Optic neuritis
An approach to
Diagnosis and Classification

Disclosures

NIHR UK

Overview

- Background: SLCTRIMS 2024
- Visual: 2 flow-charts
- Repeat: 3 clinical scenarios
- New: PIRA as optic neuritis
- Validation: of ICON 2022 criteria
- Conclusion

SLCTRIMS 2024

Symposium 4

Neuro ophthalmology of Demyelinating Disorders

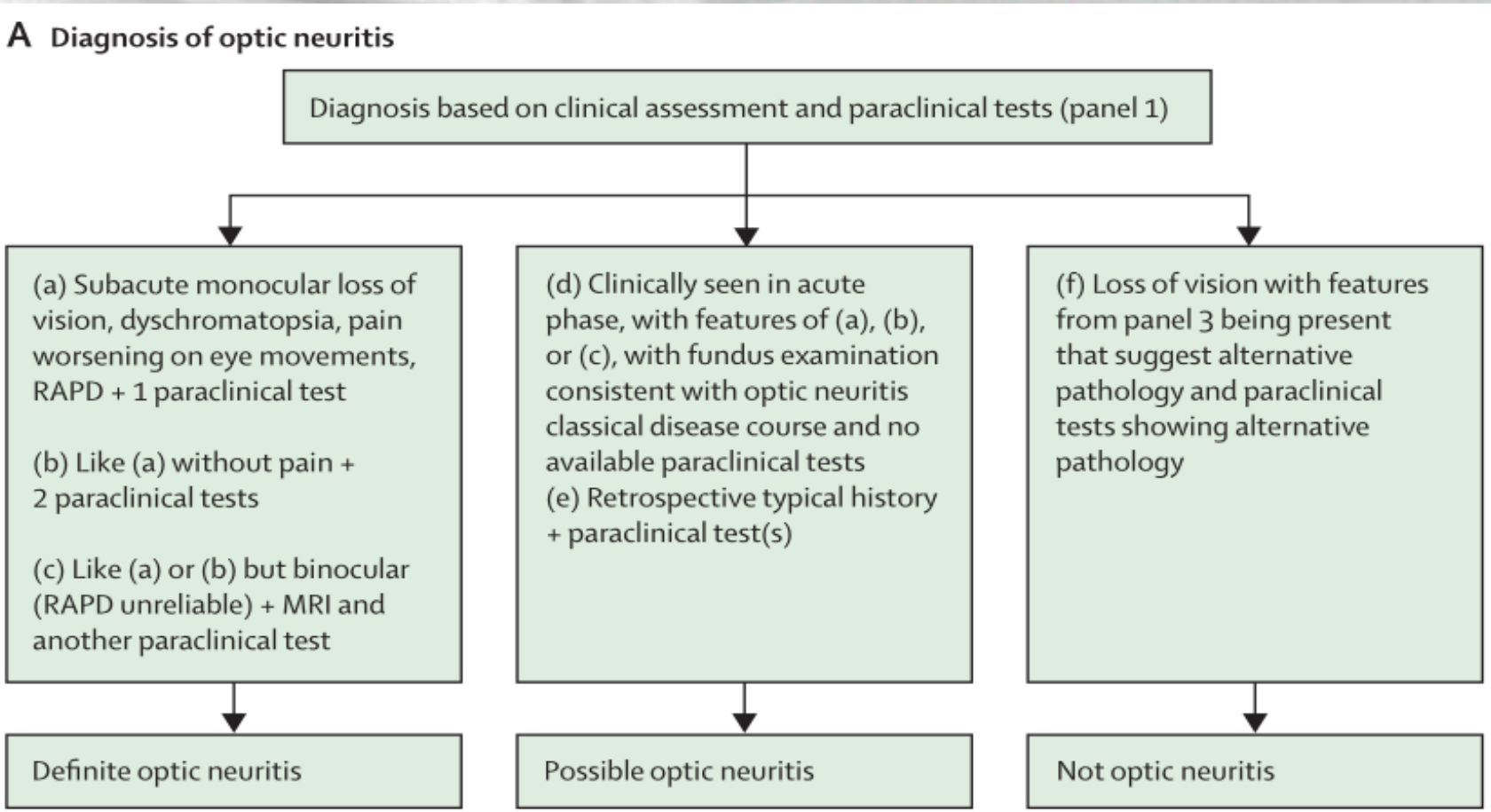
The ICON 2022 Diagnostic Criteria for Optic Neuritis

Axel Petzold
Moorfields Eye Hospital, VU Medical Centre, Amsterdam, The Netherlands
UCL Institute of Neurology, Queen Square, London, United Kingdom

Optic Neuritis in MOGAD

John Chen
Mayo Clinic Rochester, Minnesota, USA

Diagnostic Criteria



SL TRIMS

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සියලුම ICON 2022 කතුවරුන් මෙහි ලැයිස්තුගත කළ යුතුය

Lancet Neurology 2022;21:1120-1134, DOI:10.1016/S1474-4422(22)00200-9

ඔප්ටික් නියුරිටිස් වර්ගීකරණය සම්බන්ධයෙන් සම්මුතියක් නොමැති අතර නිශ්චිත රෝග විනිශ්චය නිර්ණායක නොමැත. මෙම යථාර්ථයෙන් අදහස් කරන්නේ පළමු ප්‍රකාශනය ලෙස ඔප්ටික් නියුරිටිස් ඇති ආබාධ හඳුනා ගැනීම අභියෝගාත්මක විය හැකි බවයි. ඉදිරිපත් කිරීමේදී ඔප්ටික් නියුරිටිස් පිළිබඳ නිවැරදි රෝග විනිශ්චය බහු

பார்வை நரம்பு அழற்சி நோய் கண்டறிதல் மற்றும் வகைப்பாடு

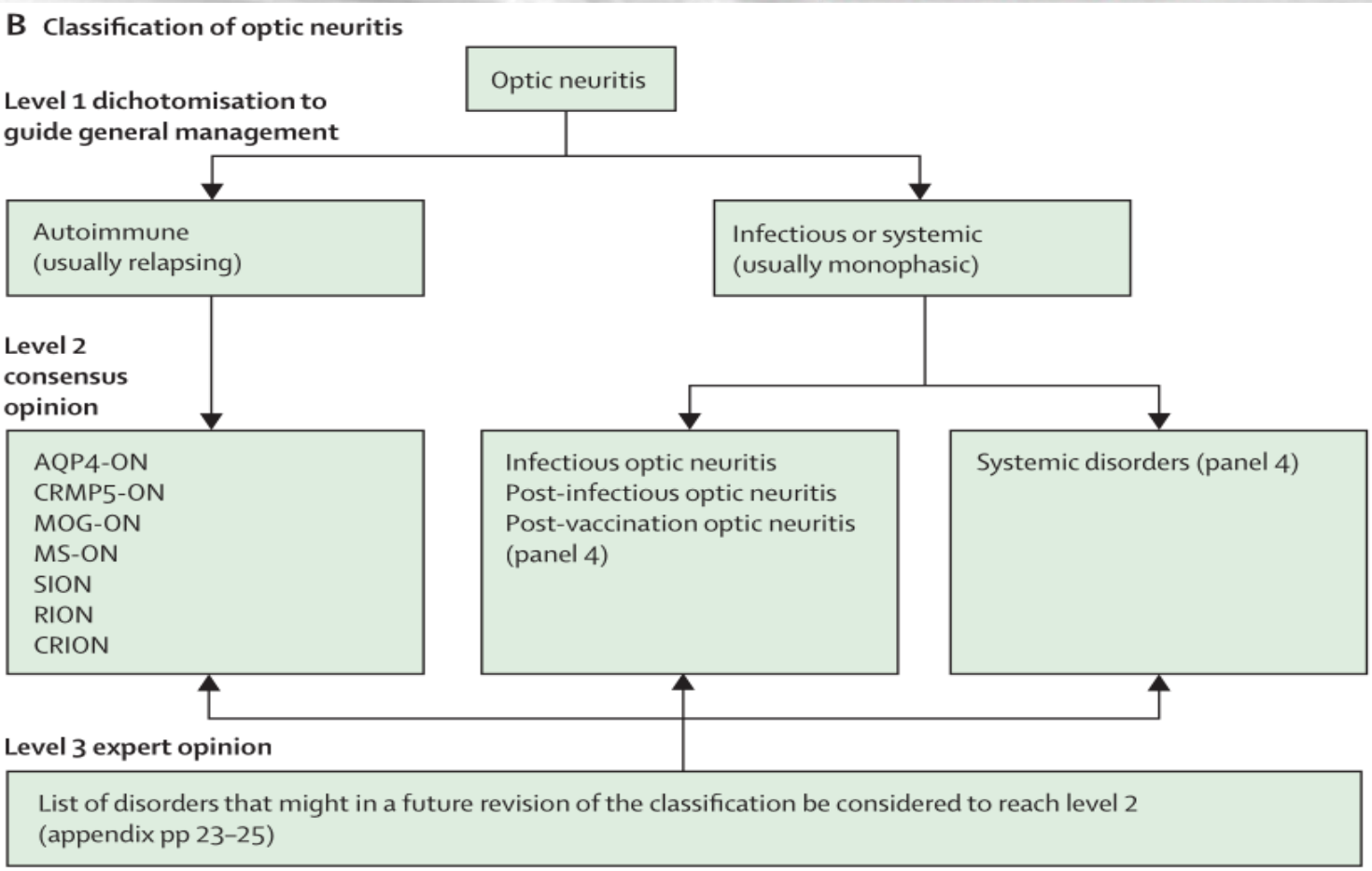
அனைத்து ICON 2022 ஆசிரியர்களும் இங்கே பட்டியலிடப்பட வேண்டும்

லான்செட் நரம்பியல் 2022;21:1120-1134, DOI:10.1016/S1474–4422(22)00200–9

பார்வை நரம்பு அழற்சியின் வகைப்பாடு குறித்து ஒருமித்த கருத்து இல்லை, மேலும் துல்லியமான கண்டறியும் அளவுகோல்கள் கிடைக்கவில்லை. இந்த உண்மை என்னவென்றால், பார்வை நரம்பு அழற்சியை முதல் வெளிப்பாடாகக் கொண்ட கோளாறுகளைக்

UCL

Classification



Application

Panel 1: **Diagnostic criteria for optic neuritis**

Clinical criteria

- A: Monocular, subacute loss of vision associated with orbital pain worsening on eye movements, reduced contrast and colour vision, and relative afferent pupillary deficit
- B: Painless with all other features of (A).
- C: Binocular loss of vision with all features of (A) or (B).

Paraclinical criteria

- OCT: Corresponding optic disc swelling acutely or an inter-eye difference in the mGCIPL of >4% or >4 µm or in the pRNFL of >5% or >5 µm within 3 months after onset.
- MRI: Contrast enhancement of the symptomatic optic nerve and sheaths acutely or an intrinsic signal (looking brighter) increase within 3 months.
- Biomarker: AQP4, MOG, or CRMP5 antibody seropositive, or intrathecal CSF IgG (oligoclonal bands).

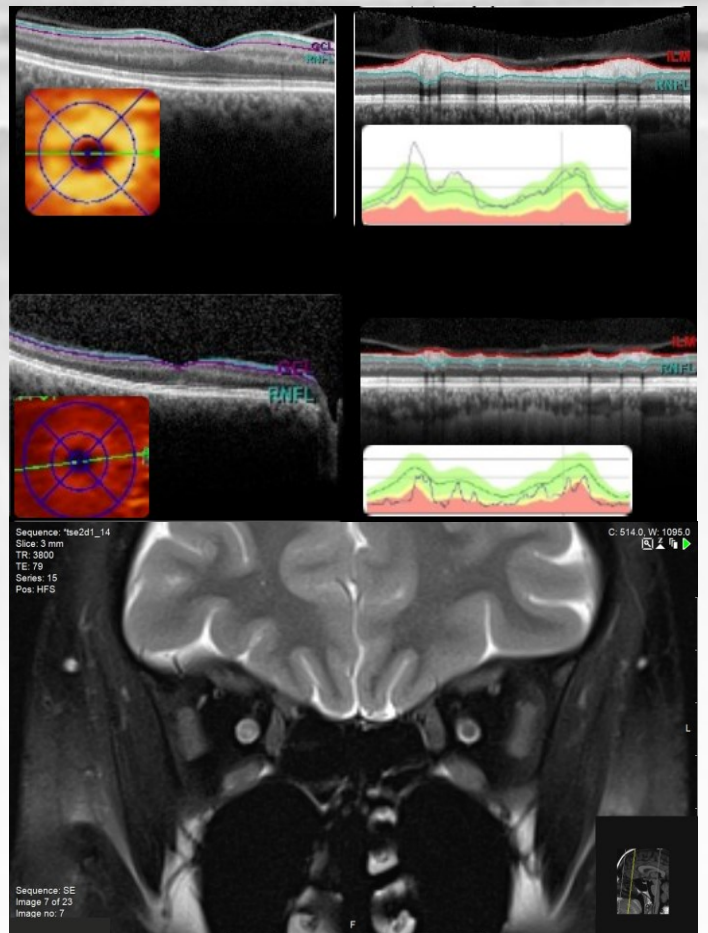
Application of the clinical and paraclinical criteria

Definite optic neuritis

- (A) and one paraclinical test
- (B) and two paraclinical tests of different modality
- (C) and two different paraclinical tests of which one is MRI

Possible optic neuritis

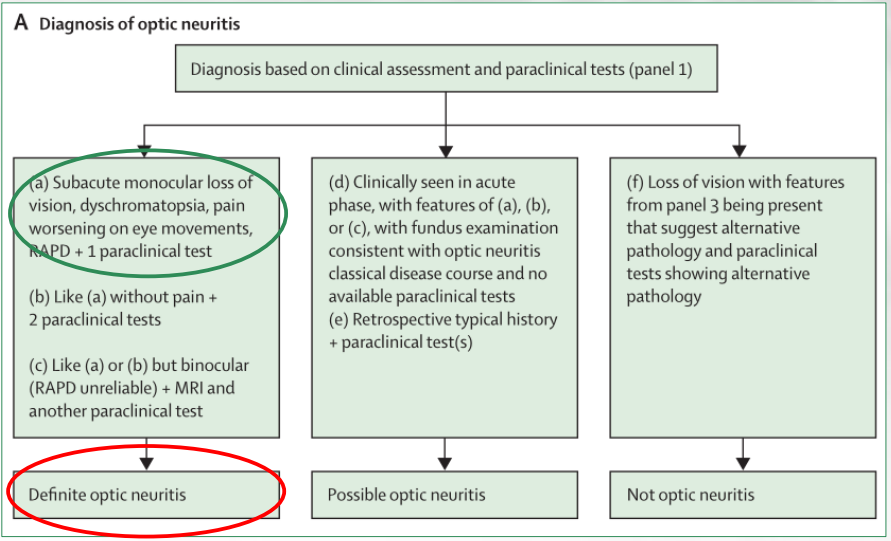
- (A), (B), or (C) if seen acutely but in absence of paraclinical tests, with fundus examination typical for optic neuritis and consistent with the natural history during follow-up
- Positive paraclinical test or tests, with a medical history suggestive of optic neuritis

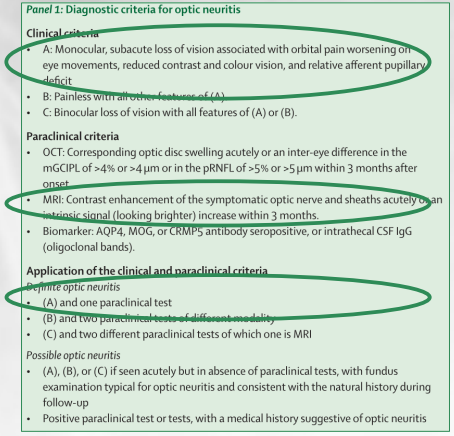


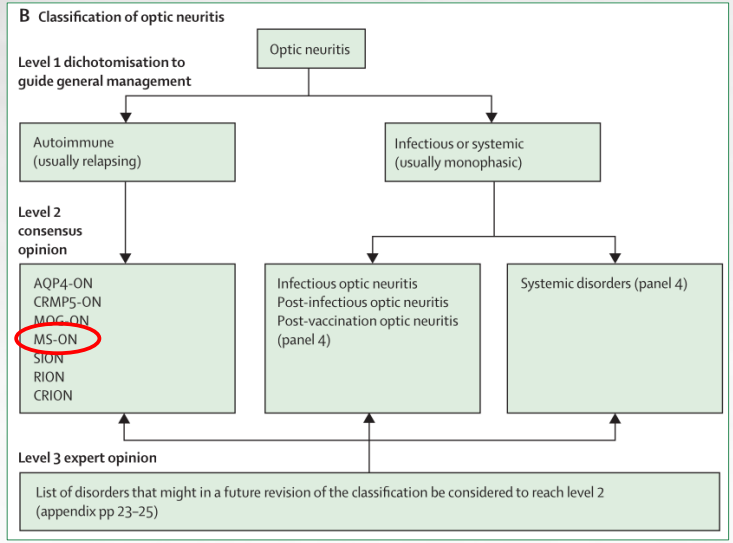
1st Case

- 34y old Caucasian female patient
- 7d RE pain, worsening on eye movements
- Dyschromatopsia & VA RE 6/9, LE 6/5
- Right RAPD
- Reports: fatigue, cognitive problems, urinary incontinence, depressi
- PmHx: right sided numbness lasting ~1m, 3y ago
- MRI: DIS & DIT & 3 Gd+ non-symptomatic lesions

Practical exercise: 1st Case



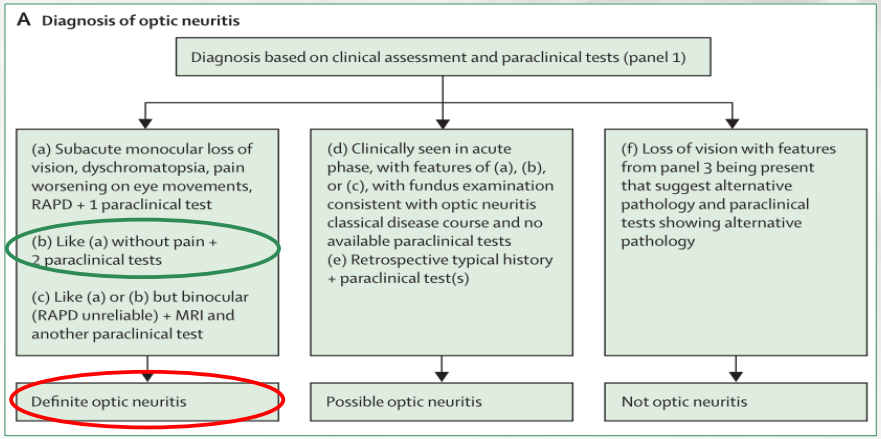


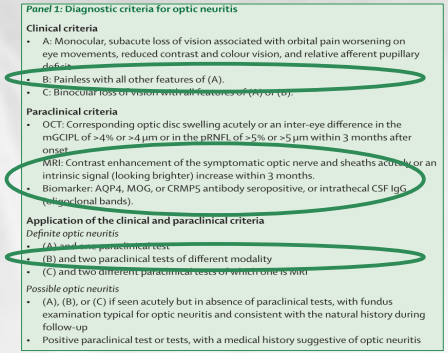


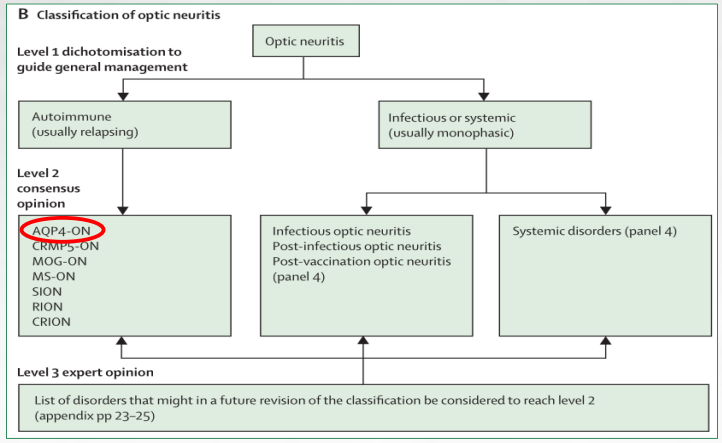
2nd Case

- 28y old, Afrocaribbean male
- Painless loss of vision LE (6/38)
- Dyschromatopsia
- Left RAPD
- Corticosteroid responsive relapses over ~21y fup
- Acutely MRI shows a swollen, Gd+, left optic nerve.
- AQP4 seropositive

Practical exercise: 2nd Case





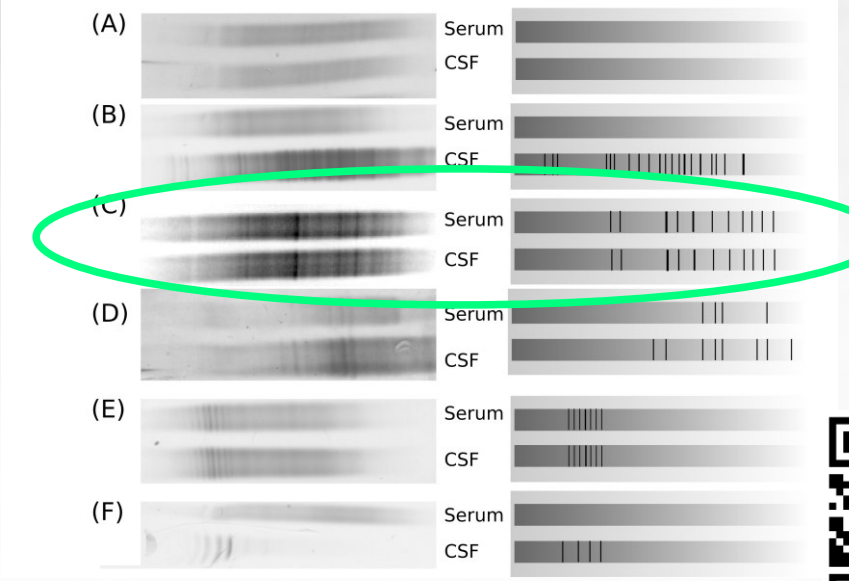


3rd Case

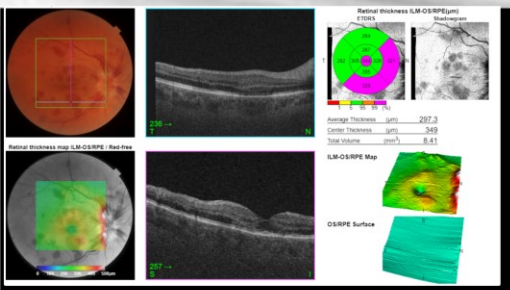
- 64 year old female receives AZ COVID vaccination
- 14 days later ocular pain, worsening on eye movements
- 2 days later sequential binocular loss of vision
- IVMP (5d, 500mg) given 23d after onset
- Excellent functional recovery of vision @ 1y fup
  - RE 6/9, Ishihara 15/17
  - LE 6/7.5, Ishihara 17/17

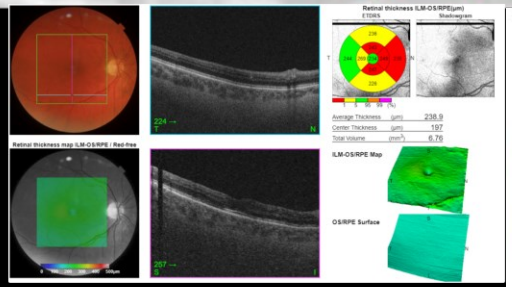
3rd Case

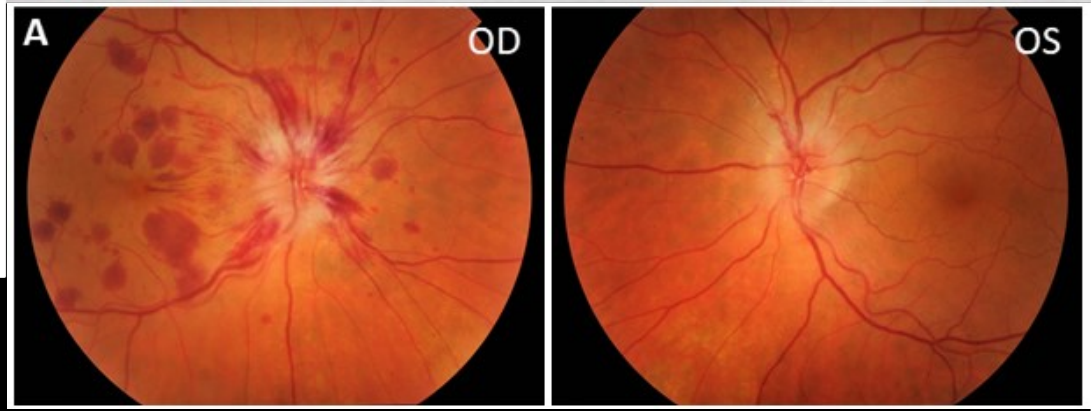
- OCT: see next slides for different devices.
- MRI: increased signal (FLAIR, T2) for optic nerves, no contrast enhancement.
- Biomarker:
  - MOG & AQP4 negative
  - IgG: matched bands

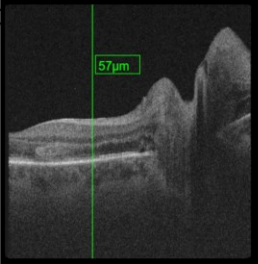


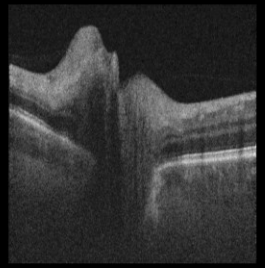
3rd Case

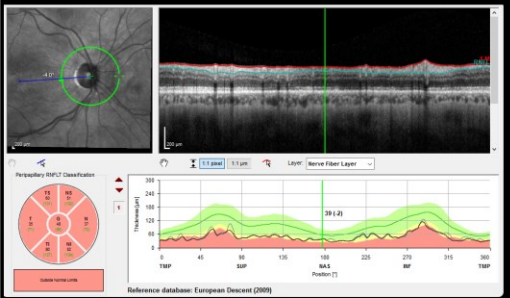

Retinal thickness ILM-OS/RPE(µm)
ETDRS
Average Thickness (µm) 297.3
Center Thickness (µm) 349
Total Volume (mm³) 8.41
ILM-OS/RPE Map
OS/RPE Surface

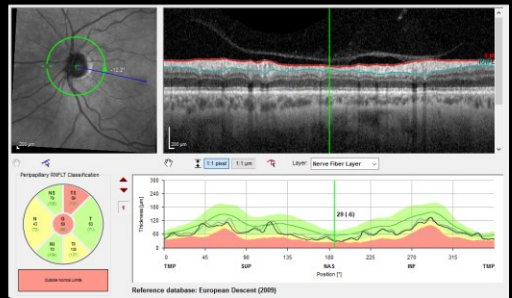

Retinal thickness ILM-OS/RPE(µm)
ETDRS
Average Thickness (µm) 236.9
Center Thickness (µm) 197
Total Volume (mm³) 6.76
ILM-OS/RPE Map
OS/RPE Surface

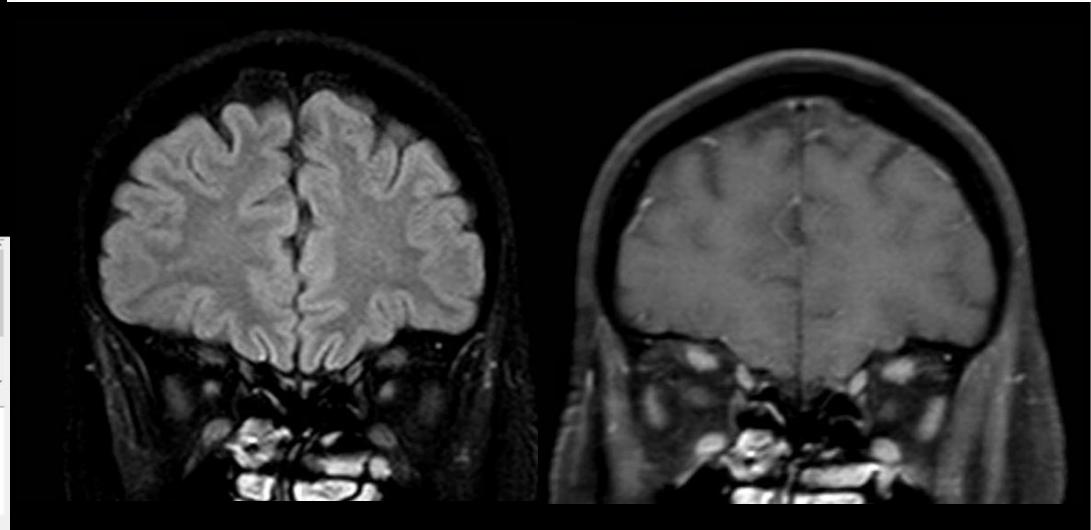

A
OD
OS


57µm

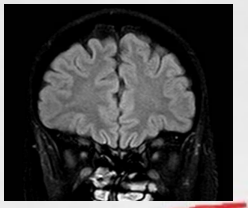



Peripapillary RNFLT Classification
39 (-2)
Reference database: European Descent (2009)


Peripapillary RNFLT Classification
29 (-6)
Reference database: European Descent (2009)

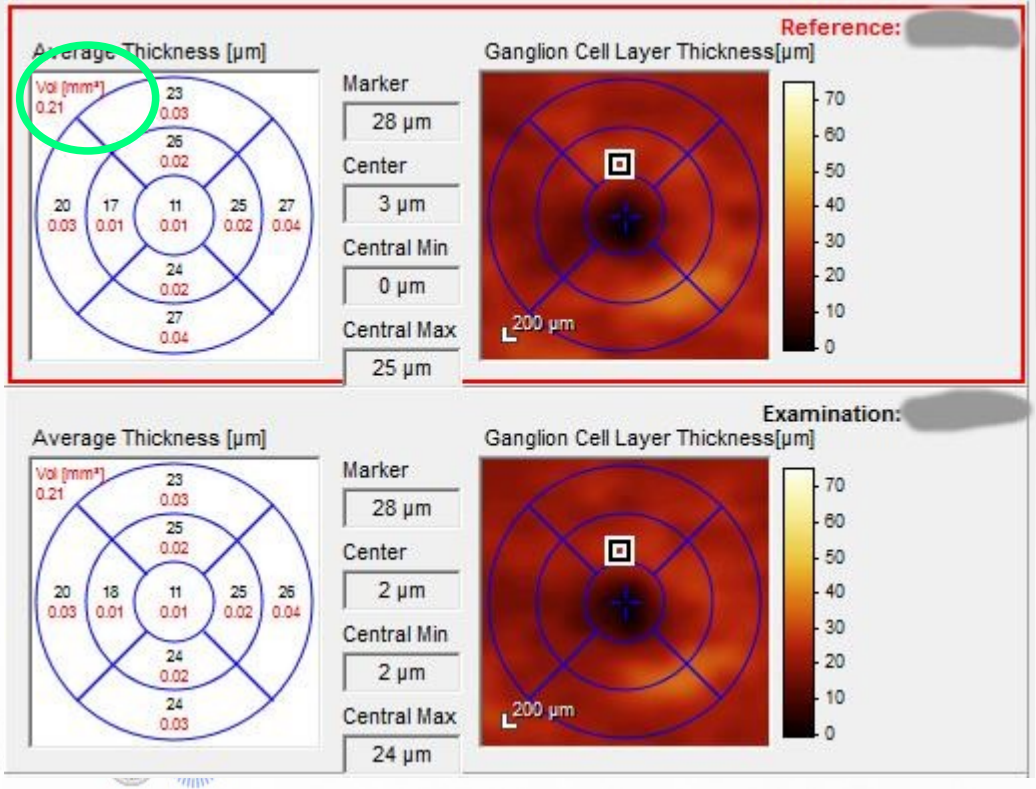


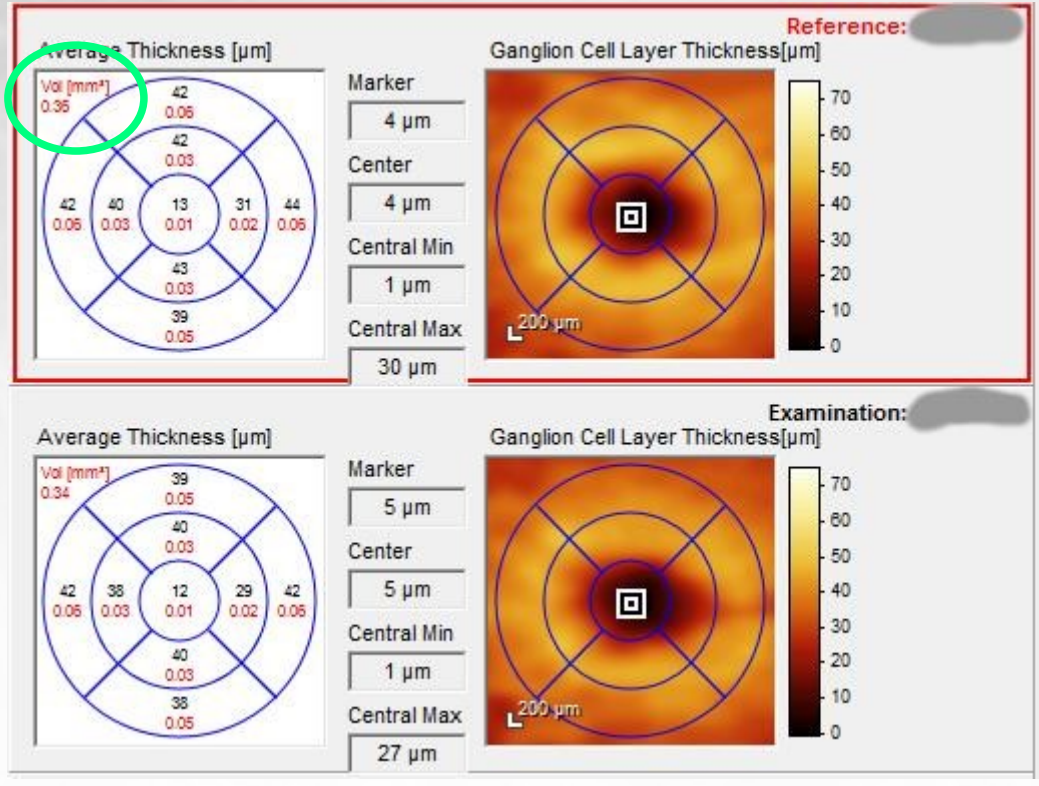
Retinal asymmetry



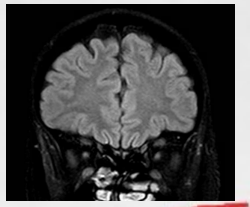
RE mGCL 0.21

LE mGCL 0.36 **IEPD: 62%**





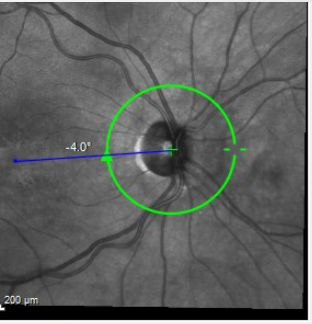
Retinal asymmetry

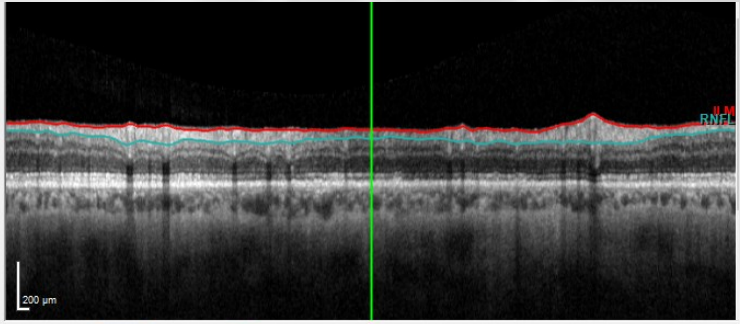


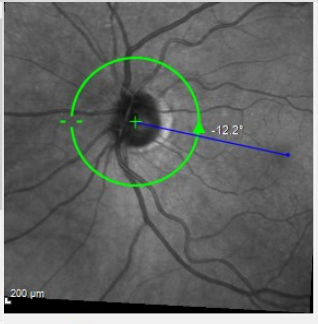
RE pRNFL 48 µm

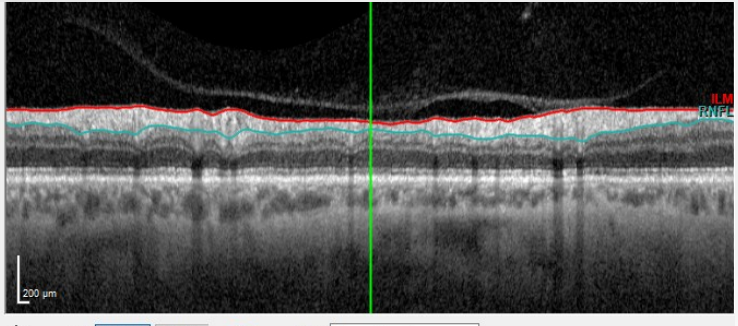
LE pRNFL 69 µm

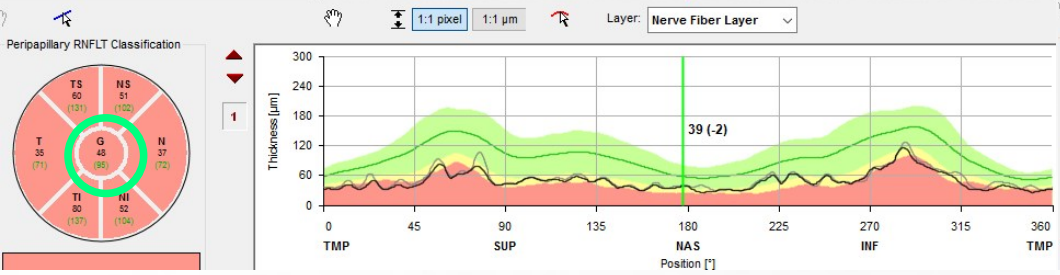
IEPD: 31%

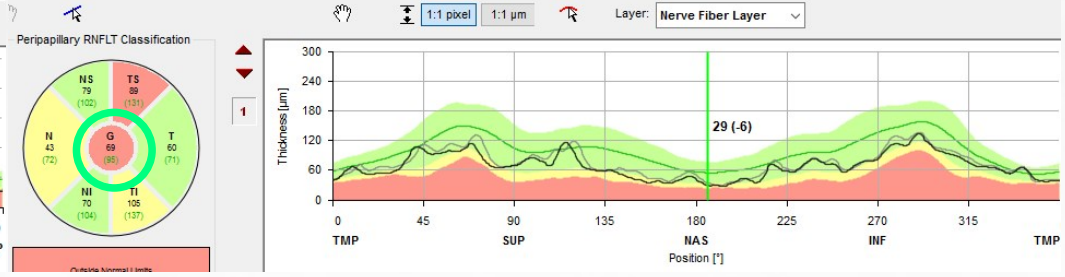




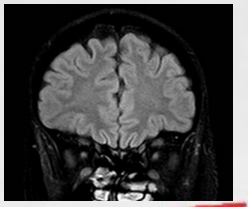






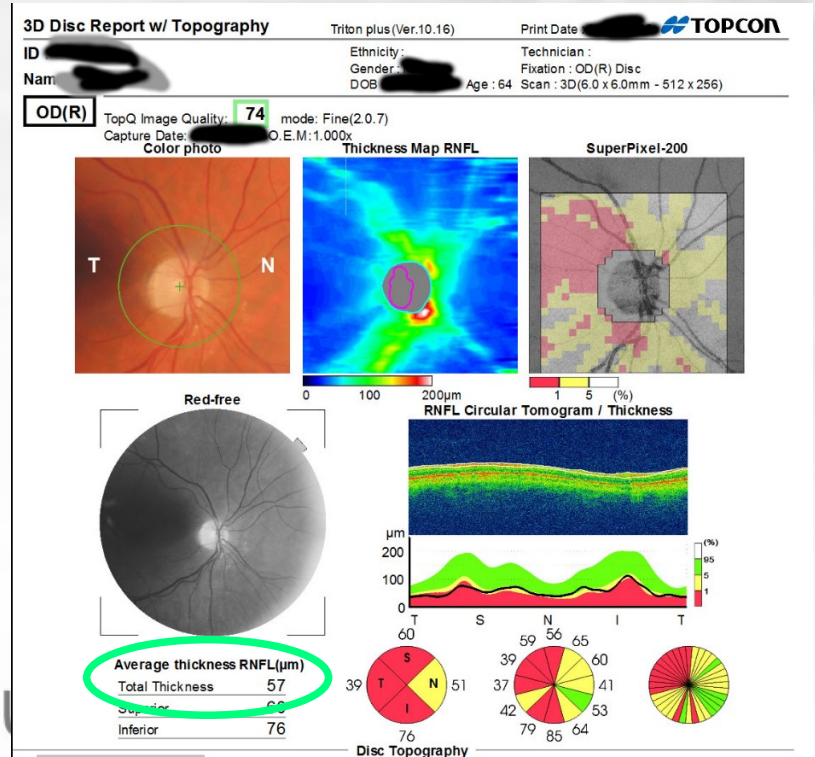


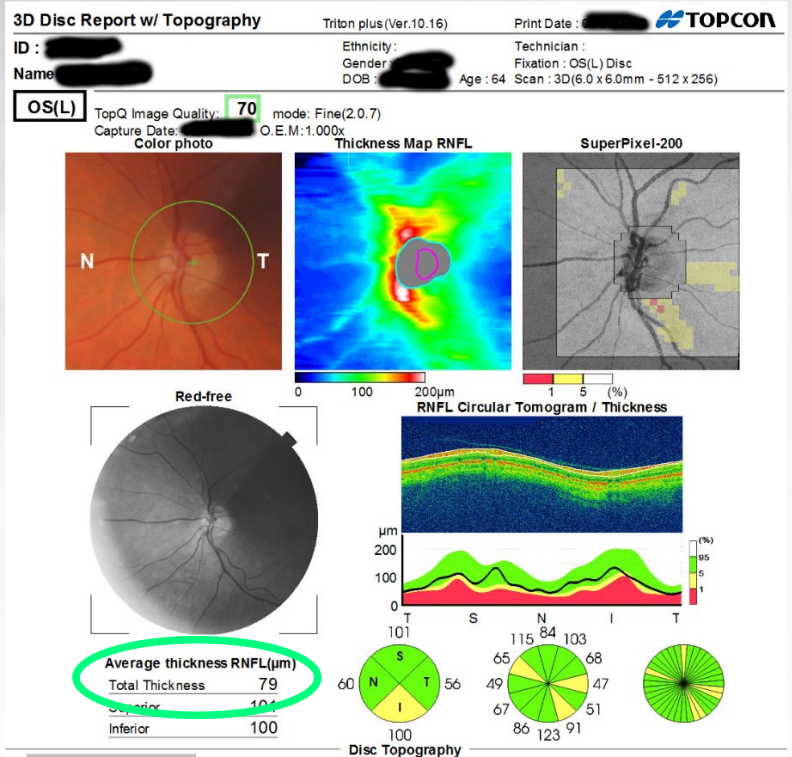
Retinal asymmetry



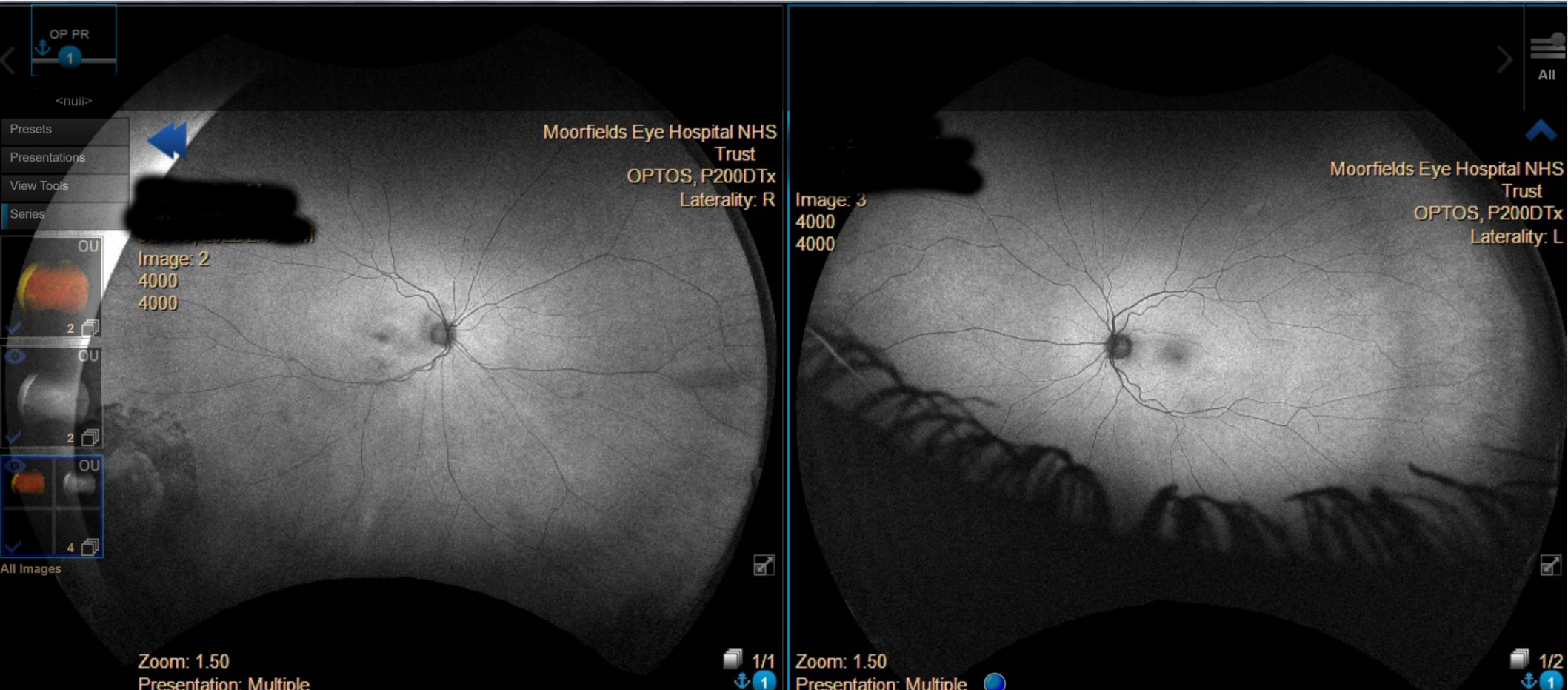
Topcon RE pRNFL 57 µm

LE pRNFL 79 µm **IEPD: 28%**



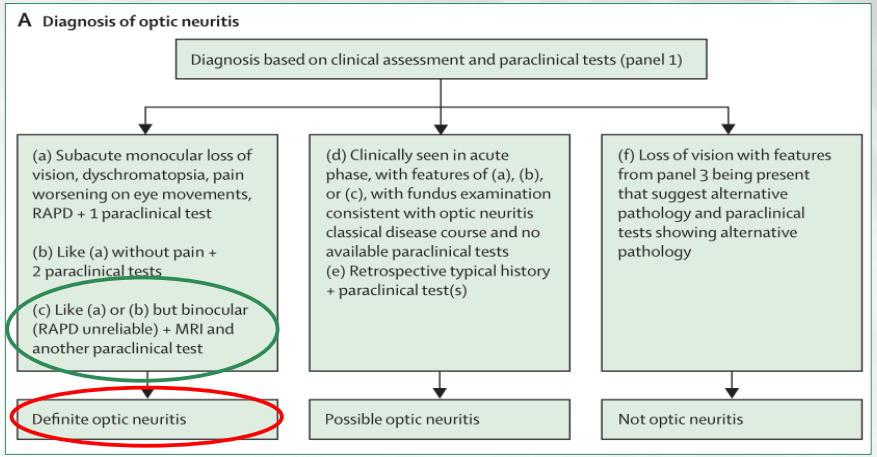


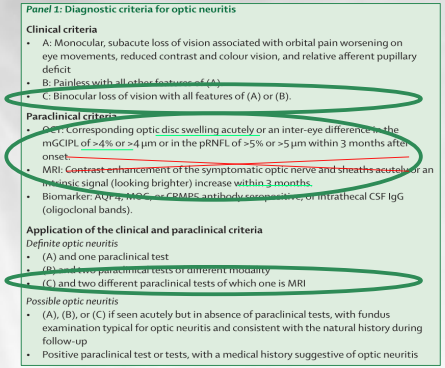
Autofluorescence

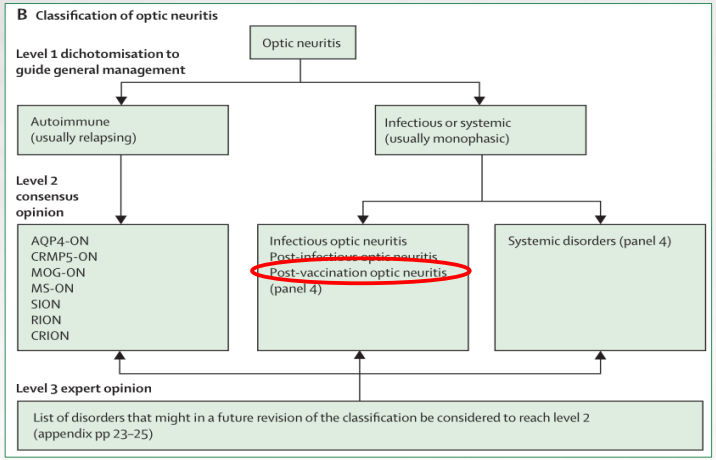


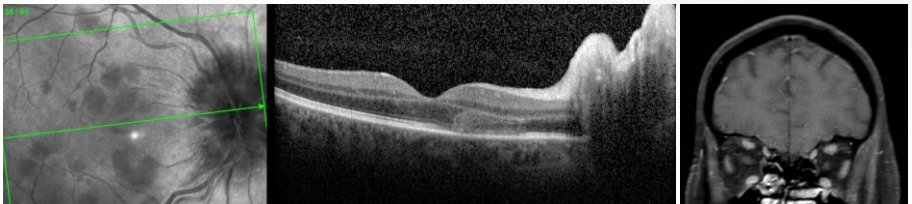
Practical exercise: 3rd Case

IEPD: mGCL 62% (>4%), pRNFL 28-32% (>5%)









In acute pre-laminar ON the MRI may not show contrast enhancement

3 clinical scenarios of increasing complexity

- Case 1: is this MS ?

Scenario A: painful, monocular, subacute LOV, dyschromatopsia, RAPD+

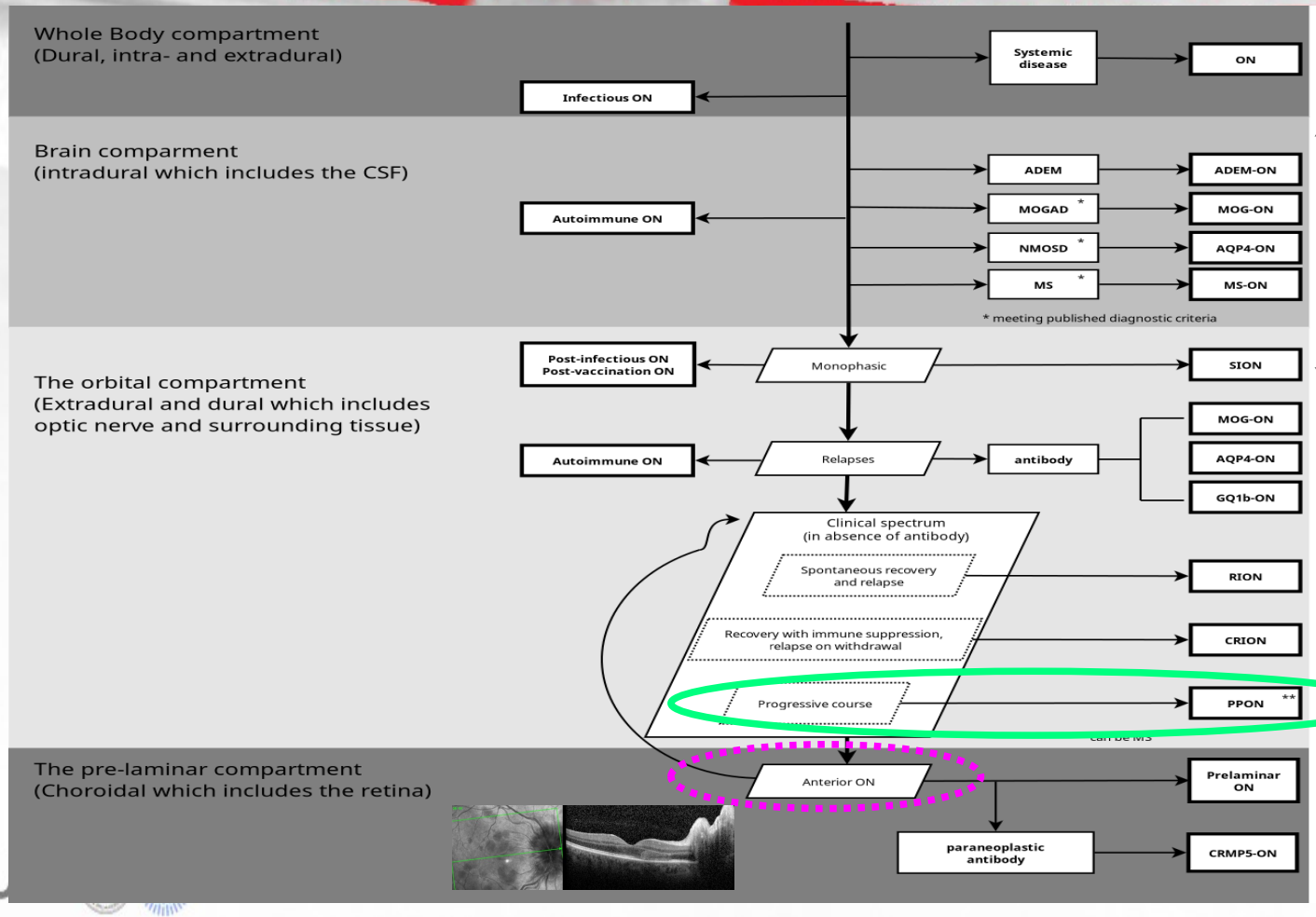
- Case 2: is this NMOSD ?

Scenario B: no pain, monocular, subacute LOV, dyschromatopsia, RAPD+

- Case 3: was this caused by the Covid vaccination ?

Scenario C: binocular, subacute LOV, dyschromatopsia, RAPD unreliable

Anatomy



Dr. Brain

Dr. Eye

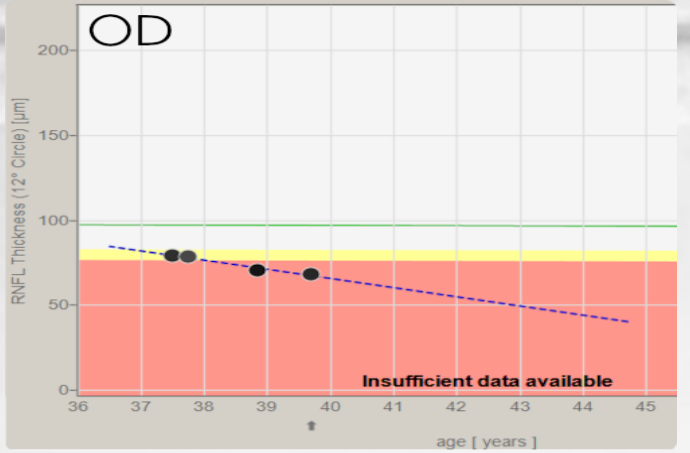
Primary progressive ON

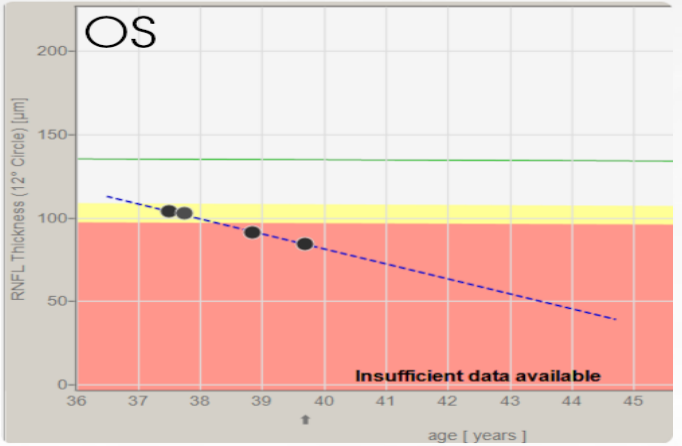
PPON

Primary progressive optic neuritis. Diagnosis requires progressive atrophy or progressive visual loss, or both for >12 months. Diagnosis of PPON is based on time and applies to all subforms of ON that present with a progressive rather then a relapsing disease course.

4th Case: PPON

- 27 year lady with MS, takes Dimethyl Fumarat
- VA:
  - 2022 RE 6/9 LE 6/24
  - 2023 RE 6/18 LE 6/24
  - 2024 RE 6/48 LE 6/60
- pVEP delaid, pERG reduced N95:P50, ffERG normal. MRI: stable.
- OCT confirms progression independent of relapse activity.

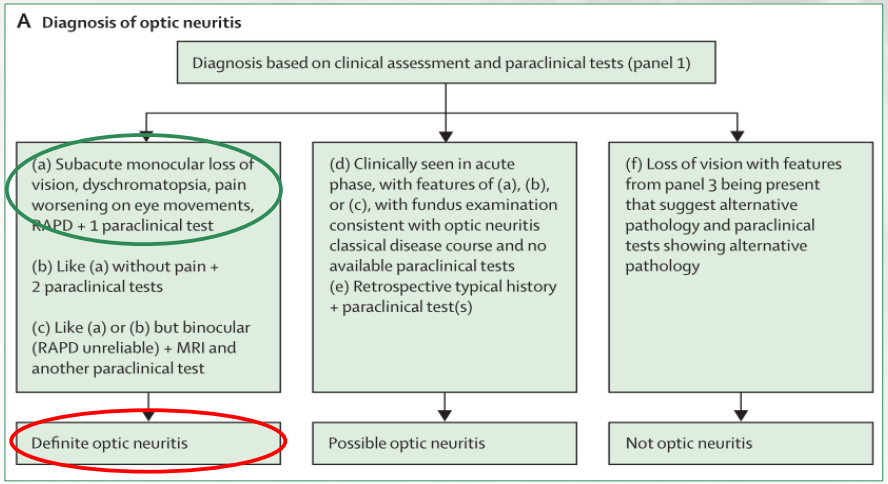


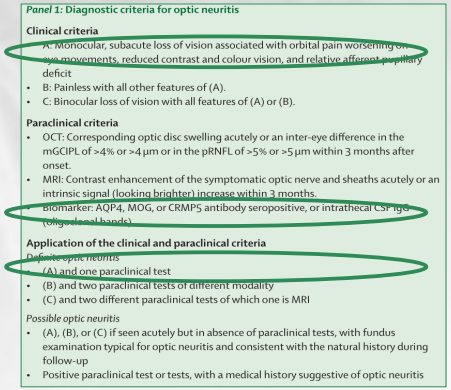


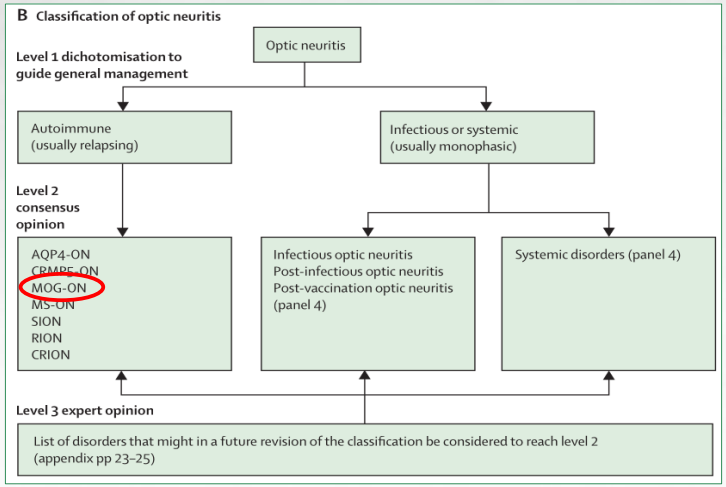
5th Case

- 54y old woman RE pain worsening on eye movements
- 4d later
  - RE vision loss (HM)
  - RE dyschromatopsia
- Right RAPD
- MOG seropositive

Practical exercise: 5th Case

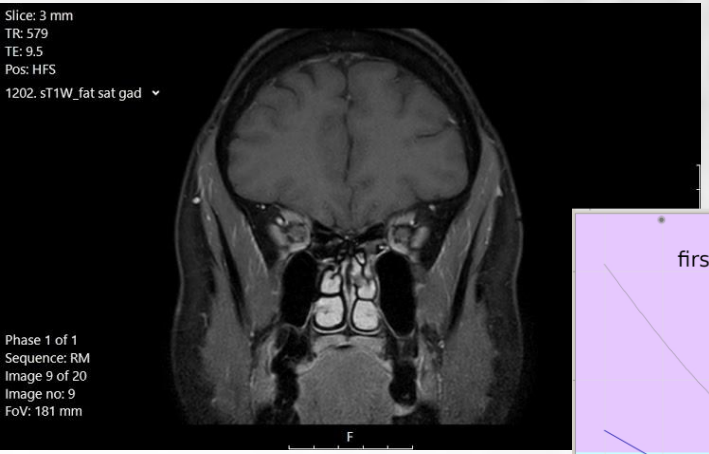


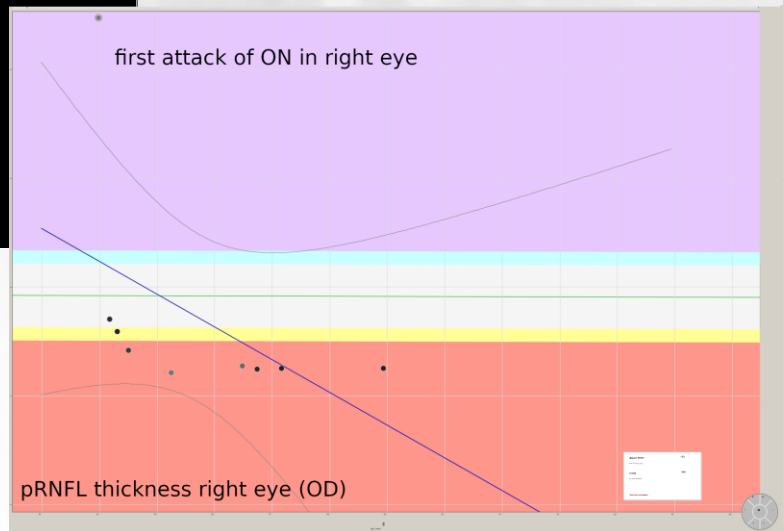


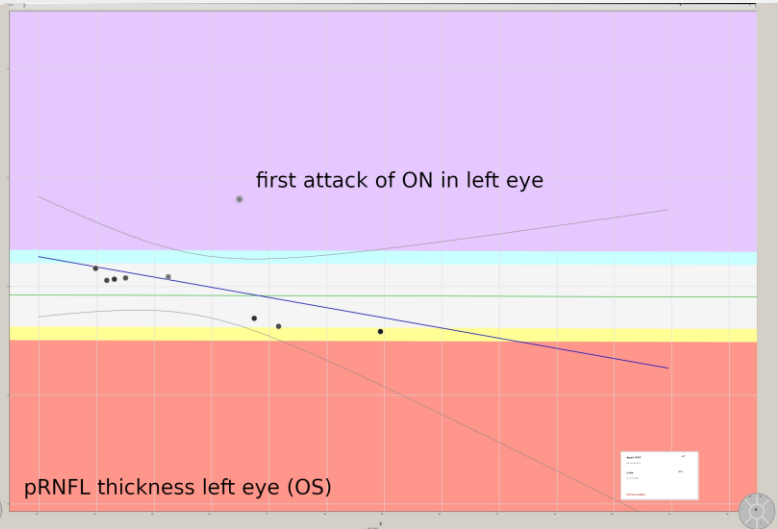


Case 5: treatment

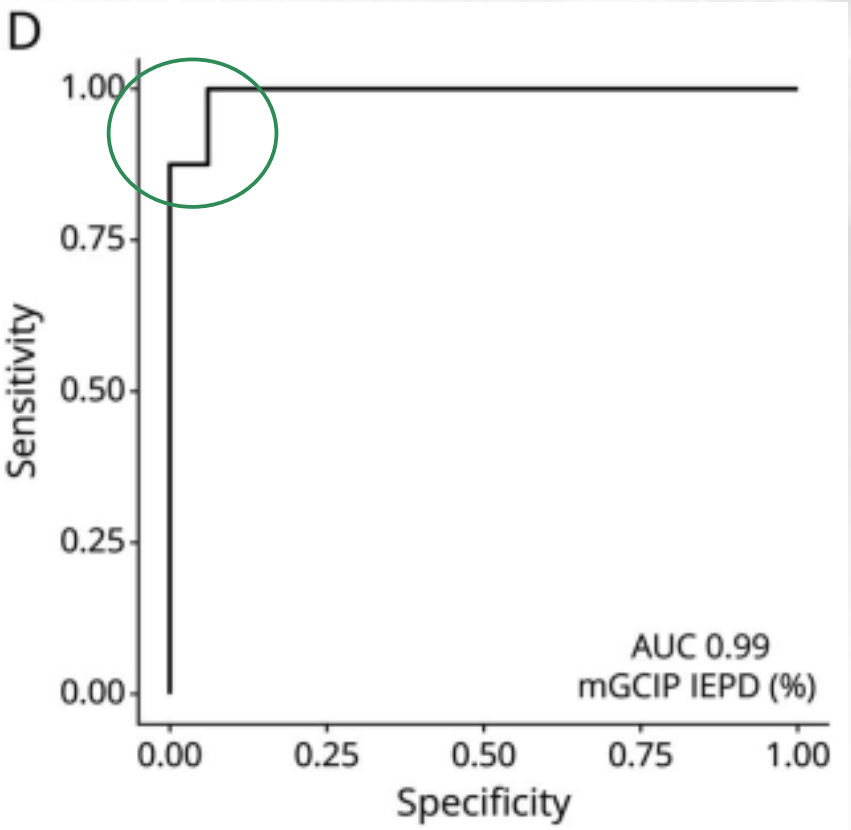
Corticosteroids for RE within 2 weeks after onset. Pain stopped within hours after 1st dose
3 years later relapse of MOG-ON in LE. Corticosteroids for LE within 1 week after onset. Pain stopped within hours. Less severe pRNFL atrophy in LE if compare to RE.





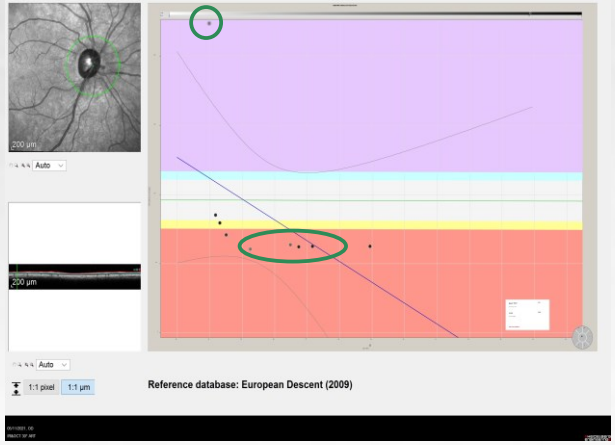


Validation of OCT in MOG-ON



Acutely:
severe disc swelling

Chronic:
severe atrophy



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OCT in MOG-ON

	HCs	MOG-ON
Subjects [N]	33	33
Subjects with unilateral ON [N (%)]		20 (61)
Subjects with bilateral ON [N (%)]		13 (39)
Eyes [N]	66	66
Age [y, mean (SD)]	34 (11)	39 (15)
Sex [m, N (%)]	16 (48.5)	16 (48.5)
Time since ON [y, mean (SD)]		3 (4)
pRNFL [µm, mean (SD)]	95.98 (7.91)	71.03 (24.35)
mGCIP [µm, mean (SD)]	86.48 (9.64)	67.32 (19.46)
IEAD pRNFL [µm, mean (SD)]	2.70 (2.49)	23.75 (17.50)
IEPD pRNFL [%, mean (SD)]	2.77 (2.61)	25.90 (16.85)
IEAD mGCIP [µm, mean (SD)]	2.61 (2.70)	20.60 (13.10)
IEPD mGCIP [%, mean (SD)]	2.92 (2.88)	24.94 (14.52)

Table 2 Intereye Percentage and Absolute Differences

	t	*p* Value
MOG-ON (all subjects) vs HCs		
pRNFL IEAD [µm]	−6.739	<0.001
pRNFL IEPD [%]	−7.678	<0.001
mGCIP IEAD [µm]	−6.760	<0.001
mGCIP IEPD [%]	−7.473	<0.001
MOG-ON (unilateral) vs HC		
pRNFL IEAD [µm]	−7.796	<0.001
pRNFL IEPD [%]	−8.642	<0.001
mGCIP IEAD [µm]	−8.429	<0.001
mGCIP IEPD [%]	−8.213	<0.001
MOG-ON (bilateral) vs HC		
pRNFL IEAD [µm]	−2.499	0.028
pRNFL IEPD [%]	−3.118	0.009
mGCIP IEAD [µm]	−2.389	0.043
mGCIP IEPD [%]	−2.886	0.020

OCT in unilateral MOG-ON

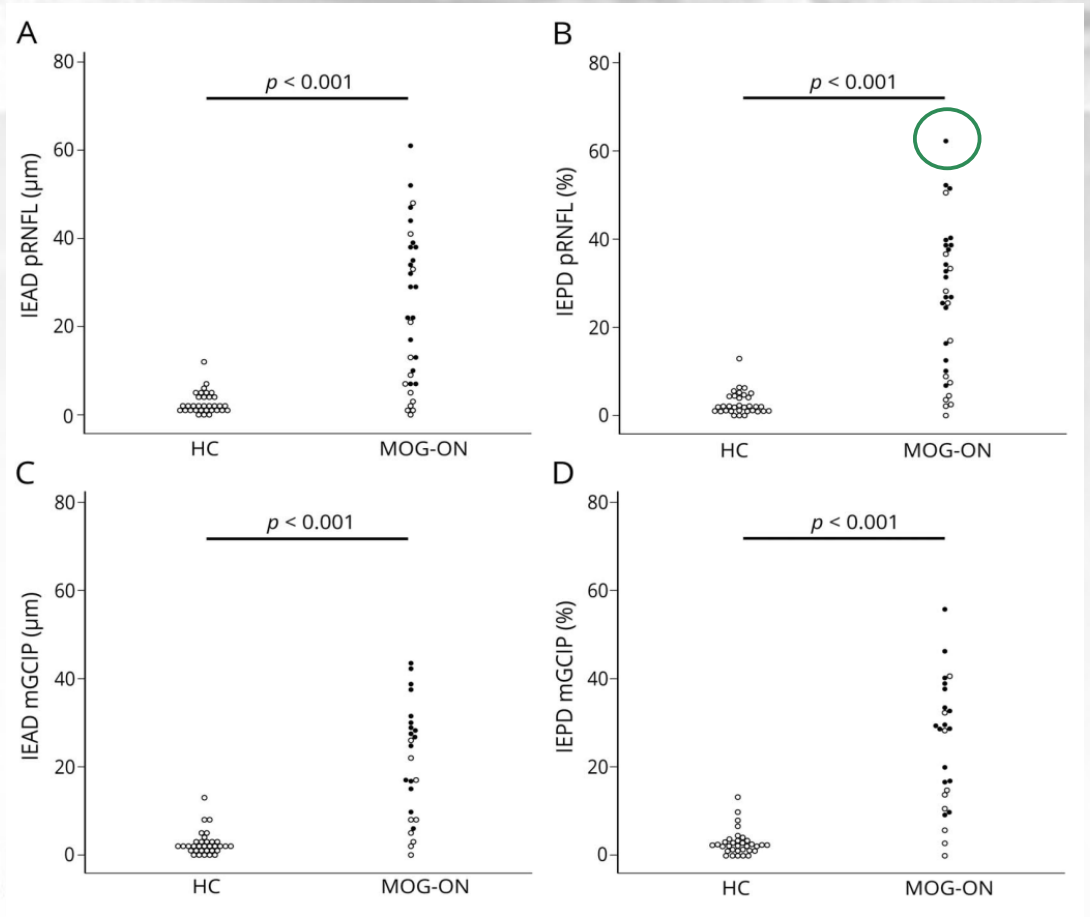
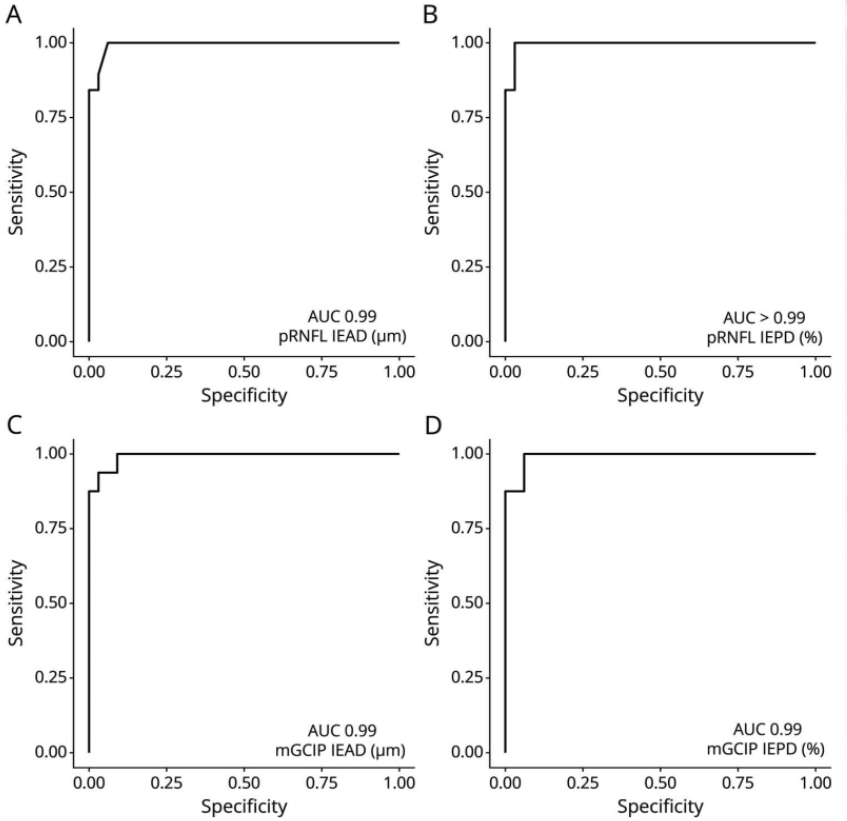


Figure 3 Diagnostic Sensitivity and Specificity of IED in Unilateral MOG-ON



OCT in bilateral MOG-ON

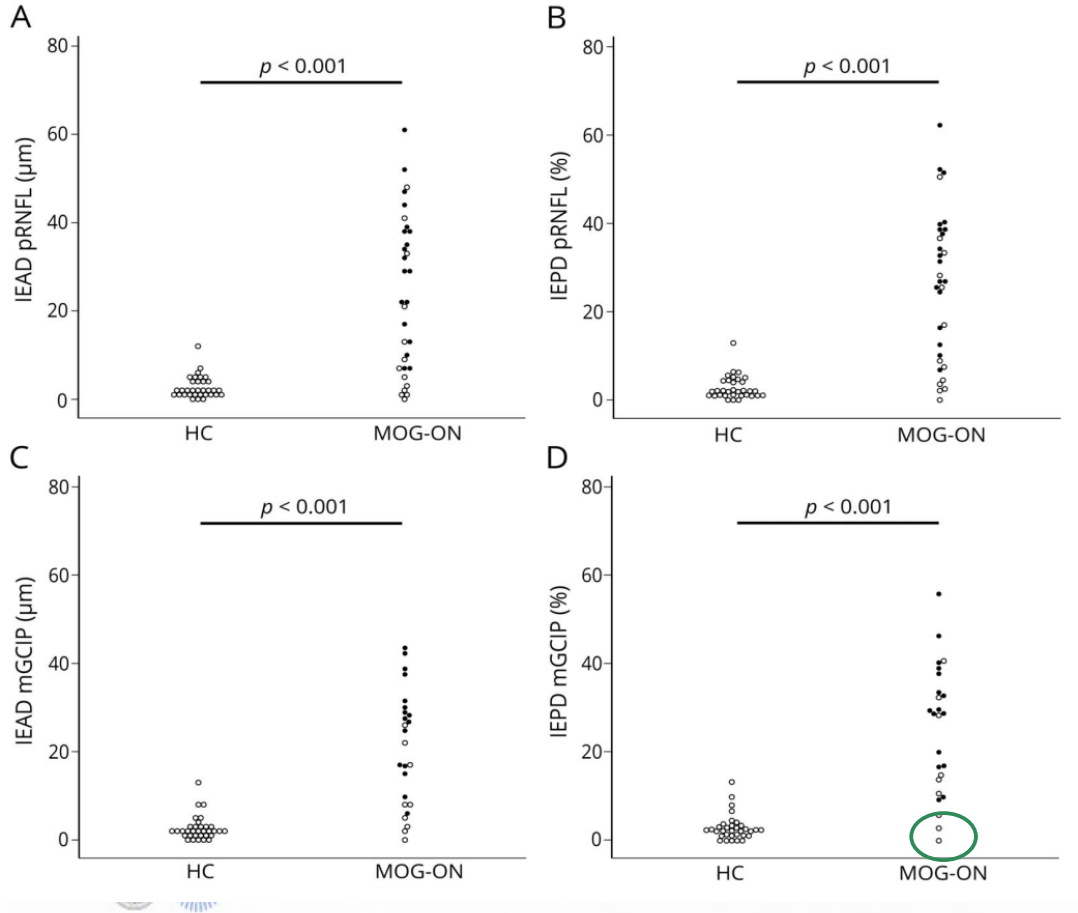
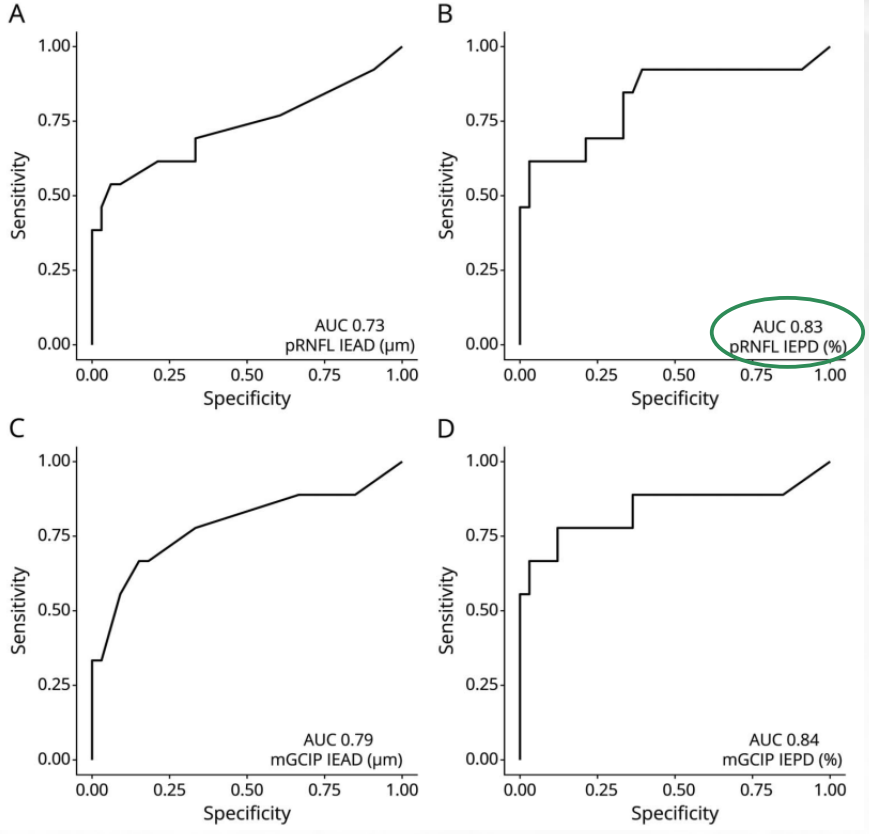


Figure 4 Diagnostic Sensitivity and Specificity of IED in Bilateral MOG-ON



Sensitivity & Specificity

Table 3 Diagnostic Sensitivity and Specificity of IED in MOG-ON

	AUC	95% CI	Specificity (%)	Sensitivity (%)	Positive predictive value	Negative predictive value
MOG-ON vs HCs						
pRNFL IEAD	0.89	0.80–0.98	79	84	0.80	0.83
pRNFL IEPD	0.93	0.86–1.0	82	84	0.82	0.84
mGCIP IEAD	0.92	0.83–1.0	82	88	0.83	0.87
mGCIP IEPD	0.94	0.86–1.0	82	92	0.84	0.91
MOG-ON (unilateral) vs HC						
pRNFL IEAD	0.99	0.98–1.0	79	≥99	0.74	0.99
pRNFL IEPD	>0.99	0.98–1.0	82	≥99	0.77	0.99
mGCIP IEAD	0.99	0.98–1.0	82	≥99	0.77	0.99
mGCIP IEPD	0.99	0.98–1.0	82	≥99	0.77	0.99
MOG-ON (bilateral) vs HC						
pRNFL IEAD	0.73	0.53–0.93	79	62	0.53	0.84
pRNFL IEPD	0.83	0.67–0.98	82	62	0.57	0.84
mGCIP IEAD	0.79	0.58–1.0	82	67	0.59	0.86
mGCIP IEPD	0.84	0.63–1.0	82	78	0.63	0.90

Validation of OCT in AQP4-ON

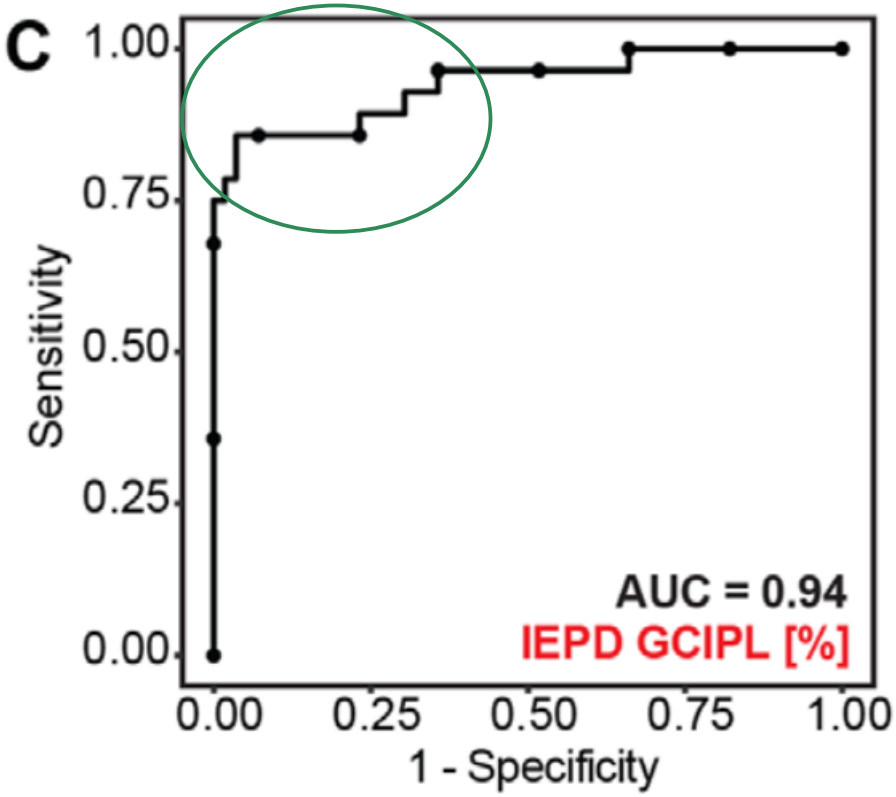


Table 1 Demographic overview

	HC	NMOSD-NON	NMOSD-ON
Subjects (n)	62	45	28
Eyes (n)	124	90	56
Patients with a disease duration <10 years (n)	.	43	21
Patients with ON as first manifestation (n)	.	.	17
Age (year, mean±SD)	37.7±10.2	39.0±10.4	38.8±12.1
Sex (male, n (%))	20 (32)	2 (4)	3 (11)
Time since ON (year, median (min–max))	.	.	2.8 (0.7–19.5)
Time since onset (year, mean±SD)	.	3.8±4.0	6.5±5.6

curve (AUC) metrics.

Results The discriminative power was high for NMOSD-ON versus HC for IEAD (pRNFL: AUC 0.95, specificity 82%, sensitivity 86%; GCIPL: AUC 0.93, specificity 98%, sensitivity 75%) and IEPD (pRNFL: AUC 0.96, specificity 87%, sensitivity 89%; GCIPL: AUC 0.94, specificity 96%, sensitivity 82%). The discriminative power was high/moderate for NMOSD-ON versus NMOSD-NON for IEAD (pRNFL: AUC 0.92, specificity 77%, sensitivity 86%; GCIP: AUC 0.87, specificity 85%, sensitivity 75%) and for IEPD (pRNFL: AUC 0.94, specificity 82%, sensitivity 89%; GCIP: AUC 0.88, specificity 82%, sensitivity 82%).

Conclusions Results support the validation of the IED metrics as OCT parameters of the novel diagnostic ON criteria in AQP4+NMOSD.

⇒ OCT parameters of novel diagnostic ON criteria are applicable in AQP4+NMOSD.

Validation of ON Criteria

Journal of Neurology
https://doi.org/10.1007/s00415-024-12335-y

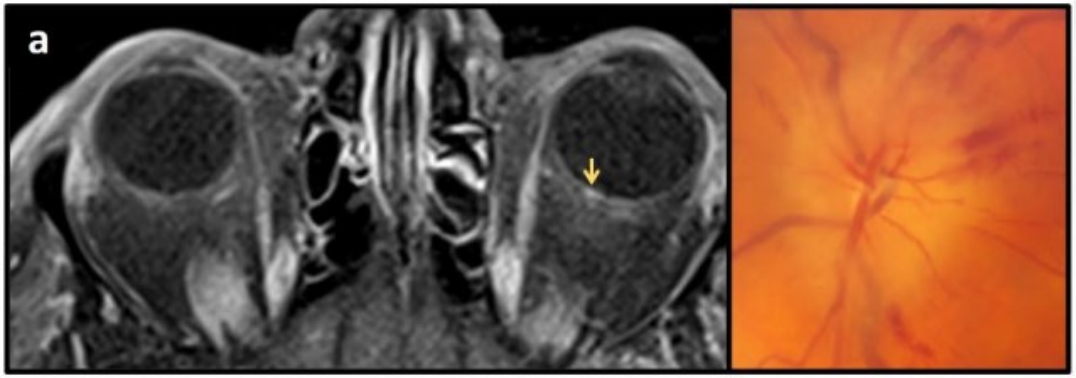
ORIGINAL COMMUNICATION

Check for updates

Applying the 2022 optic neuritis criteria to noninflammatory optic neuropathies with optic nerve T2-hyperintensity: an observational study

Fernando Labella Álvarez[1,6] · Valérie Biousse[1,5,6] · Rasha Mosleh[1,2,6] · Amit M. Saindane[3,4] · Nancy J. Newman[1,4,5,6]

150 patients
acute to chronic



Specificity 97.4 %

4 patients with an ischaemic optic neuropathy had MRI Gd+ of the optic nerve head.

Validation of ON Criteria

Journal of Neurology
https://doi.org/10.1007/s00415-024-12540-9

SHORT COMMENTARY

Diagnostic criteria for optic neuritis in the acute and subacute phase: clinical uses and limitations

Z. Duvigneaud[1] · P. Lardeux[1] · S. Verrecchia[1] · L. Benyahya[2] · R. Marignier[2,3] · C. Froment Tilikete[1,3]

257 patients subacute

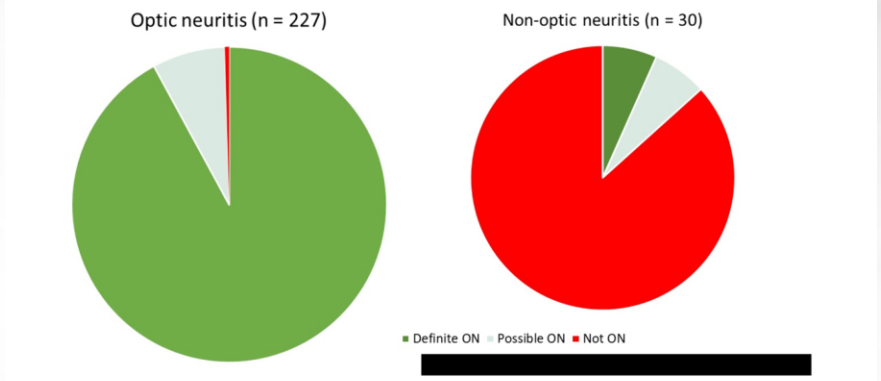


Fig. 1 Representation of the contingency table. Left: among 227 final diagnoses of optic neuritis, one false-negative was found with the new diagnostic criteria. Right: among 30 final diagnoses of non-optic neuritis, four false-positives were found with the new diagnostic criteria

Based on prevalence of 88% authors calculate sensitivity 99.5%, Specificity 86.7%.

1 false negative: neurosyphilis

4 false positive: 2 LHON, 2 infiltrative.

(2/257: specificity 99.3%)

Conclusion

- Practical application of ICON 2022 criteria for diagnosing and classifying ON
- PPON as a potential model for PIRA
- Retinal asymmetry: inter-eye percentage (%) difference is optimal
- ICON 2022 criteria show excellent diagnostic accuracy in retrospective validation studies

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Thank you