

2024 NMO Roundtable Conference of the Guthy Jackson Charitable Foundation

Imaging Biomarkers of Disease Status & Relapse

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Imaging biomarkers of disease status & relapse

Spinal cord involvement

Optic nerve involvement

Spinal cord involvement – acquisition protocol

Sagittal and axial T2-weighted MRI
& Post-contrast T1-weighted images
with complete visualization of the spinal cord

Single/multiple intramedullary T2-hyperintensities
Involving grey and/or white matter
Acutely with contrast enhancement

Spinal cord involvement – acute phase sagittal MRI



Lesion location:

Cervical or thoracic, not useful for differential diagnosis
(but conus involvement should trigger testing for MOG-ab)

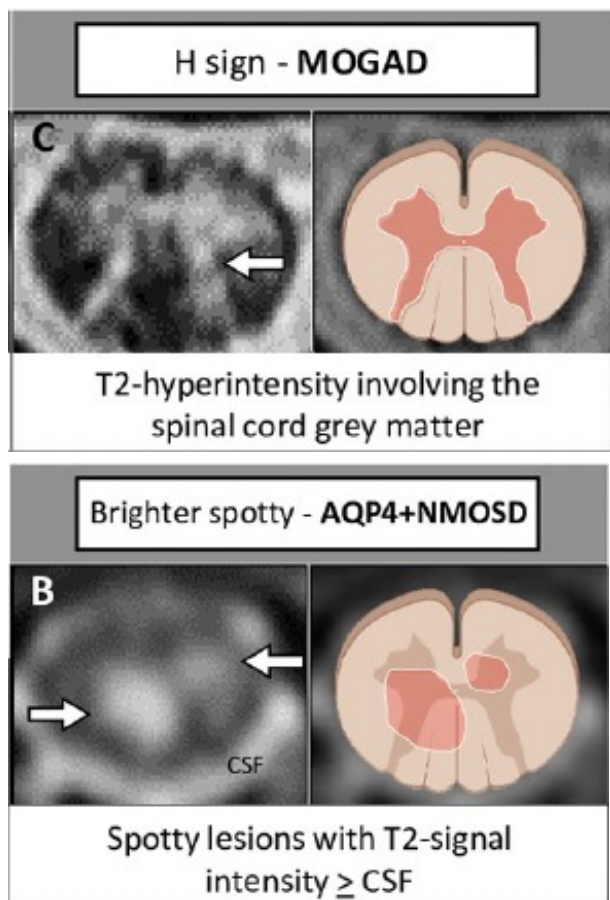
Lesion length (cut-off 3 segments):

Short T2-hyperintense lesions often centrally located & together with T1 hypointensity in 14-15% of AQP4+NMOSD. BUT 92% of NMOSD with short lesions will subsequently have longitudinally-extensive lesions

Longitudinally extensive T2-hyperintense lesions are most common in NMOSD (up to 90% of recurrent cases) and include focal cord swelling, concomitant T1-hypointensity (70%)

Cacciaguerra et al. Frontiers 2022

Spinal cord involvement – acute phase axial MRI



Lesion location:

Central pure gray matter involvement or mixed gray-white matter involvement, usually affecting > 50% of the cross-sectional area

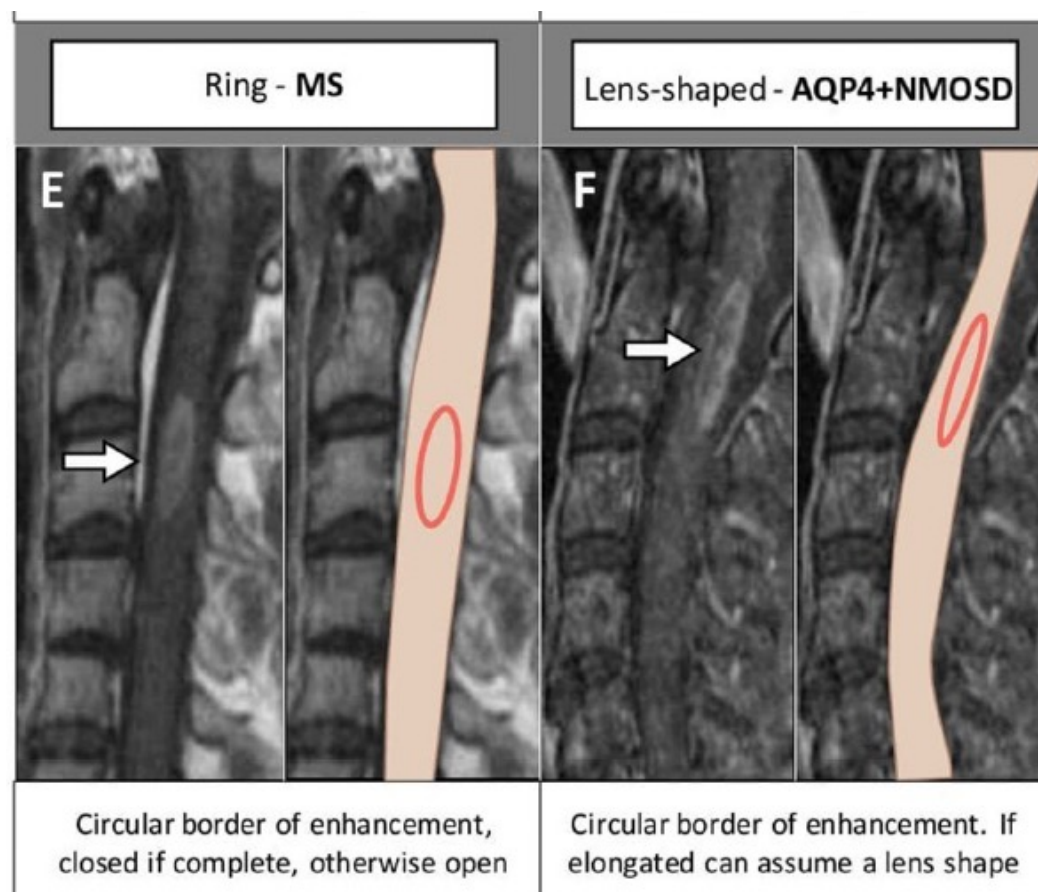
Key findings:

H-shape common in MOGAD (30%) but also seen in AQP4+NMOSD (10%)

Brighter spotty lesions (30-50%) in AQP4+ NMOSD

Cacciaguerra et al. Frontiers 2022

Spinal cord – acute phase MRI enhancement



Enhancement:

Lesion enhancement common: often longitudinally extensive, patchy or ring-like (up to 30%), rarely persists >3 months

Ring enhancement can be lens- or ellipsoid shaped (vs. ring in MS)

Longitudinally extensive leptomeningeal enhancement possible but less common

Cacciaguerra et al. Frontiers 2022

Spinal cord involvement – chronic phase

Follow-up MRI with same sequences ~ 3 months after baseline
with complete visualization of the spinal cord

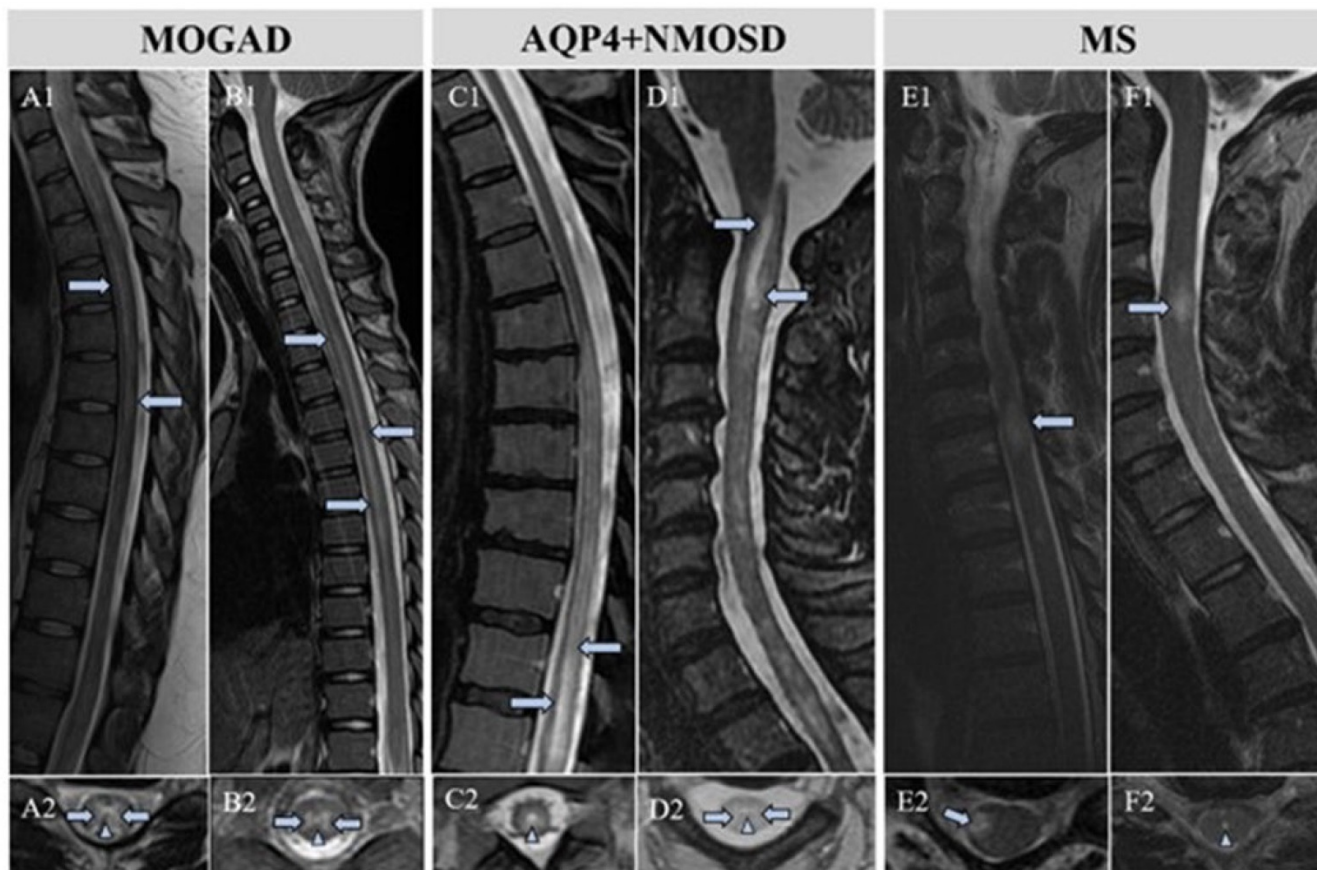
Fragmentation: into shorter lesions within 3 months or resolution
(~5%, CAVE MOGAD)

Persistent enhancement for >2 months only in 12% of AQP4+NMOSD

Focal atrophy in AQP4+NMOSD and MS

Cacciaguerra et al. Frontiers 2022

Spinal cord involvement – what's new?



Central canal T2-hyperintensity:

Pseudo-dilatation of ependymal canal (local edema) causing brighter T2-signal

Frequent in MOGAD (29%) and AQP4+NMOSD (35%), but not MS

T1-hypointensity more common in AQP4+NMOSD (46%) vs. MOGAD (11%)

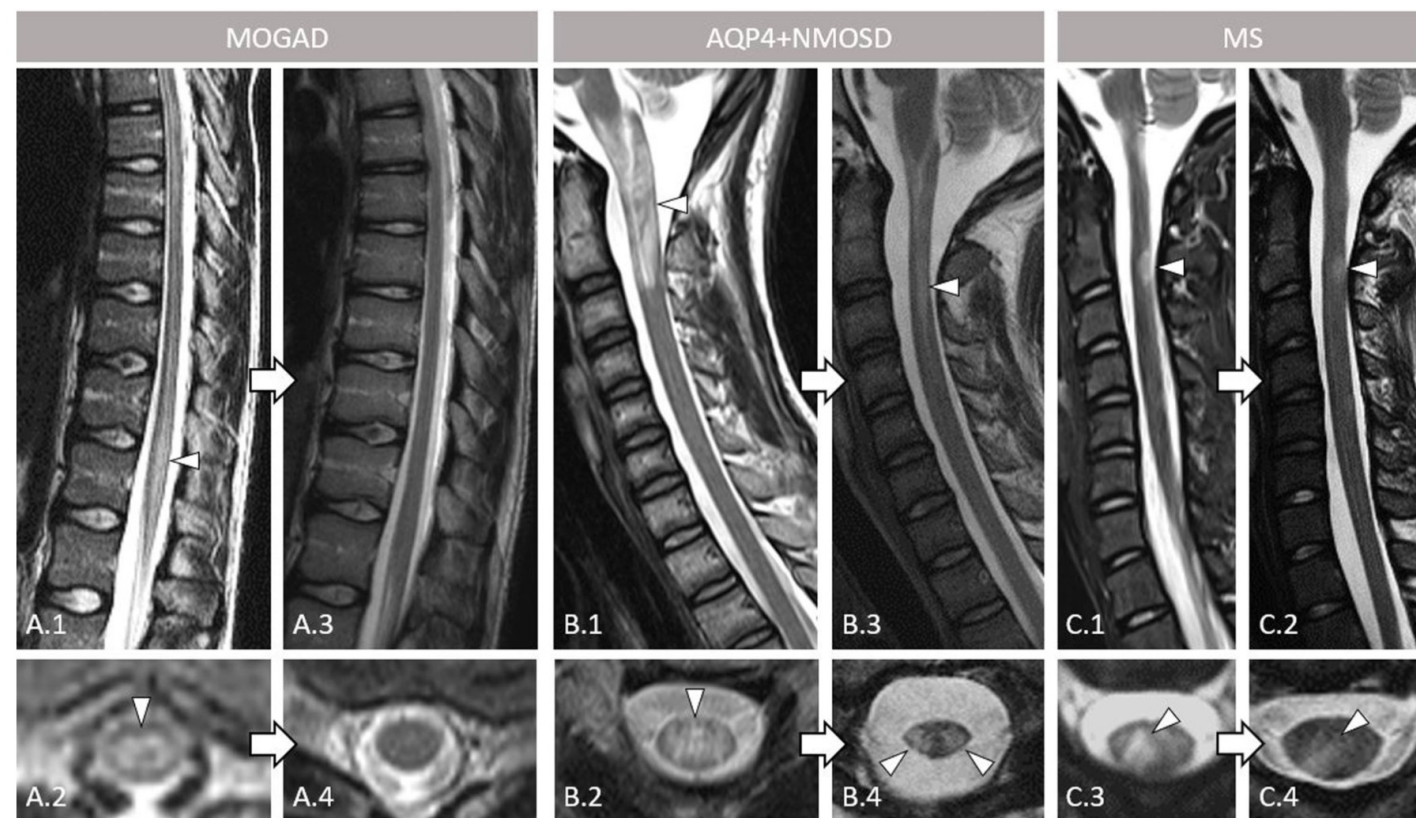
37 AQP4-IgG+ NMOSD

63 MOGAD

26 MS

Webb et al J Neurol Sci 2023

Spinal cord involvement – what's new?



Lesion resolution in pediatric disease:

Follow-up MRI ~1.5-2 years after acute MRI

Resolution of index T2-lesion: 0% in AQP4+NMOSD vs. 67% in MOGAD vs. 8% in MS

Resolution of all T2-lesions: 0% in AQP4+NMOSD vs. 58% in MOGAD vs. 8% in MS

Persistent enhancement: 29% in AQP4+NMOSD vs. 0% in MOGAD vs. 0% in MS

8 AQP4-IgG+ NMOSD

21 MOGAD

27 MS

14 (4-16) years

7 (2-17 years)

15 (3-17 years)

Redenbaugh et al Mult Scler 2023

Optic nerve involvement – acquisition protocol

T2-weighted orbital MRI with orbital fat saturation
& Post-contrast T1-weighted images
OCT ring scan (RNFL) and macular scan (GCIPL) of both eyes

Ramanathan et al. MSJ 2015

Optic nerve involvement – acute phase orbital MRI



Laterality:

Bilateral (82% AQP4+NMOSD, 84% MOGAD) > unilateral (MS)

Enhancement (100%):

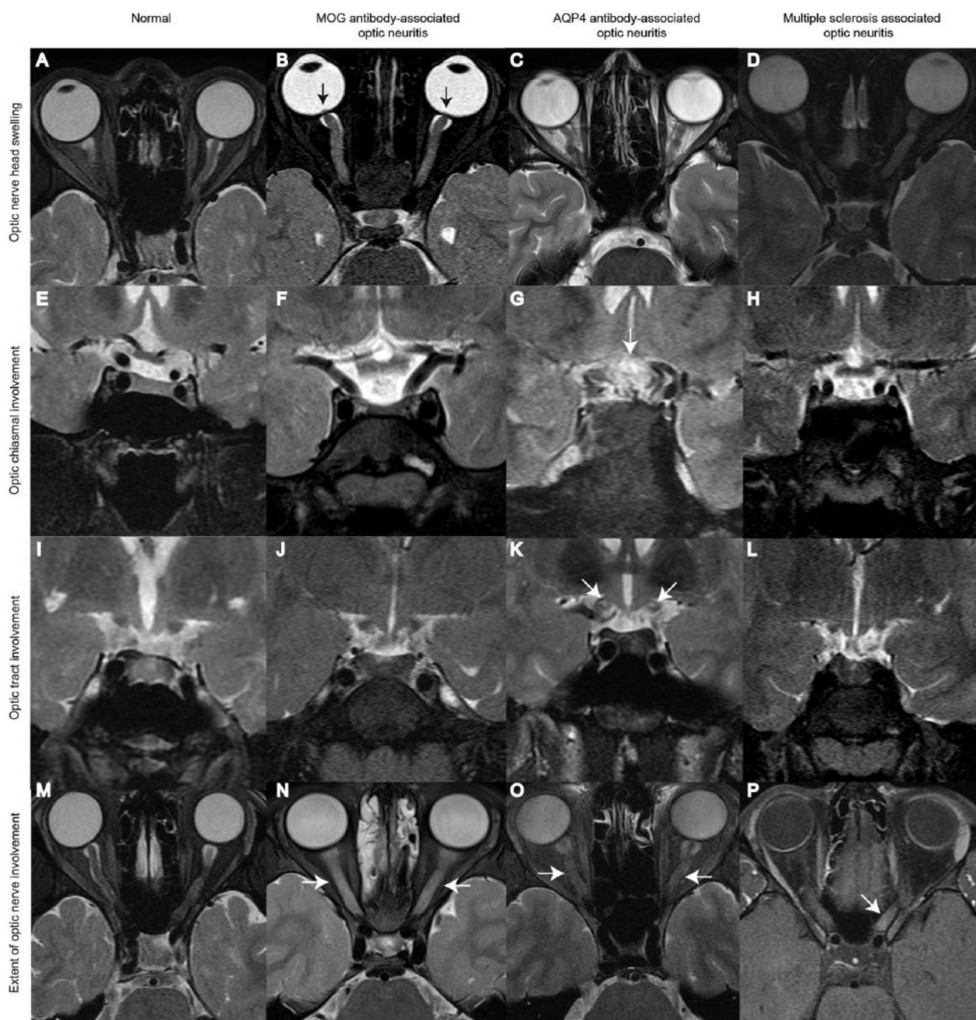
Bilateral intracanalicular optic nerve enhancement in AQP4+NMOSD vs. retrobulbar (MOGAD & MS)

Optic nerve swelling:

Bilateral (AQP4+NMOSD, MOGAD) > unilateral (MS)
Can be absent in AQP4+NMOSD

Ramanathan et al. MSJ 2015

Optic nerve involvement – acute phase orbital MRI



Location:

ONH (9%): bilateral (MOGAD) vs. absent (AQP4+NMOSD, MS)

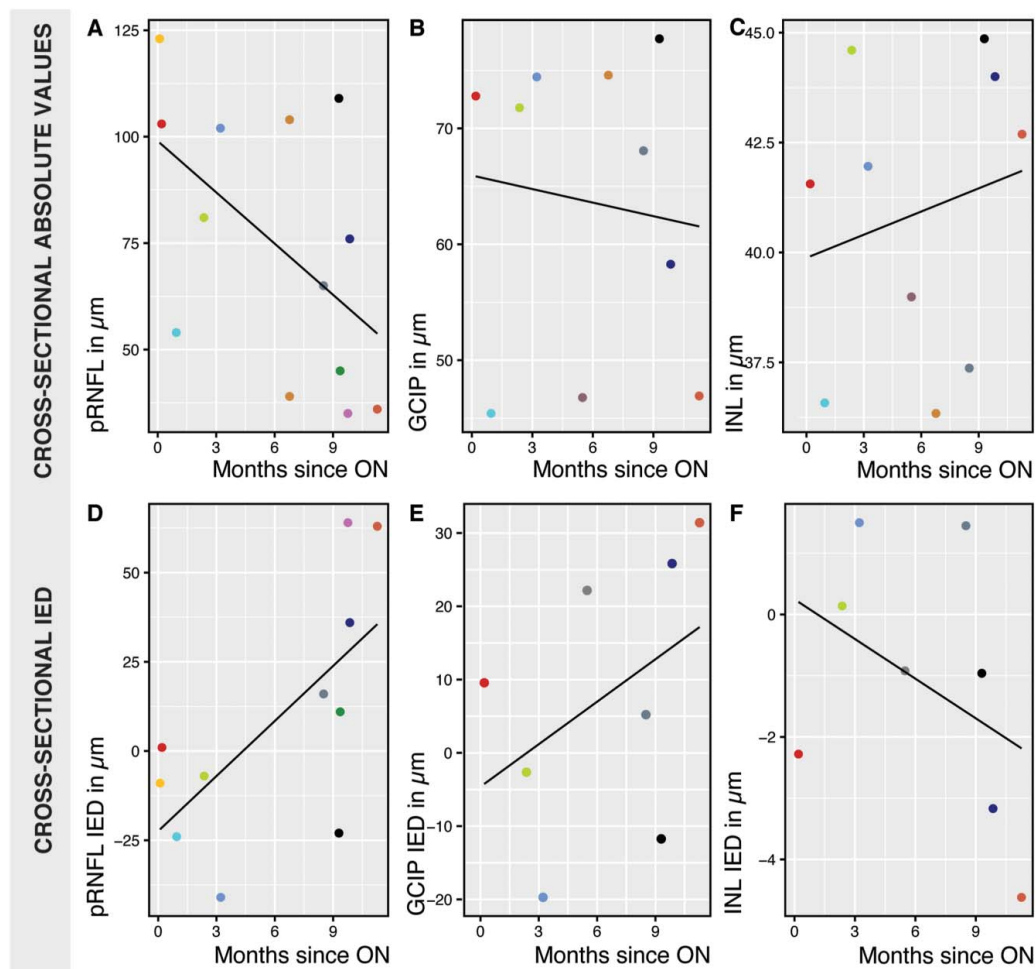
Chiasm (64%): involved in AQP4+NMOSD, but not MS & MOGAD

Optic tract (bilateral 45%): involved in AQP4+NMOSD, but not MS & MOGAD

Longitudinally extensive in AQP4+NMOSD (100%) & MOGAD (95%) [median 23mm] but mostly focal in MS [median 10mm]

Ramanathan et al. MSJ 2015

Optic nerve involvement – acute phase OCT



Acute OCT findings

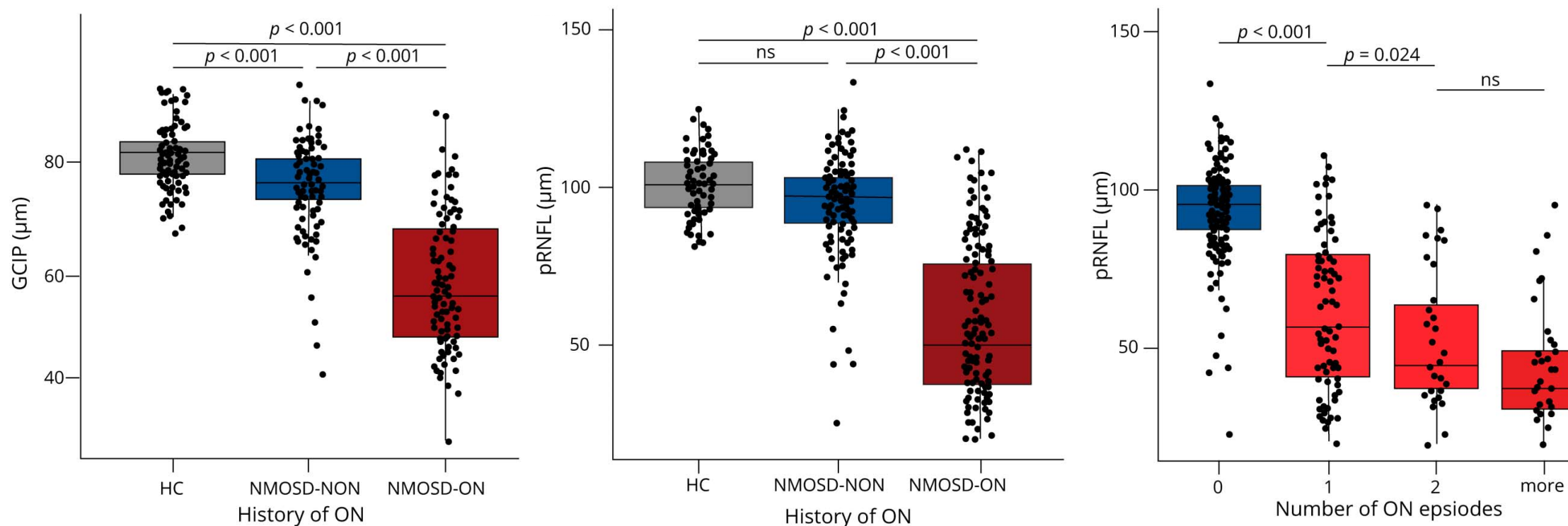
No severe disc edema (consider MOG-ab testing)

Post-acute OCT findings

Fast thinning of GCIPL (and subsequent RNFL)

Oertel et al. J Neuroophth 2023

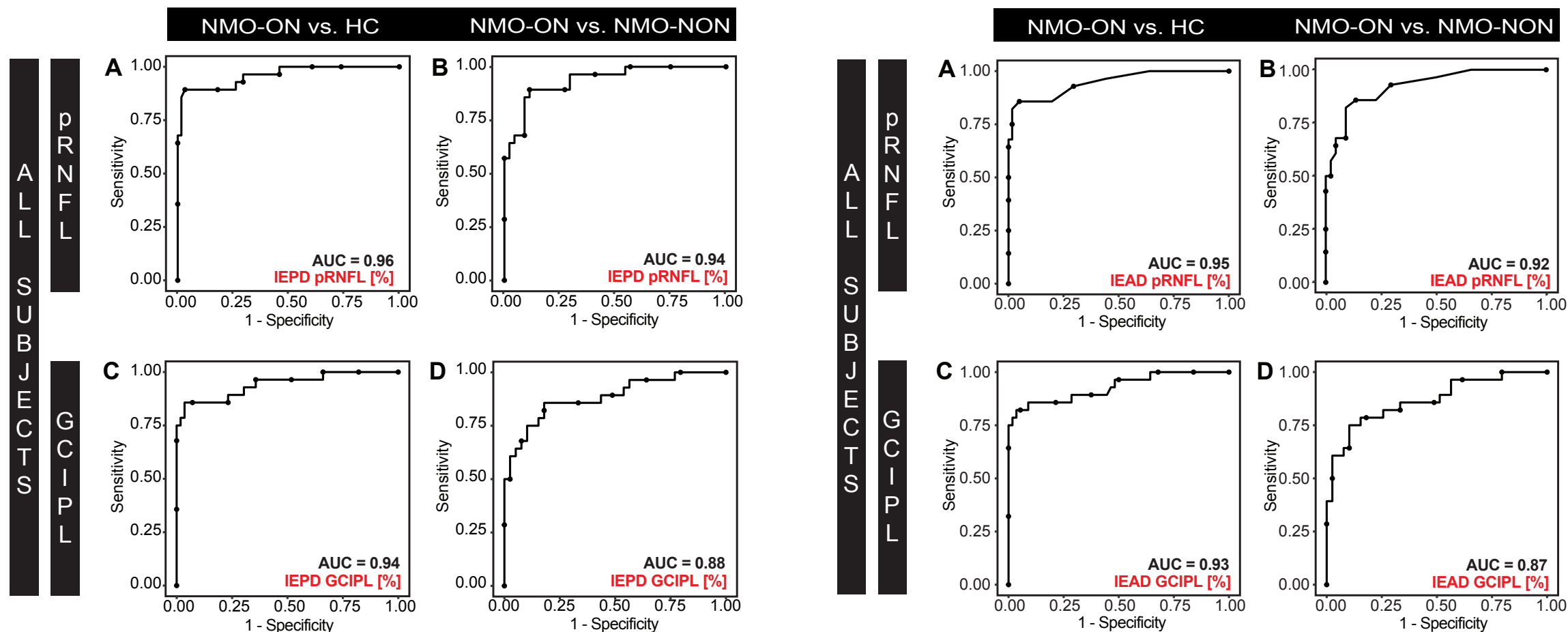
Optic nerve involvement – chronic phase OCT



283 AQP4-IgG+ NMOSD 72 HC

Oertel et al. Neurology – Neuroimm & Neuroinflamm 2021

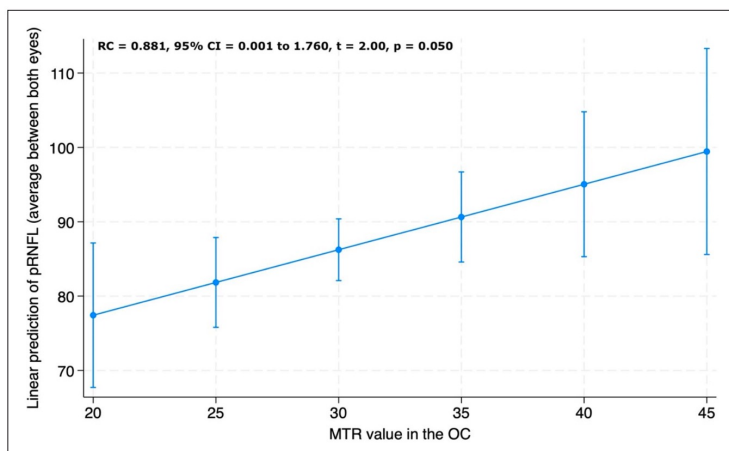
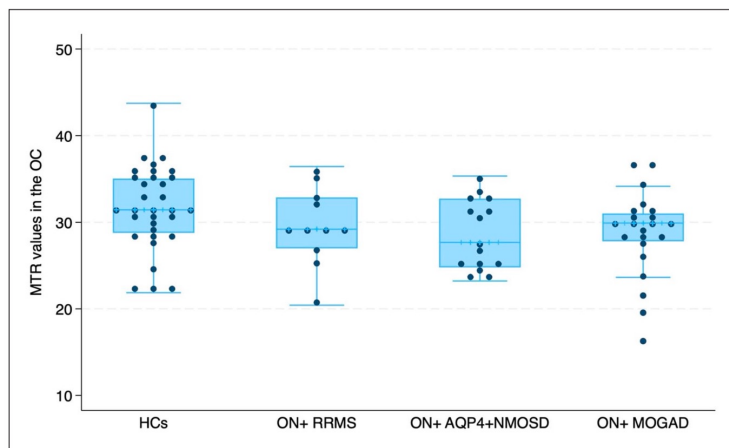
Optic nerve involvement – chronic phase OCT



73 AQP4-IgG+ NMOSD 62 HC

Oertel et al. Journal Neurol Neurosurg Psych 2023

Optic nerve involvement – what's new?



Magnetisation transfer ratio (MTR) as a promising MRI technique to quantify chiasmal involvement

Measurement of the exchange of proton magnetization between tissue macromolecules and mobile water molecules

Associated with myelin content, early demyelination & axonal loss

ON+ optic chiasmal MTR lower in AQP4+NMOSD ($p=0.02$) & MOGAD ($p=0.01$) vs. HC, but not RRMS

ON- optic chiasmal MTR lower in AQP4+NMOSD vs. HC ($p=0.04$), but not RRMS or MOGAD

24 AQP4-IgG+ NMOSD

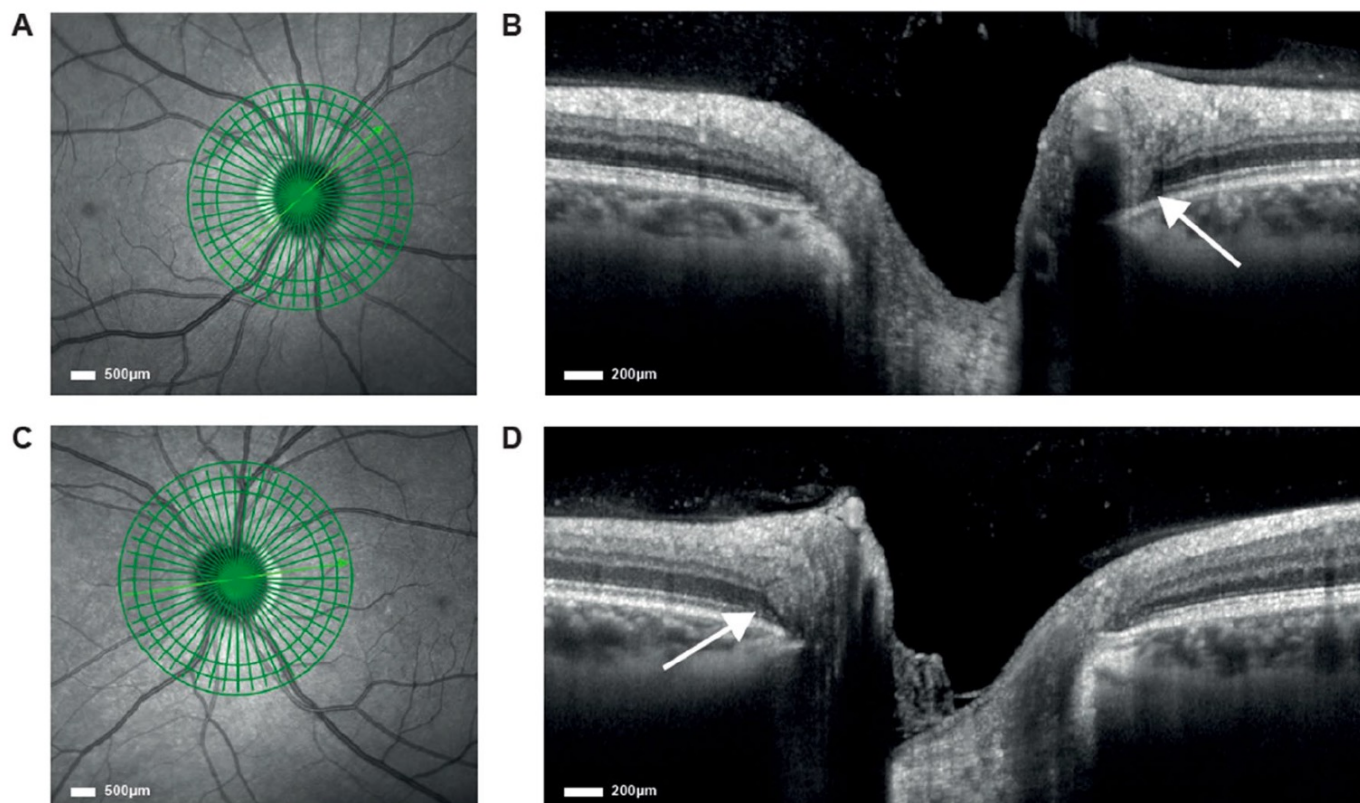
28 MOGAD

28 MS

32 HC

Bianchi et al. MSJ 2024

Optic nerve involvement – what's new?



Peripapillary hyperreflective ovoid mass-like structures (PHOMS)

17% AQP4+NMOSD vs. 14% MOGAD vs. 4% HC

No association with neuroaxonal damage

Pathophysiological significance unclear

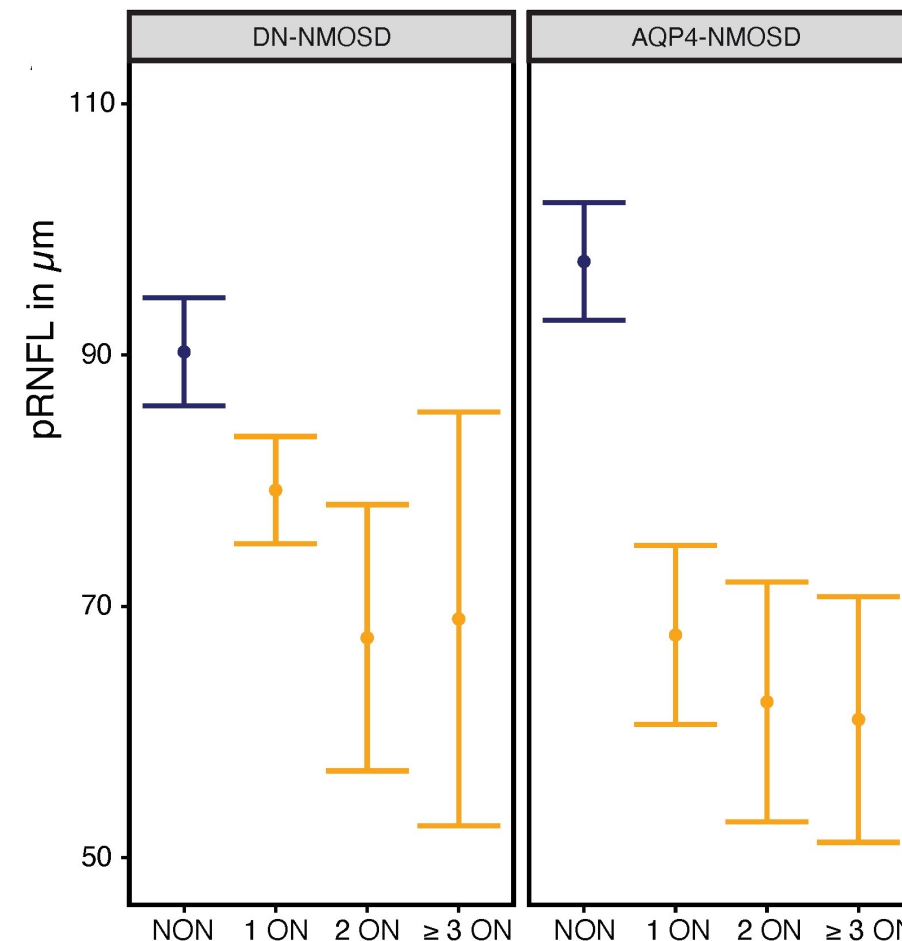
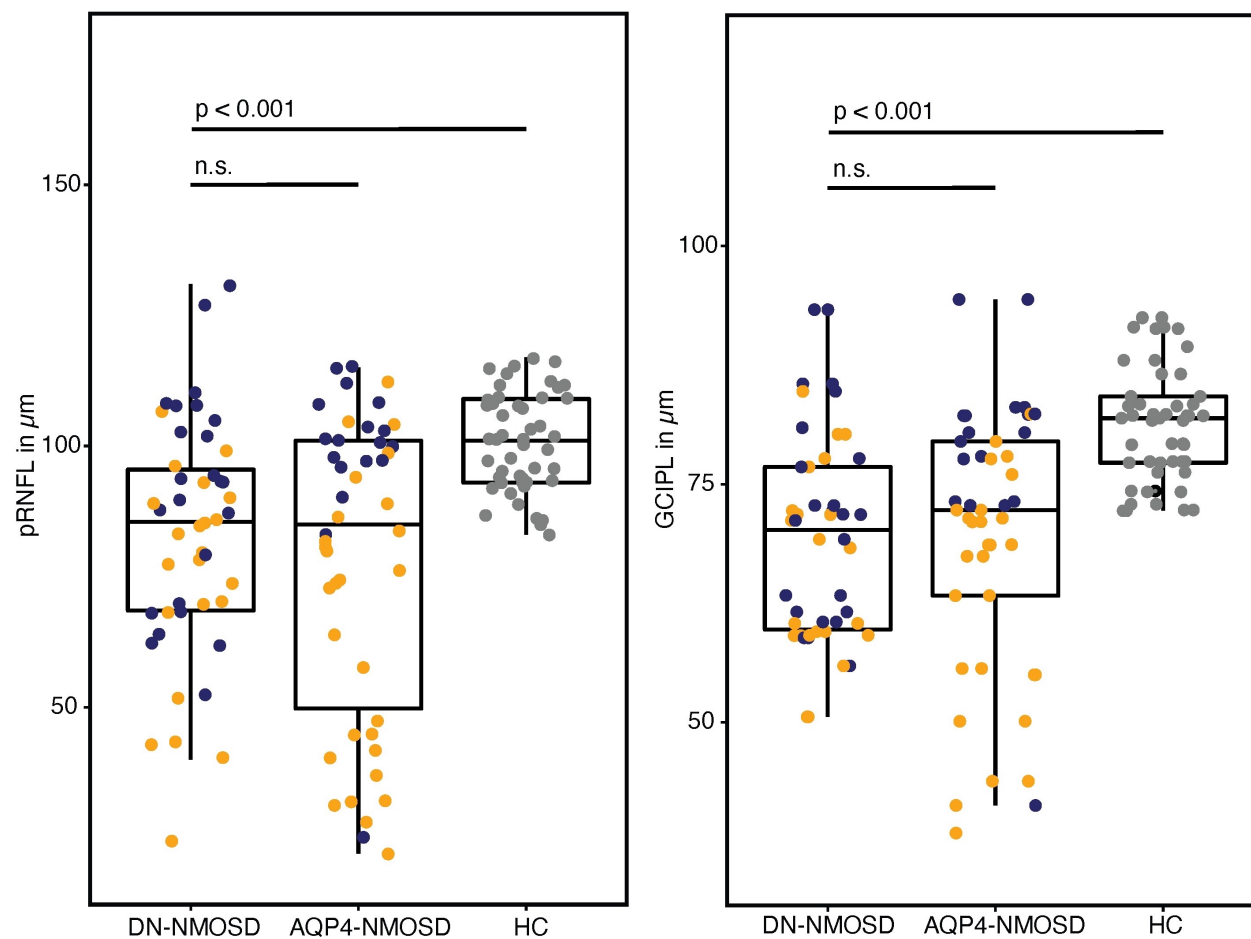
47 AQP4-IgG+ NMOSD

44 MOGAD

47 HC

Gernert et al. Neurology – J of Neurology 2023

Optic nerve involvement – what's new?



25 AQP4-IgG+ NMOSD

25 DN-NMOSD

33 HC

Oertel et al. Neurology – Neuroimm & Neuroinflamm 2024

Acute Optic Neuritis Network (ACON)

Verifying functional benefits of early corticosteroids in optic neuritis employing a global, multi-racial prospective study including people with MS-ON, AQP4-IgG+ ON, and MOG-IgG+ ON.

Primary outcome	High-contrast visual acuity at 6 mo. (stratified by diagnosis and days since onset)
Secondary outcomes	Low-contrast visual acuity
	pRNFL, GCIPL (OCT)
	Brain lesion number/volume, ON characterization score (MRI)
	QoL and PROM (including NEI-VFQ)



Asseyer et al. Frontiers 2023

Thank you.



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