Differential diagnosis of non-MS optic neuropathies

8th Istanbul MS Days
17-OCT-2023;15:30-15:50
axel petzold

Disclosures

Stichting MS Research NL
NIHR UK, UCSF, Amsterdam UMC
Novartis, Roche, Heidelberg Academy

The ICON 2022 story

THE LANCET Neurology

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Optic Neuropathies

Published: September 22, 2022

Executive Summary

Optic neuropathies can reflect a wide range of pathophysiologies, both acquired and inherited. This Series provides an update on the clinical, imaging, and laboratory findings that differentiate these disorders, allowing clinicians to focus their diagnostic studies and optimise treatments. Multimodality optic nerve imaging—including fundus photography, optical coherence tomography, and MRI—has greatly advanced the diagnosis and follow-up of patients with optic neuropathies. Also reviewed in this Series, new evidence shows that optic neuritis can frequently indicate autoimmune neurological disorders, including multiple sclerosis and the recently recognised disease categories of aquaporin-4 antibody-associated neuromyelitis optica spectrum disorder and myelin-oligodendrocyte glycoprotein antibody-associated disease. Early clinical recognition of optic neuritis is, therefore, important for prognosis and treatment. Also reviewed in the Series, a unifying feature in the pathophysiology of hereditary disorders of the optic nerve is mitochondrial dysfunction. Treatments are emerging for optic neuropathies, including immunotherapies and genetic therapies.

Series

Imaging of the optic nerve: technological advances and future prospects
Valérie Biousse, Helen V Danesh-Meyer, Amit M Saindane, Cédric Lamirel, Nancy J Newman
The Lancet Neurology
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Optic neuritis and autoimmune optic neuropathies: advances in diagnosis and treatment
Jeffrey L Bennett, Fiona Costello, John J Chen, Axel Petzold, Valérie Biousse, Nancy J Newman, Steven L Galetta
The Lancet Neurology
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Understanding the molecular basis and pathogenesis of hereditary optic neuropathies: towards improved diagnosis and management
Nancy J Newman, Patrick Yu-Wai-Man, Valérie Biousse, Valerio Carelli
The Lancet Neurology
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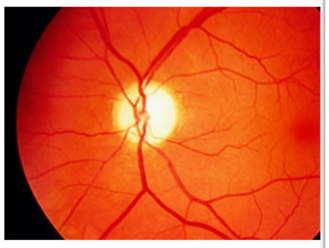

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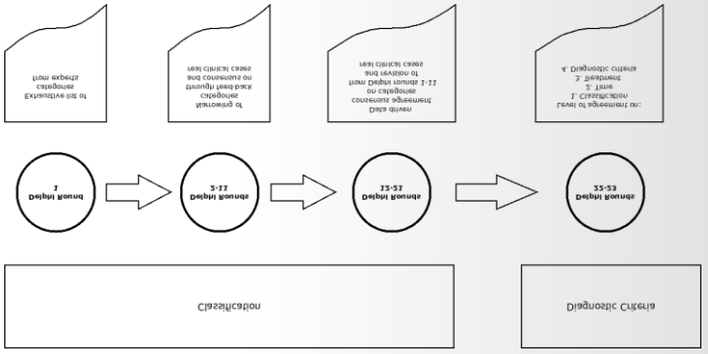
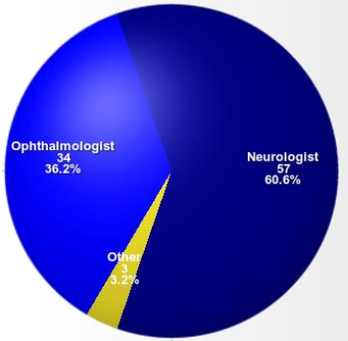
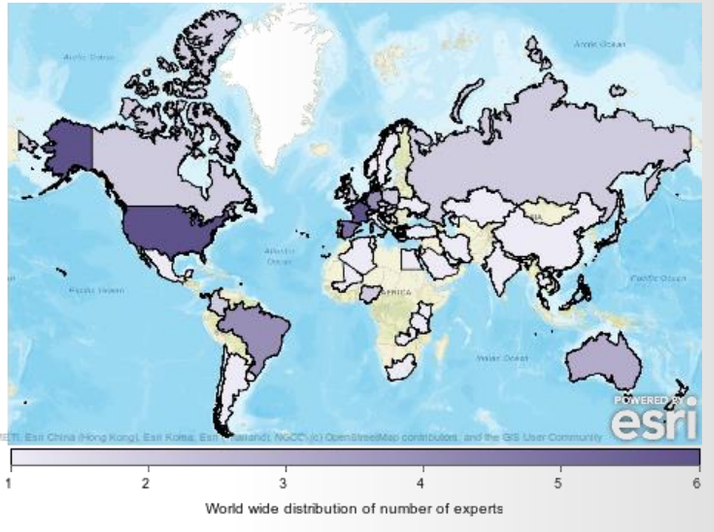
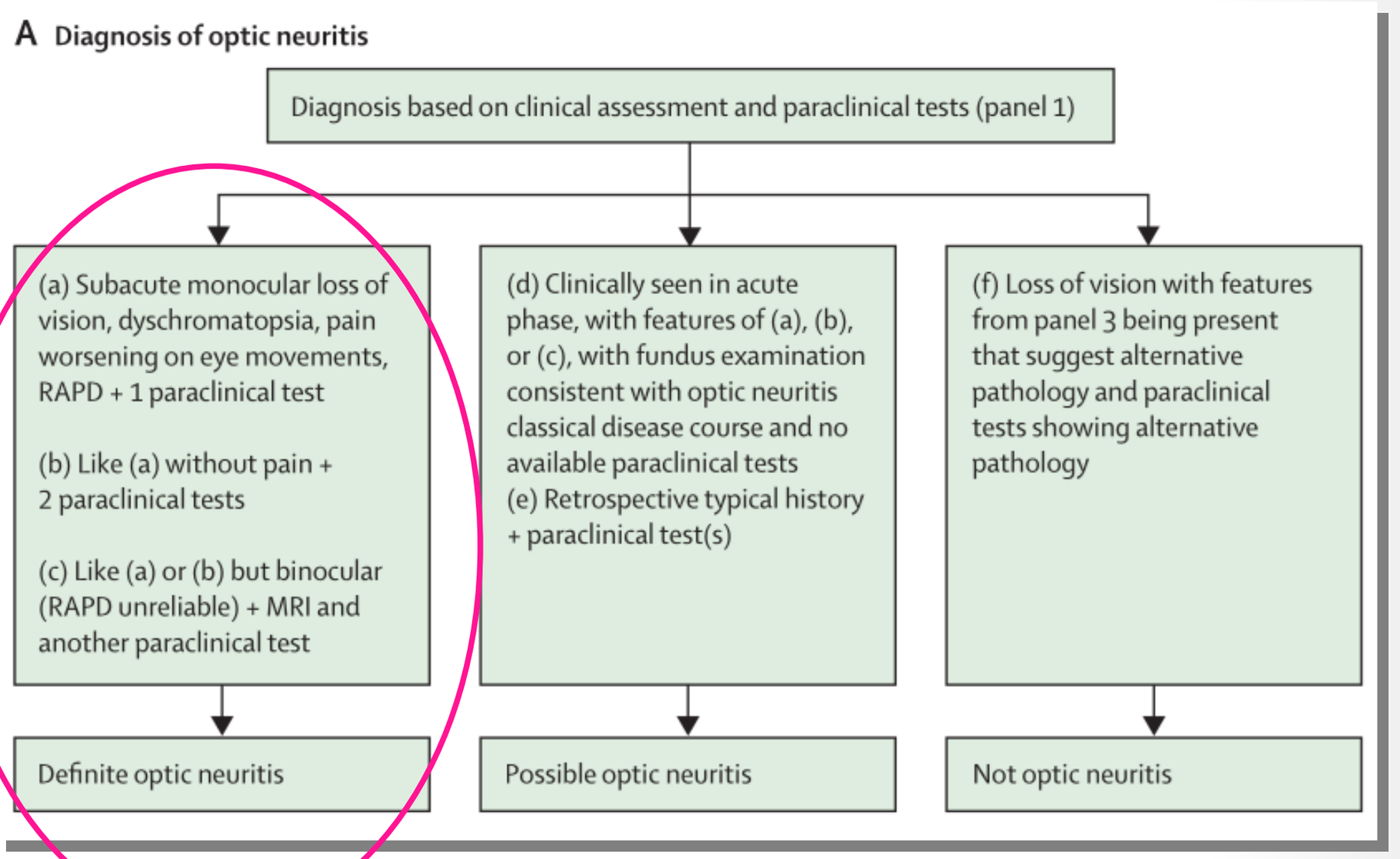


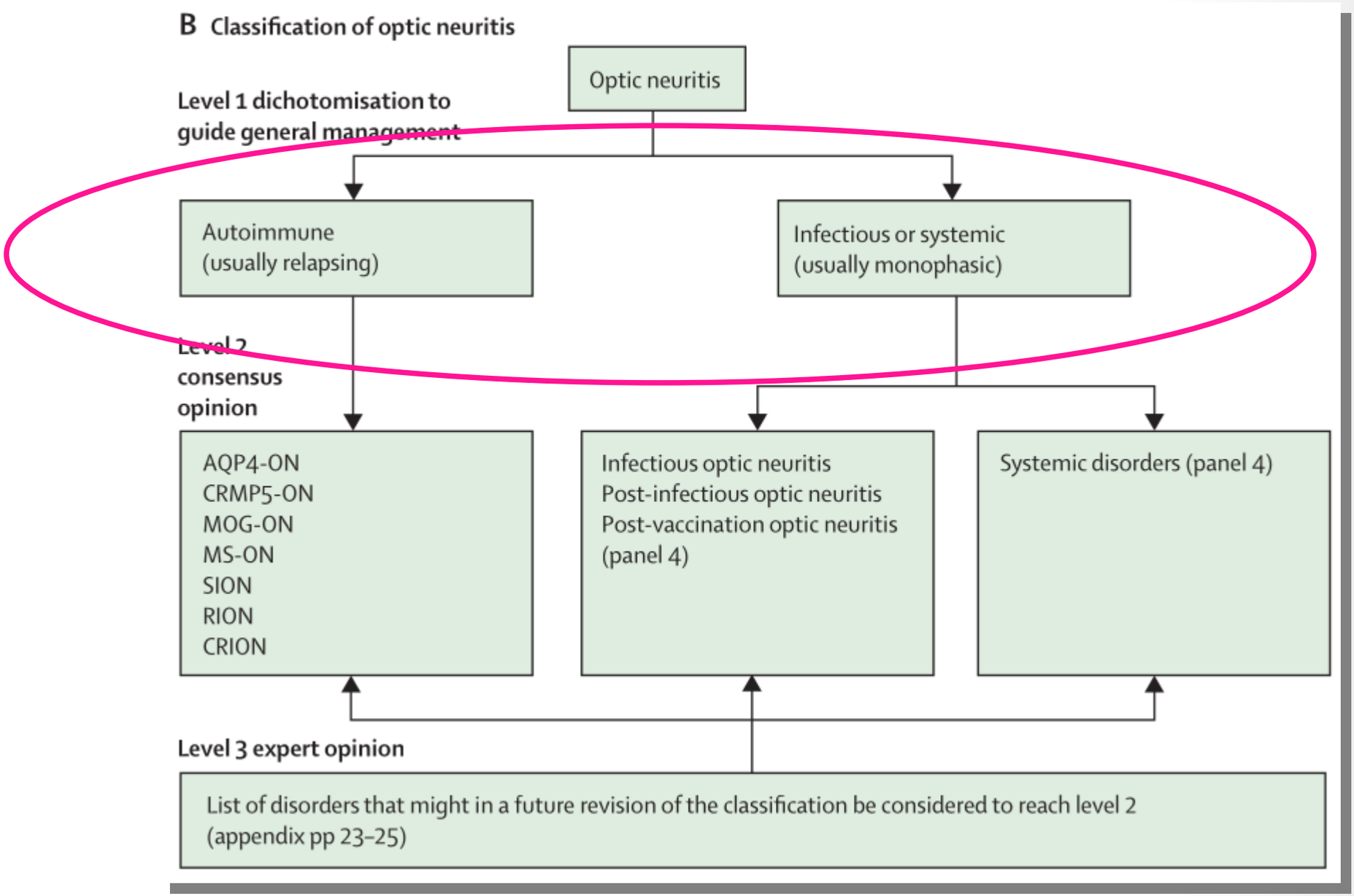




ICON 2022 Diagnostic Criteria



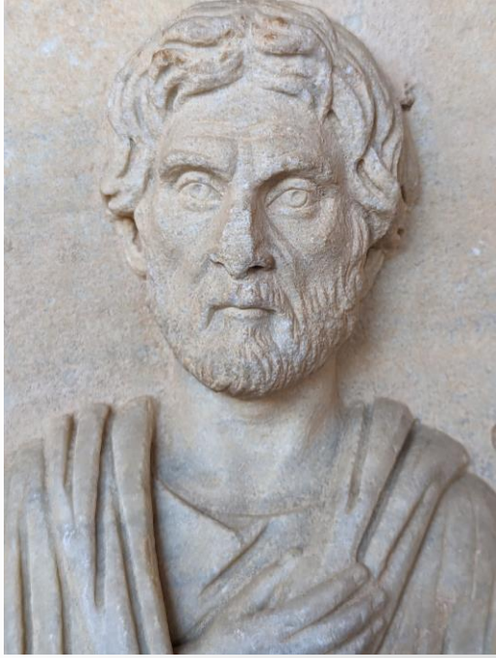
ICON 2022 Classification



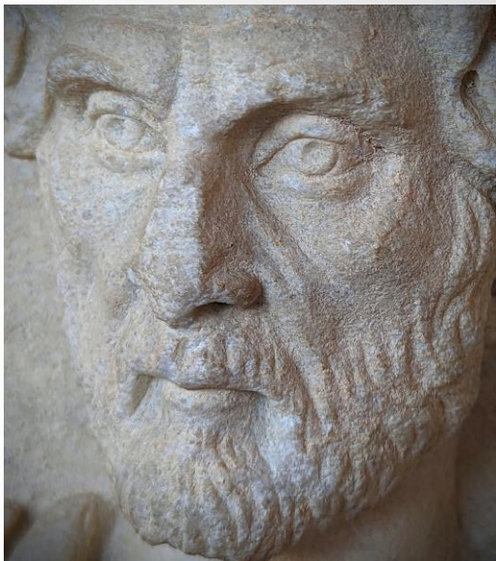
1st Case

- 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, depression
- PmHx: right sided numbness lasting 1m, 3y ago
- MRI: DIS & DIT & 3 Gd+ non-symptomatic lesions

2nd Case

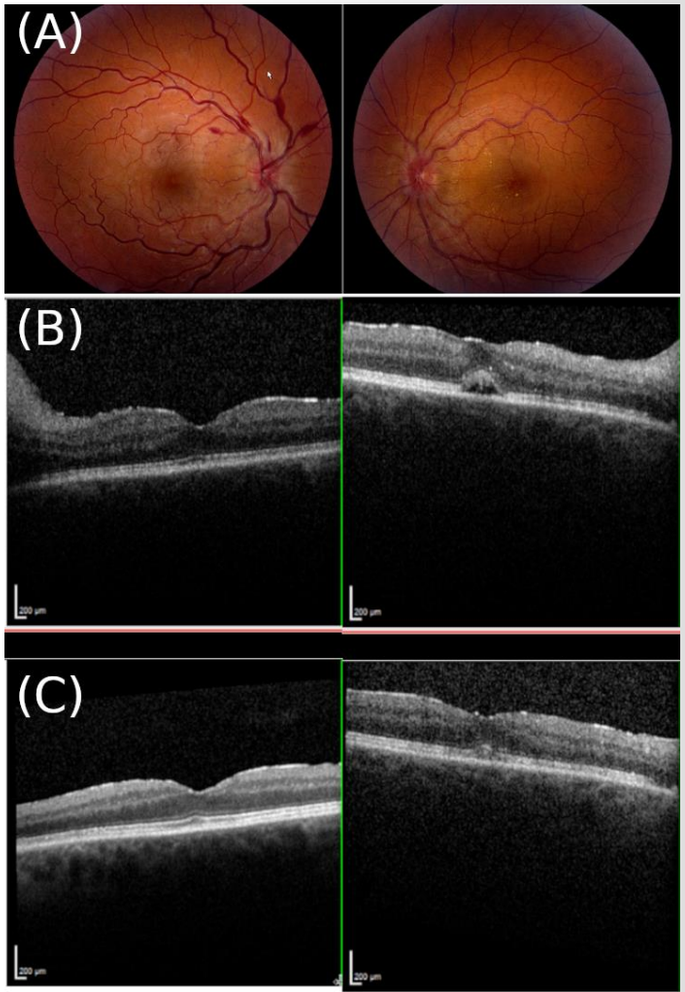


- 28y old, Afrocaribbean male
- Painless loss of vision LE (6/38)
- Dyschromatopsia
- L RAPD
- Several steroid responsive episodes over ~20y fup
- OCT: pRNFL atrophy LE (IEPD >5%)
- MRI a swollen, Gd+, left optic nerve. Brain & spinal cord normal
- AQP4 seropositive



3rd Case

- 72 year old male develops febrile illness in Vietnam
- 2-3 weeks later bilateral, sequential, painless loss of vision (PL)
- no RAPD (but both pupils constrict with accomodation)
- Fundus:
  - Bilateral disc edema
  - RE hemorrhages
  - LE macular scar, CMO
- No recovery @ 6m fup (IVMP given ~6w after onset)



3 Scenarios

- Case 1: is this MS ?

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

- Case 2: is this NMO ?

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

- Case 3: what is this ?

  Scenario C: binocular, subacute LOV, dyschromatopsia, no pain, RAPD unreliable

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).

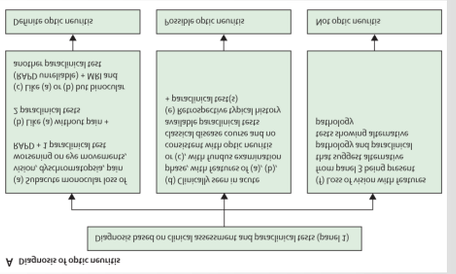
Application of the clinical and paraclinical criteria

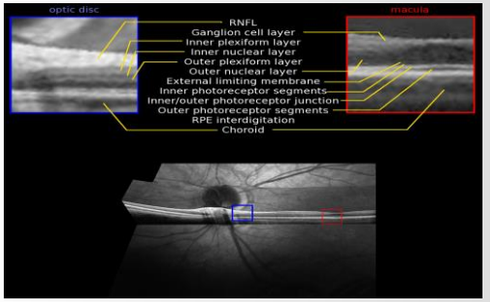
Definite optic neuritis

- (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

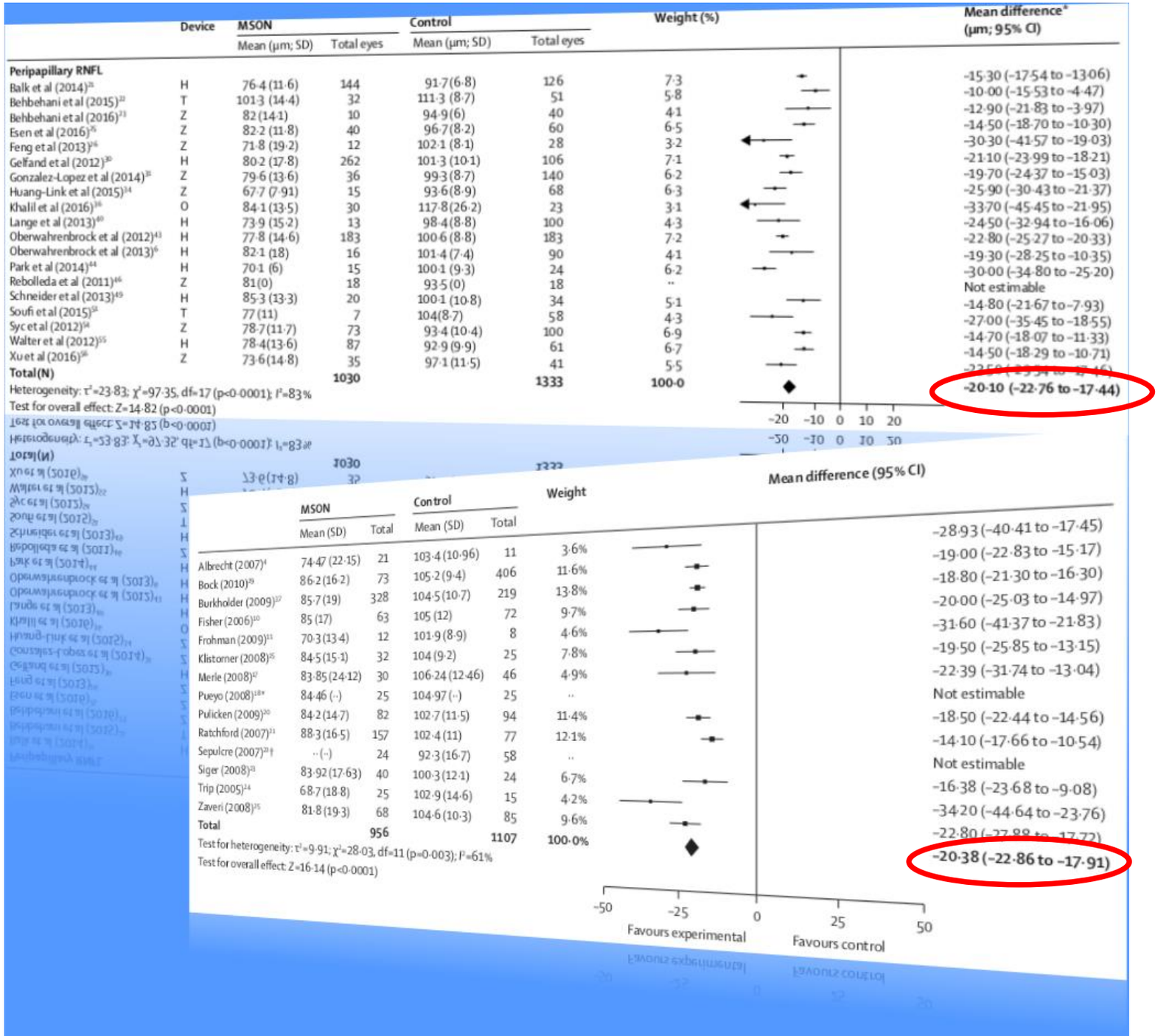
- (A), (B), or (C) if seen acutely but in absence of paraclinical tests, with fundus examination typical for optic neuritis and consistent with the natural history during follow-up
- Positive paraclinical test or tests, with a medical history suggestive of optic neuritis





TLN 2022

OCT in MS-ON



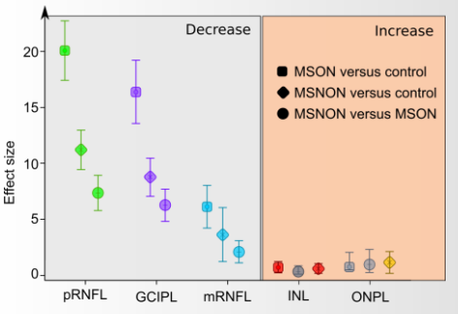
pRNFL atrophy

TLN 2010

20.10 (17.44-22.76) µm

TLN 2017

20.38 (17.91-22.86) µm



4th Case

- 37y old woman 18 month ago
  - expanding central scotoma
  - Periocular pain, score 9/10
  - Photo phobia
- Headaches improved with topiramate
- Visual function with 3 more attacks:
  - BCVA RE 6/9.5, LE 6/24
  - Normal colour vision
  - Left RAPD

4th Case

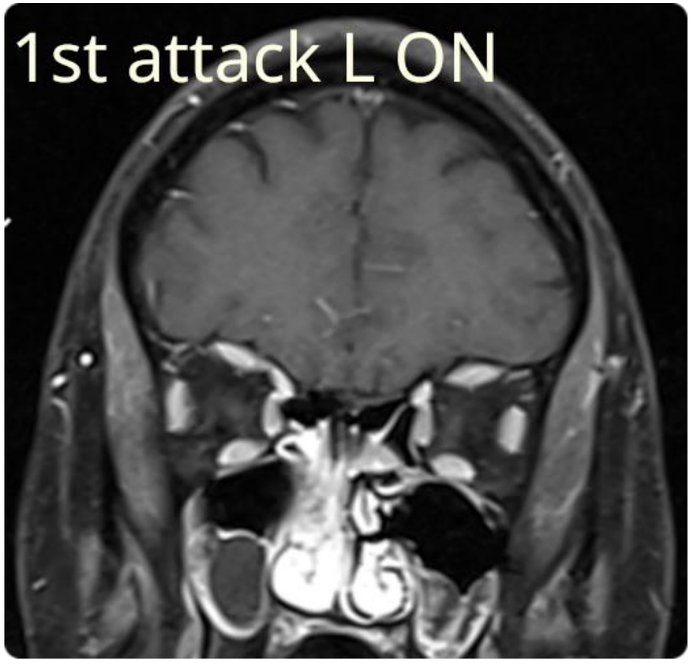
PmHx:

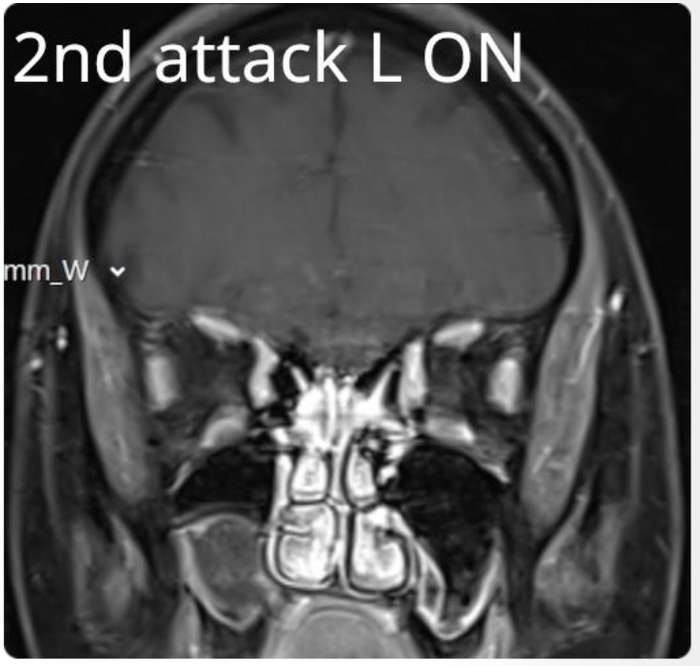
- Recurrent oral ulcers for 9 years
- Erythematous digital nodules & facial rash
- Musculoskeletal pain & fatigue
- GI problems (bloating, diarrhoea, steatorrhoea)

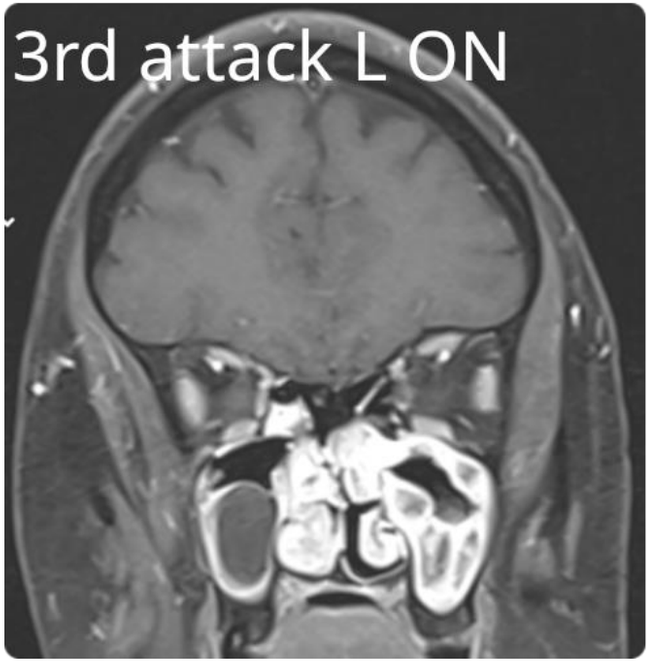
Management in referring hospital:

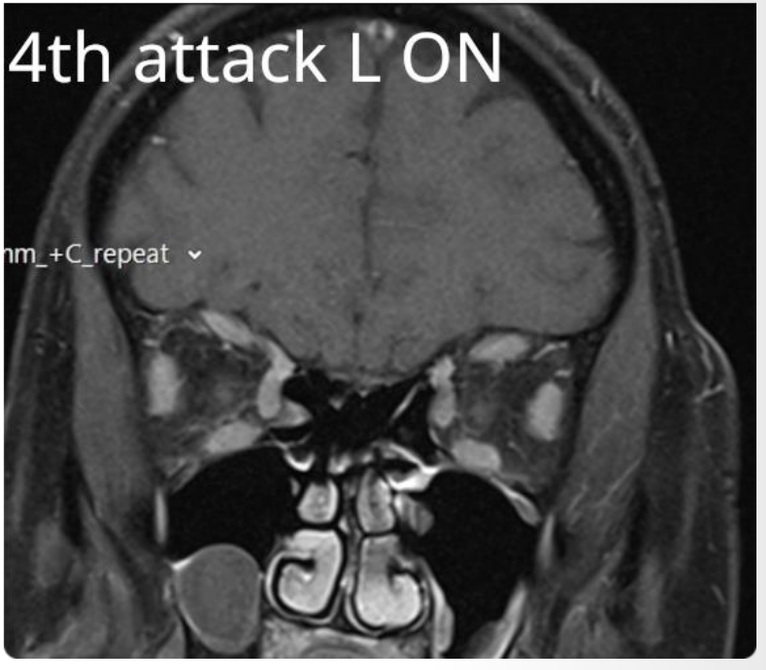
- High dose IV corticosteroids repeatedly for suspected relapsing optic neuritis
  & repeat MRI

MRI


1st attack L ON

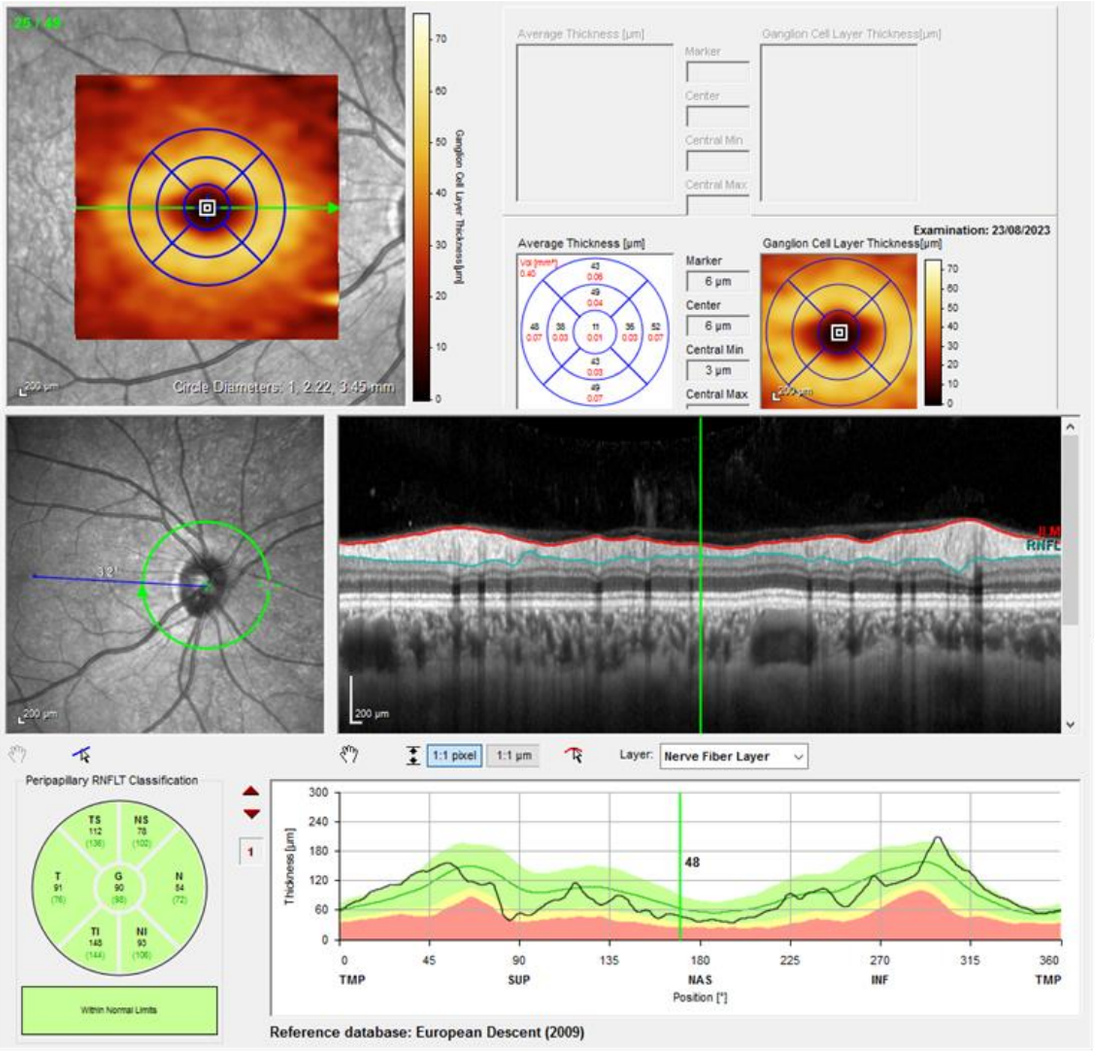

2nd attack L ON
mm_W

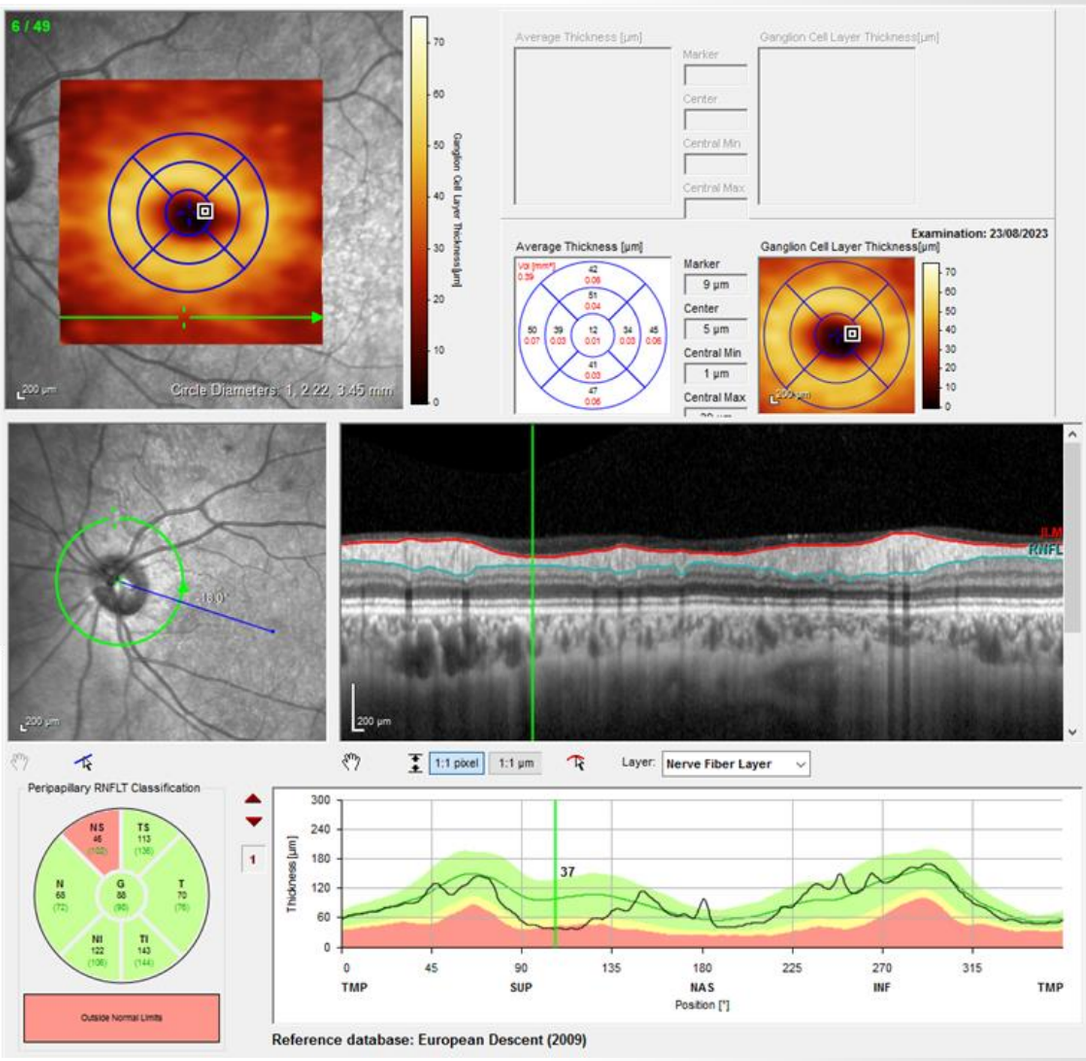

3rd attack L ON


4th attack L ON
nm_+C_repeat

OCT

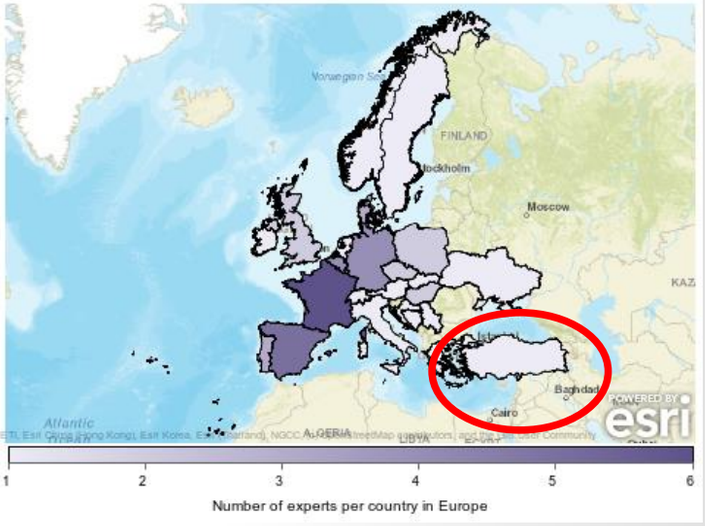
IEPD macular = 2.5% (less than the 4% required)
IEPD disc = 3% (less than the 5% required)





4th Case

- ICON 2022: not optic neuritis
  - Not clinically
  - Not with para-clinical tests



- Dx: acute L superior BRVO pattern recognition on OCT

- DD: Behçet's disease
- National Behçet's Centre @Birmingham

Outlook

ANNALS of Clinical and Translational Neurology
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REVIEW

Artificial intelligence extension of the OSCAR-IB criteria

Axel Petzold[1,2], Philipp Albrecht[3], Laura Balcer[4], Erik Bekkers[5], Alexander U. Brandt[6], Peter A. Calabresi[7], Orla Galvin Deborah[8], Jennifer S. Graves[9], Ari Green[10], Pearse A Keane[1], Jenny A. Nij Bijvank[2], Josemir W. Sander[11,12,13], Friedemann Paul[14], Shiv Saidha[7], Pablo Villoslada[15], Siegfried K Wagner[1], E. Ann Yeh[16], the IMSVISUAL, ERN-EYE Consortium[a]

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November 2023; 10 (6) RESEARCH ARTICLE
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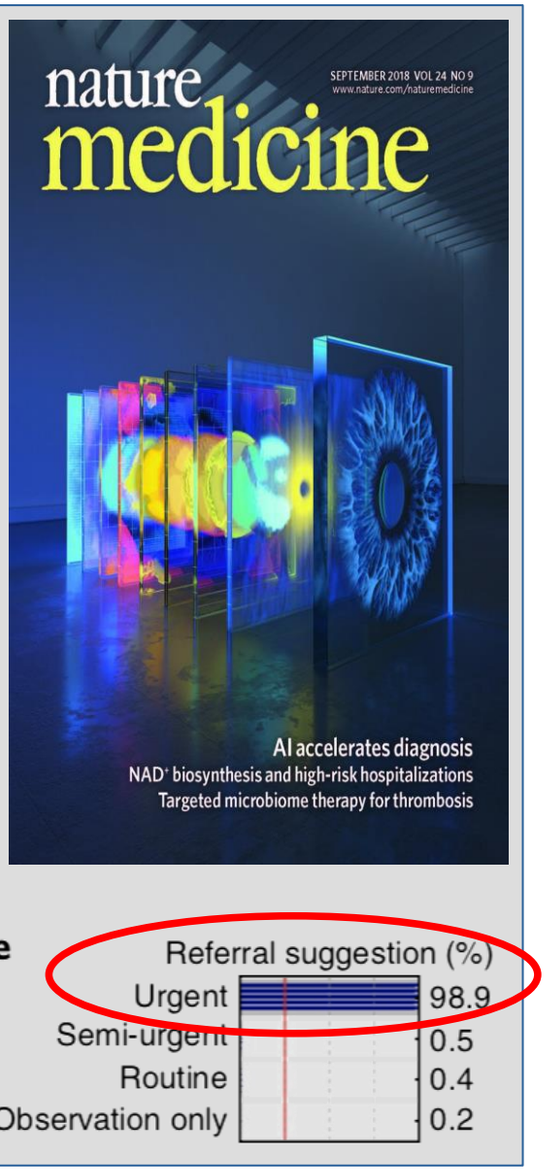
The OSCAR-MP Consensus Criteria for Quality Assessment of Retinal Optical Coherence Tomography Angiography

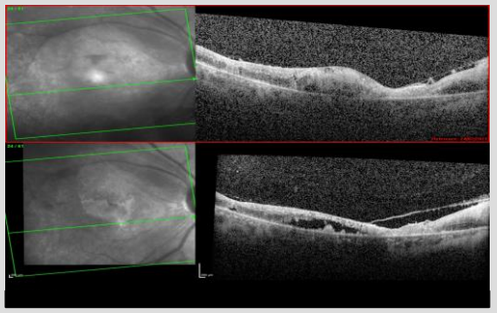
Rebecca Wicklein, Charmaine Yam, Christina Noll, Lilian Aly, Nicolas Banze, Eva Feodora Romahn, Elisabeth Wolf, Bernhard Hemmer, Frederike C. Oertel, Hanna Zimmermann, Philipp Albrecht, Marius Ringelstein, Carmen Baumann, Nikolaus Feucht, Josef Penkava, Joachim Havla, Jonathan A. Gernert, Christian Mardin, Eleni S. Vasileiou, Anneke Van Der Walt, Omar Al-Louzi, Sergio Cabello, Angela Vidal-Jordana, Julia Krämer, Heinz Wiendl, Jana Lizrova Preiningerova, Olga Ciccarelli, Elena Garcia-Martin, Veronika Kana, Peter A. Calabresi, Friedemann Paul, Shiv Saidha, Axel Petzold, Ahmed T. Toosy, Benjamin Knier, ; on behalf of IMSVISUAL Consortium

5th case

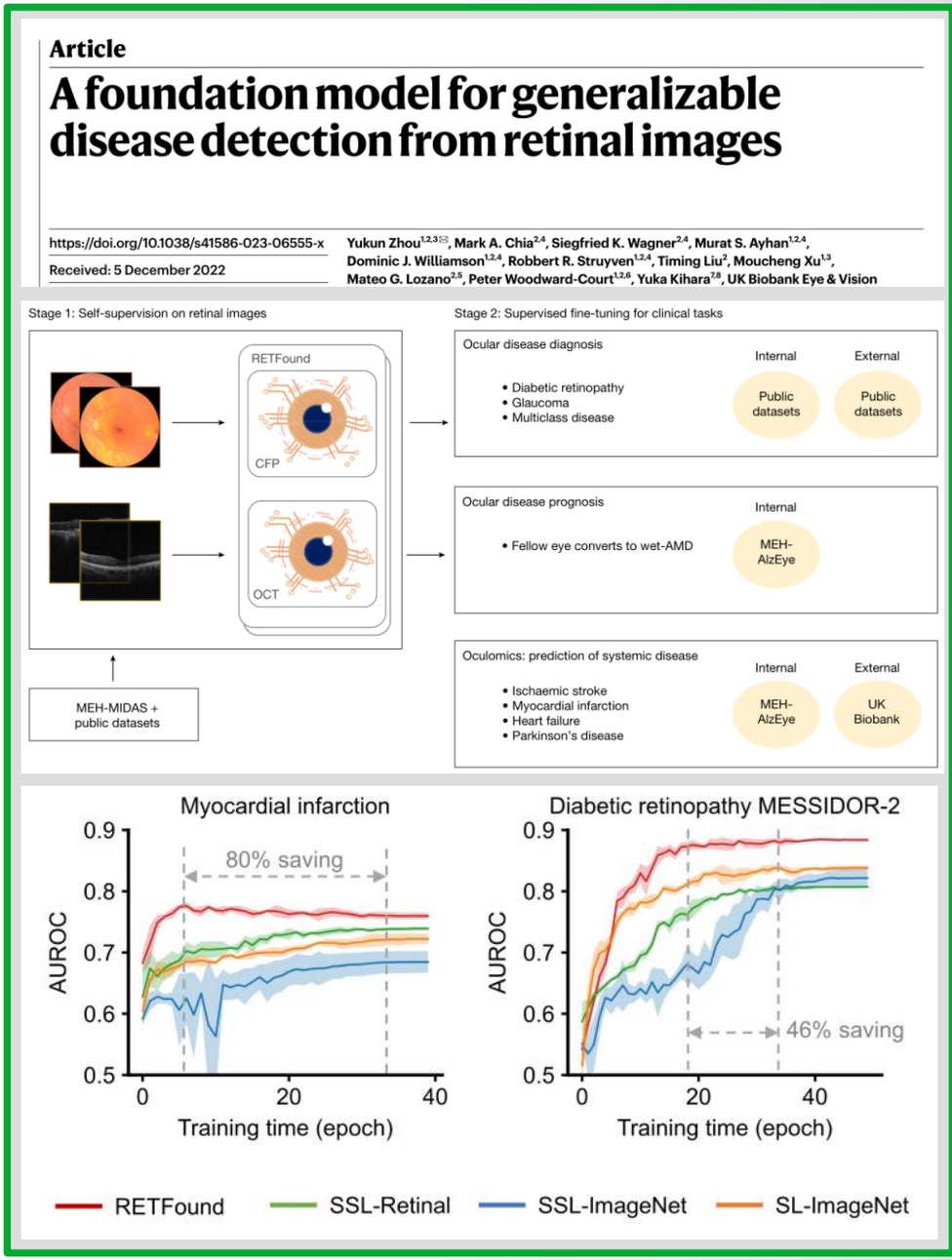
- 32 year old woman with RRMS
- Natalizumab for > 10 years
- Develops progressive cloudy vision in right eye
- Started on corticosteroids for suspected MS-ON
- MRI: no enhancement of right optic nerve, no new lesions
- Vision continues to worsen (HM)
- 22 days after onset seen @MEH
- OCT: …

OCT & AI





- 5th case: VZV vitritis
- Observation: 1.71%
- Routine: 24.09%
- Semi-Urgent: 46.39%
- Urgent: 27.80%



Nature Medicine 2019

Summary

- Clinical approach to ON differential diagnosis
- ICON 2022 Diagnostic Criteria
- ICON 2022 Classification
- 5 Cases: 4 not MS-ON
  - 3 clinical scenarios
- Outlook: AI, pattern recognition, non-supervised learning, EUNOS 2024

Teşekkürler ederim