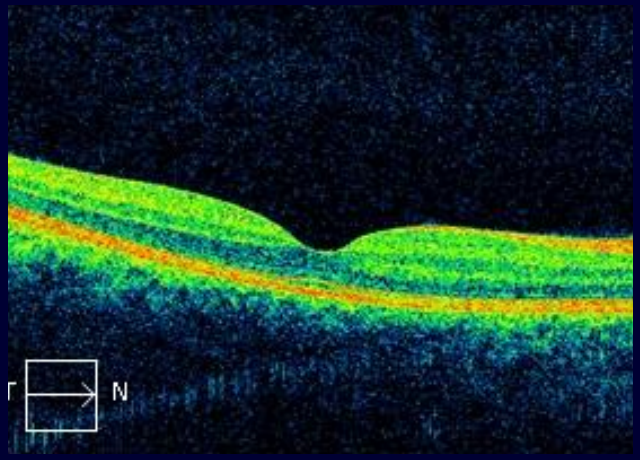
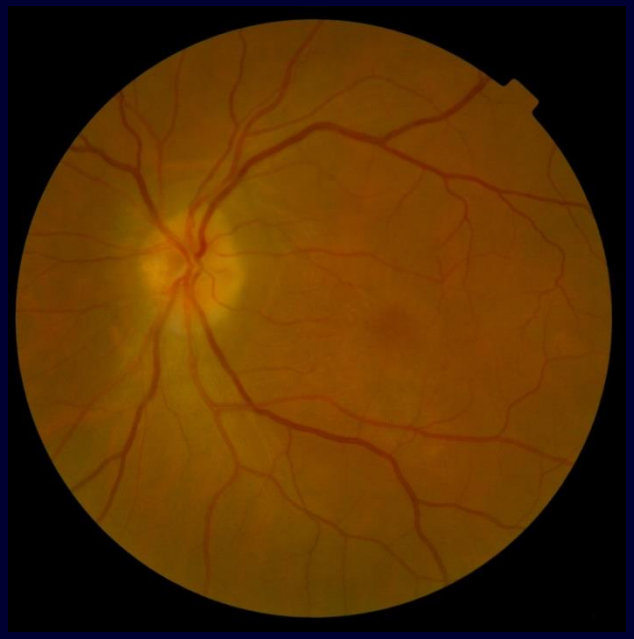
OCT in Multiple Sclerosis: Case by Case





Steven L. Galetta, MD
Philip K. Moskowitz, MD, Professor and Chair
Professor of Ophthalmology
New York University School of Medicine, New York, USA

The speaker has no financial interest in any of the tests or devices discussed in this presentation

The Value of OCT in MS Cases

- Subtle or Subclinical Disease
- Key in Differential Diagnosis
- Predict Progression of Disease

Case Scenario 1
(Early or Subtle Disease)

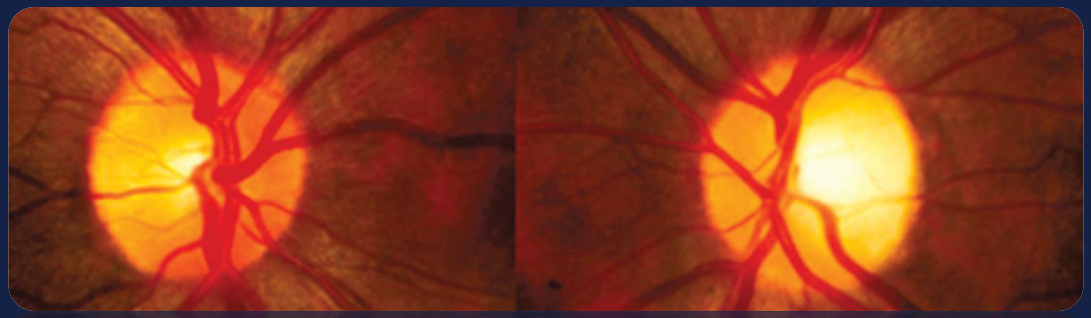
A 33-year-old woman who was referred to the clinic after having a transient episode of numbness in the right arm and right leg.

She has history of having an episode of transient decreased vision in the left eye 8 months ago; since then the vision in the left eye has improved

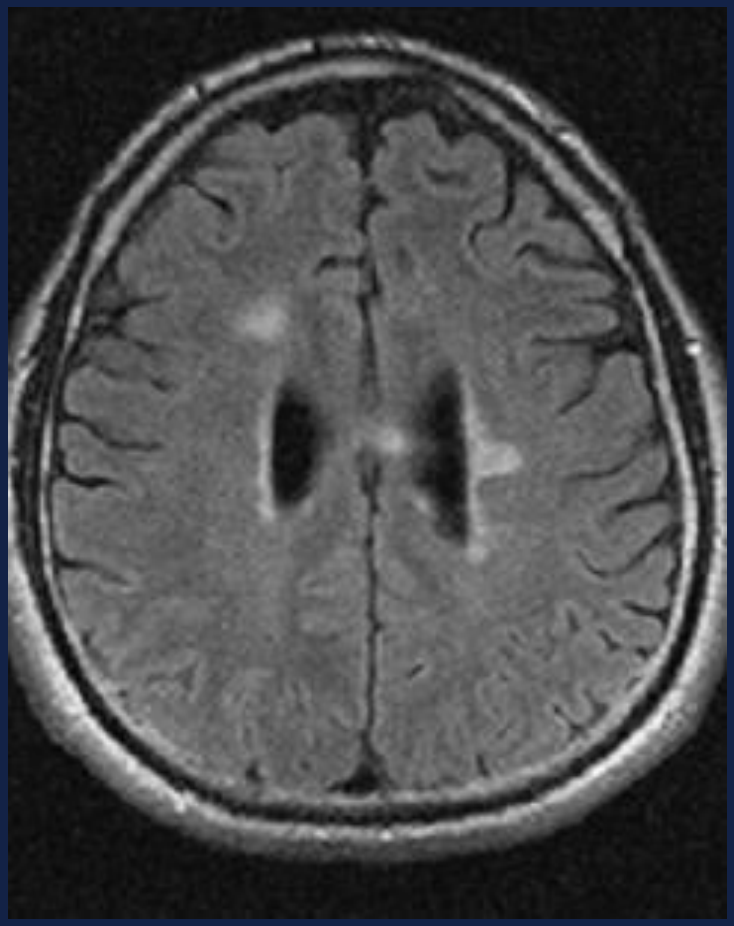
Past medical history was unremarkable

On examination, visual function was said to be normal in both eyes

The left optic disc was pale temporally; OCT RNFL 78 microns in left eye



MRI Showed Scattered T2 Changes



30-Year-Old Woman

- Relapsing-remitting multiple sclerosis (MS)
- Acute optic neuritis (ON) in the right eye 10 years ago
- Typical, stable brain MRI, normal spine
- On IFN beta-1a weekly, compliant

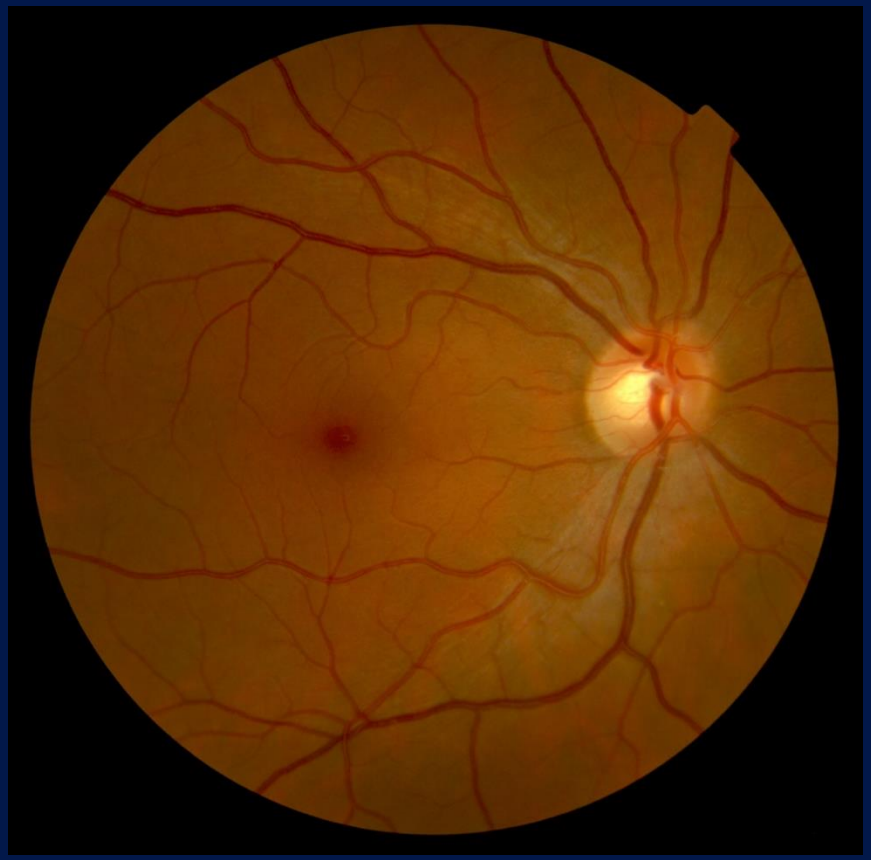
New Right Eye Pain

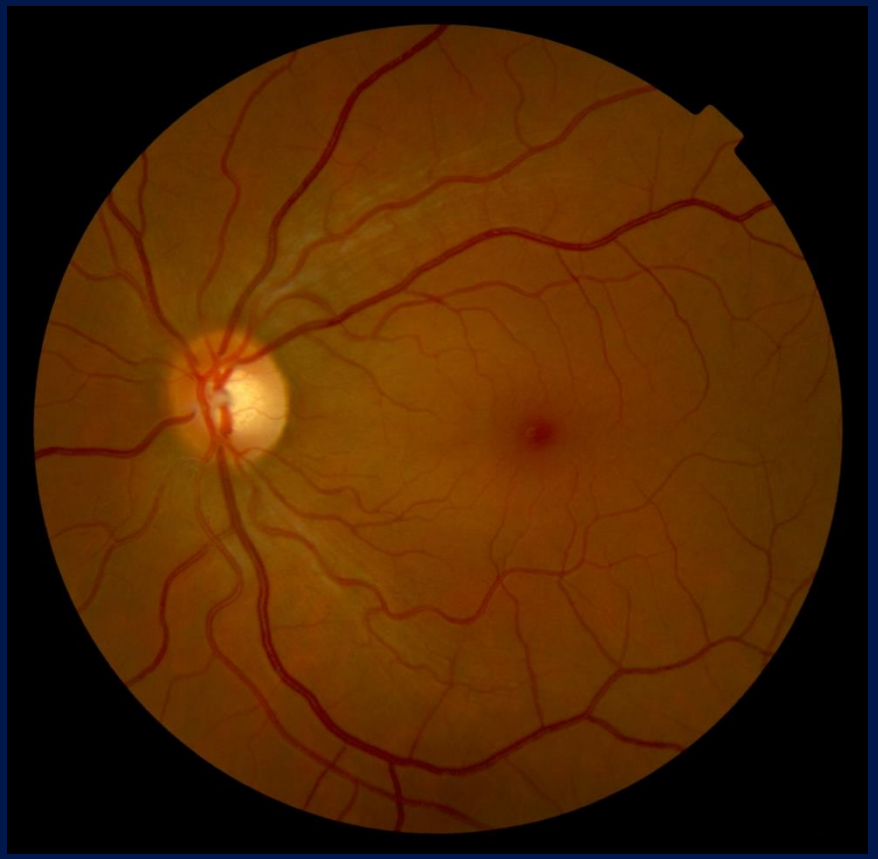
- “The same” as her pain with ON during the episode 10 years ago
- Worse on eye movement, pushing on globe, putting on makeup
- No visual symptoms

Examination
(1 day later)

- Visual acuities 20/15 -2 OU
- Pupils equal, brisk, no APD
- Visual fields, color: full
- Normal ocular motility (pain)

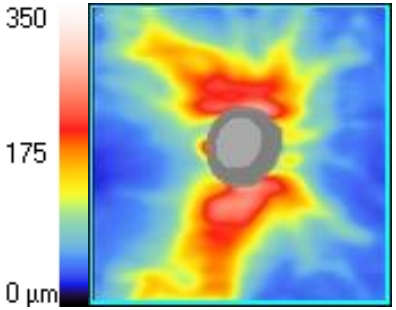
Examination





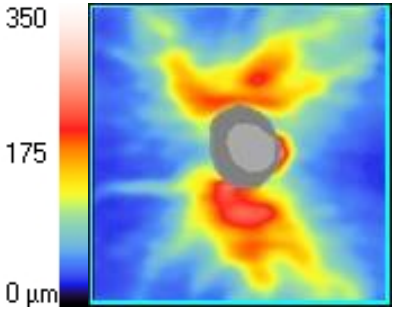
OCT Retinal Nerve Fiber Layer (RNFL) Thickness

RNFL Thickness Map



	OD	OS
Average RNFL Thickness	115 µm	108 µm
RNFL Symmetry	90%	
Rim Area	1.22 mm²	1.15 mm²
Disc Area	1.97 mm²	1.90 mm²
Average C/D Ratio	0.62	0.63
Vertical C/D Ratio	0.62	0.59
Cup Volume	0.287 mm³	0.278 mm³

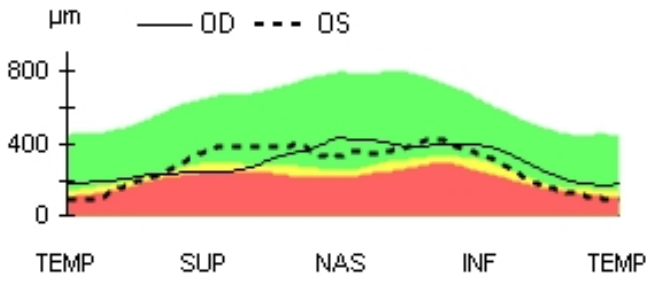
RNFL Thickness Map



RNFL Deviation Map

Disc Center(0.06,0.21)mm
Extracted Horizontal Tomogram

Neuro-retinal Rim Thickness



RNFL Thickness

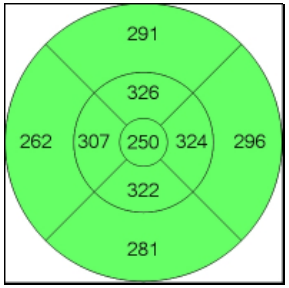
RNFL Deviation Map

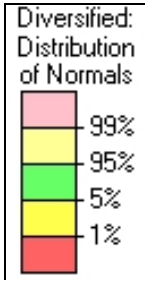
Disc Center(0.06,0.18)mm
Extracted Horizontal Tomogram

OCT Macular Thickness

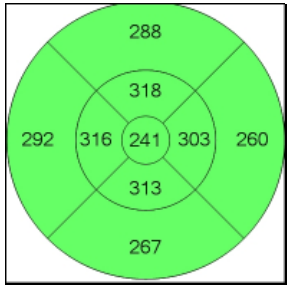
OD OCT Fundus

OD ILM-RPE Thickness





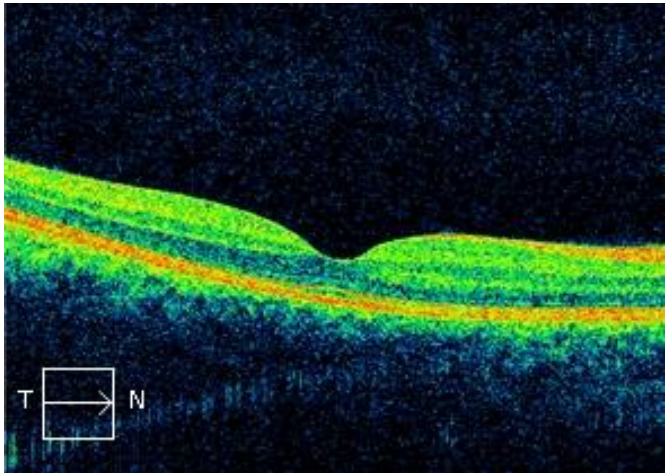
OS ILM-RPE Thickness



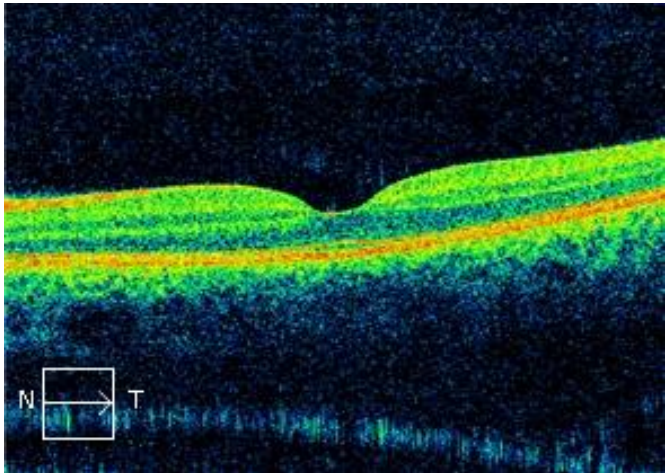
OS OCT Fundus

ILM - RPE	OD	OS
Thickness Central Subfield (µm)	250	241
Volume Cube (mm³)	10.4	10.1
Thickness Avg Cube (µm)	288	281

OD Horizontal B-Scan **BScan:** 64



OS Horizontal B-Scan **BScan:** 63

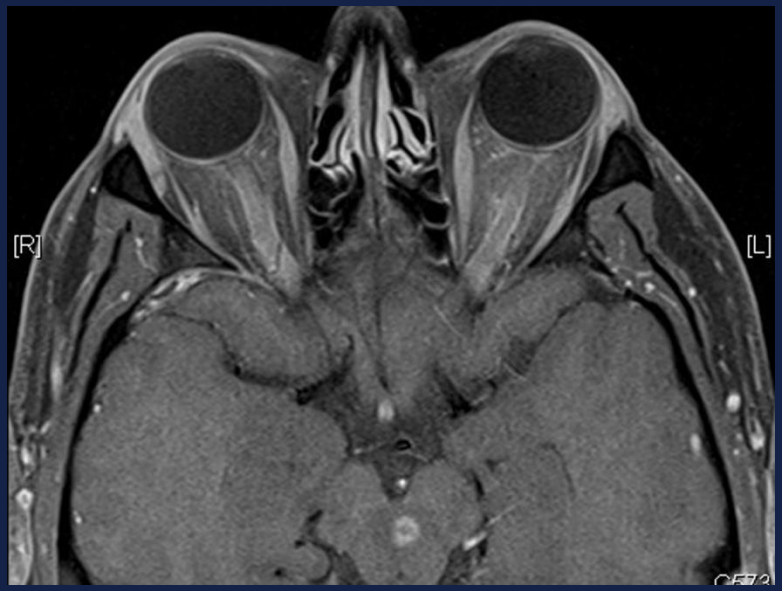


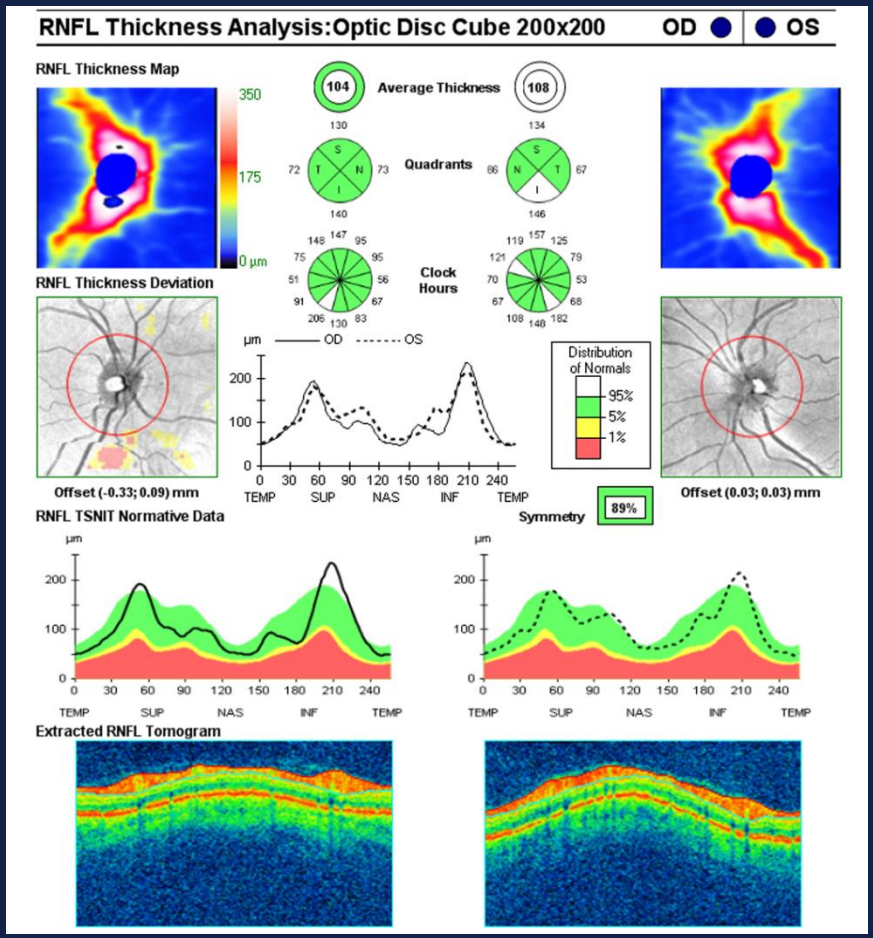
Acute Optic Neuritis – Pain Without Obvious Visual Loss

- More frequent than we think?
- Our case: hint of disc swelling
- OCT was helpful clinically to detect

Case Scenario 2
(The Differential Diagnosis)

NMO and OCT


[R]
[L]

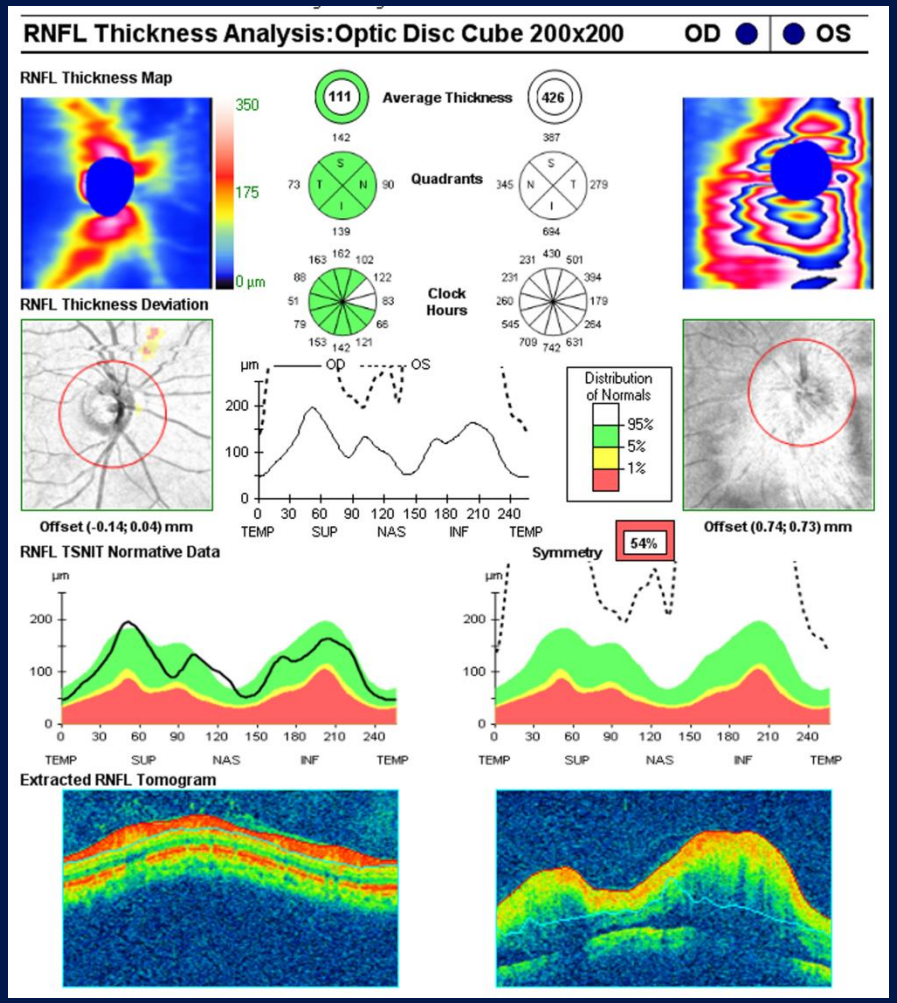

RNFL Thickness Analysis:Optic Disc Cube 200x200
OD
OS
RNFL Thickness Map
350
175
0 µm
104
Average Thickness
108
130
134
Quadrants
140
146
Clock Hours
RNFL Thickness Deviation
µm
OD
OS
200
100
0
0 30 60 90 120 150 180 210 240
TEMP SUP NAS INF TEMP
Distribution of Normals
95%
5%
1%
Offset (-0.33; 0.09) mm
Offset (0.03; 0.03) mm
Symmetry
89%
RNFL TSNIT Normative Data
Extracted RNFL Tomogram

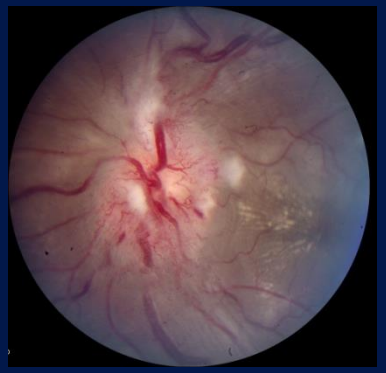
NMO and OCT

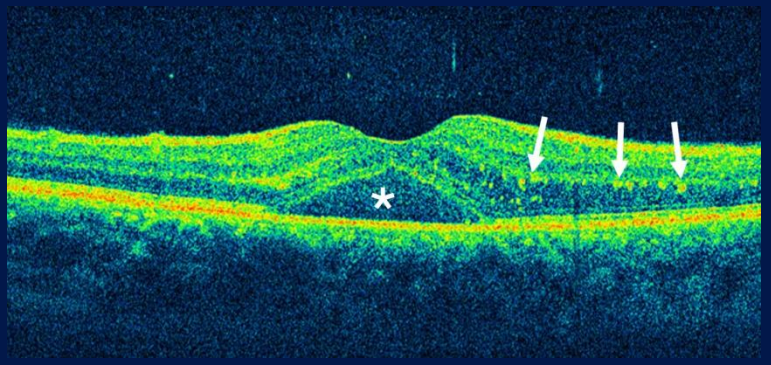
- Average RNFL thickness
  - NMO - 63 microns
  - Typical optic neuritis- 88 microns
  - Controls- 102 microns
- 60 microns or less suggests NMO
- Diffuse loss vs. temporal loss in ON

Neurology 73:302, 2009

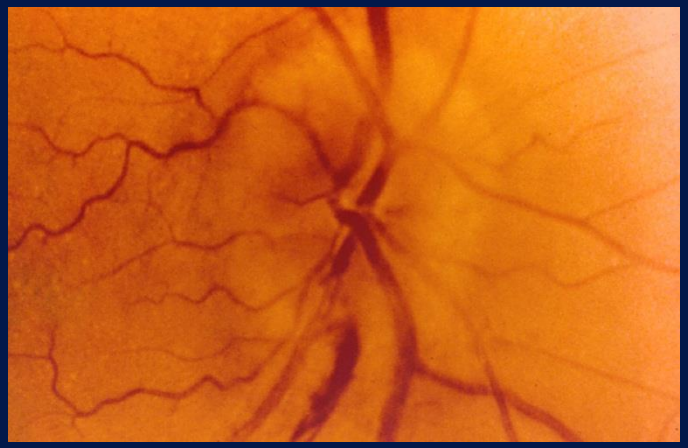
Differential? Neuroretinitis

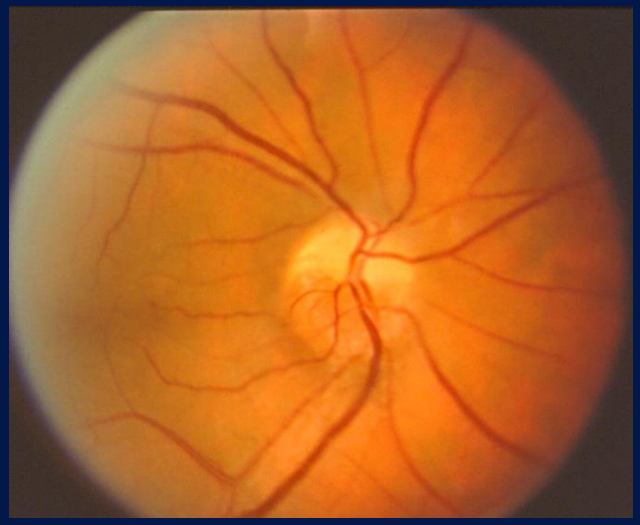


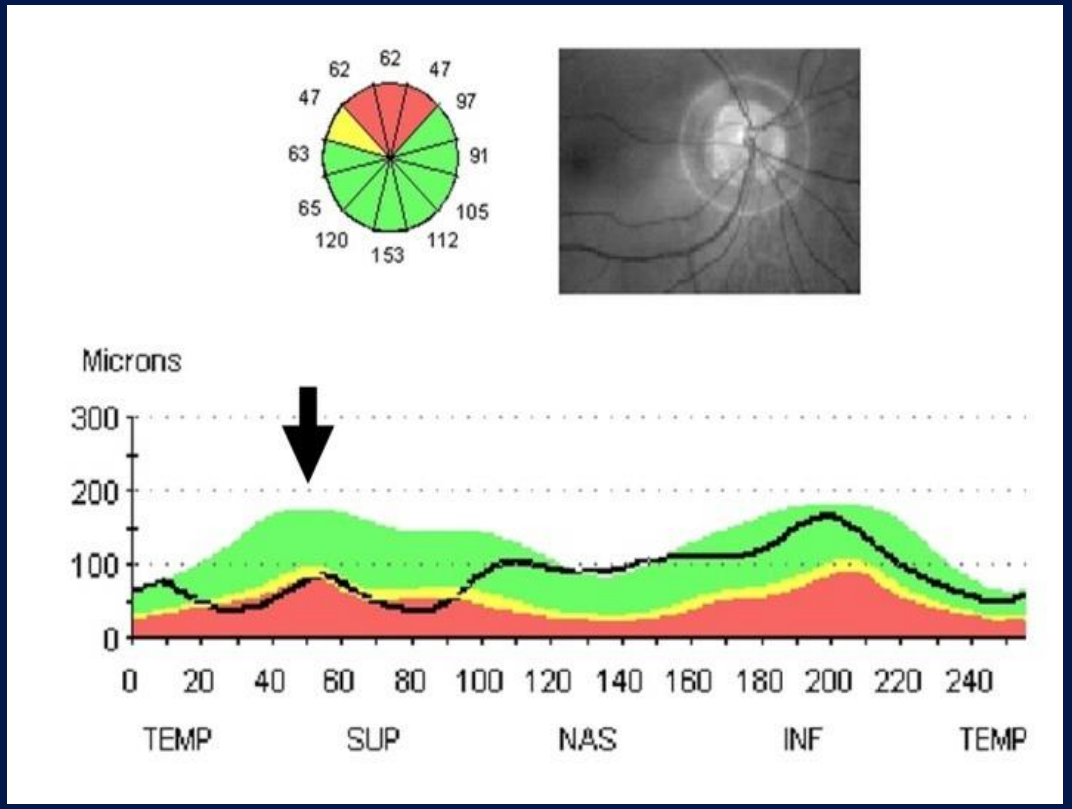




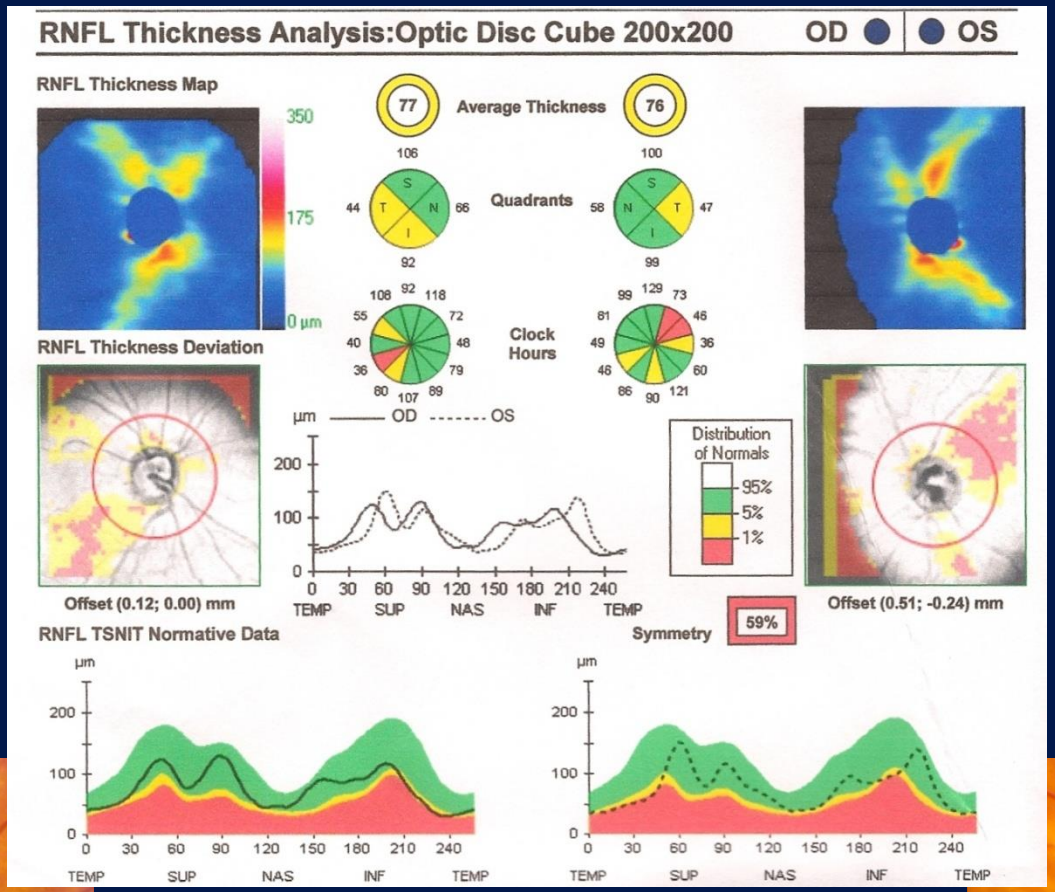
Ischemic Optic Neuropathy (Older Patients)

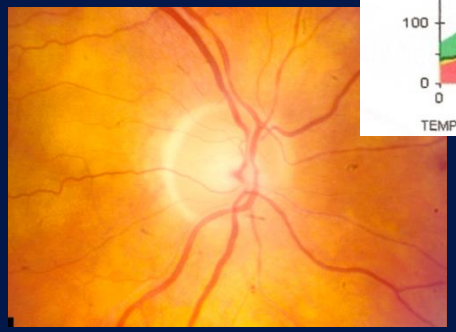


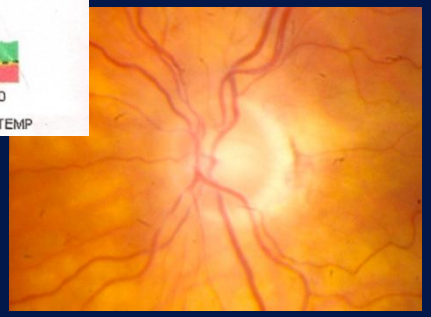




Optic Neuropathy: Copper Deficiency



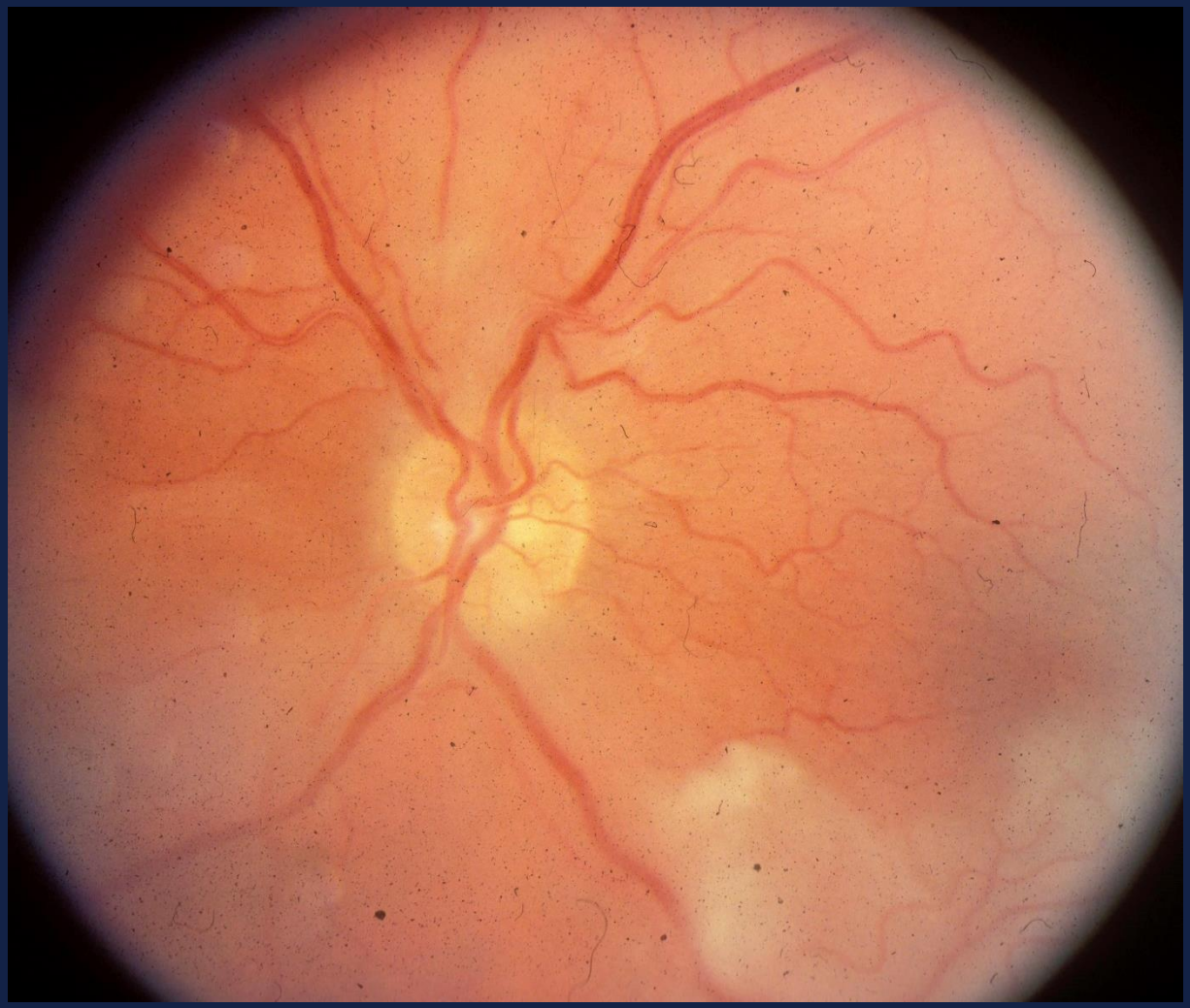


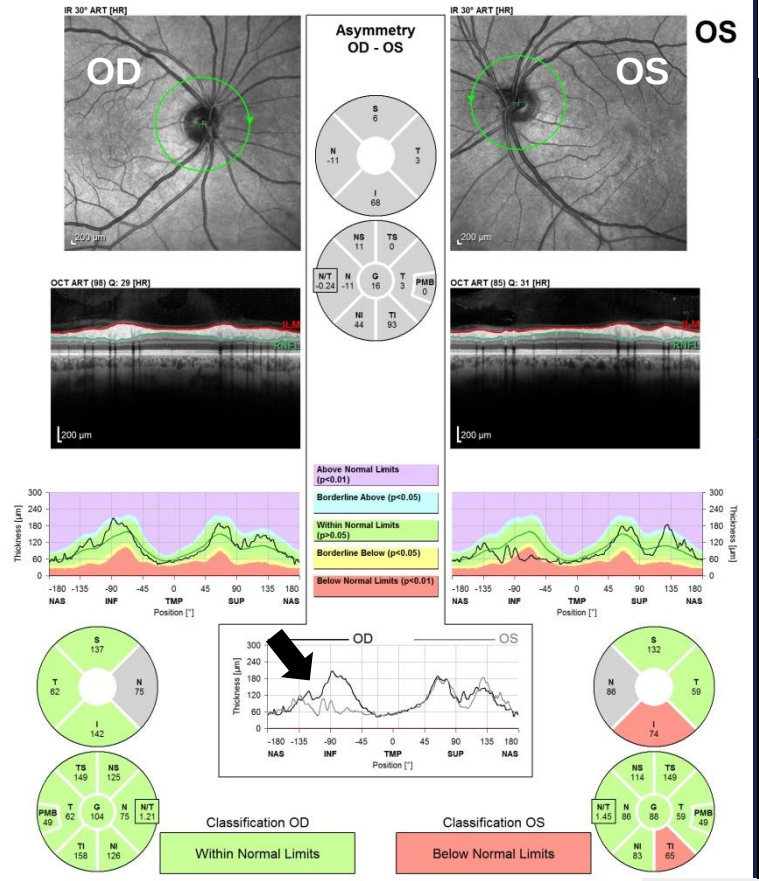


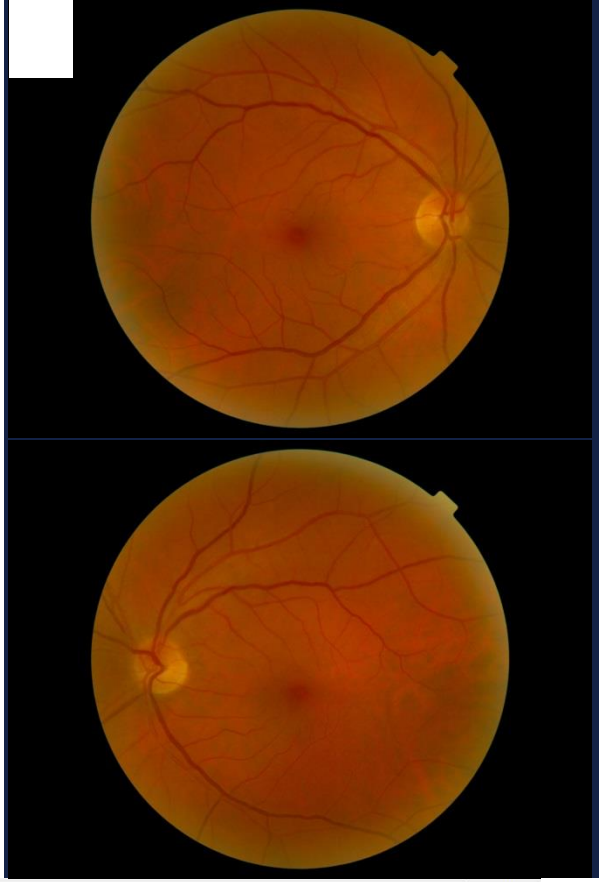
Susac Syndrome

- Encephalopathy
- Retinal artery occlusions
- Sensorineural hearing loss

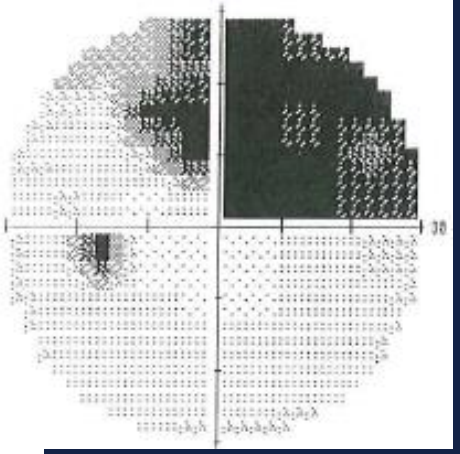
Left Eye Fundus

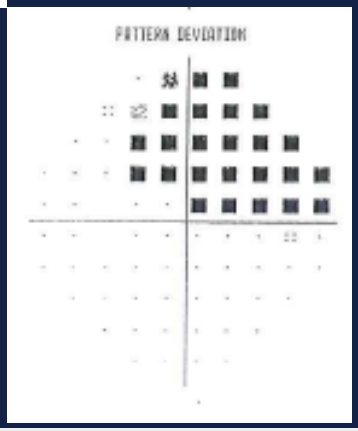


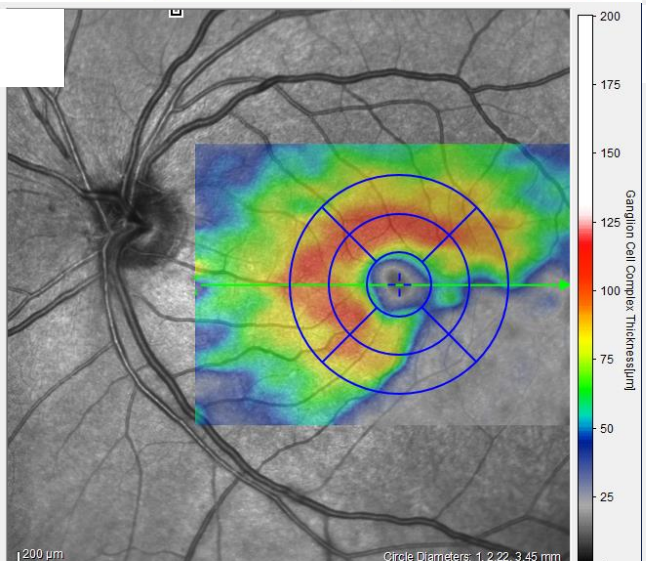

IR 30° ART [HR]
OD
Asymmetry
OD - OS
IR 30° ART [HR]
OS
OS
200 µm
OCT ART (98) Q: 29 [HR]
OCT ART (85) Q: 31 [HR]
200 µm
200 µm
Above Normal Limits (p<0.01)
Borderline Above (p<0.05)
Within Normal Limits (p>0.05)
Borderline Below (p<0.05)
Below Normal Limits (p<0.01)
Thickness [µm]
Position [°]
NAS
INF
TMP
SUP
NAS
OD
OS
Classification OD
Within Normal Limits
Classification OS
Below Normal Limits

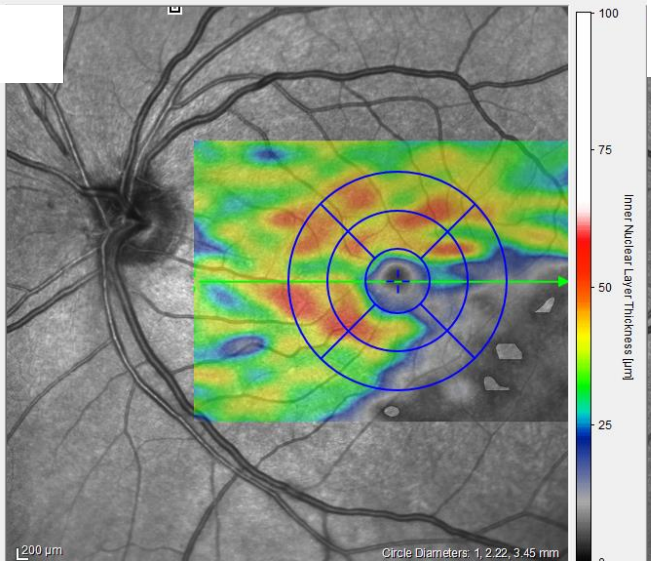


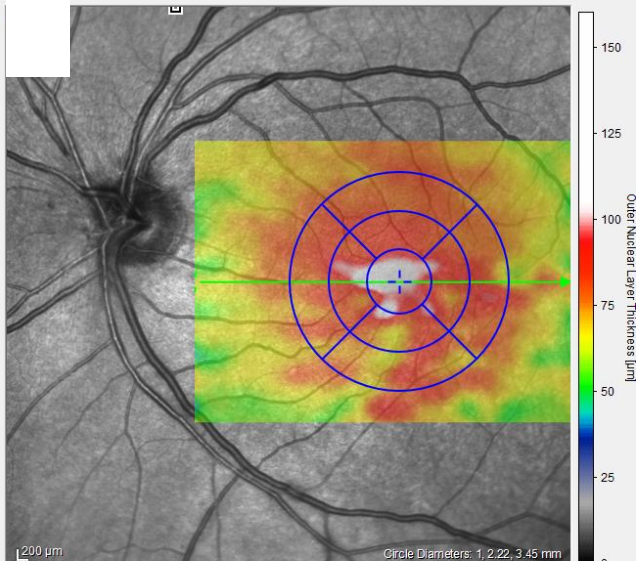
c

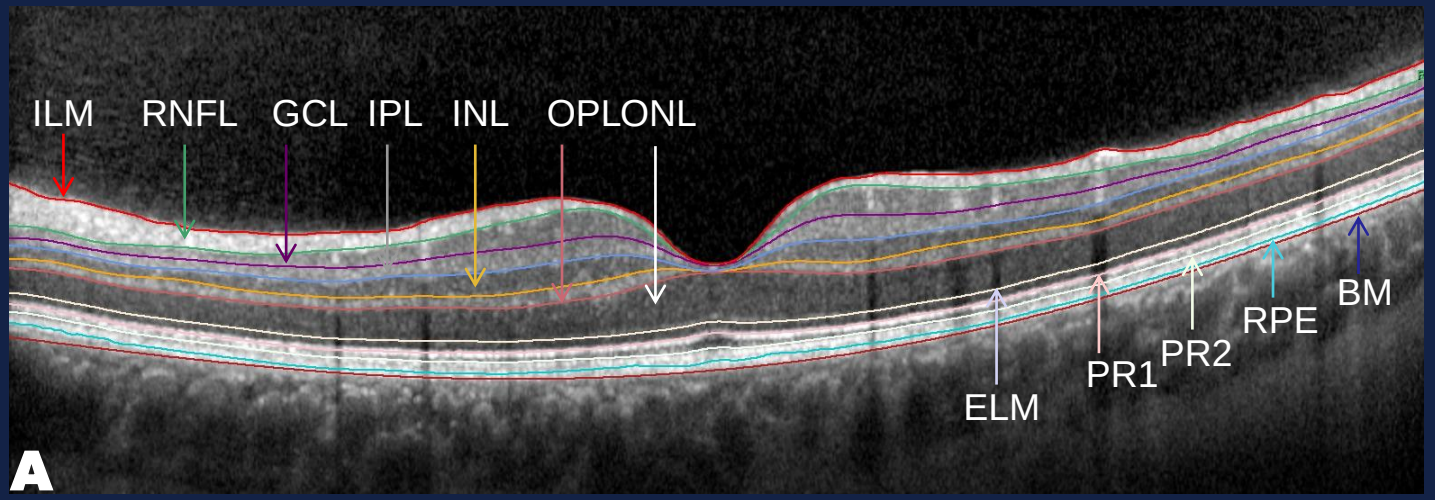


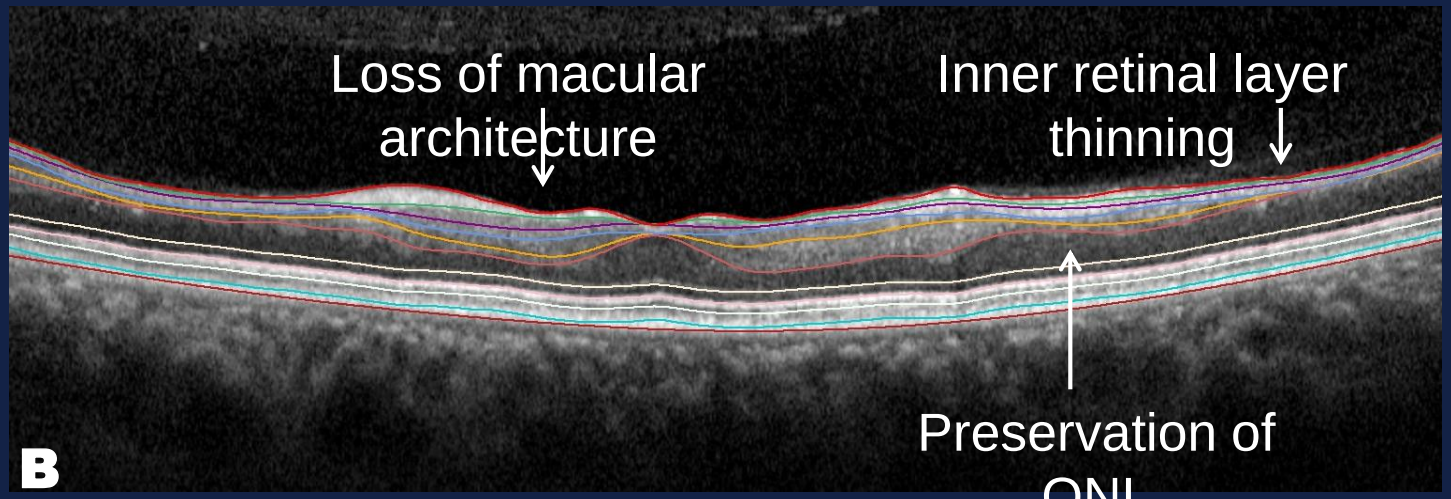

PATTERN DEVIATION


200 µm
Circle Diameters: 1, 2.22, 3.45 mm
Ganglion Cell Complex Thickness [µm]


200 µm
Circle Diameters: 1, 2.22, 3.45 mm
Inner Nuclear Layer Thickness [µm]


200 µm
Circle Diameters: 1, 2.22, 3.45 mm
Outer Nuclear Layer Thickness [µm]


ILM
RNFL
GCL
IPL
INL
OPLONL
ELM
PR1
PR2
RPE
BM
A


Loss of macular architecture
Inner retinal layer thinning
Preservation of ONL
B

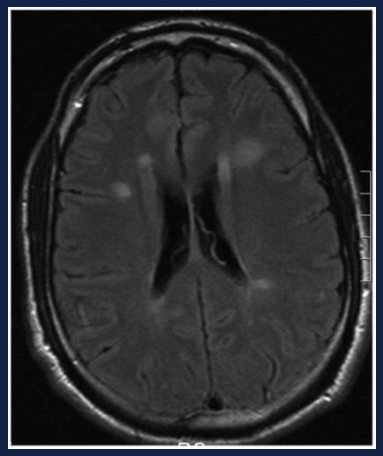
Summary for Role of OCT in Differential Diagnosis

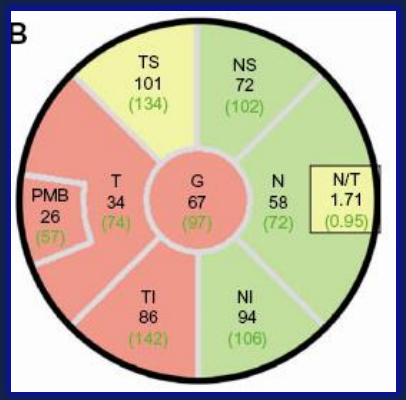
- NAION - increase RNFL early, segmental loss late, particularly superiorly
- Systemic disease - bilateral changes
- NMO - severe RNFL loss (less than 60 microns)
- Macula scans - can distinguish primary retinal lesions such as serous retinal detachment, retinal artery occlusions, inflammation

Nolan et al, *J Clin Neurosci* 2016

Case Scenario 3 (Predict Disease Progression)

Can OCT Help Predict Progression from CIS or RIS to MS?





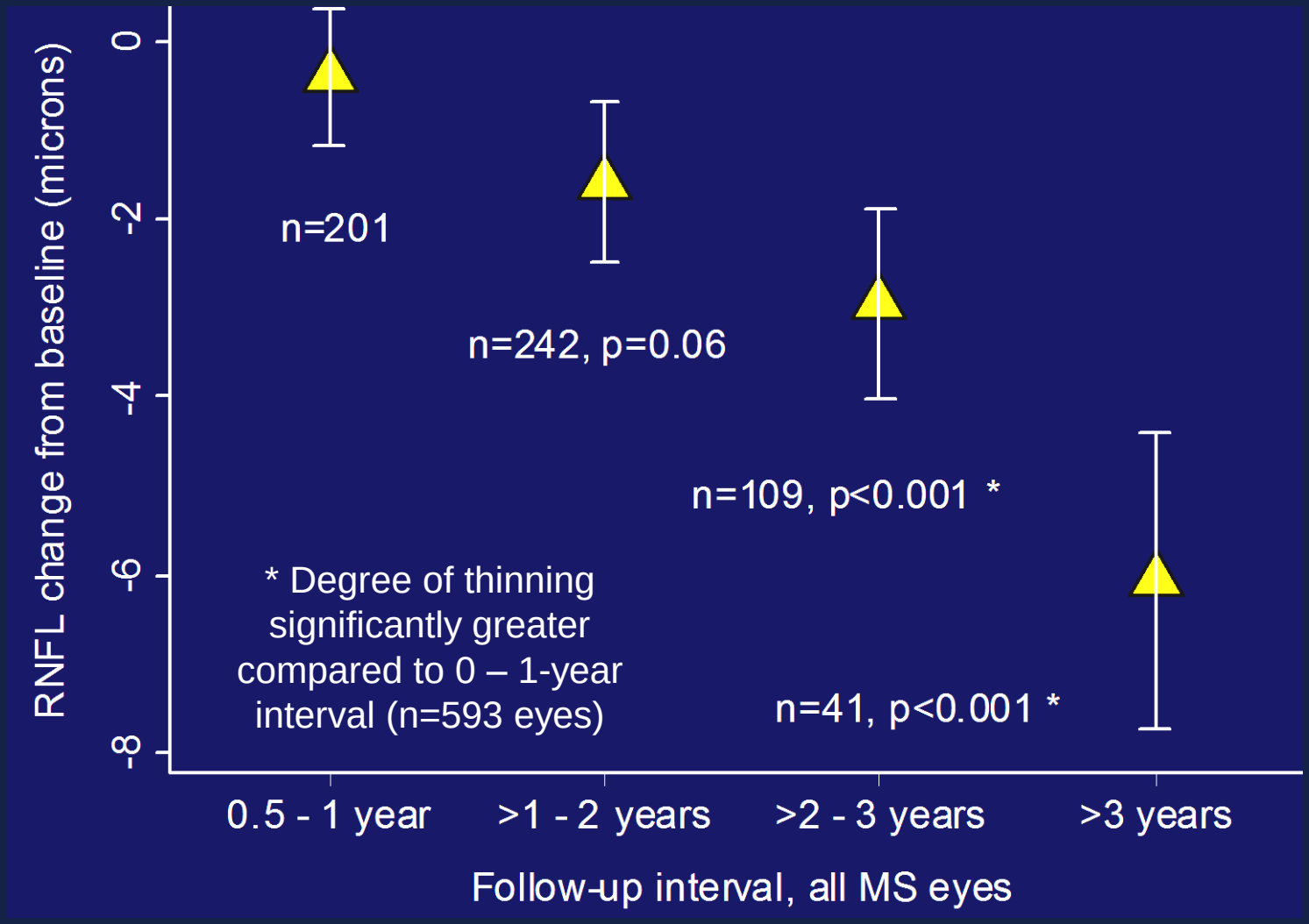
Can it help us predict progression?
What is meaningful progression?

Predicting Progression: OCT in MS

- Sub-clinical injury is common, 5 to 6 microns RNFL loss beyond test-retest variability, and predicts disability progression even if the absence of optic neuritis
- Low baseline pRNFL (87- 88 microns) predicts disability
- Ganglion cell layer loss over time mirrors brain atrophy
- In a small study of CIS (n=18) and RIS (n=20) patients, low mRNFL (25 percentile) predicted new T2 MR lesions and clinical activity in the subsequent year

Talman et al, Ann Neurol 2010, Martinez-Lapiscina, Lancet Neurol, 2016, Saidha et al, Ann Neurol, 2015, Knier et al, MS Journal, 2016, Perez-Rico et al, IVOS, 55:6127, 2014.

What Happens to the RNFL Axons Over Time in MS?



Talman et al. *Ann Neurol* 2010.

Monitoring: How Often?

VIEWS & REVIEWS

Defining the clinical course of multiple sclerosis

The 2013 revisions

OPEN

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Editorial, page 206

ABSTRACT

Accurate clinical course descriptions (phenotypes) of multiple sclerosis (MS) are important for communication, prognostication, design and recruitment of clinical trials, and treatment decision-making. Standardized descriptions published in 1996 based on a survey of international MS experts provided purely clinical phenotypes based on data and consensus at that time, but imaging and biological correlates were lacking. Increased understanding of MS and its pathology, coupled with general concern that the original descriptors may not adequately reflect more recently identified clinical aspects of the disease, prompted a re-examination of MS disease phenotypes by the International Advisory Committee on Clinical Trials of MS. While imaging and biological markers that might provide objective criteria for separating clinical phenotypes are lacking, we propose refined descriptors that include consideration of disease activity (based on clinical relapse rate and imaging findings) and disease progression. Strategies for future research to better define phenotypes are also outlined.

Neurology® 2014;83:278-286

GLOSSARY

CIS = clinically isolated syndrome; **EDSS** = Expanded Disability Status Scale; **MS** = multiple sclerosis; **NMSS** = National Multiple Sclerosis Society; **OCT** = optical coherence tomography; **PP** = primary progressive; **PR** = progressive relapsing; **PRO** = patient-reported outcomes; **RIS** = radiologically isolated syndrome; **RR** = relapsing-remitting; **SP** = secondary progressive.

In 1996, the US National Multiple Sclerosis Society (NMSS) Advisory Committee on Clinical Trials in Multiple Sclerosis defined the clinical subtypes of multiple sclerosis (MS).[1] The definitions provided consensus on terminology to describe various clinical courses of MS and highlighted areas where there was lack of consensus, or confusion. The rationale was the perceived need for clarity and consistency in defining patient groups for natural history and demographic studies, to enhance homogeneity in clinical trials, and to clarify communications among clinicians and with individuals with MS.

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International Advisory Committee on Clinical Trials of MS: Recommended at least annual assessment of disease activity by brain imaging criteria for relapsing MS

Is OCT now in the position of brain MRI was 15 years ago?

Performing OCT every 1-2 years could be an option

In Summary

- OCT is a new technology, constantly improving
- Studies demonstrate measures are promising biomarkers of subclinical, ongoing or acute MS disease activity
- Great in the differential diagnosis of visual loss
- Can OCT measurements substitute for a MR lesion in terms of dissemination in time or space?

61-Year-Old Woman

- College professor in NYC
- No significant past medical history
- Developed painful scleral “cyst” left eye 1 month prior to visit

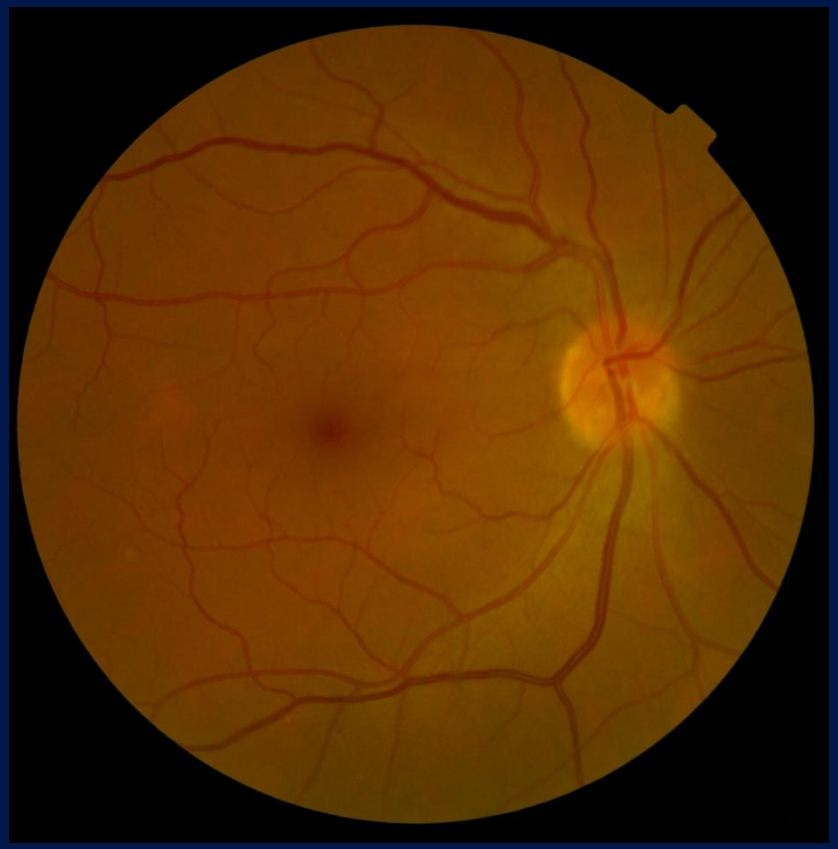
Examination
(2 weeks after visual loss, symptoms improving)

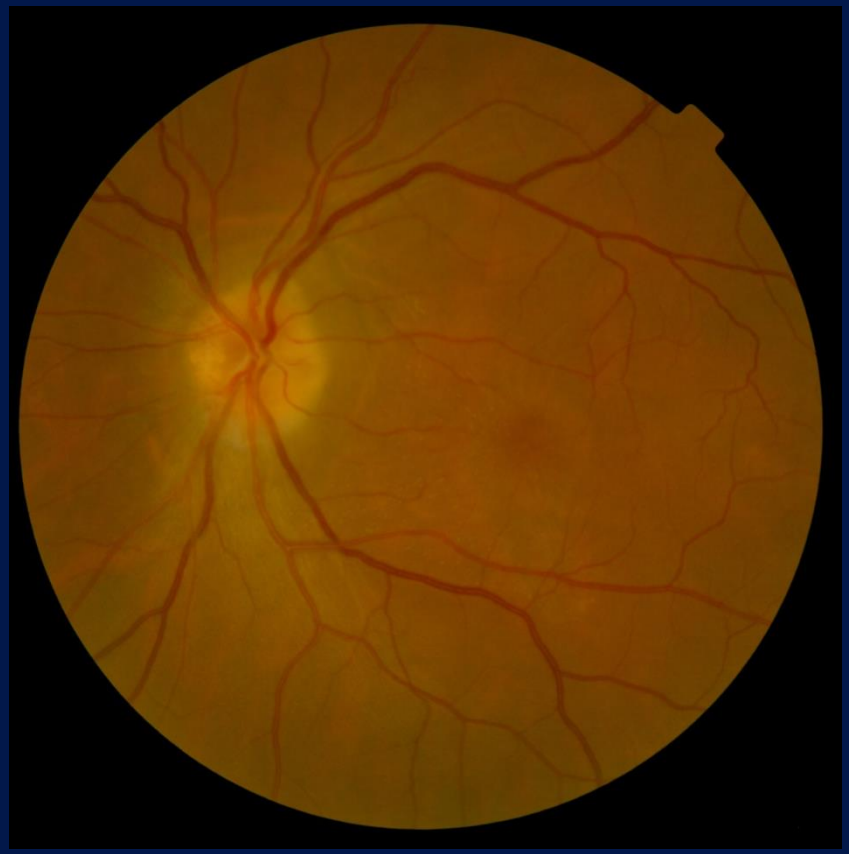
- VA 20/15 OD, 20/25 OS searching
- Pupils equal, left APD
- Visual fields: arcuate defect OS
- Normal ocular motility (no pain)

Visual Loss 2 Weeks Later

- Pain described as severe!
- Treated with topical antibiotic and corticosteroid drops
- Improved redness and pain
- Visual loss left eye, “gray donut” temporally, extending to fixation

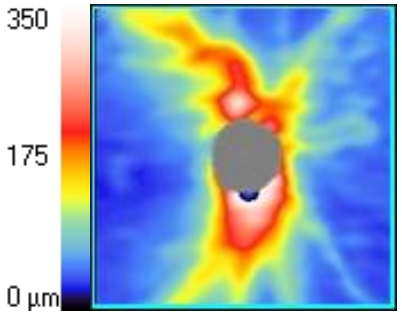
Examination





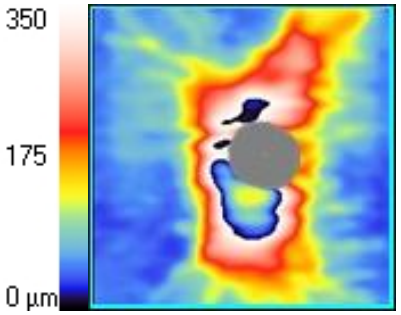
OCT RNFL Thickness

RNFL Thickness Map



	OD	OS
Average RNFL Thickness	97 µm	151 µm
RNFL Symmetry	88%	
Rim Area	1.67 mm²	1.64 mm²
Disc Area	1.66 mm²	1.53 mm²
Average C/D Ratio	0.07	0.07
Vertical C/D Ratio	0.06	0.07
Cup Volume	0.000 mm³	0.000 mm³

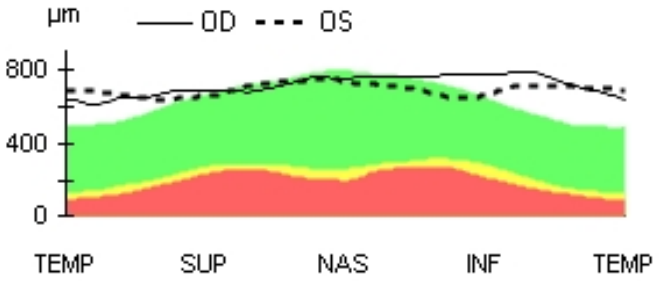
RNFL Thickness Map



RNFL Deviation Map

Disc Center(0.03,0.03)mm
Extracted Horizontal Tomogram

Neuro-retinal Rim Thickness



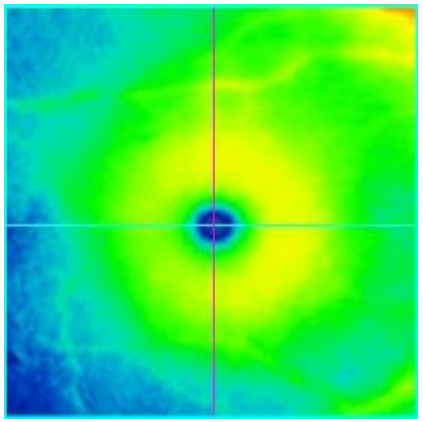
RNFL Thickness

RNFL Deviation Map

Disc Center(0.42,0.06)mm
Extracted Horizontal Tomogram

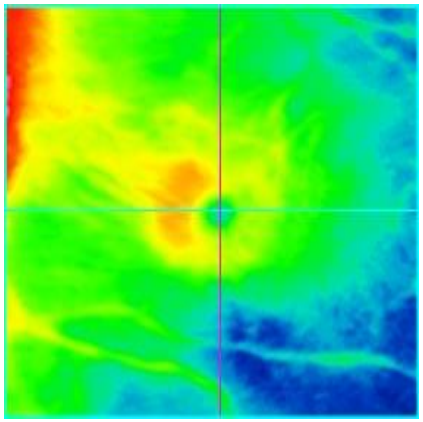
OCT Macular Thickness

OD ILM-RPE Thickness Map



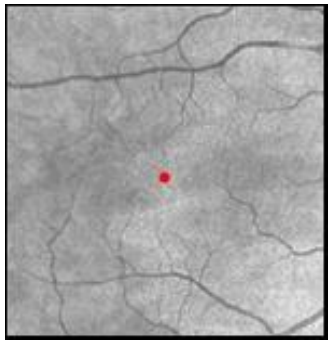
Fovea: 102, 107

OS ILM-RPE Thickness Map

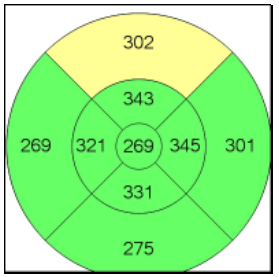


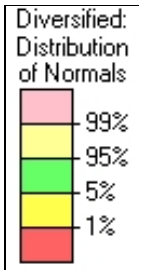
Fovea: 105, 100

OD OCT Fundus

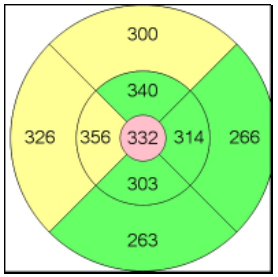


OD ILM-RPE Thickness

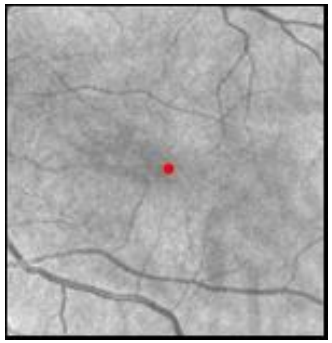




OS ILM-RPE Thickness



OS OCT Fundus



ILM - RPE	OD	OS
Thickness Central Subfield (µm)	269	332
Volume Cube (mm³)	10.6	10.8
Thickness Avg Cube (µm)	293	300

Painful Visual Loss: Look for Ophthalmologic Company!

- Patient had signs of ocular inflammation
- Pain more severe than usual for ON
- Our patient had disc drusen and edema!
- OCT helped define macular edema

In Summary

- OCT is a new technology, constantly improving
- Studies demonstrate measures are promising biomarkers of subclinical, ongoing or acute MS disease activity
- Great in the differential diagnosis of visual loss
- Can OCT measurements substitute for a MR lesion in terms of dissemination in time or space?

Differentiating Papilledema from Pseudopapilledema by OCT

- Fluorescein angiogram is best test
- Drusen have a hyper-reflective border
- RPE and Bruch's membrane bent inward in true edema
- Extent of RNFL thickness may be helpful- Drusen usually less than 120 microns.

Special Population: Patients on Fingolimod

- Fingolimod has been shown to be associated with macular edema in 0.3 to 1.2% of patients
- History of uveitis, other ocular pathology elevates risk
- Macular edema resolves in most cases when treatment is discontinued
- OCT scans of the macula are recommended before initiating treatment and follow-up at 3 to 4months and dilated fundus examination annually