

# Intralesional vein shrinking in multiple sclerosis lacks in severeness -preliminary results from a 7T MRI study

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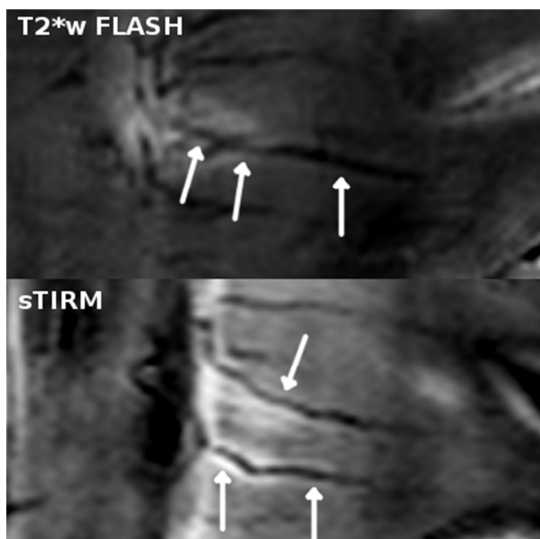
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**Background:** Vascular alterations in multiple sclerosis (MS) have been described decades ago<sup>1-3</sup> Perivascular inflammation remains a key issue in MS research. Gaining from very high spatial resolution, T<sub>2</sub>\* weighted ultrahigh field magnetic resonance imaging (MRI) at 3 Tesla (T) visualized shrunk brain veins within MS plaques *in vivo*.<sup>4</sup> However, this observation may have been confounded by partial volume effects caused by surrounding edema. We addressed this issue by developing a quantification algorithm and an MR-post processing procedure which generates a heavily susceptibility weighted turbo inversion recovery magnitude (sTIRM) image.

**Methods:** 51 patients with MS or clinically isolated syndrome (CIS) underwent 7T MRI (21 female, mean±SD age: 37,6± years). The imaging protocol included T<sub>2</sub>\* weighted (T2\*w) fast low echo shot (FLASH), turbo inversion recovery magnitude (TIRM), and susceptibility weighted imaging (SWI, n=18). STIRM was calculated as the sum of the co-registered, homogenized TIRM and the unmodified SWI using the MIPAV software package (version 7.0.1). Veins that were continuously displayed and showing a kinking of less than 30° were included. To determine mean venous diameter, intra-, pre-, and postlesional venous voxels were manually marked by two trained observers in consensus reading using the OsiriX software package (Osirix version 5.7, 32bit). Consequently we quantified venous diameters at predefined cross-sections of the same veins in two independent studies, using either T<sub>2</sub>\*w or sTIRM sequences. Differences between vein sections were assessed using Wilcoxon signed-rank test.

**Results:** We detected 2416 MS lesions on T<sub>2</sub>\*w FLASH images. As expected, the majority of these lesions was characterized by a central vein and – to a much smaller extent - a hypointense rim at the edge of the plaque. In total, we could analyze 330 venous parts (T<sub>2</sub>\*w, n=195, 72 prae-, 94 intra- and 29 postlesional parts; sTIRM, n=135, 43 prae-, 64 intra- and 28 postlesional parts) of 94 (T<sub>2</sub>\*w) veins (sTIRM n=64) meeting the inclusion criteria. We observed significant intralesional venous shrinking when analyzing T<sub>2</sub>\*w images (p=0.034, postlesional parts, p=0.339 praelesional parts). However, venous shrinking was not statistical significant on sTIRM images (p=0.359 postlesional parts, p= 0.349 praelesional parts).

**Conclusions:** Our results confirm initial reports showing venous shrinking within MS lesions.<sup>3</sup> Intralesional venous thinning was significant in T2\*w imaging but not in sTIRM, suggesting that the T2\*w analysis could be influenced by artifacts such as partial volume effects. Hence, thinning of intralesional veins in MS is most likely not as severe as previously expected. Future combined sTIRM-MRI and histopathological studies may prove whether intralesional vein shrinking is associated with increased inflammation or clinical disease progression.



**Figure 1.** T<sub>2</sub>\*w weighted FLASH imaging visualizing intralesional vein shrinking. This phenomenon is also visible in images derived from the sTIRM approach but to a smaller extent.

## References

1. Tanaka R, Iwasaki Y, Koprowski H. Ultrastructural studies of perivascular cuffing cells in multiple sclerosis brain. *Am J Pathol* 1975;81:467-478.
2. Adams CW. Perivascular iron deposition and other vascular damage in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1988;51:260-265.
3. Dawson J. The histology of disseminated sclerosis. *Trans Roy Soc Edinb* 1916;50:517.
4. Gaitán MI, de Alwis MP, Sati P, Nair G, Reich DS. Multiple sclerosis shrinks intralesional, and enlarges extralesional, brain parenchymal veins. *Neurology* 2013;80:145-151.