

CAUTION, STEEP HILL AHEAD: MANAGING KERATOCONUS IN CLINICAL PRACTICE: ARE YOU READY TO CONQUER KERATOCONUS?

MELISSA BARNETT, OD, FAAO, FSLs, FBCLA
SHALU PAL, OD, FAAO, FSLs, FBCLA, FIAOMC




Image credit: Tom Arnold, OD

1

KC DEFINITION

- Abnormal topography:
 - Skew deviation
 - Corneal curvature measure $\geq 48D$
 - Hemi-meridional steepening
- Abnormal posterior shape:
 - OCT
 - Tomography
- Abnormal corneal thickness and distribution
- Clinical noninflammatory corneal thinning


Image credit: Tom Arnold, OD

5

KC DEFINITION

According to the 2015 Global Consensus on Keratoconus and Ectatic Disease, mandatory findings to diagnose keratoconus are:

1. Abnormal posterior ectasia
2. Abnormal corneal thickness distribution
3. Clinically non-inflammatory corneal thinning



Gomes JA, et al. Cornea. 2015 Apr;34(4):559-69.

6

NORMAL STROMA

- Helix to microfibrils to fibrils to lamella
 - Natural crosslinking to keep it strong
- Orthogonal in the center and circumferential in the periphery
- Interweaving at the front and stacking in the back
 - Strong Bowmans, weaker posterior

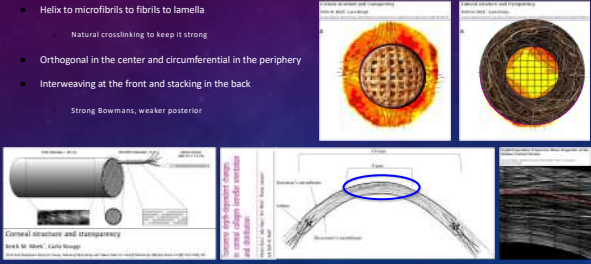
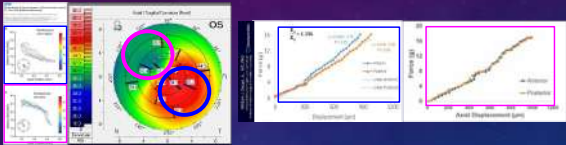


Image credit: Tom Arnold, OD

7

KERATOCONUS BIOMECHANICS

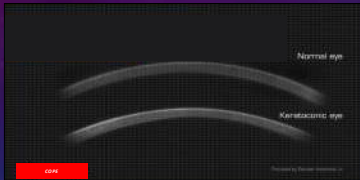


- Scarcelli: Brillouin Microscopy: Focal weakness
- Dupps: Optical Coherence Elastography: Anterior weakening, homogeneous

Image credit: Tom Arnold, OD

8


VISUALIZATION OF KERATOCONUS VS NORMAL



- High Speed Scheimpflug Video Comparison

Image credit: Tom Arnold, OD

9



KC DEFINITION


- Abnormal topography:**
 - Skew deviation
 - Corneal curvature measure $\geq 48D$
 - Hemi-meridional steepening
- Abnormal posterior shape:**
 - DCF
 - Tomography
- Abnormal corneal thickness and distribution**
- Clinical noninflammatory corneal thinning**

National Eye Institute, National Institutes of Health
Photo Tom Arnold, MD

10

KC DEFINITION

- Abnormal posterior ectasia
- Abnormal corneal thickness distribution
- Clinically non-inflammatory corneal thinning



Gomes JA, et al. Cornea. 2015 Apr 1;34(4):399-69.

11

Keratoconus:

A sight-threatening disease

Previously estimated 1:2000 (1986 US), more recent estimate 1:375 (2017 Netherlands)

1 out of 5 people with keratoconus will need a corneal transplant

Awareness is growing

"He was getting worse, we kept going to the doctor and saying 'Hey, he is really struggling with this'"
April 5, 2019


"For all his career, his life even, Steph Curry has had issues with his eyes. He said he has a condition called Keratoconus"
The Advocate - April 5, 2019



12

PREVALENCE AND RISK FACTORS FOR KC GLOBALLY

- Meta-analysis**
 - 29 articles
 - 7,158,241 participants
 - 15 countries
- Prevalence of KC in the whole population**
 - 1.38 per 1000 population
- In studies reporting sex prevalence of KC**
 - Men - 20.6 per 1000
 - Women - 18.33 per 1000



Hossein H, Heydari, S, Hooshmand, E, et al. The Prevalence and Risk Factors for Keratoconus: A Systematic Review and Meta-Analysis. Cornea. February 2020, Volume 39, Issue 2, 249-270.

13

INCIDENCE AND PREVALENCE OF KERATOCONUS

Reference	Prevalence	Geography
Kennedy et al. 1986	0.05% or 1:2000	US
Jonas et al. 2009	2.3%	India
Milodot et al. 2011	2.5%	Israel
Xu et al. 2012	0.9%	China
Hosheini et al. 2014	2.5%	Iran
Godtfredt et al. 2017	0.26% or 1:375	Netherlands
Tamara Nieto et al. 2018	4.78%	Saudi Arabia
Chen et al. 2020	1.2% or 1:84	Australia
Hosheini et al. 2020*	0.14% or 1:700	Global Meta-Analysis

1:2000¹
Based on a registration study in Olmsted County, Minnesota, conducted between 1935-1992; diagnosis was based on the detection of scissors reflex with retinoscopy and keratometry outcomes

1:375²
4.4 million patients in the Netherlands from a mandatory health insurance data base; topography utilized

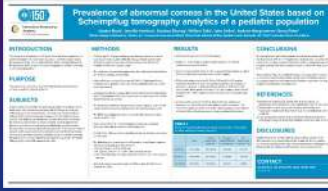
Hosheini H, et al. Cornea. 2020 Feb 1;39(2):263-70.

Kennedy RA, Bourne WM, Dyer JA. Am J Ophthalmol 1986;101(3):267-73.
Godtfredt DA, et al. American journal of ophthalmology. 2017 Mar 1;175:169-72.

14

NEW US BASED PREVALENCE STUDY

- IKA & ICO United States Pediatric Data
- Prevalence of 1:352
- Why? ADVANCED SCREENING DEVICES!!!



15

HOW COMMON IS KERATOCONUS?

American Journal of Ophthalmology
Volume 163, Issue 3, March 1996, Pages 267-271

A 48-Year Clinical and Epidemiologic Study of Keratoconus
Robert H. Kennedy W.D., William M. Brazner M.D., John A. Coar M.D.

1 in 2,000

Age-specific Incidence and Prevalence of Keratoconus: A Nationwide Registration Study

DANIELE A. GORRONELO, G. ARDINE DE VITO, CLAUDIO L. LUTERWAL, SAMUELE BORDO, AND ROBERTO FA. VIGORE

1 in 375

Ophthalmology
Publishes in Advance 2020
In Advance Online First


Prevalence of Keratoconus Based on Scheimpflug Imaging: The Raine Study

1 in 84

16

COMORBID CONDITIONS IN KC

- Allergic rhinitis
- Asthma
- Atopic dermatitis
- Aortic dissection
- Sleep apnea
- Collagen vascular diseases
- Diabetes
- Mitral valve prolapse
- Down syndrome




Moore JY, Lee J, Park YH, et al. "Incidence of Keratoconus and Its Association with Systemic Comorbid Conditions: A Nationwide Cohort Study from South Korea", Journal of Ophthalmology, vol. 2020, Article ID 3493654, 6 pages, 2020. <https://doi.org/10.1155/2020/3493654>

18

COMORBIDITIES IN KC


- Vigorous eye rubbing
- Atopy
- Ocular allergies
- Eczema
- Floppy eyelid syndrome
- Ethnicity
- Pregnancy



19

EYE RUBBING AND KC

- Chronic abnormal eye rubbing is associated with KC
- Repetitive gentle and vigorous knuckle-grinding rubbing associated with progression of KC



- Rabinowitz
- Case-control study
- 218 KC patients
- 183 healthy age-matched controls
- Eye rubbing present in 83% of KC patients compared to 58% controls

Rabinowitz YG, Sakic V, Tello A, Ruzick D, Garcia JD. Genetics of chronic corneal mechanical trauma in the etiology of keratoconus. Exp Eye Res. 2021 Jun;207:108328. doi: 10.1016/j.exer.2020.108328. Epub 2020 Oct 24. PMID: 32888532

20

ASSOCIATION BETWEEN SLEEP APNEA AND KC

- Meta-analysis *Optometry and Vision Science*
- Between 2012 and 2016 and involving 33,844 subjects (16,922 patients with KC, 16,922 controls)
- KC 1.8x more likely to have sleep apnea than general population
- Prevalence of sleep apnea in the general population around 5% (many likely underdiagnosed)
- Sleep apnea in around 9% of pts with KC¹
- With severe sleep apnea, risk of death 1.5- 2x higher than those without KC²
- Use of a CPAP device in those with severe disease significant increase in QOL³

1. Pellegrini M, Bucchieri G, Frascarelli A, et al. Obstructive Sleep Apnea and Keratoconus: A Systematic Review and Meta-analysis. Optom Vis Sci. 2020 Jun;97(5):514-524. doi: 10.1097/OPT.0000000000001167. PMID: 31892272.
2. Fildes RA. Obstructive sleep apnea severity and obstructive sleep apnea in keratoconus. Contact Lens Spect. 2013;28(1):24-28. doi: 10.1097/CLS.0b013e318281705c. PMID: 23921493.
3. Boudreau S, Boudreau R, Fortin CA, et al. Impact of continuous positive airway pressure (CPAP) on quality of life in patients with obstructive sleep apnea (OSA). J Sleep Res. 2016 Jun;25(6):753-758. doi: 10.1111/jsr.12346. Epub 2016 May 10. PMID: 26941171. https://doi.org/10.1111/jsr.12346

21

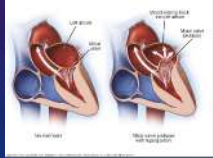
MITRAL VALVE PROLAPSE (MVP)

Occurs when valve between the heart's left atrium and left ventricle doesn't close properly

During MVP, the valve bulges (prolapses) upward, or back into the atrium

Prevalence 2-3%

Treatment may or may not be indicated

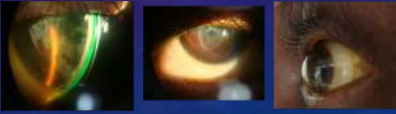


Rahimovskikh T, Zubov M. "Association Between Acute Corneal Melthion in Patients with Keratoconus and Mitral Valve Prolapse". Contact Lens Spect. 2011; 36(7): 154-157

22

HYDROPS AND MITRAL VALVE PROLAPSE

- Hydrops affects 5% patients with KCN
- Prevalence of mitral valve prolapse in patients with corneal hydrops due to KC is 65%

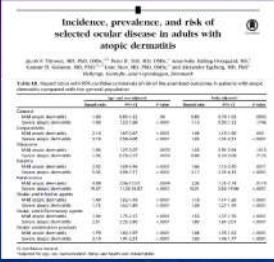


Rabbanihah, J, Zahra, M. "Association Between Acute Corneal Hydrops in Patients with Keratoconus and Mitral Valve Prolapse." Cornea 2011, 30(2): 154-157.

23

ATOPIC DERMATITIS


- Atopic Dermatitis
 - Danish registry study
 - Allergists exploring associated eye diseases
 - Mild AD: 3.06 Hazard ratio
 - Severe AD: 10.01 Hazard ratio
 - 100x more likely to have KC



24

RISK FACTORS FOR KC

- Age
- Genetics
- Family history



25

PATHOGENESIS OF KC

Evidence of the role of VXX1 and SOD1 (1%) in the pathogenesis of KC

Highlighting the effect of genetic factors


Autosomal dominant and sporadic pattern most common pattern in familial KC

26

COMORBIDITIES IN KC

- Down syndrome
- Connective tissue disorders
- Marfan syndrome
- Ehlers-Danlos syndrome

Wing span much greater than height
Long and slender fingers/toes
Hyperflexibility of joints
Long narrow face



27

GENETIC DISEASES

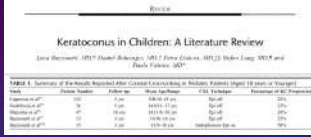
- Down Syndrome:** 622% increased risk = always screen
 - Collagen-related abnormalities and KC linked to chromosome 21
 - Down syndrome may be associated with more eye rubbing and possibly also a higher frequency of atopy
 - Thinner corneas in Down syndrome without manifest keratoconus
- Ehlers Danlos**
 - Associated with generalized corneal thinning and Keratoconus
 - SNPs of consistently associated with keratoconus in case-control panels as well as in a familial panel.



28

PEDIATRIC KC

- Literature review
- KC greatest incidence in Middle-Eastern populations
 - Incidence:** 1/2,000 (not prevalence)
- Epithelium-off CXL as soon as disease progression
- PK more common technique of pediatric keratoplasty
 - Deep anterior lamellar keratoplasty ideal surgical option due to healthy endothelium
- KC in children is more aggressive than that in adults
- To preserve good visual acuity, early diagnosis and appropriate treatment is crucial



Buzonetti L, Bhringer D, Liskova P, et al. Cornea. 2020;39(11):1721-1727. doi: 10.1097/ICO.0000000000002420

29

PREGNANCY

- Change due to rise in pregnancy-related hormones (estrogen and relaxin)
- Alter the biomechanical properties of the cornea and increase its refractive power

30

PREGNANCY AND KC

- 100% of eyes in the pregnancy group experienced significant KC progression
- None of the control eyes demonstrated disease progression
- No evidence of reversal after pregnancy
- No long-term follow-up data

Badrinar M, Jafarizad A. Topographic, tomographic, and biomechanical corneal changes during pregnancy in patients with keratoconus: a cohort study. Acta Ophthalmol.

31

PREGNANCY AND KC

- Case-controlled report
- 22 patients with bilateral KC
- 11 intended to become pregnant
- 11 did not intend to become pregnant
- Compared refractive and topographic data
 - Before pregnancy
 - During the third trimester
 - 6 months postpartum

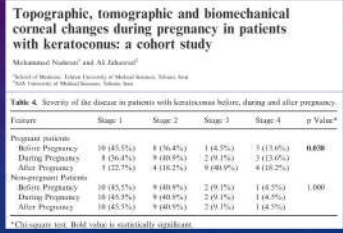


Table 4. Severity of the disease in patients with keratoconus before, during and after pregnancy.

Patients	Stage-1	Stage-2	Stage-3	Stage-4	p Value*
Pregnant patients					
Before Pregnancy	10 (45.5%)	8 (36.4%)	1 (4.5%)	3 (13.6%)	0.038
During Pregnancy	8 (36.4%)	9 (40.9%)	2 (9.1%)	3 (13.6%)	
After Pregnancy	1 (4.5%)	4 (18.2%)	9 (40.9%)	8 (36.4%)	
Nonpregnant Patients					1.000
Before Pregnancy	10 (45.5%)	8 (40.9%)	2 (9.1%)	1 (4.5%)	1.000
During Pregnancy	10 (45.5%)	8 (40.9%)	2 (9.1%)	1 (4.5%)	
After Pregnancy	10 (45.5%)	8 (40.9%)	2 (9.1%)	1 (4.5%)	


*Chi-square test. Bold values is statistically significant.

Badrinar M, Jafarizad A. Topographic, tomographic, and biomechanical corneal changes during pregnancy in patients with keratoconus: a cohort study. Acta Ophthalmol.

32

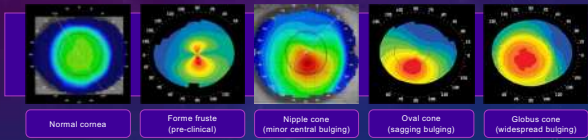
FACTORS THAT REDUCE KC RISK

- Smoking
 - Reduced prevalence in KC patients
 - Smoking may increase corneal collagen cross-linking
- Diabetes
 - Diabetic hyperglycemia may increase corneal collagen cross-linking
 - Diabetic patient with KC have less severe disease



33

CORNEAL TOPOGRAPHY IN KC



Normal cornea Forme fruste (pre-clinical) Nipple cone (minor central bulging) Oval cone (sagging bulging) Globus cone (widespread bulging)

41

ECONOMIC IMPACT OF KC

- Modeled a hypothetical cohort of people with clinically significant KC
- Defined by the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study
- Included costs of
 - Clinic visits
 - Fitting fees
 - Contact lenses
 - Surgical procedures
 - Complications
- Survival curves of corneal transplants and complications
- Modeled using data from the 2007 Australian Graft Registry

The Lifetime Economic Burden of Keratoconus: A Decision Analysis Using a Markov Model

REINALD L. REBERTSCH, STEVEN AC KEMIS, JEFFREY J. WALLINE, AND MAE G. GORDON

Rebertsch RL, Kemis SA, Walline JJ, Gordon MO. The lifetime economic burden of keratoconus: a decision analysis using a markov model. Am J Ophthalmol. 2011; May;151(5):768-773.e2. doi: 10.1016/j.ajo.2010.10.034. Epub 2011 Feb 18. PMID: 21330364; PMCID: PMC3074341.

42

ECONOMIC IMPACT OF KC

- Expected value of the lifetime cost of the treatment of KC over myopia **\$25,168**
- Factors that most influenced the lifetime cost
 - Probability of initial corneal transplant
 - Subsequent regraft
- Combining corneal transplant with the significantly impaired vision-related QoL and relatively young onset of disease
- Expected lifetime cost of treatment of KC
 - Significant cost to patients and payors
- Economic burden of the treatment of KC represents a significant public health concern


The Lifetime Economic Burden of Keratoconus: A Decision Analysis Using a Markov Model

REINALD L. REBERTSCH, STEVEN AC KEMIS, JEFFREY J. WALLINE, AND MAE G. GORDON


Rebertsch RL, Kemis SA, Walline JJ, Gordon MO. The lifetime economic burden of keratoconus: a decision analysis using a markov model. Am J Ophthalmol. 2011

43

ECONOMIC BURDEN OF KC



Patients pay more than \$25,000 for cost of care over their lifetime post-diagnosis



46% of patients pay more than \$1,000 annually for treatment costs

Source: <https://www.nkcf.org/living-keratoconus/>

44

CHANGES IN THE QUALITY-OF-LIFE OF PEOPLE WITH KERATOCONUS

- Evaluated changes that occurred in V-QoL over 7 years of follow-up.
- Prospective study
- 1,166 participants for seven years

Changes in the Quality-of-Life of People with Keratoconus

REBERTSCH RL, KEMIS SA, WALLINE JJ, GORDON MO. CHANGES IN THE QUALITY-OF-LIFE OF PEOPLE WITH KERATOCONUS: A PROSPECTIVE STUDY OF SEVEN YEARS OF FOLLOW-UP. Ophthalmology. 2010;117(12):2315-2322.

Rebertsch RL, Kemis SA, Walline JJ, Gordon MO. Changes in the quality-of-life of people with keratoconus: a prospective study of seven years of follow-up. Ophthalmology. 2010;117(12):2315-2322. doi: 10.1016/j.ophtha.2010.04.024. Epub 2010 Jun 24.

45

CHANGES IN THE QUALITY-OF-LIFE OF PEOPLE WITH KERATOCONUS

- All scales showed modest decline except ocular pain and mental health.
- Baseline factors were not associated with longitudinal change in NEI-VFQ scores.
- Significantly larger declines in V-QoL associated with
 - 10 letter decline in high-contrast binocular VA
 - 3.00D increase in corneal curvature
- In multivariate analysis, factors associated with a 10-point decline in NEI-VFQ scale scores.
 - KCN is associated with significantly impaired V-QoL that continues to decline over time.

Changes in the Quality-of-Life of People with Keratoconus

REBERTSCH RL, KEMIS SA, WALLINE JJ, GORDON MO. CHANGES IN THE QUALITY-OF-LIFE OF PEOPLE WITH KERATOCONUS: A PROSPECTIVE STUDY OF SEVEN YEARS OF FOLLOW-UP. Ophthalmology. 2010;117(12):2315-2322.

Rebertsch RL, Kemis SA, Walline JJ, Gordon MO. Changes in the quality-of-life of people with keratoconus: a prospective study of seven years of follow-up. Ophthalmology. 2010;117(12):2315-2322. doi: 10.1016/j.ophtha.2010.04.024. Epub 2010 Jun 24.

46

QUALITY OF LIFE IN PATIENTS WITH KC

- National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25)
 - 30 patients with KCN
 - 20 RGP wearers
 - 10 non-contact lens wearers
 - 30 healthy patients (control group)

Research Article

Vision Related Quality of Life in Patients with Keratoconus

SIVDA, APTEVA, KEMIS, ALBERT ALBA, TAYLOR GREGG, TRAVIS ALBERT, AND TRAVIS BERGER

Sivda RA, Apte VA, Kemis SA, Albert AL, Taylor G, Gregg T, Albert T, Berger T. Vision related quality of life in patients with keratoconus. Ophthalmology. 2010;117(12):2315-2322. doi: 10.1016/j.ophtha.2010.04.024. Epub 2010 Jun 24.

47

QOL KC

- CL wearers had better BCVA compared with non-CL wearers (P = 0.028)
- ★ Vision related quality of life worse in patients with KC
 - Success with CLs and maintaining better visual acuity may improve vision related quality of life.

Research Article
Vision Related Quality of Life in Patients with Keratoconus
 Serda Aydin Korum,¹ Ahmet Altun,² Tugba Gencoglu,³ Sezen Altunay,⁴ and Ferihs Tengiz⁵
¹Tugba Aydin, MSc, MEd, PhD, and Ferihs Tengiz, MD, PhD, Department of Ophthalmology, Faculty of Medicine, Istanbul Kültür University, Istanbul, Turkey
²Ilhan University of Health Sciences, Department of Ophthalmology, Istanbul, Turkey
³Ilhan University of Health Sciences, Department of Ophthalmology, Istanbul, Turkey
⁴Ilhan University of Health Sciences, Department of Ophthalmology, Istanbul, Turkey
⁵Ilhan University of Health Sciences, Department of Ophthalmology, Istanbul, Turkey

Table 2. Mean VQOL scores according to the groups (P = 0.001, **P < 0.001).

Visual Function	Keratoconus group	Control group	P
General health	85.0 ± 20.4	79.7 ± 15.9	0.001*
Visual vision	88.5 ± 24.4	80.7 ± 20.4	0.001**
Visual pain	94.0 ± 10.4	78.4 ± 17.0	0.001*
Specialized vision	74.5 ± 21.0	85.5 ± 15.0	0.001**
Distance vision	84.0 ± 18.5	84.7 ± 8.7	0.38
Near vision	85.0 ± 23.5	80.7 ± 15.8	0.001**
Visual disability	85.0 ± 27.4	80.7 ± 15.8	0.001**
Health & Well-being	77.2 ± 26.4	80.4 ± 21.0	0.001**
Dependence	84.7 ± 26.4	80.4 ± 21.0	0.214
Living vision	80.0 ± 17.0	81.4 ± 8.0	0.313
Functional vision	88.7 ± 17.4	81.4 ± 8.7	0.001**
Overall composite score	73.1 ± 17.7	81.2 ± 15.0	0.001**

48

KCN: Old Mantra

Diagnose → Monitor → Spec/CL → PKP/DALK

49

KCN: New Mantra

Diagnose **Early** → Stop Progression → Rehabilitate VA

50

MODERN KERATOCONUS MANAGEMENT

- Diagnose Early
- Stop progression
 - CXL
- Improve Vision
 - Surgical procedures
 - Specialty contact lenses
- Monitor Often
- DALK vs PK as last resort

51

CORNEAL COLLAGEN CROSSLINKING

- Approved in the US April 2016
- FDA approved for progressive KC
- Revolutionary in the treatment of KC
- Several randomized controlled trials
- Safe and effective to halt ectatic progression

© 2016 American Medical Association. All rights reserved. From: Diagnosis to Therapeutics. KRC Month. August 2016. doi:10.1055/a-0684-100617. Published online 2016. doi:10.1055/a-0684-100617.

52

FDA-Approved iLink Cross-Linking Procedure For the Treatment of Progressive Keratoconus

Product Platform

Photrexa[®] Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution)¹
 and
 Photrexa[®] (riboflavin 5'-phosphate ophthalmic solution)¹
 are photoenhancers indicated for use with the
 iKXL[®] ultraviolet light delivery system in corneal collagen cross-linking
 Procedures.²

53

FDA-APPROVED ILINK CROSS-LINKING PROCEDURE

Indications

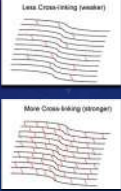
- Progressive Keratoconus & Corneal Ectasia Following Refractive Surgery (Post-LASIK Ectasia)

Procedure involves:

- Epithelium removal (Epi-off)
- 30 min riboflavin application & 30 min exposure 365 nm UVA light, 3.0 mW/cm²
- Intraoperative corneal thickness minimum: 400 microns

Activated riboflavin and reactive oxygen species interact in cornea to form crosslinks: stiffens cornea

- Laboratory studies suggest 328.9% increase in biomechanical rigidity⁴



54

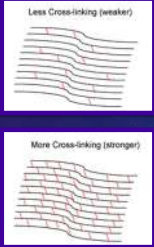

Mechanism of Action

Corneal collagen cross-linking combines the use of ultra-violet (UV) light and riboflavin (vitamin B2) drops.

The absorption of UVA by riboflavin generates radical riboflavin and singlet oxygen to form cross-links.¹

Corneal Cross-Linking:

- Creates new corneal collagen cross-links
- Results in a shortening and thickening of the collagen fibrils
- Leads to the stiffening of the cornea²

55

FDA-APPROVED ILINK CROSS-LINKING PROCEDURE

No other riboflavin solutions or UV devices have been FDA-approved for corneal cross-linking clinical use in the U.S.

Patients ages 14 – 65 were included in FDA studies


Cross-Linking not advised during pregnancy

Ulcerative keratitis can occur; most common ocular adverse reaction was corneal opacity (haze)

Other side effects may include punctate keratitis, corneal striae, dry eye, corneal epithelium defect, eye pain, light sensitivity, reduced visual acuity & blurred vision.






56

THE PROCEDURE



57


FDA-APPROVED ILINK CROSS-LINKING PROCEDURE SUMMARY

- Remove epithelium.
 
- Soak cornea with Photrexa® Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution).
 
 - 30 minutes
- Check for flare.
 
- Once flare is observed, measure corneal thickness.
 
 - If corneal thickness is less than 400 µm, instill 2 drops of Photrexa (riboflavin 5'-phosphate in ophthalmic solution) until the corneal thickness increases to at least 400 µm.
- Irradiate for 30 minutes.
 
 - Continue applying Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) during irradiation.

58

Patient Counseling

- Patients should be advised NOT to rub their eyes for the first five days after their procedure.
- Patients may be sensitive to light and have a foreign body sensation.
- They should be advised of possible discomfort in the treated eye and that sunglasses may help with light sensitivity.
- If patients experience severe pain in the eye or any sudden decrease in their vision, they should be advised to contact their eye care provider immediately.
- If the bandage contact lens that was placed on the patient's eye on the day of treatment falls out or becomes dislodged, the patient should be advised not to replace it and to contact their eye care provider immediately.



59

CROSS-LINKING HEALTH ECONOMICS MODEL

60

FDA-APPROVED ILINK REDUCES HEALTHCARE COSTS & INCREASES QALY

Compared to conventional treatment, FDA-approved cross-linking was associated with:

- Lower total direct medical costs (-\$8,677; \$30,994 vs. \$39,671) and more QALYs (quality-adjusted life years, 7.88; 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.

Scenario	ILINK Cost	CONV Cost	ILINK QALY	CONV QALY
Base	\$30,994	\$39,671	21.80	19.93
ILINK	\$22,317	\$39,671	21.80	19.93
CONV	\$30,994	\$39,671	21.80	19.93
ILINK + Prod	\$13,640	\$39,671	21.80	19.93
CONV + Prod	\$30,994	\$39,671	21.80	19.93
ILINK + Prod + OOP	\$9,392	\$39,671	21.80	19.93
CONV + Prod + OOP	\$30,994	\$39,671	21.80	19.93

61

ECONOMIC BENEFIT OF FDA-APPROVED CROSS-LINKING MAXIMIZED WITH EARLY INTERVENTION

Modeled Outcomes at Different Baseline Ages

- Intervention at a younger age maximizes both cost savings and QALYs gained.
- Scenario analyses where the baseline age was increased in 10-year increments indicated that the economic benefits of FDA-approved cross-linking decreased as patients' age at the time of treatment increased.

62

INSURANCE COVERAGE FOR FDA-APPROVED ILINK

63

Payer Coverage Status

FDA-approved cross-linking is broadly covered in the U.S.

- 6 National and
- 62 Regional Health Plans
- 96% of Commercial Lives Covered

All 50 states

For a comprehensive up to date list of increasing approved carriers, please visit www.livingwithkc.com

64

CORNEAL TRANSPLANTATION

65

Full thickness or penetrating keratoplasty (PK)

Full thickness corneal transplant

66

Modern day lamellar transplant surgery: Anatomically targeted replacement of corneal tissue

Epithelium
Bowman's layer
Stroma
Descemet's membrane
Endothelium

LSCT: Limbal epithelial Stem Cell Transplantation

DALK: Deep Anterior Lamellar Keratoplasty

DSAEK / DMEK: Posterior lamellar or endothelial Keratoplasty

67

Graft survival – how long the graft stays clear

Lower endothelial cell counts and hypoxia

PK 2007 657 cells/mm²

Endothelial cell density (cells/mm²)

Post-operative time (months)

Ambrósio J. Predicting endothelial cell loss and long-term graft survival. Invest Ophthalmol Vis Sci. 2003; 44: 3328-3331.

68

RISK OF GRAFT REJECTION

- Higher risk
 - Vascularized corneas
 - Previous rejection
 - Herpetic and ocular surface disease
- Lower risk
 - Non-vascularized corneas
- Endothelial rejection most common
 - Use corticosteroid drops for at least one year
 - Life long risk of rejection

Superior neovascularisation and edema

Khodadoust line

69

RISK OF GRAFT REJECTION

- Require routine monitoring, at least twice a year
- Recognize rejection and refer as emergency
- Any sign of inflammation (often atypical such as ciliary redness, cells in the anterior chamber, precipitates, edema)
- Reevaluate CL fit and material
- Ensure that the corneal physiology and the ocular surface are not disturbed by the lens (avoid hypoxia, inflammation, neovascularization)
- Inform patient of urgent symptoms = redness, photophobia, pain, decreased visual acuity
- Symptoms can occur anytime during lifetime

70

What are Intacs?

- 150° Arcs of PMMA (same as rigid lens)
- Placed between stromal layers
- Inner Diameter = 6.8 mm
- Outer Diameter = 8.1 mm
- Hexagonal-Shaped
- Intacs are
 - replaceable
 - removable
 - upgradable

71

How Intacs work

- Inserts Placed at least 70% Depth
- Inserts Separate Corneal Lamellae
- Results in a Shortened Corneal Arc Length
- The Central Cornea Flattens
- Thicker Inserts Increase Flattening

The diagram illustrates the mechanism of Intacs. On the left, a cross-section shows a pink Intacs insert being inserted into the stroma of the cornea, separating the lamellae. On the right, a 3D grid shows the cornea after insertion, which has become flatter. Below this, two diagrams of a human figure show the arc length of the cornea: a normal, curved arc on the left and a shorter, flatter arc on the right, labeled 'Normal Cornea' and 'Intacs' respectively.

72

Intacs FDA approval

- Approved for the treatment of Myopia in 1999
- Approved as a treatment for keratoconus in 2004
- Approved expanded range of sizes in 2010

Do Intacs make a specialty contact lens fit easier or more difficult?

73

IRREGULAR CORNEAS: WHERE DO I START?

A grid of six clinical photographs showing different types of corneal irregularities, such as keratoconus, keratic precipitates, and other corneal pathologies.

74

IRREGULAR CORNEAS: WHERE DO I START?

A grid of six clinical photographs showing contact lenses fitted on eyes with irregular corneas. The lenses are labeled: RGP, Piggyback, Recessed CL System, Soft/Soft KC, Hybrid, and Scleral.

75

WHY CHOOSE A CORNEAL GP?

- Rigid optics → Good vision!
- Wide range of parameters
- Easily obtained

A yellow diamond-shaped road sign with the text 'OPTIONS JUST AHEAD' in black letters, set against a background of a road stretching into the distance.

76

WHY CHOOSE A CORNEAL GP?

- Corneal lenses are less costly and often less complex than other CL options

Two rectangular road signs on a post. The top sign points to the right and says 'SIMPLE'. The bottom sign points to the left and says 'COMPLEX'.

77

MATERIAL CONSIDERATIONS

- High oxygen, but stable, materials
 - Usually high minus powers
 - Movement may be compromised
 - Stability important for good vision
 - Flexure
 - Warpage



78

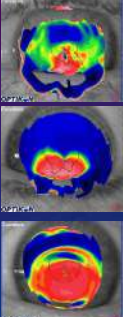
DESIGN CONSIDERATIONS

- Reverse Geometry Design
 - Oblate (periphery steep) cornea
 - Eg. post-RK
 - Normal Eye
- Prolate Design
 - Prolate (centrally steep) cornea
 - Eg. keratoconus

79

CONE TYPES


- Nipple (or central)
- Oval (usually inferior-temporal)
- Globus (or generalized)
- PMD (near lower limbus)
- Undefinable?



80

ASSESSING THE CONE

- Where?
- How large?
- How steep?



81

ASSESSING THE CONE

- Where?
 - Central: 28.7%
 - Off-center:
 - Below horizontal: 87.8%
- How large?
 - Nipple (3 mm): 28.7%
 - Oval (3-5.5 mm): 44.3%
 - Globus (5.0 mm or above): 6.7%
- How steep?

82


BASIC FITTING CONCEPTS

- Small, central cone (eg. Nipple cone)
 - small diameter (<9.0 mm)
- Larger, more decentered cone (eg. Oval cone)
 - larger diameter (10.0-12.0 mm)
- REALLY BIG or extremely decentered cone (eg. Globus or PMD)
 - really big!
 - Scleral/Mini-scleral design

83

BASIC FITTING CONCEPTS


- The steeper the cone:
 - Steeper the base curve
 - Smaller the back optic zone



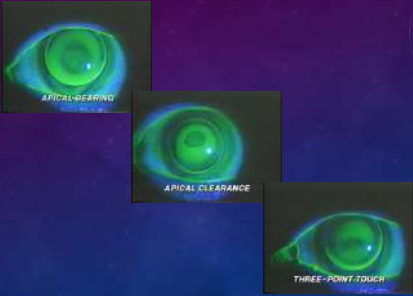
84

DIAGNOSTIC FITTING

- Start with central (apical) fit
 - Look for light (feather) touch



85



86

DIAGNOSTIC FITTING

- Start with central fit
- Second: peripheral fit
 - Only after central fit achieved
 - Flatten or steepen accordingly



87

CORNEAL GP COMFORT & KERATOCONUS

- No association with disease severity
- No association with apical (central) fitting relationship
- Minimal peripheral clearance may decrease comfort

Variables Affecting Rigid Contact Lens Comfort in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study Optom & Vis Sci, March 2004 81(3):382-388

88

PERIPHERAL CLEARANCE



- Minimal acceptable
- Average
- High acceptable

Variables Affecting Rigid Contact Lens Comfort in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study Optom & Vis Sci, March 2004 81(3):382-388

89

DIAGNOSTIC FITTING

- Start with central fit
- Assess peripheral fit
- Determine final lens diameter
 - Nipple cones
 - Start small (8.5-9.0 mm)
 - Steeper cone, go smaller
 - Oval cones
 - Increase OAD to aid centration
 - Decrease OAD to aid removal

90

DIAGNOSTIC FITTING

- Key performance characteristics
 - Centration
 - Pupil within back optic zone
 - Movement
 - "adequate" lens movement



91

PIGGYBACK (PB) LENS SYSTEM

- Definition
 - A corneal GP lens is placed over a soft lens
 - GP provides good vision
 - Soft:
 - Protects cornea
 - Improves comfort
 - Helps centration and stabilization of the lens



92

PIGGYBACK FITTING PRINCIPLES

- Improved GP and soft lens materials provide better oxygen permeability and prevent corneal edema and hypoxia
- Use high DK RGP lens and daily replacement soft lenses
- **Plus powered soft lens - flatten the RGP fit**
- **Minus powered soft lens - steepen the RGP fit**

93

ADVANTAGES

- Better comfort than standard RGP CL
- No corneal compromise or complications
- No hypoxia
- Improved comfort compared with RGP lens alone
- Same or increased wearing time vs. the RGP lens worn alone
- Same or better visual acuity

94

DISADVANTAGES

- More difficulty and inconvenience with piggyback lens system
- Loss of GP lens
- Damage to soft lens
- Multiple lens care systems

95

PIGGYBACK (PB) LENS SYSTEM

- Indications
 - Poor comfort with a corneal GP
 - Minor corneal abrasion with GP wear
 - Temporary use of soft lens

96


PIGGYBACK (PB) LENS SYSTEM

- Challenges
 - Extra cost
 - Extra hassle
 - Daily disposable soft minimizes added care

97

PIGGYBACK (PB) LENS SYSTEM


- Fitting Tips- Approach #1
 - Fit corneal GP first
 - Then fit "near plano" soft lens underneath
 - Good for temporary use (i.e. abrasion)



98

PIGGYBACK (PB) LENS SYSTEM

- Fitting Tips- Approach #2
 - Fit soft lens first
 - If steep cornea, fit minus lens
 - Provides flatter fitting surface
 - If flat cornea, fit plus lens
 - Provides steeper fitting surface
 - Then fit GP lens to front surface of SCL



99

CUSTOM SOFT LENSES

- Indications
 - Corneal GP intolerance
 - Mild to moderate corneal irregularities
 - Simple to transition from a soft toric contact lens
- Challenges
 - Vision may not be as good as that provided by rigid optics
 - Added thickness may lead to corneal hypoxia

100

Manufacturer	Contact Lens Name
ABB Optical Group	Concise K
	KeraSoft IC & KeraSoft Thin
Acculens	Soft K
Advanced Vision Technologies	Soft K & Soft K Definitive
	NaturaSOFT IC & ICR
Alden Optical	NovaKone & NovaKone Toric
Art Optical	KeraSoft Thin
Continental	Continental Kone
GP Specialists	YamaKone IC
Gelflex USA	Keratoconus Lens
Marietta	Soflex
Metro Optics	Revitaleyes & Revitaleyes Definitive
	KeraSoft Thin
Ocu-Ease, Optech	Ocu-Flex K
TruForm Optics	KeraSoft IC & KeraSoft Thin
United Contact Lens	UCL K-Lens
Visionary Optics	HydroKone & HydroKone Toric
X-Cal Contacts	Flexlens ARC & Flexlens Tri-Curve

SPECIALTY SOFT CONTACT LENSES FOR KERATOCONUS
TABLE ADAPTED FROM CLINICAL MANUAL OF CONTACT LENSES FIFTH EDITION AND THOMPSON ET AL

101

HYBRID LENSES

- Definition
 - Rigid center
 - Soft skirt
- Indications
 - Those who can't tolerate a corneal GP
- Challenges
 - Proper lens movement
- Empirical fitting

102

A Trip Beyond Limbus

Irregular Corneas: Evolution of Hybrid CL

Redefining Hybrid platform for irregular corneas

- Fitting Parameters: Central and junctional SAG depth
- Metabolic requirement: Higher gas diffusion constant (DK)
- Comfort/Cost/Compliance: Junctional adherence
- Comfort: Surface wetting chemistry

103

A Trip Beyond Limbus

Irregular Corneas: Evolution of Hybrid CL

104

A Trip Beyond Limbus

Irregular Corneas: Evolution of Hybrid CL

Proper Vault Maintains Semi-Sealed Environment 2 minute tear exchange

UltraHealth Lens Design

105

ULTRAHEALTH LENS DESIGN

106

EMPIRICAL FITTING

- Provide a topography (PDF or raw data) with the following information
- Keratometry readings
- Eccentricity data, often listed as E, E squared, CEI, Shape factor, or Q value
- Manifest Rx
- Prior RGP/Scleral base curve and power with over Rx
- HVID

107

EMPIRICAL FITTING

- A first lens will be designed and ordered from the measurements
- Alternatively, a first lens from the diagnostic set will be recommended as a starting point for an in-office fitting
- Ideal fit
- 100 microns clearance over apex
- After settling, 40-50 microns centrally and feather clearance at the inner landing zone (ILZ)

Microscopy fitting on ICC used to verify the fit. Note the thin bearing ring on the inner landing zone.

108

CLINICAL APPLICATIONS FOR HYBRID LENSES

- Corneal Ectasia
 - Off-center and central nipple cones
 - PRK/LASIK Ectasia
 - PMD
 - Keratoglobus
- Post-surgical Corneas
 - PKP
 - Intacs
 - Collagen Crosslinking (CXL)
- Post-refractive surgery
 - s/p corneal perforation
 - s/p RK/IK
 - s/p HSV stromal scar

Post SK (nodule removed) and INTACS
Image: Clark Chang, MD

Post INTACS
Image: Jeff Sormino, OD

109

SCLERAL LENSES

Photo credit: Tom Arnold, OD

110

MAIN SCLERAL LENS INDICATIONS

- Visual rehabilitation in irregular corneas
- Therapeutic treatment of ocular surface disease
- Correction of refractive error in normal or healthy eyes

111

SCLERAL LENS: INDICATIONS

- Corneal ectasias
 - Primary corneal ectasias
 - Advanced (notably decentered) keratoconus
 - Keratoglobus
 - Pellucid marginal degeneration
- Secondary corneal ectasias
 - Post-LASIK
 - Post-PRK
 - Post-RK

112

SCLERAL LENS: INDICATIONS

- Corneal transplants
- Trauma
- Corneal scars
- Corneal degenerations or dystrophies
 - Salzmann's nodular degeneration
 - Terrien's marginal degeneration

113

THERAPEUTIC SCLERAL LENS INDICATIONS

- Neurotrophic Keratitis
- Exposure Keratitis
- Dry Eye Syndrome
- Graft vs Host Disease
- Steven Johnson Syndrome
- Ocular Cicatricial Pemphigoid
- Chemical Burns
- Limbal Stem Cell Failure
- Sjogren's Disease
- Persistent Epithelial Defects

114

SCLERAL LENS INDICATIONS

- Inflammatory conditions
 - Limbal stem cell deficiency
 - Ocular cicatricial pemphigoid
- Neovascularization with hybrid lens designs
- Poor comfort with traditional gas permeable designs
- High refractive error

115

SCLERAL LENSES: CONTRAINDICATIONS

- Corneas with significant edema from reduced endothelial cell count
- Fuch's corneal dystrophy
- Glaucoma?

116

SCLERAL LENS EDUCATIONAL RESOURCES

- Increasing amount of literature corresponding with increased adoption
- First dedicated educational textbook

117

NEWEST SCLERAL LENS EDUCATIONAL RESOURCES

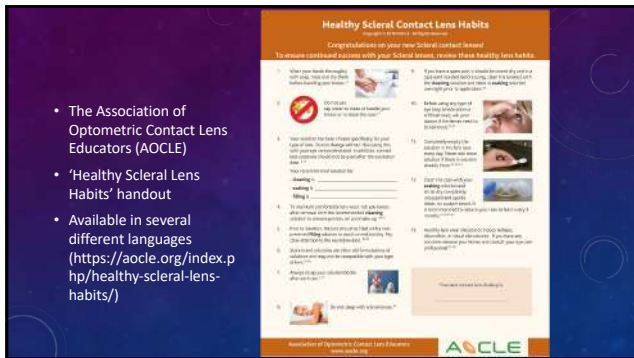
- Continued increase in publications
- Second dedicated educational textbook and new educational supplements

118

APPLICATION AND REMOVAL

- Difficulty with lens handling greater in scleral (63%) compared to rigid corneal lens wearers (40%)
- Scleral lens handling primary reason for scleral lens drop out
- Patient education materials are helpful

119



- The Association of Optometric Contact Lens Educators (AOCLE)
- 'Healthy Scleral Lens Habits' handout
- Available in several different languages (<https://aocle.org/index.php/healthy-scleral-lens-habits/>)

120



121

RINSE AND APPLICATION SALINE					
NaCl 0.9% Inhalation Solution	LacriPure (Menicon)	ScleralFil (B+L)	Nutrifill (Contamac)	VibrantVue Scleral Saline (ABB)	Puriflens (The Lifestyle Company)
No buffers, no preservatives	No buffers, no preservatives	Contains borate buffer, no preservatives	Phosphate buffer, no preservatives, contains electrolytes	No buffers, no preservatives	Contains borate buffer, no preservatives
Off-label	FDA approved	FDA approved	FDA approved	FDA approved	FDA approved
3 ml or 5 ml vials	5 ml vials	10 ml vials	10 ml vials	5 ml vials	4oz bottle
Available in box of 100 vials	Available in box of 30 vials	Available in box of 30 vials	Available in box of 30 vials	Available in box of 100 vials	Bottle replaced every 15 days

122

DISINFECTION AND STORAGE SOLUTIONS

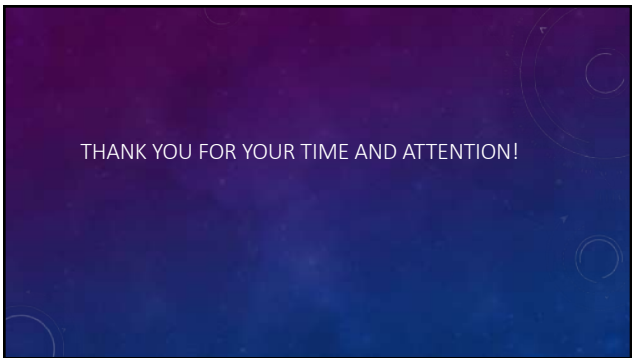
Reminder: avoid abrasive cleaners so as not to prematurely remove plasma or other surface treatments.

123

General Guideline Created by AOA/AAO/GPLI/CLMA. Joint publication in OVS.

TECHNICAL REPORT
 Technical Report: Guidelines for Handling of Multipatient Contact Lenses in the Clinical Setting

124



125