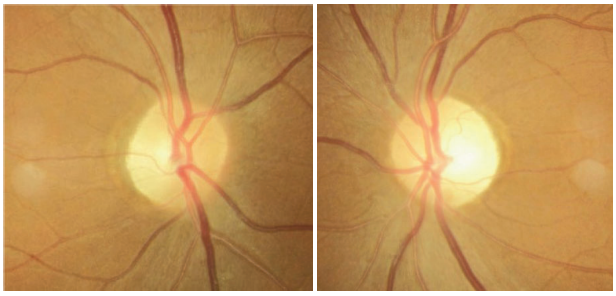


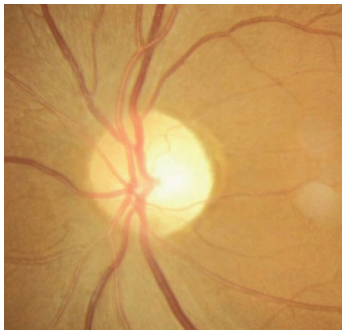
Optometry's Role in MS

Elizabeth A. Steele, OD, FAAO
bsteele@uab.edu

Disclosures: Dr. Beth Steele

- None

- Diagnosis/Early Intervention
- Treatment of Acute Optic Neuritis
- Monitoring for Chronic Change
- High Risk Medication
- Co-Management



Multiple Sclerosis – the most common disability in young adults

- Autoimmune demyelinating disease
  - Leads to neurodegeneration, disability
  - Secondary vascular dysregulation
  - Poorly understood etiology/associations
- Treatments:
  - Anti-inflammatory
  - more effective in early phases of disease
  - aim is to decrease the frequency of relapses and to delay disease progression

Who Gets MS?

- Young Adults
- Kids – rare
- Prevalence is increasing:
  - 1-6 in 100,000 worldwide (Japan, other Asian countries in particular)
  - 140 in 100,000 in US

Carvalho IV, Dos Santos CS, Amaral J, Ribeiro JA, Pereira C, Pais RP, Palavra F. Multiple sclerosis under the age of ten: the challenge of a rare diagnosis in a special population - a case series. Front Neurosci. 2023 Dec 20;17:1297171. doi: 10.3389/fnins.2023.1297171. PMID: 38174051; PMCID: PMC10761493.

MS Classification

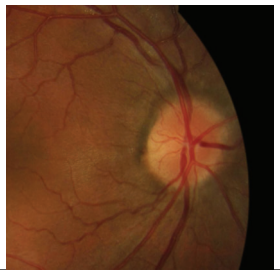
- Relapsing-Remitting – most common (85%); will often progress to secondary-progressive
- Secondary-Progressive - symptoms worsen over time, with or without relapses and remissions
- Primary-Progressive - uncommon (10%); symptoms slowly worsen over time, without relapse/remission
- Progressive relapsing – rare (5%); continuous progression of disease with acute relapses but no remissions; often without recovery

Diagnosis and Early Intervention

What is Optometry's Role?

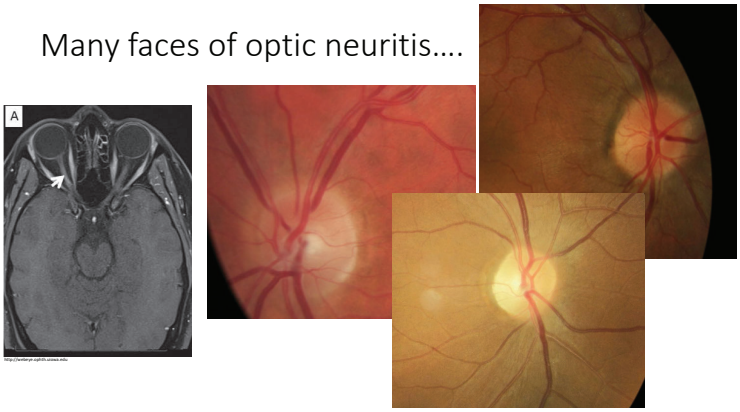
Optic Neuritis in MS

- Up to 70% develop ON throughout disease course
- Often presenting sign—up to 30%
  - Indicates less severe disease course ?
- Acute vs. previous event
- Presentation
  - Visual function
  - Pupil – APD
  - Eye pain – up to 92%
  - And… *no other cause*

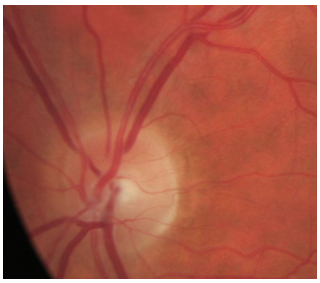


Sakai, et al. J Neuroophthalmology, 2011

Many faces of optic neuritis….



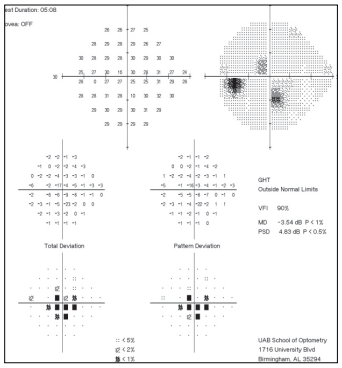
Optic Neuritis: At initial presentation…..



1. What is the cause?
   - 50% in US will show signs of MS
2. Typical or atypical ON?
3. Clinically Isolated (Clinically Isolated Syndrome, CIS)?
   - 75% will be diagnosed with MR in 15 years *(ONTT)*
   - When to treat with MS medications?

Visual Function in ON

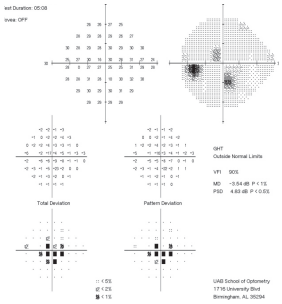
- More severe initial presentation ➔ worse visual prognosis
  - Up to 59% report impaired visual function at 1 year
- VA – often "good"
- Contrast sensitivity, color
- VF loss
  central scotoma – 90%
- VEP
  ↓ amp, ↑ latency



Nakajima H et al. BMC Neurology, 2010.

VF Loss in Demyelinating Disease

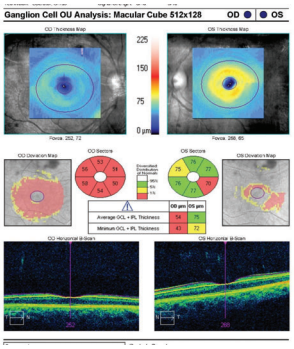
- Often seen as presenting symptom – crucial to early diagnosis!
- MS
  - Most common is central scotoma – 90%
- NMO
  - Only 54% with central scotoma
  - 33% central and non-central
  - 13% non-central (mostly altitudinal)



Nakajima H et al. BMC Neurology, 2010.

Earlier detection of MS with OCT

- Immediate treatment may improve prognosis
  - Correlates with lesion load on MRI
- Abnormalities in retinal tissues w/ and w/o history of ON
  - Subclinical ON?
  - Retrograde degeneration?
  - Thinning of RGCs independent of ON?
- Predictive value
  - Papillomacular bundle
  - GCC
  - Peripapillary RNFL



Sakai, et al. J Neuroophthalmology, 2011
Behbahani R. J Neurological Sciences 2015

Adding the Optic Nerve in Multiple Sclerosis Diagnostic Criteria

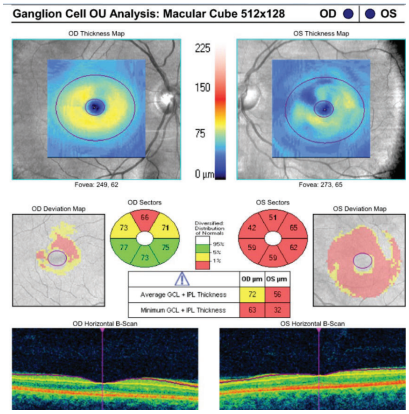
A Longitudinal, Prospective, Multicenter Study

Optic Neuritis is not currently part of diagnostic criteria in 2017

- MRI of ON
- VEP
- OCT
- ONH topography

OCT over time

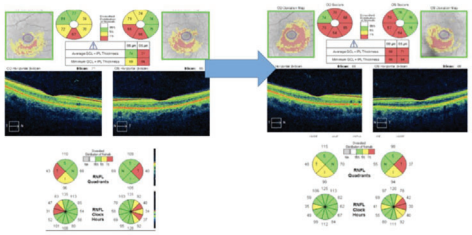
- Acute: thickening of inner retinal layers
- Atrophy
  - ≤2mos *dramatic* thinning
  - 10–40 µm of RNFL loss within 3–6 months
- Disease activity: ↑rate of GCL thinning



Sakai, et al. J Neuroophthalmology, 2011
Behbahani R. J Neurological Sciences 2015

OCT appearance with flare ups

- Acute optic neuritis = inner retinal thickening noted in the central ganglion cell complex as well as in the peripapillary RNFL
- May not present as "abnormally" thick according to the instrument's normative database, unless first event
- Existing atrophy (thinning) from previous episode = less cellular function and nerve fibers which do not as actively swell



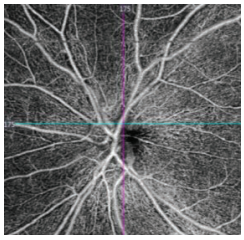
BMJ Journals

British Journal of Ophthalmology

Home / Archive / Volume 102, Issue 4

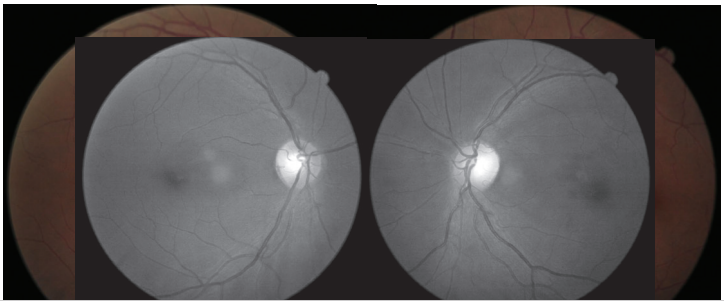
Optical coherence tomography angiography enhances the detection of optic nerve damage in multiple sclerosis

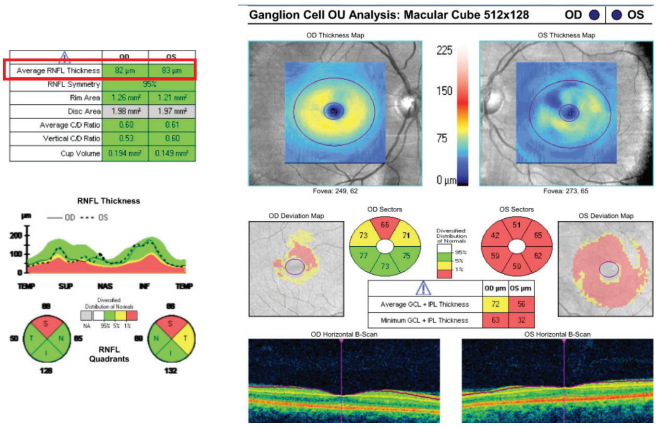
Rebecca I Spain[1, 2], Liang Liu[3], Xinbo Zhang[3], Yali Jia[3], Ou Tan[3], Dennis Bourdette[1, 2], David Huang[3]

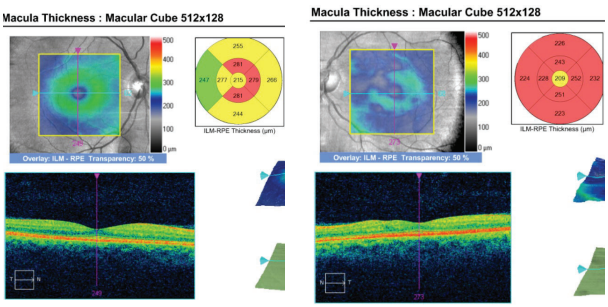


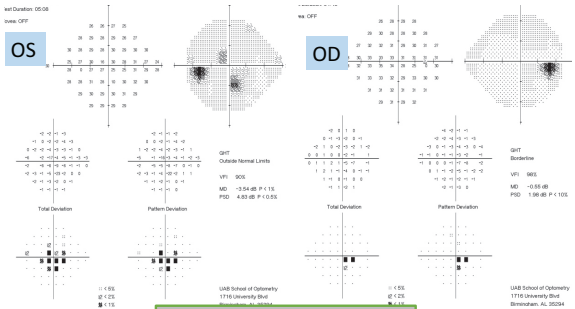
- 42 AA female
- R/v: headache
- Father has glaucoma
- ROS: arm weakness

- BVA 20/20 after corrected significant cylinder
- Pupils normal
- Color (HRR) normal OD, OS
- IOP 21, 20



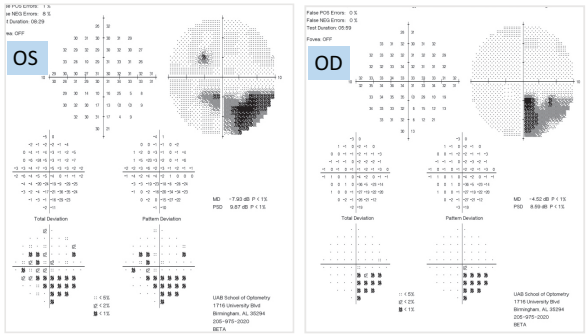






Glaucoma, or …. ?

10-2



Imaging considerations for this patient…??

- CT vs. MRI
  - With FLAIR
  - With fat suppression if acute ON
  - DWI also noted useful
- ±contrast
- ±angiography
- Location to scan
- ±urgency

Neuromyelitis optica (NMO; NMOSD)
AKA Devic's

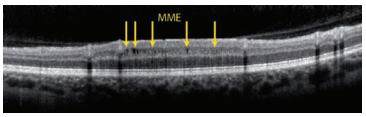
- Rare CNS inflammatory disorder
  - Monophasic or recurrent attacks of optic neuritis
  - →Acute transverse myelitis
- 1-2% of demyelinating disease in US
  - 40% in Thailand
- Diagnosis: Anti-Aquaporin4 Ab (AQP4)
  - 20% will test negative, but may be positive for anti-MOG Ab

Prognosis and Treatment for NMO

- W/in 5 years onset:
  - 50% are blind in both eyes
  - 50% are unable to walk
  - 20% die from respiratory failure
- Treatment – plasma exchange / immunosuppresants
  - Exacerbated by some MS therapies
  - For ON – steroids may not be adequate

Differentiation – can be crucial early on

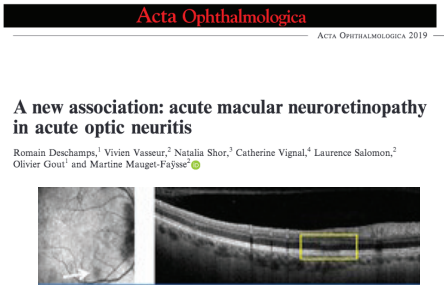
- Atypical/more aggressive presentation – think NMOSD
  - *Severe* loss of VA
- Can treat ON before results are in for better visual prognosis
- OCT
  - More RNFL and RGC layer thinning
  - Higher incidence microcystic macular edema (~24%)
  - Less likely to have subclinical damage



Bennett JL, et al. Multiple Sclerosis Journal, 2015.

…and Acute Macular Neuroretinopathy!

- At onset of acute ON
- Mostly in patients with those with anti-MOG Abs


Acta Ophthalmologica

Acta Ophthalmologica 2019

A new association: acute macular neuroretinopathy in acute optic neuritis

Romain Deschamps,[1] Vivien Vasseur,[2] Natalia Shor,[3] Catherine Vignal,[4] Laurence Salomon,[2] Olivier Gout[1] and Martine Mauget-Faÿsse[2]

MS vs. NMOSD – Clinical Presentation of Optic Neuritis

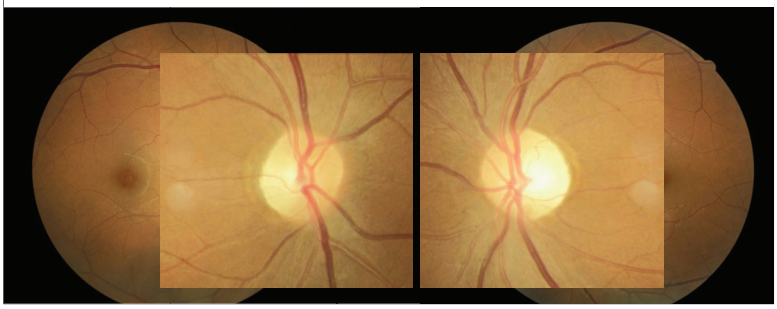
	MS	NMOSD
Optic Nerve Exam	Segmental atrophy	Non-segmental atrophy accompanied by vascular changes
Visual Field / Function	VA reduced moderately Central VF loss – 90%	Severe reduction in VA Central and noncentral – 33% Altitudinal defect – 13%
OCT	Subclinical thinning often noted	Thinning is "attack-related" and much more severe More likely to have macular edema

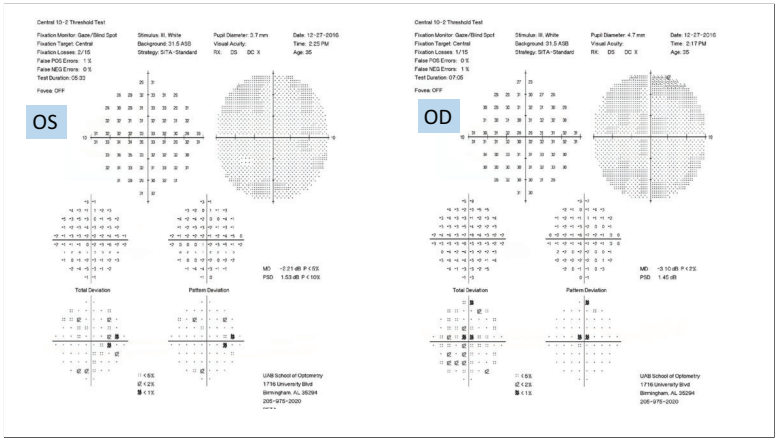
Other demyelinating neuropathies

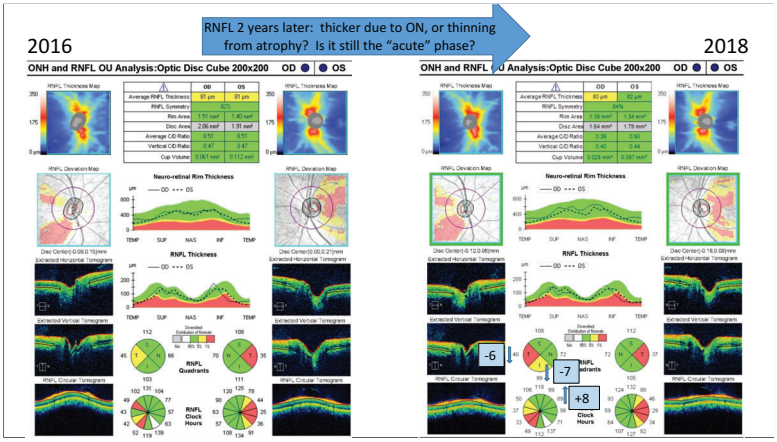
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- Distal Acquired Demyelinating Symmetric Neuropathy
- Multifocal Motor Neuropathy
- Multifocal Acquired Demyelinating Sensory
- Motor Neuropathy (the Lewis–Sumner Syndrome)

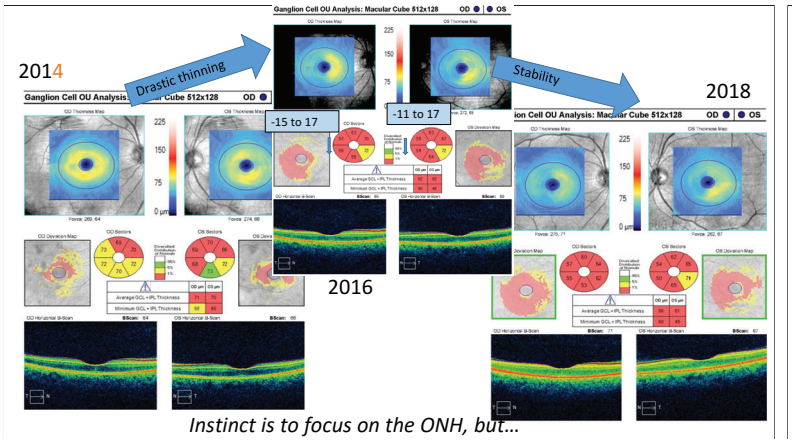
Known MS. 2018 - *Sudden decline in VA starting last week, progressively worse*

20/400 OD, 20/20 OS
APD OD
Red cap 30% OD









Instinct is to focus on the ONH, but…

Treatment of Acute Optic Neuritis

1. *IV steroids*
2. *Oral steroid*
3. *No steroids*
4. *(in trials: immunosuppression, neuroprotection and remyelination)*

Optic Neuritis Treatment Trial, circa 1992

The New England
Journal of Medicine
©Copyright, 1992, by the Massachusetts Medical Society
Volume 326 FEBRUARY 27, 1992 Number 9

A RANDOMIZED, CONTROLLED TRIAL OF CORTICOSTEROIDS IN THE TREATMENT OF ACUTE OPTIC NEURITIS

- IV steroids over oral
  - 1000mg IV methylpred x 3 days
  - Speeds recovery of vision; reduces recurrences
- Controversy. Delayed onset of MS vs. no long term benefit?

Research

JAMA Neurology | Original Investigation

Effect of Treating Acute Optic Neuritis With Bioequivalent Oral vs Intravenous Corticosteroids

A Randomized Clinical Trial

Sarah A. Morrow, MD, MS, FRCPC; J. Alexander Fraser, MD, FRCPC; Chad Day, BScH; Denise Bowman, BAH; Heather Rosehart, BScH; Marcelo Kremenchutzky, MD; Michael Nicolle, MD, PhD, FRCPC

- Bioequivalent Oral Steroid–
  - oral prednisone (1250-mg over 3 days) vs. high dose IV over 3 days
  - No significant differences in VA, Contrast Sensitivity, VEP at 1 month or 6 months
- Steroid "Smoothie"

Literature Review of Oral vs. IV

- *Oral methylprednisolone has comparable efficacy and adverse effect profiles to intravenous methylprednisolone for the treatment of optic neuritis. The analysis suggests oral administration is more cost-effective than intravenous administration; …*

Pietris J, et al. Semin Ophthalmol. 2024. doi: 10.1080/08820538.2023.2287100. Epub 2023 Dec 27. PMID: 38013424.

REVIEW ARTICLE

Updates and Controversies in the Management of Acute Optic Neuritis

Ethan Meltzer, MD,† and Sashank Prasad, MD**

- Immunomodulation therapies
- Neuroprotective therapies

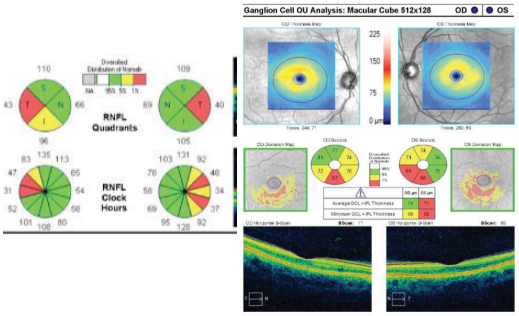
- *EPO*
- *IVIg*
- *LINGO-1*
- *Clemastine fumarate ….*

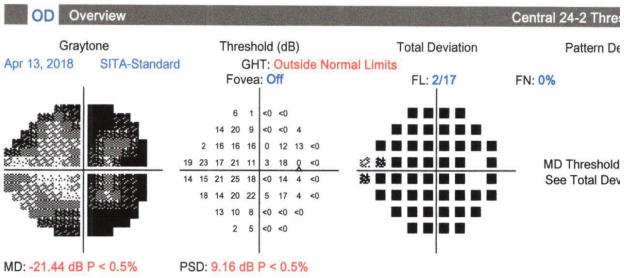
Asia-Pac J Ophthalmol 2018

39 WM with progressive, relapsing MS

- Avoids tx due to SEs
- 20/60 OD, +APD

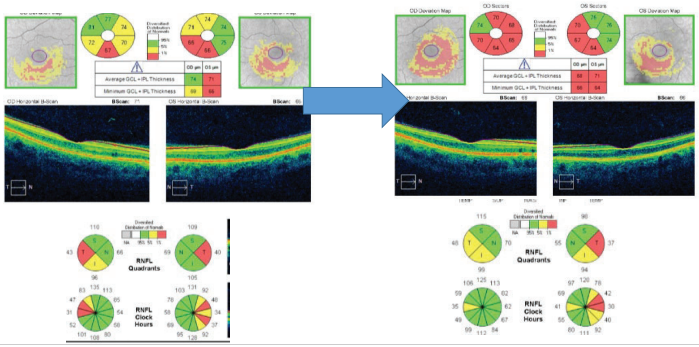
- RNFL and GCC thinning both eyes

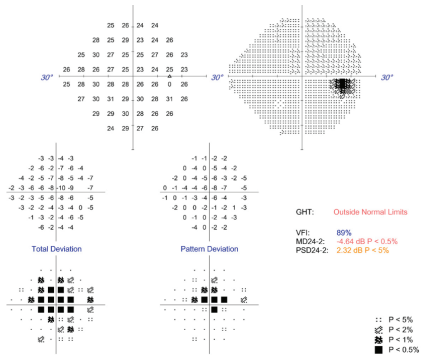




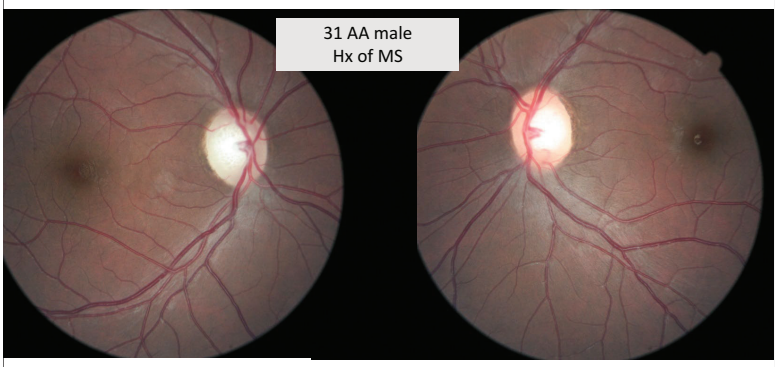
1 month post steroid infusion

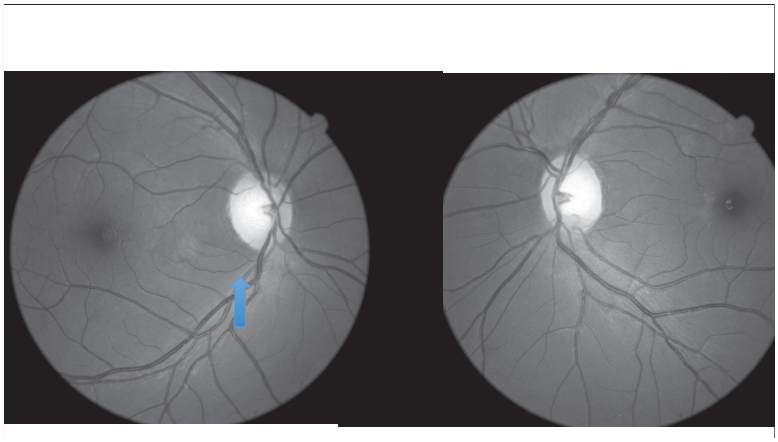
- 20/40
- (-)APD
- VF improved

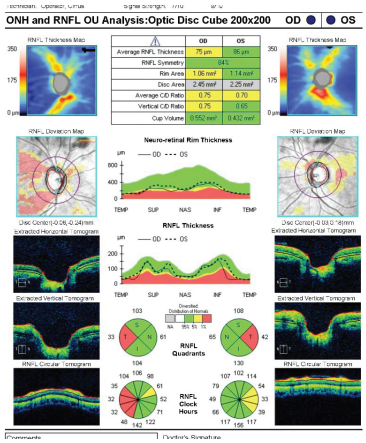


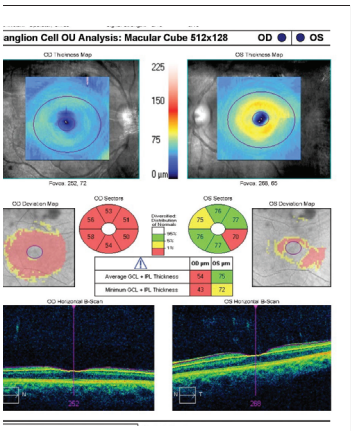


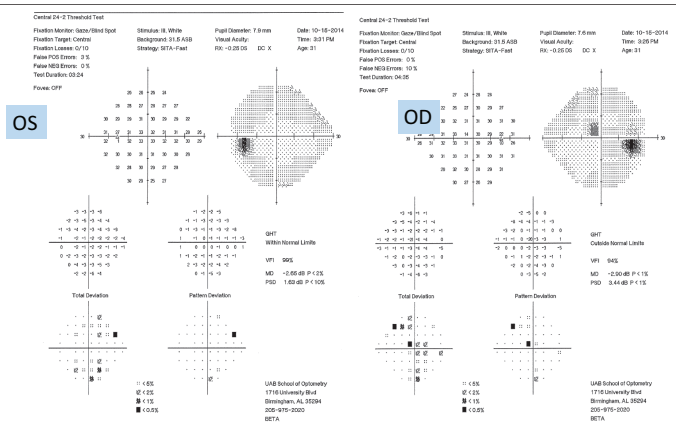
Baseline Testing and Monitoring for Chronic Change in Visual Function











35 year old with relapsing remitting MS

- Here today for doctor-directed Gilenya pre-treatment examination
- Medications:
  - *Gilenya*
  - *Lyrica*
  - Oral Prednisone 10mg
  - Steroid infusions – as needed for ON and other relapses

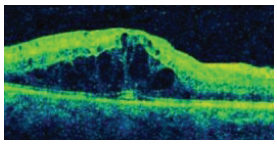
Fingolimod-Associated Macular Edema (FAME)

- 0.5% of patients taking lower dose
  - Up to 20% risk for patients with diabetes or hx uveitis
- Mostly unilateral
- May be asymptomatic
- ➔*Baseline exam, then q4 weeks for 1st 4 months*


American Journal of Ophthalmology Case Reports
Volume 4, December 2016, Pages 67-70

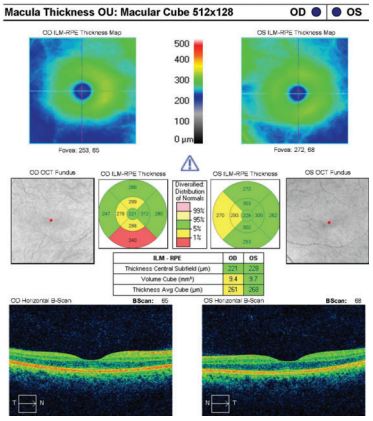
Case report

Acute onset of fingolimod-associated macular edema

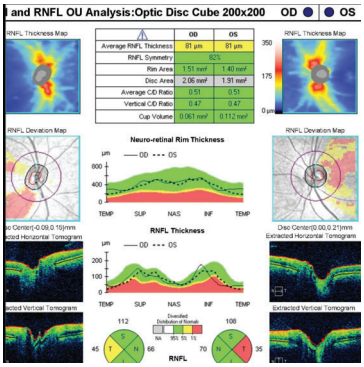


2016

- Dx of MS and baseline visit for Gilenya
- (-)CME
- 20/40 best corrected
- Coding?
  Z79.899 – Long-term use of high risk drug

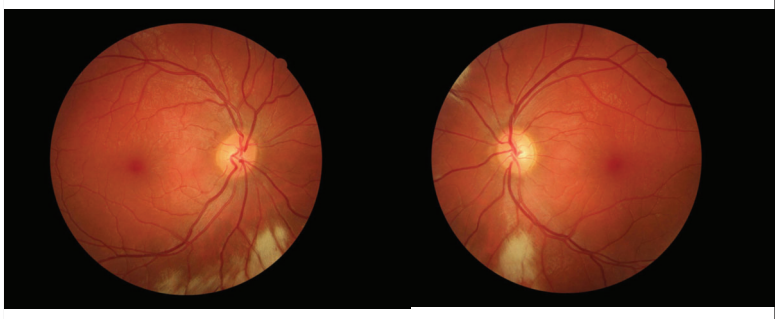


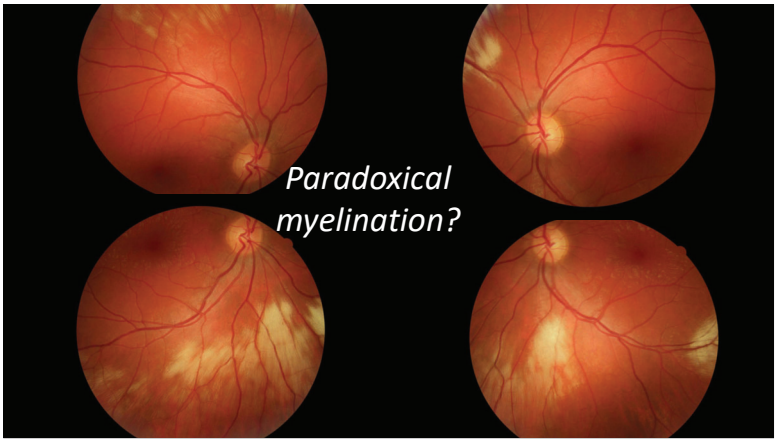
2016

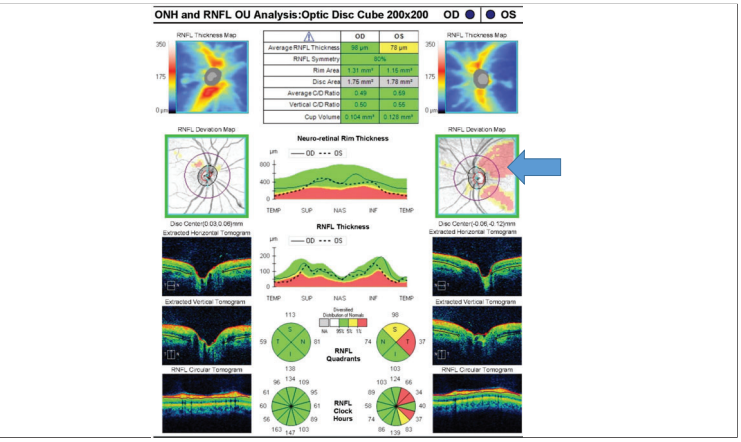


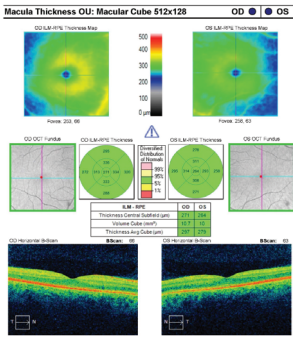
30 WF with relapsing remitting MS x 4 years

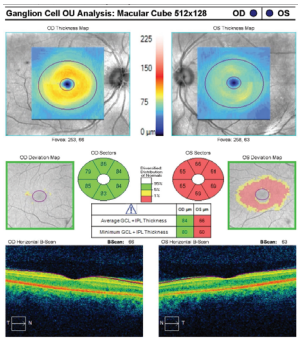
- Presenting sign was optic neuritis OS in April of 2015
- 20/20 OD, OS
- Red Cap – 90% OS
- Medications
  - Tecfidera 240mg

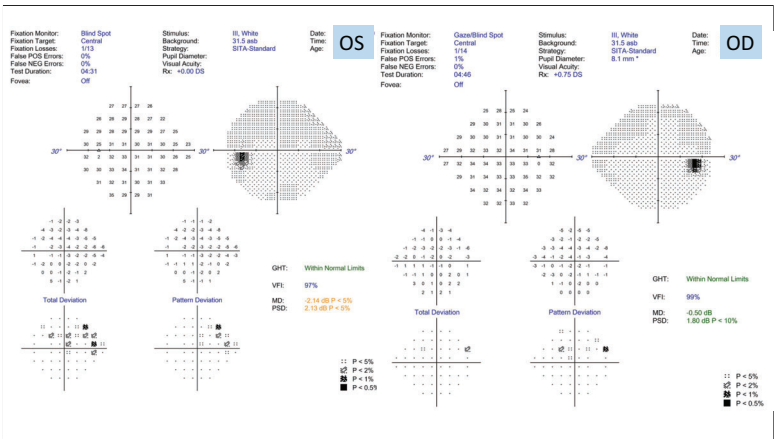








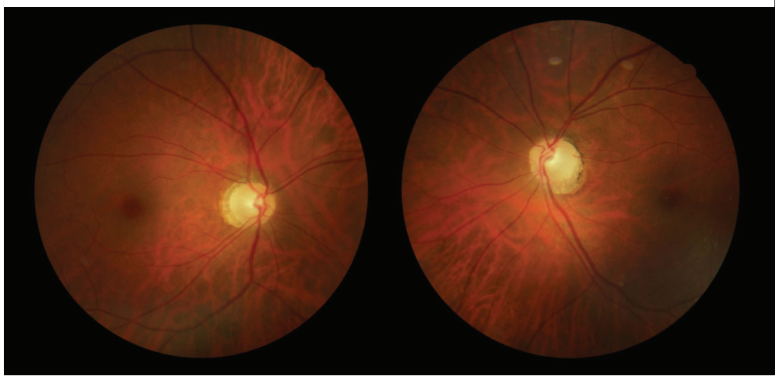




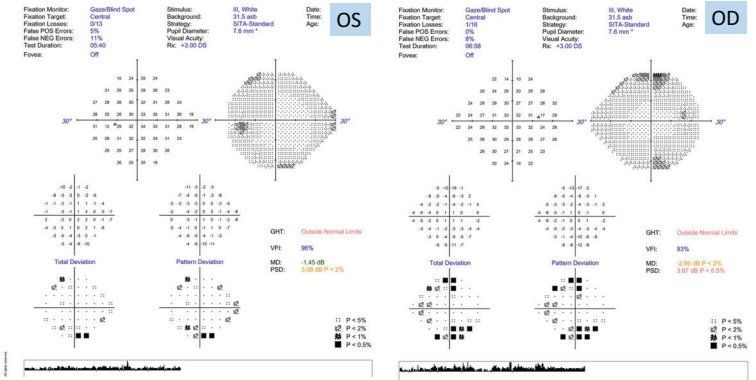
68 AAF

- MS diagnosed 11 years ago in 2008
  - Reports MS flare up since September 2018
  - Last infusion of Ocrevus 02/2019, with improvement
- Today
  - BCVA 20/30 OD, OS
  - Pupils normal
  - IOPs 12
- *AND:* Open-angle glaucoma suspect OU secondary to ONH appearance, +FHx (mother, sister)

2019



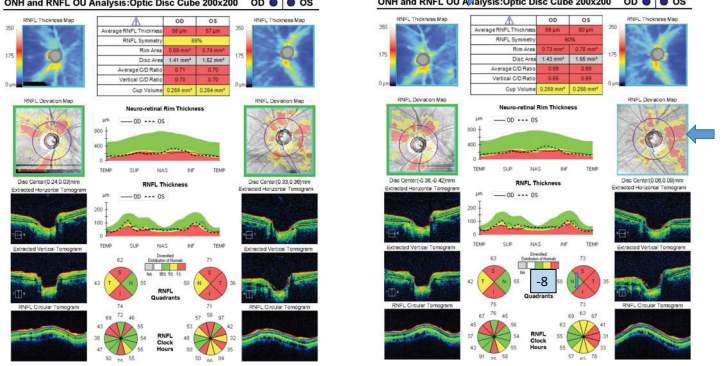
Last Year VF: 2018



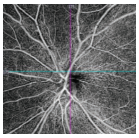
2018

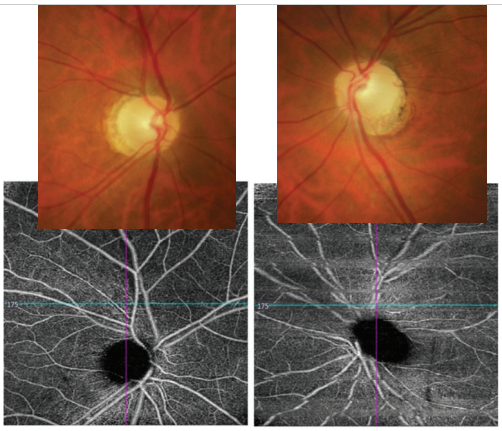
RNFL –some change nasally OS

2019



2019
OCT-A





2018

GCC –some change nasally OS

2019