# Understanding Corneal Cross linking for Your Patient

Jim Owen, OD, MBA, FAAO
encinitasod@cox.net

Keratoconus

- Adolescent onset
- Progresses over 10-20 years
- Prevalence: 50-230/100,000[1]
- Incidence
  - 1/100,000 in general population[2]
  - 2% in patients seeking surgical correction of refractive errors[3]
- About 20% of patients with KC require corneal transplantation
- KC is the indication for 5000 (15%) corneal transplants performed each year in the US[4]

Characteristics of Keratoconus

- Reduced corneal rigidity in eyes with keratoconus
- Reduced likelihood of keratoconus progression with age (physiological cross-linking)[1]
- Diabetes protects against development of keratoconus – glycation2
- Cigarette smoking protects against development of keratoconus – unknown toxins in cigarette smoke
- Diabetes protects against development of keratoconus[3]

Methods Of Stiffening the Cornea

- Glutaraldehyde crosslinking (prosthetic heart valves)
- Formaldehyde (pathology specimens)
- Aldehyde sugars (diabetes)
- UVA-induced crosslinking (dentistry)

Methods Of Stiffening the Cornea -Riboflavin Absorption SpectrumCollagen Cross-Linking

History

- Studied since 1994
- University of Dresden
- Theo Seiler
- Eberhard Spoerl
- Gregory Wollensak

  III International Congress of Corneal Cross-linking
- Abbreviations in literature confusing
- CCC
- C3R

- CCL

- Universal standard going forward - CXL

Corneal Collagen Cross-Linking Mechanism of Action

- Riboflavin excited by UVA radiation into triplet state, generating reactive oxygen species
- Reactive oxygen species create covalent bonds between collagen molecules
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Sites For Collagen Cross-Linking

- UVA Corneal Absorption in Presence of Riboflavin
- Effects of Corneal Cross-Linking
- Confocal Micrograph at 300 microns

Treatment Protocol

- Riboflavin 0.1% q 2 minutes/30 minutes
- Fluorescence in Anterior Chamber
- Riboflavin q 2 minutes and UV Light for 30 minutes
- UV Light for 30 Minutes
- Bandage Contact Lens

Cross-Linking and Keratoconus / Keratometry Over Time Questions

- Does it really work?
- Is it really safe?
- How long does the effect last?
- Does the epithelium have to be removed?[1]

Epi-on CXL

- Pinelli R and Boxer-Wachler B
- Benefits of no pain
- Very difficult (questionable) to get Riboflavin into corneal stroma
- Insufficient Riboflavin penetration can lead to UVA over-exposure and damage to ocular structures.

Prospective Randomized Trial Design: Australia

- Christine Wittig, Grant Snibson, Mark Whiting, Laurie Sullivan, Richard Lindsay, Hugh Taylor
- Inclusion criteria
- Keratoconus
- Documented progression over 12 mo.
- CT > 400µ
- Age 16-50
- No corneal surgery or other pathology
- Cross-over at 6 months if progression in control eyes

Prospective Randomized Trial $K_{max}$ and $K_{min}$ Prospective Randomized Trial

CXL – Possible Side Effects

- Endothelial Cell Loss
- Crystalline lens opacity
- Pain
- Infection
- Stromal Haze
- Delayed Epithelial healing
- Retinal damage

Riboflavin + UVA Effect Conclusions -CXL

- Halts progression of ectatic corneal diseases
- Decreases corneal curvature and thickness
- Regularizes corneal surface
- Improves UCVA and BSCVA
- Effect lasts indefinitely
- Offers safe and effective treatment for conditions with no currently available treatment and may avoid
- 15% of corneal transplants
- Disability, cost, loss of productivity, CTL

Regulatory Status

- International
- CE Mark
- Distributed internationally
- United States
- Investigational
- Combination product
- Device: UVA light source
- Drug: Riboflavin

CXL Clinical Trial* USA

- Prospective, block-randomized treatment
- Progressive keratoconus
- Corneal ectasia after LASIK
- CXL of one eye/subject
- Outcome measures
- $K_{max}$ at 3 months
- BSCVA, UCVA
- Optional crossover of control eyes and treatment of untreated fellow eyes at three months
- 1-year follow-up

Inclusion Criteria

Learning Obectives

- Understand the basic science behind corneal cross-linking
- Understand how crosslink changes clinical measurements in keratoconus and ectasia
- Understand the treatment criteria and protocolo