

eFigure1. Examples of peripapillary RNFLT classification (A) and macular ganglion cell layer 1-3.45 mm EDTRS grid (B).

A) Thickness of the various sectors into which the peripapillary scan is divided: temporal (T), nasal (N), superior temporal (TS), inferior temporal (TI), superior nasal (NS), inferior nasal (NI), papillomacular bundle (PMB), and the nasal-to-temporal ratio (N/T). In the center, framed in magenta, is the general thickness value (G), which had to be considered when evaluating the difference in pRNFL thickness in μm and percentage.

B) At the top left, the total volume of the ganglion cell layer is framed in red. The inner ring thicknesses, on which the average inner ring thickness has been calculated [es. $(41+30+37+42)/4$], are framed in green.

	ON (25 patients)	HC (5 patients)	P value
Age, y ^a	32.2 ± 10.8	30.8 ± 8.41	1.000 ⁺
Female, n (%)	16 (64)	4 (80)	0.640 ⁺⁺
MS-ON, n (%)	10 (40)	0	
MOG-ON, n (%)	6 (24)	0	
SION, n (%)	9 (36)	0	

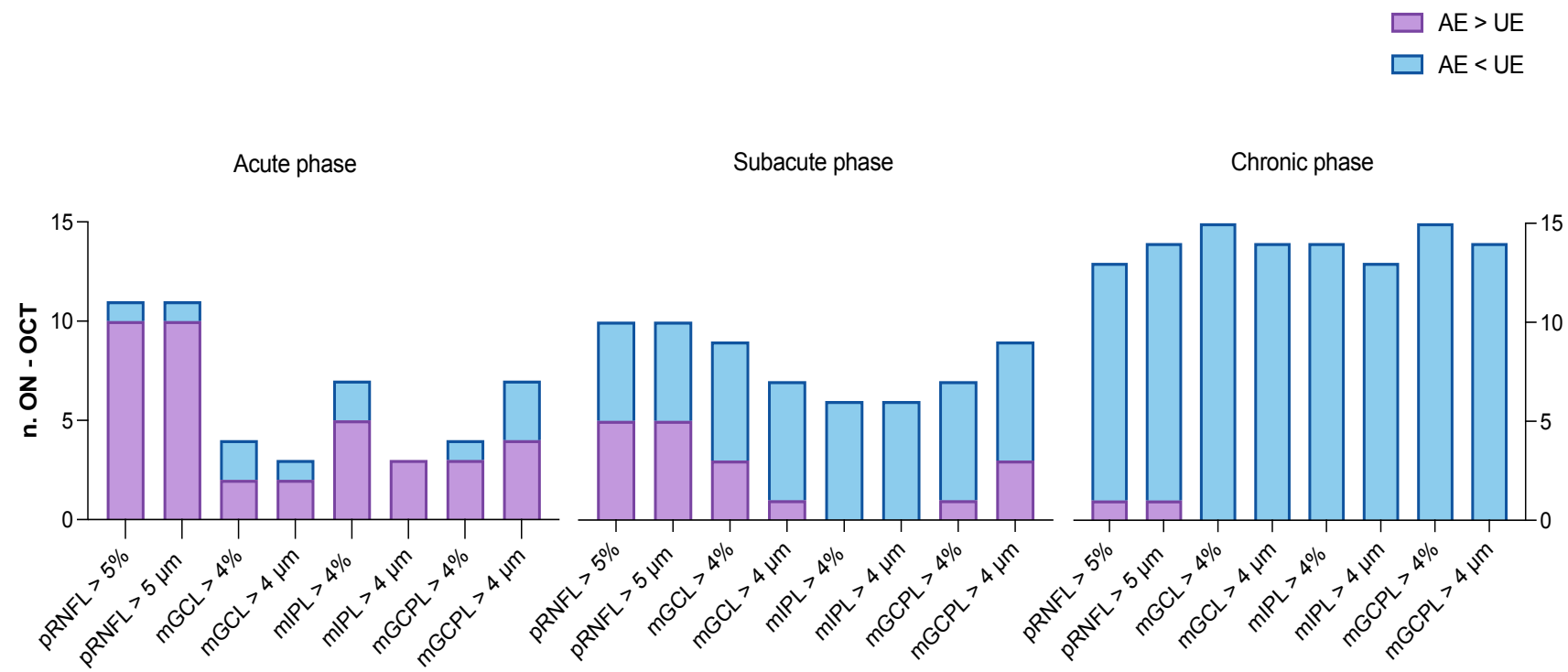
eTable1. Baseline Demographic and Clinical parameters of patients and controls included in the study. Abbreviations: ON = optic neuritis; HC = healthy control; MS-ON = Multiple sclerosis-associated optic neuritis; MOG-ON = myelin oligodendrocyte glycoprotein antibody-associated optic neuritis; SION = single isolated optic neuritis. ^a Mean ± SD. + *p*-value from U-test for group mean comparison ++ *p*-value from Fisher test

	Disc scan ON	Disc scan HC	Macular scan ON	Macular scan HC
n.	44	9	42	8
≤ 7 days from onset, n (%)	16 (36.4)	5 (55.6)	15 (35.7)	4 (50)
> 1 and ≤ 12 weeks from onset, n (%)	11 (25)	1 (11.1)	10 (23.8)	1 (12.5)
≥ 3 months from onset, n (%)	17 (38.6)	3 (33.3)	17 (40.5)	3 (37.5)

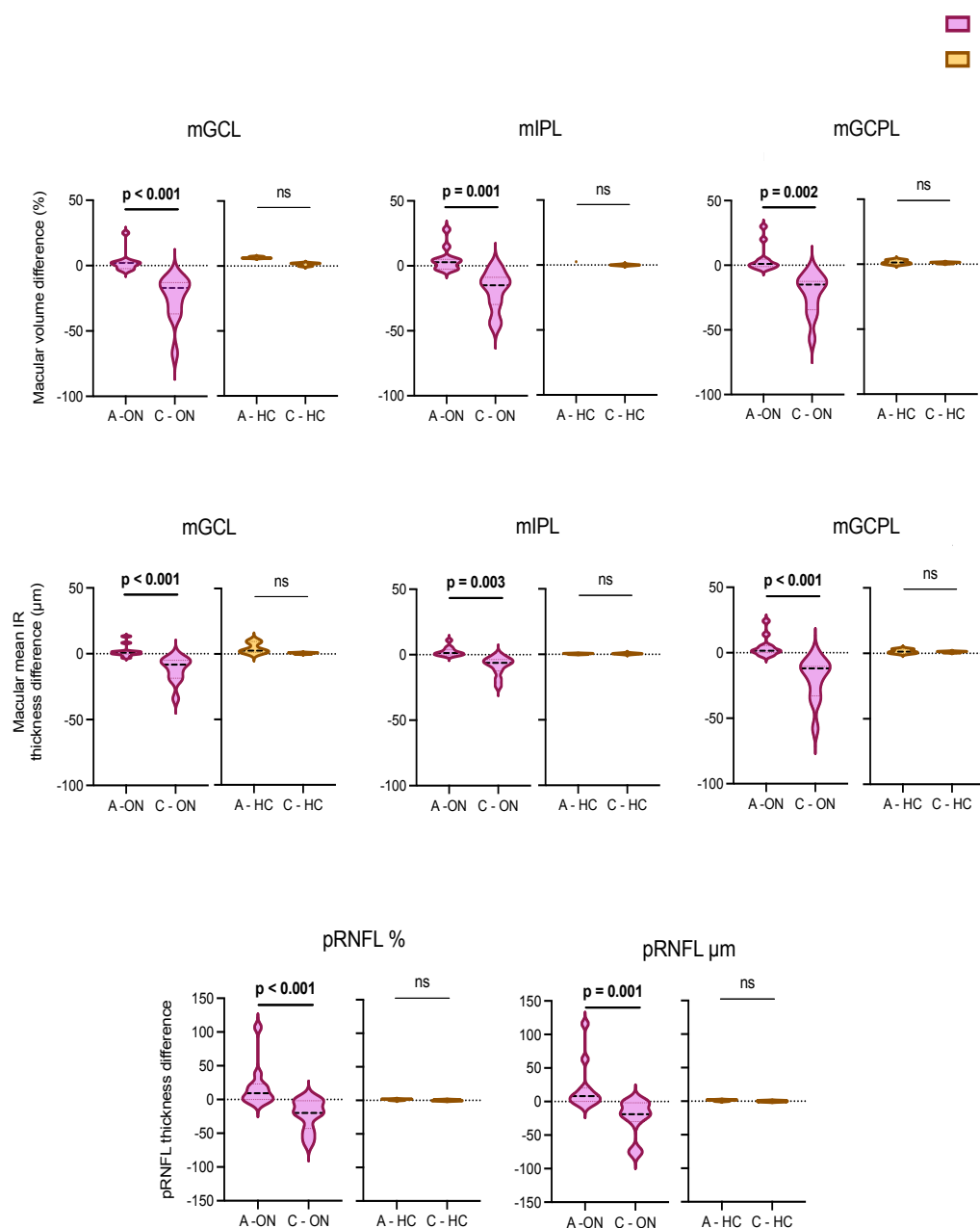
eTable2. Optic disc scan and macular scan OCTs distribution based on time of symptoms onset.

	Acute phase			Subacute phase			Chronic phase		
	ON OCT	HC OCT	p value	ON OCT	HC OCT	p value	ON OCT	HC OCT	p value
n. disc scan	16	5		11	1		17	3	
n. macular scan	15	4		10	1		17	3	
pRNFL difference >5%, n (%)	11 (68.75%)	0		10 (90.9%)	0		13 (76.4%)	0	
pRNFL difference >5µm, n (%)	11 (68.75%)	1 (20%)		10 (90.9%)	1 (100%)		14 (82.3%)	0	
mGCL volume difference > 4%, n (%)	4 (26.6)	0		9 (90%)	0		15 (88.2)	0	
mGCL mean IR difference > 4 µm, n (%)	3 (20%)	1 (25%)		7 (70%)	0		14 (82.3%)	0	
mIPL volume difference > 4%, n (%)	7 (46.6)	0		6 (60%)	0		14 (82.3%)	0	
mIPL mean IR difference > 4 µm, n (%)	3 (20)	0		6 (60%)	0		13 (76.4%)	0	
mGCPL volume difference > 4%, n (%)	4 (26.6)	0		7 (70%)	0		15 (88.2%)	0	
mGCPL mean IR difference > 4 µm, n (%)	7 (46.6)	0		9 (90%)	0		15 (88.2%)	0	
pRNFL difference % ^a	35 ± 63.1	1.28 ± 2.48	0.099	13.7 ± 61.1	4.70 ± NaN	1.000	19.9 ± 24.4	0.067 ± 0.9	0.064
pRNFL difference µm ^a	36.5 ± 64.5	1.40 ± 2.61	0.136	18.9 ± 67.3	5.0 ± NaN	1.000	20.2 ± 27.4	0 ± 1	0.056
GCL volume difference % ^a	1.03 ± 7.28	1.05 ± 1.22	0.450	22.1 ± 26.4	2.0 ± NaN	0.727	24.2 ± 18.1	1.3 ± 1.15	0.008**
GCL mean IR difference µm ^a	0.53 ± 4.75	3.31 ± 4.25	0.147	11.3 ± 14.4	3.5 ± NaN	0.364	12.1 ± 9.8	0.58 ± 0.519	0.002**
IPL volume difference % ^a	2.79 ± 8.71	2.58 ± 0.05	0.763	15 ± 15.3	2.50 ± NaN	0.305	18.6 ± 14.6	0 ± 0	0.045*
IPL mean IR difference µm ^a	1.10 ± 3.72	0.31 ± 0.37	1.000	5.8 ± 7.89	0.25 ± NaN	0.484	8.19 ± 6.46	0.5 ± 0	0.035*
GCPL volume difference % ^a	2.67 ± 9.67	1.10 ± 0.89	0.340	18.9 ± 21.3	2.20 ± NaN	0.727	21.8 ± 16.2	1.13 ± 1.15	0.006**
GCPL mean IR difference µm ^a	1.78 ± 8.32	1.38 ± 1.36	0.841	18.1 ± 22.5	3.75 ± NaN	0.727	20.2 ± 16.1	1.08 ± 0.52	0.017*

eTable3. Optic neuritis (ON) vs Healthy controls (HC) peripapillary and macular volumes and thicknesses. pRNFL thickness differences (expressed as % and µm), and volume and mean inner retina (IR) thickness differences of mGCL, mIPL, and mGCPL in the affected eye compared to the contralateral eye, across the three phases: acute (within 7 days from onset), subacute (7 days to 3 months from onset), and chronic (>3 months from onset). Blue values report a reduction in the affected eye compared with the fellow-eye, while purple an increase. ^aMean ± SD. * *p value* < 0.05 ** *p value* < 0.01



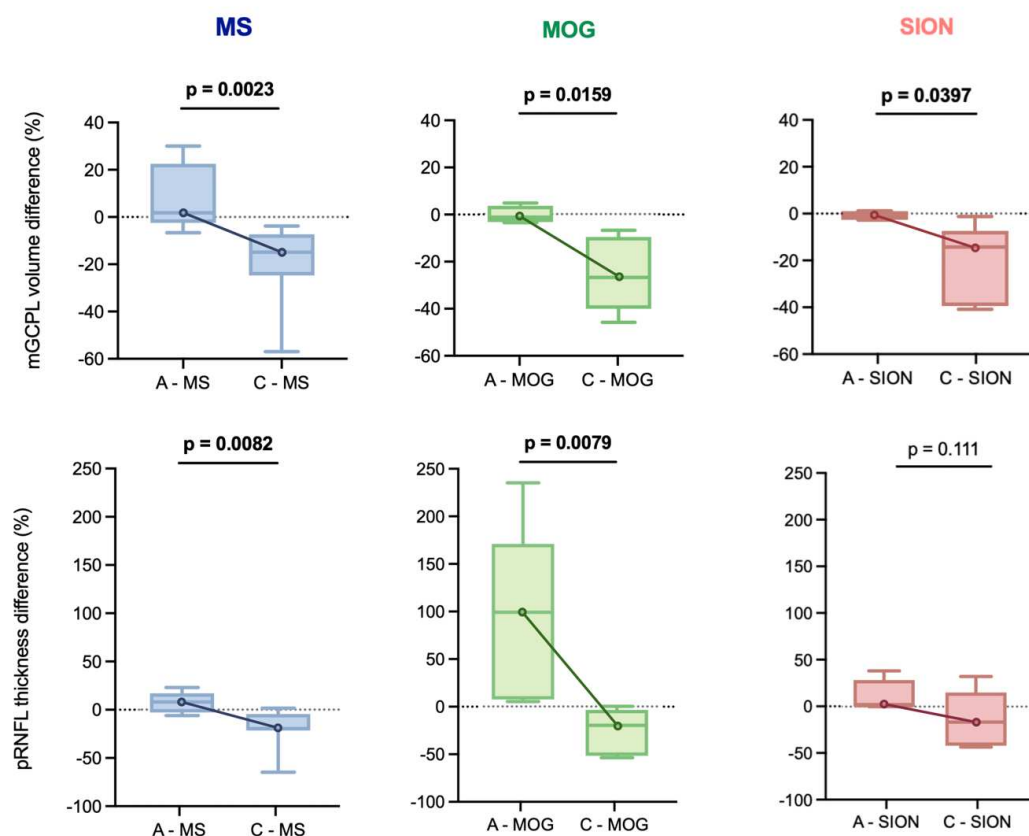
eFigure2. Significant inter-eye asymmetry in patients across the acute, subacute and chronic phase. The figure shows the n. of OCT with pRNFL thickness difference above 5 % and 5 μ m and with mGCL, mIPL and mGCPL volume difference > 4% and mean IR thickness difference > 4 μ m. In the acute phase: significant asymmetry is more frequently due to an increase in the volume or thickness of the affected eye compared to the unaffected contralateral eye. In the subacute phase: in the pRNFL 50% of cases shows increased thickness of the affected eye compared to the unaffected contralateral eye; in mGCL, mIPL and mGCPL the asymmetry is mostly due to a decrease in volume or thickness of the affected eye compared to the unaffected contralateral eye. In the chronic phase: significant asymmetry mostly due to a decrease in volume or thickness of the affected eye compared to the unaffected contralateral eye. Abbreviations: ON: optic neuritis; HC: Healthy control; IR: inner ring; AE > UE: Affected eye increased (in volume or thickness) compared to Unaffected eye; AE < UE: Affected eye decreased (in volume or thickness) compared to Unaffected eye.



eFigure3. Longitudinal changes in mean differences of retinal layer volumes and thicknesses between the acute and chronic phases in patients with optic neuritis (ON) and healthy controls (HC) who underwent OCT at both time-points. Statistical analyses were conducted using the Wilcoxon test for paired samples in both groups. Abbreviations: A-ON: Acute phase in optic neuritis; C-ON: Chronic phase in optic neuritis; A-HC: Acute phase in healthy controls; C-HC: Chronic phase in healthy controls.

	Acute phase			Subacute phase			Chronic phase			Acute vs Chronic phase (p value)		
	MS ON	MOG ON	SION	MS ON	MOG ON	SION	MS ON	MOG ON	SION	MS ON	MOG ON	SION
n. disc scan	6	5	5	5	3	3	7	5	5	6 vs 7	5 vs 5	5 vs 5
n. macular scan	6	4	5	4	3	3	7	5	5	6 vs 7	4 vs 5	5 vs 5
pRNFL IEPD	7.65 ± 11.3	91.1 ± 93.6	11.7 ± 16.6	45.2 ± 76.8	-13.2 ± 6.9	-11.8 ± 50.8	-19.7 ± 21.9	-26.3 ± 24.6	-13.9 ± 30.7	0.0082**	0.0079**	0.111
pRNFL IEAD	6.84 ± 10.7	94 ± 93	14.6 ± 27.2	49.8 ± 91.7	-15 ± 6.0	1.3 ± 35	-19.7 ± 25.2	-30 ± 31.7	-11.0 ± 28.5	0.0117*	0.0079**	0.092
GCL volume IEPD	2.97 ± 11.4	0.63 ± 3.3	-0.98 ± 1.9	-30.3 ± 28.2	-23.2 ± 27.9	-9.9 ± 28.5	-23.3 ± 20.4	-27.9 ± 19.8	-21.7 ± 16.3	0.0012**	0.0159*	0.0397*
GCL mean IR IEAD	2.86 ± 6.84	-1.06 ± 2.5	-1.0 ± 1.4	-14.8 ± 15.3	-11 ± 15	-6.7 ± 17.1	-11.1 ± 11.2	-13.7 ± 9.5	-11.9 ± 10.0	0.0093**	0.0635	0.0079**
IPL volume IEPD	6.64 ± 12.7	0.02 ± 4.7	0.38 ± 3.3	-19.2 ± 17.5	-16.3 ± 14.8	-8.0 ± 16.3	-15.3 ± 15.9	-22.1 ± 11.8	-19.7 ± 17.3	0.0146*	0.0159*	0.0397*
IPL mean IR IEAD	2.84 ± 5.02	0.0 ± 3.2	-0.1 ± 1.3	-8.94 ± 9.5	-6.7 ± 7.9	-0.7 ± 4.7	-7.32 ± 7.9	-9.3 ± 4.4	-8.3 ± 7.2	0.0082**	0.0159*	0.0317*
GCPL volume IEPD	7.64 ± 14.2	-0.37 ± 3.7	-0.86 ± 1.8	-25.2 ± 23.2	-20.3 ± 21.9	-9.1 ± 22.9	-19.7 ± 18.1	-25.4 ± 15.9	-21.1 ± 16.7	0.0023**	0.0159*	0.0397*
GCPL mean IR IEAD	5.71 ± 11.8	-0.62 ± 5.3	-1.0 ± 2.7	-24.2 ± 24.3	-17.7 ± 22.9	-10.2 ± 26.6	-18.4 ± 19.0	-23 ± 13.9	-19.9 ± 16.8	0.0082**	0.0159*	0.0317*

eTable4. Multiple sclerosis - optic neuritis (MS ON) vs MOGAD – optic neuritis (MOG-ON) vs single isolated optic neuritis (SION) peripapillary and macular volumes and thicknesses. pRNFL thickness differences (expressed as % and μm), and volume and mean inner retina (IR) thickness differences of mGCL, mIPL, and mGCPL in the affected eye compared to the contralateral eye (expressed NOT as absolute value), across the three phases: acute (within 7 days from onset), subacute (7 days to 3 months from onset), and chronic (>3 months from onset). All OCT data are reported as Mean ± SD. Abbreviations: IEPD: inter-eye percentage differences; IEAD: inter-eye percentage differences). * *p value < 0.05*; ** *p value < 0.01*



eFigure4. Longitudinal changes in mean differences in % of pRNFL and mGCPL from acute to chronic phases in patients with MS-ON, MOG-ON or SION. A) Mean macular volume difference in %, B) Mean macular IR thickness difference in μm , C) mean pRNFL thickness in % and μm . *Statistical analyses were conducted using the Mann Whitney test in every group.* Abbreviations: A – MS: Acute phase in multiple sclerosis, C-MS: Chronic phase in multiple sclerosis; A – MOG: Acute phase in MOGAD, C – MOG: Chronic phase in MOGAD; A – SION: Acute phase in single isolated ON C – SION: Chronic phase in single isolated ON.