Differences in MRI findings with various Disease Modifying Therapies

MRI has emerged as one of the most important measures of MS disease activity. It is the only method of directly seeing the lesions of MS. For every MS attack that patients are aware of, there are, on average, ten silent MRI lesions. Thus, MRI provides almost ten times as many events to count compared to counting attacks. In addition, measuring lesions that enhance with gadolinium contrast allows lesions that have active inflammation to be counted. MRI can also be used to measure whole brain injuries through measures of atrophy. These three measures (lesions, inflammation and atrophy) all correlate to the clinical state of patients. However, the correlation is not sufficiently good to allow MRI to completely substitute for clinical measures such as attacks and disability. The FDA requires that a clinical measurement like attack rate or disability be used as the primary outcome for studies, so MRI measures are used as secondary rather than primary outcome measures.

It is tempting to compare the MRI findings between various studies of MS medications. However, such comparisons are not scientifically valid. The patients enrolled in different studies have differences that cannot be corrected for. One example is the difference in disease severity, with more recent studies enrolling patients that are earlier in the disease course and with fewer attacks per year. Patients come from different regions that have differences in the timing of diagnosis, different treatments and different genetic backgrounds. Many differences are due to factors that cannot even be identified. Because of the impossibility of identifying and correcting for the differences in these populations, scientists strongly discourage comparisons across different studies.

Nevertheless, comparisons have been made and are frequently discussed among those deciding on the use of DMTs. These comparisons are often driven by marketing of particular medications with data selected to favor that particular product. Such comparisons are strongly discouraged. Examples of MRI measurements of lesions in large phase III studies include:
- Avonex: 13.2% improvement in lesion volume compared to 0.65% in the placebo group
- Betaseron: 5.6% improvement in lesion volume compared to 11.9% in the placebo group
- Copaxone: 12.3% worsening in lesion volume compared to 20.6% in the placebo group
- Gilenya: 10.6% worsening in lesion volume compared to 33.8% in the placebo group
- Mitoxantrone: 1.1 new lesions compared to 5.5 in the placebo group
- Rebif: 3.8% improvement in lesion volume compared to 10.9% in the placebo group
- Tysabri: 1.9 new lesions compared to 11 in the placebo group

Note that Extavia was approved using data from the Betaseron study. Different MRI outcomes were used in these various studies, including number and volume of enhancing lesions, number of patients with enhancing lesions, new lesion volume and number, number of patients with new lesions, etc. The use of different MRI outcomes in different studies makes it difficult to compare studies. Notice that the studies for mitoxantrone and Tyasbri did not include measures of volume. Copaxone and mitoxantrone did not include MRI outcomes in the original studies. Copaxone, in
particular, was the recipient of negative marketing because of the lack of data regarding MRI outcomes. This lead to a separate study to determine the effect of Copaxone on MRI outcomes. A second study was also done to include MRI outcomes for mitoxantrone. While this study showed a positive benefit on MRI outcomes with mitoxantrone, it should be pointed out that the dose used in the MRI study was completely different that the dose used in clinical practice. Avonex, in particular, has been criticized because the changes in lesion volume on MRI was not statistically significant. However, the placebo group did unusually well on this outcome making it difficult for the medication to surpass it. Also, other MRI outcome measures did show a benefit to the medication.

It is also important to acknowledge that none of the current medications are expected to improve MRI findings. However, several studies have found that patients in the treated group (and often the placebo group) have had improvements in MRI findings. MS attacks are often accompanied by large lesions on MRI, which gradually shrink over several weeks. Patients often enroll in studies because they are having active disease with attacks. These patients often have large acute lesions on MRIs that shrink during the course of the study. This accounts for the decrease in lesion volume in patients in these studies. Also, if patients have fewer attacks during the course of the study, there will be a decrease in large acute lesions and a decrease in overall lesion volume. None of these findings indicate an actual shrinkage of the chronic lesions of MS.

It is also important to note the primary importance of MRI in studies of MS treatments. MRI findings cannot prove a benefit of treatment on clinical activity or disability. Rather, MRI provides an important check that treatments are truly affecting the underlying biology of the disease, leading to a decrease in inflammation and new disease activity. Furthermore, MRI provides proof that these findings are not due to a placebo effect.

Since we believe that MRI findings cannot be scientifically compared between different studies, we strongly advise that patients make decisions on which DMT to use based on other factors. We believe that only head-to-head studies of medications can accurately predict which one is stronger. Information about head-to-head studies can be found elsewhere on our website.