The Most Updated KCN Management Guide

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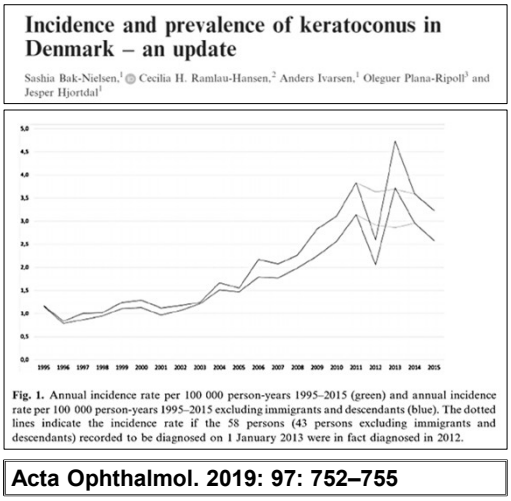
Financial Disclosure: Clark Y. Chang, OD, MS, FAAO, FSLS

- EssilorLuxottica (Sr. Director, Medical & Surgical Operations)
- Oculus
- Wills Eye Hospital (Director of Specialty CL, Cornea Service)

The opinions expressed in this presentation are my own and do not represent the views of my employers

KCN Global Prevalence: Meta-Analysis

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



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

Studies Outside of U.S. Suggest Prevalence May be Higher in Certain Populations

*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

Underestimate KC Impact & Urgency to Tx

- Public health impact is disproportionate to its prevalence and clinical severity…resulting in a loss of QoL not likely to be reflected by clinical measures such as visual acuity
- Scores for CLEK patients on all scales were between patients with category 3 and category 4 age-related macular degeneration (AMD)
- Demonstrated KC is associated with significantly impaired V-QoL that continues to decline over 7-year (despite many CLEKS patients wears CLs)
- Negative impact on emotional well-being even in early KC stages due to concerns over progression & the potential need for PKP (Kymes SM et al, 2008).

Quality of Life in Keratoconus

STEVEN M. KYMES, PHD, JEFFREY J. WALLINE, OD, PHD, KARLA ZADNIK, OD, PHD, MAE O. GORDON, PHD, AND THE COLLABORATIVE LONGITUDINAL EVALUATION OF KERATOCONUS (CLEK) STUDY GROUP

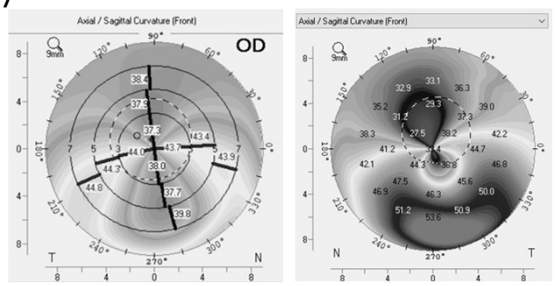
Published in final edited form as:
Am J Ophthalmol. 2008 April ; 145(4): 611–617. doi:10.1016/j.ajo.2007.11.017.

Changes in the Quality of Life of People with Keratoconus

Steven M. Kymes, PhD[1,2,3], Jeffrey J. Walline, OD, PhD[4], Karla Zadnik, OD, PhD[4], John Sterling, OD[5], and Mae O. Gordon, PhD[1,2] for the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study Group

Consensus publication statements…..

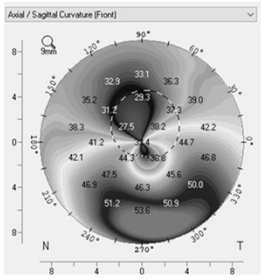
- True unilateral keratoconus does not exist
- Central pachymetry is the least reliable indicator for diagnosing KCN
- Thinning location and pattern are aspects that distinguish KCN, PMD, and keratoglobus
- KCN and PMD are best differentiated by a combination of
  - Full tomographic corneal thickness map
  - Slit-lamp examination
  - Anterior curvature map
  - Anterior tomographic elevation map

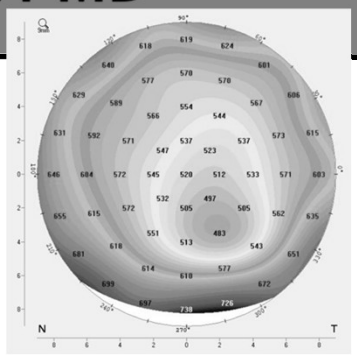


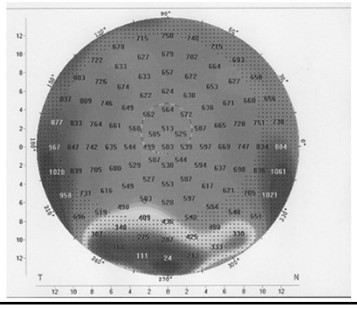
Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrósio R Jr, Guell JL, Malecaze F, Nishida K, Sangwan VS; Group of Panelists for the Global Delphi Panel of Keratoconus and Ectatic Diseases. Global consensus on keratoconus and ectatic diseases. Cornea. 2015 Apr;34(4):359-69.

A Personal Tip on Decoding True PMD

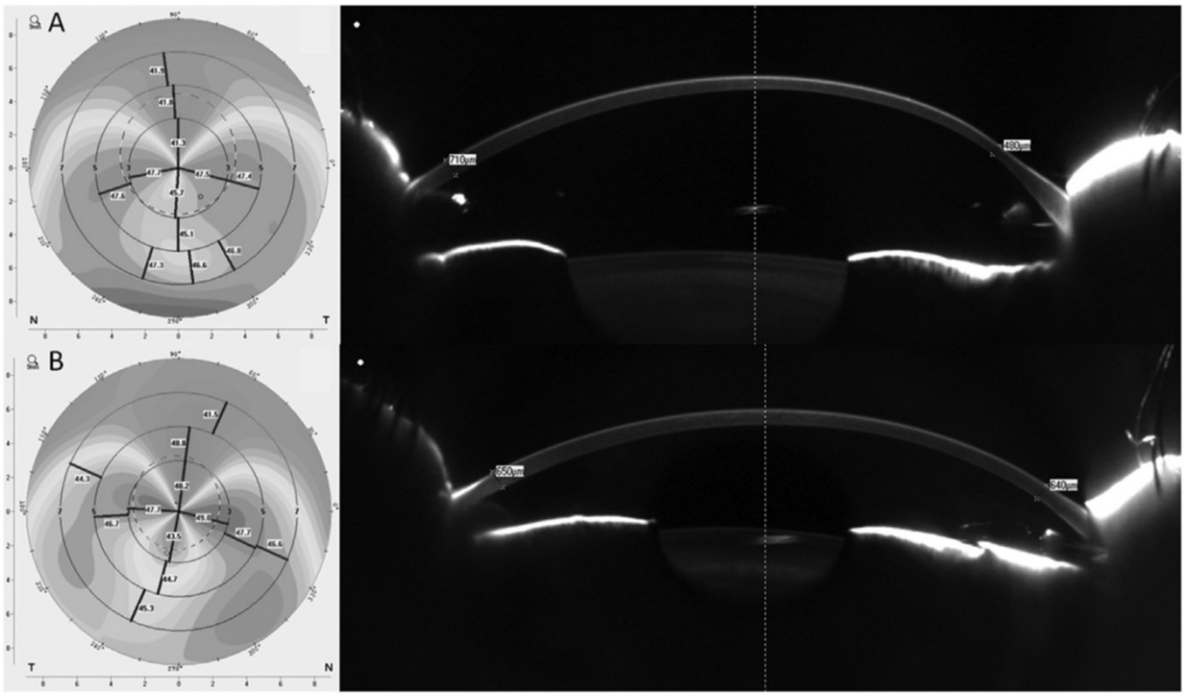
- Open up Pach Map to full diameter
  - Right click on Pach map
  - Uncheck Max Diam 9.0mm
- Inspect Scheimpflug image – Segments 5-8







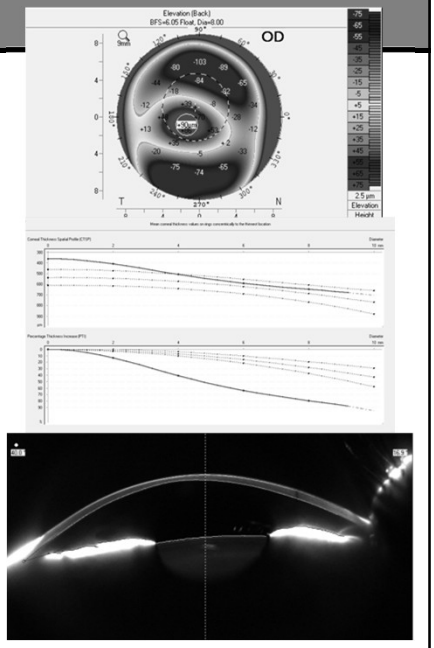
Belin MW, Asota IM, Ambrosio R, Khachikian SS. What's In a Name: Keratoconus, Pellucids Marginal Degeneration and Related Thinning Disorders. Am J Ophthalmol 2011; 152(2): 157-162.



Pircher N, Lammer J, Holzer S, Gschließer A, Schmidinger G. Corneal crosslinking for pellucid marginal degeneration. J Cataract Refract Surg. 2019 Aug;45(8):1163-1167. doi: 10.1016/j.jcrs.2019.03.018. Epub 2019 Jul 2. PMID: 31272773.

KCN - Early Diagnosis & Pearls

- Criteria "<u>mandatory to diagnose</u> KCN"
  - Abnormal posterior elevation (ectasia)
  - Abnormal corneal thickness distribution
  - Non-inflammatory corneal thinning
- Diagnosing <u>mild or subclinical</u> KCN
  - "Posterior corneal elevation abnormalities must be present"
  - "Best current and most widely available diagnostic test to diagnose early keratoconus is tomography (Scheimpflug or optical coherence tomography)"



Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrósio R Jr, Guell JL, Malecaze F, Nishida K, Sangwan VS; Group of Panelists for the Global Delphi Panel of Keratoconus and Ectatic Diseases. Global consensus on keratoconus and ectatic diseases. Cornea. 2015 Apr;34(4):359-69.

Possible KCN Signs and Symptoms

Look out for warning signs in medical history

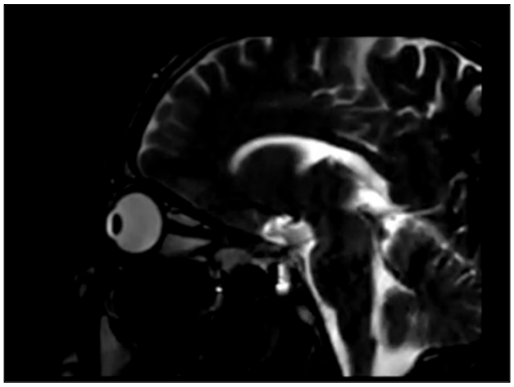
- Family history of KCN
- Chronic eye rubbing and/or atopic eye diseases
- Systemic associations - Down syndrome - Connective tissue disorders

Listen carefully to subjective symptoms

- Reduced visual quality or loss of vision
- Glare, halo, ghosting, and/or monocular diplopia (esp. at night)
- Frequent changes in glasses Rx or contact lens refits

Look out for refractive & keratometric anomalies

- Distortion of mires on keratometry
- Error messages on autorefractors
- Increasing astigmatism and/or high baseline astigmatism
- Unsatisfactory vision correction attempts & progressive loss of VA
- Unexplained amblyopia

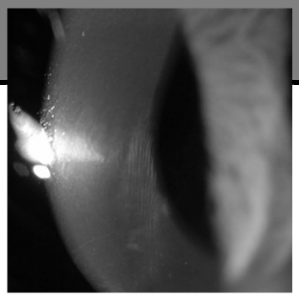


Gatinel, D., & Savatovsky, J. *Novel Investigation of Eye Rubbing with Dynamic Medical Imaging* . [Video]. Rothschild Foundation.

The American Academy of Ophthalmology Corneal Ectasia Preferred Practice Pattern recommends <u>prompt</u> referral of patients who have been diagnosed with progressive keratoconus to an ophthalmologist who can perform corneal cross-linking.[1]

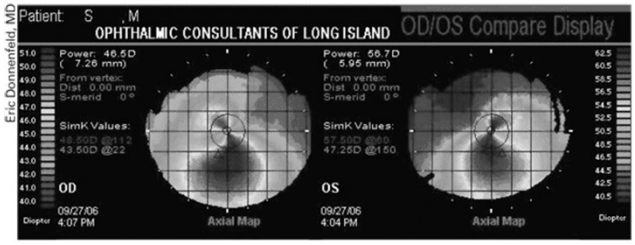
1. Garcia-Ferrer FJ, Akpek EK, Amescua G, Farid M, Lin A, Rhee MK, Varu DM, Musch DC, Mah FS, Dunn SP; American Academy of Ophthalmology Preferred Practice Pattern Cornea and External Disease Panel. Corneal Ectasia Preferred Practice Pattern®. Ophthalmology. 2019 Jan;126(1):P170-P215

KC Detection - Past



- Central K > 47 D and/or **increases** in Ks
- High baseline Cyl (ie, >2D)
- (Frequent) **Increases** in Cyl
- (Frequent) **Increases** in Myopia
- Unexplained BCVA <20/20 or reduced Vr-QoL
- Irregular (scissor) reflex

KC Detection – Past/Present



An eye like this, with skewed astigmatism, is a relative contraindication for a multifocal intraocular lens and limbal relaxing incisions, say experts.

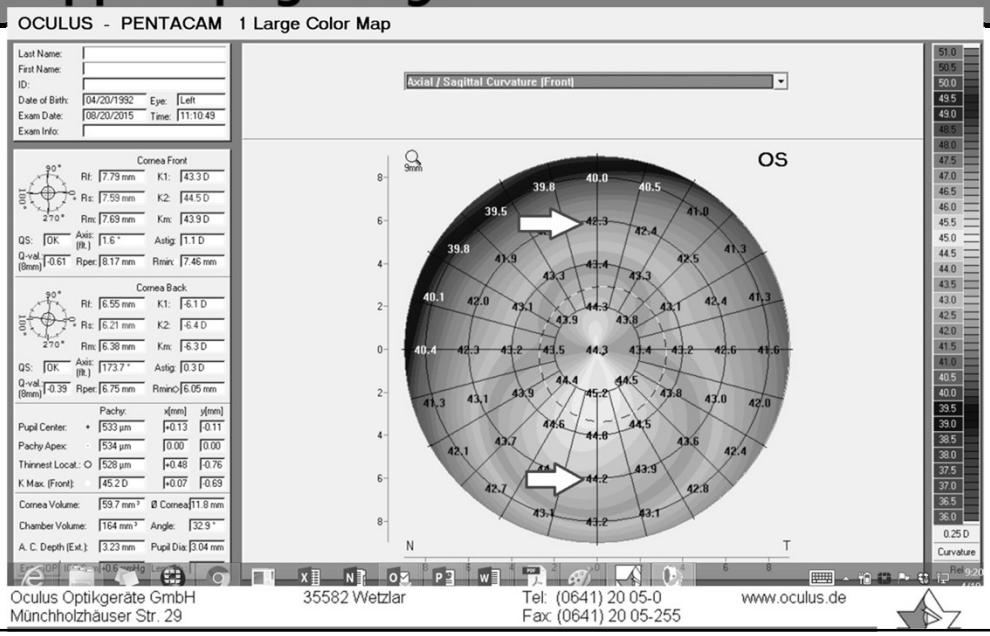
Summary of Topography Findings

- Central K > 47D[1] or **increases** in Ks
  - **Sim-K astigmatism** > 1.5D[1]
- Non-Orthogonal topo pattern
  - **Asymmetry** and/or radial skew >21 Deg[1]
- I/S Ratio (Hemi-meridianal steepening)
  - At 6mm diameter, I/S ≥ 1.8 – 2.0 is likely abnormal
  - At 6mm diameter, I/S ≥ 1.4 is questionable
- **"Small" & consistent increases** in the above risk characteristics over time

1. Rabinowitz YS. Videokeratographic indices to aid in screening for keratoconus. J Refract Surg 1995;11:371-9.

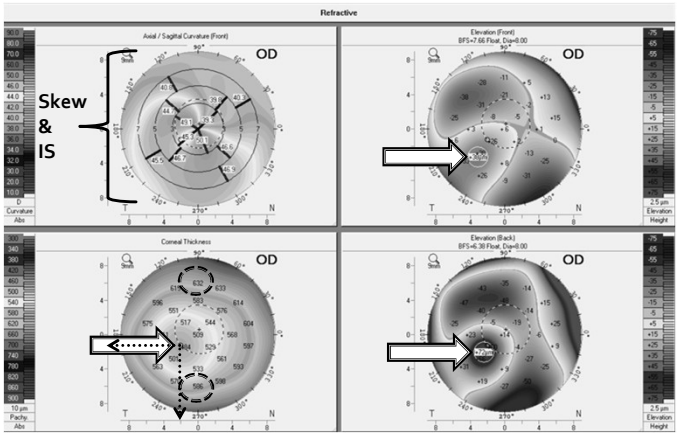
I/S Ratio Suspicious

44.2 - 42.3 = 1.9D



KC Detection - Present

- Posterior elevation **>18mi** (myopia) & **>28mi** (hyperopia)
  - Anterior elevation >8mi
  - Elevation values are specific for BSF reference shape
- On pachymetry map
  - **Interocular asymmetry** at thinnest location **≥ 25mi** (less than **1%** population)
  - Apical decentration of > 0.8 mm or
  - > 50mi disparity between superior & inferior cornea
- Personally, rate of pachymetric distribution & changes over time are more weighted



KC Detection & Monitoring - Present

Derivation of Keratoconus Pattern

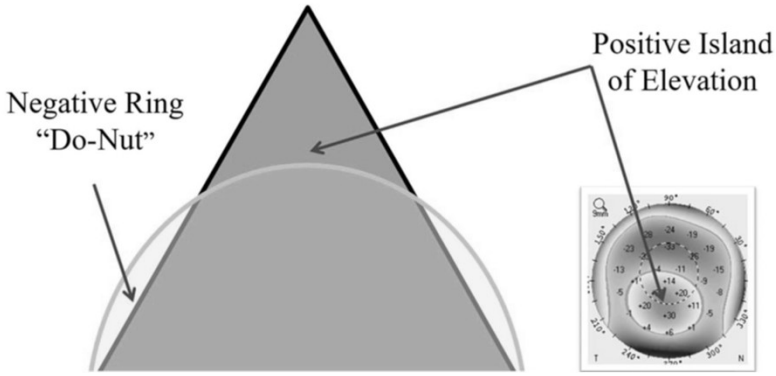
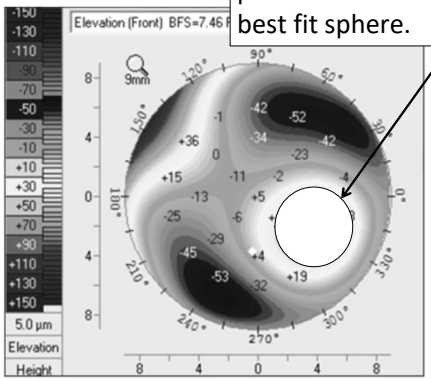
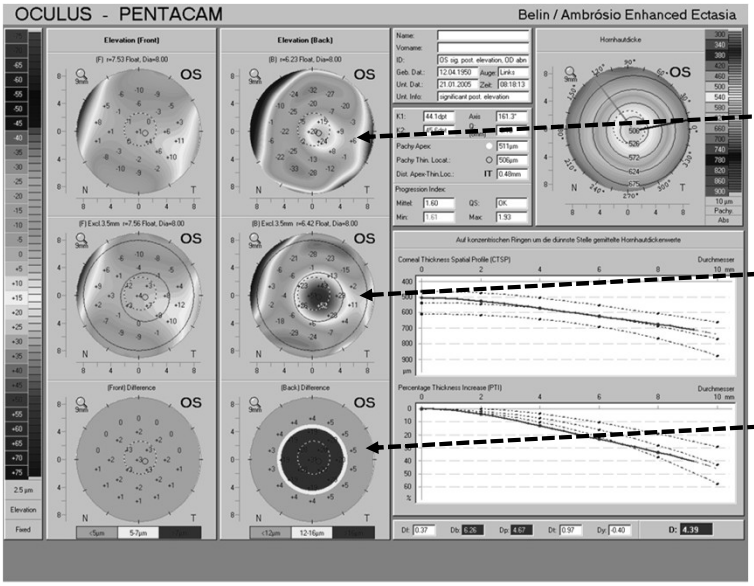


Figure adapted from "Belin MW, Jang HS, Borgstrom M. Keratoconus: Diagnosis and Staging. Cornea. 2022 Jan 1;41(1):1-11. "

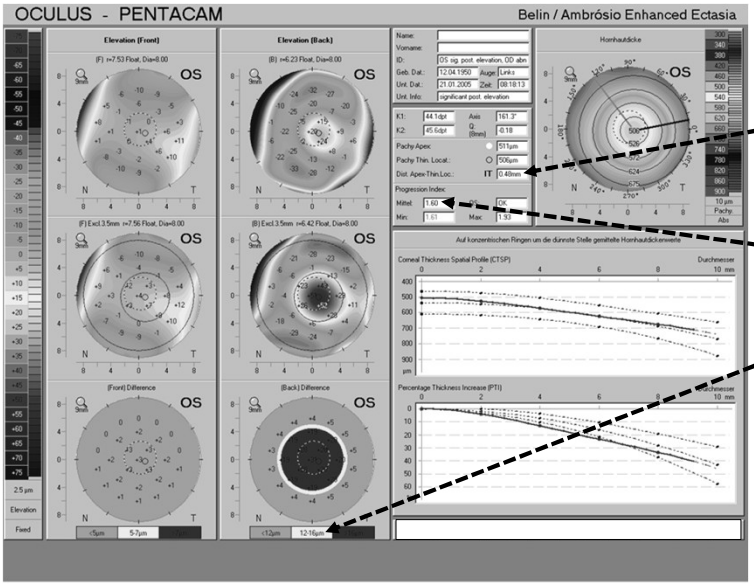
The Belin/Ambrosio excludes a 3mm-4mm zone at the thinnest point to normalize the best fit sphere.



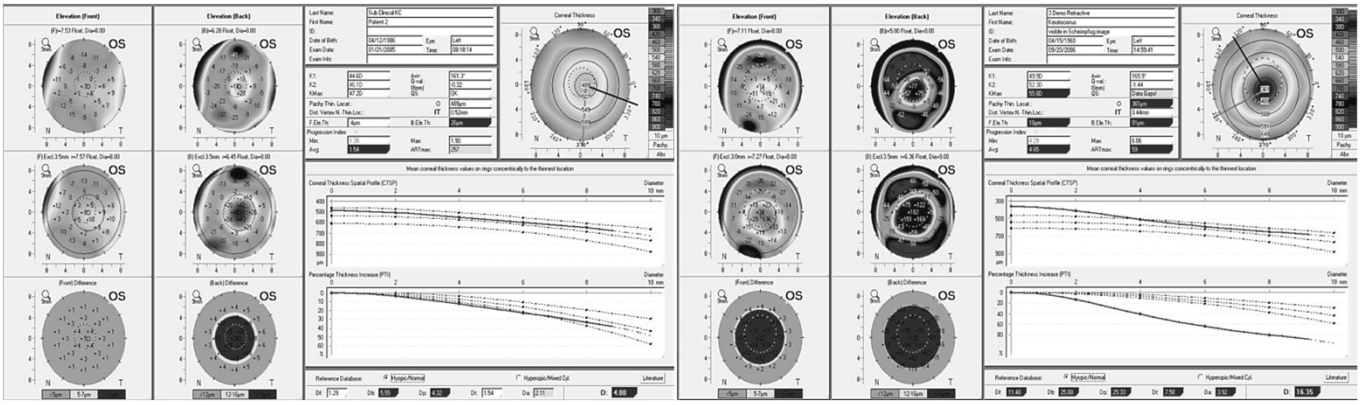
BAD: Enhanced Ectasia Display



BAD: Enhanced Ectasia Display



KC Detection & Monitoring - Present

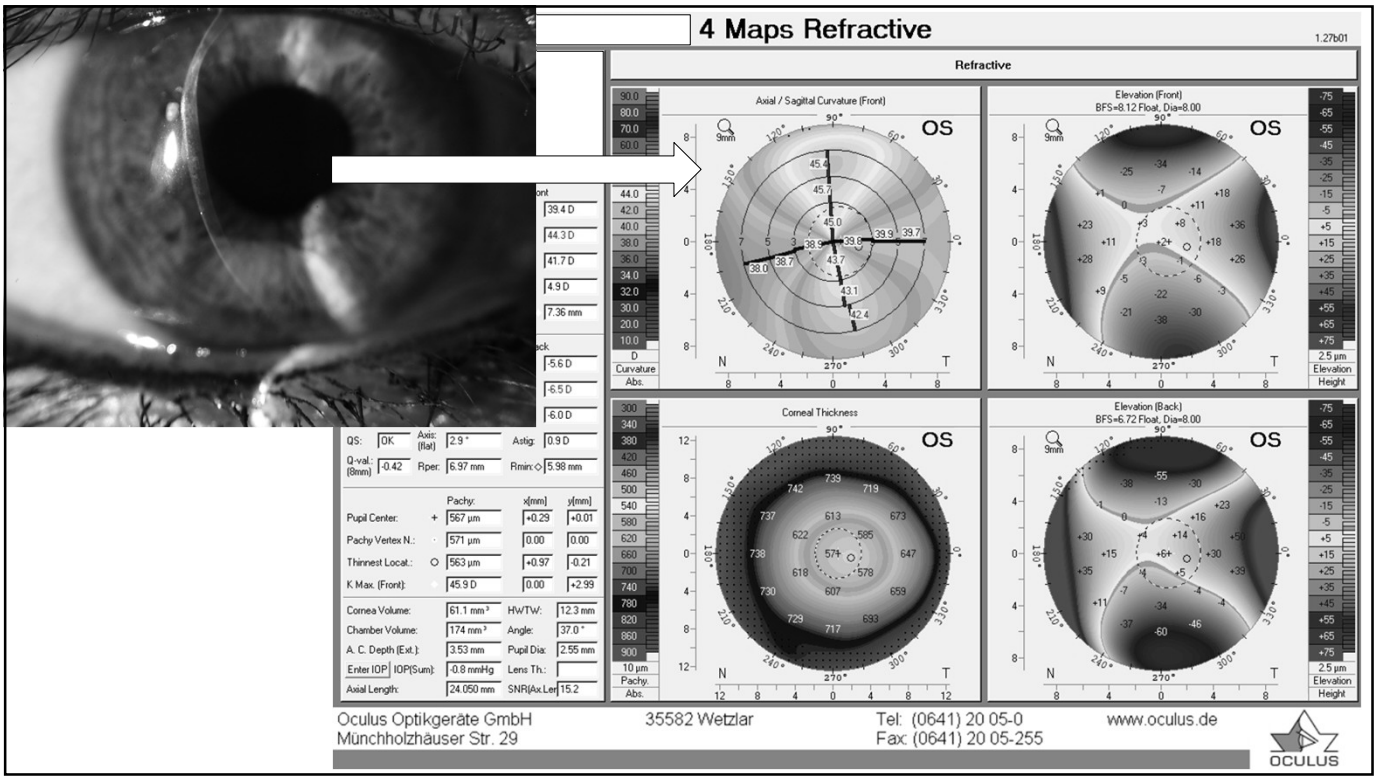


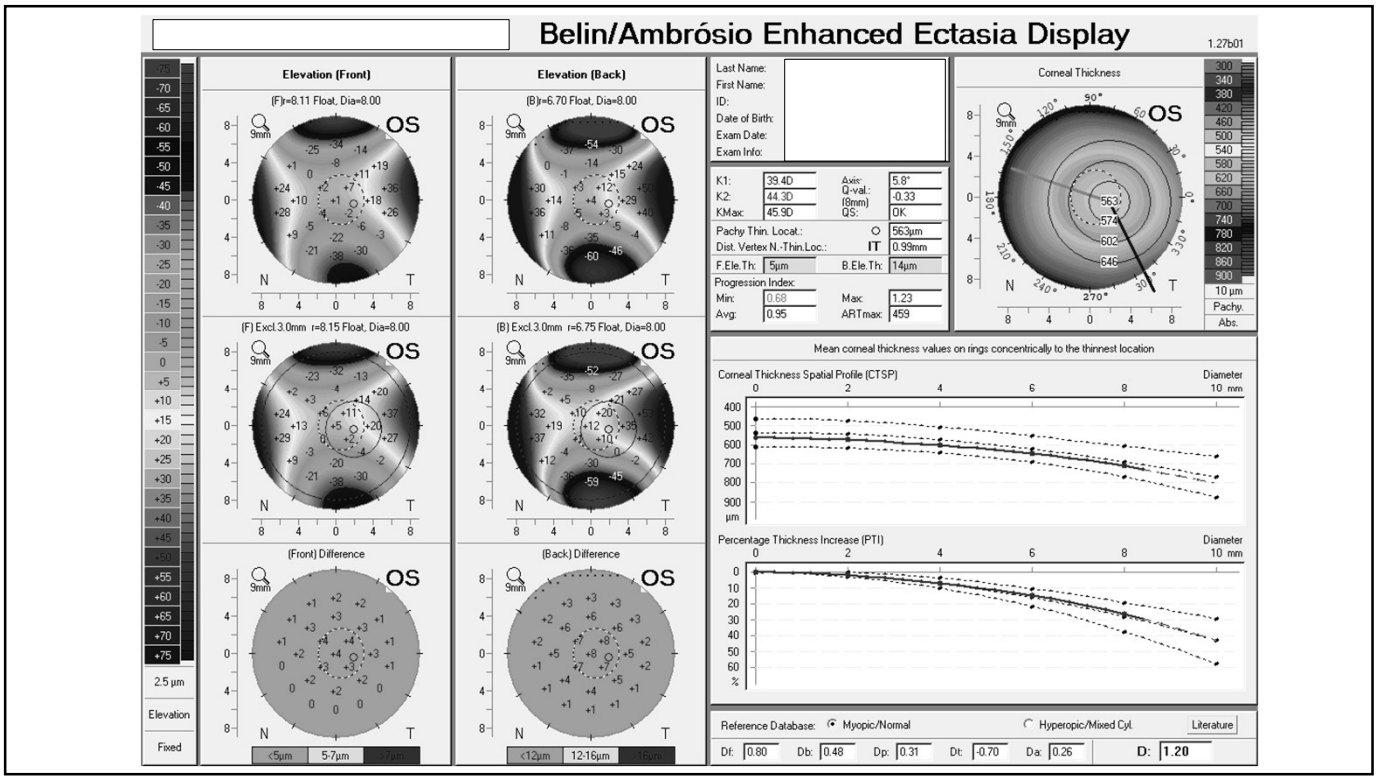
Final "D" - Sensitivity 0.941 / Specificity 0.944

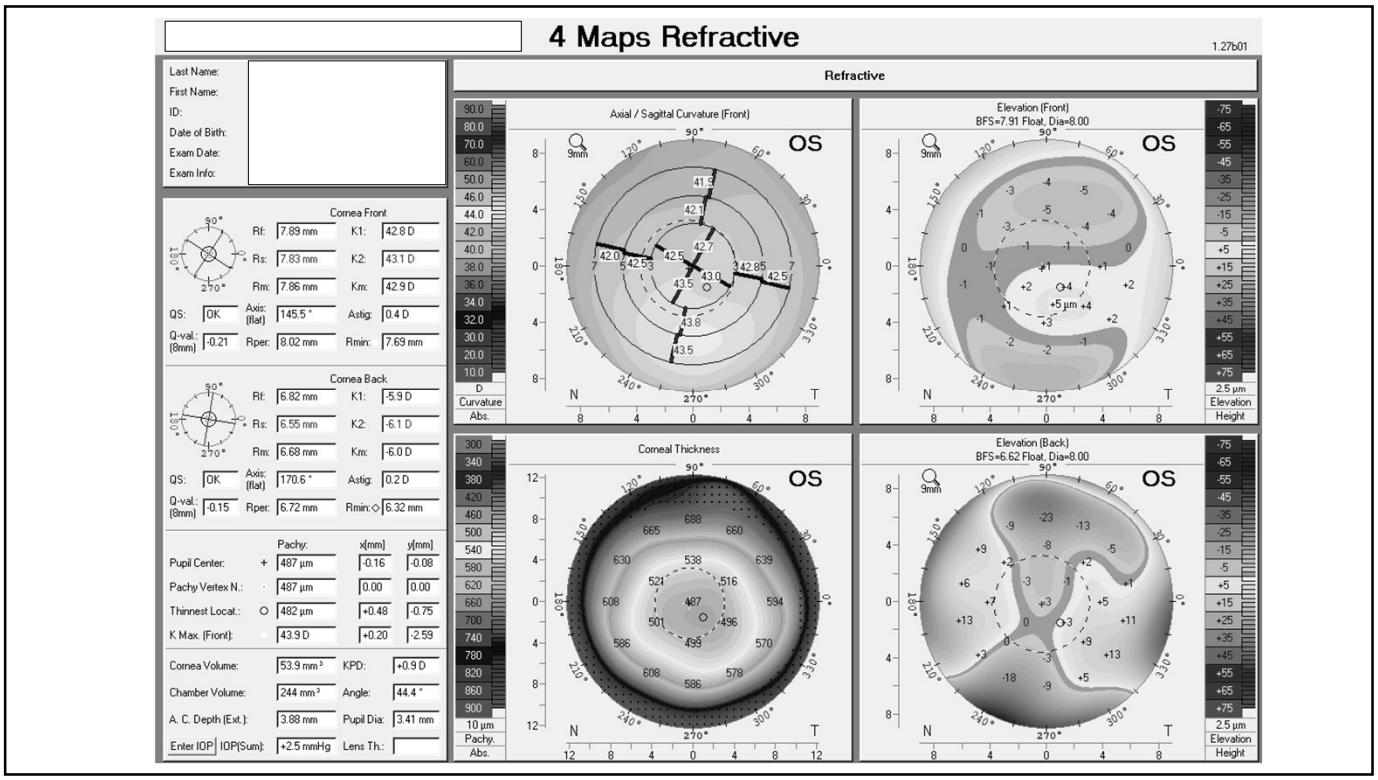
MAKING THE DIAGNOSIS

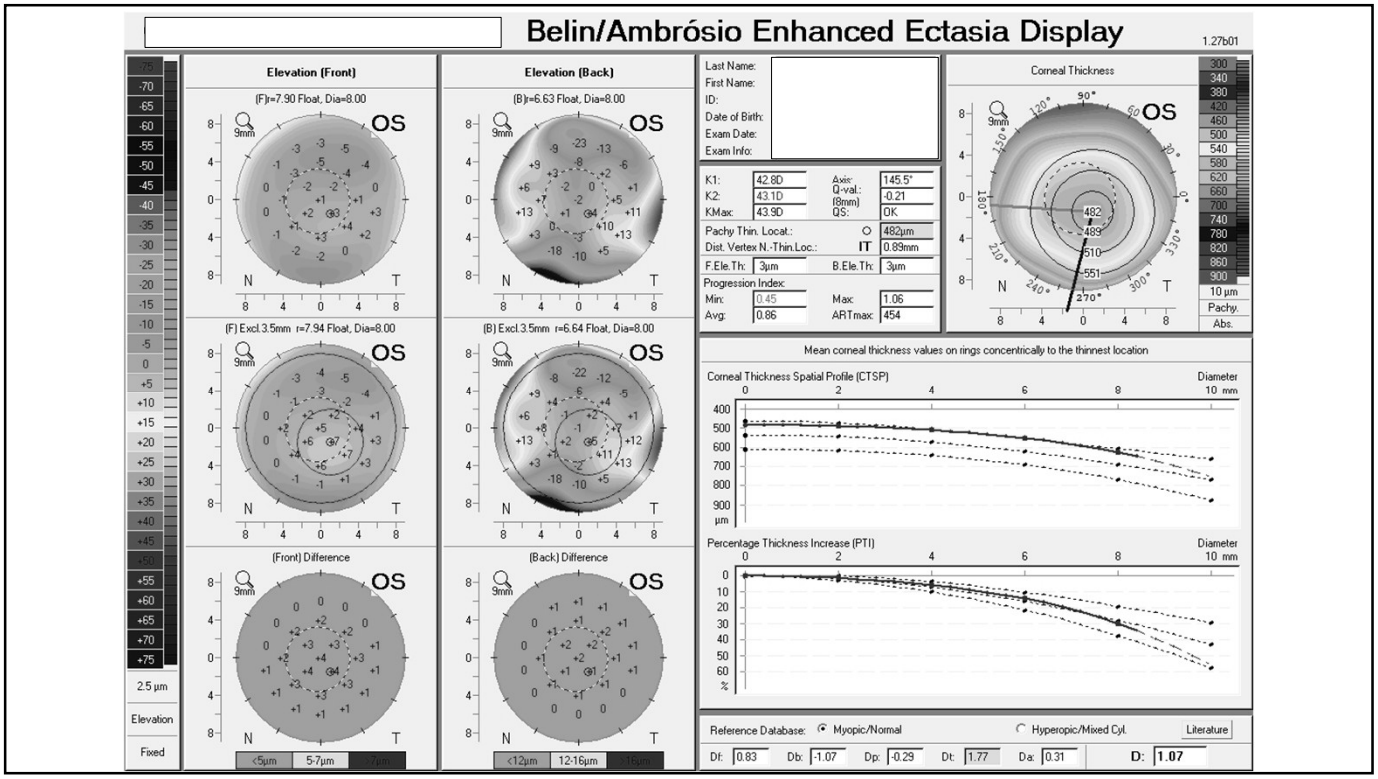
- Delayed acquired asymmetric corneal astigmatism
- Asymmetric BCVA, reduced VA Quality or Loss of BCVA
- Topography
  - Inferior Steepening
  - Skewed Radial Axis (ie, >20 degree)
- Tomography
  - Front/Back Elevation
  - Abnormal Pachymetric Progression
  - Regression Analysis
- Aberrometry
  - Elevated vertical coma*

*Buhren J, Kuhne C, Kohnen T. Defining subclinical keratoconus using corneal first-surface high-order aberrations. Am J Ophthalmol 2007 Mar;143(3):381-9.

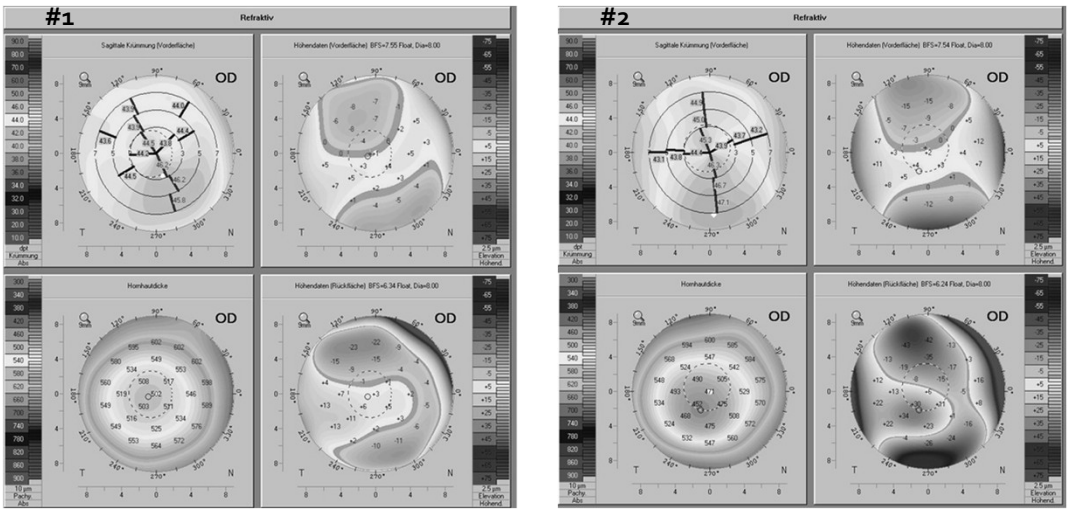

4 Maps Refractive
1.27b01
Refractive
Axial / Sagittal Curvature (Front)
Elevation (Front)
BFS=8.12 Float, Dia=8.00
Corneal Thickness
Elevation (Back)
BFS=6.72 Float, Dia=8.00
OS
Oculus Optikgeräte GmbH
Münchholzhäuser Str. 29
35582 Wetzlar
Tel: (0641) 20 05-0
Fax: (0641) 20 05-255
www.oculus.de
OCULUS


Belin/Ambrósio Enhanced Ectasia Display
1.27b01
Elevation (Front)
(F)r=8.11 Float, Dia=8.00
Elevation (Back)
(B)r=6.70 Float, Dia=8.00
(F) Excl.3.0mm r=8.15 Float, Dia=8.00
(B) Excl.3.0mm r=6.75 Float, Dia=8.00
(Front) Difference
(Back) Difference
Corneal Thickness
Mean corneal thickness values on rings concentrically to the thinnest location
Corneal Thickness Spatial Profile (CTSP)
Percentage Thickness Increase (PTI)
Reference Database: Myopic/Normal
Hyperopic/Mixed Cyl.
Literature
D: 1.20
OS


4 Maps Refractive
1.27b01
Refractive
Last Name:
First Name:
ID:
Date of Birth:
Exam Date:
Exam Info:
Cornea Front
Rf: 7.89 mm
Rs: 7.83 mm
Rm: 7.86 mm
K1: 42.8 D
K2: 43.1 D
Km: 42.9 D
QS: OK
Axis: (flat) 145.5 °
Astig: 0.4 D
Q-val.: (8mm) -0.21
Rper: 8.02 mm
Rmin: 7.69 mm
Cornea Back
Rf: 6.82 mm
Rs: 6.55 mm
Rm: 6.68 mm
K1: -5.9 D
K2: -6.1 D
Km: -6.0 D
QS: OK
Axis: (flat) 170.6 °
Astig: 0.2 D
Q-val.: (8mm) -0.15
Rper: 6.72 mm
Rmin: 6.32 mm
Pachy: x[mm] y[mm]
Pupil Center: 487 µm -0.16 -0.08
Pachy Vertex N.: 487 µm 0.00 0.00
Thinnest Locat.: 482 µm +0.48 -0.75
K Max. (Front): 43.9 D +0.20 -2.59
Cornea Volume: 53.9 mm³
KPD: +0.9 D
Chamber Volume: 244 mm³
Angle: 44.4 °
A. C. Depth (Ext.): 3.88 mm
Pupil Dia: 3.41 mm
Enter IOP
IOP(Sum): +2.5 mmHg
Lens Th.:
Axial / Sagittal Curvature (Front)
Elevation (Front)
BFS=7.91 Float, Dia=8.00
Corneal Thickness
Elevation (Back)
BFS=6.62 Float, Dia=8.00
OS
D
Curvature
Abs.
10 µm
Pachy.
2.5 µm
Elevation
Height


Belin/Ambrósio Enhanced Ectasia Display
1.27b01
Elevation (Front)
(F)r=7.90 Float, Dia=8.00
Elevation (Back)
(B)r=6.63 Float, Dia=8.00
(F) Excl.3.5mm r=7.94 Float, Dia=8.00
(B) Excl.3.5mm r=6.64 Float, Dia=8.00
(Front) Difference
(Back) Difference
<5µm
5-7µm
<12µm
12-16µm
Last Name:
First Name:
ID:
Date of Birth:
Exam Date:
Exam Info:
K1: 42.8D
K2: 43.1D
K.Max: 43.9D
Axis: (8mm) 145.5°
Q-val.: -0.21
QS: OK
Pachy Thin. Locat.: 482µm
Dist. Vertex N.-Thin.Loc.: IT 0.89mm
F.Ele.Th: 3µm
B.Ele.Th: 3µm
Progression Index:
Min: 0.45
Max: 1.06
Avg: 0.86
ART max: 454
Corneal Thickness
Mean corneal thickness values on rings concentrically to the thinnest location
Corneal Thickness Spatial Profile (CTSP)
Diameter 10 mm
Percentage Thickness Increase (PTI)
Reference Database: Myopic/Normal Hyperopic/Mixed Cyl. Literature
Df: 0.83 Db: -1.07 Dp: -0.29 Dt: 1.77 Da: 0.31 D: 1.07
2.5 µm
Elevation
Fixed

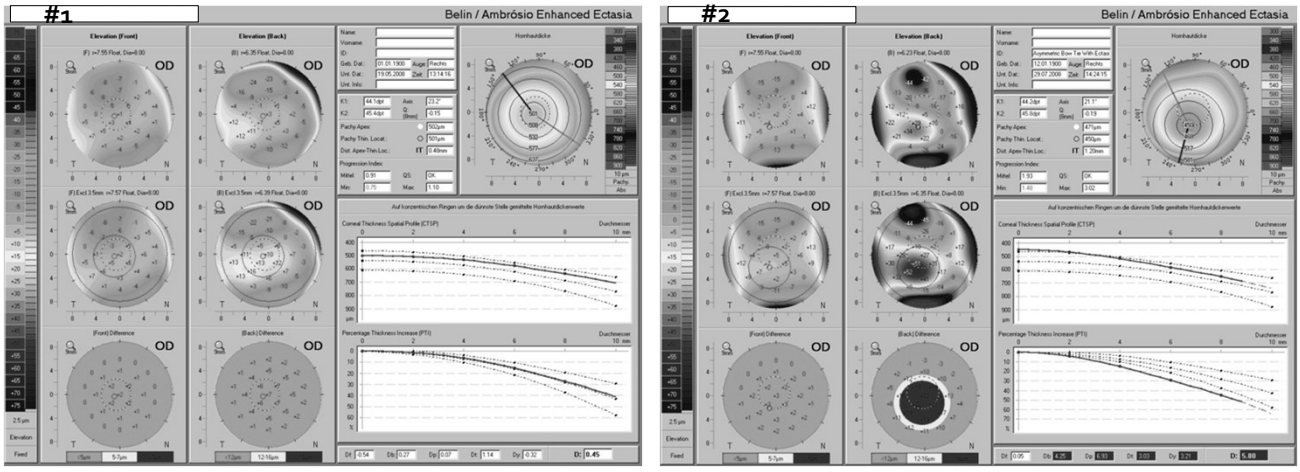
What About These Cases?



Which is Keratoconus? Both? Neither?

With courtesy from Renato Ambrosio

What About These Cases?



WNL

Keratoconus

With courtesy from Renato Ambrosio

KC Progression & Monitoring Pearls

SPECIAL ARTICLE

Global Consensus on Keratoconus and Ectatic Diseases

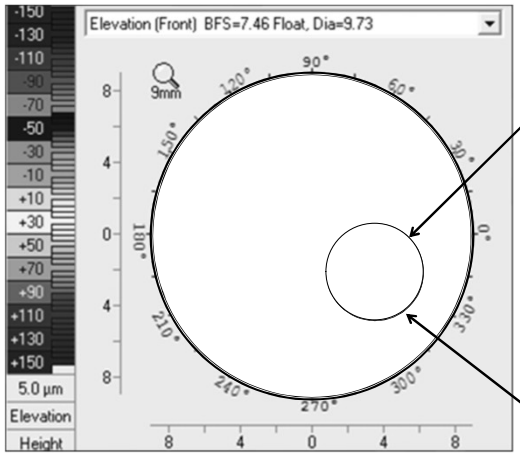
José A. P. Gomes, MD, PhD, Donald Tan, MD, PhD,† Christopher J. Rapuano, MD,‡ Michael W. Belin, MD,§ Renato Ambrósio, Jr, MD, PhD,¶ José L. Guell, MD,‖ François Malecaze, MD, PhD,** Kohji Nishida, MD,†† and Virender S. Sangwan, MD‡‡, the Group of Panelists for the Global Delphi Panel of Keratoconus and Ectatic Diseases*

- Ectasia progression is defined by a consistent change in <u>at least 2</u> of the following parameters:
  - Progressive steepening of the anterior corneal surface
  - Progressive steepening of the posterior corneal surface
  - Progressive thinning and/or an increase in the rate of corneal thickness change from the periphery to the thinnest point

** ”Although progression is often accompanied by a decrease in BSCVA, a <u>change in both uncorrected visual acuity and BSCVA is not required</u> to document progression”

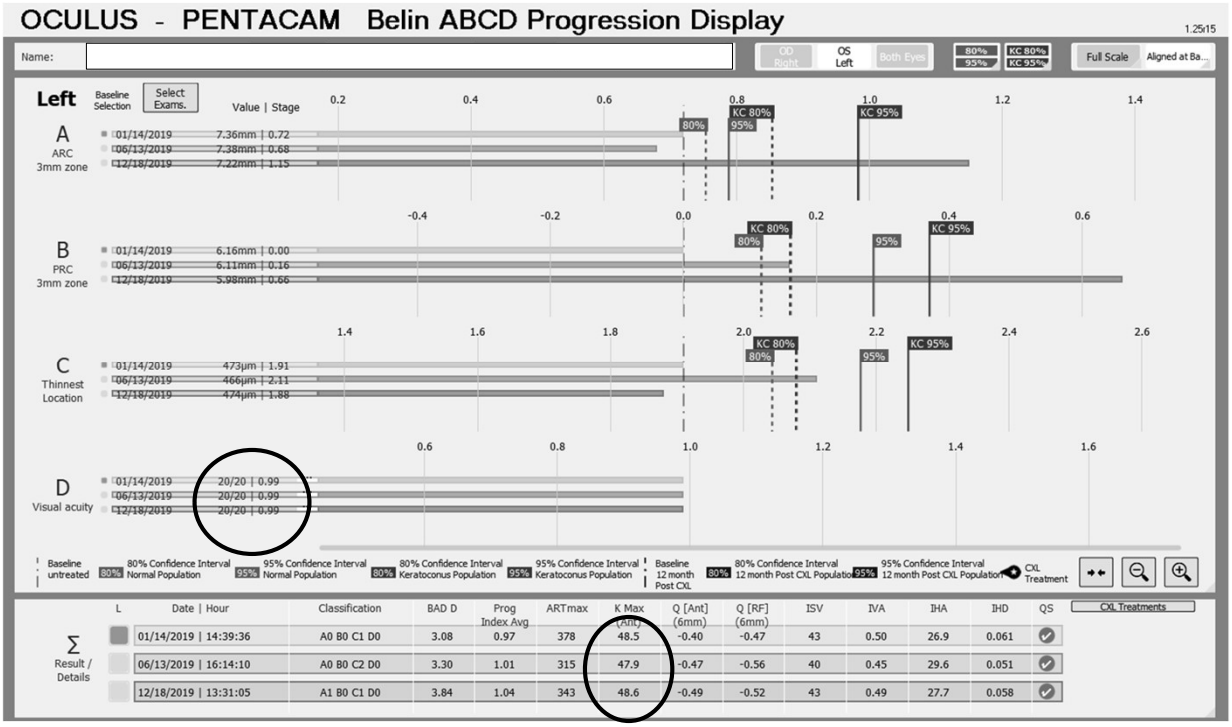
KC Detection & Monitoring - Present

Radius of Curvature Measured at Thinnest Corneal Point



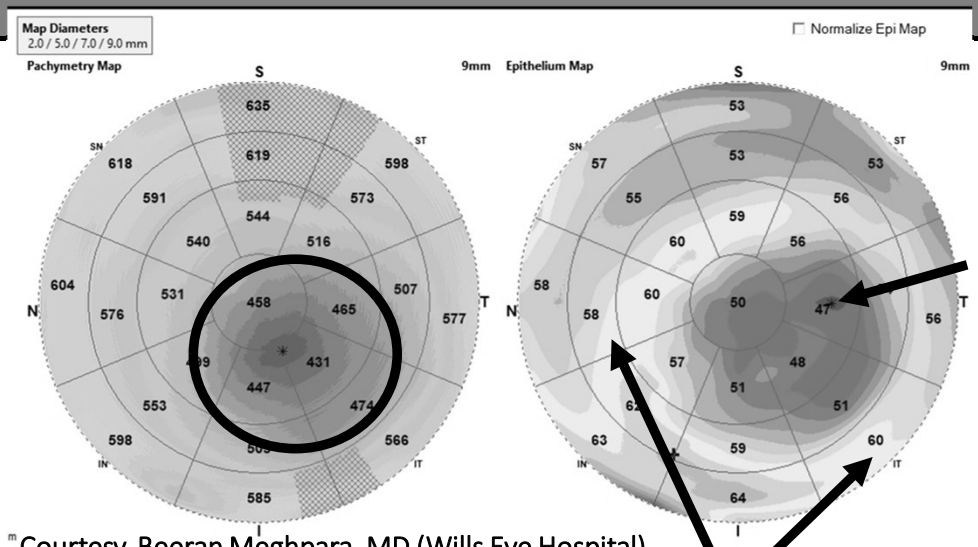
The Belin/Ambrosio excludes a 3mm-4mm zone at the thinnest point to normalize the best fit sphere.

The Belin ABCD Staging measures the ROC and pachymetry in this area to assess severity and track progression.



Courtesy, Beeran Meghpara, MD (Wills Eye Hospital)

Keratoconus



Apical thinning

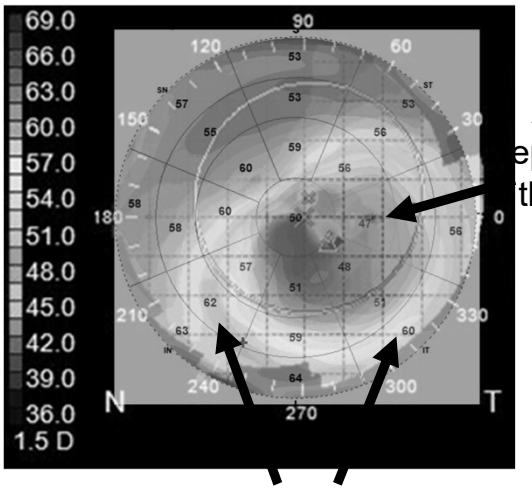
Thin epithelium at apex

Hyperplasia surrounding cone

Courtesy, Beeran Meghpara, MD (Wills Eye Hospital)

WillsEye Hospital

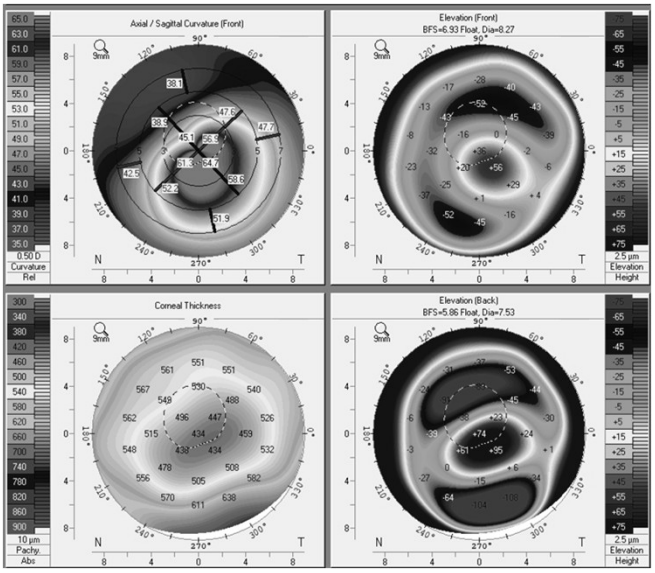
Adjunctive Confirmation of KCN via OCT



Apical epithelial thinning

Hyperplasia surrounding cone

Courtesy Beeran Meghpara, MD (Wills Eye Hospital)



Detecting Keratoconic Thinning with OCT "Pachymetric Indices":

- **KC vs Control eval of focal thinning & asymmetric parameters at 5 vs 7mm[1]**
  - Lower MCT ($P < 0.001$)
  - Greater I-S & SN-IT ($P < 0.001$)
  - More negative Min-Med & Min-Max ($P < 0.001$)
  - BUT, higher asymmetry in 5mm zone

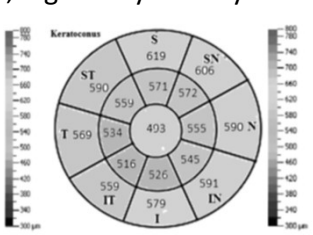


Table 3: The result of receiver operating characteristics analysis to differentiate eyes with keratoconus from normal eyes

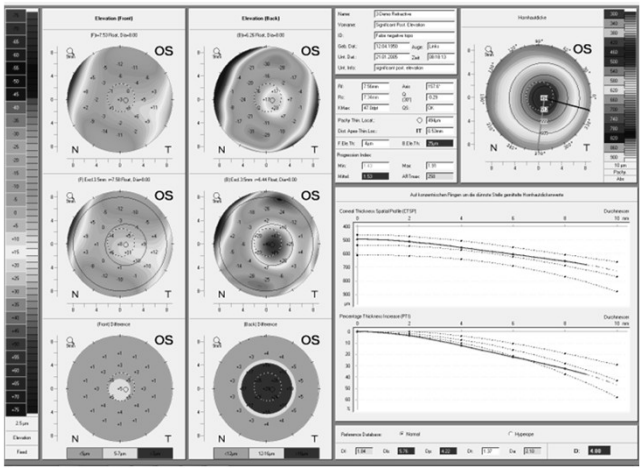
Variable (μm)	Normal versus KCN G1				Normal versus KCN G2			
	AUC (95% CI)	Cut-off	Sensitivity	Specificity	AUC (95% CI)	Cut-off	Sensitivity	Specificity
Central corneal thickness	**0.822** (0.730-0.893)	≤520	87.80	60.37	**0.902** (0.826-0.956)	≤508	87.82	73.08
Minimum thickness	0.759 (0.660-0.842)	≤516	51.22	88.68	0.865 (0.782-0.929)	≤497	56.34	96.50
Minimum–median thickness	**0.805** (0.711-0.880)	≤−40	82.93	66.0	**0.892** (0.813-0.948)	≤−45	85.67	78.85
Minimum–maximum thickness	0.679 (0.575-0.772)	≤−123	41.46	88.68	0.779 (0.678-0.856)	≤−106	80.5	61.5
Total corneal thickness (5 mm)								
S	0.685 (0.581-0.777)	≤565	63.40	77.70	0.701 (0.605-0.798)	≤560	56.1	76.92
I	0.793 (0.697-0.870)	≤542	80.49	64.15	0.862 (0.779-0.928)	≤529	75.6	86.5
N	0.721 (0.619-0.808)	≤552	75.60	66.04	0.704 (0.607-0.800)	≤547	68.3	73.1
T	0.742 (0.641-0.826)	≤724	58.5	79.2	0.768 (0.675-0.854)	≤530	65.9	75.0
SN	0.708 (0.606-0.798)	≤577	82.9	56.6	0.697 (0.593-0.789)	≤565	67.5	67.3
IT	0.789 (0.692-0.866)	≤540	80.41	60.38	0.855 (0.766-0.920)	≤518	77.5	84.62
ST	0.699 (0.597-0.791)	≤548	56.10	77.36	0.773 (0.626-0.815)	≤539	58.5	70.1
IN	0.764 (0.666-0.846)	≤547	75.61	67.9	0.776 (0.678-0.856)	≤527	63.41	88.46
I-S	0.694 (0.593-0.787)	≤−40	48.78	86.80	0.807 (0.701-0.873)	≤−41	68.50	86.54
SN-IT	0.694 (0.590-0.785)	>37	63.4	67.3	0.80 (0.706-0.879)	>42	77.50	74.50
Total corneal thickness (7 mm)								
S	0.647 (0.538-0.740)	≤632	73.2	52.8	0.717 (0.614-0.805)	≤642	80.0	53.66
I	0.758 (0.658-0.840)	≤592	80.0	56.98	0.799 (0.709-0.879)	≤595	85.2	59.62
N	0.693 (0.589-0.784)	≤608	80.0	47.17	0.704 (0.600-0.794)	≤609	82.93	46.2
T	0.707 (0.604-0.796)	≤548	46.3	88.8	0.738 (0.637-0.824)	≤541	46.3	92.3
SN	0.686 (0.582-0.778)	≤625	79.9	52.8	0.724 (0.622-0.812)	≤624	85.4	53.8
IT	0.746 (0.646-0.830)	≤578	80.4	54.72	0.772 (0.680-0.859)	≤585	85.3	53.8
ST	0.671 (0.566-0.764)	≤608	78	56	0.708 (0.605-0.798)	≤608	85.4	57.7
IN	0.731 (0.566-0.764)	≤577	63.4	75.5	0.716 (0.607-0.800)	≤575	58.5	78.8
I-S	0.640 (0.536-0.738)	≤−53.4	41.46	80.0	0.636 (0.519-0.724)	≤−22	78.0	45.0
SN-IT	0.633 (0.526-0.730)	>28	80.11	44.24	0.640 (0.533-0.738)	>43	65.0	60.78

**The highest AUCs highlighted. AUC: Area under the receiver operating characteristic curve, CI: Confidence interval, KCN: Keratoconus, KCN G1: Mild KCN group, KCN G2: Moderate and sever KCN groups, S: Superior, I: Inferior, N: Nasal, T: Temporal, SN: Supranasal, IT: Infratemporal, ST: Supratemporal, IN: Infranasal, I-S: Inferior-superior, SN-IT: Supranasal-infratemporal

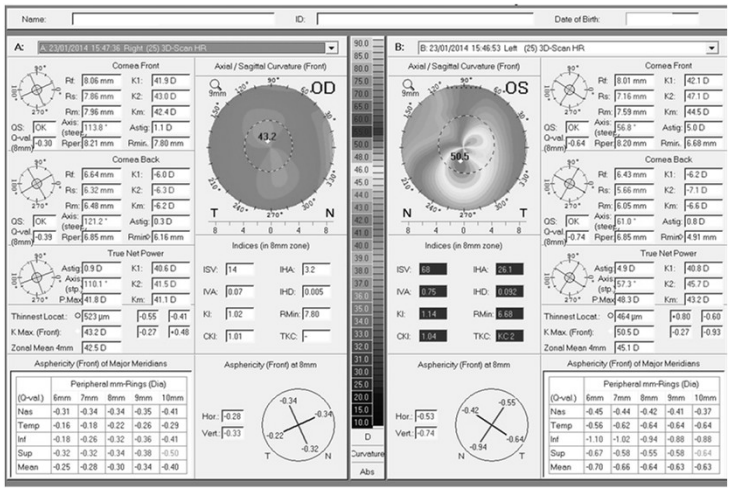
1. Hashemi H, Heidari Z, Mohammadpour M, Momeni-Moghaddam H, Khabazkhoob M. Distribution Pattern of Total Corneal Thickness in Keratoconus versus Normal Eyes Using an Optical Coherence Tomography. J Curr Ophthalmol. 2022 Jul 26;34(2):216-222.

KCN Detection – Future

NOT FDA APPROVED in US

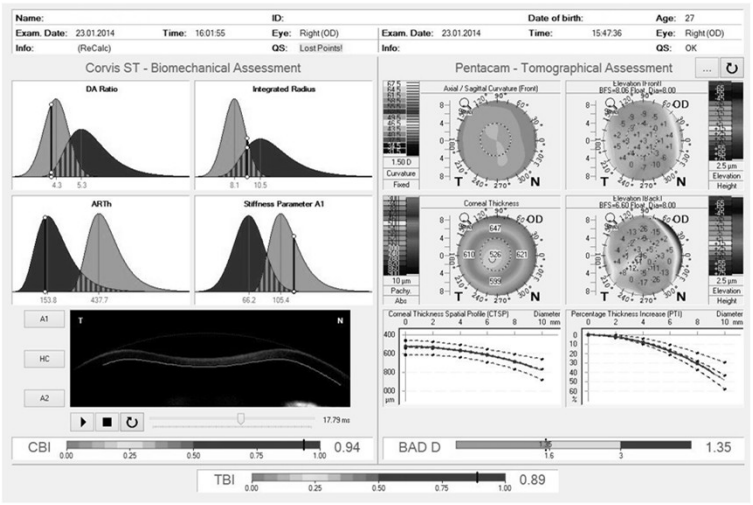


Unilateral Keratoconus?



Unilateral / FFKC case: Grade 2 OS, Tomographically normal OD

Tomographical / Biomechanical Assesment OD



"Biomechanical changes likely occur before tomographic changes" – Cynthia Roberts OD, PhD

CBI (0.94) and TBI (0.89) already abnormal OD

NOT FDA APPROVED in US

Biomechanical Assessments of High-Fluence Corneal Crosslinking with Supplemental Oxygen Using Optical Coherence Elastography in *ex vivo* Rabbit Eyes

POSTER #2049 - B0483

Behrouz Tavakol, Stuart Elmhurst, Jason Hill, Clark Chang, Alex Yildizyan, David Usher

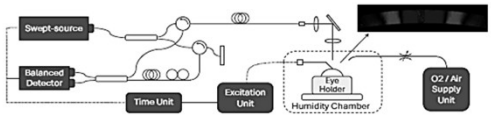
Glaukos Corp, Burlington, MA

Purpose

- Oxygen has been proposed to be the critical rate limiting step to the biomechanical outcomes of corneal crosslinking, especially when involving high UV fluence and/or transepithelial applications.
- The biomechanical impacts of supplemental oxygen and epithelial presence during high-fluence UVA corneal crosslinking were investigated using Optical Coherence Elastography (OCE).

Methods

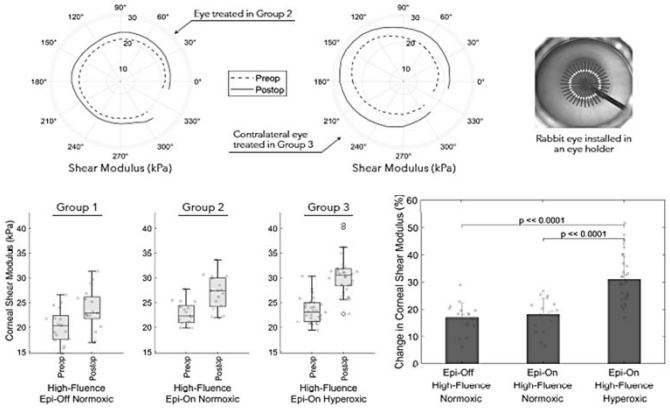
- A total of 80 fresh New Zealand White rabbit eyes (paired) were treated with UVA crosslinking KXL iLink systems.
- Eyes were stabilized to room temperature and 15 mmHg intraocular pressure (IOP) prior to any operations.
- Eyes were randomized and separated into three treatment groups.
- The epithelium was removed for eyes in Group 1 which received a 10-minute soak of a riboflavin solution. Eyes in Groups 2 and 3, with the epithelium intact, received trans-epithelial (epi-on) riboflavin solutions.
- Eyes in Group 3 received supplemental oxygen maintained at a >90% level. Eyes in Group 1 and 2 received air supply at the same flow rate as supplemental oxygen rate for Group 3.
- All groups received a fluence of 10 J/cm² at an irradiance of 30 mW/cm² with 1s:1s pulsing for 11 minutes 6 seconds.
- Eyes were placed in chambers to prevent dehydration during IOP stabilization and treatment time.



- An in-house built OCE was used to scan eyes twice immediately before and after UVA treatment to obtain average shear moduli, which were later used in paired and unpaired t-test analyses.

Results

- A significant change in shear modulus pre/post UVA treatment was observed in all groups.
- No significant difference was found between changes in shear moduli in Groups 1 and 2 (p=0.6).
- The increase in Group 3 (31%) was found to be significantly higher than both Group 1 (17%) and 2 (18%) (p<<0.0001).



Conclusions

The oxygen enriched epi-on procedure significantly outperformed both epi-off and epi-on high-fluence procedures without supplemental oxygen. Experiments support the hypothesis that oxygen availability in stroma is rate limiting for high-fluence UVA crosslinking. Furthermore, the presence of the epithelium did not adversely affect crosslinking efficacy for the normoxic procedures.

References

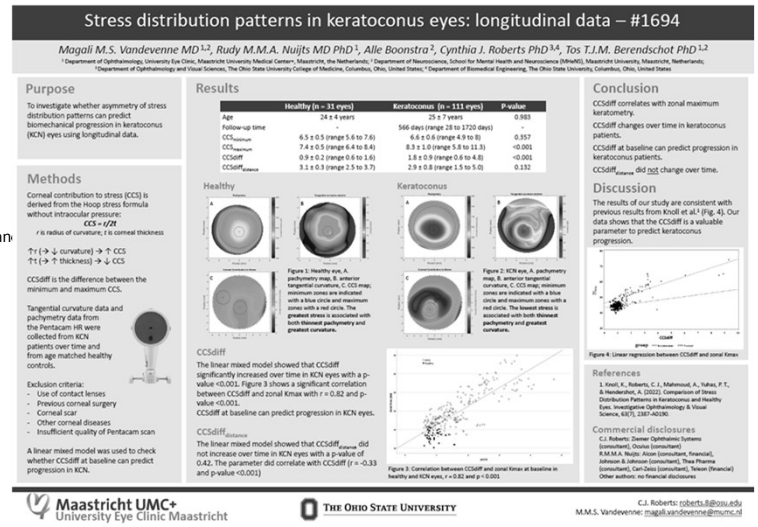
1. Seiler TG, Komninou MA, Nambiar MH, Schuerch K, Frueh BE, Büchler P. Oxygen Kinetics During Corneal Cross-linking With and Without Supplementary Oxygen. Am J Ophthalmol. 2021 Mar;223:368-376. doi: 10.1016/j.ajo.2020.11.001.
2. Hill J, Liu C, Deardorff P, Tavakol B, Eddington W, Thompson V, Gore D, 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. doi: 10.1080/02713683.2019.1669663.

GLAUKOS

KC Detection - Future

- Artificial Intelligence
  - Deep machine learning with initial expert validation/guidance

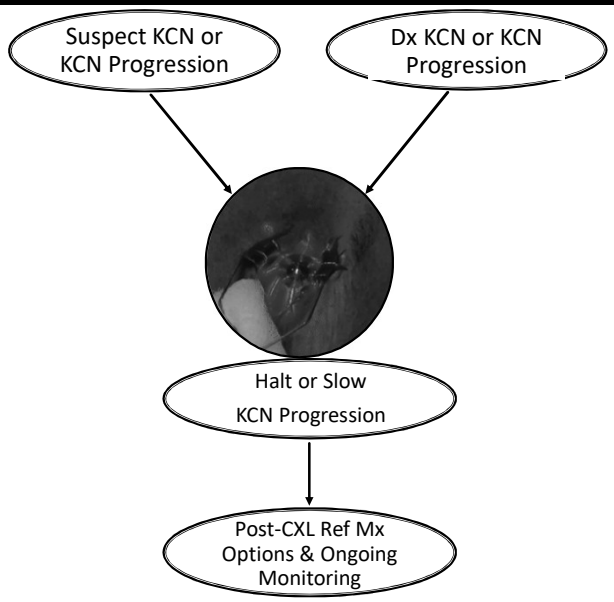
AA Siddiqui, J Ladas, JK Lee. Artificial intelligence in cornea, refractive, and cataract surgery. Curr Opin Ophthalmol . 2020 Jul;31(4):253-260



Breaking KCN Cycle & Collaboration Opportunity

Keratoconus (KCN) is an ideal condition for collaboration between optometrists & ophthalmologists

1. **The 1st challenge** is detecting KC early before vision is compromised
2. **The 2nd challenge** is to prevent further corneal changes and corresponding loss of vision that may lead to a corneal transplant
3. **The 3rd challenge** is helping patients see better, wherever they are in the KCN staging



When To Consider Additional Corneal Imaging?

- 1. Frequent Refractive changes
- 2. Frequent CL refit
- 3. K ≥ 47D
- 4. BCVA < 20/20 with no anatomical explanation
- 5. Subjective visual complaints and/or worsening symptoms
- 6. Family Hx
- 7. Medical Hx (ie, atopic eye disease, chronic eye rubbing)

What Got Epi-Off CXL Approved By FDA

Inclusion Criteria

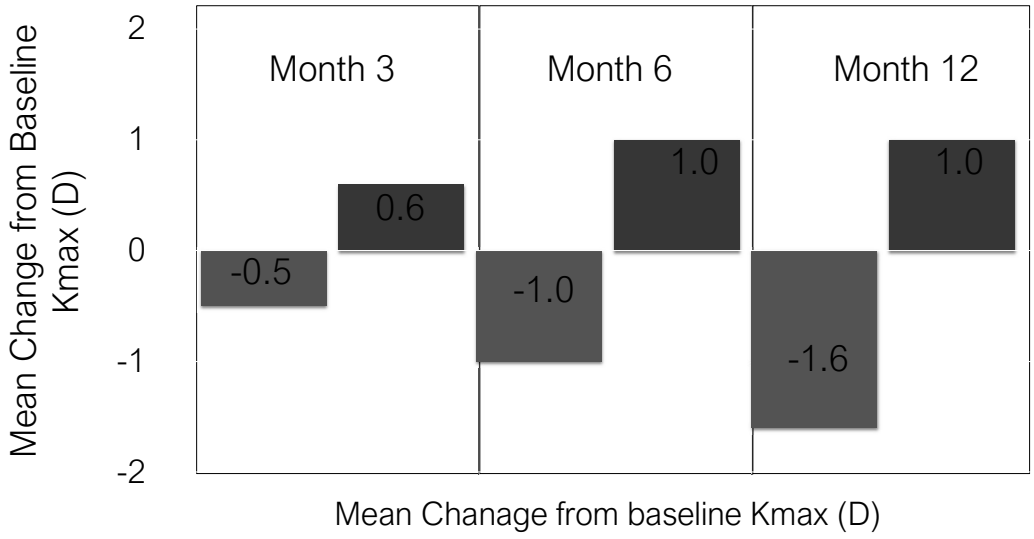
- 14 YO or older in age (up to 65 YO)
- Dx of KCN or ectasia s/p refractive surgery
- Axial topo consistent with KCN
  - K of 47 or greater
  - I:S ratio > 1.5
- BSCVA worse than 20/20 on ETDRS chart
- Corneal thickness **300 microns or greater**

Progression ≤ 24 Months

- Increase in 1 D in steepest K value, or
- Increase of 1 D in manifest astigmatism, or
- Myopic shift of 0.5 D on subjective manifest refraction, or
- Decrease of 0.1 mm in the back optical zone radius in rigid contact lens wearers

1. Hersh PS, Stulting RD, Muller D, Durrie DS, Rajpal RK; United States Crosslinking Study Group. United States Multicenter Clinical Trial of Corneal Collagen Crosslinking for Keratoconus Treatment. Ophthalmology. 2017 Sep;124(9):1259-1270.

Progressive KCN Mean Change Kmax (D)



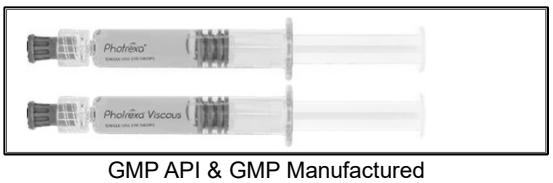
FDA-Approved Epi-Off CXL Protocol

Indications

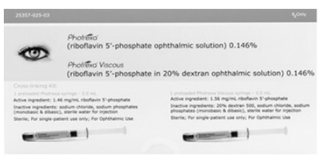
- Progressive Keratoconus & Corneal Ectasia Following Refractive Surgery (Post-LASIK Ectasia)

Approved Drug-Device Platform

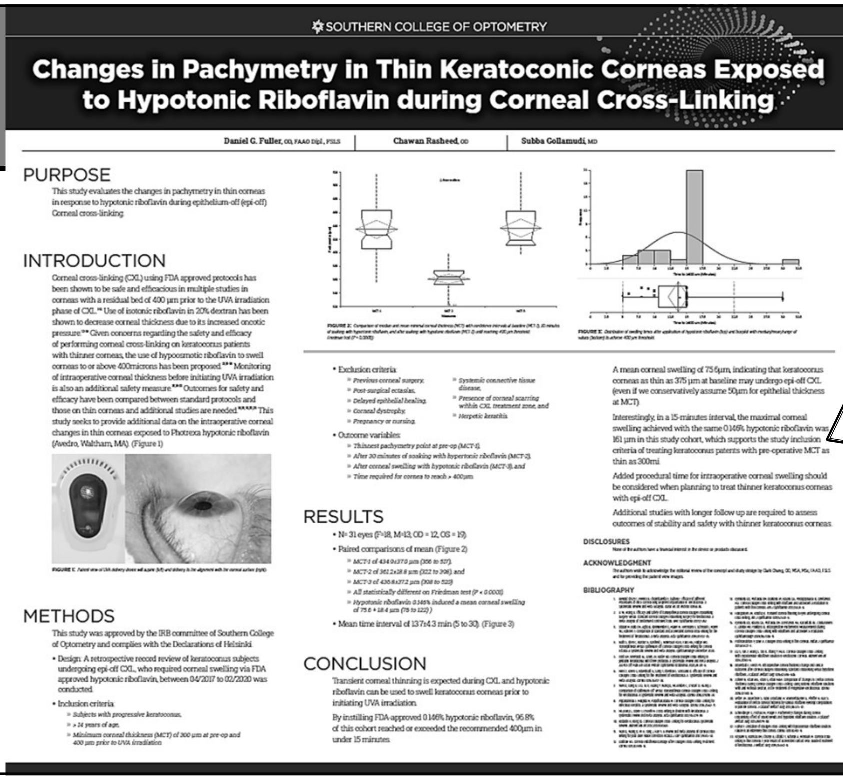
- **Photrexa® Viscous** (riboflavin 5'-phosphate in 20% dextran ophth soln)[1]
- **Photrexa®** (riboflavin 5'-phosphate ophth soln)[1]
- **KXL®** ultraviolet light delivery system in corneal collagen cross-linking Procedures.[2]



GMP API & GMP Manufactured



[1] Manufactured for Avedro. | [2] Manufactured by Avedro



SOUTHERN COLLEGE OF OPTOMETRY

Changes in Pachymetry in Thin Keratoconic Corneas Exposed to Hypotonic Riboflavin during Corneal Cross-Linking

Daniel G. Fuller, OD, FAAO Dipl., FSLS | Chawan Rasheed, OD | Subba Gollamudi, MD

PURPOSE

This study evaluates the changes in pachymetry in thin corneas in response to hypotonic riboflavin during epithelium-off (epi-off) Corneal cross-linking.

INTRODUCTION

Corneal cross-linking (CXL) using FDA approved protocols has been shown to be safe and efficacious in multiple studies in corneas with a residual bed of 400 µm prior to the UVA irradiation phase of CXL. Use of isotonic riboflavin in 20% dextran has been shown to decrease corneal thickness due to its increased oncotic pressure. Given concerns regarding the safety and efficacy of performing corneal cross-linking on keratoconus patients with thinner corneas, the use of hypoosmotic riboflavin to swell corneas to or above 400microns has been proposed. Monitoring of intraoperative corneal thickness before initiating UVA irradiation is also an additional safety measure. Outcomes for safety and efficacy have been compared between standard protocols and those on thin corneas and additional studies are needed. This study seeks to provide additional data on the intraoperative corneal changes in thin corneas exposed to Photrexa hypotonic riboflavin (Avedro, Waltham, MA). (Figure 1)

METHODS

This study was approved by the IRB committee of Southern College of Optometry and complies with the Declarations of Helsinki.

- Design: A retrospective record review of keratoconus subjects undergoing epi-off CXL, who required corneal swelling via FDA approved hypotonic riboflavin, between 04/2017 to 02/2020 was conducted.
- Inclusion criteria:
  - Subjects with progressive keratoconus,
  - > 14 years of age,
  - Minimum corneal thickness (MCT) of 300 µm at pre-op and 400 µm prior to UVA irradiation
- Exclusion criteria:
  - Previous corneal surgery,
  - Post-surgical ectasias,
  - Delayed epithelial healing,
  - Corneal dystrophy,
  - Pregnancy or nursing,
  - Systemic connective tissue disease,
  - Presence of corneal scarring within CXL treatment zone, and
  - Herpetic keratitis
- Outcome variables:
  - Thinnest pachymetry point at pre-op (MCT-1),
  - After 30 minutes of soaking with hypertonic riboflavin (MCT-2),
  - After corneal swelling with hypotonic riboflavin (MCT-3), and
  - Time required for cornea to reach > 400µm

RESULTS

- N= 31 eyes (F=18, M=13, OD = 12, OS = 19)
- Paired comparisons of mean (Figure 2)
  - MCT-1 of 434.0±37.0 µm (356 to 527),
  - MCT-2 of 361.2±18.8 µm (322 to 398), and
  - MCT-3 of 436.8±37.2 µm (398 to 520)
  - All statistically different on Friedman test (P < 0.0001)
  - Hypotonic riboflavin 0.146% induced a mean corneal swelling of 75.6 ± 18.4 µm (75 to 122))
- Mean time interval of 13.7±4.3 min (5 to 30). (Figure 3)

CONCLUSION

Transient corneal thinning is expected during CXL and hypotonic riboflavin can be used to swell keratoconus corneas prior to initiating UVA irradiation.

By instilling FDA-approved 0.146% hypotonic riboflavin, 96.8% of this cohort reached or exceeded the recommended 400µm in under 15 minutes.

A mean corneal swelling of 75.6µm, indicating that keratoconus corneas as thin as 375 µm at baseline may undergo epi-off CXL (even if we conservatively assume 50µm for epithelial thickness at MCT).

Interestingly, in a 15-minutes interval, the maximal corneal swelling achieved with the same 0.146% hypotonic riboflavin was 161 µm in this study cohort, which supports the study inclusion criteria of treating keratoconus patients with pre-operative MCT as thin as 300mi.

Added procedural time for intraoperative corneal swelling should be considered when planning to treat thinner keratoconus corneas with epi-off CXL.

Additional studies with longer follow up are required to assess outcomes of stability and safety with thinner keratoconus corneas.

DISCLOSURES

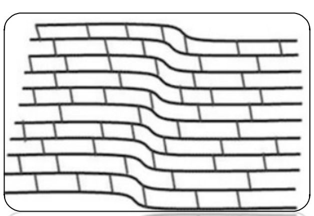
ACKNOWLEDGMENT

BIBLIOGRAPHY

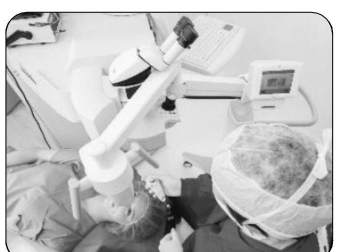
Conclusion

- In a 15 minutes interval, the maximum swelling achieved with 0.146% hypotonic riboflavin was 161µm in this study cohort
- This supports the study inclusion criteria of treating keratoconus patients **with pre-op MCT as thin as 300µm**

Patient Q&A: Does it "take away" keratoconus?



Aim of cross-linking is to halt or slow disease progression



Cross-Linking is <u>NOT</u> a refractive procedure

Post-op evaluation for visual correction & ongoing corneal monitoring are still recommended

Patient Q&A: Why do I need CXL?

1. CXL may improve lifetime outcomes & economic burdens

4,000 **Eyes individually simulated across 2,000 patients**

- *Mean age at baseline 31 yrs., mean follow-up 52.3 yrs.*
- *4:1 ratio of slow to fast progressors.*

26% **Reduction in rate of PK in iLink treated eyes vs. control**

- *Slow-progressors: 0.3% iLink and 8.7% control eyes underwent PK.*
- *Fast-progressors: 2.5% iLink and 92.7% control eyes underwent PK.*

28 Yrs **Fewer years spent in advanced stages of disease (AK 3 & 4)**

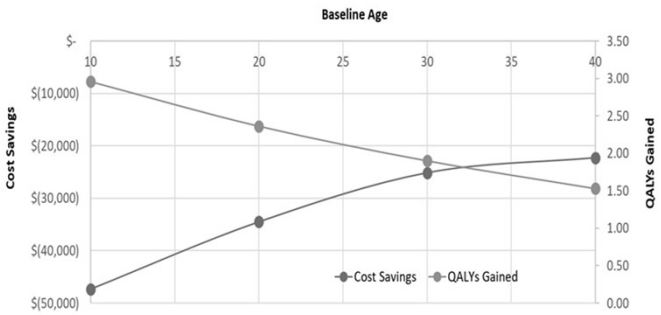
- *Drives impact on lost productivity; out-of-pocket costs (lens type).*

Lindstrom R, Berdahl J, Donnenfeld E. Cross-Linking versus Conventional Management for Keratoconus: A Lifetime Economic Model. *J Medical Economics* 2020.

Patient Q&A: Why do I need CXL?

1. CXL may improve lifetime outcomes & economic burdens

- **Compared to conventional treatment, iLink was associated with:**
  - **Lower total direct medical costs** (-$8,677; $30,994 vs. $39,671) and **more QALYs** (quality-adjusted life years,1.88; 21.80 vs. 19.93)
  - **Reduction in lifetime costs of $43,759** (including loss of productivity), and lifetime reduction in out-of-pocket costs of $4,248
  - **US national savings of $150 MM per year** with conservative prevalence estimates (1 in 2000), increasing to $736 MM with prevalence 1 in 375
- **Intervention at a younger age maximizes both cost savings and QALYs gained**



Lindstrom R, Berdahl J, Donnenfeld E. Cross-Linking versus Conventional Management for Keratoconus: A Lifetime Economic Model. *J Medical Economics* 2020.

Patient Q&A: Why do I need CXL?

2. CXL early may results in better QoL

REVIEW

Measurement of Quality of Life in Keratoconus

Himal Kandel, PhD, Konrad Pesudovs, PhD,† and Stephanie L. Watson, MBBS, PhD**

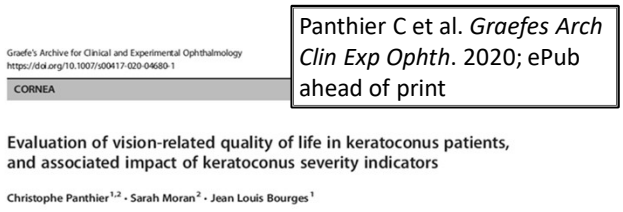
Purpose: To identify and assess the quality of questionnaires used to measure quality of life in keratoconus and guide selection of the most appropriate questionnaire for evaluating the impact of keratoconus.

Key Words: keratoconus, patient-reported outcomes, quality of life, questionnaire

(*Cornea* 2020;39:386–393)

Kandel et al *Cornea* 2020; 39:386- 393

- Many patients who have better visual acuity with contact lenses than with spectacles may not be able to wear contact lenses all day
- **Ocular pain and discomfort are significantly more in people with keratoconus wearing contact lenses**, particularly RGP contact lenses
- The impact of keratoconus on QoL therefore may be **disproportionate to the clinical measures such as best corrected visual acuity**



Graefe's Archive for Clinical and Experimental Ophthalmology
https://doi.org/10.1007/s00417-020-04680-1

CORNEA

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

Christophe Panthier[1,2] · Sarah Moran[2] · Jean Louis Bourges[1]

Panthier C et al. *Graefes Arch Clin Exp Ophth*. 2020; ePub ahead of print

- BCVA in the better eye is the most important factor contributing to patient's VR-QoL
- Clinicians should consider initially **targeting the better eye, as this may have a greater impact on the patients' quality of life**
- **CXL contributed to higher VR-QOL scores**
  - In **early stages of KC**: avoid deterioration of BCVA
  - In **late stages of KC**: decrease stress and anxiety concerning the progression of the disease

Patient Q&A: Why do I need CXL?

3. Synergy with optical rehabilitation

- FDA-approved corneal cross-linking procedure offers
  - Coverage for over 95% of commercially insured lives
  - Proven safety and efficacy
  - Slowing or halting keratoconus progression may enable patients to continue to tolerate contact lenses[1]

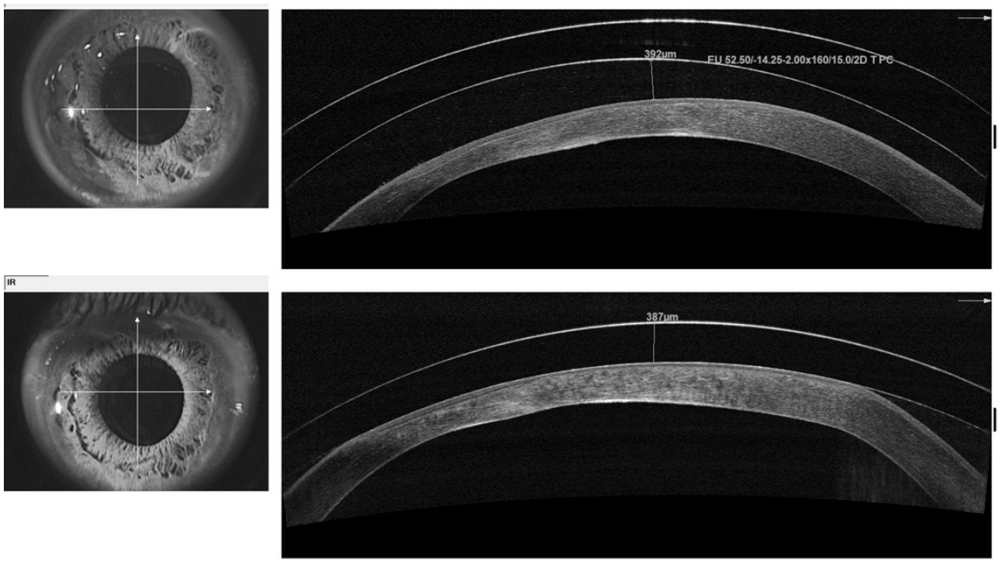
FDA-approved CXL
Slow or halt progression to help preserve vision

Scleral Lenses
Vision Rehabilitation
Address vision needs

The proprietary **iLink** epithelium-off procedure incorporates **Photrexa® Viscous** (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) *and* **Photrexa®** (riboflavin 5'-phosphate ophthalmic solution) which are photoenhancers indicated for use with the **KXL®** ultraviolet light delivery system.

1. Singh K, Bhattacharyya M, Arora R, Dangda S, Mutreja A. Alterations in contact lens fitting parameters following cross-linking in keratoconus patients of Indian ethnicity. *Int Ophthalmol*. 2018 Aug;38(4):1521-1530.

Patient Q&A: But I See Just Fine?!



Patient Q&A: Couldn't I wait longer?

Further KC worsening may occur while progressive KC eyes wait to receive CXL

- **Shah et al (UK) [1]**
  - **All 46 progressive KC worsened with wait time made longer by COVID pandemic**
  - **Typical Avg wait time is 182 ± 65 days & COVID restrictions added at least 3 mo**
  - **Worsened keratometric indices & lost nearly 1 line of VA**
- **Goh et al (New Zealand) [2]**
  - **39.6% (n=38) of 96 eyes further worsened over 153 ± 101 days**
- **Chatzis et al (Switzerland) [3]**
  - **While waiting to document KC progression in young KC patients (age 9 to 19 Yr)**
  - **88% (n=52) of 59 eyes were found to have Kmax ≥1D within 12 mo**
- **Romano et al (UK/Italy) [4]**
  - **25% of 104 eyes worsened in Kmax over 84.8 ± 62.9 days**
  - **Progressive KCN < 18 YO – Suggest no more than 6 weeks wait time**
  - **Progressive KCN ≥ 18 YO – Suggest no more than 12 weeks wait time**

1. 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.
2. Goh YW, Gokul A, Yadegarfar ME, Vellara H, Shew W, Patel D, McGhee CNJ, Ziaei M. Prospective Clinical Study of Keratoconus Progression in Patients Awaiting Corneal Cross-linking. Cornea. 2020 Oct;39(10):1256-1260.
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4. Romano V, Vinciguerra R, Arbabi EM, Hicks N, Rosetta P, Vinciguerra P, Kaye SB. Progression of Keratoconus in Patients While Awaiting Corneal Cross-linking: A Prospective Clinical Study. J Refract Surg. 2018 Mar 1;34(3):177-180

Patient Q&A: Couldn't I wait longer?

Keratoconus Natural Progression

A Systematic Review and Meta-analysis of 11 529 Eyes

Ferdi et al *Ophthalmology* 2019; 126:935- 945

- Patients **younger than 17 YO** or with **greater than 55 D Kmax** are likely to have more than 1.5 D of Kmax progression within 12 months
- **Self-reported outcome may be sensitive** in determining KC progression compared to changes in VA or Ks

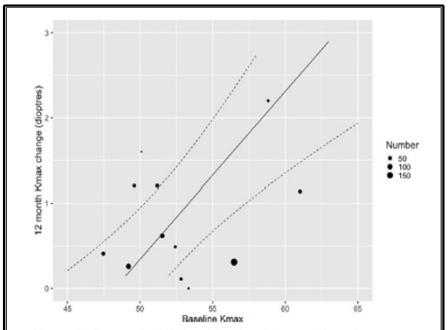


Figure 4. Scatter plot of effect of baseline K_{max} on 12-month raw mean change in K_{max} for each study included in meta-analysis. *Solid line* = predicted K_{max} change ($P = 0.003$), *dotted line* = 95% CIs, *dot size* = study sample size.

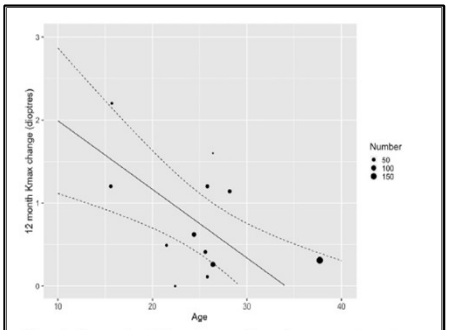


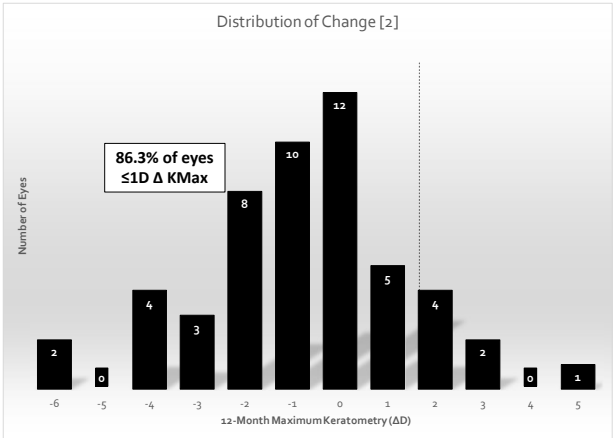
Figure 3. Scatter plot of effect of age on 12-month raw mean change in K_{max} for each study included in meta-analysis. *Solid line* = predicted K_{max} change ($P = 0.01$), *dotted line* = 95% confidence intervals (CIs), *dot size* = study sample size.

Patient Q&A: Too Much Discomfort for Younger KCN?

Background: **A published meta-analysis study of >11000 eyes demonstrated that patients with untreated progressive keratoconus ≤17 yrs of age or with ≥55 D KMax are likely to show ≥1.5D of Kmax progression within 12 months[1]**

US Real World Experience Confirms the Efficacy & Tolerability of iLink

- Retrospective study of patients with progressive keratoconus who underwent iLink at the Byers Eye Institute, Stanford University[2]
- n=57 eyes with ≥12-month follow-up, mean age 16.4 yrs ± 2.5 (**Range 12 to 22 years**) at the time of the procedure
- **Mean improvement in Kmax of -0.8 D at 12mo, -1.3D at 24mo**. **86.3% of eyes within ≤1D change** from pre-op Kmax at 12mo
- Anterior stromal haze was observed in the majority of eyes. Persistent epithelial defects were reported in 2 eyes, resolved within 1 and 6 mo after first observation, respectively.
- No other adverse effects were reported.



1. Ferdi et al. *Ophthalmology* 2019; 126:935- 945
2. Saleh et al. *Cornea*. 2021 Apr 14, Epub ahead of print.

Patient Q&A: More Complications in Younger KCN?

- Prospective, non-comparative, cohort study followed up to 24M (N=138 eyes)
  - Using iLink and Photrexa Viscous/Photrexa
  - Evaluate iLink efficacy in adults and children
  - Keratoconus & Ectasia Patients (12–65 YO)

ORIGINAL RESEARCH

Post-FDA Approval Results of Epithelium-Off, Full-Fluence, Dresden Protocol Corneal Collagen Crosslinking in the USA

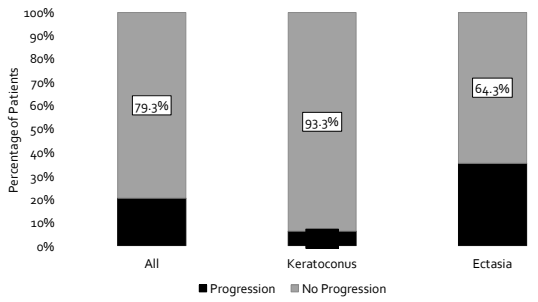
Derick O. Ansah · Jiangxia Wang · Kevin Lu · Samir Jabbour · Kraig S. Bower · Uri S. Soiberman

- Pediatric (≤18 YO) vs Adult (>18 YO)
  - Similar disease severity at presentation
  - **Similar visual & keratometric outcomes**
  - Concluded "**early intervention in pediatric patients to prevent additional damage**"
- Study did not find predilection for persistent haze in below patients
  - Younger Px
  - Thinner/Steeper Corneas
  - More Advanced KCN
  - Using both Photrexa Viscous & Photrexa

1. Ansah, Derick O., et al. "Post-FDA Approval Results of Epithelium-Off, Full-Fluence, Dresden Protocol Corneal Collagen Crosslinking in the USA." *Ophthalmology and Therapy* 9.4 (2020): 1023-1040.

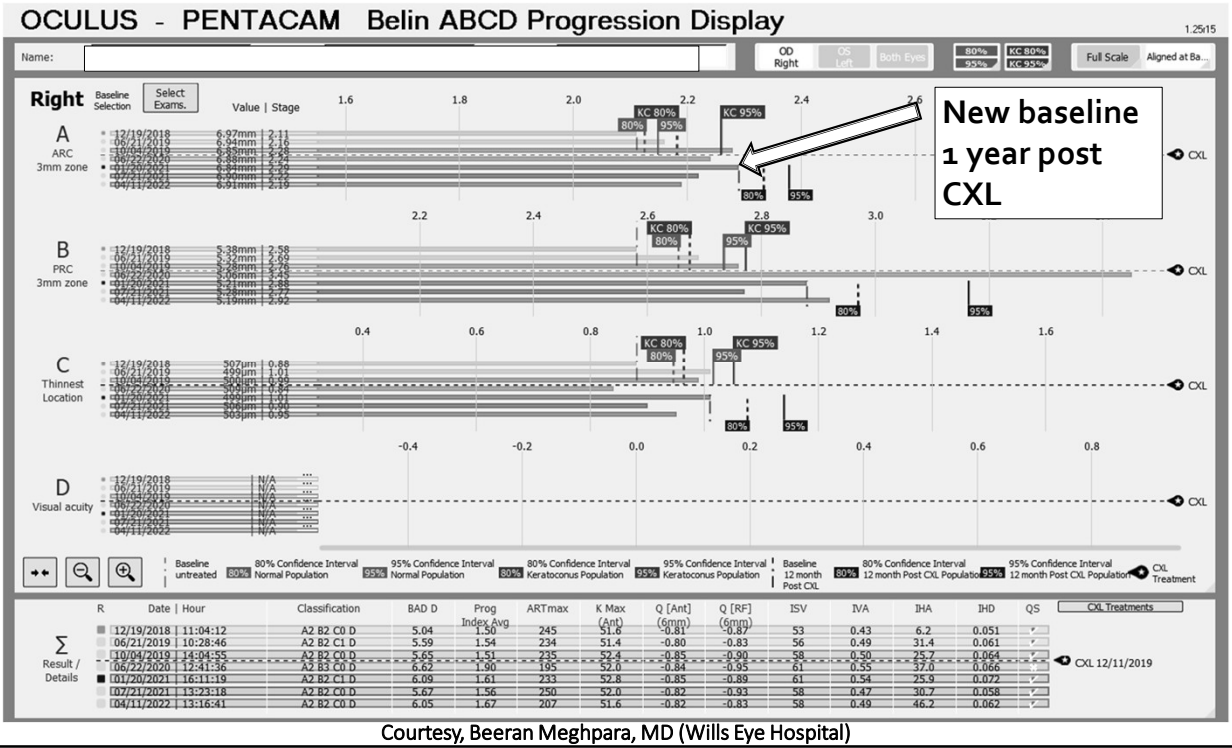
Patient Q&A: How Long does it last? 10-Yr Epi-Off CXL Outcomes in US

- In general, CXL appears to remain stable at 10 years (N=30 eyes in 16 Px – 15 KC Eyes & 15 Ectasia eyes)
  - Stable topography
    - 77% of the entire cohort
    - 87% of keratoconus eyes
    - 67% of ectasia eyes
  - Stable BSCVA
    - 86% of the entire cohort
    - 100% of keratoconus eyes
    - 71.4% of ectasia eyes
- Progression was defined
  - Steepening of Kmax ≥2D
  - Worsening in VA (UCVA or BSCVA) ≥ 2 logMar lines
  - Belin ABCD Progression display



Courtesy, Steven Greenstein, MD

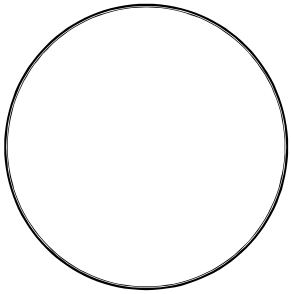
The CLEI Center for Keratoconus



Courtesy, Beeran Meghpara, MD (Wills Eye Hospital)

Post-CXL Considerations

- A bandage contact lens should be applied
- Similar to standard of care for postoperative management of PRK patients, post-op regimen varies but may include:
  - Antibiotic
  - Steroid
  - NSAID
  - Lubricating drops
  - Opioid (Vicodin, OxyContin, etc..)



- Treatment Emergent Adverse Events from Phase 3 (TEAEs)
  - Majority of AEs reported resolved **during the 1st month**
  - **Resolved within 6-months**: Corneal epithelium defect, corneal striae, punctate keratitis, photophobia, dry eye, eye pain, and decreased visual acuity

Phase 3 TEAE Examples - Progressive KCN

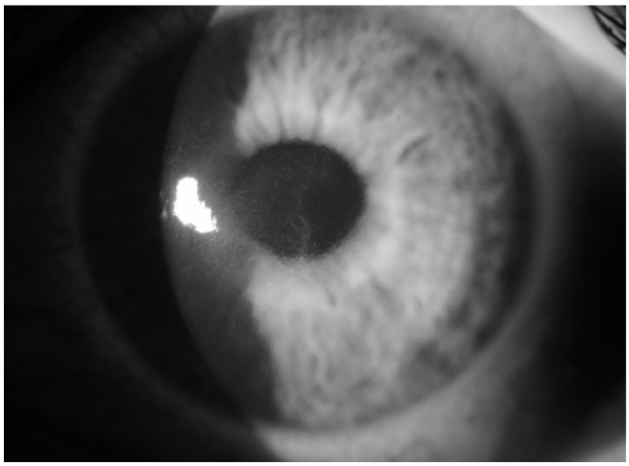
- Corneal Opacity (haze)
- Corneal Epithelium Defect
- Punctate Keratitis
- Corneal Striae
- Eye Pain
- Blurred Vision
- Reduced Visual Acuity

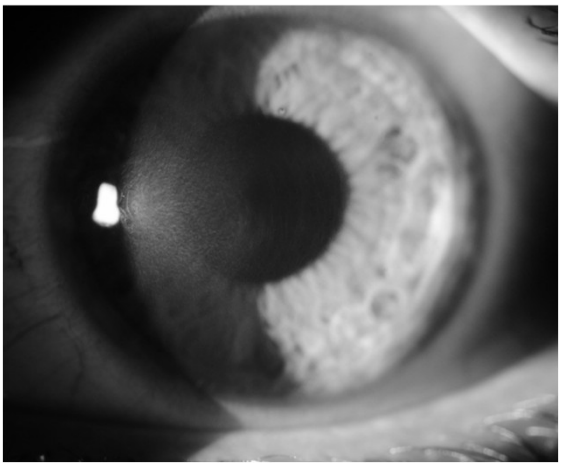
Post-CXL: General Follow-Up Schedule

VISIT	PLAN
Day 1 to 1 Week	• Topical antibiotic, steroid • Frequent lubricants • No eye rubbing • Remove BCL once epithelium heals
Month 1	• OCT Imaging • Tomography / Topography • Vision assessment • **Contact lens refitting evaluation**
Month 3, 6, 12 **(Follow-ups potentially performed and billed by diagnosing physician depending on practice preference)**	• Continued evaluation utilizing tomography / topography • Vision assessment

No Global Period! Follow-up visits can be billed to insurance

Post-CXL: CL Fitting Considerations?





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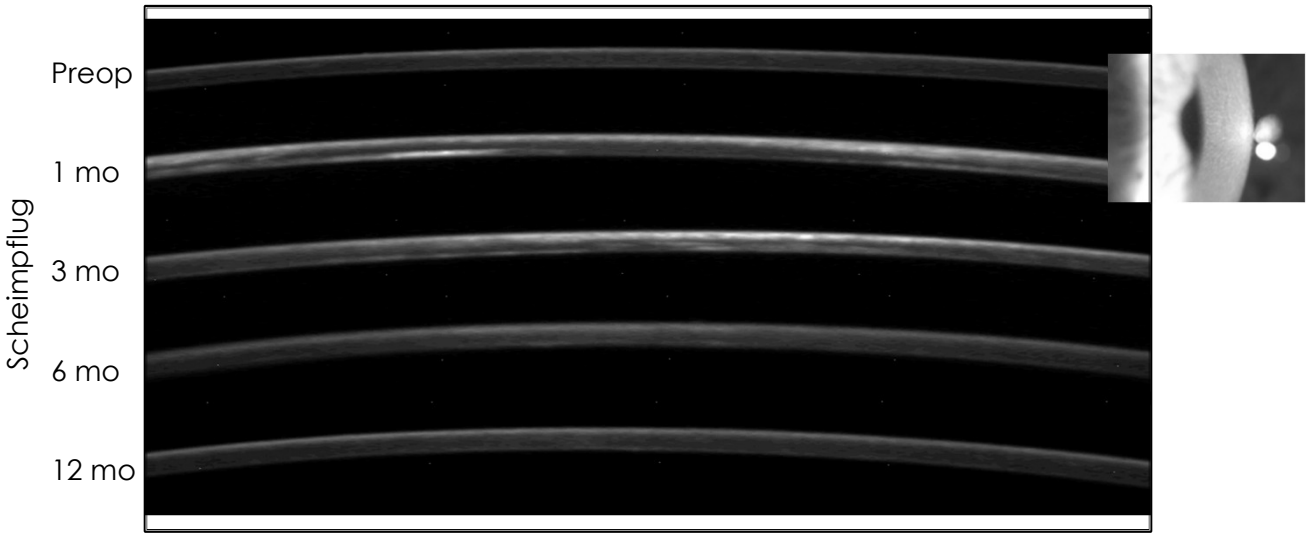
Post-CXL: CL Fitting Considerations?



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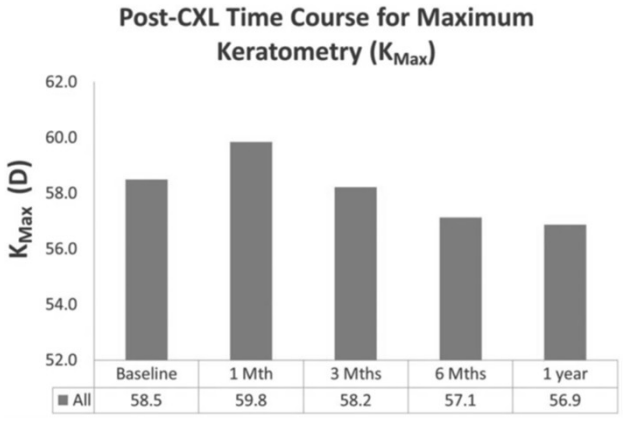
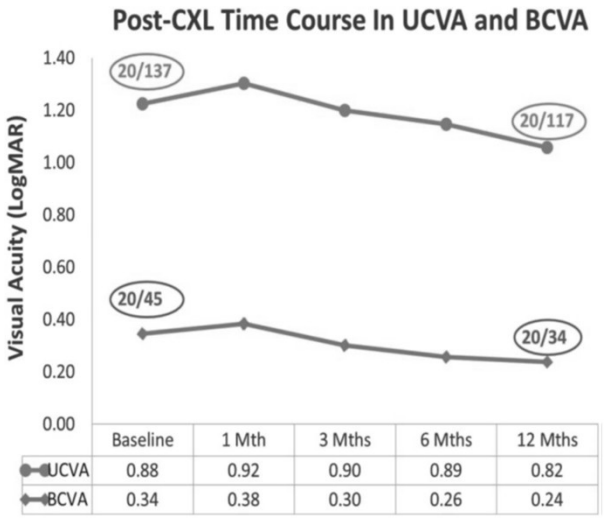
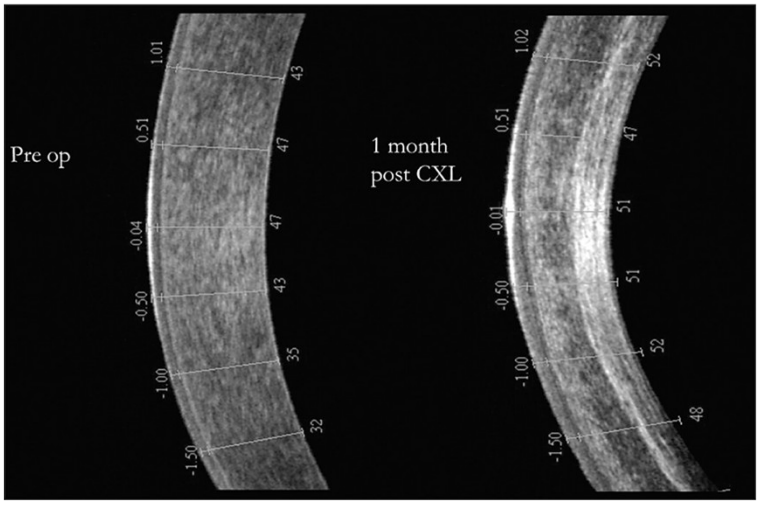
Post-CXL: CL Fitting Considerations?

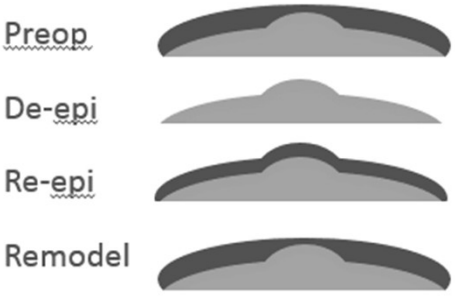




Chang CY, Hersh PS. Corneal collagen cross-linking: a review of 1-year outcomes. Eye Contact Lens. 2014 Nov;40(6):345-52.

Post-CXL: CL Fitting Considerations?

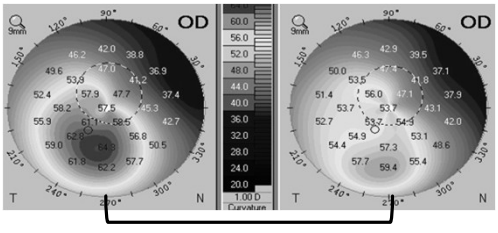




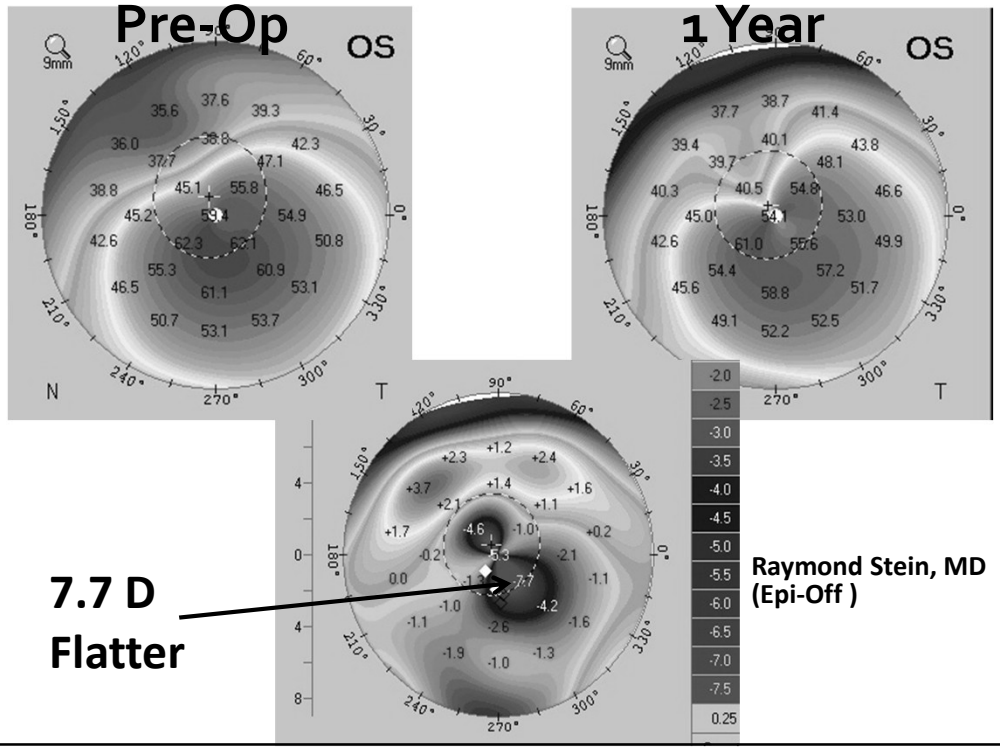
Rocha KM, Perez-Straziota CE, Stulting RD, Randleman JB. Epithelial and stromal remodeling after corneal collagen cross-linking evaluated by spectral-domain OCT. J Refract Surg. 2014 Feb;30(2):122-7.

Post-CXL: When to Start CL Fitting?

- Scleral lenses significantly improve BCVA and visual functioning and vr-QoL[1]
- Initial apical epithelial hyperplasia & subsequent remodeling may continue up to 12-24 months
  - My personal protocol: allow approx 4 weeks after CXL before consider refit
    - Ideally, patient RTC at 4 weeks with habitual lens to examine fit & VA
    - If acceptable, wait longer to allow for more corneal regularization prior to new CL fitting
    - If non-functional or new CL wearer, consider CL fitting (or at least CL refraction)
    - Many advanced contact lens options exist today, but may need to increase follow-up frequency during the first 12 months after CXL



1. EO Kreps, K Pesudovs, I Claerhout, C Koppen. Mini-Scleral Lenses Improve Vision-Related Quality of Life in Keratoconus. Cornea. 2021 Jul 1;40(7):859-864



Post-CXL: When to Start CL Fitting?

Figure 1: 3-point-touch type of fitting of rigid gas-permeable lens before corneal cross-linking

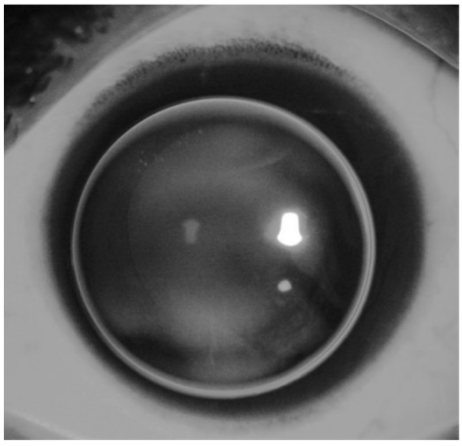
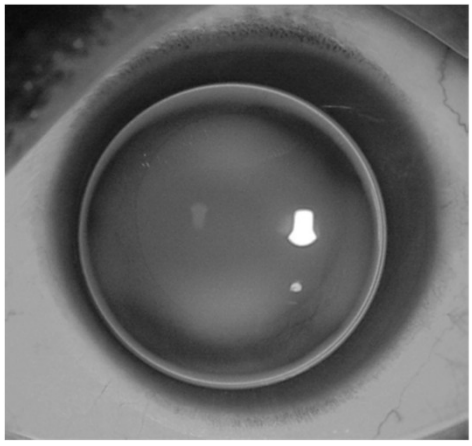


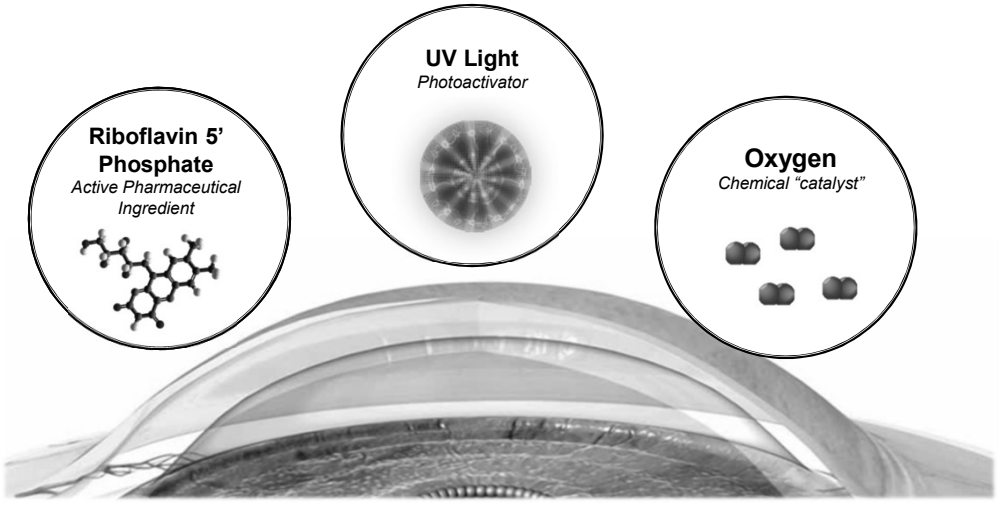
Figure 2: The same patient of Figure 1 showing pooling of fluorescein with rigid gas-permeable lens after corneal cross-linking as seen using Wratten filter



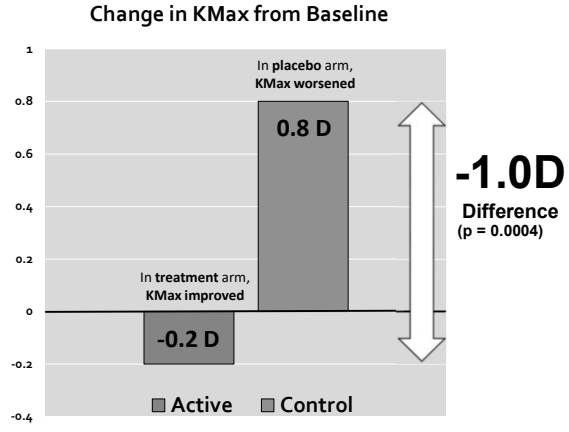
1. Mandathara PS, Kalaiselvan P, Rathi VM, Murthy SI, Taneja M, Sangwan VS. Contact lens fitting after corneal collagen cross-linking. Oman J Ophthalmol. 2019 Oct 11;12(3):177-180.

Enhancing CXL Mechanism of Action

- Corneal collagen cross-linking combines UV light + Riboflavin (vitamin B2) drops
- *UV light and oxygen activate the pharmaceutical agent to form additional covalent bonds within the intracellular matrix of the collagen stroma (= corneal stiffening)*



Glaukos Epi-On US Phase III Pivotal Trial : Top Line Outcomes



Randomized Controlled Trial

- enrolled **279 eyes** with documented progressive keratoconus (189 Epi-on treatment; 90 placebo control)

Achieved primary efficacy outcome

- by demonstrating **-1.0 D** difference in change in Kmax from baseline in treated vs. placebo arms at 6 months (p=0.0004).

Well-tolerated procedure

- majority of adverse events were mild and transient in nature; no change in corneal endothelial cell counts over course of trial.
- **98%** of placebo eyes elected to cross-over for Epi-on treatment

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

43RD CONGRESS OF THE ESCRS 12-16 SEPTEMBER 2025
COPENHAGEN 2025
Bella Center, Copenhagen - Denmark

Clinical Outcomes Of Topography-Guided Oxygen-Supplemented Transepithelial-Accelerated Corneal Crosslinking For Progressive Keratoconus

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David Gunn,[1] FRANZCO, MBBS(Hons)
Clark Y. Chang[2] OD, MSA, MSc

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[2]Wills Eye Hospital, Cornea Service, Philadelphia, Pennsylvania.

STUDY OVEVIEW

PURPOSE

To investigate how topography-guided epithelium-on crosslinking (customized epi-on CXL), along with oxygen supplementation, impacts procedural efficacy and the improvement in best corrected visual acuity (CDVA) among patients with progressive keratoconus (KCN).

STUDY OVERVIEW

In this retrospective study, we enrolled patients with progressive keratoconus (KCN) who had undergone oxygen-supplemented, topography-guided epithelium-on crosslinking (Epi-on CXL) using the Mosaic system (Glaukos, Burlington, MA).

Outcome measures:

- Corrected distance visual acuity (CDVA)
- Maximum keratometry (Kmax)
- Regularization index

At baseline and 12 months

*Evidence of KC progression defined as (*within 12 months postoperatively)
- increase in myopic spherical equivalent of 0.50 diopters (D) or greater,
- increase in astigmatism of 1 D or greater,
- increase in Kmax of 1 D or greater
- increase in the mean simulated keratometry in the central 3.0mm zone of 1 D or greater

CONCLUSION

Oxygen-supplemented epithelium-on crosslinking (epi-on CXL) with customized UVA energy distributions, guided by the baseline topography, was shown to be effective in corneal stabilization and regularization across a wide range of keratoconus severity.

The results of this study demonstrate the sustained improvement of best corrected distance visual acuity, higher order aberrations, and corneal regularization index as well as corneal biomechanical stability in patients with progressive keratoconus, as observed at the 24+ months follow-up.

COPENHAGEN 2025

43RD CONGRESS OF THE ESCRS 12-16 SEPTEMBER 2025

COPENHAGEN 2025

Bella Center, Copenhagen - Denmark

CORNEAL BIOMECHANICAL CHANGES IN PROGRESSIVE KERATOCONUS AFTER OXYGEN SUPPLEMENTED TRANSEPITHELIAL ACCELERATED CORNEAL CROSSLINKING

SIX MONTHS OUTCOMES

Brendan Cronin, MBBS (Hons), DipOphthSci, B.Com, FRANZCO

QUEENSLAND EYE INSTITUTE, BRISBANE, AUSTRALIA

No relevant conflicts of interest to declare.

COPENHAGEN 2025

Customized Remodeled Vision (CurV)
Topo-guided Epi-On CXL

avedro

Treatment Plans

O_2 Epi-On CXL (Group 1)

Broad zone treatment

Same energy level across the treatment zone

O_2 Topo-guided Epi-On CXL (Group 2)

Customized to patient's Specific corneal topography

Variable energy levels across the treatment zone

Cone localized treatment

94

QUEENSLAND eye INSTITUTE

DR BRENDAN CRONIN OPHTHALMOLOGIST

ASCRS ANNUAL MEETING APRIL 22–26, 2022 | WASHINGTON, D.C.

CONCLUSIONS

- Dynamic Scheimpflug analyzer can provide in-vivo biomechanical evidence of CXL efficacy that may assist in determining the viability of novel CXL techniques.

95

- In our study of 2 different oxygen-supplemented, pulsed (1:1) transepithelial accelerated CXL, significant corneal stiffening was observed at 6 months after both O_2 epi-on CXL and Topo-guided O_2 epi-on CXL.

Corneal Transplants: Modern Day Risk Factors

- "Future research should examine if young patients with these conditions may benefit from more frequent follow-up and/or early CXL to reduce the need for subsequent keratoplasty." [1]
- N.B. – Atopic diseases & Down syndrome were not associated with higher risk of KP in the study[1]

Logistic Regression Co-variates		Odds Ratio (95% CI, Univariate Model)	P value
Age (Reference 10 - 19 Yrs)			
	20 – 29 Yrs	1.87	< 0.001
	30 – 39 Yrs	1.81	<0.001
	40 – 49 Yrs	1.70	<0.001
Ocular Conditions			
	Corneal Hydrops	3.19	< 0.001
	Glaucoma	0.56	<0.001
	Contact Lens	0.70	<0.001
Systemic Conditions			
	Leber Congenital Amaurosis	2.23	0.059
	Sleep Apnea	1.63	<0.001
	Diabetes Mellitus	1.27	<0.001
	Depression	1.26	0.004

1. Thanitcul C, Varadaraj V, Canner JK, Woreta FA, Soiberman US, Srikumaran D. Predictors of Receiving Keratoplasty for Keratoconus. Am J Ophthalmol. 2021 Nov;231:11-18.

Reduction of Corneal Transplant Utility

Oslo University Hospital

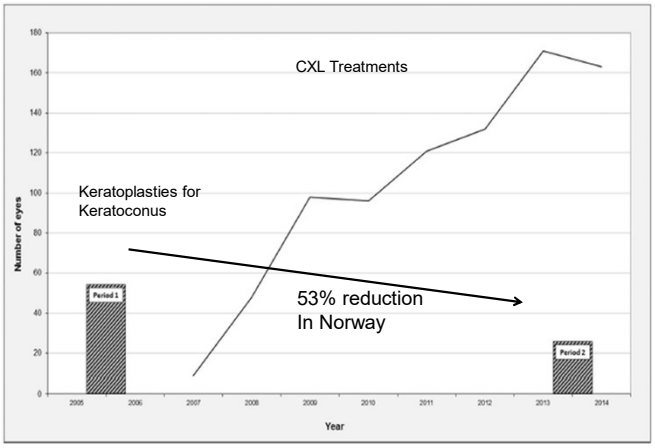

FIGURE 1. The annual number of CXL treatments from 2007 to 2015 (blue line), and the number of keratoplasties for keratoconus in period 1 (2005–2006) and period 2 (2013–2014).

Sandvik et al., Cornea 2015;34:991–995

Questions?
Thank you

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