Investigation of lesion volume dynamics in MS patients as detected by Voxel-Guided Morphometry – A multi center study

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Disclosures

Presenting author Matthias Kraemer, Andreas Dabringhaus, Stefan Hoffmann and Achim Gass: Nothing to disclose

Johannes Gregori is Managing Director of Mediri GmbH

Ulf Schulze-Topphoff, Benedict Rauser, Benjamin Ettle are employees of Novartis Pharma GmbH

The final responsibility for the content lies with the authors.

Background and objective

In multiple sclerosis (MS), brain atrophy is known to occur in early as well as later stages of the disease. While an interrelationship between white matter lesion formation and consecutive grey matter atrophy has been demonstrated in MRI morphometric studies (Sepulcre et al., Arch Neurol. 2009 Feb;66(2):173-9; Mühlau et al., Mult Scler. 2013 Oct;19(11):1485-92), recently, chronic active lesions (‚smouldering lesions‘) have gained increasing interest as a possible marker for disease activity.

Yet a possible in vivo marker for occurrence and intraindividual structural development for such smouldering lesions is lacking.

Objective

- **To detect chronic active lesions in T1-weighted volumetric native MRI scans (MPRAGE) of MS patients and characterize their intraindividual volume dynamics over time. This includes differentiation of shrinking, enlarging and structurally constant lesions as a possible correlate for active versus inactive MS lesions.**

Methods: MRI datasets and VGM analysis

581 MRI datasets in 200 relapsing-remitting MS patients (2 - 5 per individual) from a 3-year multi-centre observational INSPIRATION-MRI study were investigated using Voxel-Guided-Morphometry (VGM), a method for intraindividual detection and quantification of structural changes in volumetric native MRI scans (T1–weighted MPRAGE sequence) over time (Kraemer, Schormann IEEE Trans Med Imaging. 2003 Jan;22(1):62-74.

VGM uses a three-step procedure consisting of coarse and fine linear alignment and a final non-linear transformation process for registration of 3D MRI data sets from different time points. Thus, regional volume changes are detected within the whole brain volume on a voxel-by-voxel basis. Chronic active lesions were identified and differentiated into chronic shrinking vs. chronic enlarging lesions.

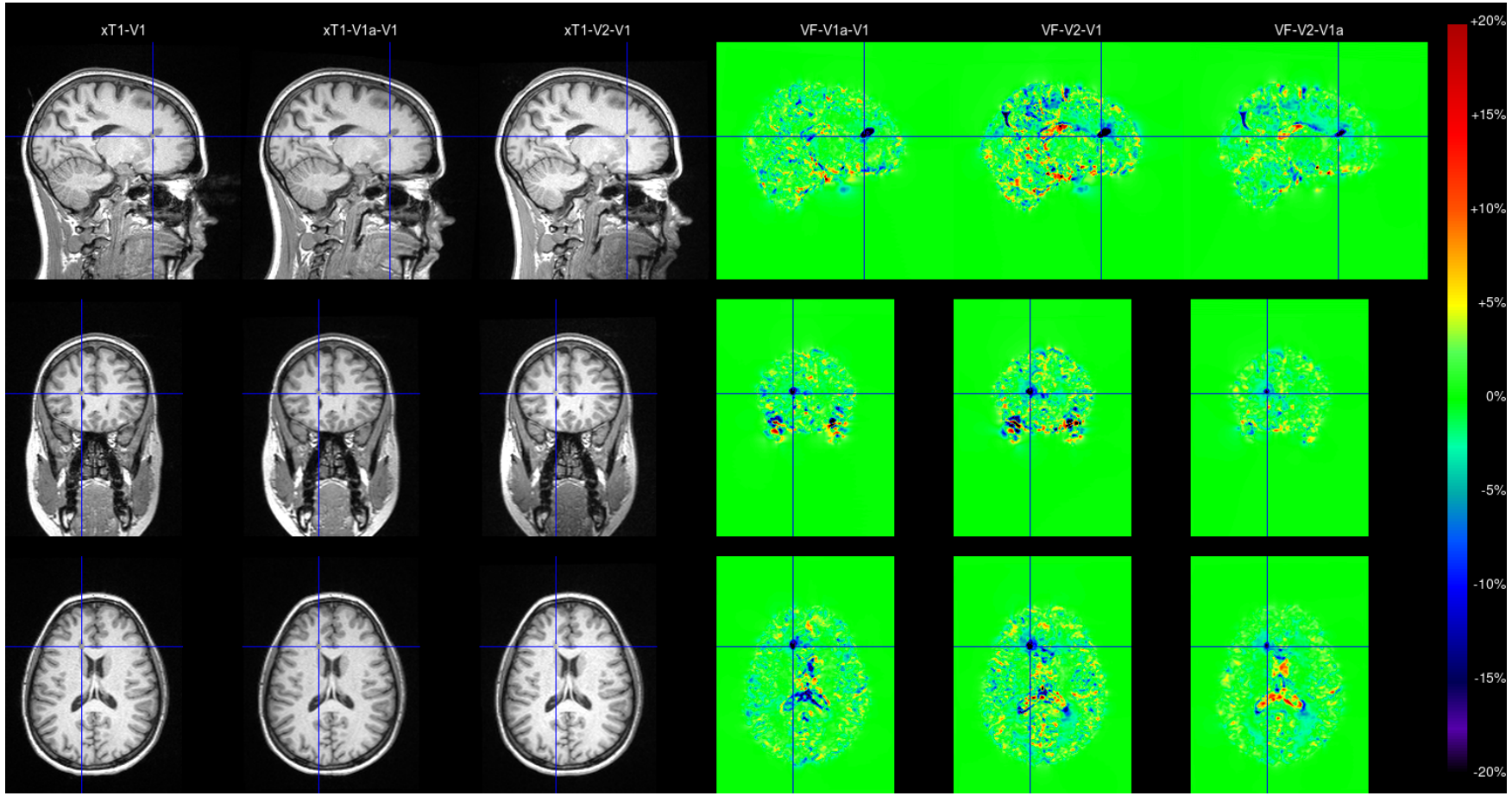
Results

- Intervals between consecutive scans varied between 53 and 1199 days, mean = 443 days. In total, 2419 active lesions were identified, characterized and quantified, corresponding to a mean active lesion load of 12 lesions per patient.

- In chronic shrinking lesions, mean volume change was -33% (from -11% to -59%), in chronic enlarging lesions mean volume change was +53% (from 29% to 425%). We found a mean annual volume decrease for white matter of 0.17% and gray matter of 0.12%.

- 31 patients exclusively demonstrated chronic enlarging lesions, in 16 patients only chronic shrinking lesions were detected, and 119 patients were found to have a mixture of both types of active lesions. In 34 patients, no active lesions were identified.

Results



Chronic shrinking lesion adjacent to the anterior horn of the right lateral ventricle, marked by crosshair.

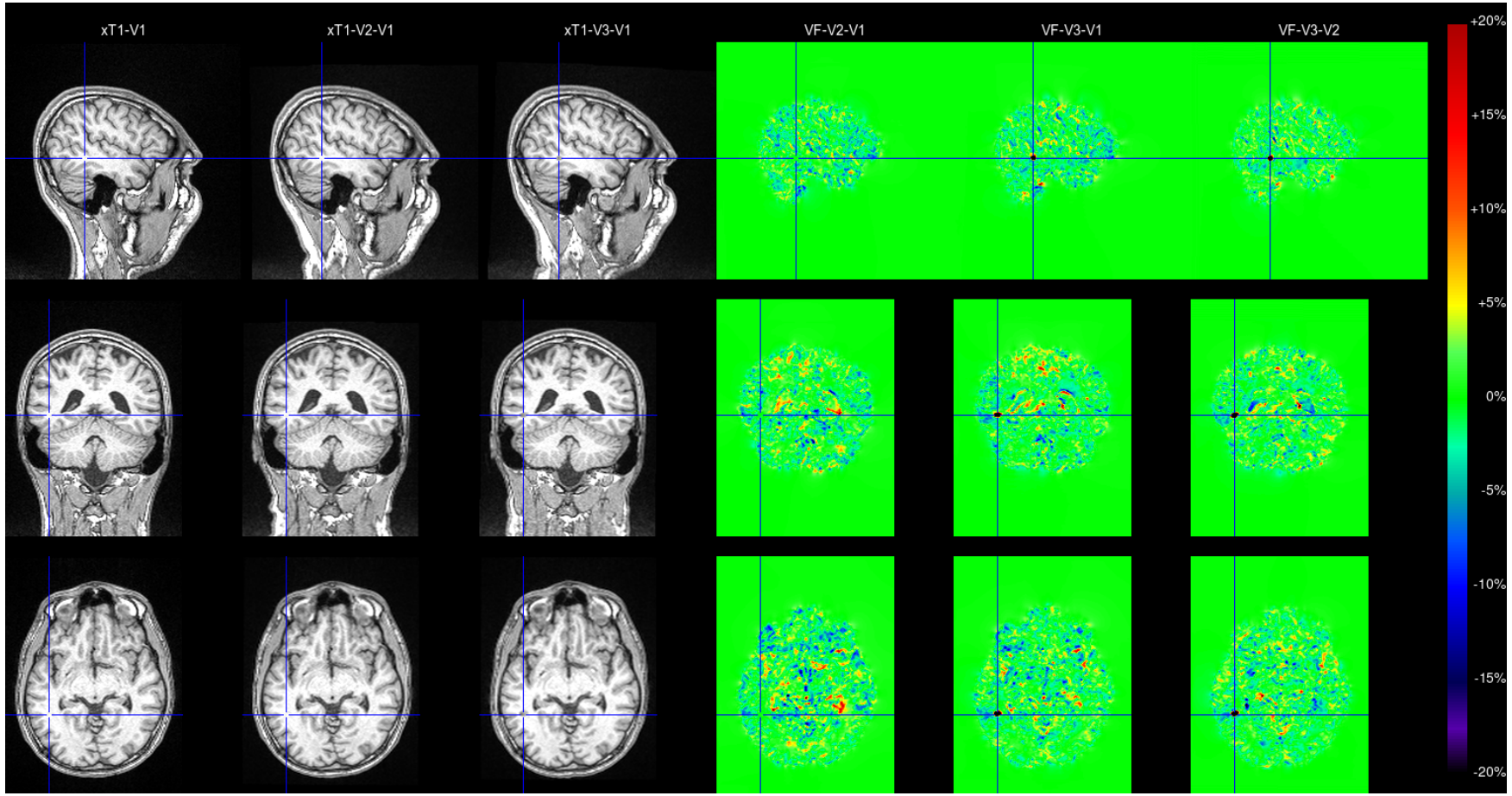
Left: linearly aligned MRI scans over three time points (initial scan on the left, second one after 4 months, third one after 14 months)

Right: Anatomically corresponding colour-coded volume fields as determined by VGM. First column: Alignment of second scan (V1a) to initial scan (V1). Second column: Alignment of third scan (V2) to initial scan. Third column: Alignment of third scan (V2) to second scan (V1a)

Volume reduction is represented by blue colour, volume enlargement by yellow and red colours. No volume change is indicated by light green colour.

Colour scale encoding on the right.

Results



New and secondarily chronic enlarging lesion in right temporal white matter, marked by crosshair.

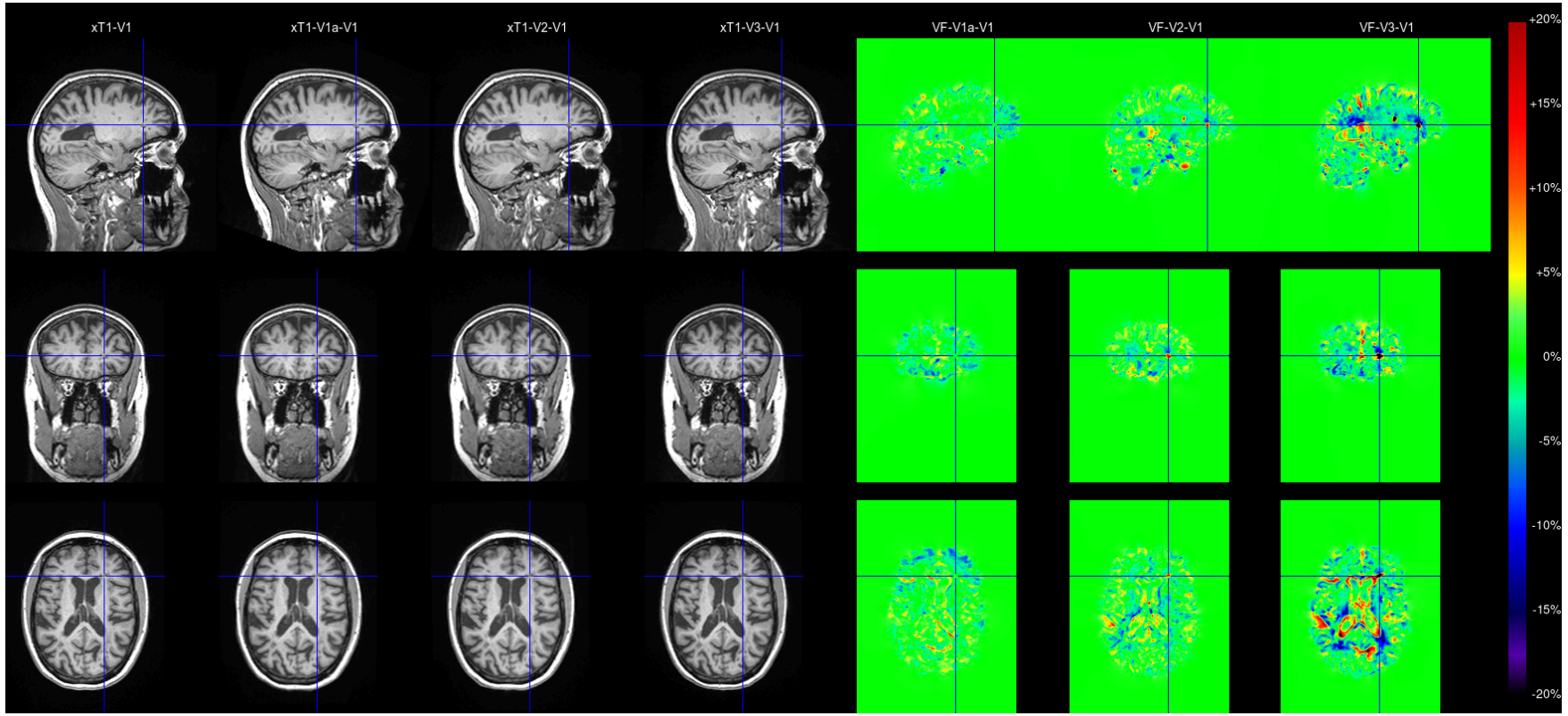
Left: linearly aligned MRI scans over three time points (initial scan on the left, second one after 11 months, third one after 35 months)

Right: Anatomically corresponding colour-coded volume fields as determined by VGM. First column: Alignment of second scan (V2) to initial scan (V1). Second column: Alignment of third scan (V3) to initial scan. Third column: Alignment of third scan (V3) to second scan (V2)

Volume reduction is represented by blue colour, volume enlargement by yellow and red colours. No volume change is indicated by light green colour.

Colour scale encoding on the right.

Results



Chronic enlarging lesion adjacent to the anterior horn of the left lateral ventricle, marked by crosshair.
Left: linearly aligned MRI scans over four time points (initial scan on the left, second one (V1a) after 3 months, third one (V2) after 12 months, fourth one (V3) after 36 months)
Right: Anatomically corresponding colour-coded volume fields as determined by VGM. First column: Alignment of second scan (V1a) to initial scan (V1). Second column: Alignment of third scan (V2) to initial scan. Third column: Alignment of fourth scan (V3) to initial scan.
Volume reduction is represented by blue colour, volume enlargement by yellow and red colours. No volume change is indicated by light green colour.
Colour scale encoding on the right.

Conclusions

- In 83% of investigated patients, chronic active lesions were detected using Voxel-Guided Morphometry in intraindividual longitudinal T1-weighted native 3D-MRI datasets (MPRAGE). These could be further differentiated into chronic shrinking and chronic enlarging lesions.

- Chronic active (smouldering) MS lesions may be regarded as a correlate of MS activity resulting in structural brain damage. These lesions and their structural development over time are detected intraindividually using Voxel-Guided Morphometry.

- Chronic active MS lesions may thus represent an additional biomarker for MS disease activity.

- The correlation between such lesions and clinical development of the disease needs to be further investigated.

Thank you