OCT in Neuro-Ophthalmic Disorders: Papilledema, MS & other Neurodegenerative Diseases

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Key Points

- OCT analysis of papilledema vs. pseudopapilledema
- OCT analysis of chiasmal compression
- OCT in neurodegenerative disease
  - Multiple sclerosis
  - Parkinson’s disease
  - Alzheimer’s disease
  - TBI

Definition of Papilledema

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

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)

Stages of Papilledema (Frisen Grading Scale)

Disclosures

- King Devick Technologies (scientific advisory board)
- Heidelberg Engineering (professional advisory board)
- Illinois Society for the Prevention of Blindness (clinical research grants)
Grade I

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

Grade II

- Circumferential halo of optic disc edema

Grade III

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

Grade IV

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

Grade V

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

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

Kupersmith MJ, et al. IOVS 2011
32 y/o AA Woman

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

- C/o chronic daily headaches
- + synchronous pulsatile tinnitus
- BMI: 42
- BVA:
  - 20/20 OD
  - 20/20 OS

MRI/V consistent with IIH
- LP = 32 cm H2O (normal cytology)
- Rx acetazolamide 500 mg bid
- Follow-up x 3 months
43 y/o AA Woman

- C/o chronic daily headaches & SPT x 1 year
- BMI: 32
- BVA:
  - 20/20 OD
  - 20/20 OS

40 y/o AA Woman

- C/o chronic daily Has
- + SPT
- BMI = 44
- BVA:
  - 20/40 OD
  - 20/40 OS
38 y/o AA Woman

- Medical history = SLE
- Tx with po prednisone
- Approx. 200 lb weight gain (>400 lbs.)
- BVA:
  - 20/20 OD
  - 20/20 OS
Cont.

- MRI / MRV consistent with IIH
- Lost to follow-up
- F/U 5 mos. later complaining of progressive severe HA (10/10)
- BVA:
  - 20/20 OD
  - 20/20 OS
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
F/U x 6 mos

- Rx Diamox (500 mg BID)
- Weight loss (approx. 25 lbs.)
- Improvement in headaches
F/U x 14 mos
• D/C Diamox x 3 months
• Weight loss (BMI reduction from 38 to 30)
• Headache free
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

Malmqvist L, et al. J Neuro-ophthalmol 2018

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

Marsxyld L, et al. J Neuro-ophthalmol 2018

OCT Characteristics of Optic Disc Drusen

- Always located above the lamina cribrosa
- 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
- Peripapillary hyper-reflective ovoid mass-like structures (PHOMS) may represent bulging axons and should not be considered as ODD

Malmqvist L, et al. J Neuro-ophthalmol 2018
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

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
6 y/o Hispanic Female

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

8/14/13

8/16/19

85

86

87

88

89

90
“A patient can have as many diseases as he damn well pleases.”

John Hickum, MD

21 y/o Caucasian Woman

- c/o chronic daily headaches with SPT x several months
- Normal neurologic exam
- BVA:
  - 20/20 OD
  - 20/20 OS
- BMI: 38

NFL:
- 181 microns OD
- 202 microns OD
• MRI findings consistent with IIH
• Rx acetazolamide 250 mg bid
• f/u x 8 mos:

OCT Analysis of Chiasmal Compression

• 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
40 Y/O Caucasian Man

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

GCC analysis:
Bi-nasal GCC thinning

Magnetic Resonance Imaging

103
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• OCT GCC analysis more sensitive than perimetry for detection of early chiasmal compression

Blanch RJ, et al. Pituitary 2018

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31 y/o Caucasian Man

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

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OCT in Neurodegenerative Disease

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

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

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OCT Findings in Optic Neuritis

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

45 y/o Woman

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

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

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

31 y/o Woman

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

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

- 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

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
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

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


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How do OCT Parameters Correlate with Visual Function?

Temporal Predilection

OCT in Neurodegenerative Disease
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

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

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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”

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
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

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)

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

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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
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


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

Results: Visual Pathway Structure

|       | Controls   | Athletes
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<tbody>
<tr>
<td></td>
<td>(n=104, 208 eyes)</td>
<td>(n=14, 28 eyes)</td>
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<tr>
<td>Average RNFL thickness, µm, mean ± SD</td>
<td>94.3 ± 0.9</td>
<td>83.5 ± 2.8</td>
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<tr>
<td>Average GCC thickness, µm, mean ± SD</td>
<td>81.6 ± 0.5</td>
<td>76.7 ± 2.1</td>
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</tbody>
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Visual Function: Low Contrast Acuity

|       | Controls   | Athletes
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<tr>
<td></td>
<td>(n=104, 208 eyes)</td>
<td>(n=14, 28 eyes)</td>
</tr>
<tr>
<td>Binocular 2.5%</td>
<td>38.6 ± 0.5</td>
<td>31.7 ± 2.1</td>
</tr>
<tr>
<td>Binocular 1.25%</td>
<td>29.8 ± 0.6</td>
<td>26.4 ± 2.0</td>
</tr>
<tr>
<td>Monocular 2.5%</td>
<td>30.8 ± 0.6</td>
<td>24.4 ± 2.0</td>
</tr>
<tr>
<td>Monocular 1.25%</td>
<td>21.2 ± 0.8</td>
<td>16.3 ± 2.0</td>
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Leong D, et al. J Neuro-ophthalmol 2018

OCT Findings in Military Veterans with TBI vs. Healthy Controls

- 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

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

Key Points

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Thank you!