Corneal Cross Linking for Keratoconus and Ectasia

Keratoconus
- Responsible for 15% of all corneal transplants in the US
- About 22% of patients with keratoconus require a PKP with a mean duration of 8.8 years
- Develops during the ages of 12-20 most commonly
- Males = Females
- Bilateral and asymmetric

CA-200 Basic module
Fast and comfortable image acquisition

High quality of keratoscopic images

Map is presented within the maximum scale measured of the cornea. This map shows immediately the actual astigmatism. More then 3 colors present a suspected high astigmatism.
Elevation Maps of the cornea (BFS)

- The normal cornea is prolate, \( Q < 1 \), meaning that meridional curvature decreases from center to periphery.
- Prolateness of the normal cornea causes it to rise centrally above the reference sphere. This is a central hill.
- Immediately surrounding the central hill is an annular sea where the cornea dips below the reference surface.
- In the far periphery, the prolate cornea again rises above the reference surface, producing peripheral highlands.

4 combinations of mapping

Axial Absolute Normalized

Tangential Tangential Absolute Normalized

Ectasia Diagnosis and Management

17 months post-op

Pre-op

- Note: central pach: 514
- Thinnest pach: 507
- Normal topography (left lower map)
- Yet elevated and eccentric posterior elevation (right upper map)

Post-op

Note: post-op
Belin/Ambrosio Enhanced Ectasia
Differences in fitting the sphere

A normal cornea looks pretty same, independent which fitting method is used.

An abnormal cornea looks different. With the "enhanced" fitting the cone is more pronounced.

Belin/Ambrosio Enhanced Ectasia
Standard BFS
Enhanced BFS
Difference between normal and enhanced BFS

Belin/Ambrosio Enhanced Ectasia

Indicators of potential early keratoconus
1. Topography- inferior steepening
2. Wavefront RMS elevated
   –Especially peripheral aberrations
3. Irregularity index (e.g. IS or Rabinowitz)
4. Peripheral thickness changes (pachymetry)
5. Astigmatism variance between eyes
6. Steep K’s (>47D)
CA-200 Topography of a patient with Keratoconus

iTrace of a patient with Keratoconus

A case of advanced keratoconus

PMD

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Peripheral Thickness Comparisons

• If peripheral pachs are not > 20 microns from central this is a sign of potential keratoconus
Orbscan FF Keratoconus Indices

1. Number of Abnormal maps
2. Posterior surface float (difference) > 0.050D
3. 3MM and 5MM irregularity
4. Peripheral thickness changes
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Variance Between Eyes

- Astigmatism > 1.00D between eyes

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Treatment Options

CXL
Corneal Cross-Linking

- First introduced by Theo Seiler MD
- Involves saturating the cornea with riboflavin (Vit B2)
- Expose cornea to UV light (370 nm) for 30 minutes
- Riboflavin absorbs UV light and produces singlet oxygen
- Causes cross-linking of collagen fibers and extracellular matrix proteins
- To protect the endothelium:
  - Soak cornea for 30 minutes prior
  - Debride corneal epithelium
  - Ensure riboflavin has penetrated the AC

Corneal Collagen Cross-Linking

- Riboflavin prevents penetration of uv light
- Older corneas vs. younger corneas and progression of keratoconus
- CXL appears to be the first technology than can halt the progression of ectasia

CORNEAL CROSSLINKING with Riboflavin 0.1% (Vit B2) increases corneal rigidity by 328.9%

Role of benzalkonium chloride (BAK) on the corneal epithelium

Corneal epithelium tight junctions are the most important barrier for Riboflavin permeability

BAK (=contained in many eye drop concentrations 0.0075%-0.02) loosens epithelial tight junctions and enhances permeability for pharmaceutical agents

RICROLIN TE® = Hypotonic ophthalmic solution containing Riboflavin 0.1% and enhancers helping the Riboflavin pass through the intact corneal epithelium
RIBOFLAVIN 0.1% TE (TRANSEPITHELIAL) PENETRATION INTO THE ANTERIOR STROMA (89–99 microns by PENTACAM)

UVA -Riboflavin
• 30 minutes of drops and UV radiation exposure
• Strengthen collagen bonds

UVA -Riboflavin: Post-operative Care
• Interim Results from a multicenter clinical trial on CXL in the US
• Shows that CXL halts keratoconus and ectasia after LASIK
• Improves vision

UVA -Riboflavin: Ongoing US Clinical Trials
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UVA - Riboflavin: Ongoing US Clinical Trials

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UVA - Riboflavin: Ongoing US Clinical Sites

• Penny Asbell - New York, NY
• David Hardten - Bloomington, MN
• Ron Krueger - Cleveland, OH
• Tom Mauger - Columbus, OH
• George Waring - Columbus, OH
• Gregory Pamel - New York, NY
• Robert Rivera - Phoenix, AZ
• Stephen Slade - Houston, TX
• Doyle Stulting - Atlanta, GA
• Steven Dell - Austin, TX
• Mark Speaker - New York, NY
• Darcy Wolsey - Salt Lake City, UT

UVA - Riboflavin: Ongoing US Clinical Trials

• Cornea is stronger and increased stiffness but:
• also thinner (compacted?)
• 292 patients enrolled, 3 & 6 month data:
  – 182 keratoconus eyes and 139 post-Lasik ectasia
  – 1:2 sham group
  – statistical improvement in average corneal curvature values

UVA - Riboflavin: Ongoing US Clinical Trials

• No change in manifest Rx
• Statistical improvement in BCVA
• Complications in 321 eyes treated:
  – 4 infiltrates
  – 4 delayed re-epithelialization
  – 1 case of uveitis
• No cases of corneal haze in the clinical trial but occurs occasionally in international experience: resolves with time

UVA - Riboflavin: Longer term data

• 71 eyes of 58 patients (KCN and ectasia) treated
• 41 received a sham but were treated at 3 months for ethical considerations
• 1 year - statistical improvement in UDVA and BCDVA
• Stabilization curve noted
• On average K’s flattened by 1.7D
• Results were best for keratoconus > post-lasik ectasia > control

Other potential applications

• Combine CXL with Intacs
• ICR has been shown to flatten the cornea in 80% of the cases
• CXL has been shown to halt progression of the disease

Intacs for Keratoconus

Other potential applications

• Physician sponsored IND for infectious keratitis treatment
  – Ulcers limited to 250 microns
  – May also help with infectious load
• Treatment of corneal edema
  – Cross linking reduces imbibition pressure
  – Internationally it appears to work for 3 mo to 12 mo duration

Conclusions

• Diagnosing keratoconus early is critical to effective treatment
• CXL is likely to become the standard of care for ectasia management
• Patients are more educated than in the past and expect to see doctors who know the answers to their eye care questions and can communicate that knowledge

THANK YOU!

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