Perivascular spaces in MS patients at 7 Tesla MRI: a marker of neurodegeneration?

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Target audience: Radiologists.

Purpose: To analyze enlarged perivascular spaces - Virchow Robin Spaces (VRS) - in multiple sclerosis (MS) patients, using high resolution 7T MRI. Additionally, we try to gain insight into the pathological substrate of VRS; is this related to inflammatory or neurodegenerative aspects of MS?

Methods: 34 MS patients and 11 age and gender-matched healthy controls were examined at a whole-body Philips 7T MRI system. Frequency and size (i.e. cross-section and area) of through-plane VRS were measured manually on 3D T1-weighted images (MPRAGE, TR = 7.0 ms, TE = 2.9 ms, TI = 1129 ms, flip angle 8°, acquired resolution 0.8x0.8x0.8 mm^3, reconstructed resolution 0.49x0.49x0.40 mm^3, acquisition time 9.43 min) at five different levels in the brain (Figure 1), and compared between groups with the Mann-Whitney-U test. 3D FLAIR (TR = 8000 ms, TE = 303 ms, TI = 2325 ms, flip angle 100°, acquired resolution 0.8x0.8x0.8 mm^3, reconstructed resolution 0.49x0.49x0.4 mm^3, acquisition time 12.48 min) images were used for MS lesion detection. Supratentorial brain atrophy was quantified using a modified version of the FreeSurfer 5.3 processing stream, computing supratentorial brain volume fraction (sBVF) (Figure 2). Correlations of VRS counts with clinical variables, lesion count and sBVF were assessed using Spearman's rank correlation coefficient.

Results: Overall, MS patients displayed more VRS (group total 508, median 11 per patient) than healthy controls (group total 73, median 4 per healthy control), *P*=0.001. The increased VRS frequency was most pronounced in the convexity of the brain: 77% of the MS patients showed VRS compared to only 46% of the healthy controls (*P*=0.032) at level A. The size of VRS did not differ between both groups. Mean sBVF was lower in MS patients (0.60, SD=0.06) compared to controls (0.65, SD=0.04) (*P*=0.012), indicating a higher degree of supratentorial brain atrophy in MS patients. The number of VRS in MS patients was associated with sBVF (rho=-0.396, *P*=0.020), as well as with age (rho=0.421, *P*=0.013) and disease duration (rho=0.405, *P*=0.022), but interestingly not with lesion count (*P*=0.220).

Discussion: To our knowledge, this is the first study to implement brain atrophy measurements in MS patients at 7T MRI. Main limitation of the study concerns the limited size of our cohort. Therefore, we were not able to perform stepwise linear regression modeling to identify the main predictors of VRS in MS, or perform analyses per clinical subtype of MS. In the future, further studies are necessary to investigate the actual content of VRS in MS, and to determine the relevance of VRS in terms of the correlation with physical or cognitive disability, for differentiating MS clinical subtypes, or predicting disease progression.

Conclusion: Ultra-high field 7T MRI reveals an increased number of VRS in MS. The finding that VRS are associated with supratentorial brain atrophy, but not with lesion count, suggests that VRS might rather serve as a neurodegenerative than an inflammatory marker in MS.

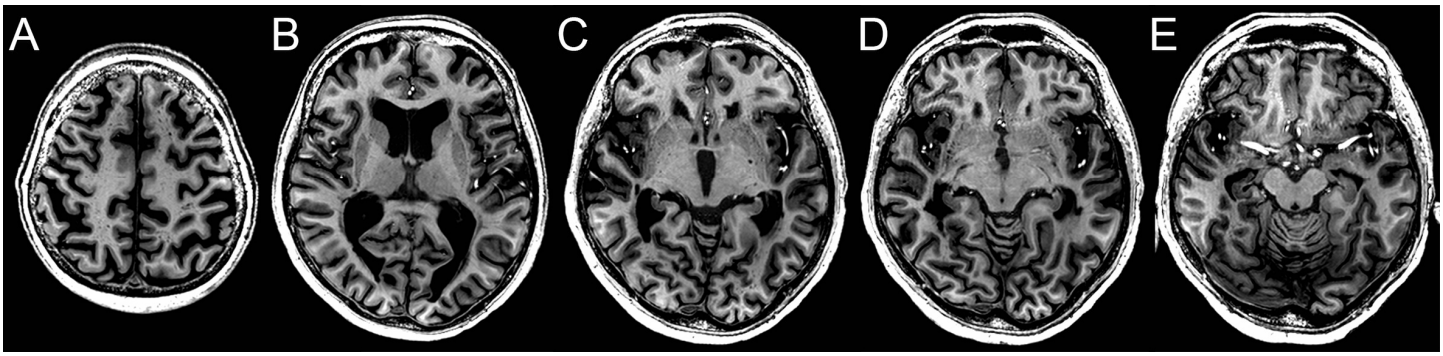

Figure 1. *Five different levels in the brain used for VRS analysis, based on the following anatomical landmarks: A) handknob, to analyze VRS in the vertex; B) where the crus anterius is the widest; C) anterior commissure; and D) the transition between third ventricle and aqueduct, to analyze VRS in the basal ganglia; and E) where the interpeduncular distance is the largest, to analyze VRS in the midbrain.*

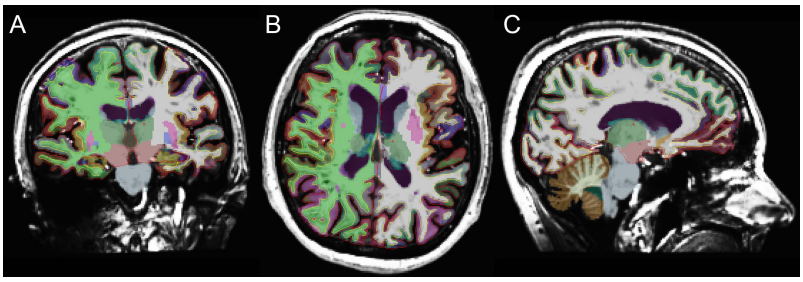

Figure 2. *Segmentation used for atrophy quantification in MS.*

	MS	HC
Gender (F/M)	22/12	6/5
Age (years)	43.0 (SD=7.9)	38.8 (SD=10.5)
EDSS	4 (0-7.5)	-
Disease duration (yrs)	9.4 (SD=5.8)	-
VRS count	11 (1-66)	4 (2-24)
VRS area (mm^2)	2.9 (1.2-17.5)	2.9(1.9-7.0)
VRS cross-section (mm)	2.1 (1.0-11.9)	2.1 (1.4-3.1)
Lesion count	77.2 (SD=65)	4.6 (SD=4.7)
sBVF	0.60 (SD=0.06)	0.65 (SD=0.04)

Table 1. *Clinical and MRI data of MS patients and controls. Note. MS = multiple sclerosis; HC = healthy control; F = female; M = male; SD = standard deviation; EDSS = Extended Disability Status Scale; VRS = Virchow Robin Space; sBVF = supratentorial brain volume fraction. Data are presented as mean (SD) or median (range).*