

**My MRI worsened but I didn't. Should I change my disease-modifying treatment?  
No.**

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It is imperative to recognize multiple sclerosis (MS) patients with high risk of disability progression as soon as possible and offer them more potent treatment.

Conventional (enlarging T2, novel T2 and Gd lesions) and unconventional (brain atrophy) MRI parameters are putative biomarkers of the disease progression.

The data about influence of early conventional MRI parameter worsening (without clinical progression or relapses) on early or late disability in treated MS patients are controversial and available mainly for interferons beta. Some of the studies showed that the development of new T2 or Gd enhancing lesions in the first year of interferon beta treatment predicted second and third year disease activity or worse late clinical outcome, but some of the studies were negative. In a single study from Barcelona the first-year MRI activity did not predict clinical worsening of the disease in the next two years in patients treated with glatiramer acetate.

There are many caveats which need to be considered when interpreting comparative MRI data in the treated MS patients.

How many novel silent T2 MRI lesions have to be present in the first year for a poor early or late prognosis? One, two or three? In the interferon beta studies different number of early new T2 lesions predicted worse future outcome.

One has to be aware that the clinical effects of interferons beta and glatiramer acetate are delayed therefore novel T2 lesions could appear before the start of efficacy of the agents.

The substantial problem of all injectable drugs is adherence to the therapy. In a large recent study from Germany only 30-40% from more than 50.000 patients were adherent to the injectables.

Furthermore, there is also a problem of an interpretation reliability of paired MRI data among neuroradiologists. In a study from Cleveland for example between-rater variability was high for enlarging T2 lesions, intermediate for novel T2 lesions and low only for Gd enhancing lesions.

So far there are no data which would indicate that patients treated with oral drugs or monoclonal antibodies have a poor prognosis with 'MRI only' worsening.

It is even more difficult to include unconventional MRI parameters, such as brain atrophy measurements into early therapeutic decision making. The majority of disease modifying drugs have moderate and inconsistent effect on brain volume which is often delayed (e.g. pseudoatrophy).

Therefore, taking into account also a less favorable safety profile of more potent drugs, common clinical reasoning is crucial in the management of an individual with MS and escalation therapy should be given to patients with more realistic risk of poor prognosis.

