Rapid Fire: Clinical Application of OCT Enhanced Depth Imaging

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Disclosure Statement:
Robert Dunphy has been a paid consultant for Heidelberg Engineering, no current financial interests.
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Overview

• “Windowing” OCT for enhanced information about outer retinal and choroid structure
• Glaucoma
• Choroid thickness and qualities
• Choroid in DM
• Choroid in AMD
• Choroid in Maculopathies
Challenging Assumptions

- Prevalence of uncommon disorders
- Assumptions about the choroid
- Parameters of the nerve head
- Relationship between choroid features and retinal disease manifestation
- Directed imaging studies of critical regions of the retina
Assumptions

• Choroid is regular and symmetric
• Choroid is stable
• CDR represents status of rim tissue
• Clinical disease states are identifiable by their ophthalmoscopic presentation
Imaging deeper structural features in glaucoma

- Traditional paradigm - cup / disc estimation
- ONH surface contour
- OCT peripapillary circle scan
- Inner retinal ganglion cell population

- Intrapapillary structural reference and features - 3D model of ONH
- Lamina cribrosa features
SDOCT BMO Anatomy

Chauhan after Strouthidis et al., Invest Ophthalmol Vis Sci., 2009
Minimum Rim Width

Bruch’s membrane

Bruch’s membrane opening (BMO)

border tissue
Regionalize and Parameterize OCT data sets relative to anatomic landmarks
BMO-MRW Exceeds RNFL and Horizontal rim width

Enhanced Detection of Open-angle Glaucoma with an Anatomically Accurate Optical Coherence Tomography–Derived Neuroretinal Rim Parameter

Objective: Neuroretinal rim assessment based on the clinical optic disc margin-GMH lacks a sound anatomic basis for 2 reasons: (1) The GMH is not reliable as the outer border of rim tissue because of clinically and geographically variable extensions of Bruch’s membrane (BM) inside the GMH and (2) measurement variability of rim margin definition in the optic nerve head (ONH). The rim margin rim width (BMO-MRW) is a parameter that quantifies the rim from its true anatomic outer border (BMH) and accounts for its variable configuration. We report the diagnostic capability of BMO-MRW.

Methods: Cross-sectional open-angle glaucoma is ... and healthy controls (n = 30).

Fig. 3. The receiver operating characteristics (ROC) curves illustrating the diagnostic performance of optic nerve head rim area (RNFLT), BMO-Rim area (BMO-MRA), and Bruch’s membrane opening horizontal rim width (BMO-MRW) and Bruch’s membrane opening horizontal rim width (BMO-MRW) compared globally. Also shown are the 2-diameter points of the global Mondiaz Reference Analyzer (MRA) from confocal scanning laser tomography (CSLT). MRA1, where “0-degrees” cases were classified as normal; and MRA2, where “45-degrees” cases were classified as abnormal. Useful metrics are indicated respectively.

Enhanced Depth Imaging of the Optic Nerve and Surrounds

Doug Rett OD FAAO
AAO Chicago 2017
Lamina Cribrosa Imaging

- **Lamina cribrosa (LC)**
  - **Thickness**
    - Thickest in healthy eyes
    - Less thick in eyes with high-pressure glaucoma
    - Thinnest in eyes with normal-tension glaucoma
      - Has been noted to thin before any defect in MD index on visual field testing
    - Thickness is hard to judge (SS-OCT?)
  - **Position**
    - Migrates posteriorly as glaucoma progresses
    - The more glaucomatous damage there is, the deeper the LC migrates
    - Position is hard to quantify
      - LC curvature index exists, but not practical
Lamina Cribrosa Depth

- Has always been useful, but never had a standardized reference.
- Now we use the line between Bruch Membrane Openings (BMO)
  - Helpful because only uses anterior face of LC
- Average readings (interpatient variability)
  - 344um for normal
  - 448um for advanced glaucoma
- Caution, BMO can be variable
  - Choroidal Thickness
  - Glaucomatous eyes experience “hoop stress”

(5)
The initial site of RGC injury is likely the LC\textsuperscript{6}.

LC is a pressure valve
- Flexible beams of LC act to ease the pressure differential between the relatively high-pressure environment in the eye to the low-pressure region in the cerebrospinal fluid space\textsuperscript{7}.

Shear stress and compressive stress
- The deformation of the LC may cause kinking and pinching of the axons passing through the laminar pores, promoting blockade of the axoplasmic flow. In addition, LC deformation may compress the laminar capillaries, thereby causing ischemic insult to the axons.

Pressure and vascular mechanisms are intertwined!
Lamina Cribrosa and Glaucoma progression

• Circle scan limitations
  – Superficial retinal changes
  – Line segmentation errors

• Cup-to-disc ratio limitations
  – Only horizontal and vertical
  – Quite subjective and can be difficult to judge

• Objective measurements of LC thickness and position would be helpful to use for progression detection
Normal Tension Glaucoma and LC

- Drance’s hemorrhages are more common in NTG\(^3\)
- LC is thinner and more posteriorly positioned in NTG\(^4\)
- The area where the LC is remodeled correlates with the location of disc hemorrhages
Optic Pits and LC

- Pits can be acquired or congenital
- Optic pits represent a localized area of susceptibility of the LC to IOP associated structural changes
- Need to identify them and, if found, treat pressure aggressively
  - Highly correlative with RNFL loss
Choroidal Thickness and EDI

• Blood flow to the choroid is the highest per tissue mass in the body\textsuperscript{10}
Peripapillary Perfusion Confusion

• It is controversial whether the peripapillary choroid even perfuses the prelaminar region of the ONH\textsuperscript{11, 12}
  – Question of whether the SPCAs and circle of Zinn-Haller branches join the choroid or simply pass through it. Hayreh says yes, they are considered part of the choroid when they pierce sclera.

• SUMMARY:
  – Peripapillary choroid is a small part of entire choroid
  – Blood supply of peripapillary choroid is a small part of entire ONH perfusion
  – Thus, change in choroidal blood flow does not necessarily reflect change in ONH perfusion

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Glaucoma and Choroidal Thickness

• Important to be matched to:
  – Age
  – Axial-length
  – Time of Day

• No difference in sub-foveal choroidal thickness (**SFCT**) between POAG patients and non-glaucoma patients\(^8\)

• No difference in peripapillary choroidal thickness (**PPCT**) between glaucoma and non pts EXCEPT maybe in temporal region in NTG pts\(^9\)

• Some studies show no difference anywhere
  – Meta-analysis of 22 studies using EDI found “no significant difference in both SFCT and PPCT between OAG and NTG pts and controls”\(^{10}\)
Different Mechanisms of Glaucoma → Different Uses of EDI for Glaucoma

• Open angle glaucoma
  – No big change in PPCT; but EDI useful in LC structural changes like:
    • LCD (LC Depth)
    • LC bowing
    • FLCD (Focal LC Defects)

• Closed angle glaucoma
  – Water drinking test shows a greater increase in choroidal thickness in angle closure glaucoma patients than in OAG pts

• Normal tension glaucoma
  – Driven by perfusion, and this seems to be the only type of glaucoma which correlates with PPCT
  – Temporal region thinning could explain increase in beta zone PPA
Literature

Enhanced Depth Imaging in Diabetes and Age-related Macular Degeneration

Rachel Currin, OD FAAO
AAO Chicago 2017
EDI-OCT macular imaging

Enhanced visualization of outer retinal layers
EDI-OCT macular imaging

Enhanced visualization of the choroid
Choroidal thickness in disease

Ocular disease

- Diabetic retinopathy*
- Age-related macular degeneration*
- Central serous chorioretinopathy
- Uveitis
- Myopic degeneration

Systemic disease

- Diabetes
- Cardiovascular disease
- Carotid artery disease
- Renal disease
- Autoimmune disease
- Alzheimer’s dementia

Choroidal thickness in diabetes

Mixed reports in the literature

- Many confounding factors! (ophthalmic + systemic)

- Studies must control for:
  - AGE
  - REFRACTIVE ERROR
  - AXIAL LENGTH
  - DIRUNAL FLUCTUATION
Choroidal thickness in diabetes

Subfoveal + perifoveal choroid is **THINNER** in diabetics compared to non-diabetics\(^1,2,3,4\)

- Endothelial degeneration / capillary dropout
- Reduced choroidal blood flow\(^5\)

1. Esmaeelpour et al. Retina 2010
2. Querques et al. IOVS 2012
3. Kim et al. IOVS 2013
5. Nagaoka et al. BJO 2004

Choroidal thickness in diabetes

Unclear relationship with level of NPDR and with DME
- No relationship\(^1,2\)
- Increasing thickness with increasing levels\(^3,4\)

Initial ischemic phase $\rightarrow$ choroidal thinning

Subsequent exudative/proliferative stage (mediated by VEGF) $\rightarrow$ choroidal thickening

1. Xu et al. Ophthalmology 2013
2. Lee et al. Ophthalmology 2013
3. Kim et al. IOVS 2013
Choroidal thickness in diabetes

Figure 1. Fundus photograph (first row), FA (second row), and EDI-OCT (bottom row). First column: no DR. Second column: severe NPDR. Third column: untreated PDR. Fourth column: PRP treated DR. Fifth column: severe NPDR with DME of SRD-type. SFCT is indicated in the figure of EDI-OCT. Arrowheads indicate hyperreflective line of the choroid-scleral interface on EDI-OCT. Green markings indicate ChT measured with the caliper program of the Heidelberg Eye Explorer software of EDI-OCT.
Choroidal thickness in diabetes

• **Thinning** occurs in PDR after PRP\(^1,2\)
  – Ablation of vessels
  – Reduction of VEGF

• Intravitreal anti-VEGF initially hastens PRP-induced choroidal thinning\(^3\)

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1. Kang et al. Retina 2017
2. Kim et al IOVS 2013
Choroidal thickness in diabetes

• Diabetic choroidal thinning occurs before clinical retinopathy, independent of A1c\(^1\)
  – No predictive / longitudinal studies to date

• Baseline choroidal thickness may predict DME treatment response with intravitreal anti-VEGF \(^2\)
  – Anatomical + functional response
  – Thinner choroid at baseline = worse outcome

EDI-OCT imaging in ARMD

• Increased outer retinal visibility


• Increased visibility of the choroid
Choroidal thickness in ARMD

Mixed literature – **NO EFFECT**\(^1,2\) vs **THINNING**\(^3,4\), in both dry and wet ARMD

2. Jonas et al. Retina 2014
4. Sigler et al. IOVS 2013
Choroidal thickness in ARMD

No relationship between ARMD status and choroidal thickness according to histology studies, except for end-stage dry ARMD (GA) (thinner)

Sohn et al. IOVS 2014
Choroidal thickness in ARMD

No relationship between ARMD status and choroidal thickness by EDI-OCT, according to AREDS2 classification of AMD and when accounting for age.

Choroidal thickness in ARMD

**Drusen subtype** may matter when analyzing choroidal thickness
Choroidal thickness in ARMD

**Drusen subtype** may matter when analyzing choroidal thickness

Pachydrusen phenotype =
- Irregular/complex shape to the drusen
- Scattered distribution of drusen
- Reddish hue to the choroid
- Featureless choroid

**Thicker choroid in dry ARMD** characterized by pachydrusen, with thin vs normal choroid in other forms of dry ARMD
Choroidal thickness in ARMD

Choroidal thickness may predict response to anti-VEGF (anatomical and functional) in wet ARMD\textsuperscript{2,3}

– Thinner choroid at baseline carries worse prognosis

Choroidal thickness in ARMD

Choroidal thickness may **differentiate between wet ARMD and mimickers**

**THICKER choroid in:**

- Adult-onset vitelliform foveomacular dystrophy\(^1\)
- Polypoidal choroidal vasculopathy\(^2,3\)
- Central serous chorioretinopathy\(^3\)

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1. Coscas et al. IOVS 2014
Enhanced Depth Imaging: The Clinical Features Underlying Central Serous Chorioretinopathy

James M. Caruso, O.D., F.A.A.O.
American Academy of Optometry • Chicago
October 2017
Overview

• ID choroidal involvement in Central Serous Chorioretinopathy (CSCR)
• Identify populations at risk
• Entertain this possible Dx among patients with RPE abnormalities not overtly CSCR
• Review key literature
• Incorporation of clinical presentations (acute and chronic) with enhanced depth imaging spectral domain optical coherence tomography (EDI-OCT) interpretation
History of CSCR

- Central recurrent retinitis 1866
- Idiopathic flat detachment of the macula by Walsh
- Central angiospastic retinopathy by Gifford
- Central serous retinopathy by Straatsma
- Idiopathic central serous chorioretinopathy by Gass et al in 1967
Initially there is choroidal hyperpermeability with congestion of the choriocapillaris along with exudation of protein and fluid. RPE pump decompensation occurs over time with the formation of a pigment epithelial detachment.

Eventually, RPE defect develops, leading to leakage into the subretinal space. This leads to elevation of the neurosensory retina and a neurosensory retinal detachment.
Epidemiology

• Most common vision-threatening retinopathy after AMD, diabetic retinopathy, and BRVO
• Reported annual incidence was 9.9 per 100,000 individuals for men and 1.7 for women
• More common among Caucasians and may be particularly severe among Asians and Hispanics
• Age typically between 20-55
• Refractive error
# Risk Factors and Associations

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<th>REPORTED RISK FACTORS AND ASSOCIATIONS WITH CENTRAL SEROUS CHORIORETINOPATHY</th>
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<td><em>Helicobacter pylori</em> infection</td>
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<tr>
<td>Autoimmune disorders</td>
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From Yanoff and Duker, Ophthalmology, 3rd ed.
EDI-OCT and CSCR

- Imamura et al. performed a study of 19 patients with CSCR
- Mean age 59.3
- 17 of 19 patients (89.5%) were men
- 12 (63.2%) patients exhibited bilateral clinical disease
- The subfoveal CT was measured from the outer border of the retinal pigment epithelium to the inner scleral border via enhanced depth imaging
- They found a mean subfoveal CT to be 505 um (range 439 to 573)
- Those with unilateral CSCR, CT was also increased in the disease-free fellow eye
- Increased CT represented ischemia, vascular dilatation, and hyperpermeability
EDI-OCT and CSCR

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EDI-OCT: Horizontal and Vertical Line Scans
Genetic Predisposition

• EDI-OCT has provided stronger evidence for a genetic contribution to the pathophysiology of CSCR

• In 14 out of 27 families of CSCR patients (52%), at least one relative presented with multiple areas of RPE irregularities suggestive of chronic or asymptomatic disease (Weenink et al)

• These relatives possessed CT greater than 395 μm, suggesting that pachychoroid could be an inherited condition with a possible dominant transmission pattern
EDI-OCT and New Pathophysiology Hypothesis

• Previous hypotheses have included abnormal ion transport across the RPE
• The advent of ICGA and EDI-OCT has shown choroidal alterations, suggestive of choroidal vascular compromise, ischemia, and hyperpermeability of the choriocapillaris
• Increase in CT in patients with CSCR visualized by EDI-OCT further supports the idea of vascular congestion and elevated hydrostatic pressure
EDI-OCT and New Pathophysiology Hypothesis

- Mineralocorticoid Receptors (MR) are expressed in the neurosensory retina, RPE, and choroid, suggesting that CSCR could result from MR over-activation
- The MR has two natural ligands, aldosterone and cortisol, that bind to MR with the same affinity
- Studies have evidenced that MR over-activation via either overexpression of the receptor in the vessels, or acute administration of its ligands (aldosterone and cortisol) produces choroidal enlargement
- PEARL: CSCR may be due to over-activation of the mineralocorticoid receptor, which has more recently become a new target for treatment (MR antagonists)
Case #1: Acute

- 40 year-old Caucasian male
- Sudden onset blur OS after feeling a small “pop”
- HTN (Amlodipine), Anxiety, Hyperlipidemia
- BVA OD 20/20 OS 20/40-
- Entrance testing, SLE, IOP normal
EDI-OCT visualized the PED and a hyperreflective flow within the SRF overlying a pachychoroid
EDI-OCT showing increased subfoveal CT
4 week follow-up
4 week follow-up
2 month follow-up
2 month follow-up
4 month follow-up
12 months
Increased CT in fellow eye
Case #2: Chronic

- 68 year-old Caucasian male presented for exam
- Past ocular Hx: Dry AMD, DES
- Medical Hx: PTSD, HTN, Gout, GERD, ED
- Medications: Methadone, Atenolol, Allopurinol, Omeprazole, Sildenafil, AREDS 2 Vitamins
- BVA OD 20/50 OS 20/25
- Entrance testing: AG (+) metamorphopsia OD>OS
- SLE, IOP WNL
Choroidal Thickness After Treatment: Laser Photocoagulation vs. PDT

• Maruko et al evaluated twenty patients (20 eyes)
• Used EDI-OCT to measure subfoveal CT and height of the serous retinal detachment before and after treatment.
  – eyes with classic CSCR were treated with laser photocoagulation
  – eyes with chronic CSCR, which are not amenable to LP, were treated with half-dose verteporfin photodynamic therapy
Choroidal Thickness After Treatment: Laser Photocoagulation vs. PDT

- There were 12 eyes in the LP group and 8 eyes in the PDT group. The serous subretinal fluid resolved in both groups after treatment.
  - LP = mean CT was 345 uM at baseline and 340uM at 4 weeks
  - PDT= mean CT 389 uM at baseline, 462 uM at 2 days, and then reduced rapidly to 360 at 1 week and 330 uM at 4 week mark

- PEARL: The subretinal fluid resolved in both disease groups; however, the CT measured via EDI-OCT (indicating reduced hyperpermeability as seen during ICGA) was only reduced after PDT
Conclusion

• Review of MHx is imperative
  – Identify risk factors (FHx, Social Hx, Meds)
• Determine who is at greatest risk by evaluating outer retina/ RPE / choroid
• Consider referral for PDT with failure of fluid to regress and before decrease in BVA becomes irreversible
• Clinical Pearl: CSCR is not merely an ocular disease, but a manifestation of a systemic vascular alteration that leads to an increase in CT, indicating ischemia and hyperpermeability
References


