

# T2 Relaxometry in Tumefactive Demyelinating Lesions: A Case Study

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## Abstract

**Objective:** The study aimed to characterize tumefactive demyelinating lesions by magnetic resonance imaging multicomponent T2 relaxation.

**Methods:** Quantitative T2 mapping of the intra/extracellular water was compared with conventional T2-weighted Fluid-Attenuated Inversion Recovery (FLAIR) and contrast-enhancement T1-weighted imaging.

**Results:** Tumefactive demyelinating lesions showed typical open-ring-like contrast enhancement, with no T2 hypointense rim on both FLAIR and T2-weighted but a clear heterogeneity in the intra/extracellular water maps. The intra/extracellular water T2 mapping showed a rim of shorter T2 in the same area of ring enhancement and a longer T2 in the central portion of the lesion.

**Conclusions:** Intra/extracellular water T2 mapping has a unique potential to evidence heterogeneity features and a rim of shorter T2 in tumefactive demyelinating lesion and deserves to be further investigated.

**Keywords:** Quantitative MRI, T2 lesions, multiple sclerosis, MRI

## INTRODUCTION

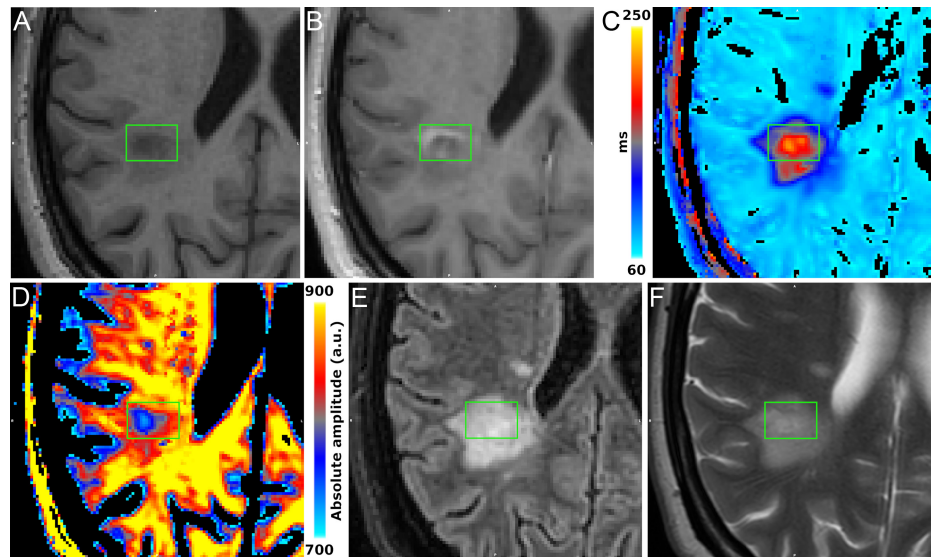
Tumefactive multiple sclerosis or tumefactive demyelinating lesion (TDL) is one of the variants of multiple sclerosis (MS) and is the consequence of central nervous system idiopathic inflammatory demyelinating diseases.<sup>1</sup> Tumefactive demyelinating lesions are not a rare occurrence with a prevalence in the range of 1.4%-8.2% of MS patients.<sup>2</sup> The radiological presentation of patients with TDL is variable and atypical for demyelinating disease due to the differences in size and location of the lesion. Tumefactive demyelinating lesions can be a challenging scenario for clinicians due to difficulties distinguishing them from other conditions, such as neoplasm or infection, and because they can be caused by a heterogeneous range of disorders.<sup>1-3</sup>

Magnetic resonance imaging (MRI) characterization of the myelin component can provide information on demyelinating diseases, offering greater insight into MS-driven pathology and its clinical manifestations.<sup>4</sup> To date, several techniques have been identified and one of the methods is based on the analysis of the transverse relaxation times (T2) of the axonal tissue, with multi-echo sequences and multi-exponential analysis (T2 relaxation). The multi-component nature of the white matter has been established, attributing to each component a different T2, of which at least 1 component is due to water trapped in the myelin lipid membrane and the other to the intra/extracellular water.<sup>5</sup> The application of multi-component T2 relaxometry in MS has been mainly focused on the myelin water pool, that is, myelin water fraction, and the intra/extracellular water (IEW) was only occasionally investigated in diffusely abnormal white matter.<sup>6</sup>

Herein, we describe a case of TDLs assessed for the first time by IEWT2 relaxation, combined with conventional FLAIR, T2-weighted, and post-contrast T1-weighted MRI. We aimed to investigate whether IEWT2 can provide additional information, especially concerning TDL heterogeneity.

## CASE PRESENTATION

A 44-year-old female, affected by relapsing-remitting MS, was recruited from an institutional review board-approved study on the application of T2 relaxometry in MS. The patient had disease onset at the age of 28, with clinical relapses at ages 30 and 31, when she started treatment with a first-line disease-modifying therapy (DMT) until the age of 42 when she experienced clinical relapse with Expanded Disability Status Scale (EDSS) of 2.5. After steroid treatment with benefit, the patient changed therapy with fingolimod (approved as second-line DMT in Europe). The patient was fine until she presented relapse with EDSS 3.5 and underwent the MR examination described in the following.



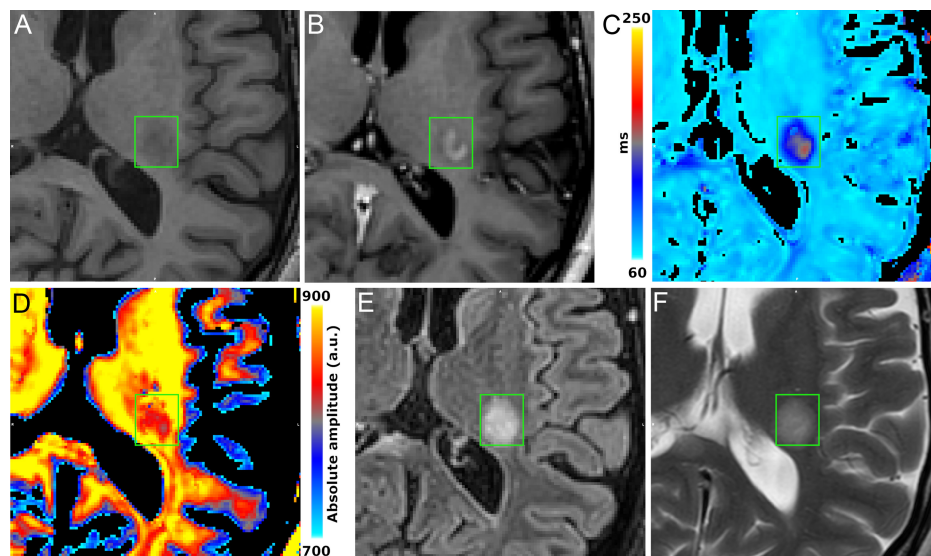
**Figure 1.** From top to bottom: T1-weighted images (pre- and post- contrast enhancement), maps of the intra-extracellular water component (IEwT2 map on the left and the corresponding amplitude on the right), T1-weighted images (FLAIR on the left and T2-image on the right). The green rectangular contour identifies the same region on all the different images/maps. IEwT2, T2 mapping of the intra/extra-cellular water.

The patient underwent conventional MRI, including FLAIR, T2-weighted, and pre- and post-contrast T1-weighted sequences. Additionally, multi-component T2 relaxation was performed by a multi-echo sequence with 32 equally spaced echoes (10-320 ms). The T2 decay signal was decomposed into 3 main components: myelin water below 40 ms, intra-extracellular water (IEw) between 40 and 250 ms, and free water above 250 ms. The obtained IEwT2 mapping was compared with conventional T2, FLAIR, and T1 imaging. Two active TDLs plaques were identified (Figures 1 and 2), showing open-ring contrast enhancement, with no T2 hypointense rim on both FLAIR and T2-weighted images, which resulted in homogeneous hyperintensity, but a clear heterogeneous pattern in the IEw maps. The IEwT2 showed a rim of shorter T2 in the same area of ring enhancement and a longer

T2 in the central portion of the TDLs. Finally, in the 2 TDLs, quantitative IEwT2 showed a T2 that increases with the size of the lesion.

## DISCUSSION

Pseudotumoral TDLs occur in MS and related diseases and are considered an atypical manifestation of central nervous system demyelination. Lesions are called “pseudotumoral” as they may be mistaken for neoplasm, leading to morbidity from brain biopsy and other procedures, delays in appropriate treatment, and unnecessary anguish for patients.<sup>2</sup> Although some radiological characteristics can help make a differential diagnosis easier, a cerebral biopsy may still be necessary. Helpful MRI characteristics that favor a tumefactive demyelinating lesion include size, surrounding edema, a T2 hypointense rim,



**Figure 2.** From top to bottom: T1-weighted images (pre- and post- contrast enhancement), maps of the intra-extracellular water component (IEwT2 map on the left and the corresponding amplitude on the right), T1-weighted images (FLAIR on the left and T2-image on the right). The green rectangular contour identifies the same region on all the different images/maps. IEwT2, T2 mapping of the intra/extra-cellular water.

open-ring enhancement, and the presence of other more typical MS demyelinating lesions elsewhere on the MRI.<sup>2</sup>

Contrast enhancement shaped as an open ring or a crescent circumscribed to the white matter is considered a specific neuroimaging sign for differential diagnosis and distinguishing demyelinating lesions from neoplasms and infections.<sup>7</sup> Furthermore, the presence of a T2 hypointense ring around the lesion is also a feature that may point toward the diagnosis.<sup>3</sup> Such T2 hypointense rim is often present in the same area of ring enhancement with the majority of lesions showing some degree of associated T1 hypointensity.<sup>1</sup> Hypointense T2 rims have also been associated with non-tumefactive ring-enhancing MS lesions.<sup>8</sup> In a study of 54 patients presenting radiographically with TDL (1 of the largest published cohorts of patients), 42% showed a T2 hypointense rim.<sup>9</sup> Moreover, in the patients with a tumefactive onset, the absence of a T2 hypointense rim resulted in an appreciably (although not significant) longer conversion time to MS compared to the patients with a T2 hypointense rim. In that study, no other radiological characteristics of TDLs had any correlation with conversion to MS.<sup>11</sup>

In the reported case, no clear T2 hypointense ring was visible on both FLAIR and T2-weighted images in 2 TDLs, while IEwT2 evidenced a clear heterogeneous pattern, with a rim characterized by a shorter T2. In a recent study, quantitative IEwT2 mapping resulted in higher sensitivity than conventional FLAIR to detect subtle brain tissue alterations,<sup>10</sup> suggesting that current T2 relaxometry, at the price of lower spatial resolution, can offer improved T2 resolution than FLAIR. The reported case demonstrated that IEwT2 can also provide more information than conventional T2 imaging, due to the intrinsic discrimination between the amplitude and the T2 decay of the signal, allowing much better detection of T2 lesion heterogeneity. This unique potential deserves to be further investigated in TDLs and in other ring-enhancing and/or heterogenic MS lesions.

**Informed Consent:** Written informed consent was obtained for the participant

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – U.R., P.F.; Design – U.R., S.M., P.F.; Supervision – B.G.; Data Collection and/or Processing – P.B., U.R., S.M.; Analysis and/or Interpretation – U.R., P.B., S.M., P.F.; Literature Search – U.R., P.B., P.F.; Writing Manuscript – U.R., P.B., P.F.; Critical Review – B.G.

**Declaration of Interests:** The authors declare that they have no conflicts of interest.

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