WOO UNIVERSITY

Neuro Ophthalmic Disorders

Leonard Messner, OD

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WELCOME!

Host: Dr. Stephanie Woo

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- For a 2-hour webinar attendees must be online for a minimum of 100 minutes
- For a COPE certificate, please fill out the survey link in the chat. Also, the survey link will appear when the webinar ends.
- CE certificates will be delivered by email and sent to ARBO with OE tracker numbers
- **CE certificates will be emailed within 4 weeks**
- Ask questions using the zoom on-screen floating panel

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Speaker Bio – Dr. Leonard Messner

Leonard V. Messner is the Vice President for Strategy & Institutional Advancement at the Illinois College of Optometry. He holds the rank of Professor of Optometry at ICO.

Dr. Messner is the immediate past Chair of the Neuro-ophthalmic Disorders Special Interest Group of the American Academy of Optometry and is currently a member of the steering committee of the Academy's Fellows Doing Research SIG. His predominant area of clinical practice and scholarly activity is the evaluation and management of individuals with neuro-ophthalmic disorders. He has published and lectured extensively in the area of neuro-ophthalmic disorders.

In addition to other awards and honors, he is a 24-time recipient of the "Teacher of the Year" award at the Illinois College of Optometry.

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Financial Disclosures for Dr. Leonard Messner

- King-Devick Technologies (scientific advisory board)
- Heidelberg Engineering (professional advisory board)

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Thank you! Please join us for our next COPE event

Date: October 14, 2021
Time: 5:30 pm PST
Speakers: Dr. Peter Hersh, Dr. Steven Greenstein and Dr. John Gelles
Topic: Corneal Inlays for Keratoconus: Past, Present, Future
COPE: One hour live CE

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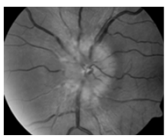
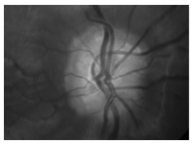
OCT in Neuro-ophthalmic Disorders: Papilledema, Pseudopapilledema, MS & Other Neurodegenerative Diseases

Leonard V. Messner, OD, FAAO
Professor of Optometry
Vice President for Strategy & Institutional Advancement
Illinois College of Optometry

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Key Points

- OCT analysis of papilledema vs. pseudopapilledema
- OCT analysis of chiasmal & retrochiasmal lesions
- OCT in neurodegenerative disease
  - Multiple sclerosis
  - Parkinson's disease
  - Alzheimer's disease
  - TBI

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Definition of Papilledema

- Swelling and elevation of the optic nerves due to elevated intracranial pressure (ICP)

10

Definition of Pseudopapilledema

- An anomalous elevation of one or both optic nerve without optic disc swelling and typically with a small or absent optic cup (may or may not be associated with optic disc drusen)

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Stages of Papilledema (Frisen Grading Scale)

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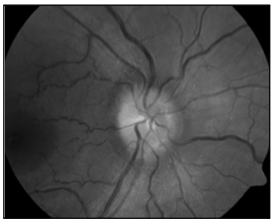
Grade I

- C-shaped halo of optic disc edema with sparing of the temporal papillomacular bundle fibers



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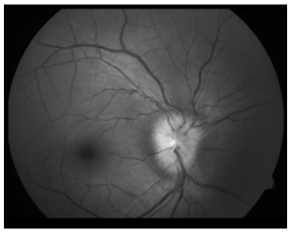
Grade II

- Circumferential halo of optic disc edema



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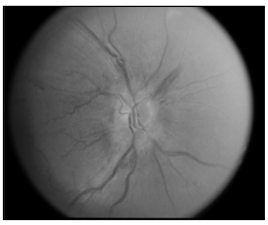
Grade III

- All of Grade II findings + obscuration of major vessels as they leave the disc



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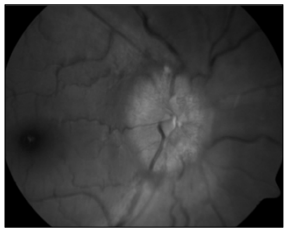
Grade IV

- All of Grade III findings + obscuration of major vessels on the surface of the disc



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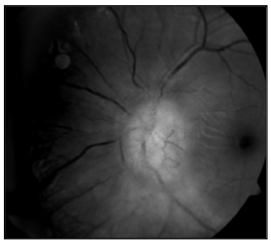
Grade V

- All of Grade IV findings + obscuration of all vessels on the surface of the disc



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OCT Analysis of Papilledema

- Increased NFL/MRW thickness:
- Elevation of nerve head (>0.8 mm from RPE to apex)
- Maintenance of central cup (until late disease)
- Subretinal hyporeflective space between photoreceptor layer and RPE (recumbent “lazy V”)
- Peripapillary inner retinal folds (T>N)
- *Inward deflection of RPE/BM (N>T)*
  - *67% with papilledema*

Flores-Rodriguez P, et al. *Ophthalmic Physiol* 2012
Lee KM, et al. *Ophthalmology* 2011
Kupersmith MJ, et al. *IOVS* 2011

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32 y/o AA Woman

- C/o progressive headaches am > pm
- BMI: 41
- BVA:
  - 20/20 OD
  - 20/20 OS

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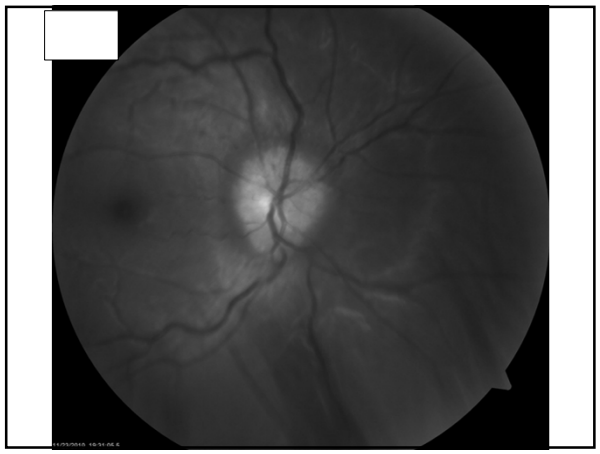

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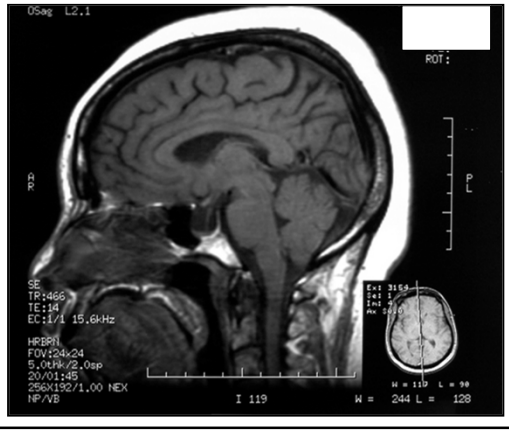

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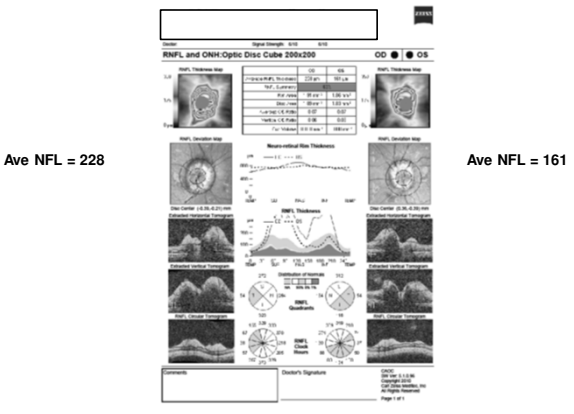

Ave NFL = 228

Ave NFL = 161

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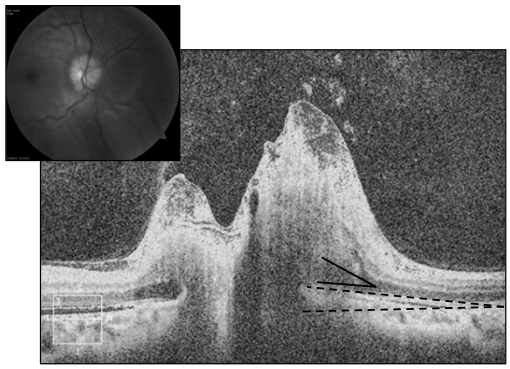

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28 y/o AA Woman

- C/o chronic daily headaches
- + synchronous pulsatile tinnitus
- BMI: 39
- BVA:
  - 20/20 OD
  - 20/20 OS

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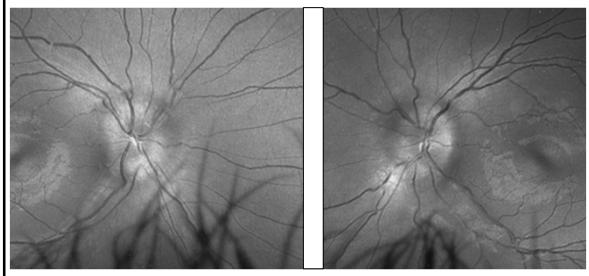

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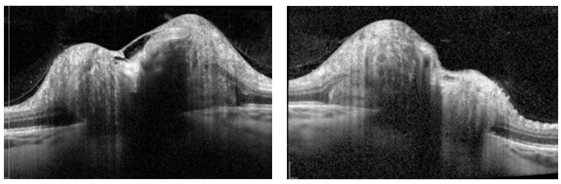

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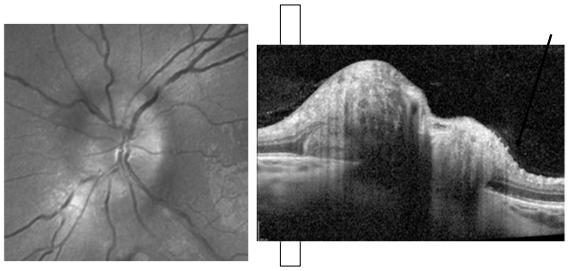

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40 y/o AA Woman

- C/o chronic daily HAs
- + SPT
- BMI = 44
- BVA:
  - 20/40 OD
  - 20/40 OS

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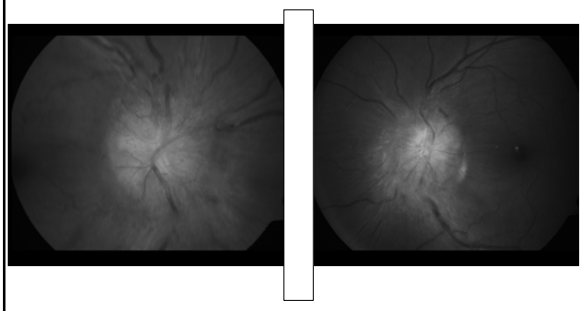

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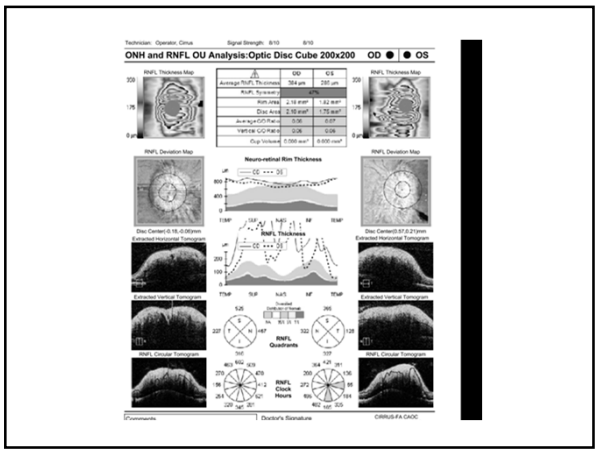

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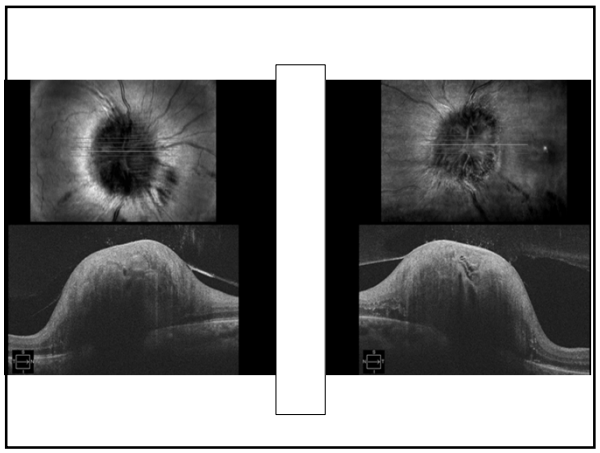

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32 y/o Hispanic Woman

- c/o progressive, debilitating headaches x 2 mos.
- Normal neurologic exam
- BVA:
  - 20/20 OD
  - 20/20 OS
- BMI: 38

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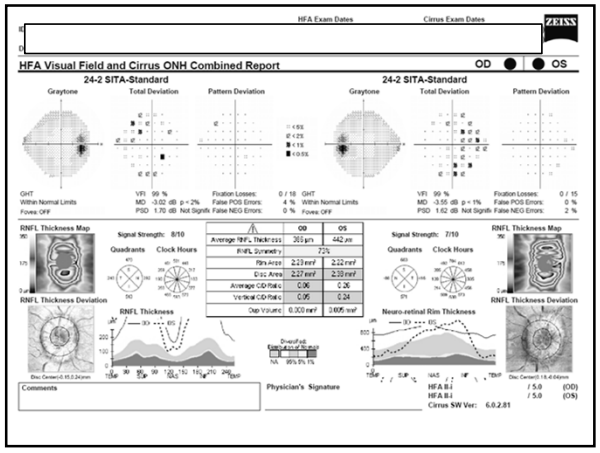

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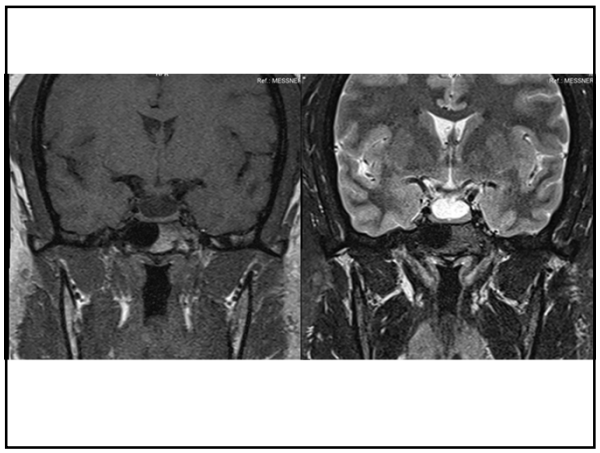

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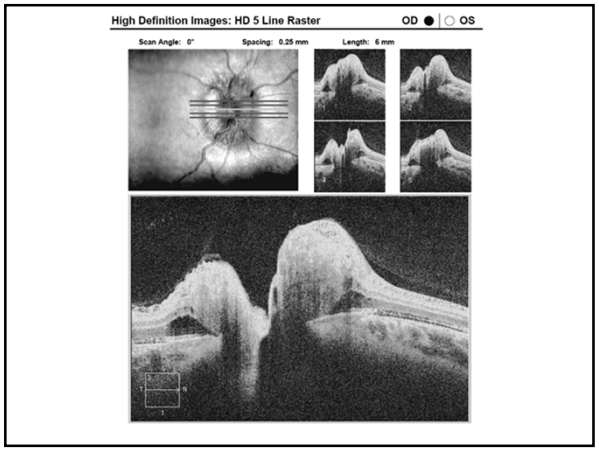

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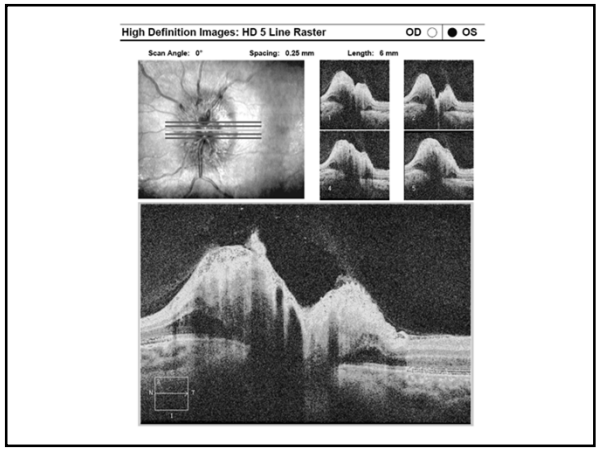

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F/U x 6 mos

- Rx acetazolamide (500 mg BID)
- Weight loss (approx. 25 lbs.)
- Improvement in headaches

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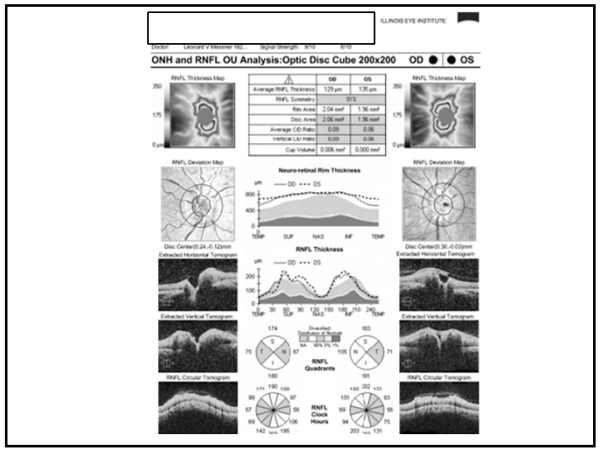

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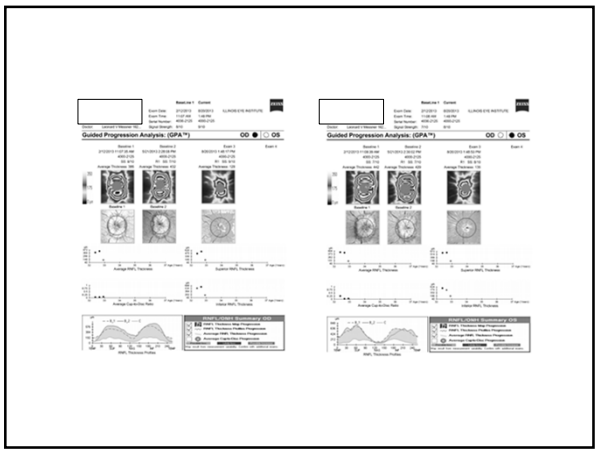

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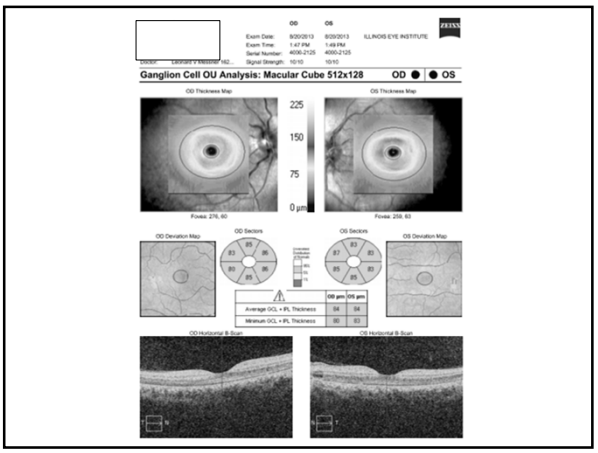

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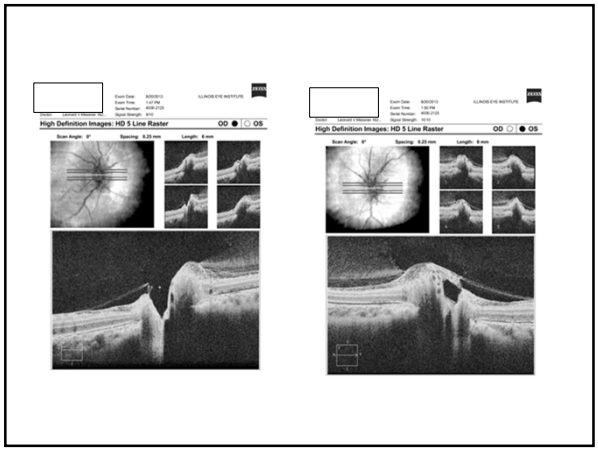

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F/U x 14 mos

- D/C Diamox x 3 months
- Weight loss (BMI reduction from 38 to 30)
- Headache free

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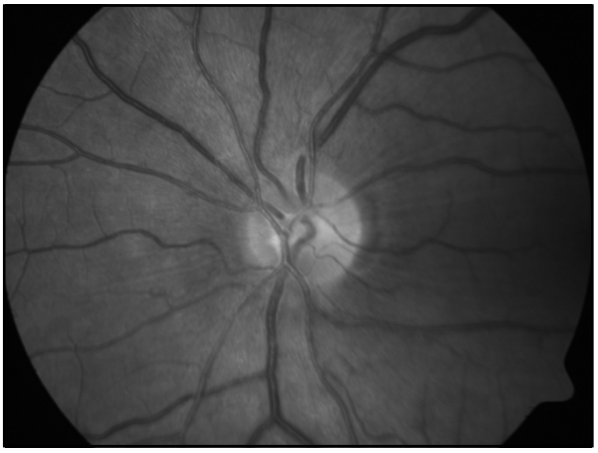

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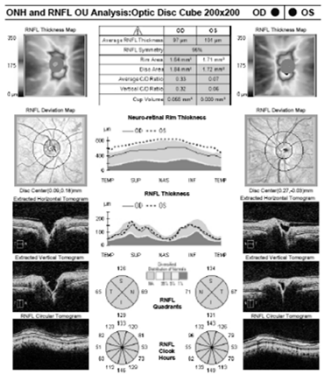

Total RNFL Reduction

OD: 386 to 97
OS: 442 to 101

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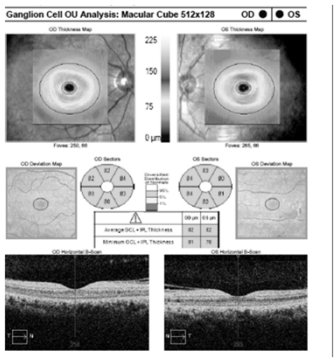

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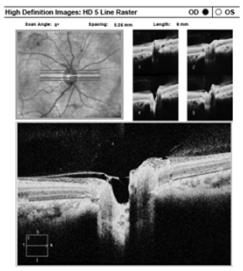

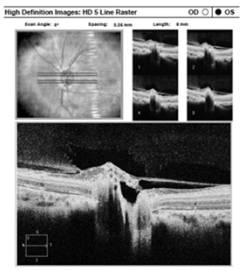

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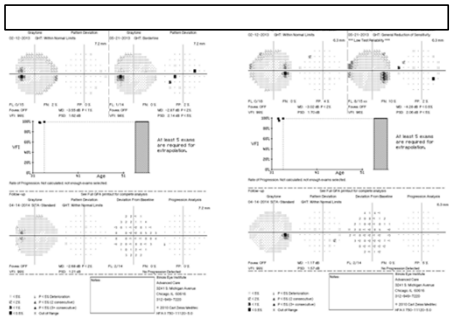

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Polling Question #1

Which of the following is not an OCT characteristic of papilledema?

a) RNFL thickening
b) Elevation of the optic disc
c) Subretinal hyporeflective space between photoreceptor layer and RPE (recumbent "lazy V")
d) Outward deflection of the RPE/Bruchs complex

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OCT Analysis of "Pseudoapilledema"

- Increased NFL thickness (+/-)
- Elevation of nerve head
  - Less than with papilledema (RPE to apex <0.8 mm)
- Lumpy, irregular internal nerve contour (disc drusen)
- No "lazy V" hyporeflective pattern
- Absence of central cup
- Neutral / negative RPE/BM deflection

Flores-Rodriguez P, et al. *Ophthalmic Physiol* 2012
Lee KM, et al. *Ophthalmology* 2011
Kupersmith MJ, et al. *IOVS* 2011

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Optic Disc Drusen

- Colloid bodies within substance of optic nerve head (anterior to lamina cribrosa)
- Degeneration of NFL axons (owing to narrow posterior scleral foramen/Bruchs membrane opening)
- Extracellular deposition of axoplasmic material with ultimate calcification
- NFL may be thickened (typically < 7 clock hours) or thinned

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OCT Characteristics of Optic Disc Drusen

- Always located above the lamina cribrosa (portion may be retrolaminar)
- Always have signal-poor core
- Often seen with hyper-reflective margin (most prominent superiorly)
- Sometimes seen as conglomerates of multiple ODD with internal reflectivity of the signal-poor core
- Hyper-reflective horizontal lines may be precursor to ODD (or artifact-prelaminar location common)
- Peripapillary hyper-reflective ovoid mass-like structures (PHOMS) may represent bulging axons and should not be considered as ODD
  - (evident 360 degrees-corresponding "blurred" disc margins)
  - Associated with CVO, myopic disc tilt, optic neuritis, other optic neuropathies)

Malmqvist L, et al. *J Neuro-ophthalmol* 2018
Fraser C. NANOS 2021

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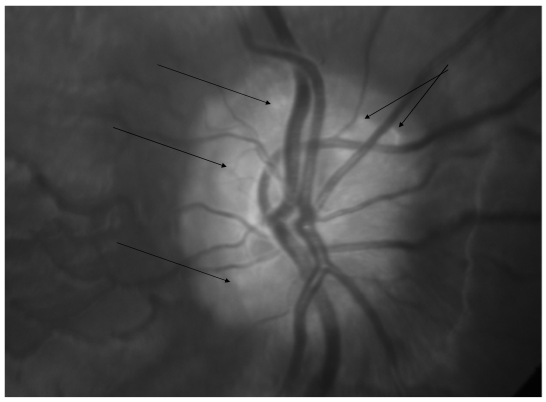

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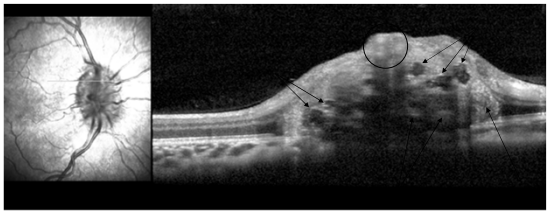

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33 y/o Hispanic Woman

- Consult for evaluation of ODE OS
- BVA
  - 20/20 OD
  - 20/20 OS
- Normal neurologic exam
- No HAs. synchronous pulsatile tinnitus, diplopia or transient vision loss

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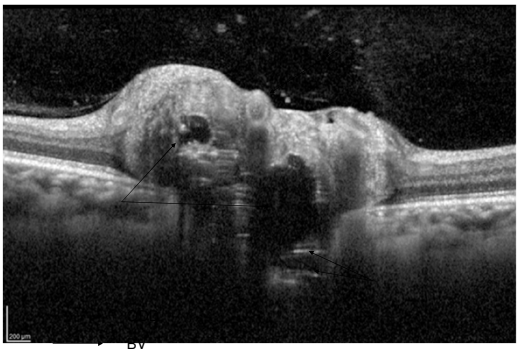

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29 y/o AA Woman

- Consult for evaluation of papilledema
- BVA
  - 20/20 OD
  - 20/20 OS
- Normal neurologic exam
- History of migraine headaches
- No synchronous pulsatile tinnitus, diplopia or transient vision loss

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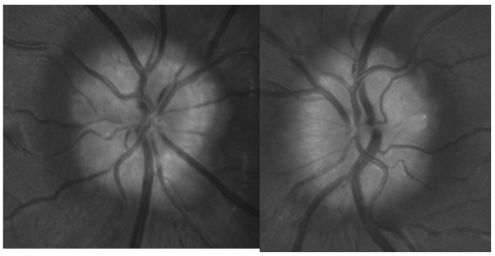

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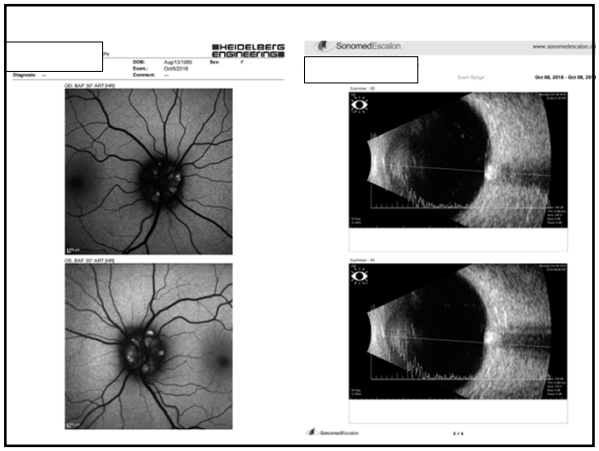

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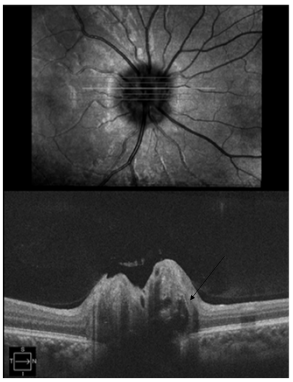

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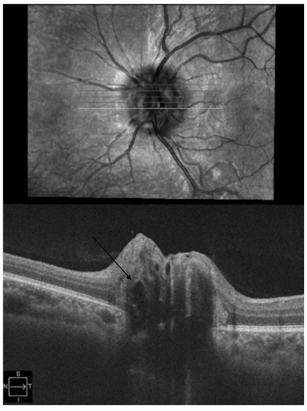

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62 y/o AA Woman

- C/o blurry vision OD > OS over past year
- H/o DED (Tx = ATs)
- BVA
  - 20/25 OD
  - 20/25 OS
- No headaches, synchronous pulsatile tinnitus, diplopia or transient vision loss

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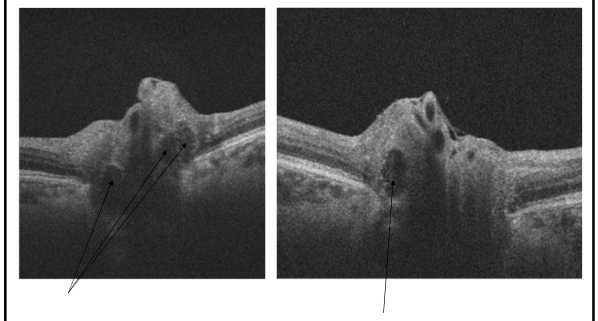

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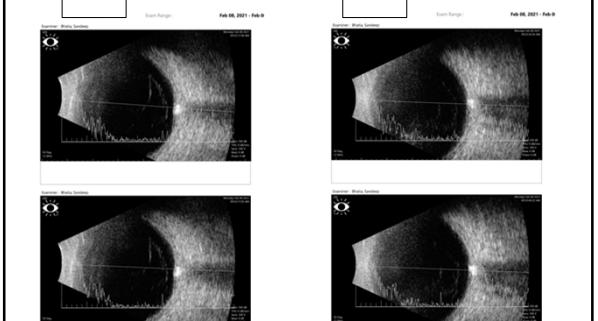

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7 y/o Hispanic Male

- BVA
  - 20/20 OD
  - 20/20 OS
- Normal neurologic exam
- No headaches, synchronous pulsatile tinnitus, diplopia or transient vision loss

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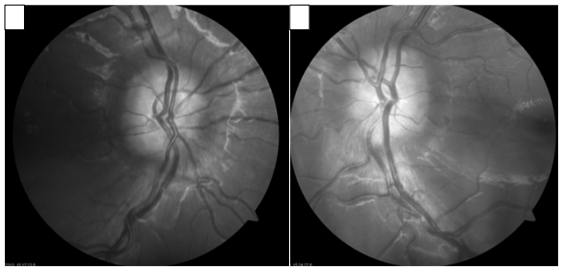
8/14/13



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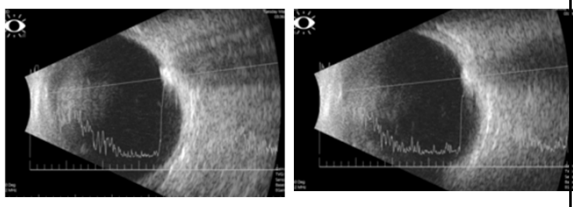

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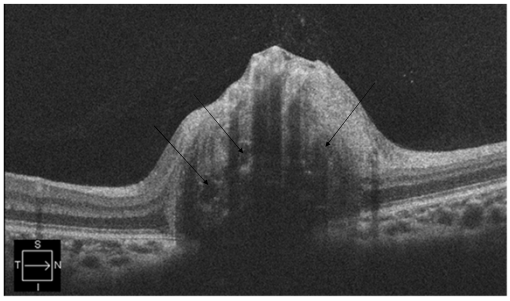

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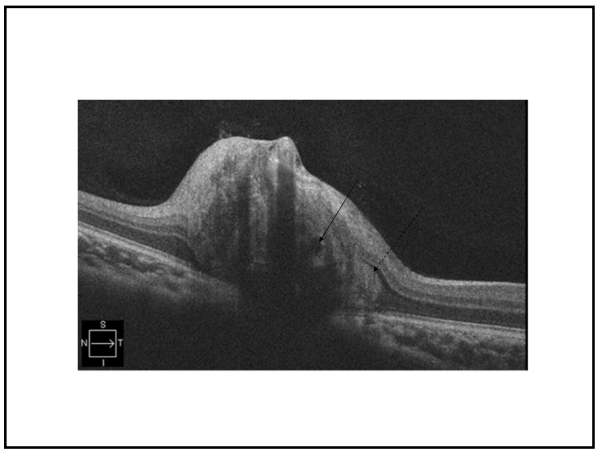

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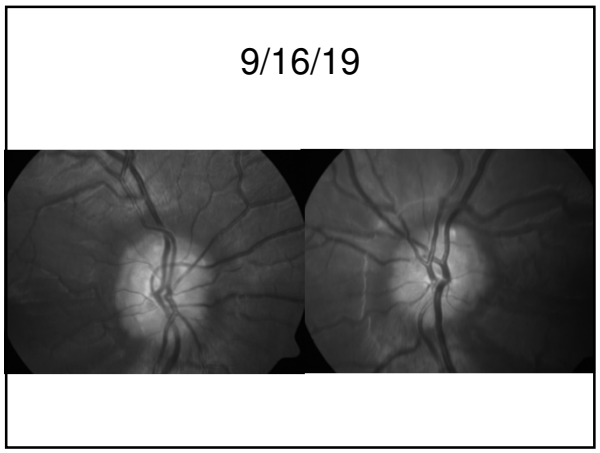

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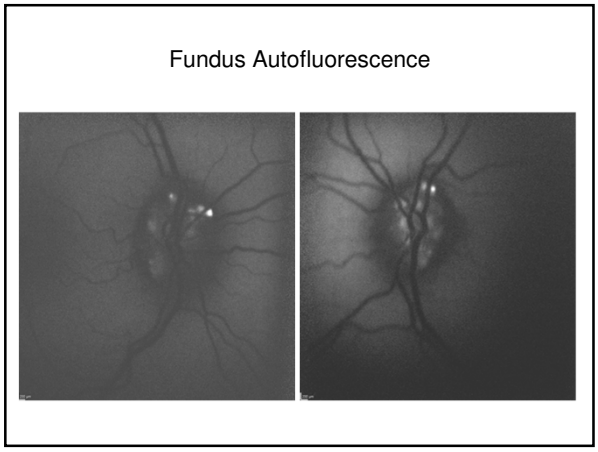

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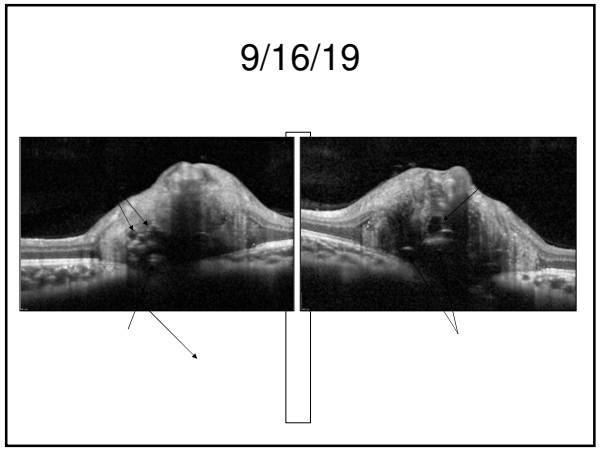

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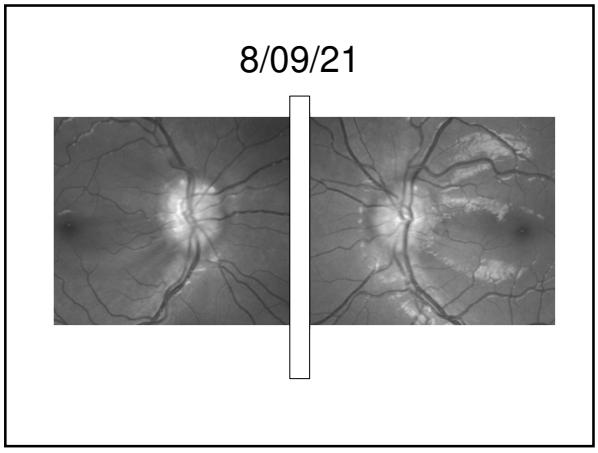

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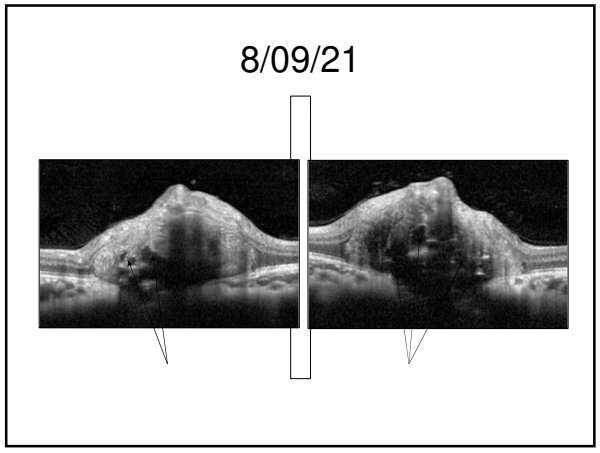

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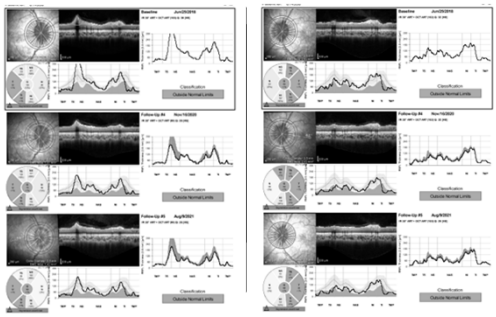
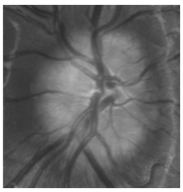
8/09/21

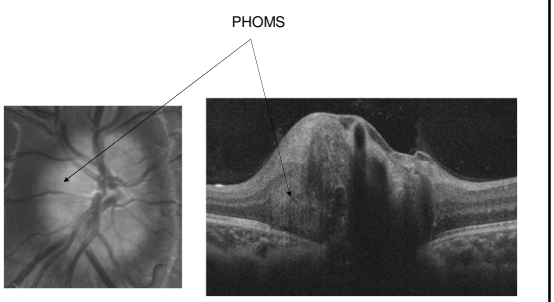


79

What is that white ring around the disc?



80



81

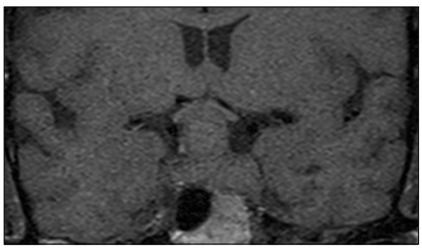
Polling Question #2

Which of the following is not an OCT characteristic of optic disc drusen?

a) Presence of a signal poor core
b) Association with hyper-reflective horizontal lines
c) Presence of a hyper-reflective surround
d) PHOMS are precursors to optic disc drusen

82

OCT Analysis of Chiasmal & Retrochiasmal Lesions



83

OCT Analysis of Chiasmal Lesions

- Nasal optic nerve fibers decussate in the paracentral region of the chiasm
- Crossed fibers most vulnerable to compressive damage
- These fibers sub-serve the nasal aspect of the optic nerve & ganglion cell complex

- **Absence of central cup**
- **Neutral / negative RPE/BM deflection**

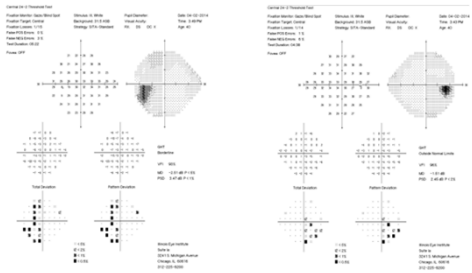
Neeranjali S, et al. IOVS 2015

84

40 Y/O Caucasian Man

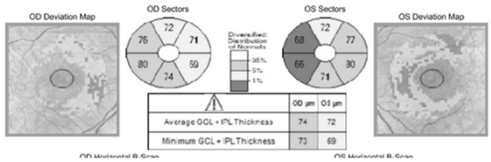
- C/o progressive side-vision loss, both eyes
- Several months duration
- BVA:
  - 20/20 OD
  - 20/20 -2 OS

85



86

GCC analysis:
Bi-nasal GCC thinning



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89

90

Optical coherence tomography retinal ganglion cell complex analysis for the detection of early chiasmal compression

Richard J. Blanch[1,2,3] · Jonathan A. Micieli[3] · Nelson M. Oyesiku[4] · Nancy J. Newman[1,4,5] · Valérie Biousse[1,5]

Published online: 10 August 2018

Abstract
Purpose To report patients with sellar tumors and chiasmal compression with normal visual fields, who demonstrate damage to the retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) on optical coherence tomography (OCT).
Methods Seven patients with sellar tumors causing mass effect on the optic chiasm without definite visual field defect, but abnormal GCC are described. GCC/RNFL analyses using Cirrus-OCT were classified into centiles based on the manufacturer's reference range.
Results In seven patients with radiologic compression of the chiasm by a sellar tumor, OCT-GCC thickness detected compressive chiasmopathy before visual defects became apparent on standard automated visual field testing. Without OCT, our patients would have been labelled as having normal visual function and no evidence of compressive chiasmopathy. With only OCT-RNFL analysis, 3/7 patients would still have been labelled as having no compression of the anterior visual pathways.
Conclusions These patients show that OCT-GCC analysis is more sensitive than visual field testing with standard automated perimetry in the detection of compressive chiasmopathy or optic neuropathy. These cases and previous studies suggest that OCT-GCC analysis may be used in addition to visual field testing to evaluate patients with lesions compressing the chiasm.

Keywords Pituitary adenoma · Sellar mass · Chiasmal compression · Optic neuropathy · Visual field test · Optical coherence tomography · Ganglion cell complex analysis

- OCT GCC analysis more sensitive than perimetry for detection of early chiasmal compression

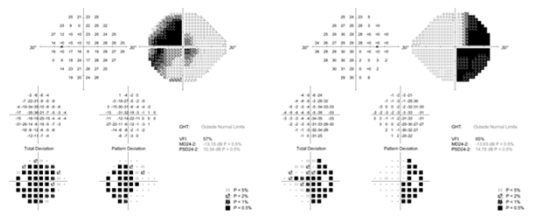
Blanch RJ, et al. *Pituitary* 2018

91

31 y/o Caucasian Man

- History of motor vehicle accident with subsequent bitemporal hemianopia
- BVA:
  - 20/40 OD
  - 20/80 OS

92



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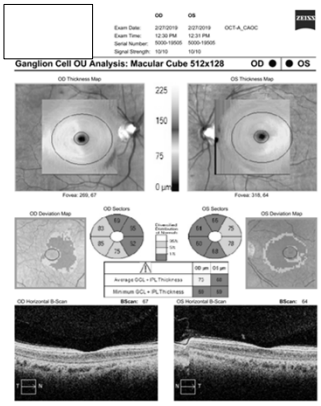

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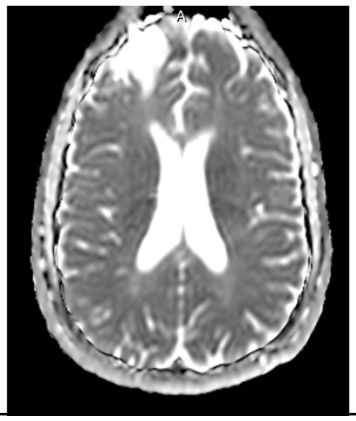

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OCT Analysis of Retrochiasmal Lesions

- Insult of ipsilateral temporal axons and contralateral nasal axons → ipsilateral temporal GCIPL thinning and contralateral nasal GCIPL thinning
- Correlation with other clinical findings:
  - Contralateral homonymous hemianopia
  - Contralateral "bow tie" optic atrophy and RAPD (optic tract lesions)

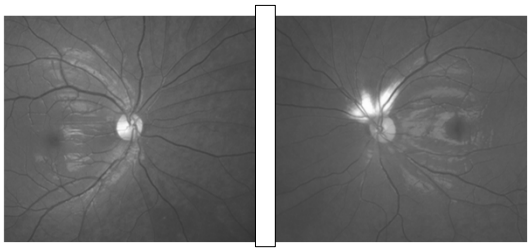
Micieli JA, et al. *Ophthalmology* 2018
Muhlemann F, et al. *Neurology* 2020

97

21 y/o Female

- History of left hemispherectomy at age 12 for intractable epilepsy
- Right-sided hemiparesis
- Aphasia
- BVA:
  - 20/25 OD
  - 20/20 OS
- 1+ RAPD OD

98



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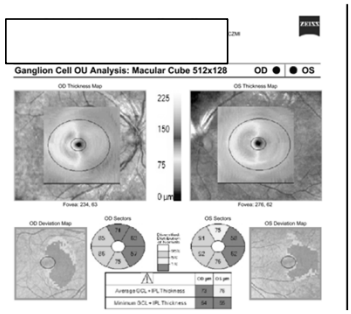
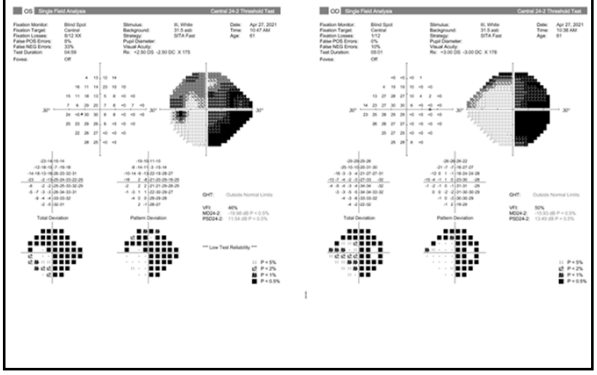


100

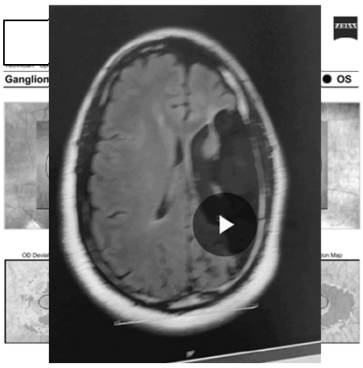
61 y/o Male

- History of cerebral palsy with right-sided hemiparesis
- Concomitant OAG (latanoprost qhs)
- BVA:
  - 20/25 OD
  - 20/25 OS

101



102



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Rapid homonymous hemi-macular atrophy of the optical coherence tomography ganglion cell complex after stroke

Arshia Eshtiaghi[1] Jonathan A Micieli[2,3]

[1]Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
[2]Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada
[3]Kensington Vision and Research Centre, Toronto, Ontario, Canada

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Accepted 16 March 2021

DESCRIPTION

A 44-year-old man developed sudden-onset right-sided weakness, aphasia and blurred vision after a cardiac valvuloplasty. Initial CT and CT angiography of the head showed early ischaemic changes involving the left medial temporal lobe, occipital lobe and thalamus with a left P2 occlusion. He was not a candidate for hyperacute therapy given his recent surgery and was already on dual antiplatelet therapy. He had improvement in his weakness and aphasia and was seen in ophthalmology consultation 1 month after the onset of stroke. He was found to have a visual acuity of 20/20 in both eyes, a complete right homonymous hemianopsia and optical coherence tomography (OCT) of the macular ganglion cell–inner plexiform layer (GCIPL) showed left homonymous hemi-macular atrophy. OCT of the retinal nerve fibre layer (RNFL) showed early inferonasal thinning, but the overall thickness was within the normal range (figure 1).

The cell bodies of the retinal ganglion cells are located in the ganglion cell layer of the retina. Their axons first travel in the RNFL, then in the optic nerve, optic chiasm and optic tract before they synapse in the lateral geniculate nucleus, after which information is conveyed to the visual cortex.[2] Disruption of the post-geniculate visual pathway will manifest as hemi-macular atrophy of the OCT GCIPL, but this takes at least several

- Pre-geniculate lesions = rapid GCIPL thinning (1 month)
- Post-geniculate lesions = delayed GCIPL thinning (5-6 months

Eshtiaghi A, et al. *BMJ* 2021

104

Polling Question #3

Which of the following is an OCT characteristic of chiasmal insult?

a) Bitemporal GCC thinning
b) Binasal GCC thinning
c) Homonymous GCC thinning
d) Diffuse, bilateral GCC thinning

105

OCT in Neurodegenerative Disease

- Multiple sclerosis
- Parkinson's disease
- Alzheimer's disease
- TBI

106

OCT in Neurodegenerative Disease

- Multiple sclerosis
- Parkinson's disease
- Alzheimer's disease
- TBI

107

Why use OCT in the evaluation of MS patients?

- OCT allows for detailed evaluation of CNS non-myelinated axons
- OCT provides reliable and reproducible measures of "neuroaxonal structure" within the CNS that correlates with other measures of disease severity & progression (standardized disease progression algorithms)
- Incorporation of OCT, low-contrast acuity measurement & vision-specific QOL measures incorporated into MS clinical trials

Kappos L, et al. *Lancet* 1999
Kanda T, et al. *Radiology* 2015
Balcer LJ. *J Neuroophthalmolo*2014
Costello F, et al. *Eye and Brain* 2018

108

OCT Findings in Optic Neuritis

- Acute optic neuritis associated with RNFL & GCL-IPL thinning of 20% - 40% X 3 months

Petzold A, et al. *Lancet Neurol* 2017
Balcer LJ. *Neuroophthalmol* 2014
Sakai RE et al. *J Neuroophthalmol* 2011
Fisher JB, et al. *Ophthalmology* 2006

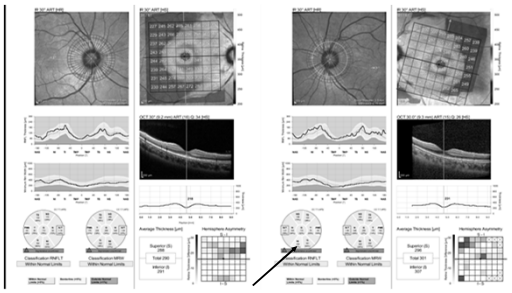
109

45 y/o Woman

- Recent-onset monosymptomatic optic neuritis OS
- BVA:
  - 20/20 OD
  - 20/500 OS

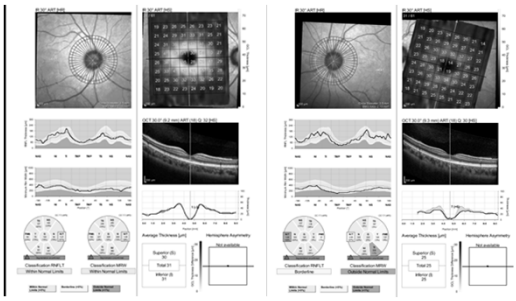
110

July 29, 2019 (BVA: 20/500 OS)



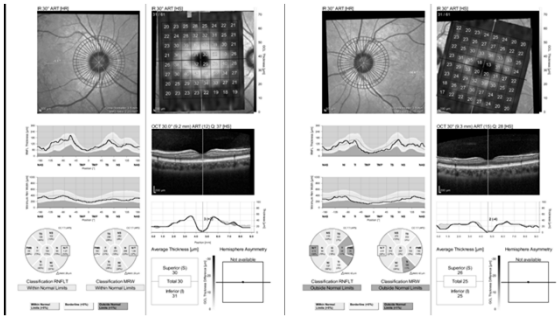
111

September 29, 2019 (BVA: 20/20 OS)



112

February 3, 2020 (BVA: 20/20 OS)



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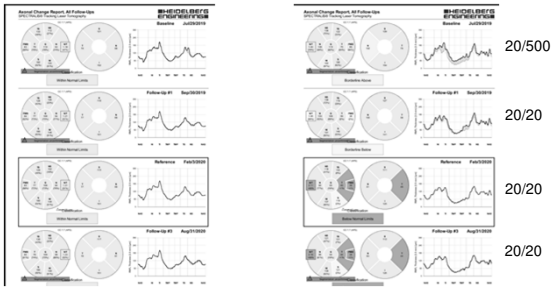
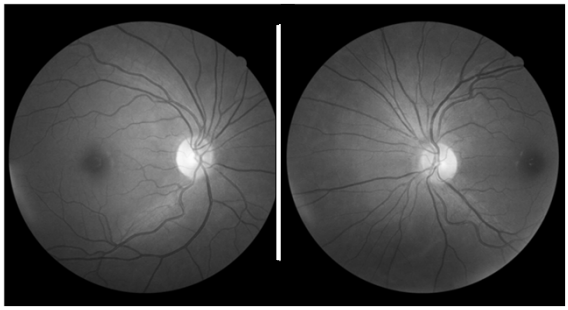


114

31 y/o Woman

- 10-year Hx of RRMS
- Meds:
  - Ocrevus (ocrelizumab)
- Prior optic neuritis OD
- BVA:
  - 20/20 -1 OD
  - 20/20 OS

115



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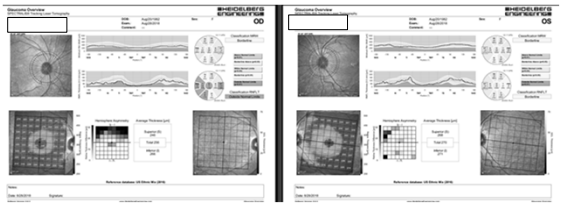

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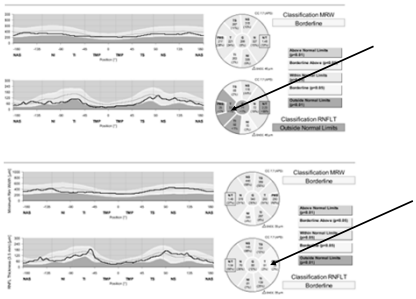


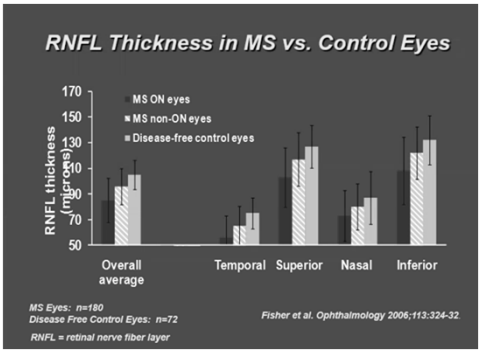
118

OCT Findings in MS

- Thinning of RNFL & GCIPL occurs over time with MS in the absence of optic neuritis (thinning of 12%)

Balcer LJ. *Neuroophthalmol* 2014
Sakai RE et al. *J Neuroophthalmol* 2011
Fisher JB, et al. *Ophthalmology* 2008

119



Slide courtesy of Laura Balcer, MD

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AMERICAN ACADEMY OF OPHTHALMOLOGY

Retinal and Optic Nerve Degeneration in Patients with Multiple Sclerosis Followed up for 5 Years

Elena Garcia-Martin, PhD,[1,2] Jose R. Ara, PhD,[2,3] Jesus Martin, PhD,[2,3] Carmen Almarcegui, PhD,[2,4] Isabel Dolz, PhD,[2,4] Elisa Vilades, MD,[1,2] Lanea Gil-Arribas, PhD,[1,2] Francisco J. Fernandez, PhD,[1,2] Vicente Polo, PhD,[1,2] Jose M. Larrosa, PhD,[1,2] Luis E. Pablo, PhD,[1,2] Maria Satue, PhD[1,2]

- Thinning of RNFL & increased VEP latencies with MS
- Normal standard assessments of vision (VA, color vision & visual fields)
- RNFL thinning greatest temporal and inferior temp
- Thinning correlation with decreased QOL

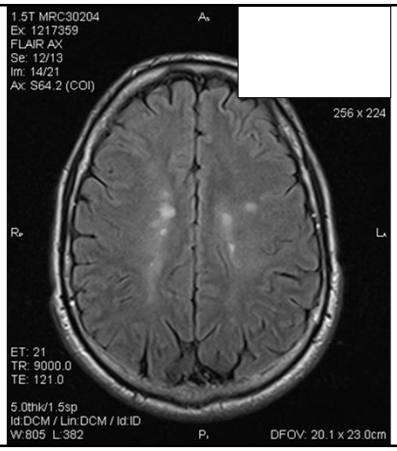
Garcia-Martin E, et al. *Ophthalmology* 2017

121

30 y/o AA Woman

- 1-year Hx of RRMS
- Meds:
  - Ocrevus (ocrelizumab)
  - baclofen
- No prior history of optic neuritis
- BVA:
  - 20/20 OD
  - 20/20 OS

122



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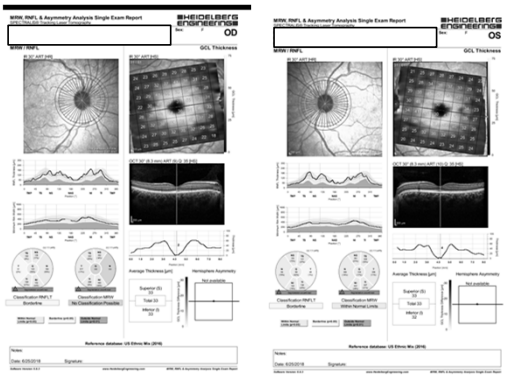

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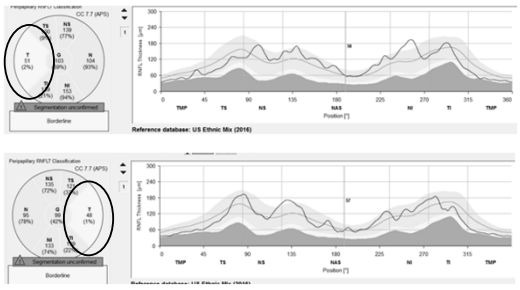
Temporal Predilection



125

Active MS is associated with accelerated retinal ganglion cell/inner plexiform layer thinning

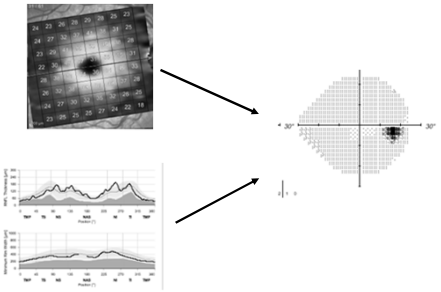
Ratchford, John N. MD; Saidha, Shiv MRCPI; Sotirchos, Elias S. MD; Oh, Jiwon A. MD, FRCPC; Seigo, Michaela A. ScB; Eckstein, Christopher MD; Durbin, Mary K. PhD; Oakley, Jonathan D. PhD; Meyer, Scott A. PhD; Conger, Amy COA; Frohman, Teresa C. BS; Newsome, Scott D. DO; Balcer, Laura J. MD, MSCE; Frohman, Elliot M. MD, PhD; Calabresi, Peter A. MD

- Longitudinal study of ganglion cell/inner plexiform (GCIP) layer q 6 months in 164 MS patients (59 health controls)
- Exclusion if development of optic neuritis
- Faster rates of GCIP thinning if:
  - Relapses (42% faster, p = 0.007)
  - New gad-enhancing lesions (54% faster, p < 0.001)
  - New T2 lesions (36% faster, p = 0.002)
- Highest annual rates of GCIP thinning if combination of new gad-enhancing lesions, new T2 lesions & disease duration < 5 yrs. (70% faster in patients with all three characteristics vs. without, p < 0.001)

Ratchford JN, et al. *Neurology* 2013

126

How do OCT Parameters Correlate with Visual Function?



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Macular Ganglion Cell and Inner Plexiform Layer Thickness Is More Strongly Associated With Visual Function in Multiple Sclerosis Than Bruch Membrane Opening–Minimum Rim Width or Peripapillary Retinal Nerve Fiber Layer Thicknesses

James Nguyen, BS, Alissa Rothman, BS, Natalia Gonzalez, MD, Ama Avornu, BA, Esther Ogbuokiri, BS, Laura J. Balcer, MD, MSCE, Steven L. Galetta, MD, Elliot M. Frohman, MD, PhD, Teresa Frohman, PA-C, Ciprian Crainiceanu, PhD, Peter A. Calabresi, MD, Shiv Saidha, MBBCh, MD, MRCPI,

- BMO-MRW, PPRNFL & GCIPL all reduced in MS vs. healthy controls
- GCIPL thickness is a stronger overall marker of visual impairment as compared to BMO-MRW & PPRNFL

Nguyen J, et al *J. Neuro-Ophthalmol* 2019

128

Polling Question #4

Which segment of the NFL is most likely to show thinning in the setting of multiple sclerosis?

a) Nasal
b) Temporal
c) Superior
d) Inferior

129

OCT in Neurodegenerative Disease

- Multiple sclerosis
- Parkinson's disease
- Alzheimer's disease
- TBI

130

Dopamine and Retinal Function

- Dopamine is released by retinal amacrine cells and binds to D1 and D2 receptors
- Responsible for light adaptation, circadian rhythm, cell survival and eye growth
- Reduction in retinal dopamine levels → retinal and NFL thinning

Witkovsky P. *Documenta Ophthalmologica* 2004
Sengupta P, et al. *Ann Indian Acad Neurol* 2018

131

Review

Optical Coherence Tomography in Parkinson's Disease: Is the Retina a Biomarker?

Jee-Young Lee[1,2,*], Jeeyun Ahn[3,4], Tae Wan Kim[3,4] and Beom Seok Jeon[1,4]
[1]Department of Neurology, Seoul National University-Seoul Metropolitan Government Boramae Medical Center, Seoul, Republic of Korea
[2]Department of Ophthalmology, Seoul National University-Seoul Metropolitan Government Boramae Medical Center, Seoul, Republic of Korea
[3]Department of Neurology and Movement Disorders Center, Seoul National University Hospital, Seoul, Republic of Korea
[4]College of Medicine, Seoul National University, Seoul, Republic of Korea

- RNFL thinning in PD associated with visual hallucinations & with PD duration and severity
- Potential for OCT as a surrogate biomarker of disease activity/progression

Lee JY, et al. *J Parkinson's Disease* 2014

132

OCT Findings in Parkinson's Disease

- Global reduction in RNFL thickness, ganglion cell complex thickness and macular volume
  - RNFL thinning Temporal > nasal
  - Thinning of OCT parameters correlate with severity and duration of PD

Sengupta P, et al. *Ann Indian Acad Neurol* 2018
Aydin TS, et al. *Kaohsiung J Med Sci* 2018
Yidiz D, et al. *Ann Indian Acad Neurol* 2019

133

OCT in Neurodegenerative Disease

- Multiple sclerosis
- Parkinson's disease
- Alzheimer's disease
- TBI

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Alois Alzheimer, MD (1906)

- South-West German Psychiatrists' Meeting presentation on pre and post-mortem findings of Auguste Deter - *"On a Peculiar Disease of the Cerebral Cortex"*

135

Alzheimer's Disease

- Progressive dementia with loss of neurons and the presence of two main microscopic neuropathological hallmarks: extracellular amyloid plaques and intracellular neurofibrillary tangles

Gheorghita M, et al. *Rom J Psychopharmacol* 2010

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The NEW ENGLAND JOURNAL of MEDICINE

Vol. 313 No. 8 OPTIC NEUROPATHY IN ALZHEIMER'S DISEASE — HINTON ET AL. 483

OPTIC-NERVE DEGENERATION IN ALZHEIMER'S DISEASE

DAVID R. HINTON, M.D., ALFREDO A. SADUN, M.D., PH.D., JANET C. BLANKS, PH.D., AND CAROL A. MILLER, M.D.

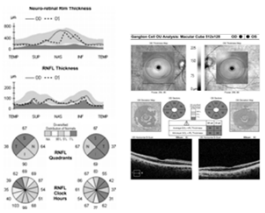
Abstract Alzheimer's disease is a dementing disorder of unknown cause in which there is degeneration of neuronal subpopulations in the central nervous system. In postmortem studies, we found widespread axonal degeneration in the optic nerves of 8 of 10 patients with Alzheimer's disease. The retinas of four of the patients were also examined histologically, and three had a reduction in the number of ganglion cells and in the thickness of the nerve-fiber layer. There was no retinal neurofibrillary degeneration or amyloid angiopathy, which are typically seen in the brains of patients with Alzheimer's disease. The changes we observed in the patients with Alzheimer's disease were clearly distinguishable from the findings in 10 age-matched controls and represent a sensory-system degeneration that occurs in Alzheimer's disease. Study of the retina in patients with this disease may be helpful diagnostically, and isolation of the affected ganglion cells may facilitate molecular analysis of the disorder. (N Engl J Med 1986; 315:485-7.)

- 1986 study post mortem study of optic nerves in patients with AD
- Wide-spread axonal degeneration in 8/10 optic nerves
- Specificity for larger M-cell degeneration

137

OCT Findings in AD

- RNFL & paramacular thinning in AD vs. controls (Polo V, et al. *Eye* 2014)
- RNFL thinning (superior quadrant selectivity with mild cognitive impairment/early AD) parallels dementia progression in AD (Liu D, et al. *BMC Neurol* 2015)
- RNFL and superior retinal thickness/GCIPL thinning (Cunha JP, et al. *Graefe's Arch Clin Exp Ophthalmol* 2017



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Alzheimer's & Dementia

Retinal Imaging

Retinal thickness in Alzheimer's disease: A systematic review and meta-analysis

Jurre den Haan[a,*], Frank D. Verbraak[b,c], Pieter Jelle Visser[a,d], Femke H. Bouwman[a]

- Meta-analysis of 25 studies involving 887 AD patients, 216 MCI patients and 864 health controls
- AD & MCI patients had thinner RNFL ($p < 0.0001$) & macular thickness ($p = 0.0001$) as compared to healthy controls

ML1

den Haan J, et al. *Alzheimer's & Dementia* 2017

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Polling Question #5

Which of the following statements is true about the RNFL in the setting of Alzheimer's disease?

a) Shows progressive thinning over time
b) Shows progressive thickening over time
c) There is no relationship between NFL thickness and Alzheimer'

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OCT in Neurodegenerative Disease

- Multiple sclerosis
- Parkinson's disease
- Alzheimer's disease
- TBI

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Diffuse Axonal Injury (DAI)

- Rapid axonal stretching
- Axoplasmic stasis with focal axonal swelling ("axonal varicosities" / "axonal bulbs")
- Ionic imbalance (Ca++ and K+)
- Accumulation of candidate proteins – amyloid precursor protein (APP)
- Microtubular disarrangement
- Dispersal and accumulation of preivascular neurofibrillary tau tangles

Johnson VE, et al. *Exp Neurol* 2012

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Evidence for OCT as a Potential Surrogate Biomarker of Chronic Traumatic Encephalopathy

- Approx. 50% of brain devoted to vision and visual motor function
- Opportunity for retrograde axonal degeneration into the optic nerve
- Identification of TDP-43 retinal deposition in autopsied eyes from CTE subjects

Goodwill V, et al. *Invest Ophthalmol Vis Sci* 2020

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Slide 139

ML1 Messner, Leonard, 8/8/2021

Original Contribution

Visual Structure and Function in Collision Sport Athletes

Danielle Leong, OD, PhD, Christina Morettin, OD, Leonard V. Messner, OD, Robert J. Steinmetz, OD, Yi Pang, MD, OD, PhD, Steven L. Galetta, MD, Laura J. Balcer, MD, MSCE

- Multi-center study of 46 collision sport athletes as compared to age-matched healthy controls
  - Illinois Eye Institute/Illinois College of Optometry
  - NYU Langone Medical Center/Department of Neurology
- Comparison of OCT, low contrast acuity, rapid number naming & quality of life among boxers/retired NFL players vs. age-matched controls

Leong D, et al. *J Neuro-ophthalmol* 2018

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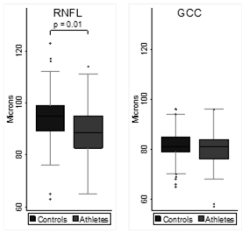
Results: Visual Pathway Structure



	Controls (n=104, 208 eyes)	Athletes	
		Boxing Athletes (n=14, 28 eyes)	Football Athletes (n= 29, 58 eyes)
Average RNFL thickness, µm, mean ± SD	94.3 ± 0.9	83.5 ± 2.8 *p* < 0.001	93.0 ± 1.9
Average GCC thickness, µm, mean ± SD	81.6 ± 0.5	76.7 ± 2.1 *p* = 0.02	81.2 ± 1.2

Leong D, et al. J Neuro-ophthalmol 2018

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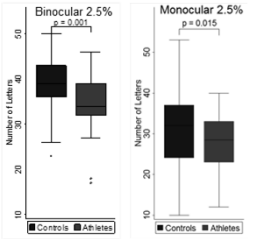
Visual Function: Low Contrast Acuity



	Controls (n=104, 208 eyes)	Athletes	
		Boxing Athletes (n=14, 28 eyes)	Football Athletes (n= 29, 58 eyes)
Binocular 2.5%, mean (letters/70)	38.6 ± 0.5	31.7 ± 2.1 *p* = 0.002	36.6 ± 1.0
Binocular 1.25%, mean (letters/70)	29.8 ± 0.6	26.4 ± 2.0	29.8 ± 0.8
Monocular 2.5%, mean (letters/70)	30.8 ± 0.6	24.4 ± 2.0 *p* = 0.003	29.2 ± 1.1
Monocular 1.25%, mean (letters/70)	21.2 ± 0.8	16.3 ± 2.0 *p* = 0.03	21.1 ± 1.2

Leong D, et al. J Neuro-ophthalmol 2018

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Eye and Brain

Dovepress

ORIGINAL RESEARCH

Investigating possible retinal biomarkers of head trauma in Olympic boxers using optical coherence tomography

- Longitudinal, OCT macular & RNFL thickness analysis of 16 Olympic boxers over 18 months
- Comparison to 20 healthy controls
- Progressive macular & RNFL thinning in boxers as compared to healthy controls

Childs C, et al. Eye and Brain 2018

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OCT Findings in Military Veterans with TBI vs. Healthy Controls

- Longitudinal OCT study of veterans with mTBI vs. controls
- Significant progression of RNFL thinning among mTBI cohort (1.25 microns/year) as compared to controls (0.1 microns/year)

Kardon R, et al. NANOS Meeting 2019

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OCT, it's not just for glaucoma and retinal disease anymore!

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Thank you!

ILLINOIS EYE INSTITUTE

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Thank you! Please join us for our next COPE event

Date: October 14, 2021
Time: 5:30 pm PST
Speakers: Dr. Peter Hersh,
Dr. Steven Greenstein and Dr. John Gelles
Topic: Corneal Inlays for Keratoconus: Past, Present, Future
COPE: One hour live CE

Visit WooU.org for a full list of upcoming CE events!

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