Marshall B.
KETCHUM UNIVERSITY
Southern California College of Optometry

Joint SCCO | USC | VA Symposium

Live Interactive CE Webinar | AM Session

Sunday | September 19, 2021 | 8:00 a.m. - 11:50 a.m.

Joint SCCO | VA | USC Symposium

Marshall B. KETCHUM UNIVERSITY
Southern California College of Optometry
Department of Continuing Education

Sunday, September 19

Pacific Time Zone | Live Webinar | Pending COPE-Approval

Morning Session

8:00 a.m. - 8:55 a.m.
Keratoconus in Youth: An Urgent Issue?
Gloria Chiu, OD

8:55 a.m. - 9:50 a.m.
Updates in Clinical Glaucoma Management
Brian Song, MD

10:00 a.m. - 11:50 a.m.
Refer or Relax? Macula
Steven Ferrucci, OD

11:50 a.m. - 12:10 p.m.
Break

Afternoon Session

12:10 p.m. - 1:05 p.m.
Optic Disc Edema
Jessica Chang, MD

1:05 p.m. - 2:00 p.m.
Herpetic Eye Disease
Brian Toy, MD

2:10 p.m. - 3:05 p.m.
The Calm in the Eye of the Storm: Re-Purposed Medications for COVID-19
Judy Tong, OD

3:05 p.m. - 4:00 p.m.
IPC: A Case for Collaboration
John Nishimoto, OD and Julie Tyler, OD

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Instructor Biographies

Marshall B. KETCHUM UNIVERSITY
Southern California College of Optometry
Department of Continuing Education

Gloria Chiu, OD

Associate Professor of Clinical Ophthalmology, USC Roski Eye Institute

Dr. Gloria Chiu completed her Bachelor of Arts from the University of California, Berkeley. She remained at the University of California, Berkeley, where she obtained her Doctor of Optometry degree in 2008. Following completion of her residency in Cornea and Contact Lenses at Southern California College of Optometry, Dr. Chiu pursued further fellowship training in Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) treatment at the Boston Foundation for Sight. Dr. Chiu developed and supervises the USC PROSE service and is actively conducting research in the areas of irregular corneas and ocular surface disease.

Brian Song, MD

Assistant Professor Of Clinical Ophthalmology & Director of Education, USC Department of Ophthalmology

Dr. Brian J. Song is Assistant Professor of Clinical Ophthalmology and Director of Education in the Department of Ophthalmology at the USC Keck School of Medicine. He received his undergraduate degree from Johns Hopkins University and his medical degree from the University of Texas Medical Branch. He then completed his ophthalmology residency at the Harkness Eye Institute of Columbia University Medical Center – New York Presbyterian Hospital followed by a glaucoma fellowship at the UCLA Stein Eye Institute. His current research interests include ophthalmic ultrasound and imaging methods to evaluate optic nerve biomechanics and blood flow abnormalities in glaucoma.

Steven Ferrucci, OD

Chief, Optometry Section at Sepulveda VA Ambulatory Care Center
Professor, MBKU | SCCO

Dr. Steven Ferrucci, a 1994 graduate of the New England College of Optometry, completed his Residency in Primary Care/Hospital Based/Geriatric Optometry at the Sepulveda VA Hospital in Sepulveda CA. He is currently Chief of Optometry at the Sepulveda VA Ambulatory Care Center and Nursing Home. He is also the Residency Director at his sight, and a Professor at the Southern California College of Optometry at Marshall B. Ketchum University. Dr. Ferrucci has lectured extensively, with a special interest in Diabetes, Diabetic Eye Disease, Age-Related Macular Degeneration, and Fluorescein Angiography. He has also published several articles in optometric journals, including The New England Journal of Optometry, Optometry and Vision Science, Optometry: Journal of The AOA and Review of Optometry. Currently, he serves on the Editorial Board for both Review of Optometry and Optometry Times. He is an active member in the American Optometric Association and the California Optometric Association, as well as a fellow in both the American Academy of Optometry and the Optometric Retinal Society.

Jessica Chang, MD

Clinical Assistant Professor of Ophthalmology, USC Roski Eye Institute

After undergraduate studies at Yale University, Dr. Jessica Chang spent a year doing volunteer work in China and then attended Duke University School of Medicine. As a medical student, she was selected as a Howard Hughes Medical Institute NIH Research Scholar and spent two years at the National Eye Institute doing basic and clinical research in ophthalmology. She then completed ophthalmology residency at the Wilmer Eye Institute, followed by American Society of Ophthalmic Plastic and Reconstructive Surgery fellowship training in Oculoplastics and Neuro-ophthalmology.

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Instructor Biographies

Marshall B. KETCHUM UNIVERSITY
Southern California College of Optometry
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Brian Toy, MD

Assistant Professor of Clinical Ophthalmology, Director of Clinical Informatics and Information Technology
Service Chief of the Uveitis and Ocular Inflammation Service, USC Roski Eye Institute

Dr. Brian Toy is a vitreoretinal fellow and clinical instructor at the USC Roski Eye Institute. He graduated magna cum laude from the University of California, Berkeley, with a degree in bioengineering, received an MD with distinction from the University of California, San Francisco, and completed a clinical research fellowship at the National Institutes of Health. He completed an internship at Santa Clara Valley Medical Center, a major county healthcare system in the Bay Area, and then completed an ophthalmology residency at Stanford University. Toy's professional interests include retinal imaging, telemedicine and safety net care, particularly as applied to diabetic retinopathy. Outside of work, he enjoys hiking, skiing, and spending time with friends and family.

Judy Tong, OD

Associate Professor & Assistant Dean of Residencies | MBKU | SCCO

Dr. Judy Tong is an Associate Professor of Optometry and Assistant Dean of Residencies at the Southern California College of Optometry of the Marshall B. Ketchum University. She received her BS degree in Genetics from the University of California, Berkeley and her OD degree from the Southern California College of Optometry. She completed a one-year residency in Primary Care Optometry at the Eye Institute of the Pennsylvania College of Optometry (Salus University). As the Assistant Dean of Residencies since November 2003, Dr. Tong serves to provide global administrative and educational direction to 24 residency programs across 6 different states. Her main academic responsibility is teaching anterior segment diseases, basic and advanced procedures including lasers, injection, and suturing. Dr. Tong is one of the core instructors of the glaucoma certification courses and grand rounds program in California. Dr. Tong's research activities include being the Principal Investigator and Co-Investigator on two phase III antibiotic drug trials and major allergy study.

John Nishimoto, OD, MBA

Professor & Senior Associate Dean for Professional Affairs, MBKU | SCCO

Dr. John Nishimoto received a Doctor of Optometry degree from the Southern California College of Optometry in 1987. In 1988, he completed a one-year residency in Hospital-Based Geriatric Optometry at the West Los Angeles VA Medical Center. Dr. Nishimoto is currently a Professor and the Senior Associate Dean for Professional Affairs. In 1997, he received a Health Care Executive Masters in Business Administration from the University of California, Irvine. Dr. Nishimoto has been a frequent contributor of articles and lectured on topics especially related to primary care and ocular disease. He is the co-author of the text "Differential Diagnosis in Primary Eye Care." Dr. Nishimoto is also currently a clinical faculty member in primary care and ocular disease at the University Eye Center at Ketchum Health. Dr. Nishimoto is a fellow of the American Academy of Optometry and served as Chair of the Section on Ocular Disease.

Julie Tyler, OD

Primary Care Department Chair & Associate Professor, MBKU | SCCO

Dr. Julie A. Tyler received her B.A. from Creighton University and her Doctor of Optometry Degree from Indiana University School of Optometry (IU). Following graduation, Dr. Tyler completed a Residency at Nova Southeastern University (NSU) and served as Chief Resident prior to joining the faculty at NSU full-time. More recently, Dr. Tyler joined the faculty at Southern California College of Optometry (SCCO) at MBKU. Dr. Tyler has served in a variety of clinical and academic roles including chief of service and instructor of record for various clinical and didactic coursework. She has been promoted to Associate Professor and received numerous teaching awards, as well as recognition as a faculty member of Gold Key Honor Society and in 2019 was inducted into Phi Kappa Phi honor society that recognizes individuals in all academic disciplines. Dr. Tyler has authored posters and published journal articles on a variety of topics in the areas of primary care and ocular disease and is a Fellow of the American Academy of Optometry and is also a member of the COA and AOA.

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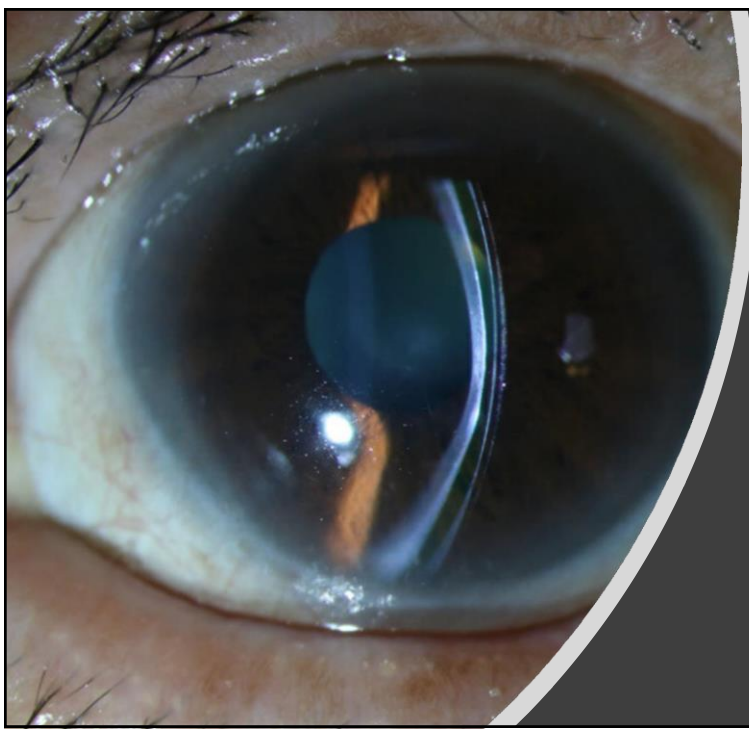
Keratoconus in Youth: An Urgent Issue?

Gloria Chiu, OD



Keratoconus in Youth: An Urgent Issue?

Southern California College of Optometry at MBKU
USC Joint Symposium
September 19, 2021

Gloria B Chiu, OD, FAAO, FSLS
Associate Professor of Clinical Ophthalmology
USC Roski Eye Institute, Dept of Ophthalmology
Keck Medicine of USC
Adjunct Faculty at Southern California College of Optometry

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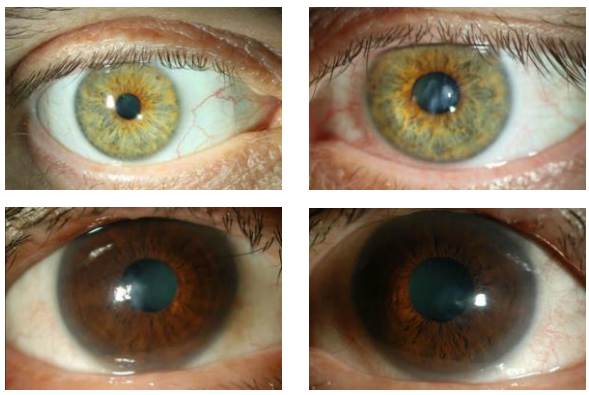
Financial Disclosures

- Avedro/Glaukos – Consultant
- Evolve Medical Education – Speaker
- Acculens – Received Honorarium

2

Keratoconus Overview

- Corneal Disorder with central thinning and steepening
  - Greek words: Kerato (cornea) and Conos (cone)
  - Bilateral
  - Asymmetric
  - Progressive
  - Non-inflammatory
- Onset
  - Teens/puberty
- Prevalence and Incidence
  - Varies with geography, ethnicity, study
  - Diagnosis often from ODs



The Open Ophthalmology Journal: Epidemiology of Keratoconus Worldwide, https://openophthalmologyjournal.com/VOLUME/12/PAGE/289/FULLTEXT/

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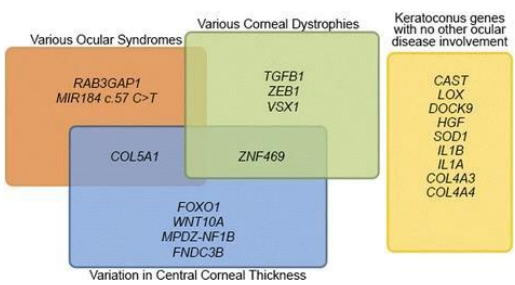
Etiology

- Genetic
  - Familial Inheritance
    - Autosomal Dominant
    - Autosomal Recessive
- Environment
  - UV exposure
  - Atopic conditions
  - Contact Lens wear
- Risk Factors
  - Family History
  - Eye rubbing
  - **Age**
- Genetic Testing
  - Universal Genetic Test
  - AvaGen test



Y Bykhovskaya, B Margines,Y Rabinowitz Genetics in Keratoconus: where are we? Eye Vis (Lond). 2016; 3: 16.

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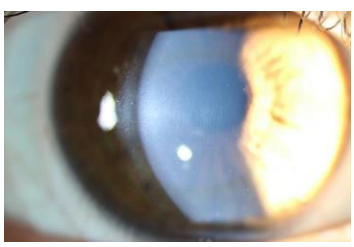
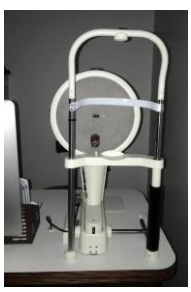
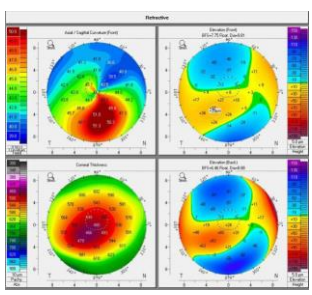
Keratoconus Diagnosis Made



Al-Mahrouqi H, Oraba SB, Al-Habsi S, Mundemkattil N, Babu J, Panchatcharam SM, Al-Saidi R, Al-Raisi A. **Retinoscopy** as a Screening Tool for **Keratoconus**. Cornea. 2019 Apr;38(4):442-445.

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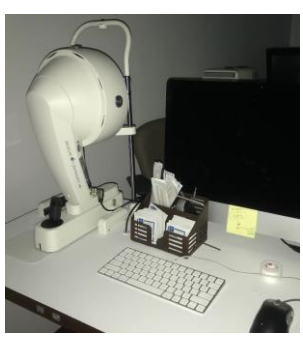
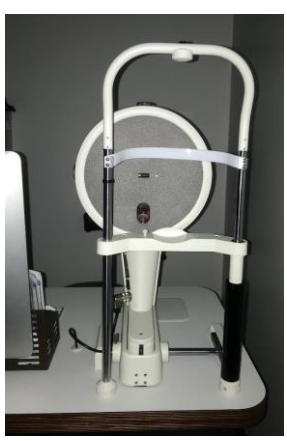
Helpful Equipment

- Corneal Topographer
  - 2-D Imaging
  - Placido disc based
  - Maps surface curvature
- Scheimpflug Tomographer
  - 3-D Imaging
  - Maps front and back corneal surface, thickness
- Anterior Segment Optical Coherence Tomography (AS-OCT)
  - Described in 1994 (Izatt JA)
    - initially for retina
  - High resolution cross-sectional imaging
    - Many applications

Izatt JA, Hee MR, Swanson EA, et al. Micrometer-scale resolution imaging of the anterior eye in vivo with optical coherence tomography. Arch Ophthalmol. 1994;112:1584–1589

6

Questions for thought

- Do you screen for keratoconus in every patient?
- Should we screen for KC in every patient?
- At what age should we start screening for KC?

7

Reported Incidence & Prevalence of keratoconus

Reference	Prevalence	Geography
Kennedy et al. 1986	0.05% or 1:2000	US
Jonas et al. 2009	2.3%	India
Millodot et al. 2011	2.3%	Israel
Xu et al. 2012	0.9%	China
Hashemi et al. 2014	2.5%	Iran
Godefrooij et al. 2017	0.26% or 1:375	Netherlands
Torres Netto et al. 2018	4.79%	Saudi Arabia
Chan et al. 2020	1.2% or 1:84	Australia
Hashemi et al. 2020*	0.14% or 1:700	Global Meta-Analysis

*Hashemi H, Heydarian S, Hooshmand E, et al. The Prevalence and Risk Factors for Keratoconus: A Systematic Review and Meta-Analysis. *Cornea*. 2020;39(2):263-270

Incidence and prevalence of keratoconus in Denmark – an update

Sashia Bak-Nielsen,[1] Cecilia H. Ramlau-Hansen,[2] Anders Ivarsen,[1] Oleguer Plana-Ripoll[3] and Jesper Hjortdal[1]

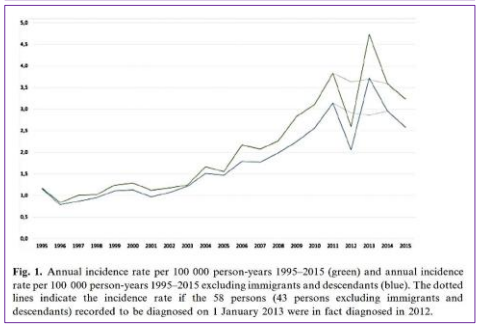


Fig. 1. Annual incidence rate per 100 000 person-years 1995–2015 (green) and annual incidence rate per 100 000 person-years 1995–2015 excluding immigrants and descendants (blue). The dotted lines indicate the incidence rate if the 58 persons (43 persons excluding immigrants and descendants) recorded to be diagnosed on 1 January 2013 were in fact diagnosed in 2012.

Acta Ophthalmol. 2019: 97: 752–755

8

Keratoconus Progression

- Study: Ferdi A, Nguyen V, Kandel H, Tan JCK, Arnalich-Montiel F, Abbondanza M, Watson S. **Predictors of progression in untreated keratoconus: a Save Sight Keratoconus Registry study.** Br J Ophthalmol. 2021 Mar 30
  - Aim to identify risk factors for progression in untreated KC pts
  - 34 centers, across Australia, New Zealand, Spain and Italy

- Steeper Max-K and younger age were the most clinically useful baseline predictors of progression
  - Every 1D steeper Max-K was associated with a 7% and 3% greater risk of worsening VA and thinning TCT, respectively
  - Each 1 year younger was associated with a 4% and 2% greater risk of steepening Max-K and thinning TCT, respectively.

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Study: A Systematic Review and Meta-analysis of 11 529 Eyes Study

- Ferdi AC, Nguyen V, Gore DM, Allan BD, Rozema JJ, Watson SL. **Keratoconus Natural Progression: A Systematic Review and Meta-analysis of 11 529 Eyes.** Ophthalmology. 2019 Jul;126(7):935-945. Epub 2019 Mar 8.
  - 41 publications in systematic review
  - 23 in meta-analysis

- Younger patients and those with K_{max} steeper than 55 D at presentation have a greater risk of progression
- **Closer follow-up and a lower threshold for cross-linking should be adopted in patients younger than 17 years and steeper than 55 D Kmax.**

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Keratoconus Progression

- Study: Ferdi A, Nguyen V, Kandel H, Tan JCK, Arnalich-Montiel F, Abbondanza M, Watson S. **Keratoconus after 40 years of age: a longitudinal comparative population-based study.** Int Ophthalmol. 2020 Mar;40(3):583-589.
  - Determine 5-yr changes in KC indices in 40-64 y/o compared to normal subjects
  - Posterior corneal steepening and thinning in keratoconus patients continue after the age of 40 years, but clinically negligible
  - Changes are independent of normal age-related changes and appear to be slower in cases with steeper and thinner corneas

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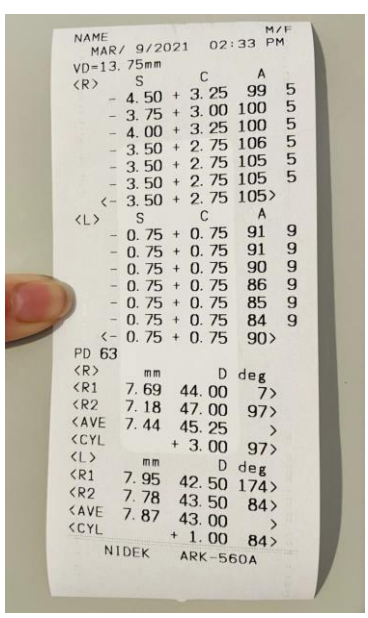
Case Example

- 31 y/o male
- Referred for CLs
- sc VA 20/30+ OD and 20/20 OS

- Final SRx:
  - -0.50 +1.50 x 150 20/20 OD
  - Plano 20/20 OS



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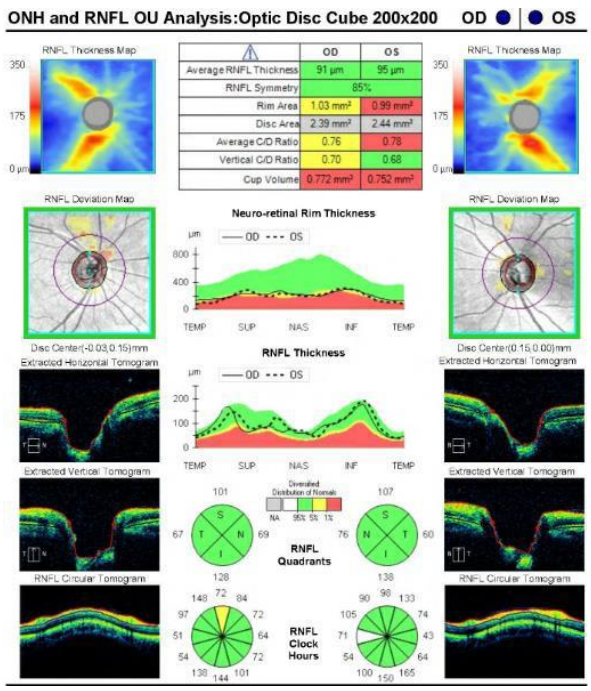

	OD	OS
Average RNFL Thickness	91 µm	95 µm
RNFL Symmetry	85%	
Rim Area	1.03 mm²	0.99 mm²
Disc Area	2.39 mm²	2.44 mm²
Average C/D Ratio	0.76	0.78
Vertical C/D Ratio	0.70	0.68
Cup Volume	0.772 mm³	0.752 mm³

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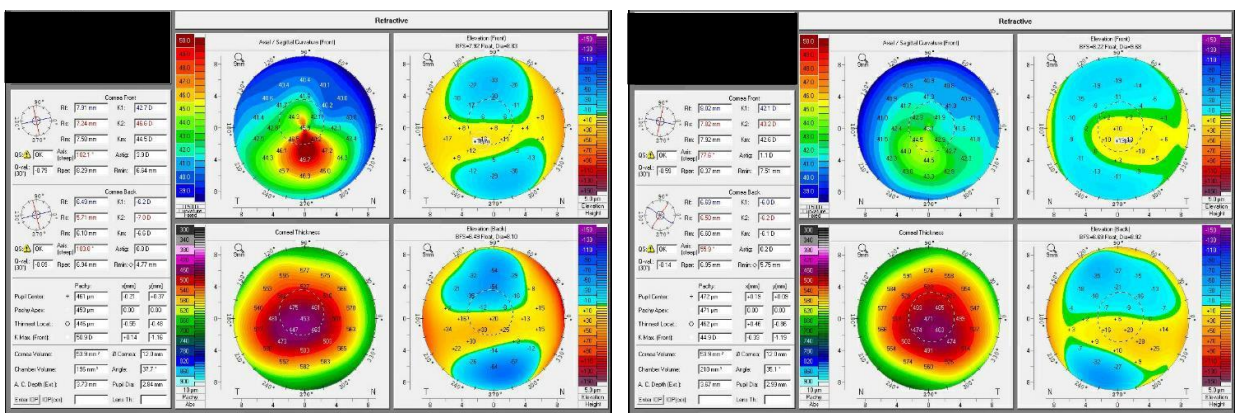
Tomography Images – Mild Keratoconus



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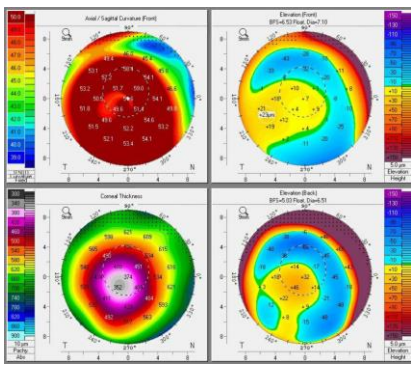
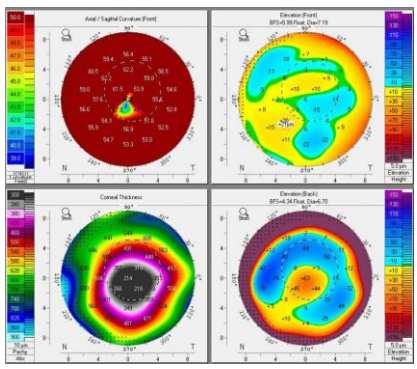
Case Example: KC Complications

- 26 y/o F
  - FHx: KC in sister
  - Hx Hybrid CL wear, switched to scleral lenses
  - s/p CXL off-label epi-on 2014 with outside MD
- 3-2019: OD: 54.6/52.1 D, 349 CCT OS: 55.3/52.8 D, 193 CCT
- 4-2020: Urgent call, White scar upon wakening OS: Hydrops





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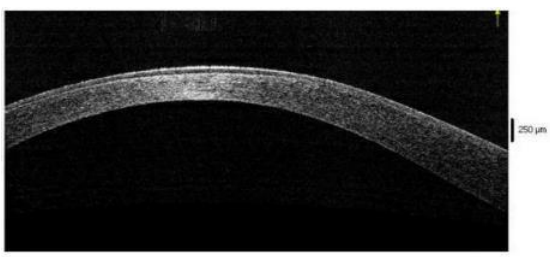
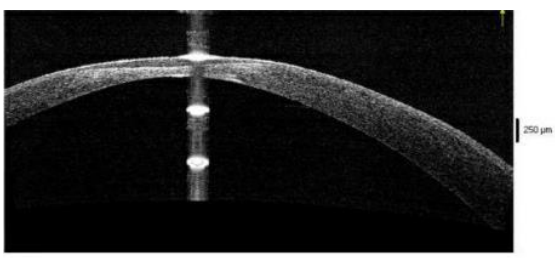
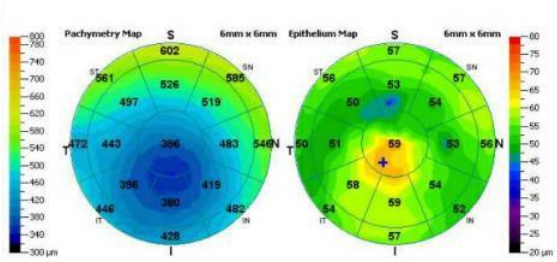
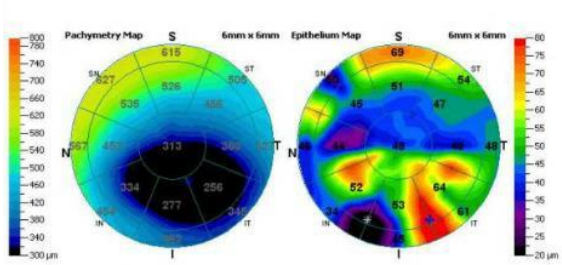
AS-OCT Images









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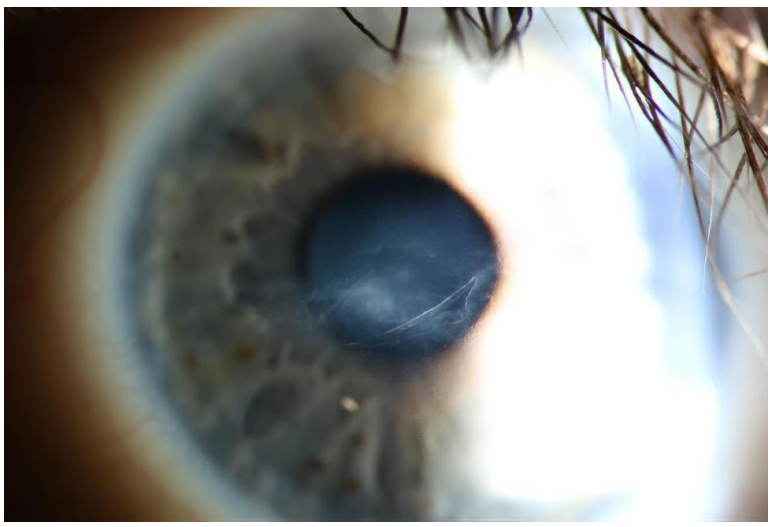
After Corneal Hydrops

BCVA 20/50-



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Case Example: Advanced KC, complications

- 25 y/o F, referred for scleral lenses OU
  - Ocular itching and admits to eye rubbing
- KC OD>OS
- CXL OS 2017
- Hydrops OD 2018
  - BCVA 20/50-60
- Does not want to have surgery

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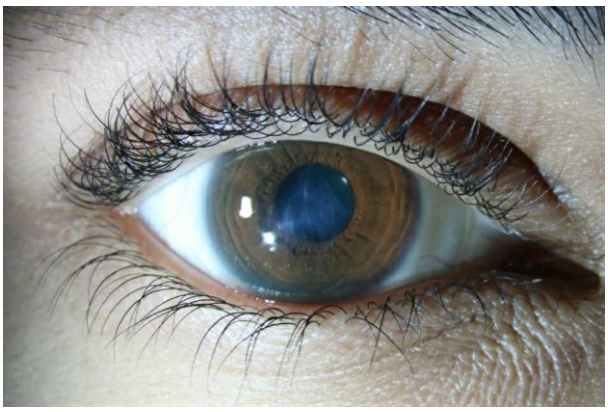
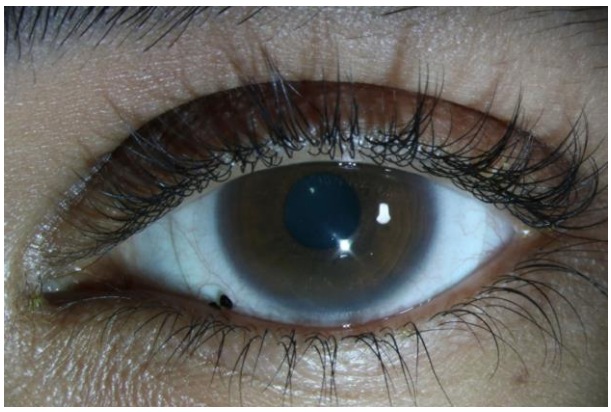
After Corneal Hydrops





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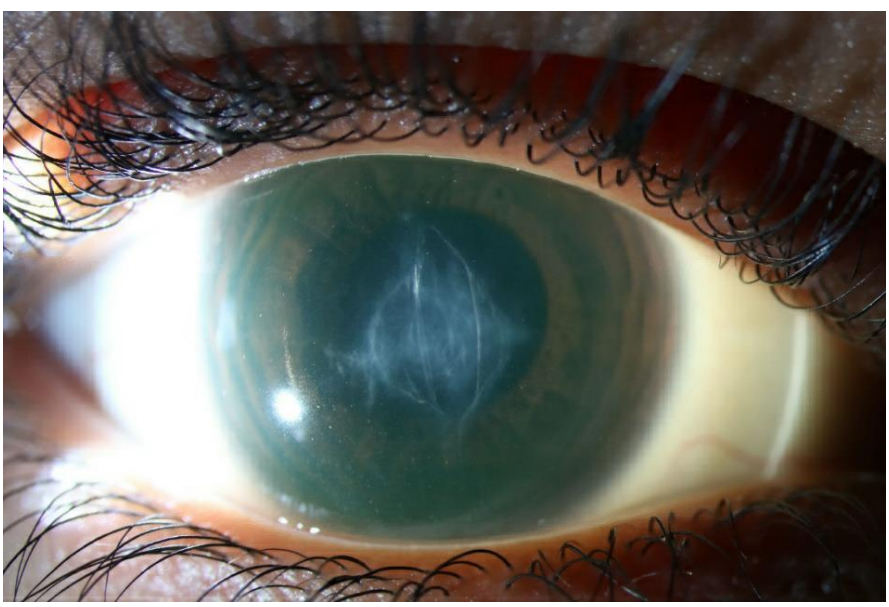

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Case Example

- 15 y/o Caucasian male
- Incoming sc VA
  - 20/300 OD
  - 20/100 OS
- Tomography Ks
  - 60.4/53.3 OD
  - 59.0/51.4 OS
- SRx BCVA
  - -1.25 +0.50 x 080 20/125 OD
  - -1.25 +1.00 x 135 20/60 OS
- Central Striae and mild scars OU
- Send immediately for CXL

1.Ferdi AC, Nguyen V, Gore DM, Allan BD, Rozema JJ, Watson SL.Ophthalmology. **Keratoconus Natural Progression: A Systematic Review and Meta-analysis of 11 529 Eyes.** 2019 Jul;126(7):935-945. doi: 10.1016/j.ophtha.2019.02.029. Epub 2019 Mar 8.
2.Shah H, Pagano L, Vakharia A, Coco G, Gadhvi KA, Kaye SB, Romano V. **Impact of COVID-19 on keratoconus patients waiting for corneal cross linking.** Eur J Ophthalmol. 2021 Mar 15:11206721211001315.

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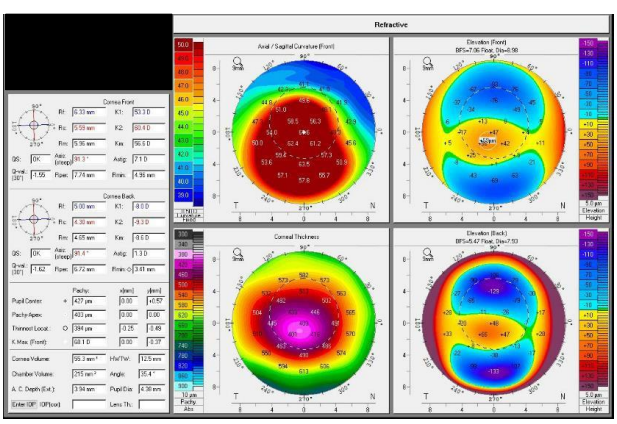
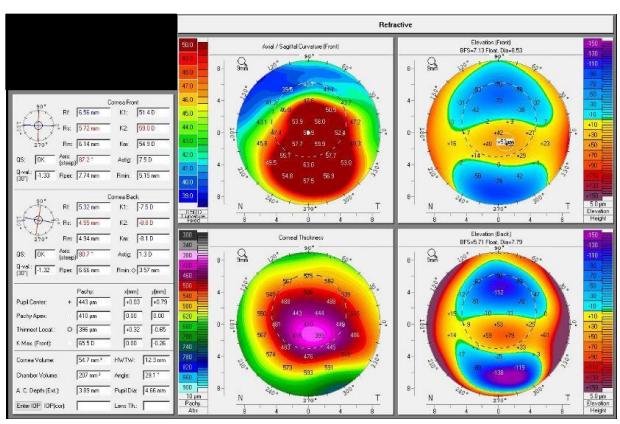
Tomography Images





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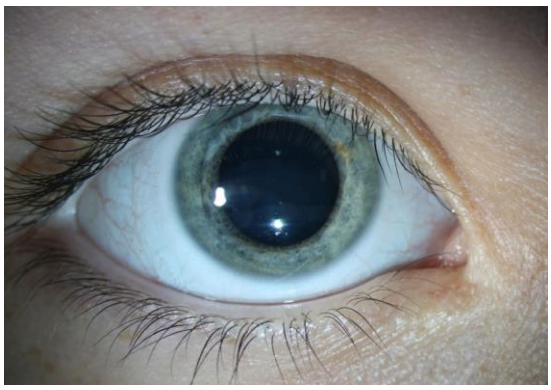
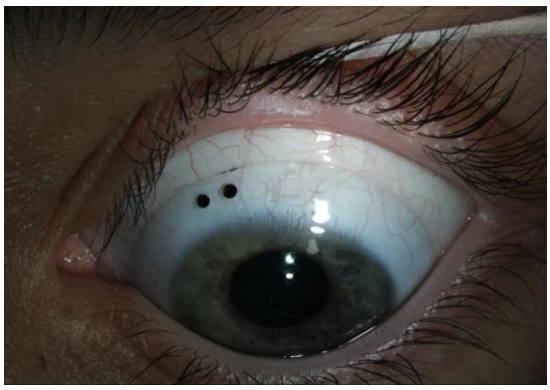
Fit with Scleral Lenses, 20/20 OD and OS





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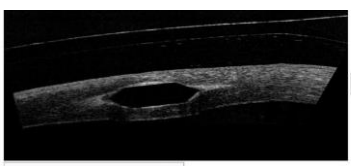
Keratoconus Procedures to Help Improve Vision

- Corneal Intacs
  - FDA approved for KC in 2004
  - "Flattens" cornea
- Topography Guided PRK (TG-PRK)
  - "Smooths" cornea, touch-up
- Corneal Transplantation
  - Replaces cornea



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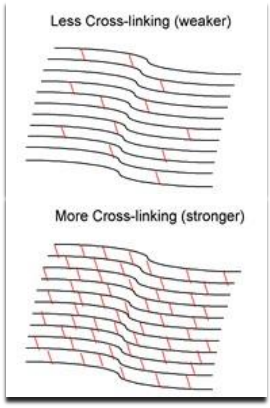
Corneal Cross-linking (CXL) to stabilize and slow progression

- FDA approved in April 2016
  - KXL UV System, with Photrexa and Photrexa Viscous (riboflavin)
- Indications:
  - Progressive Keratoconus
  - Post-LASIK Ectasia
- Procedure involves:
  - Epithelium removal (Epi-off)
  - 30 min riboflavin application
  - Intraoperative Corneal thickness minimum: **400 microns**
  - 30 min exposure 365 nm UV-A light, 3.0 mW/cm2
- Activated riboflavin and reactive oxygen species interact in cornea to form crosslinks: stiffens cornea [1]
  - 328.9% increase in biomechanical rigidity [2]



1. Beshtawi IM, O'Donnell C, Radhakrishnan H. Biomechanical properties of corneal tissue after ultraviolet-A-riboflavin crosslinking. J Cataract Refract Surg. 2013;39(3):451–62
2. Wollensak G. Crosslinking treatment of progressive kera-toconus: New hope. Curr Opin Ophthalmol. 2006;17:356–60.

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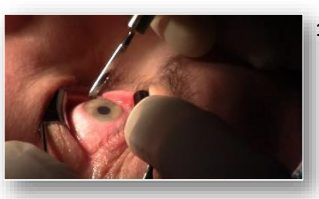
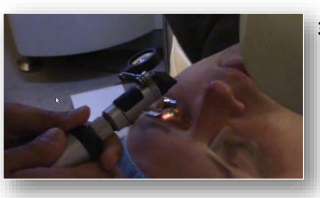
Cross-Linking Procedure Summary*



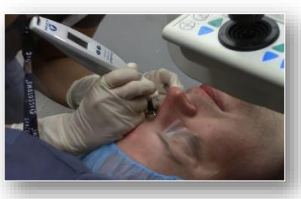
1. Remove epithelium.

2. Soak cornea with Photrexa® Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution).

30 minutes

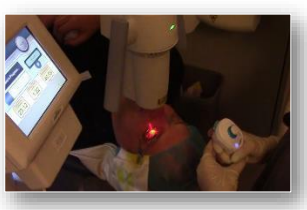


3. Check for flare.



4. Once flare is observed, measure corneal thickness.

If corneal thickness is less than 400 µm, instill 2 drops of Photrexa *(riboflavin 5'-phosphate in ophthalmic solution)* until the corneal thickness increases to at least 400 µm.



5. Irradiate for 30 minutes.

Continue applying Photrexa Viscous *(riboflavin 5'-phosphate in 20% dextran ophthalmic solution)* during irradiation.

Procedural images courtesy of Dr. Raj Rajpal

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Corneal Cross-linking (CXL)

- KXL System
  - Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran solution)
  - Photrexa (riboflavin 5'-phosphate ophthalmic solution, hypotonic; swelling effect)
  - KXL UV light delivery system
- No other riboflavin solutions or UV devices can be used in the U.S. outside of a formal IDE (device) or IND (drug) study
- No specific age range limitations
  - Patients ages 14-65, included in FDA studies
- Not advised during pregnancy

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CXL Procedure Room

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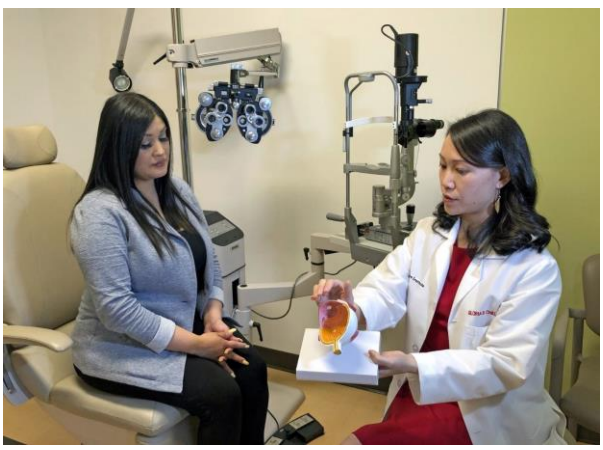
CXL Expectations

- We need to **educate** our patients
  - Aim to slow or stop progression
  - NOT refractive surgery
  - Will not remove scarring
  - Treat DES to enhance healing
  - May still need visual correction
- Recovery Period
  - Bandage Contact Lens
  - May be discomfort
  - Do not rub eyes
  - Call if sudden pain or VA decline



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CXL Post-operative Considerations

- After procedure
  - Topical Antibiotic, Steroid (NSAID)
  - Lubrication
  - Placement of bandage SCL – No eye rubbing!
- Week 1:
  - Topical meds, lubrication
  - Remove bandage SCL once epithelium healed
- Month 1:
  - Assess vision
  - Corneal Imaging – stromal remodeling
  - Consider CL fitting
- Months 3, 6, 12:
  - Assess vision – MR and BCVA often change
  - Corneal Imaging

- **Zero Global Period: Visits can be billed to insurance**

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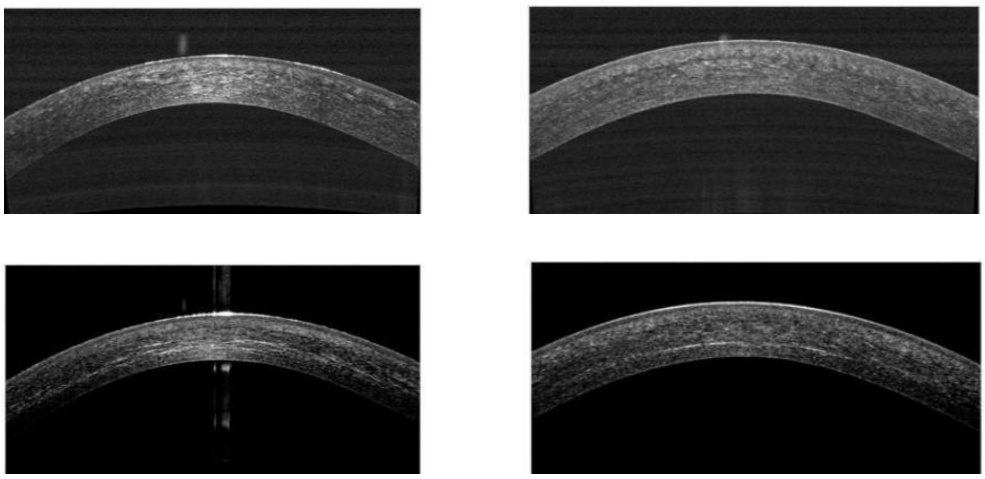
AS-OCT before CXL and 2 mo after: Corneal Remodeling – Demarcation Line



Spadea L, Tonti E, Vingolo EM. **Corneal stromal demarcation line after collagen cross-linking** in **corneal** ectatic diseases: a review of the literature. Clin Ophthalmol. 2016 Sep 19;10:1803-1810

31

Efficacy of CXL Supported by Literature

- Riboflavin/ultraviolet-a-induced collagen **crosslinking** for the treatment of **keratoconus**. Wollensak G, Spoerl E, Seiler T. Am J Ophthalmol. **2003** May;135(5):620-7. doi: 10.1016/s0002-9394(02)02220-1.
  - **Conclusions:** Collagen crosslinking may be a **new way** for stopping the progression of keratectasia in patients with keratoconus. The need for penetrating keratoplasty might then be significantly reduced in keratoconus. Long-term results are necessary to evaluate the duration of the stiffening effect and to exclude long term side-effects.
- Corneal Collagen Cross-Linking for **Keratoconus**: **Systematic Review**. Kobashi H, Rong SS.Biomed Res Int. 2017;2017:8145651. doi: 10.1155/2017/8145651. Epub 2017 Jun 11.
- Corneal collagen **crosslinking** with riboflavin and ultraviolet-A light in progressive **keratoconus**: **ten-year results.** Raiskup F, Theuring A, Pillunat LE, Spoerl E.J Cataract Refract Surg. 2015 Jan;41(1):41-6. doi: 10.1016/j.jcrs.2014.09.033.
- **Long-term results** of cornea collagen cross-linking with riboflavin for keratoconus. Agrawal V.Indian J Ophthalmol. 2013 Aug;61(8):433-4. doi: 10.4103/0301-4738.116072.

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Epi-On vs Epi-Off

- Transepithelial = Epi-ON
- All Epi-On procedures are off-label and investigational
- Many studies have evaluated and are **continuing to evaluate** for best protocol
- Studies change variables in procedure (UV light source, time, riboflavin formula)

- Efficacy and safety of transepithelial corneal collagen crosslinking surgery versus standard corneal collagen crosslinking surgery for keratoconus: a meta-analysis of randomized controlled trials. Li W, Wang B.BMC Ophthalmol. 2017 Dec 28;17(1):262. doi: 10.1186/s12886-017-0657-2.
- Prospective 2-year study of accelerated pulsed **transepithelial** corneal **crosslinking** outcomes for **Keratoconus**. Ziaei M, Vellara H, Gokul A, Patel D, McGhee CNJ.Eye (Lond). 2019 Dec;33(12):1897-1903. doi: 10.1038/s41433-019-0502-3. Epub 2019 Jul 4.PMID: 31273313
- Comparison of transepithelial corneal collagen crosslinking with epithelium-off crosslinking in progressive keratoconus. Kocak I, Aydin A, Kaya F, Koc H.J Fr Ophtalmol. 2014 May;37(5):371-6. doi: 10.1016/j.jfo.2013.11.012. Epub 2014 Mar 26.
- Transepithelial corneal crosslinking for keratoconus. Hersh PS, Lai MJ, Gelles JD, Lesniak SPJ Cataract Refract Surg. 2018 Mar;44(3):313-322. doi: 10.1016/j.jcrs.2017.12.022.

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CXL Potential Complications

- Infections
- Non-healing epithelium
- Corneal Haze
- Corneal scarring
- Endothelial cell damage
- Continued progression

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Case Example

- 16 y/o Hispanic M
- KC Dx 2018 (age 13)
- CXL OS 2019
  - Resulted in diffuse persistent K haze/scarring
- BCVA with scleral lenses
  - 20/20 OD and 20/25- OS

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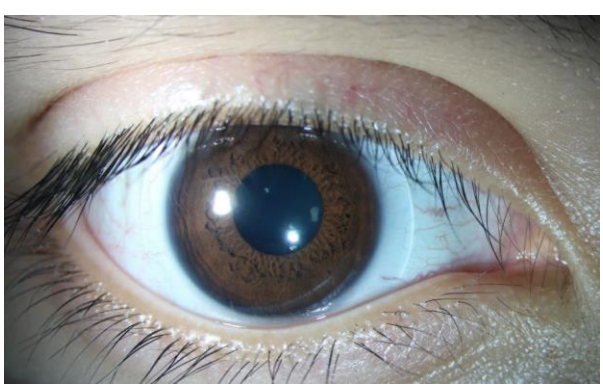
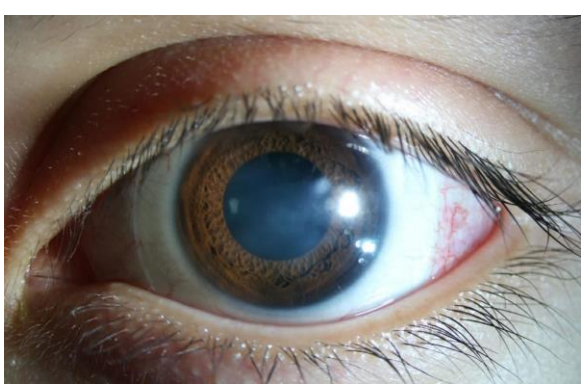
Corneal Haze s/p CXL





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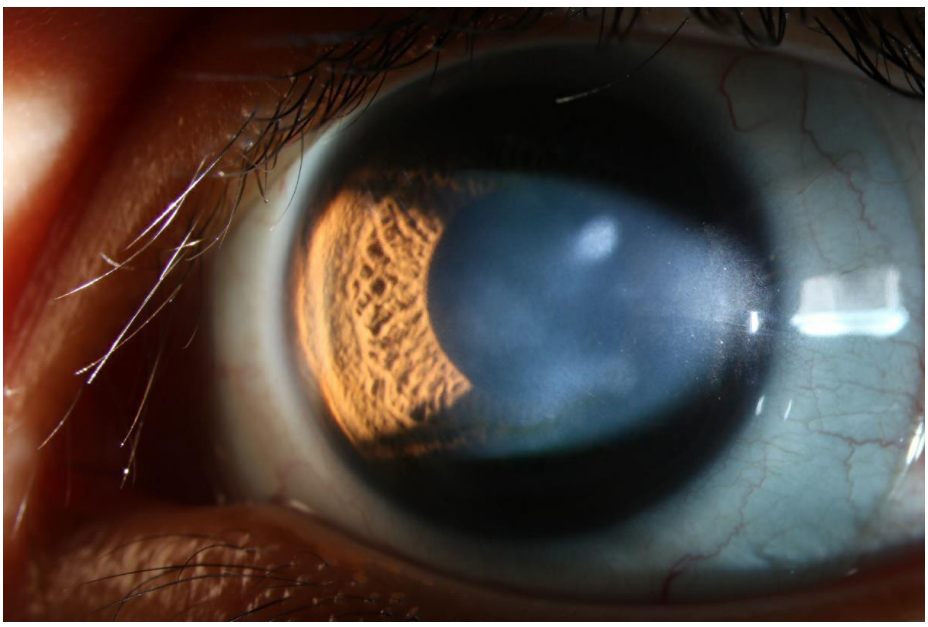

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New protocols for CXL?

- LOTS to look forward to…
- May 2019 – Enrollment completed in Phase 3 Epi-On CXL Clinical trial for progressive KC
  - Multicenter (14 centers), randomized sham-controlled study
  - Latest-generation UV light source
  - Supplemental oxygen
  - New drug to penetrate K epithelium
  - Reduce treatment time

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US Phase III Pivotal Trial of Epi-on Cross-linking Therapy

Epi-on Treatment Demonstrated the Ability to Halt or Reduce the Progression of Keratoconus versus Observed Disease Progression in a Placebo-Control Arm

279 Eyes with Progressive Keratoconus
at 14 US Clinical Sites, 2:1 Randomization

189 Active Eyes	**90 Control Eyes**
• Epi-on Ophthalmic Solution • Supplemental Oxygen • Higher Energy, Pulsed UV	• Placebo Solution • No Oxygen Delivery • Sham UV Treatment

Primary Efficacy Endpoint:
Difference of ≥ 1 D between treatment groups in mean change in Kmax from baseline at month 6

Control eyes eligible for cross-over at month 6
All eyes followed an additional 6-months

- **Achieved prospectively defined primary efficacy outcome, demonstrating Kmax treatment effect of -1.0D (p = 0.0004)**
- 98% of placebo randomized patients elected to cross-over to epi-on treatment
- Well-tolerated, majority of adverse events reported were mild and transient in nature, no change in corneal endothelial cell count over the course of the trial
- Forms the basis for planned regulatory submission (U.S. NDA) by Glaukos in 2022

Epithelium-on cross-linking is not approved by the US FDA

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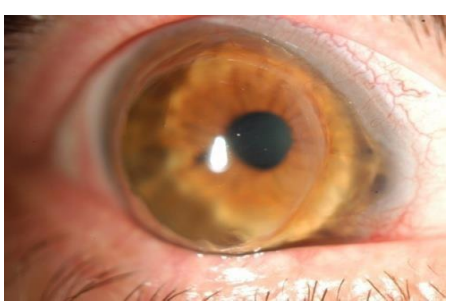
Importance of Early KC Intervention

- Preserve vision
  - Maintain ability to wear contact lenses
  - Maintain quality of life
- Prevent progression
  - Corneal striae and scars reduce BCVA
- Protect against need for surgical intervention
  - Potential complications
  - Graft rejection
  - Cost



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How To Refer?

- https://www.livingwithkeratoconus.com/
- www.livingwithkc.com

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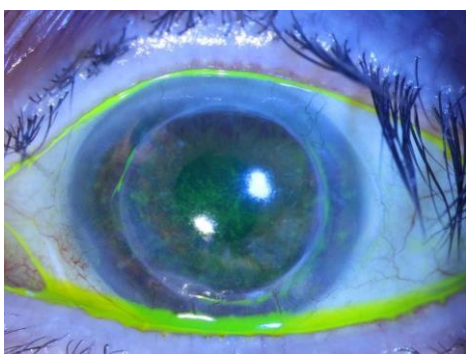
Better to Refer for 2nd Opinion or CXL

….than to Refer for a Cornea Transplant



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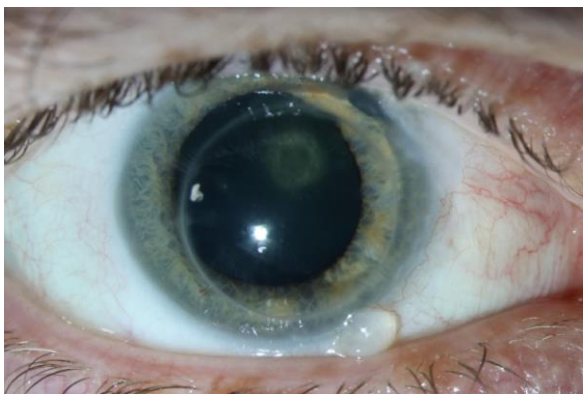
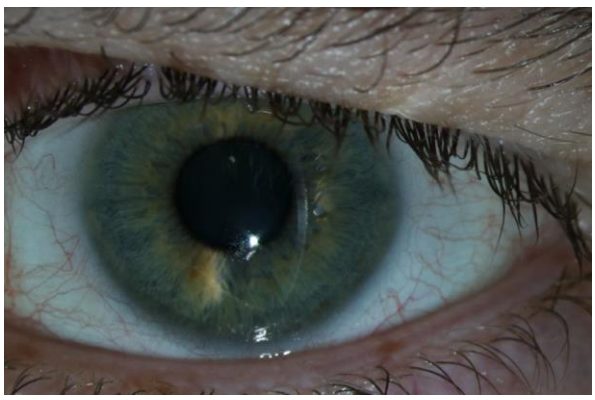
Case: Complications after Cornea Transplant





Study Conclusion: Physicians should maximize use of scleral or RGP CL because patients who successfully use CL have almost **one-fifth the risk of undergoing keratoplasty**.
Ling JJ, Mian SI, Stein JD, Rahman M, Poliskey J, Woodward MA. **Impact of Scleral Contact Lens Use on the Rate of Corneal Transplantation for Keratoconus.** Cornea. 2021 Jan;40(1):39-42.

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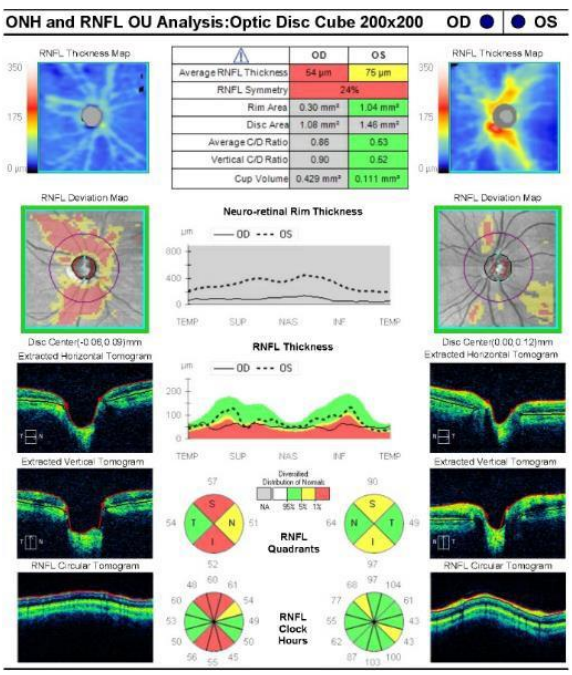

	OD	OS
Average RNFL Thickness	54 µm	75 µm
RNFL Symmetry	24%	
Rim Area	0.30 mm²	1.04 mm²
Disc Area	1.08 mm²	1.46 mm²
Average C/D Ratio	0.86	0.63
Vertical C/D Ratio	0.90	0.62
Cup Volume	0.429 mm³	0.111 mm³

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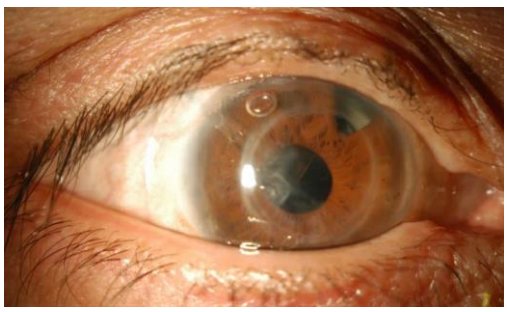
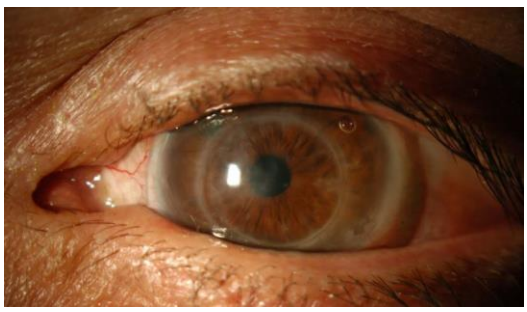
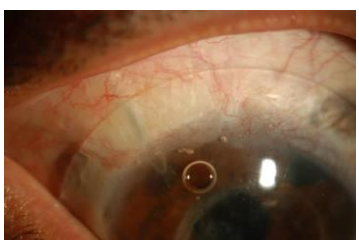
Case: Complications after Corneal Transplant

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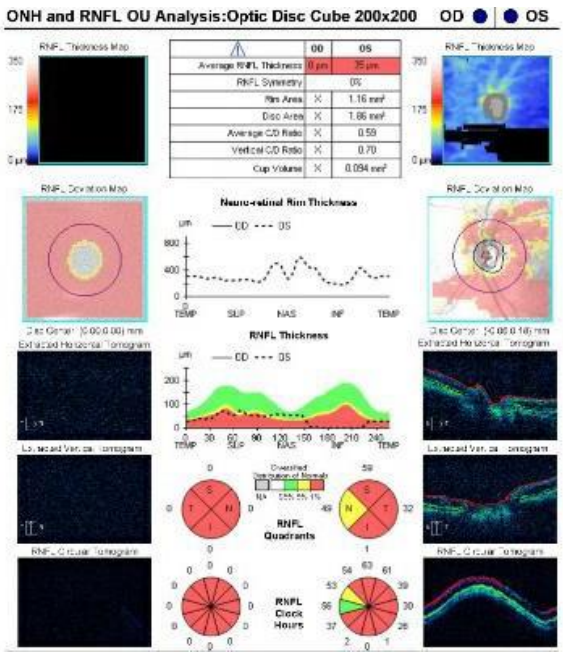
- 51 y/o Hispanic M
- PK OU 2 KC, in 30s
- Developed secondary GLC OU
- Tube-shunts OU
- Developed ET, had EOM Sx
  - Endophthalmitis OD s/p strab Sx
  - Monocular: HM VA OD
- Wears RGP OS now
  - BCVA 20/70



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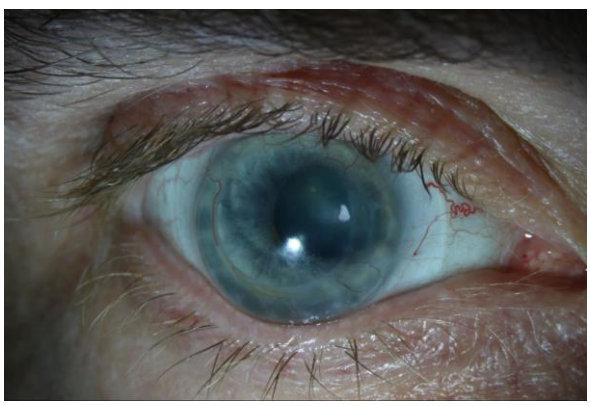
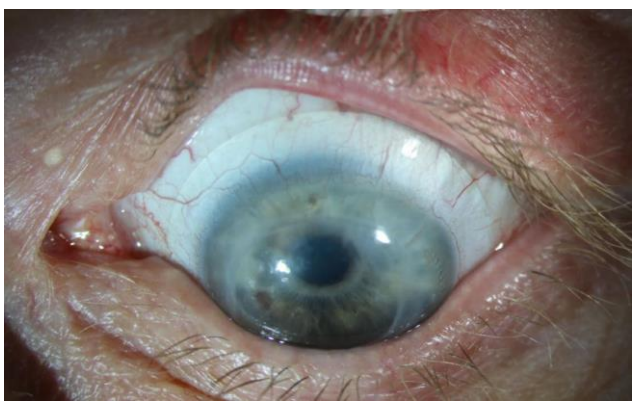
Case: Sclerals after Corneal Transplant





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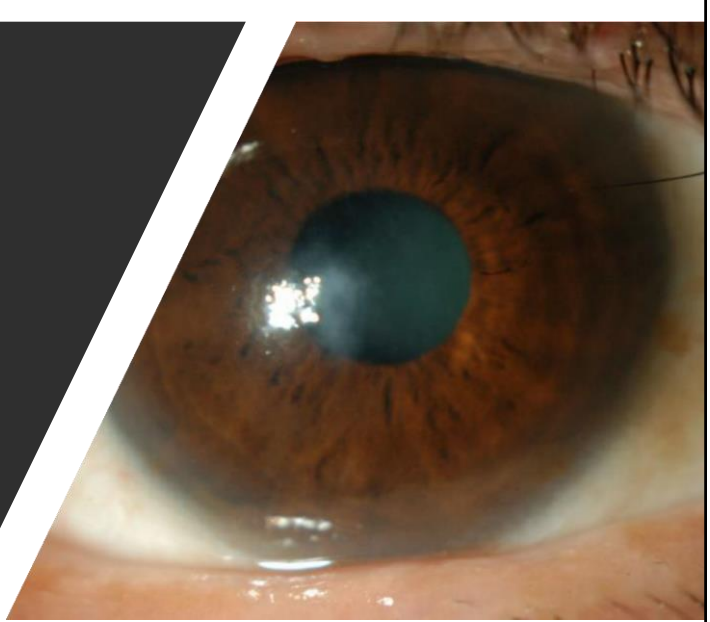
Questions for thought

- Do you screen for keratoconus in every patient?
  - 1. Look for asymmetry on K
  - 2. Asymmetry between eyes
  - 3. Abnormal/high K values (>47 D)
- Should we screen for KC in every patient?
  - Yes. Unlike before, we now have CXL to slow/halt progression
- At what age should we start screening for KC?
  - Consider baseline imaging/topography at age 10-13
- Can we screen for KC as we do for glaucoma?



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Summary

- Keratoconus tends to present in early teens
  - Earlier presentation tends to be more aggressive
  - **Closer follow-up and lower threshold for CXL should be adopted in patients < 17 years and steeper than 55 D Kmax**
- Rather than monitoring the progression, we should detect and ACT to halt/slow the progression
- Visual and physiological changes from KC can greatly affect QOV/QOL
  - Aim to prevent changes associated with advanced KC and K transplantation
- Optometrists have vital role in detection and treatment of KC

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Thank You!

Gloria B Chiu, OD, FAAO, FSLS
Associate Professor of Clinical Ophthalmology
Adjunct Faculty at Southern California College of Optometry/MBKU

USC Roski Eye Institute
Department of Ophthalmology
Keck Medicine of USC
1450 San Pablo Street, 4th Floor
Los Angeles, CA 90033
T: (323) 442-6335
usceye.org
Gloria.chiu@med.usc.edu
Instagram: @gloriachiuod

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Marshall B.
KETCHUM UNIVERSITY
Southern California College of Optometry

Updates in Clinical Glaucoma Management

Brian Song, MD

Updates in Clinical Glaucoma Management: Cases and Pearls

Brian J. Song, MD, MPH, FACS
Assistant Professor of Clinical Ophthalmology
Keck School of Medicine of USC
September 19, 2021

USC Roski Eye Institute
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No financial disclosures

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Disclosures

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- No proprietary interest in any of the devices or services mentioned in this presentation.

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2

Why This Will Be One of the Most Important Hours of this Course:

- Glaucoma is the 2nd leading cause of blindness worldwide
- We will ALL come across glaucoma cases in practice at some point
- If you are not a glaucoma specialist, the key is to recognize:
  - Which cases are urgent and require immediate attention
  - How to treat or temporize the situation until you can get more help
  - Identify the source!

Goals of Today's Talk:

- To understand that glaucoma is an "umbrella" term that encompasses multiple diseases with common features
- To appreciate the multi-factorial nature of glaucoma
- To identify when surgical intervention is needed, or even preferred
- To use real-life case examples to illustrate the above

Case 1

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5

Patient History

- 22 year old white male referred by his PCP to evaluate for “cataracts and elevated eye pressure” due to long-term steroid use
- No subjective complaints
- **PMH**
  - CNS (central nervous system) vasculitis
- **POH**
  - None

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6

Ophthalmic Vitals

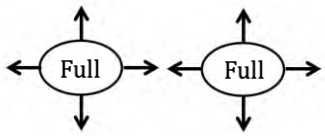
BCVA 20/20 / 20/20 -1

IOP 25 / 24

CVF: Full OU

Pupils 4 → 3, brisk, no rAPD / 4 → 3, brisk, no rAPD

EOM:

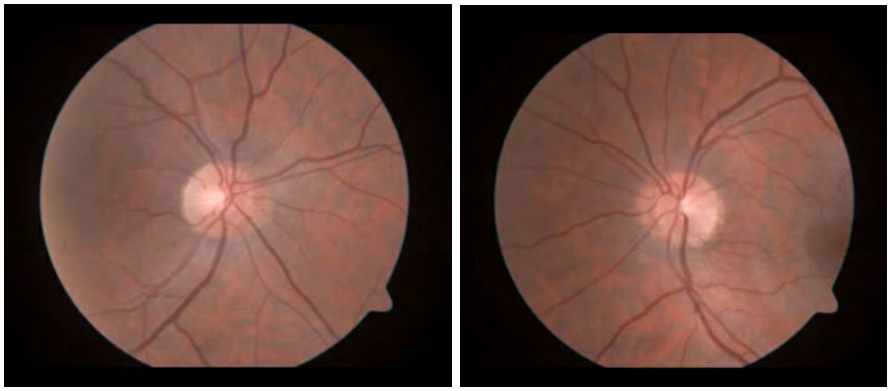


Gonioscopy: C40r1+ OU

Slit Lamp Exam

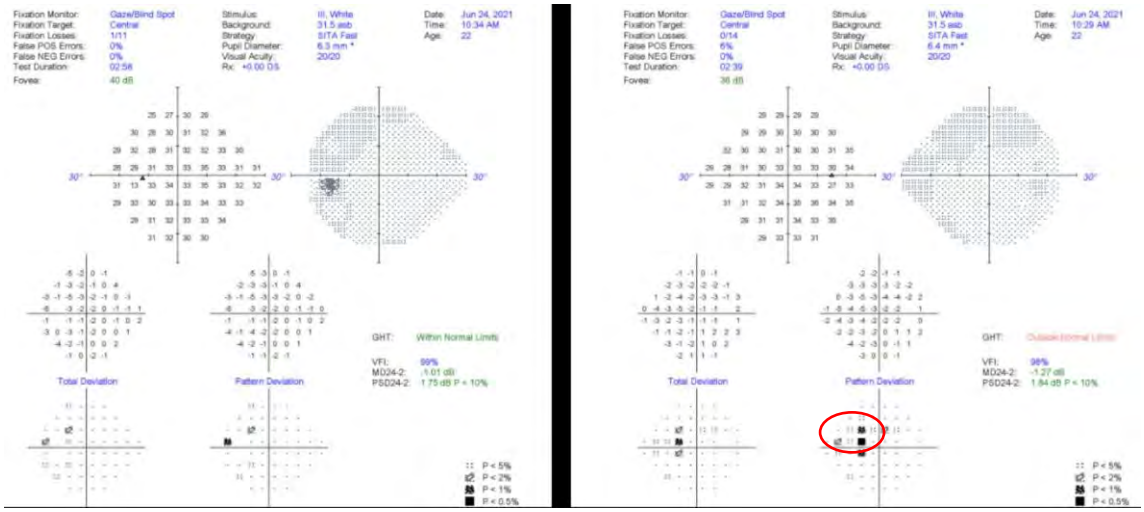
	OD	OS
Orbits/Adnexa	Normal	Normal
Lids/Lashes	**Blepharitis**	**Blepharitis**
Conjunctiva/Sclera	White and quiet	White and quiet
Cornea	**1+ SPK**	**1+ SPK**
Anterior Chamber	Deep and quiet	Deep and quiet
Iris	Flat, round	Flat, round
Lens	Clear	Clear
Anterior Vitreous	Clear	Clear

Fundus Exam

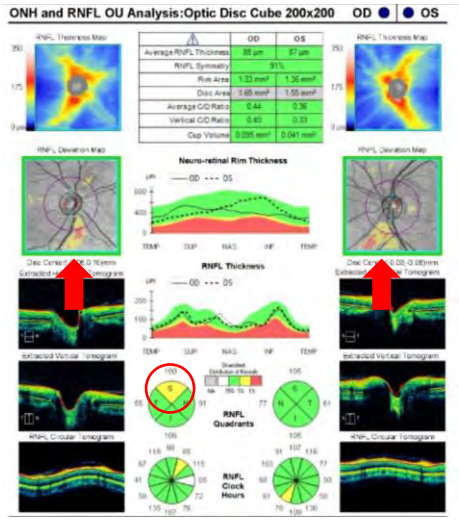


- Looks pretty normal to me?
- These small discs could not possibly be glaucoma?

Humphrey Visual Field

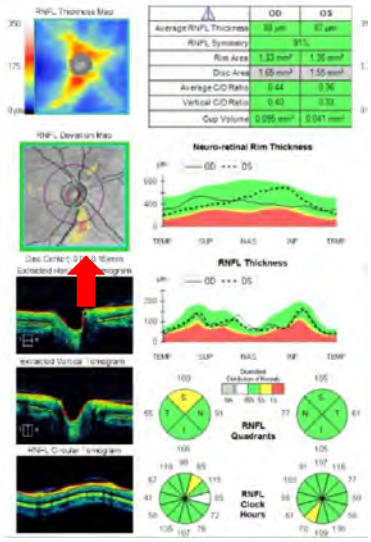


Optical Coherence Tomography (OCT)



- Quadrant scan:
  - Early superior RNFL thinning
- Does this correlate?
- What is going on?

Structure-Function Dissociation?



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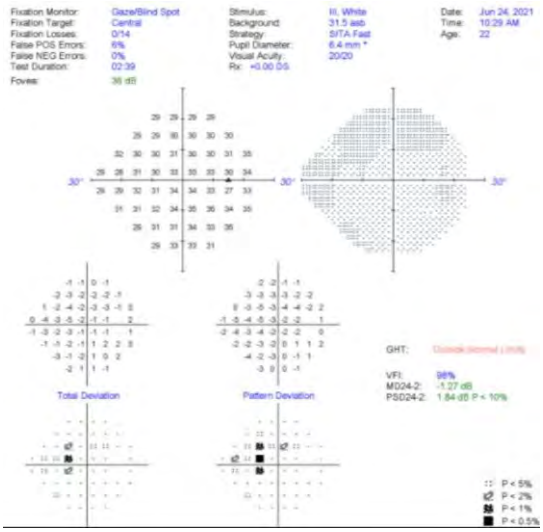


Assessment and Plan

- **<u>Mixed</u> mechanism open angle glaucoma OD > OS**
  - Primary Open Angle + Steroid Response
- What would you do next?
  - Selective laser trabeculoplasty
  - Angle surgery
  - Prostaglandin analogue
  - Rho-kinase inhibitor
  - Aqueous suppressant (beta-blocker or alpha-agonist)

COMBINED Mechanism vs MIXED Mechanism

- NOT the same thing
- ICD-9/10 and many ophthalmologists get this wrong
- COMBINED mechanism glaucoma
  - Open-angle with components of angle closure
    - e.g. Angle closure s/p LPI or cataract surgery, now with open angles
- MIXED mechanism glaucoma
  - Two or more etiologies contributing to glaucoma
    - e.g. underlying POAG with a steroid response

Pearls for Case 1

- Size matters!
  - Small discs can have small cups and still have glaucomatous optic neuropathy
- Risk factors deserve a work-up!
- Establish baselines!
- Look for structure-function correlation!
- Always interpret your own images. Do not rely on algorithms to make a diagnosis for you!



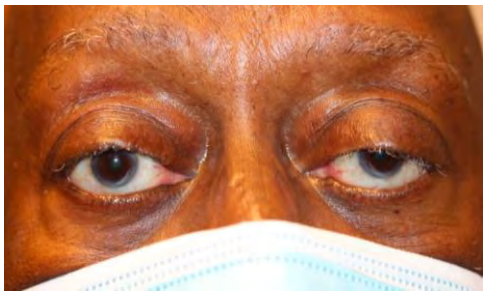
Case 2

Patient History

- 67 year old black male with thyroid eye disease (TED) OU with severe exophthalmos
- Presents May 2021 to re-establish care after being lost to follow-up since 2019

- **PMH**
  - HTN
  - Grave's disease

- **POH**
  - TED OU
  - Mixed mechanism glaucoma OU
  - Iritis OD
  - Hypertensive retinopathy OU



Past Ocular History

- Thyroid Eye Disease due to Graves Disease (dx ~ 2000)
  - s/p bilateral medial and lateral tarsorrhaphy OU 2015
  - Complicated by lagophthalmos, severe exophthalmos, and lid retraction causing exposure keratopathy and persistent retrobulbar pain
  - Thyroid disease currently inactive (CAS 0), not taking any thyroid meds. Follows closely with PCP
- Mixed Mechanism Glaucoma OS >> OD
- HTN retinopathy OU
- Iritis OD – quiescent
- Cataracts OU - visually signfiicant

Ophthalmic Vitals

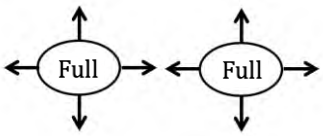
BCVA 20/25-2 / 20/50+2

IOP 24 / 27

CVF: Full OU

Pupils 4 → 3, brisk, no rAPD / 4 → 3, brisk, no rAPD

EOM:



Exophthalmometry:
Hertel 25.5 | 26 (Base: 102)

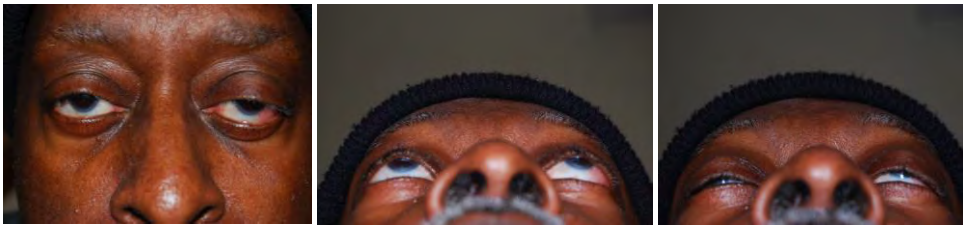
Slit Lamp Exam

	OD	OS
Orbits/Adnexa	**Proptosis**	**Proptosis**
Lids/Lashes	**Collarettes**	**Collarettes**
Conjunctiva/Sclera	White and quiet	White and quiet
Cornea	**Arcus, 3+ SPK inferiorly**	**2+ SPK inferiorly**
Anterior Chamber	Deep and quiet	Deep and quiet
Iris	Flat, round	Flat, round
Lens	**2+ NSC**	**2+ NSC**
Anterior Vitreous	Clear	Clear

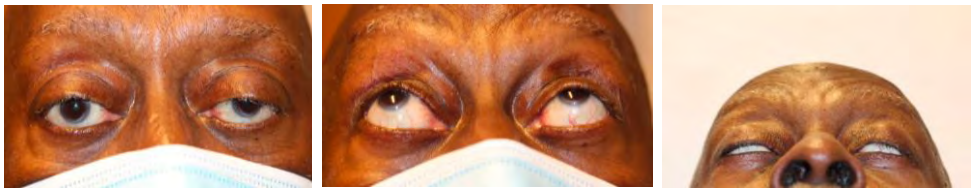
Fundus Exam

	OD	OS
CDR	0.65	0.9

December 2014:



June 2021:



Assessment & Plan

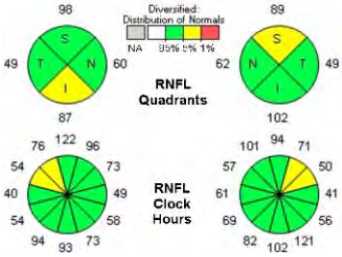
- Thyroid Eye Disease, euthyroid levels
  - Recommend orbital decompression and ptosis surgery
  - Patient defers surgery again
  - Artificial tears and lubricating ointment QHS OU PRN
  - Follow-up 4 months for reassessment for surgery

But….

OCT-RNFL

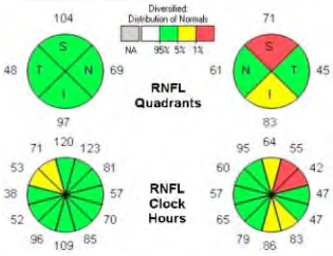
2015

	OD	OS
Average RNFL Thickness	74 µm	75 µm
RNFL Symmetry	81%	
Rim Area	1.13 mm²	0.94 mm²
Disc Area	2.07 mm²	2.21 mm²
Average C/D Ratio	0.66	0.75
Vertical C/D Ratio	0.69	0.76
Cup Volume	0.279 mm³	0.405 mm³

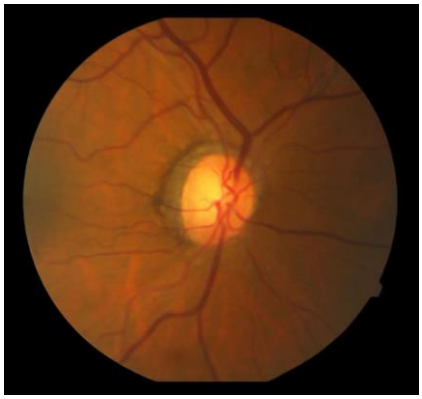


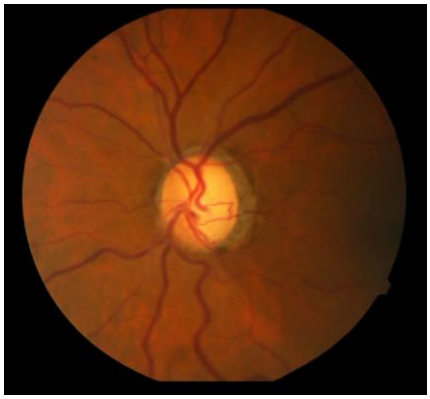
2021

	OD	OS
Average RNFL Thickness	80 µm	65 µm
RNFL Symmetry	77%	
Rim Area	1.04 mm²	0.80 mm²
Disc Area	2.07 mm²	2.28 mm²
Average C/D Ratio	0.70	0.81
Vertical C/D Ratio	0.73	0.81
Cup Volume	0.321 mm³	0.519 mm³



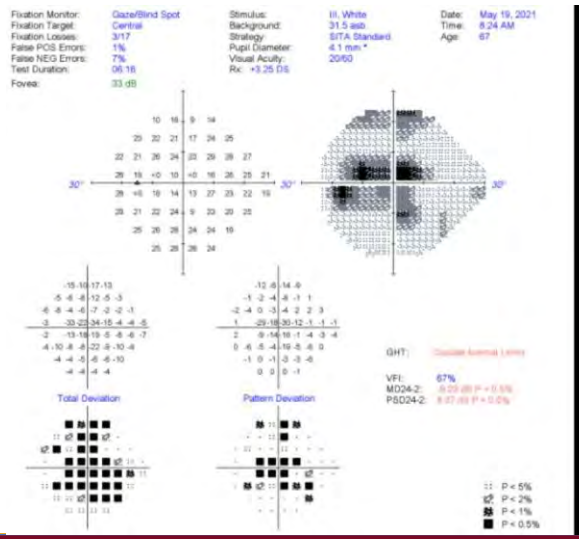
Fundus Exam

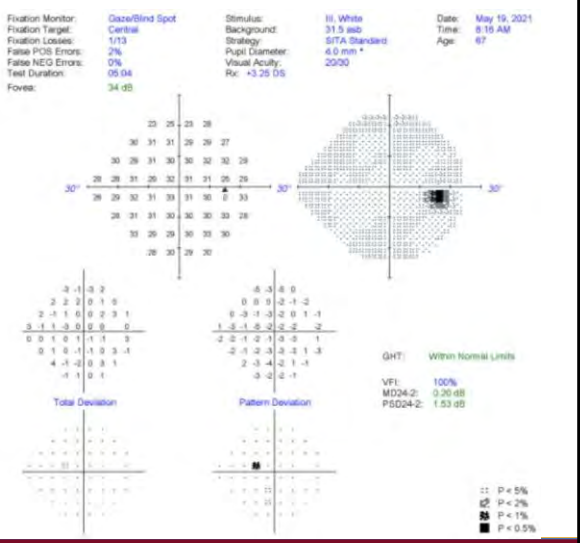




- Significant cupping OS > OD
- Is it enough to cause visual field loss?

Humphrey Visual Field





Assessment & Plan (Continued)

- Mixed Mechanism Glaucoma OS >> OD
  - Uveitic glaucoma (hx of iritis)
  - Steroid response
  - Increased episcleral venous pressure due to TED
- Intolerant to multiple topical glaucoma medications
- After counseling, patient amenable to surgical decompression
- Recommend orbital decompression to reduce episcleral venous pressure and IOP ASAP!

Surgical Course

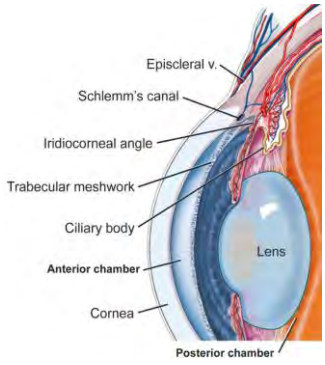
- **June 08, 2021 –** Orbital Decompression OS
  - Pre-Op: IOP 24 mmHg
  - POD#3: IOP 15 mmHg
  - POW#1: IOP 14 mmHg; significant nasal chemosis, s/p conjunctival incision and close monitoring
  - POW#3: IOP 17 mmHg
  - POM#1: IOP 20 mmHg; IOP was improving but now likely steroid response
  - POM#1.5: 15 mmHg; IOP much improved but not at target

Surgical Course

- **June 08, 2021 –** Orbital Decompression OS
  - Pre-Op: IOP 24 mmHg
  - POD#3: IOP 15 mmHg
  - POW#1: IOP 14 mmHg; significant nasal chemosis, s/p conjunctival incision and close monitoring
  - POW#3: IOP 17 mmHg
  - POM#1: IOP 20 mmHg; IOP was improving but now likely steroid response
  - POM#1.5: 15 mmHg; IOP much improved but not at target
- **June 22, 2021 –** Orbital Decompression OD
  - Pre-Op: IOP 27 mmHg
  - POD#1: IOP 15 mm Hg
  - POD#6: nasal chemosis– drained in clinic
  - POW#2: IOP 21 mmHg; IOP was improving but now likely steroid response
  - POM#1: IOP 17 mmHg

Glaucoma – An Extension of Thyroid Disease?

- Mechanisms for IOP elevation
  - Congestive orbitopathy with secondary elevation of **episcleral venous pressure**
    - Conventional aqueous humor drainage → aqueous and episcleral veins
  - Increased retrobulbar pressure
  - Contraction of extra-ocular muscles with increased pressure on the globe
  - Increased mucopolysaccharide deposition within the trabecular meshwork
  - Genetic predisposition
- Ocular hypertension in TED estimated to be ~3.1%–24%
  - Strong risk factor for open-angle glaucoma (OAG)
- Progression to glaucoma in TED estimated to be ~0.8–13%
- Association between OAG and TED (?) is controversial



Treatment of Thyroid Eye Disease

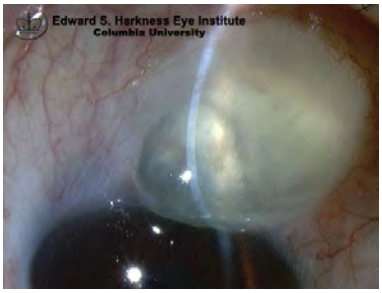
- Reduce IOP
- Corneal protection
- Comfort
- Cosmesis
- Prevention of irreversible damage to cornea or optic nerve
  - i.e. Exposure keratopathy or optic neuropathy

Medical Treatment

- **Corticosteroids** traditionally used in *active disease* → reduce inflammation and lower IOP
- **IOP lowering medications**
  - Aqueous suppression
    - Alpha-2 agonists (i.e. Brimonidine); β blockers (i.e. Timolol); Carbonic anhydrase inhibitors (i.e. Dorzolamide, Brinzolamide, Acetazolamide, Methazolamide)
  - Prostaglandin analogues
    - Periorbital fat atrophy / atrophy of adipocytes may be helpful?
    - Eftekhari et al. demonstrated decreased adipocyte density with orbital injection of bimatoprost compared to control orbits injected with saline (2018)
  - Rho kinase inhibitors
    - Increased trabecular outflow; decreased aqueous production and episcleral venous pressure

Surgical Treatment

- Orbital Decompression
  - Lowers IOP by decreasing episcleral venous pressure
    - Increase superior ophthalmic venous flow
    - Increase in choroidal perfusion
- Trabeculectomy / Tube Shunt
  - Beware of lid positioning!
- Minimally Invasive Glaucoma Surgery?

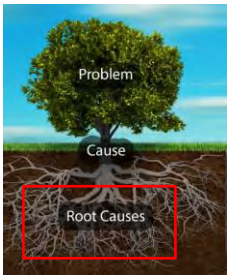


Surgical Treatment

- Angle Surgery?
  - Lowers IOP by overcoming resistance at the level of the trabecular meshwork
  - What happens if episcleral venous pressure is high though?
  - Proceed with caution!

Pearls for Case 2

- Glaucoma is oftentimes a “systemic” disease
  - Obtain a good history and be aware of the patient’s medical history
- When your roof is leaking, the answer is NOT to “buy more buckets”
  - Get to the ROOT of the problem
  - The best treatment is not always a glaucoma medication or surgery



Case 3

Patient History

- 82 year old Asian female referred by her general ophthalmologist for ocular surface disease and glaucoma progression despite maximum medical therapy
- Complains of red, irritated eyes and "tearing" OU

- **PMH**
  - Hypertension
  - History of pulmonary embolus – on Rivaroxaban
- **POH**
  - Combined mechanism glaucoma OU
  - Status post cataract surgery OU (2015)
  - Dry eye syndrome / ocular surface disease

Past Ocular History

- Combined mechanism glaucoma OU
  - Status post selective laser trabeculoplasty (SLT) OU (2018)
  - Status post trabeculectomy OU (2019)
  - Netarsudil/Latanoprost QHS OU; Brimonidine BID OU; Dorzolamide/Timolol BID OU
- Pseudophakia OU
  - Status post cataract surgery OU in 2018
- Dry Eye / Ocular Surface Disease OU
  - Artificial tears QID OU
  - Cyclosporine BID OU

Ophthalmic Vitals

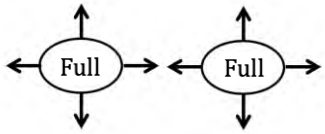
BCVA 20/25 / 20/40

IOP 14 / 11

CVF: Full OU

Pupils 4 → 2, brisk, no rAPD / 4 → 2, brisk, no rAPD

EOM:

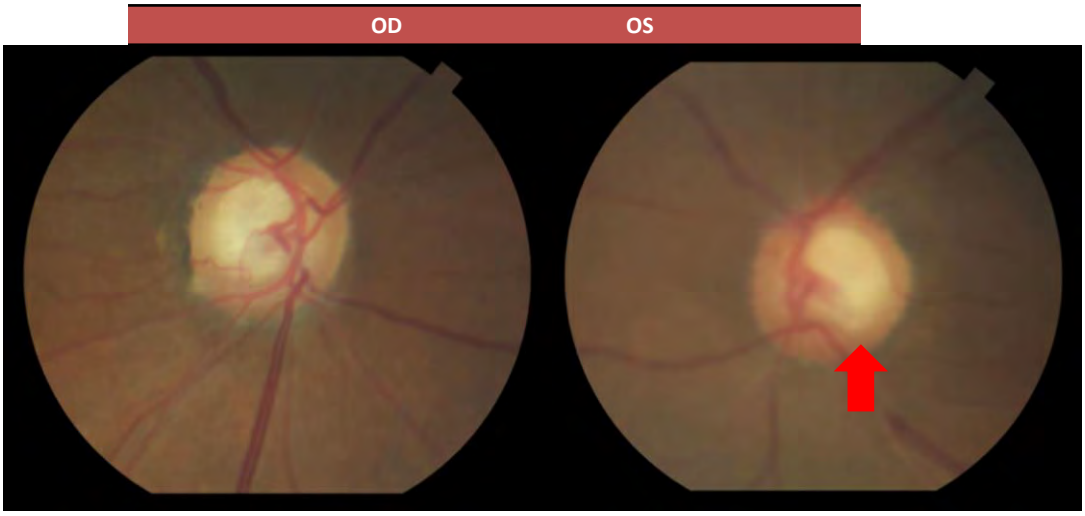


Gonioscopy: A-C35r3+ with scattered PAS OU

Slit Lamp Exam

	OD	OS
Orbits/Adnexa	Normal	Normal
Lids/Lashes	**Blepharitis, periorbitopathy**	**Blepharitis, periorbitopathy**
Conjunctiva/Sclera	**1+ injection; flat superior bleb**	**1+ injection; flat superior bleb**
Cornea	**3+ PEE**	**3+ PEE**
Anterior Chamber	Deep and quiet	Deep and quiet
Iris	Round, superior iridectomy	Round, superior iridectomy
Lens	PCIOL	PCIOL
Anterior Vitreous	Clear	Clear

Fundus Exam



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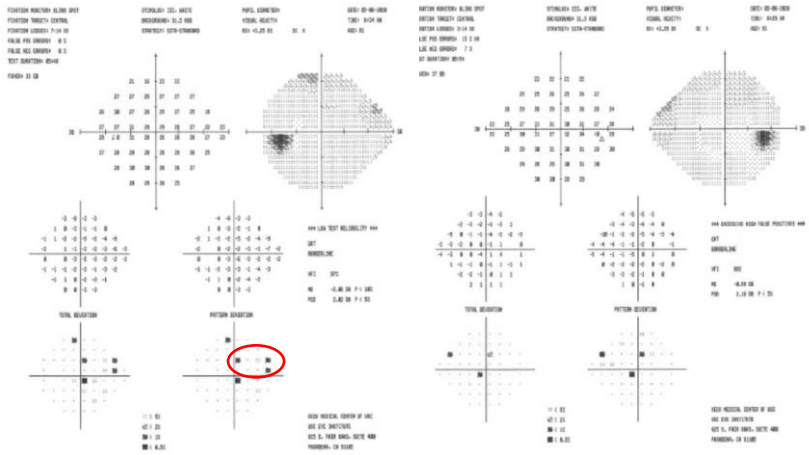
Humphrey Visual Field



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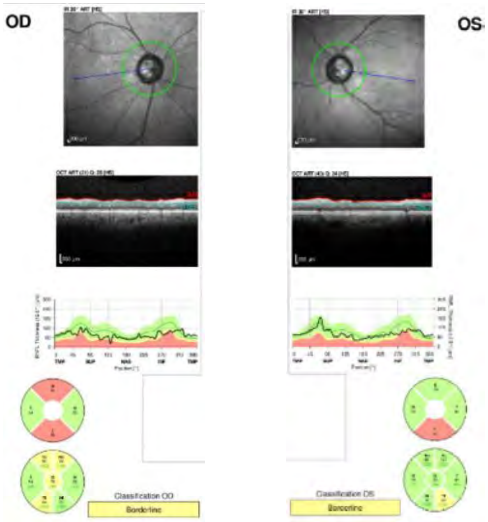
OCT-RNFL



Assessment and Plan

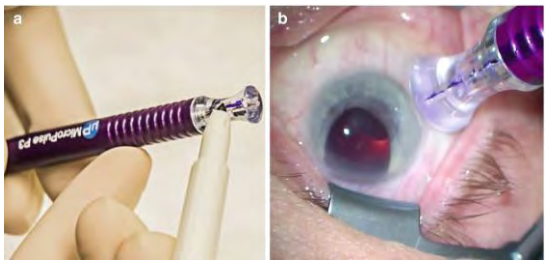
- **<u>Combined</u> mechanism open angle glaucoma OS > OD**

- What would you do next?
  - Continue present management
  - Change Dorzolamide/Timolol to preservative-free
  - Discontinue Brimonidine
  - Discontinue Netarsudil/Latanoprost combination
  - Selective laser trabeculoplasty

Clinical Course

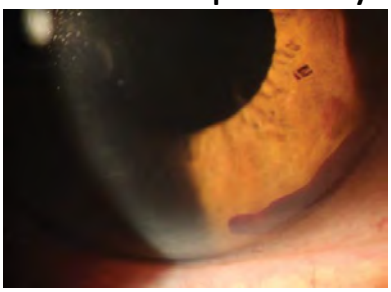
- **August 14, 2020**
  - Follow-up IOP check and reassessment of symptoms
    - IOP: 15 mmHg OD || 13 mmHg OS
    - Target IOP = low teens OU
  - Minimal change in symptoms since stopping Brimonidine and switching to Dorzolamide/Timolol preservative-free
  - Recommend micropulse cyclophotocoagulation OD first

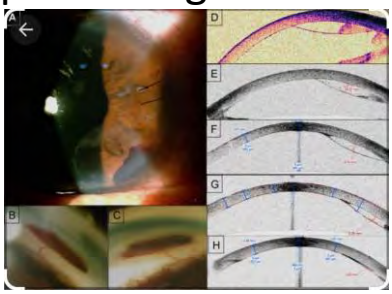
Micropulse Cyclophotocoagulation



- **Why?**
  - Patient has relatively mild glaucoma
  - Significant bleeding risk from trans-scleral filtration surgery due to anti-coagulation use

Micropulse Cyclophotocoagulation





- **How about MIGS?**
  - Significant hyphema risk due to anti-coagulation use
  - Risk of Descemet's detachment after prior trabeculectomy

Transcleral Cyclophotocoagulation

DEVICE COMPARISON	G-PROBE	G-PROBE Illuminate	MP3 PROBE
Glaucoma Treatment Stage	Refractory	Refractory	Primary Open Angle
Repeatable Procedure	Yes	Yes	Yes
MicroPulse Technology	No	No	Yes
Transillumination	No	Yes	No
Destructive	Yes	Yes	No[2]
Therapy Location	Office & OR	Office & OR	Office & OR
CPT Code	66710	66710	66710
SmartProbe Technology	Laser Parameter Memory Enabled	Laser Parameter Memory Enabled	Laser Parameter Memory Enabled
Patented Probe Design	Wedge	Wedge	Curve

- Micropulse is not believed to be cyclo-destructive
  - Delivers short pulses of energy with resting periods in between
  - Results in "cooling period" between bursts and less collateral tissue damage

Clinical Course

- **July 23, 2021**
  - Status post MP-CPC OD 11/12/2020 and OS 4/6/2021
    - IOP: 12 mmHg OD || 9 mmHg OS
    - IOP at goal on only Dorzolamide/Timolol preservative-free BID OU
  - Conjunctival hyperemia improved/resolved
  - OCT-RNFL and HVF stable from 2020

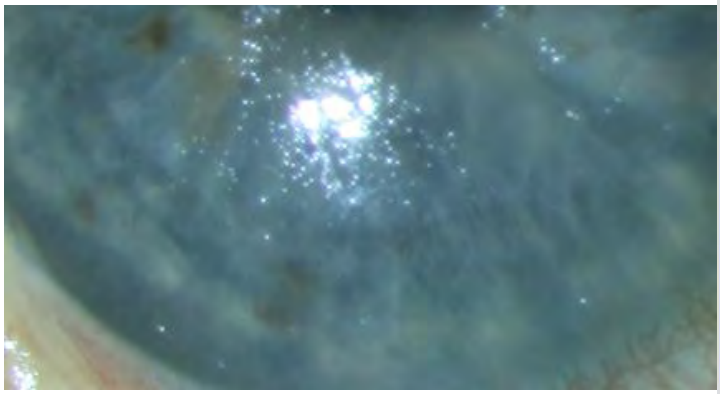
Ocular Surface Disease in Glaucoma Patients

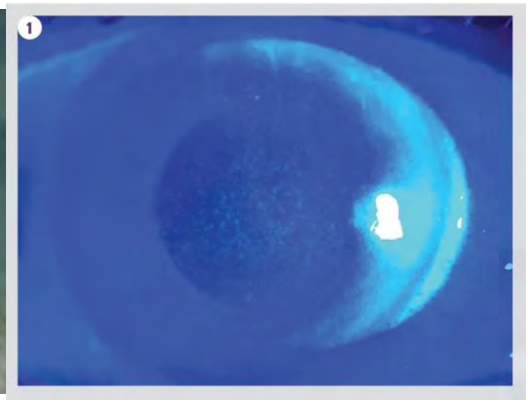
- Glaucoma treatment may cause chronic inflammation or aggravate a concomitant ocular surface disease
- Topical glaucoma medications can cause burning, irritation, itching, tearing, and decreases in visual acuity within three months of medication initiation
- Glaucoma therapy-related ocular surface disease:
  - "Imbalance of the ocular surface homeostasis caused by the toxic effect of chronic topical medication, which leads to tear film instability, epithelial damage, and inflammation."

Clinical Manifestations of Surface Issues in Glaucoma Patients

- Punctate epitheliopathy
- Dry eye disease
- Meibomian gland dysfunction and tear film instability
- Allergy
- Pseudopemphigoid

Punctate epitheliopathy/Toxic keratitis





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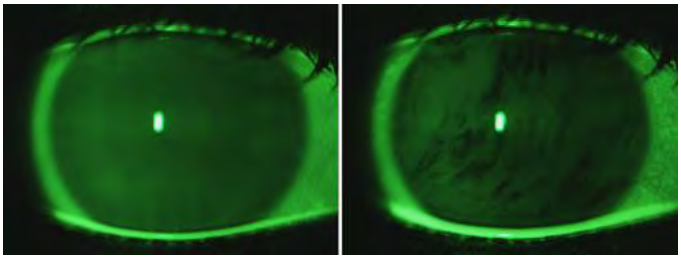
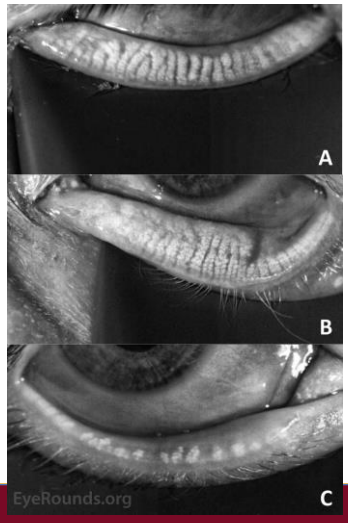
https://cdn.sanity.io/images/0vv8moc6/optometrytimes/f7f6ee77add14eaee49db47e1e414ce362e277d0-1496x878.png?auto=format

Meibomian Gland Dysfunction





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http://www.eyerounds.org/tutorials/Meibomian-gland-dysfunction-related-evap-dry-eye-syndrome/Fig4-LRG.jpg

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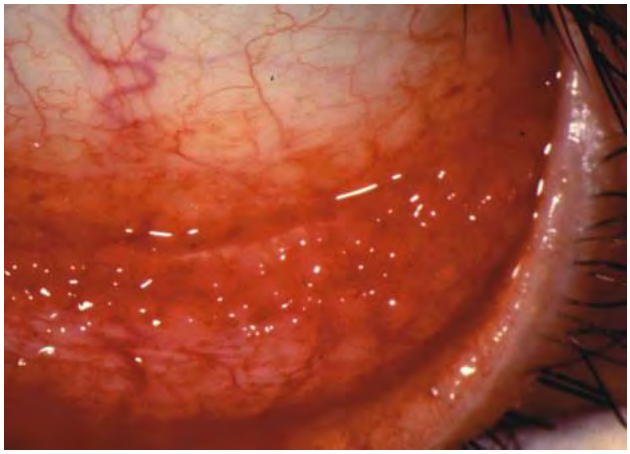
Allergy



https://lh3.googleusercontent.com/proxy/633psEd

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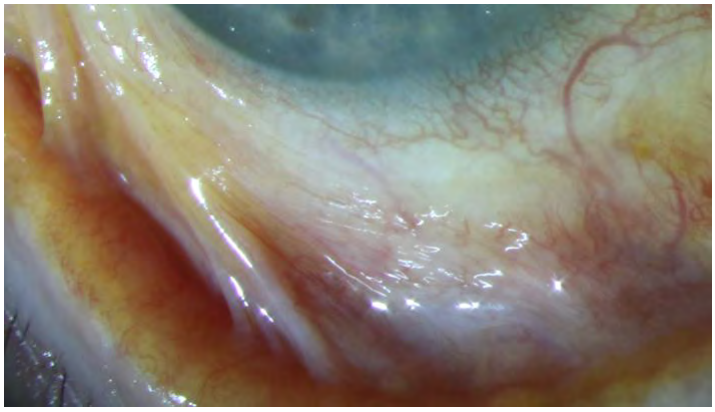
Pseudopemphigoid



https://eyewiki.aao.org/w/images/1/6/63/Pseudopemphigoid_jung.png

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Pathology of Drop Toxicity

- Preservatives
  - Benzalkonium chloride (BAK)
    - Bacteriostatic and bactericidal by destroying cell membranes
    - Pro-inflammatory and toxic
- Prostaglandin analogues (PGAs)
  - MGD and atrophy, reactivation of herpetic keratitis
- Alpha-adrenergic agonists
  - High ocular allergy rate
- Carbonic anhydrase inhibitors
  - Increased corneal thickness
- Beta-blockers
  - Reduce basal tear and alter mucus production

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Medical Treatment

- Avoid BAK preservative
- **BETTER:**
  - Alternative preservatives
    - Purite
    - SofZia
- **<u>BEST:</u>**
  - Preservative-free hypotensive medications

USC Roski Eye Institute
Keck Medicine of USC

https://2rdnmg1qbg403gumla1v9i2h-wpengine.netdna-ssl.com/wp-content/uploads/sites/3/2019/06/dryEyesDropper-163674127-770x553-650x428.jpg
https://cdn.sanity.io/images/0vv8moc6/optometrytimes/00c51c7605223b2c6edd35f010de76874d992971-1570x1298.png?auto=format

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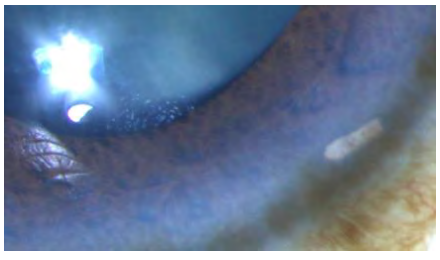
Medical Treatment

- Discontinue ineffective medications
- Lubrication without added preservatives
- Topical cyclosporine or lifitegrast
- Warm compresses/lid hygiene, IPL, thermal pulsation (if MGD present)
- New forms of drug delivery
  - Drug-eluting punctal plugs and contact lenses
  - Implants: Bimatoprost SR (Durysta)



USC Roski Eye Institute
Keck Medicine of USC

https://eyewiki.aao.org/w/images/1/2/22/Intracameral_sustained.jpg

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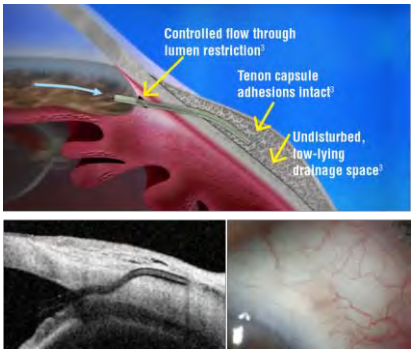
Surgical Treatment

- Selective Laser Trabeculoplasty (SLT)
- Minimally Invasive Glaucoma Surgery (MIGS)
- Filtration Surgery
  - Trabeculectomy
  - Glaucoma tube shunt
  - XEN gel stent
- Cyclophotocoagulation?



First-line option?
Treatment Paradigm shift?

THE LANCET

ARTICLES | VOLUME 393, ISSUE 10180, P1505-1516, APRIL 13, 2019

Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial

Gus Gazzard, FRCOphth • Evgenia Konstantakopoulou, PhD • Prof David Garway-Heath, MD • Anurag Garg, FRCOphth • Victoria Vickerstaff, MSc • Rachael Hunter, MSc • et al. Show all authors • Show footnotes

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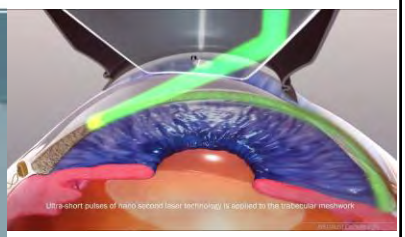

https://i.ytimg.com/vi/ablwDDKqBnM/maxresdefault.jpg

Pearls for Case 3

- Ocular surface disease is often exacerbated in glaucoma patients, especially with the use of BAK-preserved topical anti-hypotensive.
- In glaucoma patients with dry eyes, care should be taken to reduce the burden of topical glaucoma medications in order to improve quality of life and treatment compliance and effect.
  - Modern medicine affords us good options to achieve this including:
    - Selective laser trabeculoplasty
    - Drug-eluting implants
    - Minimally invasive glaucoma surgery
    - Filtration surgery
- Cyclophotocoagulation, especially micro-pulse, is a reasonable option even for well-seeing eyes in the right circumstances

Summary and Take Home Points from Today's Cases

- Glaucoma is an "umbrella" term
- Not all glaucomas are the same
  - Just like not all cancers are the same

- A *group* of diseases characterized by:
  - *Progressive* optic neuropathy
  - *Characteristic* visual field loss
  - In total, there are > 20 types of glaucoma
- Intraocular pressure (IOP) is NOT used to define glaucoma
  - Just like we do not define lung cancer by smoking
  - IOP is the primary risk factor for glaucoma, but it is not a part of its definition
  - Treat the *disease* NOT the pressure

Summary

- Glaucoma is a *central nervous system* disease with *systemic relationships*
  - If you take the time to understand the **root** cause, you and your patients will be better off

Thank You

(Virtual) Questions?

Marshall B.
KETCHUM UNIVERSITY
Southern California College of Optometry

Refer or Relax? Macula

Steven Ferrucci, OD

REFER OR RELAX: macula

Steven Ferrucci, OD, FAAO
Chief, Optometry, Sepulveda VA
Professor, MBKU/SCCO

1

Disclosures

- Alcon
- Centervue
- Genentech
- Maculogix
- Optovue
- Regeneron
- Science Based Health
- Visible Genomics

2

INTRODUCTION

- Various macula cases will be presented
- Question is should the case be referred to a retina specialist OR can you monitor it yourself
- There are no right or wrong answers, just differences of opinion
- JUST KIDDING, THERE ARE WRONG ANSWERS!

3

Dry AMD

- Currently mainstay treatment for Dry AMD revolves around prevention of progression through vitamins, nutrition and lifestyle changes
  - Rheophoresis, Laser, Anecortave Acetate did not prove effective
  - Smoking #1 modifiable risk factor for getting AMD as well as its progression!
    - One study showed 90% of pts with AMD were not advised to quit smoking
- Early detection of conversion from dry to wet may result in better treatment for patients

4

AREDS

- First large scale study looking at nutrition and ocular health
- 3640 pts followed on average for 6.3 years
  - Results released October 2001
- Results showed that 25% risk reduction to developing advanced AMD in pts with intermediate (stage 3) AMD or worse
  - 500 mg vitamin C
  - 400 IU vitamin E
  - 15 mg vitamin A (25,000 IU beta carotene)
  - 80 mg zinc
  - 2 mg copper

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AREDS 2

- AREDS 2: Enrollment ended June 2008 with ≈4200 patients followed for six years
  - Effect of lutein, zeaxanthin and omega 3 on AMD
  - Effect of eliminating beta carotene on AMD
  - Effect of reducing zinc on AMD
  - Effect of supplements on cataracts
  - Validate the AMD scale from original AREDS
- Results released May 5, 2013

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AREDS 2

- Major Conclusions:
  - The addition of lutein and zeaxanthin, DHA and EPA or both to the AREDS formulation did not further reduce the risk of progression to advanced AMD
  - Substituting L/Z (10 mg/2 mg) for beta carotene is an appropriate substitution, because of potential increased incidence of lung cancer in former smokers

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Additional findings

- Lutein and zeaxanthin did provide an additional 10% reduced risk over current supplements
  - In patients with lowest dietary intake of l/z, additional 26% reduced risk
- Decreasing zinc from 80 mg to 25 mg had no significant effect
  - No change recommended (?)
  - Deserves further study
- Competitive absorption of carotenoids

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AREDS2 Formulation

Vitamin C (500 mg)

Vitamin E (400 IU)

~~Beta-Carotene (15 mg)~~

Lutein (10 mg)/Zeaxanthin (2 mg)

Zinc (80 mg zinc oxide)

Copper (2 mg cupric oxide)

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Dark adaptomteter

- Dark adaptation is a sensitive marker for early AMD
- The AdaptDx measures dark adaptation
- A rapid test of dark adaptation using the AdaptDx has been found to have a 90% sensitivity for detecting dark adaptation impairment associated with AMD
- Decreased dark adaptation may precede clinical findings of AMD by as much as 3 years
- Dark adaptation is more sensitive than other tests such as Snellen acuity, contrast sensitivity, or visual fields which are about 25% sensitive.

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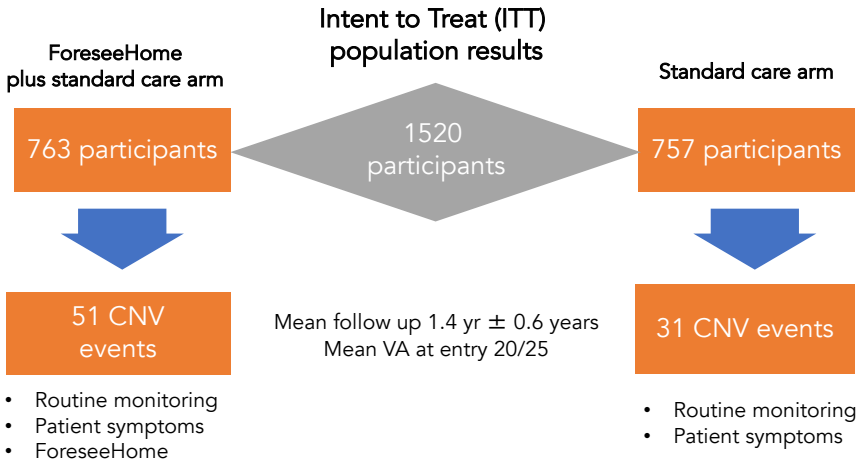
AREDS2-HOME Study



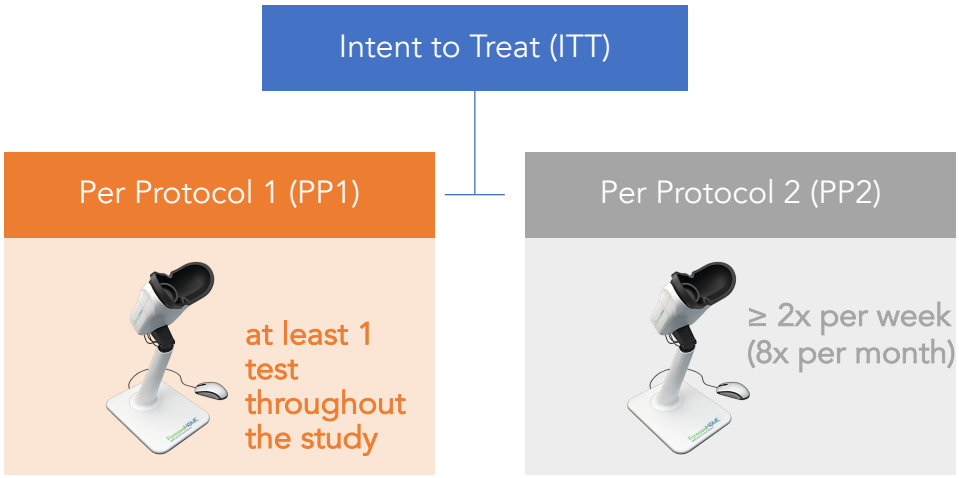
**Primary outcome:* *Change in BCVA from baseline to CNV detection*

Reference: AREDS2-HOME Study Research Group. *Ophthalmology*. 2014;121(2):535-544.

11

11

ForeseeHome Arm



Reference: AREDS2-HOME Study Research Group. *Ophthalmology*. 2014;121(2):535-544.

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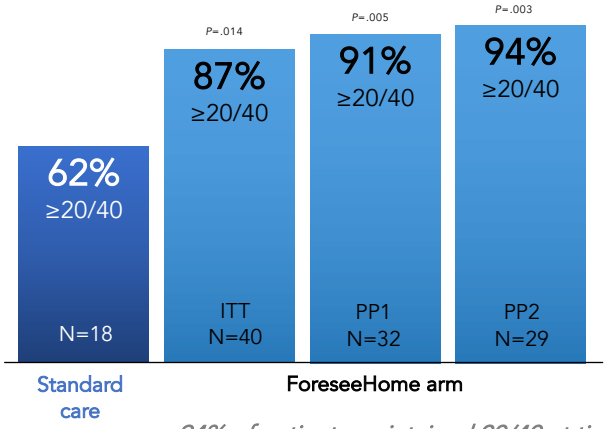
12

More patients who used ForeseeHome maintained ≥20/40 VA



50% MORE
patients maintained 20/40 or better when using ForeseeHome vs standard of care alone

94% of patients maintained 20/40 at time of wet AMD diagnosis; Absolute visual acuity at time of wet AMD diagnosis is critical to visual acuity outcomes at year 1

Reference: AREDS2-HOME Study Research Group. *Ophthalmology*. 2014;121(2):535-544.

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Home OCT

- **Notal OCT Analyzer (NOA)**
- **"Uses computer image analysis algorithm to provide automated detection of pathological fluid in exudative retinal disease, including wet AMD, macular edema and retinal vein occlusion"**
- **Performance validated in study comparing sensitivity , specificity and accuracy with 3 retinal specialist**

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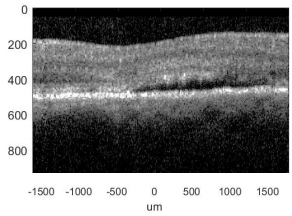
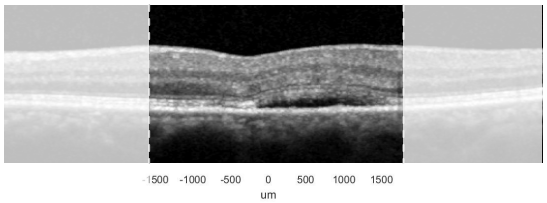
Patient Self-operated Home OCT provides high quality images

- Patient self-installed and self-operated OCT device
- Monitoring of intra- and subretinal fluid in between office visits
- Provides cross sectional images of the central 10 deg. (3 mm x 3 mm) of the macula in patients with exudative AMD
- 88 B-scans with dense 34 µm spacing ensure high sensitivity of fluid detection
- Test takes approximately 10 sec. per eye
- Device uploads OCT data to cloud

Home OCT



Heidelberg Spectralis (in-office device)



15

Home OCT Performance and Roadmap

- US clinical trial demonstrated 90% of 196 elderly wet AMD patients with VA > 20/400 could self-operate and self-capture readable images following a 2-minute video tutorial (presented at ASRS 2019)
- Human graders identified fluid with SENSITIVITY = 91.5% and SPECIFICITY = 97.0% for Notal Home OCT V2.5 when compared to commercial OCT devices (presented at ASRS 2019)
- Notal Vision's patient-operated, AI-enabled Home OCT system was granted FDA Breakthrough Device Designation Status, and was selected to participate in FDA's OCT Innovation Pilot Program
- Notal Vision plans to bring first devices to patients' homes in 2020 as part of clinical trials with a commercial launch in 2021

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Is AMD in our DNA?

- AMD is a genetic disease with known markers accounting for at least 70% of the population attributable risk
- Other 30% is environmental/lifestyle
- Risk factors
  - Non-modifiable: age, race, gender
  - Modifiable: Smoking, increased BMI, poor diet/nutrition, UV exposure

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AMD is a Genetic Disease

Population Attributable Risk	
Condition	Genetics (%)
Colorectal Cancer	35
Diabetes II	26
Coronary Artery Disease	40
AMD	70

Those with stronger genetic risk develop more advanced disease earlier in life.

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Major genetic factors

- CFH
  - Single most important genetic component
  - CFH Y402H
- ARMS2/HTRA1
  - Second most important gene in AMD
- C3
  - Another component of the complement system
- Others
  - Less important

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Genetic Factors and Risk: More than additive!

- Former Smokers: 1.29x
- Current Smokers: 2.4X
- Non-Smoker and CFH,Y402H: 7.6X
- Current smoker and CFH,Y420H: 34X

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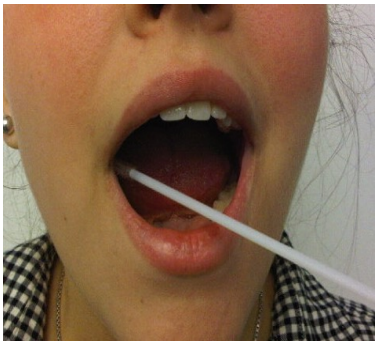
AMD Genetic Testing: Arctic DX

Macula Risk NXG

Looks at 15 SNPs as well as smoking, BMI, age and AMD status to determine AMD patients who may progress to advanced AMD and vision loss in

- 2 years
- 5 years
- 10 years



Cheek Swab

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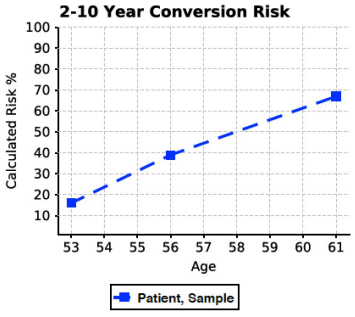
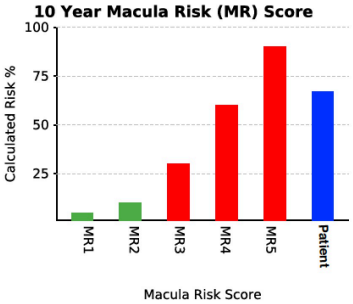
Patient Report

Risk of Conversion to GA or CNV (%) based on genetic and non genetic features

Category	2 Years	5 Years	10 Years
Patient, Sample	16	39	67
10 Year Macula Risk Score			5





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"Wet" AMD

- Neovascular "wet" AMD
  - Mainstay of treatment consists of serial intravitreal injection of anti-VEGF agents

Anti-VEGF Agents	Pegaptanib (Macugen®)	Ranibizumab (Lucentis®)	Aflibercept (Eylea®)	Brolucizumab (Beovu®)	Bevacizumab (Avastin®)
FDA approval	2004	2006	2011	2019	Not approved
Pivotal studies	VISION	ANCHOR MARINA IVAN	VIEW 1 and 2	HAWK HARRIER	CATT

  - VEGF inhibitors have demonstrated *improved visual and anatomic outcomes* compared with other therapies

VEGF = vascular endothelial growth factor.

AAO. AMD preferred practice guidelines, 2019 (www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp). Kulkarni K, Prenner JL. *Rev Ophthalmol.* 1/13/2006. (www.reviewofophthalmology.com/article/an-update-on-macugen-trials). URLs accessed 5/30/2020.

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Anti-VEGF Agents

- VEGF is a primary driver of blood vessel growth and leakage in AMD
- Anti-VEGF agents block and neutralize VEGF
  - Results in decreased intra- and sub-retinal fluid
  - May also decrease risk of scar tissue formation
- Serious adverse effects (endophthalmitis) rare
- Less serious events (subconjunctival hemorrhage, vitreous hemorrhage, floaters) are also uncommon

Pongsachareonnont P, et al. *Clin Ophthalmol.* 2018;12:1877-1885. Yeo NJY, et al. *Front Pharmacol.* 2019;10:1363. Holz FG, et al. *Br J Ophthalmol.* 2016;100:1623-1628.

American Society of Retina Specialists (ASRS). Intravitreal injections. (www.asrs.org/content/documents/fact-sheet-30-intravitreal-injections.pdf). Sukgen EA, et al. *Int Ophthalmol.* 2017;37:215-219. Living well with low vision. (https://lowvision.preventblindness.org/2013/06/25/betadine-and-eye-pain/). URLs accessed 5/30/2020

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Anti-VEGF Agents: Delivery and Dosage

- Delivered intravitreally
- Dosing schedule and agent used varies
- In general
  - Loading dose with 1 injection per month for 3 months, then inject based on FA, OCT, or other clinical findings
  - Reduces patient burden while still delivering good results

Holz FG, et al. *Br J Ophthalmol.* 2016;100:1623-1628. Kress B. *Review of Optometry.* 2019 (https://www.reviewofoptometry.com/article/antivegf-where-are-we-now). Accessed June 10, 2020. Treating Wet AMD with Anti-VEGF drugs. 2016 (https://www.reviewofophthalmology.com/article/treating-wet-amd-with-antivegf-drugs). Accessed June 10, 2020

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Anti-VEGF Agents: Outcomes

Lucentis[1]

- **94% stable vision at 2 years**
- **34–41% gained 15 letters or more**
- **Average gain of 11.3 letters at 1 year and 10.7 letters at 2 years**

Eylea[2,3]

- 95% of patients treated maintained acuity
- 7.9–10.9 letters mean improvement of vision

Beovu[4]

- ~30% gained at least 15 letters by year 1
- Less fluid and greater reduction in CST vs aflibercept
- At 1 year, half of subjects on 3-month dosing

1. Brown DM, et al. *Ophthalmology.* 2009;116:57-65.e5. 2.Nguyen QD, et al. *Invest Ophthalmol Vis Sci.* 2011;52: abstract 3073. 3. Schmidt-Erfurth U, et al. *Invest Ophthalmol Vis Sci.* 2011;52:E-Abstract 1650. 4.Dugel PU, et al. *Ophthalmology.* 2020;127:72-84.

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Other Treatment Options

Possible

- Photodynamic therapy (PDT) with verteporfin
- Intravitreal steroids in combination with PDT or anti-VEGF agents
- Laser photocoagulation
- Observation/suspension of treatment

Not advised

- Intravitreal steroids as monotherapy
- Radiation therapy
- Electrical stimulation
- Macular translocation therapy

AAO. AMD preferred practice guidelines, 2019 (www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp). Accessed 5/30/2020. Wong DT, et al. *Retina.* 2020;40:1010-1020. Giancipoli E, et al. *J Ophthalmol.* 2018:5612342. Veritti D, et al. *Expert Rev Ophthalmol.* 2010;5(5):681-688.

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Beovu (brolucizumab)

- Novartis
- FDA approved Oct 9, 2019
- Greater fluid resolution than previous agents with similar vision gains on 3 mos dosing
- Based on Hawk and Harrier Phase 3 trials

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Beovu (brolucizumab)

- Hawk and Harrier Study: compared to Eylea
  - 30% of pts gained at least 15 letters by year 1
  - Greater reduction in central retinal thickness at week 16 and 1 year than Eylea
  - Fewer pts with subretinal fluid than Eylea
  - Real key is extended dosing
    - After 3 monthly loading doses
      - By year 1, > ½ pts on 3 mos dosing
      - Rest were 2 mos dosing
  - Safety profile similar to Eylea

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Beovu update

- In Feb, 2020, American Society of Retinal Specialists (ASRS) issued a warning reporting 14 cases of retinal vasculitis following injection of Beovu
  - 11/14 were occlusive and resulted in vision loss
- In March, Novartis concluded that retinal vasculitis, retinal artery occlusion, or severe vision loss occurred in 8.75-10.08 out of 10,000 injection
- Added to warning label
  - Intraocular inflammation in 4% of pts
  - Artery occlusion in 1%
- Advised to avoid if pts had h/o inflammation to any other anti-Vegf agent

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Viagra and CSR

- Retina 2008: Fraunfelder and Fraunfelder
- 11 reported cases of CSR in men taking Viagra
  - In 8/11, pts stopped taking Viagra
  - In 6/8, vision improved with cessation
  - In 3 cases, CSR returned when started med again
  - 2 pts continued to have CSR after cessation
- Might consider recommending cessation of Viagra if active CSR, but relationship is unknown at this time

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Central Serous Retinopathy

- Common disorder of unknown etiology which typically affects men between age 20 and 45
  - Males to females 10:1
- Serous detachment of neurosensory retina due to leakage from small defect in RPE

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Central Serous Retinopathy

- Pt typically presents with fairly recent onset of blurred VA in one eye with a scotoma, micropsia, or metamorphopsia
  - VA typically 20/30-20/70
  - Often correctable with low hyperopic RX
  - Unilateral in 70% of cases

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Central Serous Retinopathy

- Appears as a shallow round or oval elevation of the sensory retina often outlined by a glistening reflex
- FA is helpful in providing definitive diagnosis
  - Classic Smoke stack appearance (occasionally)
  - Ink-blot appearance
- OCT shows marked elevation

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CSR: Risk Factors

TRADITIONAL

- Male > Female 10:1
- Age: Peak 20-45
- Type A personality
- Stress
- Pregnancy

OTHERS

- Steroid use
  - Oral
  - Topical?
  - Inhaled?
  - Injection?
- Choroidal Thickness
- Sleep apnea?
- Genes?
- Viagra?

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Central Serous Retinopathy

- 80-90% of pts will undergo spontaneous resolution and return to normal (or near normal) VA within 1-6 mos.
  - >60% resolve back to 20/20
  - Rare to have vision remain < 20/40
- Approx 40% will get recurrence
- CNVM is VERY rare occurrence, but possible

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CSR

- **When to worry/refer**
  - If VA worse than 20/70
  - If pt demographics do not support
  - If does not resolve in 6 mos
  - If gets worse rather than better
  - FA/ OCT does not support diagnosis
  - “Just doesn’t feel right”
  - Pt is unable to accept vision/prognosis

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Treatment

- Observation
- PDT
- Anti-VEGF
- Anti-corticosteroids
  - Rifampin
  - Mifepristone
  - Ketoconazole
  - Spironolactone/eplerenone
  - Finasteride
- Acetazolamide
- Aspirin
- Metoprolol
- H.pylori treatment
- Methotrexate
- Behavior Modification!

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LMH

- Lamellar Macula Hole OS
  - Also called partial thickness macular hole
- Pt ed.
- Monitor in 3 mos.
- Repeat OCT
- Consider retina referral if worsens

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LMH

- Symptoms
  - mild metamorphopsia,
  - limited acuity loss
  - stable vision
- Surgery is controversial
  - 25% to 75% improved visual acuity
- Therefore, monitoring seems reasonable

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FTMH

- Definition: Full thickness macular hole that affects all macular layers from ILM to RPE
- Size
  - Small: ≤250 um
  - Medium: 250um to 400um
  - Large ≥ 400 um
- Presence or absence of VMT
- By cause
  - Primary: Initiated by VMT (formerly idiopathic)
  - Secondary: from associated disease or trauma

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FTMH

- Small holes
  - Small rate of spontaneous closure
  - Very high surgical closure rate (almost 100%)
  - Best response to pharmacologic vitreolysis
- Medium holes
  - High surgical closure rate (>90%)
  - Decent response to pharmacologic vitreolysis
- Large holes
  - High surgical closure rate (75-90%)
  - No response to pharmacologic vitreolysis
  - ½ of all holes are large at time of diagnosis

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antiVEGF

- Lucentis, Avastin, Eylea
- Shown in multiple studies to be beneficial for DME
  - RISE
    - 18.1% of pts in sham gained ≥ 15 letters vs. 44.8% (0.3 mg) or 39.2% (0.5 mg)
    - 2.6 letters gained in sham vs. 12.5 (0.3mg) or 11.9 (0.5mg)
  - RIDE
  - READ
  - VISTA
  - VIVID

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Protocol V

- 702 pts with CI-DME with VA 20/25 or better
- 3 treatment groups
  - Eylea
  - FML
  - Observation
- At end of 2 years, rate of loss of 5 letters or more similar in all 3 groups
- Avg acuity in all 3 groups was 20/20
- Bottom line: pts with CI-DME and good VA can be observed

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DM/DME

- Refer if center involved DME/CSME evident on OCT in 1-2 weeks
- If not center involved, follow closely in 3- 6 mos
- Pt ed re role of BS/BP control
- Treatment: FML vs. serial anti-VEGF

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ERM

AGE	INCIDENCE
< 60	1.7%
60-69	7.2%
70-79	11.6%
80+	9.3%

BLUE MOUNTAIN EYE STUDY, AUSTRALIA

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ERM

- Consider surgery if:
  - VA 20/40-ish or worse
  - Symptomatic
  - Visual need of patient
- Make sure you have an experienced surgeon!!

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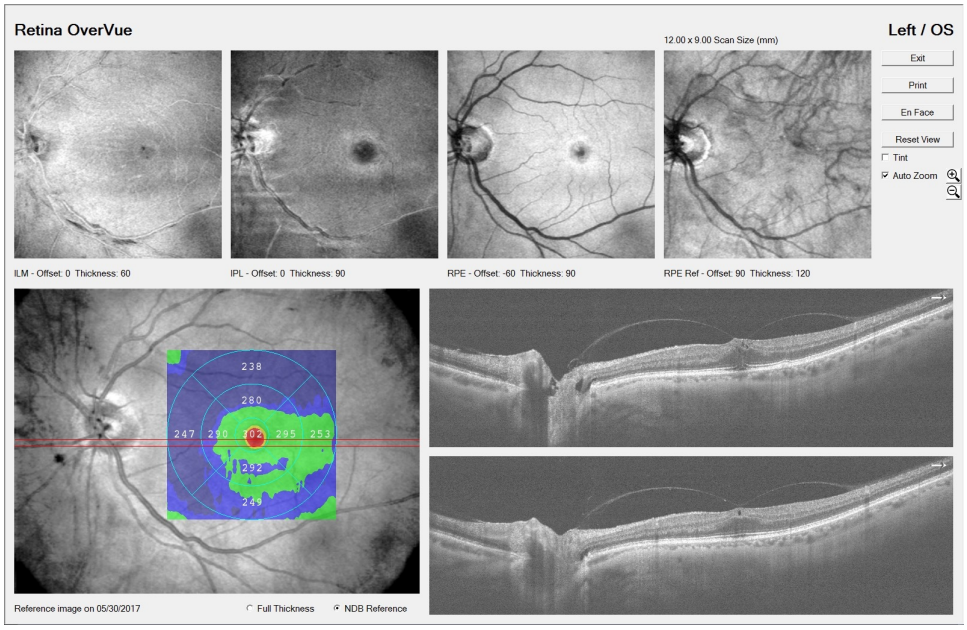
Case 7

- 70 year old male in for routine exam
- Notes mild change in distance vision, both eyes, since last exam 1 yr ago
- Thinks he needs new glasses
- 20/20 OD, 20/50 OS
  - Pt surprised that VA OS was decreased. Did not notice until exam today

48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Tint
Auto Zoom
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IPL - Offset: 0 Thickness: 90
RPE - Offset: -60 Thickness: 90
RPE Ref - Offset: 90 Thickness: 120
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247 230 302 295 253
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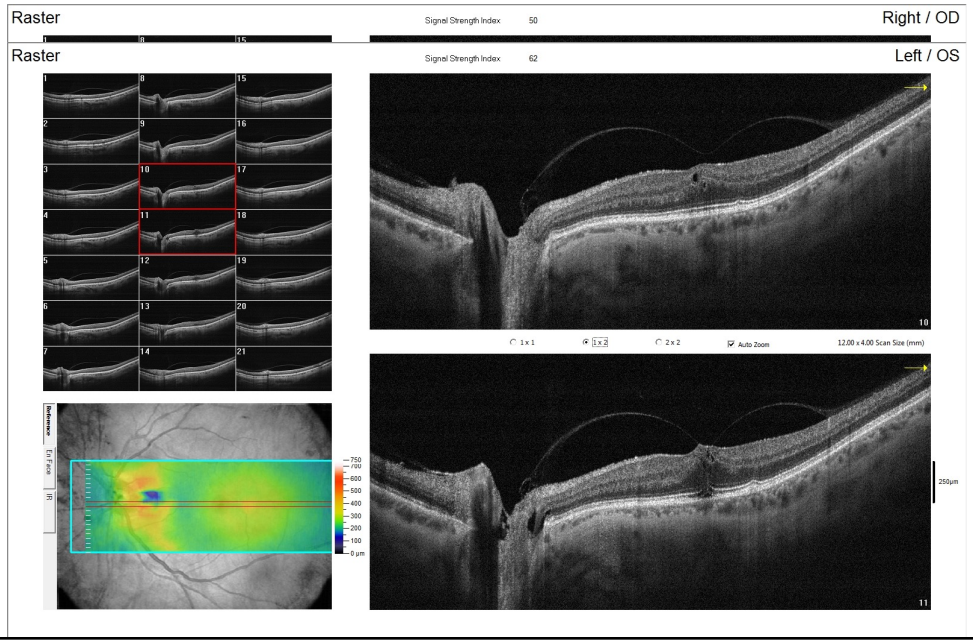
Reference image on 05/30/2017
Full Thickness
NDB Reference

49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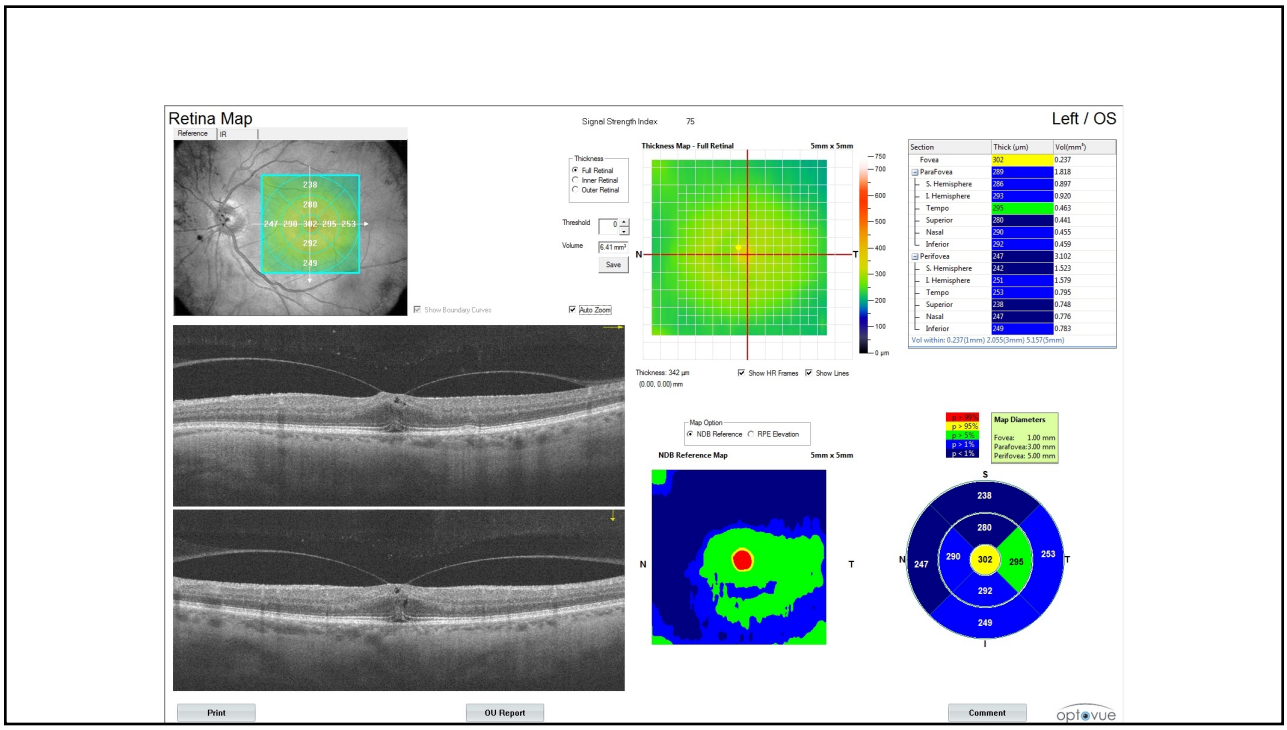
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Thickness Map - Full Retinal
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NDB Reference Map
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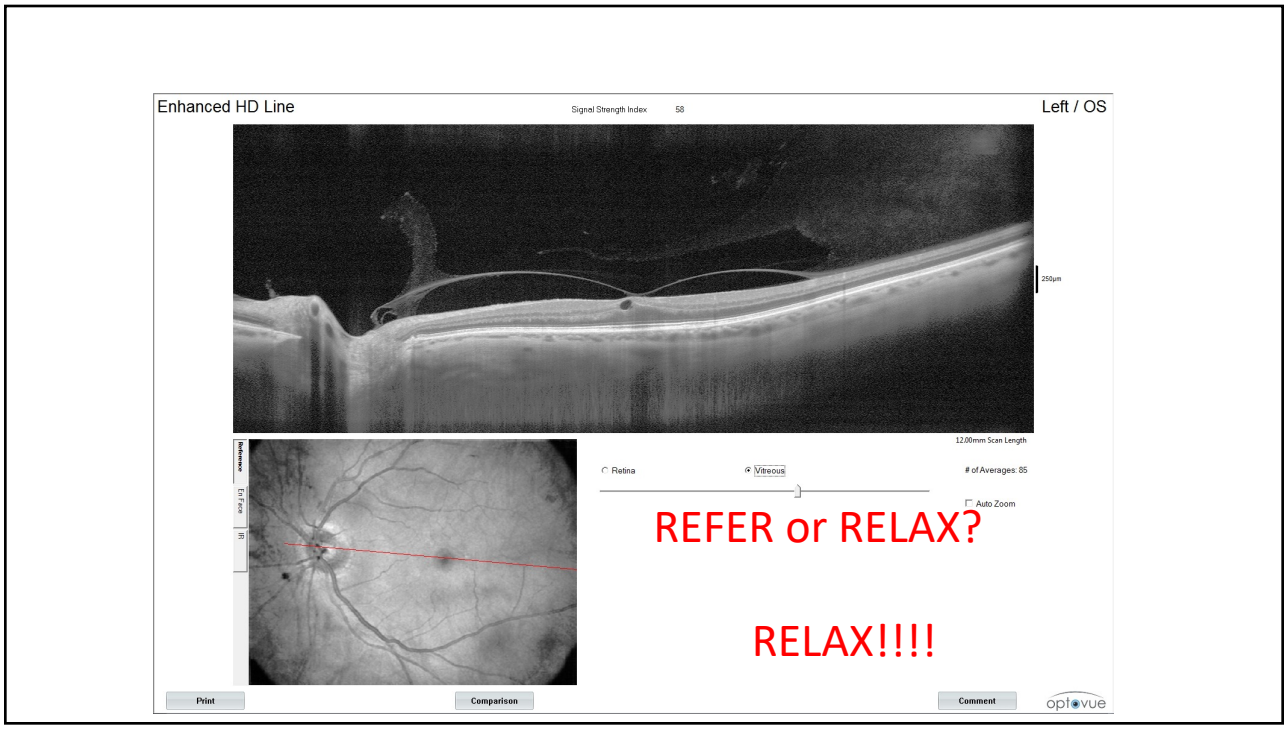
Parafovea: 3.00 mm
Perifovea: 5.00 mm
Print
OU Report
Comment
optovue

51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Signal Strength Index 58
Left / OS
12.00mm Scan Length
REFER or RELAX?
RELAX!!!!
Print
Comparison
Comment
optovue

52

BRVO/CRVO

- Management includes diagnosis and management of underlying etiology
- Most often associated with DM and HTN
- However many other possible etiologies
  - Carotid artery disease
  - Hyperlipidemia/hypercholesterolemia
  - Altered platelet function
  - Coats disease
  - Von-Hippel Lindau
  - Eales' disease
  - Trauma

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BRVO/CRVO

- At minimum, should have
  - BP evaluated
  - Fasting Blood sugars (FBS)/A1c
  - CBC
  - Lipid profile
- Additional tests might include
  - Carotid artery evaluation
  - Cardiac evaluation
  - Additional blood tests
    - ANA
    - RF
    - FTA/ABS
    - ESR

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Anti-VEGF:Lucentis

- CRUISE (CRVO) Study:
  - Vision improved > 15 letters in almost 50% of patients vs. 17% with sham at 6 mos
  - mean VA gain of almost 15 letters
- BRAVO (BRVO) Study:
  - Vision improved > 15 letters in over 60% of patients vs. 28% with sham
  - Mean VA gain of approx 18 letters
  - Few side effects in either group

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Anti-VEGF: Elyea® (afilbercept)

- FDA approved Sept, 2012 for treatment of macula edema secondary to CRVO
- COPERNICUS and GALILEO studies:
  - % of pts gaining 15 letters or more of BCVA
  - Injection q 2 mos for 24 weeks
- COPERNICUS:
  - 56% vs. 12% with sham
  - 17.3 letters gained vs. 4.o lost with sham
- GALILEO:
  - 60% vs. 22% with sham
  - 18.0 letters gained vs. 3.3 lost with sham

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CRVO/BRVO

- Refer if macula edema within 1 week
  - Laser vs. injection in BRVO
  - Injection CRVO
  - Steroids?
- Systemic workup recommended
  - DM
  - HTN
  - Cholesterol panel
  - Carotid Doppler
- Look for NV/NVI/NVA/NVG esp. in CRVO, esp. if ischemic

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