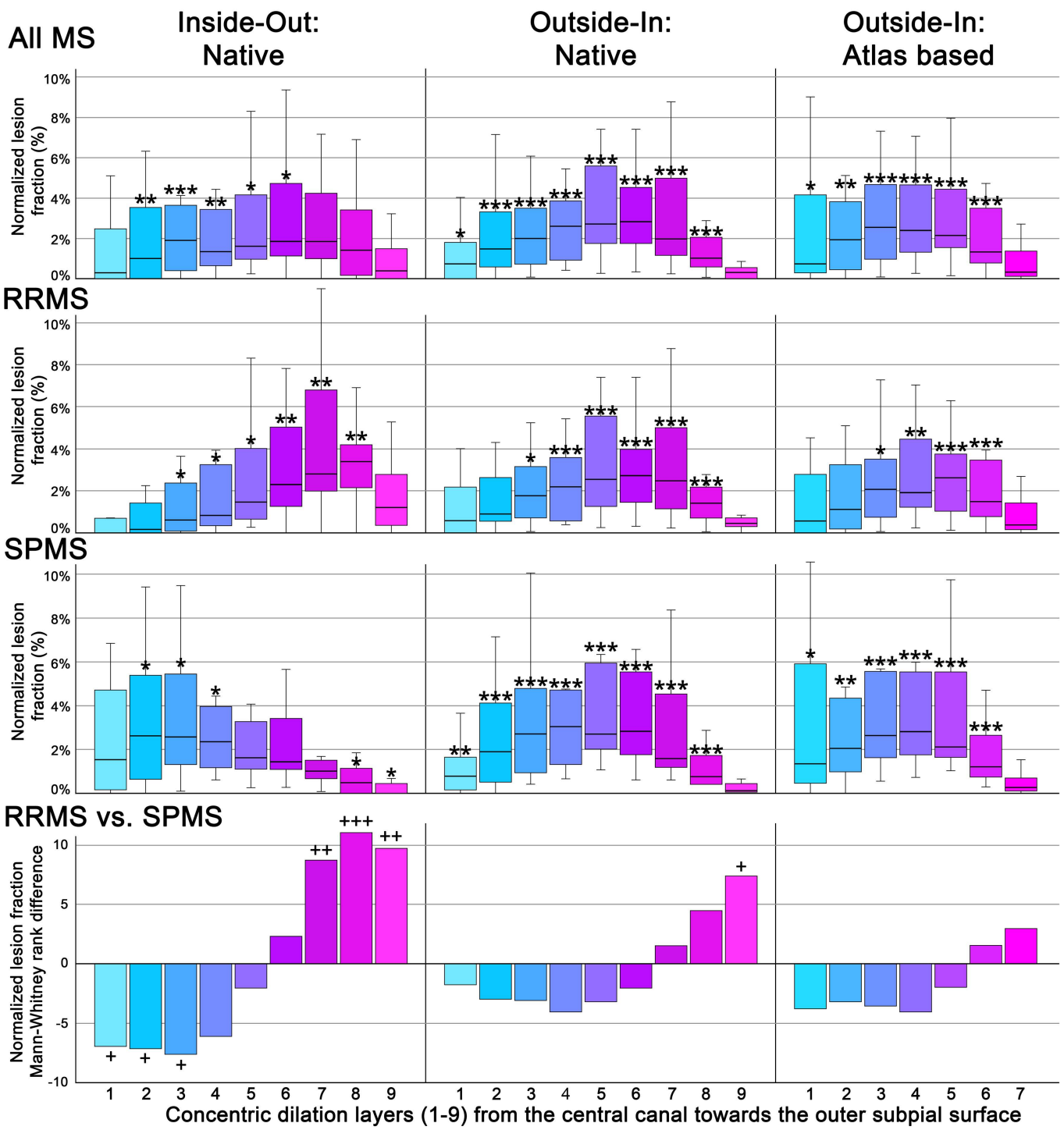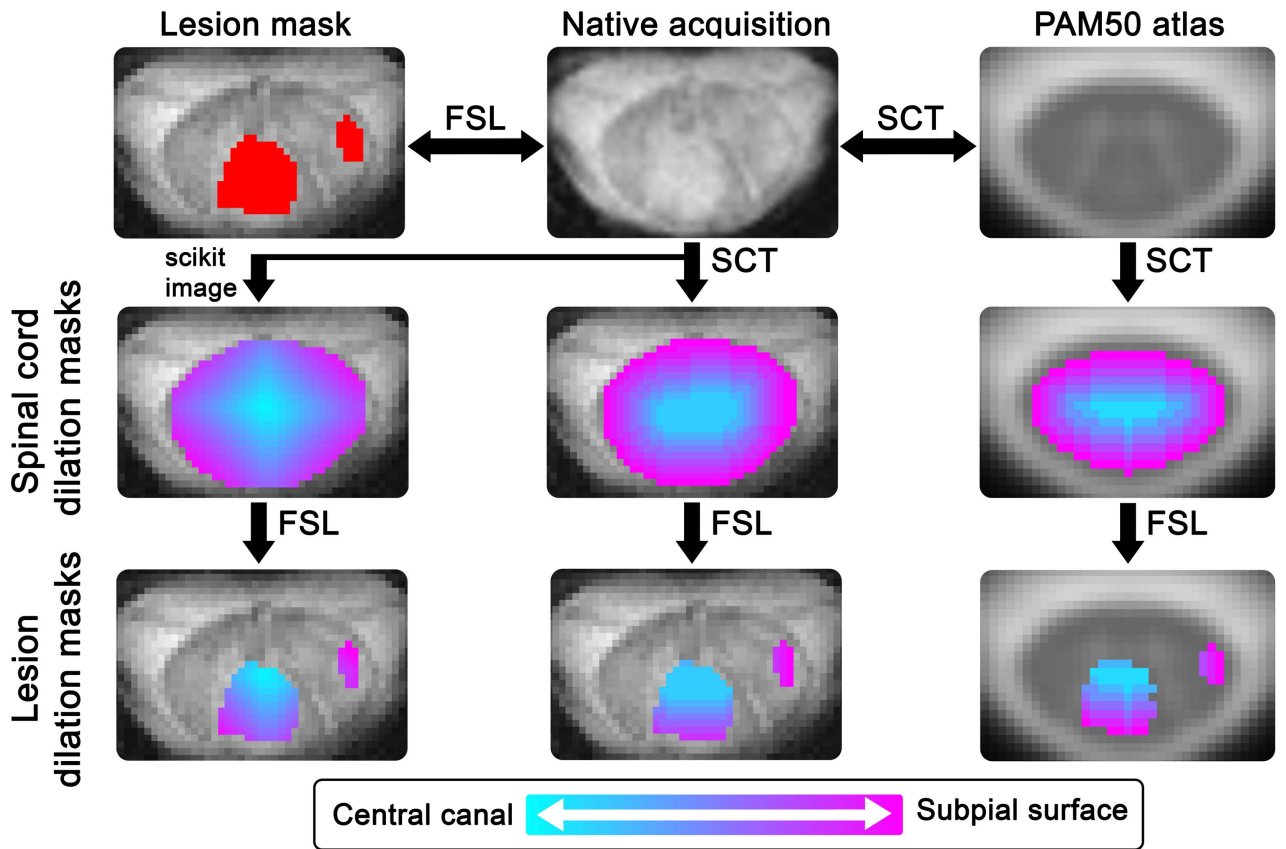**Supplementary Figure 1. Comparative spinal cord segmentation techniques: processing and results. (Upper panel) Processing pipeline.** Representative example of a native C1 lesion in an SPMS participant 33-year-old female (RRMS, EDSS: 1, DD: 2.3 years). Beginning with the native acquisition, then manual segmentation of the lesion mask in FSL. The native acquisition is then processed in Spinal Cord Toolbox to isolate the spinal cord. The inside-out technique begins in the central canal expanding towards the subpial surface, as described in the manuscript. Outside-in processing in SCT, begins by sequentially eroding the spinal cord mask. This was done in two iterations, conceptually the same but in difference spaces. The native space, as done in the inside-out method, and in the PAM50 atlas space, registered into a probabilistic template place of 50 healthy volunteers. **(Lower panel) Comparative spinal cord mapping results.** Box-and-whisker plots depict the lesioned fraction (*y*-axis) normalized to the respective radial dilation layer volume and individual MS participant lesion volume. The concentric distance (*x*-axis) of the three segmentation techniques from the central canal (layer 0, cyan) extending towards the outer subpial surface (layer 9, magenta) for the whole lesion fraction in all MS, RRMS and SPMS participants, respectively. Error bars represent the 95% confidence interval for the respective lesioned tissue dilation level. Bar graphs depict the Mann-Whitney U-test rank difference between the RRMS and SPMS subtypes for the respective dilation layers. *P*-values reported are exploratory, and therefore not corrected for multiple comparisons.

Exploratory comparison of individual level lesion fraction compared to the median of the inner-most level (*P-value <0.05, **P-value <0.01, ***P-value <0.001 by Wilcoxon Signed Rank test, two-tailed, equal variances not assumed).

Exploratory comparison of RRMS vs. SPMS participants ([+]P-value <0.05, [++]P-value <0.01, [+++]P-value <0.001, by Mann–Whitney U-test (two-tailed, equal variances not assumed).

DD = Disease Duration

Central canal ◀━━━━━━━━━━▶ Subpial surface

	Inside-Out: Native	Outside-In: Native	Outside-In: Atlas based

All MS

RRMS

SPMS

RRMS vs. SPMS

Concentric dilation layers (1-9) from the central canal towards the outer subpial surface

Supplementary table 1. *Brain and spinal cord MRI correlations.*

		Spinal cord MRI metrics										
		Cross-sectional area						Lesion fraction				
		Grey matter			White matter			Grey matter			White matter		
		r/ρ	*P*	N	*r/ρ*	*P*	N	*ρ*	*P*	N	*ρ*	*P*	N
Brain MRI metrics	**Cortical thickness**	0.13	0.46†	34	0.17	0.35†	34	0.03	0.86‡	34	-0.05	0.78‡	34
	Cortical lesion volume	-0.27	0.16‡	29	-0.26	0.18‡	29	0.19	0.33‡	29	0.30	0.12‡	29
	White matter lesion fraction	-0.27	0.13‡	34	-0.27	0.13‡	34	0.39	0.021‡*	34	0.37	0.033‡*	34

†*P-value by Spearman's rank-order correlation (two-tailed).*
‡*P-value by Pearson correlation coefficient (two-tailed).*
**Statistically significant.*

Supplementary table 2. *Clinical correlations with spinal cord and brain MRI metrics.*

		EDSS			9 - HPT			T25-FW		
		ρ	*P*	N	*ρ*	*P*	N	*ρ*	*P*	N
Spinal cord	Cross-sectional area: Grey matter	-0.31	0.069	35	-0.47	0.007*	32	-0.27	0.12	34
	White matter	-0.29	0.087	35	-0.45	0.009*	32	-0.29	0.088	34
	Lesion fraction: Grey matter	0.21	0.23	35	0.21	0.24	32	0.16	0.37	34
	White matter	0.33	0.056	35	0.31	0.09	32	0.17	0.33	34
Brain	Cortical Thickness	-0.56	0.001*	34	-0.44	0.013‡	31	-0.43	0.012*	33
	Cortical lesion fraction	0.42	0.025*	29	0.22	0.28	26	0.33	0.089	28
	White matter lesion fraction	0.35	0.042*	34	0.49	0.005*	31	0.40	0.022*	33

All correlations are reported using Spearman's rank-order correlation coefficient (ρ) for non-parametric variables.

Cortical and white matter brain lesions were normalized to the estimated total intracranial volume (eTIV)from FreeSurfer.

*Statistically significant.

9-HPT = 9-Hole Peg Test, EDSS = Expanded Disability Status Scale, N = total number of respective participants, T25-FW = Timed 25-Foot Walk