Managing Corneal Ectasia: Scleral Lenses and Corneal Collagen Cross Linking

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Disclosures

• Full time attending optometrist at Goodman Eye Center, a clinical trial site for CXL USA
• No other financial disclosures
Keratoconus

- Bilateral, asymmetric, non-inflammatory condition
- Progression is unpredictable → corneal thinning and protrusion → inducing highly irregular astigmatism
Advanced corneal findings
Treatment Options

1. Spectacles
2. Specialty Contact Lenses
3. Corneal Collagen Cross-Linking
4. Corneal Surgery
   - PKP, DALK, KPro
Scleral Lenses
Indications

• Best option for very steep/large ectasia
  – Pellucid Marginal Degeneration
  – Keratoglobus
  – Keratoconus with very steep topography

• Cons: difficult to fit, more expensive, more difficult I/R
Scleral Options

• Fenestrated or Non-fenestrated
  – Fenestrations will increase oxygen flow and create a bubble; more difficult to fit
• Toric Periphery
• Front surface torics (residual/lenticular astigmatism)
• Diameter ranges from 14.3 (mini-sclerals) to 20.2 full sclerals (24 PROSE)
• Materials: Dk as high as 141 with Boston XO₂
• Custom Sclerals:
  – Boston Foundation for Sight (PROSE)
  – EyePrint PRO: 3-D designed lens from custom mold of patient’s eye
Fitting Goals

- Complete Corneal Vault
- Scleral Alignment
- No impression ring
Curves of a Scleral Lens

- BASE CURVE / OZ
- PC1 - CORNEAL ZONE
- PC2 - LIMBAL ZONE
- PC3 - SCLERAL ZONE: LANDING CURVE
- PC4 - EDGE
- CORNEA
**Limbal Zone**

Figure (left): Excess central clearance with a bubble. Limbal bearing 360.

*Need to vault limbus to protect corneal stem cells.*

Figure (right): Completely clearing cornea, including the limbus, with 75 µ of vault.
Peripheral Fitting
Edge Lift

Excess edge lift:
• Pt sx: Awareness of edge in that region
• Bubbles in corresponding area
• Be sure to check for bubbles upon insertion
• Area for debris to enter reservoir → “foggy” vision
• Figure (left): Bubbles were not present on insertion
Conjunctival Blanching

- Indicating a tight periphery (scleral landing zone)
- Lens will have strong suction/difficulty removing the lens

If blanching causing a tight fit only in certain area, consider quadrant specific periphery or a toric periphery. If blanching is present 360, flatten the peripheral curves uniformly.
Pinguecula

- Vault lens periphery over pinguecula, or avoid it by keeping the diameter small enough not to impinge upon pinguecula
- You can also notch a segment of the periphery to avoid a pinguecula

*Note: figure on right shows tight periphery which will need to be flattened
Complications S/P Penetrating Keratoplasty

- Consider High Oxygen material eg Boston XO2
- Optimal peripheral fit to decrease suction
- Fenestration to increase Oxygen delivery
- Endothelial cell count prior to fitting
  - <700 cells/mm² preliminary corneal consult
- Average post graft cell count: 1000-2000
Mucous Debris

- Can be on surface of lens (left) or in reservoir (right).
- Greater degree of ocular surface disease → more problems with debris

Debris on surface:
- Cotton tip applicator with saline to wipe off

In Reservoir:
- Remove, clean and re-insert
- Try small amount of PF celluvisc in reservoir
- Make sure vault is not excessive
- Fix any areas of excess edge lift
Troubleshooting

• Reverse Geometry
  – PMD, post graft, oblate corneas (s/p refractive surgery)
• Diameter considerations
  • Weight (toricity in periphery

• Thickness
  – Residual astigmatism due to flexure
# Toric Peripheral Curve Capability

<table>
<thead>
<tr>
<th>Radius</th>
<th>Curve Width</th>
<th>Diameter</th>
<th>Sagittal Value</th>
<th>Sagittal Totals</th>
<th>Radius</th>
<th>Curve Width</th>
<th>Diameter</th>
<th>Sagittal Value</th>
<th>Sagittal Totals</th>
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<td></td>
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<tr>
<td>14.50</td>
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<td>18.0</td>
<td></td>
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<td>14.50</td>
<td>0.5</td>
<td>18.0</td>
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</table>

Total Diameter: 18.0
Total Sagittal Depth: 6.2048

C. Bruce Richardson Jr., FCOLSA
Houston, Texas
Follow Up Schedule

• 6 hour fit check: Make sure that the fit is still appropriate towards the end of the day.
• Check for adequate vault
• Rule out compression in periphery
• Check for staining (of conjunctiva and cornea) after lens removal
Starting a Keratoconus Fit
Large diffuse cones will usually require larger diameter KC lenses; ie Rose K IC

Small central nipple cones work well with small diameter lenses including Rose K 8.7 DIA
S/P Radial Keratotomy
Asymmetric PMD
EyePrintPRO™
Technology

- Custom imprint (mold) of patient’s eye with ocular safe polymer
- Mold provides basis for computer generated custom scleral shell
Contraindications

- Endothelial cells counts under 800
- Excessively elevated blebs
Advancements over conventional scleral lenses

- More rotationally stable → reproducible front surface toric
- Pinguecula: improved outcomes over notching
Optics

Uncorrected

Standard scleral lens

Front surface toric EyePrint Pro
Procedure

• D/C lens wear 2 days prior to imprint process
• In office imprint
• Lab manufacturing/shipping (2-3 weeks)
• Lathe manufacturing time 24 hours vs 10 min with conventional scleral
Surgical Treatment Options

• Corneal Collagen Cross Linking (CXL)
• Penetrating Keratoplasty (PKP)
• Deep Anterior Lamellar Keratoplasty (DALK)
• Keratoprosthesis (KPro)
Basic research: 1993-97 by Theo Seiler (IROC, Zurich)
First patients: 1998
Dresden protocol: 10-12mm epithelial debridement
Dresden Protocol

1. Complete epithelial debridement
2. Riboflavin 0.1% every 1-5 min for 15-30 minutes (or until Riboflavin present in AC)
3. Minimum corneal thickness 400 μ at start of UV light
4. UV light (370 nm) for 30 minutes
5. BCL until full epithelialization happens
6. Topical Ab QID until epithelialization
Cross-Linking Sites

- Over 500 centers worldwide
- Standard of care for KCN
- Patients as young as 9
- Investigational in the US
“Natural collagen cross-linking”:
- In vivo LYSYL OXIDASE catalyzes this process
  - Activates Oxygen from singlet to active triplet state
  - Causes oxidative deamination \( \rightarrow \) forms aldehyde group \( \rightarrow \) cross links with other aldehydes or amine groups (in Collagen molecules)
CXL – Basic Science

Photochemical Rxn:
Riboflavin + UVA light
• Activates Oxygen to triplet state that causes same oxidative deamination rxn → cross linking of aldehydes and amines in collagen molecules
  — Riboflavin is the “photosensitizer”
CXL – Basic Science Summary

- Corneal collagen fibers “cross-link” photochemically via the lysyl oxidative pathway or riboflavin/UVA application
  - Increased inter- and intra-fibrillar covalent bonds
- Change in the quaternary structure of the fibrils
  - Fibrils shorten, thicken
  - Fibrils move closer together
- Change in corneal elasticity
- Secondary change in GAG’s between fibrils
Animal Studies

UV + Riboflavin:

– New high-molecular-weight collagen polymer
– increased fiber diameter after cross-linking treatment
– Corneal rigidity increased by 329%
– Chemical stability of polymer indicates likely long-term corneal stability after treatment
Safety of Cross-Linking

Endothelium Damage threshold

With Riboflavin loading

3.00 mW/cm²

1.49 mW/cm²

0.74 mW/cm²

0.36 mW/cm²

0.18 mW/cm²

0.09 mW/cm²

0.06 mW/cm²
CXLUSA
Prospective Non-randomized Multicenter study evaluating Trans-epithelial ("Epi-On") CXL

• Physician-sponsored, IRB-approved clinical trial
• Proprietary UV light Source
• Enrolling patients since October 2009
• Initially started as Epithelial-Off then changed to Transepithelial in 2010.
Study Criteria

**Indications:**
- Keratoconus
- FFKC
- Pellucid Marginal Degeneration
- Post-LASIK ectasia
- RK with diurnal visual fluctuations

**Inclusion Criteria**
- Age 12 or older
- Corneal thickness >350 microns

**Exclusion Criteria**
- Visually significant apical scarring
- Pregnant/Breast Feeding
- History of Ocular Herpes Simplex Infection
CXL-USA International Sites

• Zurich, Switzerland
  Theo Seiler M.D.
  IROC - Institute for Refractive and Ophthalmic Surgery

• Brescia Italy
  Roberto Pinelli, M.D.
  Istituto Laser Microchirurgia Oculare

• Dublin, Ireland
  Arthur Cummings M.D.
  Wellington Eye Clinic
Study Information

• ClinicalTrials.gov ID NCT01189864
• Currently enrolling patients

Local Study Sites
(National Keratoconus Foundation)

• Stanford, Sacramento, San Leandro

http://www.nkcf.org/cxl-sites-in-usa-2013/#ca
Topography-Selecting Candidates
CXL - Technique

- Topical Tetracaine with BAK provided Q 15 min
  - Topical tetracaine during procedure for pt comfort
- Riboflavin 0.5% / gum cellulose Q 1 min
- Corneal absorption sponge
CXL - technique

• 15 - 90 minutes of Riboflavin drops required
  – Average ~ 50 minutes of Riboflavin instillation
• Homogeneous and complete stromal saturation with riboflavin
• Confirm saturation with slit lamp examination
• Check Pachymetry (confirm ≥ 400 μ)
• UVA applied x 30 minutes 3.0mW/cm2
CXL - Technique

- Bandage SCL x 24 hours
- Topical antibiotic qid x 1 week
- Topical steroids qid x 2 weeks, begin day 2
- Mild-moderate pain x 12-24 hours
- Topical tetracaine permitted for 24 hours
Homogeneity
Protocol Specifies Homogeneous Loading

This is Not
Concentration
Before Riboflavin Loading
Grade 0/V
Grade I/V
Grade III/V
Grade IV/V
Grade V/V
Epi-on “flare “
Epi-On CXL POD 1
Epithelial-Off CXL
Long Term Results

• 5 year study, 48 eyes (60 pts treated)
  - No patient had progression of ectasia
  • Mean improvement 2.87 D (average K)
  • Mean Improvement in BSCV by 1.4 lines
  • Improvement in BSCV  62%
  • Improvement in UCVA  74%

Cross-Linking and Keratoconus
Keratometry Over Time

Long-term Results

- 241 eyes
- Follow-up 6 months to 6 years
- Flattening: 2.68 D at 1 year; 4.84D at 3 years
- BSCVA improvement (> 1 line): 53% at 1 year
- No loss of BCVA
- No progression of KC $\rightarrow$ 99%
- 2 patients had KCN progression $\rightarrow$ repeat CXL

Raiskup-Wolf, Hoyer, Spoerl.
AJO April 2010
Cross-linking Results: 6 year Results
(Carus University Hospital, Dresden, Germany)

Frederik Raiskup-Wolf, MD et al: Collagen cross-linking with riboflavin & ultraviolet-A light in keratoconus: Long-term results; JCRS; May 2010
Complications with Epithelial-Off Cross Linking
Delayed Epithelial Healing and Infiltrate after Epi-Off CXL

Postop Day 2

Courtesy of Wm. Trattler, MD
Haze after Epi-Off CXL

Courtesy of Roy Rubinfeld MD
alpha Strep Keratitis post Epi-Off CXL

 Courtesy of Robert Fintelman, MD (Phoenix, Arizona)
Perforation after Epi-Off CXL

Courtesy of Roy Rubinfeld MD
Epi-off CXL-adverse events

- **Corneal melting in both eyes** after simultaneous corneal cross-linking in a patient with keratoconus and Down syndrome. *Ophthalmolomologie*. 2010 Oct; 107(10):951-5

- **Corneal melting** corneal collagen cross-linking for keratoconus: A case report. Labiris. *Journal of Medical Case Reports* 5:15 2012

- **Ocular surface complications** of CXL. Frucht-Perry. AAO annual meeting poster (P0367), 2012 *(11% incidence)*
Epithelial-off vs. Transepithelial cross-linking: Clinical Studies
### Cohort 1: Epithelial Off CXL, n = 23

<table>
<thead>
<tr>
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<th>Baseline</th>
<th>1 Year follow up</th>
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<tr>
<td><strong>K Average</strong></td>
<td>47.11 ± 3.5</td>
<td>45.64 ± 4.3</td>
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<tr>
<td><strong>K Min</strong></td>
<td>46.31 ± 3.4</td>
<td>43.13 ± 3.5</td>
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<tr>
<td><strong>K Max</strong></td>
<td>50.13 ± 4.0</td>
<td>49.02 ± 4.6</td>
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### Cohort 2: Transepithelial CXL, n = 16

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<td><strong>K Average</strong></td>
<td>47.50 ± 4.2</td>
<td>45.87 ± 4.0</td>
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<tr>
<td><strong>K Min</strong></td>
<td>45.36 ± 2.7</td>
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<tr>
<td><strong>K Max</strong></td>
<td>49.27 ± 4.1</td>
<td>48.13 ± 5.4</td>
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## Transepithelial corneal collagen crosslinking: Bilateral study

Massimo Filippello, MD, PhD, Edoardo Stagni, MD, David O’Brart, MD, FRCS, FRCOphth

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<td>Baseline</td>
<td>1 yr follow up</td>
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<tr>
<td>Average K</td>
<td>49.98 ± 4.46</td>
<td>47.95 ± 2.69</td>
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<tr>
<td>Steep K</td>
<td>60.30 ± 5.26</td>
<td>58.10 ± 4.20</td>
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Adverse events-Pilot Study
CXL USA San Francisco Center

• **Keratoconus Progression**
  – 0% of eyes exhibited progression after CXL (up to 9 months f/u)
  – 16 multicenter trial: ~1% progression in larger group (>10,000 eyes)

• **Vision Loss greater than 1 snellen line**
  – 0% of eyes

• **Epithelial defect**
  – 2% of eyes
  – All less than 1 mm and healed by POD #2

• **Corneal Haze**
  – 0% of eyes
OCT Cornea- Patient EW pre-op
6 weeks post op

- Microscopic cellular changes in stroma
- Hypothesis: Aldehyde/Amine covalent bonds → cross-linking / changing collagen structure
4.5 months post op

Cellular changes still present, but not as prominent
Azedro CXL Protocol- Photrex®

- Debride 9 mm corneal epithelium
- Add 1 drop of Photrex Viscous (riboflavin 5’-phosphate in 20% dextran) every 2 minutes for 30 minutes
- Check for full penetration of drop at 30 minutes, continue instilling drops if needed
- Check ultrasound pachymetry with minimum thickness 400µ
- Use UV light for 30 minutes (3 mW/cm²) with KXL system
- During UV light procedure: add Photrex drop every 2 minutes
- Place a BCL on treated eye (s) until epi defect has healed
- F/U q1 day until re-epithelialized
Questions

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