MS Repair Potential and Disease Progression from Short-Term T2 Change

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SYNOPSIS

Short-term recovery of new MS lesions on T2-weighted MRI was evaluated for its potential as a surrogate for repair potential and disease progression. We hypothesized that the rate and extent of lesion recovery from peak hyperintensity is indicative of the current repair capacity and predictive of further permanent disease progression. In such a context, greater individual lesion recovery would specify higher repair potential and/or less destructive disease activity.

INTRODUCTION

Over 80% of newly diagnosed cases of clinically definite MS fall into the relapsing-remitting (RRMS) category. A large proportion of RRMS patients eventually converts to secondary progressive stage (SPMS) within 6-10 years [1]. Hallmark of this progression is a shift from inflammatory to degenerative activity, apparent on MRI as fewer contrast-enhancing lesions and accelerated brain parenchymal atrophy. The etiology this progression is not known, but a common premise is an exhaustion of repair potential leading to accelerated damage accrual. In this context we explored the dynamics of new focal T2 hyperintensities ("T2 lesions") as early MRI signs of the stage of progression, before atrophy or disability develop. Goal is an early and specific MRI marker for this "reparatory potential", and through that, a measure of disease severity that distinguishes destructive from non-destructive activity, i.e. a dissociating metric for the component in MRI visible disease activity that does contribute to permanent damage and the component that does not.

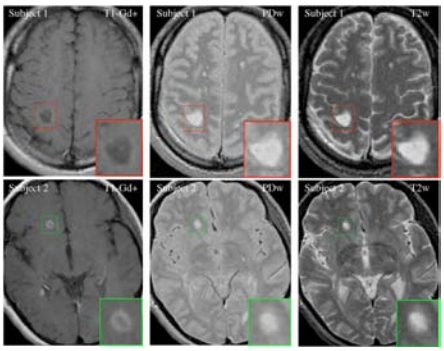

Fig.1: Example slices of 2 new lesions from 2 MS patients. Columns (left to right) show T1-Gd+, PD- and T2-weighted MRI. Evolution for these 2 lesions (PDw series) is shown in Fig.2

METHODS

The relationship of new lesion dynamics relative to later markers of progression were examined. Frequent MRI during 1 year and a one-time follow-up after 4-5 years was obtained from 26 patients (age 37±8 years) with RRMS. Time Series Modeling [2] was applied to assess the dynamics of new lesions and the level of short-term recovery. Relationships were examined between lesion evolution during the first year and atrophy (brain-parenchymal fraction, BPF) and disability (EDSS [3]) at 4-year follow-up and progression rates thereof. Lesion recovery was defined (on a per-voxel basis) as the percentage of return toward isointensity, relative to peak after first appearance. Mean residual hyperintensity across all lesion voxels was used as the complementary measure to lesion recovery (residual = 1 – recovery). New lesion activity was defined as the time of significant T2 signal change. New lesions with less than 6 months of frequent follow-up were excluded to ensure accurate estimate of the dynamics.

RESULTS

6 patients (23%) had no new lesions during the first year; the remaining 19 patients showed 231 new lesions. Example lesion time signatures for two representative lesions from patients with low and high BPF rates and disability, respectively, are shown in Figures 1 and 2. Reduced short-term lesion recovery (i.e. higher residual hyperintensity) was associated with significantly higher rates of atrophy progression (p=0.0003), as well as overall disability (p=0.002). Comparison was done via t-test at α=5% assuming equal variances. Similar relations were found for new lesion activity duration (p=0.02, Figure 3). Relationships with disability progression did not reach significance.

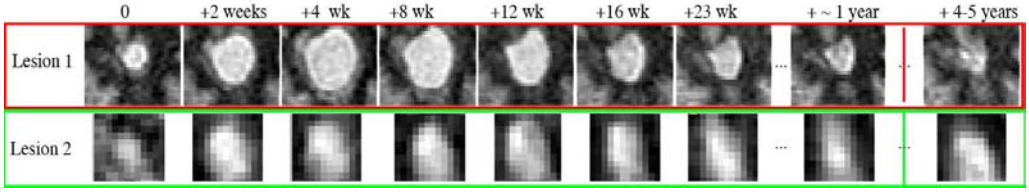

Fig.2: Example of two lesion evolution signatures for 2 MS subjects shown in Fig.1. Subject 1 had significantly lower EDSS and BPF rate than subject 2. Note that the bottom lesion is smaller and has a different time signature, leading to substantially lower recovery.

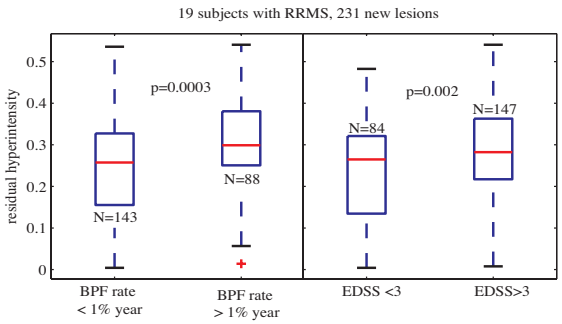

Fig.3: Residual hyperintensity of new lesions was significantly greater for patients with higher atrophy rates and also greater disability

DISCUSSION

These findings suggest that the short-term behavior of new T2 lesions has value to stage MS progression earlier, before atrophy or disability develop. Lower rates of lesion recovery may represent lower repair and greater proximity to a progressive stage. The short- and mid-term dynamics obtained from serial T2-weighted MRI appear promising as potential surrogates to stage disease progression and disease severity.

REFERENCES

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