Subacute changes in T2 signal evolution: Time-Series Modeling of Degenerative and Restorative Processes in MS

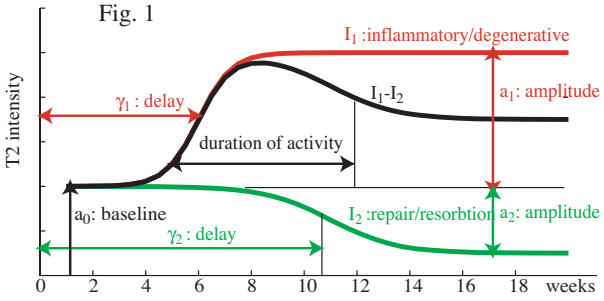
D. S. Meier[1], C. R. Guttmann[1]

[1]Dept. of Radiology, Brigham & Women's Hospital, Harvard Medical School, Boston, MA, United States

INTRODUCTION

Lesion formation in MS consists of a sequence of inflammatory/autoimmune, degenerative, and restorative processes that result in the pathological findings of demyelination and remyelination, inflammatory infiltrates, axonal loss, and fibrillary astrocytosis. Little is known about the timing, sequence, and interplay of the processes leading to white matter damage in MS. MS lesion development on MRI is commonly subdivided into an acute phase with blood-brain barrier leakage lasting a few weeks, followed by a chronic phase of T2-hyperintensity and occasional T1 hypointensity ("black holes"). To further explore the timing of pathological processes *in vivo*, the short-term dynamics of new lesion formation were characterized by applying a new parametric model to a frequent (up to weekly) MRI follow-up series of MS patients.

Fig. 1



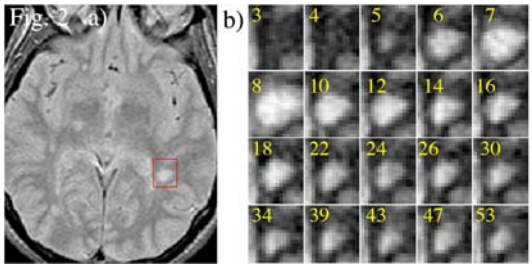
METHODS

332 new T2 lesions were identified in frequent (weekly to monthly) serial MRI of 32 MS patients over one year. The MRI data was fused into a four-dimensional volume using methods described in (1). To study the intensity dynamics of new lesion formation in terms of inflammation and degeneration versus resorbtion and repair, a pathophysiologically motivated two-process model was applied. The model (Fig.1) comprises two opposing non-linear processes representing inflammatory/degenerative and resorbtive/reparatory activity, respectively. Each process has individual strength (α), rate (β) and delay (γ). The model equation was

$$I(t) = \alpha_0 + \frac{\alpha_1}{1+e^{\beta_1(\gamma_1 - t)}} - \frac{\alpha_2}{1+e^{\beta_2(\gamma_2 - t)}}.$$

The model was fit pixel-wise through the time-series within a manually defined bounding box around each lesion (Fig.2). Peak intensity, duration and residual hyperintensity of each lesion pixel were estimated from the model parameters with respect to the baseline signal before lesion appearance. Median duration of activity was computed for each lesion and compared to duration estimates of contrast-enhancement (T1-Gd activity) (2).

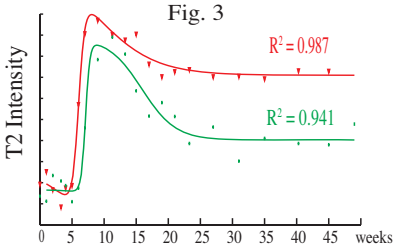
Fig. 2



RESULTS

The mathematical model described the lesion time profiles with excellent fidelity (R^2=0.72±0.14, range 0.5 to 0.996). A pair of example profiles and fits for two pixels within a single lesion are shown in Fig.3. High levels of lesion activity beyond the enhancing inflammatory phase were observed, identifying a **subacute phase** where water resorbtion and/or reparatory processes occur. Concentric patterns of hyperintensity, duration and residual damage were observed, consistent with findings of heterogeneous MS lesion histopathology. 30-50% of a new MRI lesion consisted of transient signal change with little or no residual hyperintensity. Comparison of T2 durations with enhancing activity (2) showed a clear sensitivity of T2 hyperintensities towards subacute disease activity. Whereas T1-Gd activity is predominantly observed around 1-2 weeks, subacute T2 activity extends significantly beyond (Fig.4).

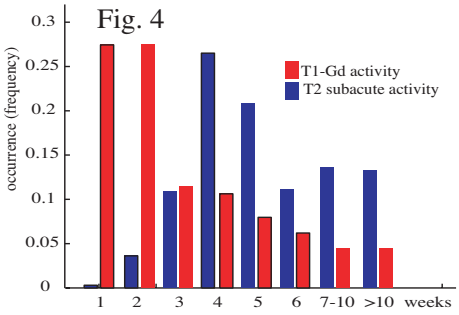
Fig. 3



DISCUSSION

The dominant short-term fluctuations in MS lesions are well described by two opposing processes of inflammation/degeneration versus resorbtion and repair. The observed **subacute phase** indicates collective MRI sensitivity toward secondary non-inflammatory processes (de- and remyelination, axonal degeneration, astrocytosis). The observed heterogeneity of evolution within lesions cautions against MRI surrogates on a per-lesion basis. The use of single-timepoint global lesion burden appears significantly confounded by transient signal change that does not represent permanent damage. The widely observed lack of clinical correlation and specificity of T2-weighted MRI is likely to stem in part from this effect.

Fig. 4



REFERENCES

1. Meier et al. NeuroImage, 2003; 20:1193-1209
2. Cotton et al. Neurology, 2003; 60:640-646

ACKNOWLEDGMENTS

This work was supported in part by funding provided by the Harvard Center for Neurodegeneration and Repair (Clinical Trials Pilot Study Grant) and the National Multiple Sclerosis Society (RG 3574-A-1).