T1-darkening as a surrogate marker for disease progression independent of relapse activity

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Introduction and Purpose

- Slowly enlarging lesions (SELs) and phase-rim lesions (PRLs) are currently considered candidates to quantify disease progression independent of relapse activity (PIRA) but are difficult to measure in clinical routine.
- We introduce a novel MRI biomarker for PIRA.

Methods

- T1-darkening is defined as a focal area within an existing T1 hypo-intense lesion that shows a significant decrease in T1 signal over time (see example in Figure 1).
- Lesions with T1-darkening are automatically computed based on 3D T1 baseline (BL) and follow-up (FU) images. Processing steps include:
  - elastic registration of BL and FU images,
  - skull stripping of BL and FU images,
  - calculation of a difference image (between FU and BL)
  - detection of hypo intensities within an existing T1 lesion

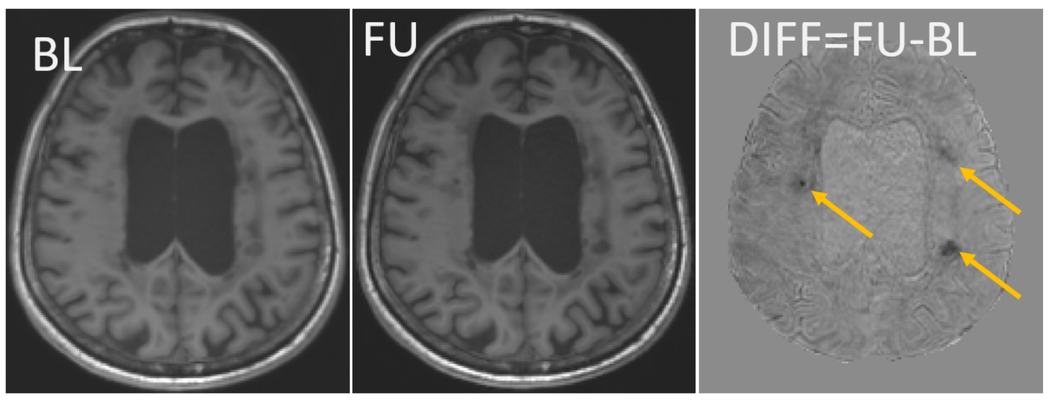

Figure 1 T1 darkening: Arrows indicate three T1 hypo intense lesions with a significant decrease in T1 signal.

- Validation: longitudinal (2-year observation time) cohort of 148 MS patients who received BL and FU 3D T1 and FLAIR and EDSS assessments. A sub-group of 87 MS patients had no relapse during the observation period.
- For each patient we calculated:
  - T2 lesion load [1]
  - number of new/enlarging T2 lesions [2]
  - percentage brain volume loss (BVL) per year [3]
  - number of lesions with T1-darkening
- The cohort was dichotomized into patients with disease progression (prog.) and non-progression (non-prog.). Disease progression: increase in EDSS between BL and FU (delta EDSS). The three longitudinal measures were compared between prog. and non-prog. group using a t-test. The comparison was repeated for a sub-cohort of patients who did not show any relapses during the observation period.

	n	age at BL [years]	EDSS BL	delta EDSS	T2 lesion load [ml] BL
all	149 (126 RRMS,23SPMS/PPMS)	41.78(11.33)	2.67(1.65)	0.19(0.72)	10.08(10.71)
without relapses	87 (71 RRMS,16SPMS/PPMS)	43.71(11.33)	2.79(1.73)	0.17(0.71)	10.56(11.7)

Table 1 MS patient cohort.

Results

- The cohort's mean age (standard deviation) was 41.7 years (11.3 years), mean EDSS at BL was 2.6 (1.6), and a mean delta EDSS was 0.2 (0.7).
- Out of the 149 patients, 51 featured prog. and 98 non-prog.
  - For all patients there was a significant difference between prog. and non-prog. for BVL/year, new/enlarging T2 lesions, and lesions with T1-darkening (Table 1).
  - For patients without relapses only BVL/year and the number of lesions with T1-darkening was significantly different between prog. and non-prog.

	all			without relapses		
	prog.	**non-prog.**	**p**	**prog.**	**non-prog.**	**p**
n	51	98		26	61	
BVL/year [%]	-0.45(0.53)	-0.21(0.43)	**	-0.45(0.4)	-0.17(0.41)	**
# new/enlarging T2 lesions	2.88(4.67)	1.36(3.14)	*	2.38(4.38)	1.21(3.39)	
# T1 darkenings	14.45(12.72)	8.19(10.47)	**	15.46(13.41)	7.15(9.94)	**

Table 1 Difference between disease prog. and non-prog. for all patients and for the subgroup of patients without relapses. Significance levels are: * $p < 0.05$; ** $p < 0.005$

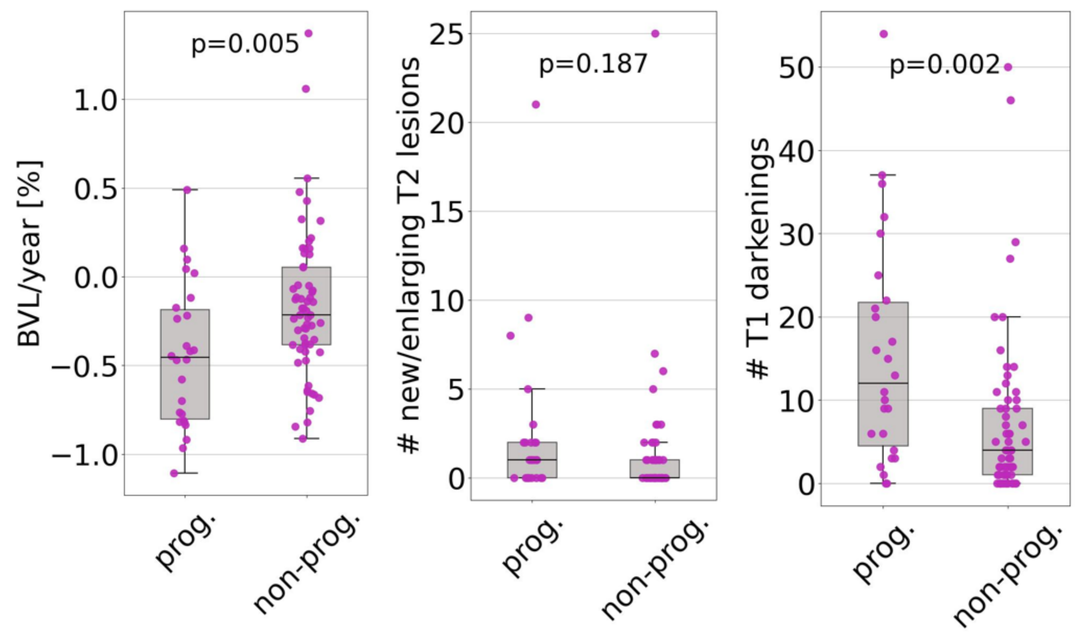

Figure 2 Difference between disease prog. and non-prog. for patients without relapses.

Conclusion

Our findings indicate that T1-darkening is an easy to measure surrogate marker for PIRA which warrants further validation in larger longitudinal cohorts.

Literature

[1] Krüger, J., et al., Infratentorial lesions in multiple sclerosis patients: intra- and inter-rater variability in comparison to a fully automated segmentation using 3D convolutional neural networks. Eur Radiol, 2021.

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[3] Opfer, R., et al., BrainLossNet: a fast, accurate and robust method to estimate brain volume loss from longitudinal MRI. Int J Comput Assist Radiol Surg, 2024.

Disclosures

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