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Rapid reduction of lesion accumulation in specific white matter tracts as assessed by lesion mapping in patients with relapsing-remitting multiple sclerosis treated with interferon beta-1a

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Introduction: Administration of interferon beta-1a (IFN β -1a) in patients with relapsing-remitting multiple sclerosis (RRMS) reduces brain lesion accumulation over time, as assessed by magnetic resonance imaging (MRI). However, it is unclear whether this reduction has treatment specific spatio-temporal characteristics.

Objective: To assess spatio-temporal characteristics of active lesions in patients treated with IFN β -1a or placebo using lesion mapping approaches in monthly-acquired MRI data.

Methods: Post-hoc analysis of MRI data from the IMPROVE study, comparing patients treated with subcutaneous IFN β -1a (44 μ g) three times weekly (n=120) versus placebo (n=60). MRI examinations were acquired at weeks 4, 8, 12 and 16 to build lesion probability maps (LPMs) of cumulative combined unique active (CUA) lesions. At each time point, differences in lesion location were assessed in several white matter (WM) tracts using predefined anatomic WM atlases. Voxel-wise comparisons assessed differences in lesion frequencies between IFN β -treated and placebo groups within general linear model framework using nonparametric permutations (p<0.05, cluster-corrected).

Results: Progressive increases in portions of WM occupied by CUA lesions was half in the IFN β -

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treated group (41cm^3 at week 4; 95cm^3 at week 16; mean $24\text{cm}^3/\text{month}$) versus the placebo group (62cm^3 at week 4; 196cm^3 at week 16; mean $48\text{cm}^3/\text{month}$). Similar results were obtained with tract analysis; reductions of 50% of lesion accumulation in IFN β -treated group in the cortico-spinal tract (CST), 52% in anterior thalamic radiation (ATR) and 65% in superior longitudinal fasciculus (SLF). At voxel-wise analysis, the IFN β -treated group LPMs showed lower frequency of CUA lesions versus placebo group from week 4. This was pronounced at week 16 in the left CST ($p<0.005$), left ATR ($p<0.005$) and right SLF ($p<0.02$).

Conclusions: Treatment with IFN β -1a rapidly reduces lesion accumulation in RRMS patients in specific WM tracts versus placebo. The highest local differences along the regions mainly involved in clinical manifestations such as CST, SLF and ATR.

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