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Financial Disclosures- Ibach

Disclosure Statement:

- Aerie - consultant/speaker
- Allergan - consultant
- Avellino -- consultant
- Bausch Health- consultant
- Dompe - consultant/speaker
- Equinox LLC-- shareholder
- Glaucos - consultant/speaker
- Heru - consultant/speaker
- Kala - consultant
- NewWorld Medical - consultant
- Ocular Therapeutix - consultant/speaker
- Ocuphire - consultant
- Oyster Point - consultant/speaker
- Sight Sciences - consultant/speaker
- Sun - speaker
- Zeiss - consultant

All relevant relationships have been mitigated

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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)

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Reported incidence & prevalence of keratoconus may be on the rise globally, largely due to improved diagnosis

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

Fig. 1. Annual incidence rate per 100,000 persons from 1995-2015 (green) and annual incidence rate per 100,000 persons from 1995-2015 including immigrants and descendants (blue). The annual incidence rate of the 10 persons 445 persons including immigrants and descendants recorded in the National Eye Survey (NEI) was in the dashed line. 2021

Acta Ophthalmol. 2019; 97: 752-755

*Wagner H, Boudreau S, Boudreau S, et al. The Prevalence and Risk Factors for Keratoconus: A Systematic Review and Meta-Analysis. Cornea. 2020;39(2):267-276

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Publication for final edited form at: *Cornea*. Advance online first. 2017 September ; 36(4): 223-232. doi:10.1016/j.jco.2017.03.001.

Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study: Methods and Findings to Date

H. Wagner¹, J.T. Barr², K. Zadnik³, and the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study Group

¹Nova Southeastern University, College of Optometry, Ft. Lauderdale, Florida

²The Ohio State University College of Optometry, Columbus, Ohio

Bilateral 96%

Eye Rubbing 50%

Genetic 13%

Source: JAMA Ophthalmol. 2017;35(10):1040-1046. doi:10.1001/jamaophth.2017.1040

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What does the KCN patient look like?

Vernal KC/Allergies

Atopic Dermatitis

Dry Eye Disease

Floppy Eyelid Syndrome

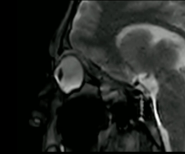
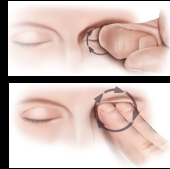
Down's Syndrome

Mitral Valve Prolapse

Ehlers-Danlos Syndrome

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KCN Risk Assessment: Eye Rubbing



Gallini, D., & Savatovsky, J. Novel investigation of Eye Rubbing with Dynamic Medical Imaging - (Video). Retusoft Foundation.

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Unstable Cornea: Refractive Surgery Ectasia

Ectatic corneal **degeneration**:

- Unilateral or bilateral
- Maybe asymmetric
- Manifests after corneal surgery
- Higher risk in big corneal ablations, eye rubbers, RK patients, mildly abnormal pre-op topo/tomography

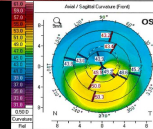
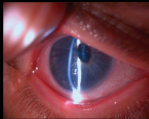


Rodman, J.B., Russell, R., Ward, M.A., et al. Risk factors and prognosis for corneal ectasia after LASIK. Ophthalmology 2003; 110:267-274.
Raf, A.S., Jafarzadeh, M., Sali, N. Progressive keratoconus after laser in situ keratomileusis. J Refract Surg 2004; 20:5718-5722.

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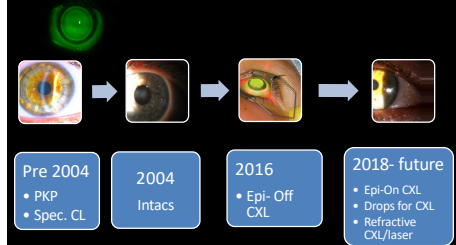
Unstable Cornea: Pellucid Marginal Degeneration (PMD)

- Later life onset (2nd to 5th decade)
- Crescent shaped band of inferior thinning
- "Crab claw" topography pattern, "beer belly" corneal appearance



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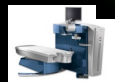
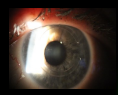
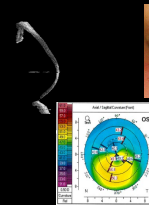
KCN Treatment Timeline



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KCN: New Mantra

Diagnose **Early** → Stop **Progression** → Maintain **BCVA Potential** for Rehabilitation



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FDA Approved Cross-Linking Ingredients

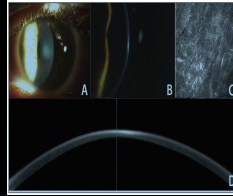


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Is CXL Safe? WHAT ARE THE RISKS?

Common Ocular AEs include:

- Corneal opacity (haze)
- Punctate keratitis
- Corneal striae
- Corneal epithelium defect
- Eye pain
- Reduced visual acuity
- Blurred vision



Resolved within 6 months: epithelium defect, corneal striae, punctate keratitis, photophobia, dry eye, eye pain, and decreased visual acuity
In 1-2% of patients, corneal epithelium defect, corneal edema, corneal opacity (haze) and corneal scar continued to be observed at 12 months

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5 Take Aways for PO Management

- Post-operative care/schedule is similar to PRK.
- Remove BCL when epithelium is closed, vision reduced.
- New glasses 1 month, specialty lens 3-4 months
- New topography/tomography 6-12 months (surgical center?)
- No global period, bill office visits.



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Refractive Tag Team Partners with CXL

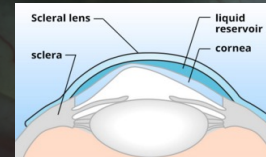
Crosslinking has opened the refractive treasure chest



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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



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Specialty lens options When & Why

Where do Intacs fit in?

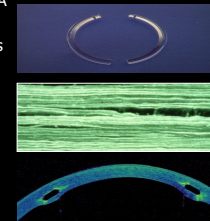
150° Hexagonal Arcs of PMMA (same as rigid lens)

Placed between stromal layers at least 70% depth

Results in shortened corneal arc length

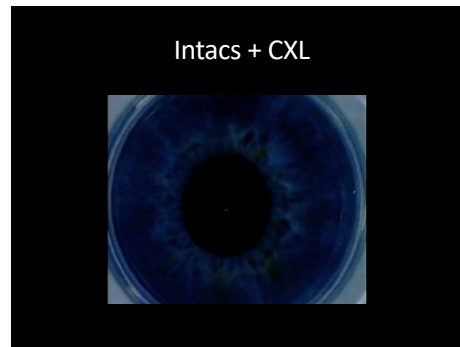
Flattens the central cornea

Intacs are replaceable
removable
upgradable

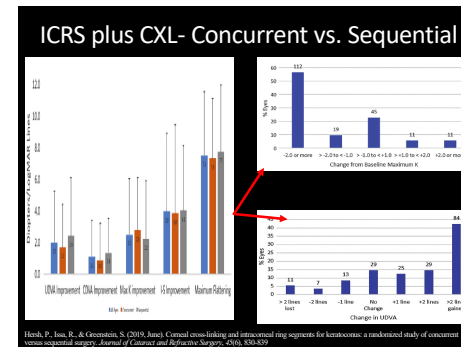


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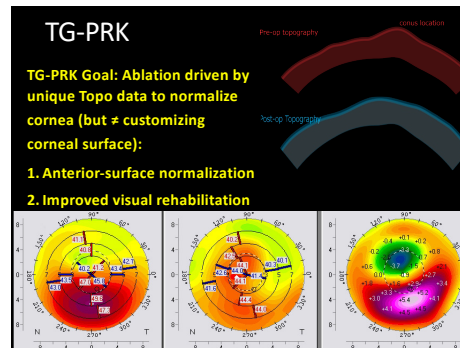
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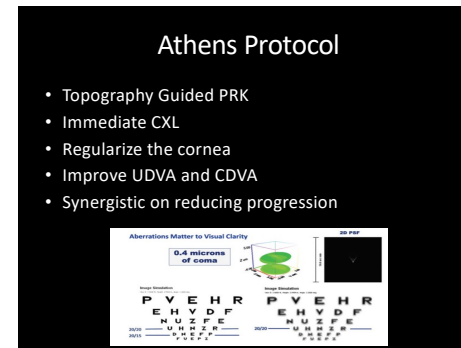
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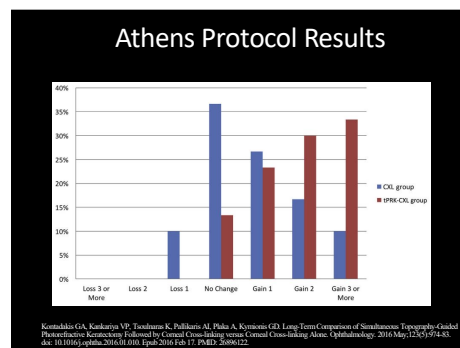
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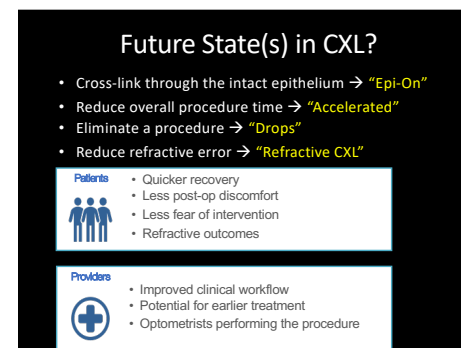
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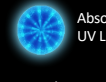
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WHAT IS STANDING IN OUR WAY?

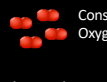
Epithelium



Prevents
Drug
Diffusion



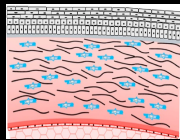
Absorbs
UV Light



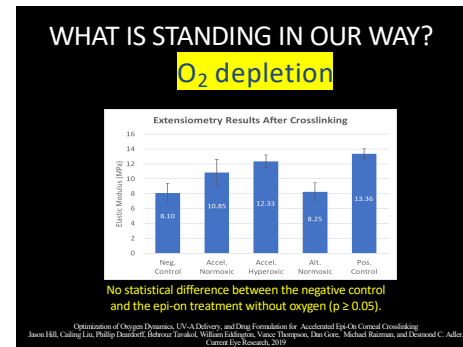
Consumes
Oxygen

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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Epi-On: US Phase III Trial- Glaukos

Increasing O₂ in Human Corneas (Hyperoxic)



DRUG FORMULATION

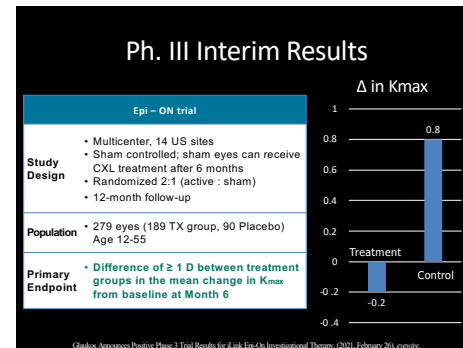


O₂ GOGGLES

SHORTER PULSED UV EXPOSURE



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Epi-SMART CXL

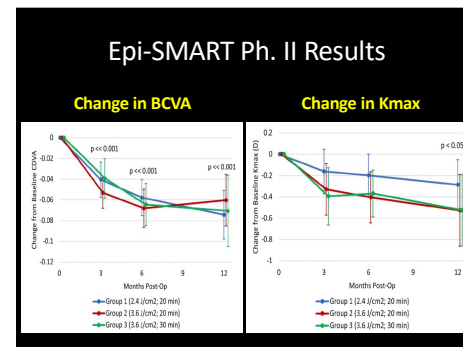



1. Epi-prep sponge to loosen epithelial junctions
2. High concentration Riboflavin with sodium iodide and Epi-prep loading sponge
3. Pulsed UV irradiance
4. 20 minute bilateral procedure

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<https://www.cdxpharmaceuticals.com/epismart>

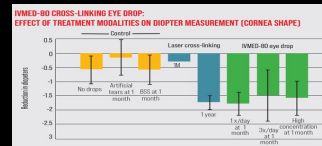
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Drops for Crosslinking?

- 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



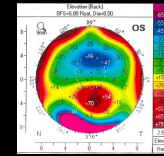
NOT FDA APPROVED in US

Kent, C. (2022, November 16). Cross-linking: Headed For The New Level. *Review of Ophthalmology*.

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Customized Cross-Linking

- Irradiation down to 3 mm
- Goal to reduce coma
- Guides treatment off max posterior float (weakest point)
- Mosaic light delivery device

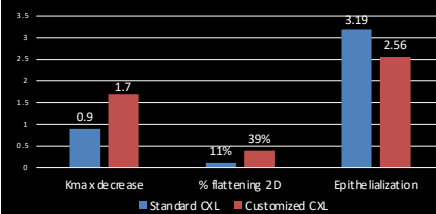


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Customized Corneal Cross-linking: One-Year Results

THEO G. SEILER, ISAAC FISCHINGER, TOBIAS KOLLER, DANIEL ZAPP, BEATRICE E. FRUEH, AND THEO SEILER



Seiler, T., Fischinger, I., Koller, T., Zapp, D., Frueh, B. E., & Seiler, T. (2016, June). Customized Corneal Cross-linking: One-Year Results. *Acta Ophthalmologica*, 94(6), 742.

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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%

Improve Vision for the Visual and Progressive Ophthalmology Research Group (VPO) 2021/2022 17 (2021) 17

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

Christophorus Pantelides^{1,2} · Sarah Morton³ · Jean Louis Bourgeois⁴

Pantelides C et al. *Graphic Arch Clin Exp Ophthalmol*. 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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Be Brave, Jump Into a Question



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