1%) reached confirmed sustained disability progression. Over a 2-year period, MS patients increased 1.9ml (10%) in their total T2-LV and decreased 1% in their whole brain volume. No relationship was observed between total T2-LV changes and disability progression. The voxel-wise classifier program revealed that over 2 years 59.3% of the total T2-LV was stable, 50.8% was new, 38.4% resolved and 1.7% atrophied into the CSF. Correlation analysis revealed that atrophied T2-LV had the highest predictive value for disability development ($r=0.44$, $p=0.0008$). This was particularly evident in SP MS. The correlation of new T2-LV and disability progression was substantially lower ($r=0.21$, $p=0.004$). Atrophied T2-LV showed a strong relationship with evolution of all non-conventional MRI measures. The relationship was particularly robust with development of whole brain atrophy, accumulation of hypointense T1-LV and DWI entropy (all $p<0.0001$). Higher occurrence or presence of relapses during the follow-up was associated with atrophied T2-LV ($p<0.0001$) and new T2-LV ($p=0.001$) (Table 4). Resolved T2-LVs did not correlate with progression of clinical and MRI outcomes.

Conclusions. Voxel-wise dynamic classification of T2-LV into new, stable, resolving and atrophied T2-LVs is an attractive quantitative MRI measure of inflammatory and neurodegenerative lesion activity and may have an important application in future clinical trials. Robust correlation of atrophied T2-LV with all clinical and MRI parameters suggests that disappearance or shrinkage of lesions into the CSF is an important mechanism of disease progression in MS.

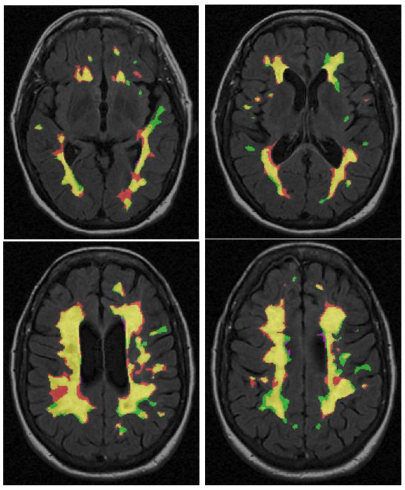

Figure 1. Voxel-wise dynamic lesion change mapping in a 36 year-old patient with relapsing-remitting MS patient over 2 years.

The figure compares two successive T2-weighted scans performed at a two-year interval in a 36-year old patient with RR MS. Voxel-wise analysis was performed on the longitudinally paired lesion masks to classify all voxels within the union of masks as new, resolving, stable, or atrophied. LV at the time of the initial scan was 40 ml, and this had increased by 2 ml by the time of the second scan, suggesting a relative stability of lesion burden over time. However, when the lesions were evaluated voxel by voxel, this stability was revealed to be only apparent (yellow areas).. Indeed, an area corresponding to 15% of the initial LV, which appeared healthy tissue on the first scan was affected by the creation of the new lesions on the second scan (red areas). In parallel, around 10% of the original lesion burden disappeared by the time of the second scan (green areas) and around 3% was lost to expansion of the ventricular space as a result of cerebral atrophy (pink area).

Legend: Yellow: stable lesion areas; red: lesion areas appearing since baseline; green: lesion areas resolving since baseline; pink: lesion areas lost to the ventricles due to atrophy.