INSIGHT

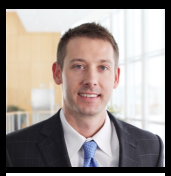
The ABCs To Keratoconus Treatment

Mitch Ibach, OD FAAO
Vance Thompson Vision- Residency Coordinator

1

Financial Disclosures—Ibach

Disclosure Statement:
Alcon – consultant/speaker
Allergan — consultant
Balance Ophthalmics – share holder
Bausch Health — consultant/speaker
C-Light Tech -- consultant
Dompé — consultant/speaker
Glaukos — consultant/speaker
iCare – consultant
Orasis – consultant
Reichert – consultant
Tarsus pharmaceuticals – consultant
Thea – consultant
Zeiss — consultant



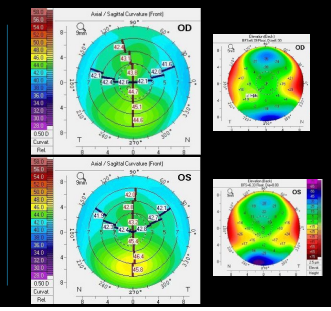
VANCE THOMPSON VISION

All relevant relationships have been mitigated

2

35 yo New Refractive Eval

- UCVA → 20/300, 20/400
- MRx → -4.75-1.00x004 20/20, -5.75-0.75x10 20/20-
- Pach → 482um, 466 um



3

Decision Time



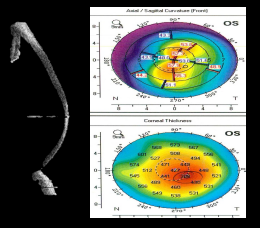




4

Unstable Cornea: Keratoconus (KCN)

- Prevalence ~1:2000 (1986, US)
  - **Estimated 1:375** (2017, Netherlands)
- Naturally occurring corneal ectasia, typically onsets in teenage yrs with:
  - Myopia,
  - Irregular astigmatism & other HOAs
  - **Loss of BSCVA & Visual quality**
- Mixed etiology:
  - **Mechanical factors (eye rubbing)**
  - Genetic factors
  - Down's Syndrome
  - Connective tissue disease (Ehlers-Danlos)



5

Prevalence of Keratoconus Based on Scheimpflug Corneal Tomography Metrics in a Pediatric Population From a Chicago-Based School Age Vision Clinic

Jennifer S. Harthan, O.D., John D. Gelles, O.D., Sandra S. Block, O.D., William Tullo, O.D., Andrew S. Morgenstern, O.D., Becky Su, O.D., Daniel Chung, B.S., Austin Yu, B.S., Steven A. Greenstein, M.D., Peter S. Hersh, M.D., and Steven Barry Eiden, O.D.

Purpose: Determine the pediatric prevalence of keratoconus (KC) using Scheimpflug corneal tomography.
Methods: A prospective observational study was done on subjects aged 3 to 18 years at the Princeton Vision Clinic, Chicago, IL. Scheimpflug tomography (Pentacam HR, OCULUS Optikgeräte GmbH) scans (Belin/Ambrósio Enhanced Ectasia BAD) yielded BAD Final D (Final D) and Back Elevation at the Thinnest Point (BETP) measurements. Criteria differentiating non-KC from KC suspects & KC were, *Non-KC*—Final [illegible]. Removing duplicate and poor-quality scans leaving 2007 subjects.
Results: Of 2007 subjects, six were classified as *KC*—prevalence of 1:334, three subjects were *KC suspects*—prevalence of 1:669, and total prevalence of *KC suspects and KC* was 1:223.
Conclusion: The prevalence of KC in children is higher than previously reported, emphasizing the importance of sensitive screening for KC at its earliest manifestation as standard in pediatric comprehensive eye examination.

KCN or KCN suspect 1 in 223

Harthan, J., Gelles, J., Block, S., Eiden, S. et al (2024, March). Prevalence of Keratoconus Based on Scheimpflug Corneal Tomography Metrics in a Pediatric Population From a Chicago-Based School Age Vision Clinic. *Eye and Contact Lens*, 50.

7

Why Listen, Why are you Here?

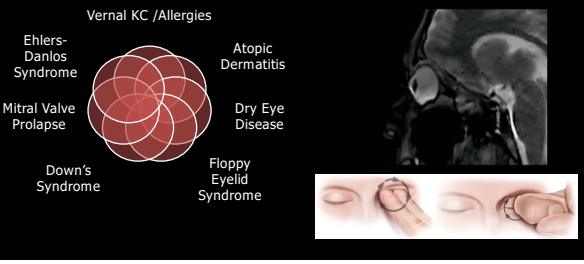
"I don't ever see KCN patients."

20 patients per day, 5 clinic days per week→ 100 pts/week

Average 2 KCN patients/month

8

What does the KCN patient look like?



9



1. Diagnose **Early**
2. Stop **Progression**
3. Rehabilitate **Vision**

11

KCN is a sight-threatening eye disease

- Although vision loss first presents in adolescence, most cases of KC go undiagnosed for decades[1-3]
  - KC is commonly diagnosed at the progressive-moderate stage with the highest prevalence in patients 18-39 years old[4-6]

90% of pediatric patients progress within 12 months without corneal collagen cross-linking treatment[7]

44% of patients 35+ experience progression[8]

References: 1. Valdez-García JC, et al. Rev Mex Oftalmol. 2014;88(3):90-98. 2. Krejza ED, et al. Cont Lens Anterior Eye. 2021;44(2):101332. 3. Hamdy V, et al. Corneal Ectasia Preferred Practice Pattern®. Ophthalmology. 2024 Apr;131(4):P150-P236. 4. Shetty C, et al. Indian J Ophthalmol. 2024;72(5):704-711. 5. Mohebbinasr N, et al. J Optom. 2009;2(4):164-172. 6. Singh RB, et al. Am J Ophthalmol. 2024;259:71-76. 7. Chatzis N, Hafezi F. J Refract Surg. 2012;28(11):753-758. 8. Ozalp O, et al. Cornea. Published online September 2, 2025. doi:10.1097/ICO.0000000000003979

12

Step 1: Diagnosing KCN

- Unhappy with Glasses
  - Myopia > 0.5D
  - Astigmatism > 1.0D
  - Patient ≠ 20/20



- Retinoscopy
  - Distorted mires
  - Scissor reflex



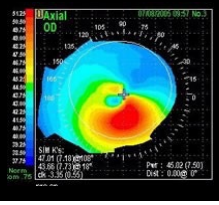
- Auto refractor/keratometer
  - error message
  - >1D increase steepest K
- Manual K's



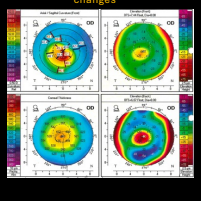
13

Gold Standard: Topography/Tomography

Topography
Keratoconus cornea



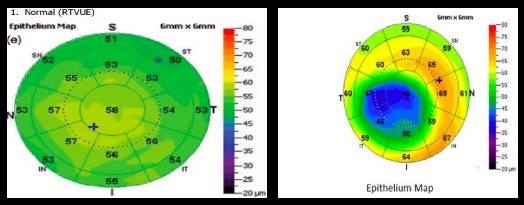
Tomography
Keratoconus cornea
Irregular/thin pachymetry, posterior float changes



14

Epithelial Mapping

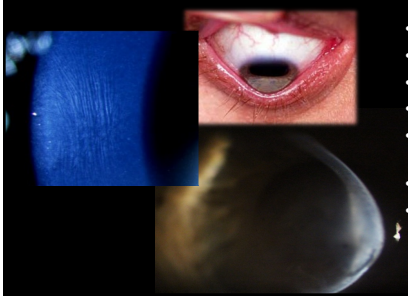
Remember the average epithelial thickness is 50-55um



Faktorovich, Ella, and Lynda Charles. "ETM Eases Diagnosis for Screening Refractive Surgery." *Ophthalmology Times*, 15 Sept. 2019.

15

Slit lamp clues for KCN?



- FLEISCHER RING
- VOGT'S STRIAE
- STROMAL THINNING
- STROMAL SCARS
- ENLARGED CORNEAL NERVES
- MUNSONS SIGN
- ACUTE HYDROPS

16

"When Do You Refer Your KCN Patient?"

ARTICLE

Keratoconus Management in the Community: A Survey of Optometrists

Angelo, Lize M.B.Ch.B., PG.Dip.Ophth.B.S.; Gokul, Akilesh B.Optom., Ph.D.; McGhee, Charles N.J. FRANZCO, Ph.D.; Ziaei, Mohammed FRANZCO, M.D.

Most optometrists would refer when the visual acuity dropped between 6/9 (20/30) and 6/12 (20/40)!!

41% reported they refer their patients once they progress on K-parameters!!



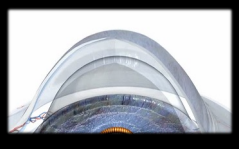


Angelo L, Gokul A, McGhee CNJ, Ziaei M. Keratoconus Management in the Community: A Survey of Optometrists. Eye Contact Lens. 2024 Jan 1;50(1):10-15.

17

Step 2: FDA Approved Cross-linking (CXL)





FDA approval dates:

April 2016 – CXL - Progressive keratoconus

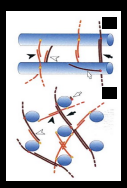
July 2016 – CXL - Corneal ectasia following refractive surgery

October 2025 – Epi-On CXL

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Cross-linking: Mechanism of Action

- Corneal cross-linking is a medical procedure in which riboflavin photosensitizer is activated with UVA light to stiffen the corneal stroma
- The absorption of UVA by the photosensitizer generates radicals and singlet oxygen to form additional covalent bonds within the intracellular matrix of the collagen lamellae
  - Creates new corneal collagen cross-links
  - Results in a shortening and thickening of the collagen fibrils
  - Leads to the stiffening of the cornea



Lewis, et al. Structure 18, 239-245 2010



19

Epi-Off Cross-linking Procedure (CXL)

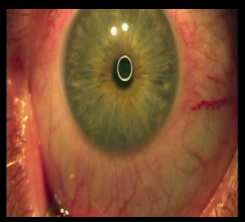
Corneal epithelium is debrided, as is done in PRK

Riboflavin eye drops (vitamin B2) are applied to the cornea.

The riboflavin film is maintained with reapplication of drops about ~2 minutes until the stroma is saturated (20-30 mins)

UVA light (365nm) is shined on the eye for 30 minutes (conventional technique)

A bandage lens is placed. Follow-up care is similar to PRK.



20

Change Over Time



Pre CXL
-5.75-0.75x10 20/20-

8 mo PO CXL
-5.25-0.50x007 20/25+

18 mo PO CXL
-4.75-0.50x24 20/20+

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The Future is now for CXL!

- Cross-link through the intact epithelium → "Epi-On"
- Reduce overall procedure time → "Accelerated"
- Less vision reduction short term → "Epi-On"

Patients
- Quicker recovery
- Less post-op discomfort
- Less fear of intervention
- Refractive outcomes

Providers
- Improved clinical workflow
- Potential for earlier treatment
- Optometrists performing the procedure

22

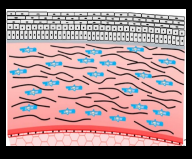
WHAT IS STANDING IN OUR WAY?

Epithelium

Prevents Drug Diffusion

Absorbs UV Light

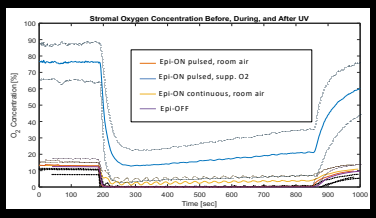
Consumes Oxygen



The epithelium limits the transmission of ***all*** CXL-required components:
- –Photosensitizer: Riboflavin
- –Photoactivator: UVA
- –Sustained Accelerant: Oxygen
- –Epithelial remodeling for MRX

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Oxygen is vital to a corneal collagen cross-linking environment, but is rapidly depleted under UV-A



Role of Oxygen
- Epithelium acts as barrier to drug and oxygen diffusion → reduced efficiency
- Supplemental oxygen enables **sustained aerobic crosslinking** under high-irradiance UV delivery
- Drives **increased reaction efficiency** vs. alternate approaches via aerobic photochemistry

Supplemental oxygen is crucial to optimizing corneal collagen cross-linking

Hill J, Liu C, Deardorff P, Tavakol B, Eddington W, Thompson V, Gore D, Raizman M, Adler DC. Optimization of Oxygen Dynamics, UV-A Delivery, and Drug Formulation for Accelerated Epi-On Corneal Crosslinking. Curr Eye Res. 2020 Apr;45(4):450-458.

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Epi-On: US Phase III Trial- Glaukos

Increasing O2 in Human Corneas (Hyperoxic)



DRUG FORMULATION



SHORTER PULSED UV EXPOSURE



02 GOGGLES

NOW FDA APPROVED in US

25

October 2025 FDA Approves Epi-On CXL (Epioxa)



Step 1: Apply Epioxa drops* ~10 minutes

Step 2: Place Boost oxygen goggles over eyes†

Step 3: deliver UV-A light with elevated irradiance lamp† ~12 minutes

EPIOXA HD and EPIOXA. Prescribing Information. Glaukos Corporation; 2025.

26

Epioxa Treatment



27

Clinical studies of Epioxa in epithelium-on CXL[1]

- Two prospective, randomized, parallel-group, sham procedure/vehicle-controlled trials evaluated the safety and efficacy of epithelium-on CXL using Epioxa in patients with keratoconus[1]
- Eligible eyes were randomized 2:1 at baseline to receive CXL treatment or sham procedure/vehicle control[Ab]
- Eyes were evaluated at Day 1, Day 3, Week 1, and Months 1, 3, 6, and 12 post-treatment
- The primary endpoint measurement was difference in change from baseline in K_{max} between the CXL treatment and sham procedure/vehicle control groups

Study 1 (NCT03442751)[1]

280 eyes of 201 patients were randomized, of which
279 eyes were treated:
- 189 eyes received CXL treatment
- 90 eyes initially received sham procedure/vehicle control

Primary endpoint: Month 6 post-treatment
Secondary endpoint: Month 12 post-treatment

Study 2 (NCT05759559)[1]

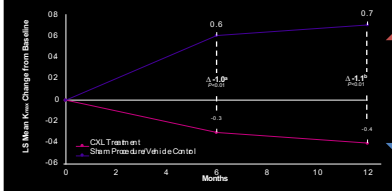
312 eyes of 208 patients were randomized, of which
312 eyes were treated:
- 200 eyes received CXL treatment
- 112 eyes received sham procedure/vehicle control

Primary endpoint: Month 12 post-treatment
Secondary endpoint: Month 6 post-treatment

IMPORTANT SAFETY INFORMATION
Warnings and Precautions
Corneal collagen cross-linking should be used with caution in patients with a history of herpetic keratitis due to the potential for reactivation of herpes keratitis.
Please see full Prescribing Information for EPIOKA HD and EPIOKA at www.Epioxa.com.

28

In Study 1, a statistically significant treatment effect was demonstrated at Month 6



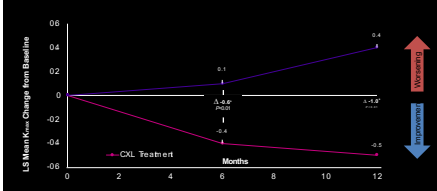
In a subgroup analysis of patients in Study 1 at Month 6, younger patients (<29 years) experienced a treatment effect of -2.0 D, as a combination of improvement in the CXL treatment arm (-0.7 D) and deterioration in the sham procedure/vehicle control arm (1.3 D). Older patients (≥29 years) did not experience improvement at Month 6 in either arm[1]

Adverse Reactions
The most common adverse reaction was conjunctival hyperaemia (31%). Other adverse reactions, occurring in 5% to 25% of eyes included: corneal opacity (haze), photophobia, punctate keratitis, eye pain, eye irritation, increased lacrimation, corneal epithelium defect, eyelid oedema, corneal striae, visual acuity reduced, dry eye, and anterior chamber flare.
Please see full Prescribing Information for EPIOKA HD and EPIOKA at www.Epioxa.com.

Reference: 1. EPIOKA HD and EPIOKA. Prescribing Information. Glaukos Corporation; 2025.

29

In Study 2, a statistically significant treatment effect was demonstrated at Month 12



In a subgroup analysis of patients in this trial at Month 12, younger patients (<30 years) experienced a treatment effect of -1.1 D, as a combination of improvement in the CXL treatment arm (-0.5 D) and deterioration in the sham procedure/vehicle control arm (0.5 D)
Older patients (≥30 years) in the CXL treatment arm experienced comparable improvement (-0.6 D) as younger patients (-0.5 D); however, in the sham procedure/vehicle control arm, older patients (-0.0 D) did not deteriorate as much as younger patients (0.5 D)[1]

IMPORTANT SAFETY INFORMATION (cont'd)
Contraindications
EPIOXA™ HD and EPIOXA™ are contraindicated in patients with known hypersensitivity to benzalkonium chloride (BAC) or any ingredients in EPIOXA HD and EPIOXA. Epithelium-on corneal collagen cross-linking is contraindicated in aphakic and pseudophakic patients without a UV-blocking intraocular lens.
Please see full Prescribing Information for EPIOKA HD and EPIOKA at www.Epioxa.com.

Reference: 1. EPIOKA HD and EPIOKA. Prescribing Information. Glaukos Corporation; 2025.

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INDICATIONS AND USAGE

EPIOXA™ HD (riboflavin 5'-phosphate ophthalmic solution) 0.239% and EPIOXA™ (riboflavin 5'-phosphate ophthalmic solution) 0.177% are photoenhancers indicated for use in epithelium-on corneal collagen cross-linking for the treatment of keratoconus in adults and pediatric patients aged 13 years and older, in conjunction with the O2n™ System and the Boost Goggles[1].

IMPORTANT SAFETY INFORMATION

Contraindications
EPIOXA™ HD and EPIOXA™ are contraindicated in patients with known hypersensitivity to benzalkonium chloride (BAC) or any ingredients in EPIOXA HD and EPIOXA. Epithelium-on corneal collagen cross-linking is contraindicated in aphakic and pseudophakic patients without a UV-blocking intraocular lens.

Warnings and Precautions
Corneal collagen cross-linking should be used with caution in patients with a history of herpetic keratitis due to the potential for reactivation of herpes keratitis.

Adverse Reactions
The most common adverse reaction was conjunctival hyperemia (31%). Other adverse reactions, occurring in 5% to 25% of eyes included: corneal opacity (haze), photophobia, punctate keratitis, eye pain, eye irritation, increased lacrimation, corneal epithelium defect, eyelid edema, corneal striae, visual acuity reduced, dry eye, and anterior chamber flare.

Keys To the Game

1. Keratoconus only
2. Doesn't define "progressive KCN"
3. 13 and above
4. No Pseudophakes

https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219910s000lbl.pdf

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Epi-SMART CXL



1. Epi-prep sponge to loosen epithelial junctions
2. High concentration Riboflavin with sodium iodine and Epi-prep loading sponge
3. Pulsed UV irradiance
4. 20 minute bilateral procedure

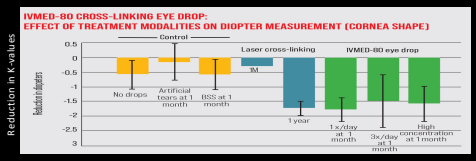
NOT FDA APPROVED in US

https://www.cxlophthalmics.com/epismart

32

Drops for Crosslinking?

- Research by Bala Ambati, MD showed the lysyl oxidase on forming crosslinks
- Lysyl oxidase is in lower concentration in KCN patients
- IVMED-80 drops applied to cornea increase copper amounts in turn activating and supporting lysyl oxidase



NOT FDA APPROVED in US

Kent, C. (2022, November 10). Cross-linking: Headed For The Next Level. *Review of Ophthalmology*.

33

Step 3: Rehabilitate Vision



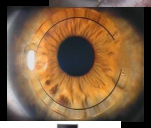
Optical correction

Vs.

Surgical options





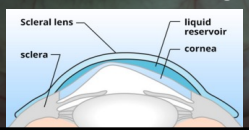




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Specialty Lenses, What's the Science?

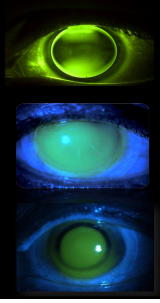
- Keratoconic patients have an irregular corneal curvature that glasses and soft lenses mold to.
- Specialty lenses with a more rigid shape, create a TEAR PRISM to mask the irregular astigmatism



35

The Power of the Tear Layer (literally)

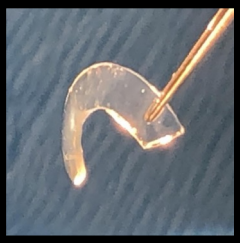
- When a GP lens is placed on the eye, the post-lens tear layer (PLTL) fills in the hills and valleys behind the contact lens
- The smooth shape of the anterior contact lens becomes the optical systems new refracting surface and 'by-passes' the irregularities of the cornea
- Patients with irregular astigmatism gain significant visual improvement in quality and acuity



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Corneal Tissue Addition Keratoplasty (CTAK)

- Developed at Cornea and Laser Eye Institute
  - Peter Hersh MD, Steven Greenstein MD, John Gelles OD
    - First procedure in 2016: Peter S. Hersh MD
- Sterilized gamma irradiated tissue – human tissue
- Customized to individual by tomography import
  - Femtosecond customizable shapes
- Implanted through femtosecond corneal channel



GOAL: Reshape and normalize the corneal topography

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CTAK Visual Acuity Improvement



Red = Statistically Significant (p≤0.05)

MRSE
Pre-CTAK
Post-CTAK

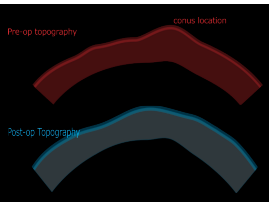
Steven, G., Yu, A., Geller, J., Hanson, E., Hersh, P. (2023, July). Corneal Tissue Addition Keratoplasty: new instrumental inlay procedure for keratoconus using femtosecond laser-shaped preserved corneal tissue. *Journal of Cataract and Refractive Surgery*. 740-746.

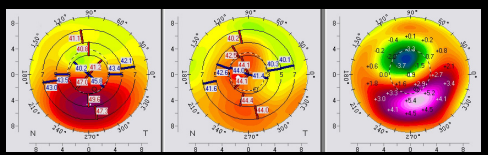
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TG-PRK

TG-PRK Goal: Ablation driven by unique Topo data to normalize cornea (but ≠ customizing corneal surface):

- **Anterior-surface normalization**
- **Improved visual rehabilitation**

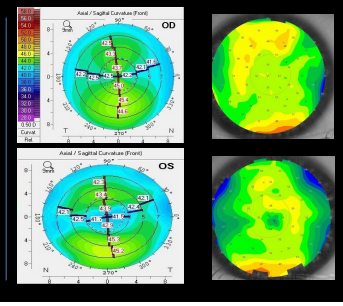




39

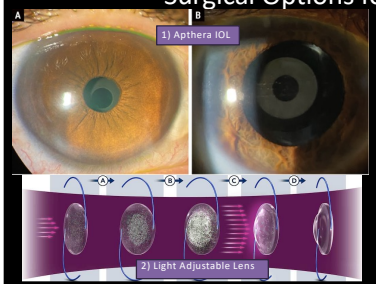
37 yo Repeat Refractive Eval

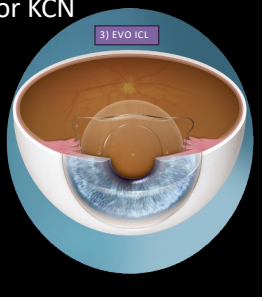
- UCVA: 20/300, 20/400
- MRx: -4.50-1.00x002 20/15, -4.75-0.50x24 20/20+
- SLE: No K haze or SPK, No K haze or SPK



40

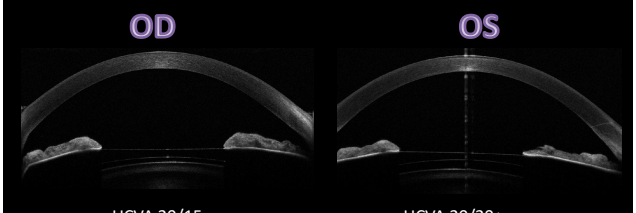
Lens Based Surgical Options for KCN





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1 Month Post Evo ICL



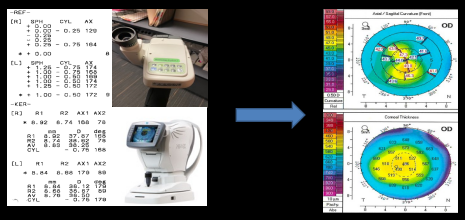
UCVA 20/15

UCVA 20/20+

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3 Things to Remember Tomorrow

1. Diagnose KCN early and refer for CXL early in the disease.



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3 Things to Remember Tomorrow

1. Diagnose KCN early and refer for CXL early in the disease.
2. Prioritize stabilizing keratoconus with CXL

95%



Evaluation of vision-related quality of life in keratoconus patients, and associated impact of keratoconus severity indicators

Christophe Panthier*,† · Sarah Moran* · Jean Louis Bourges*

Panthier C et al. *Graefes Arch Clin Exp Ophth.* 2020;

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3 Things to Remember Tomorrow

1. Diagnose KCN early and refer for CXL early in the disease.
2. Prioritize stabilizing keratoconus with CXL
3. Improve vision



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