

CXL: THE HISTORY AND CLINICAL APPLICATIONS

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Disclosure

- Presenter is on speakers panel of Alcon, Allergan, AMO, Bausch + Lomb, Merck, RPS, Odyssey, Ista, Tear Lab
- Past-President of the Optometric Council on Refractive Technology (OCRT)
- Board Member of Ocular Surface Society of Optometry (OSSO)
- Presenter has NO financial interest in any products mentioned

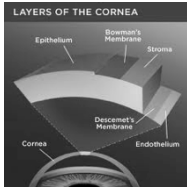
Hang on! We're gonna move fast!



Thanks to CEiB

- Optometry needs to embrace technology while not losing sight on the needs of our patients.
- Embrace Technology: Smartphones, CXL
- CEiB is keeping the OD center stage while some are trying to bypass the OD's
- Next logical step in CE
- AOA New Technology Workgroup
- OCRT Executive Board Member
 - Optometric Council on Refractive Technology
 - OCRT.ORG

Anatomy of the Cornea



The LIMelight....Get It???



CXL Is In The Fisheye Lens of FDA

- Currently under investigation
- No timeline on approval
- Insurance will not cover it
- Is approved in all European Union Countries
- We can save vision, especially in the pediatric community
- There is a race against time

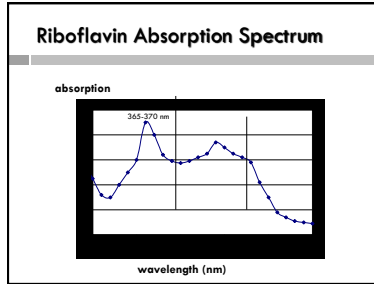
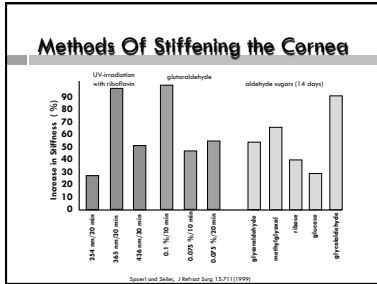
The many names...

- Corneal Collagen Cross Linking
- Collagen Cross Linking
- CXL
- Holcomb C3R
- CCL
- Ophthalmology Tanning Bed
- Sun

Can't We Just?



GE RSK-6 Sun Tanning Light

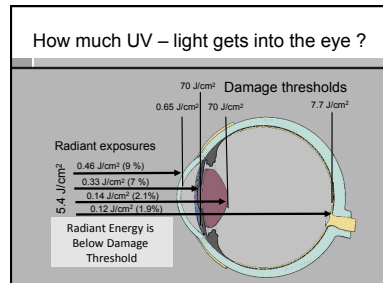


- ### Different Devices
- Avedro - USA
 - CXLUSA - USA
 - Peshke
 - IROC Innocross
 - Sooft
 - Vega X-Link
- Web-links are on the www.cxcls.org site



IS IT SAFE?????

How do we know?



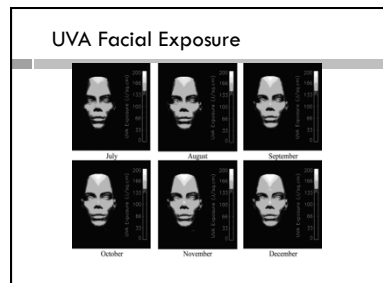
UVA Exposure Standards

PROPOSED CHANGE TO THE IRPA 1985 GUIDELINES ON LIMITS OF EXPOSURE TO ULTRAVIOLET RADIATION
 International Non-ionizing Radiation Committee
 of the
 International Radiation Protection Association


UVA Exposure Standards

Ultraviolet Radiation Guide
 Navy Environmental Health Center

2510 Walmer Avenue
 Norfolk, Virginia 23513-2617
 April 1992



Real World UV



All Exposed Tissues:

- 170-200J/cm²/day in 3-4 hrs outdoors
- ~60J/cm²/day of solar UVA

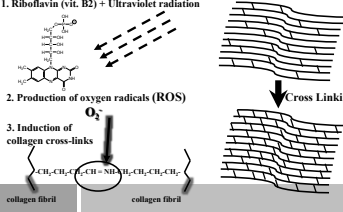
Cornea:

- 5J/cm² in 15-20 min in Summer


CXL exposure=3 mJ/cm²

Basics in Cross Linking

1. Riboflavin (vit. B2) + Ultraviolet radiation
2. Production of oxygen radicals (ROS)
3. Induction of collagen cross-links



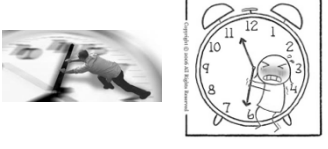
Dr Oz and Anti-Oxidants





You CANNOT Turn Back Time

WE KNOW IT WILL GET WORSE IF WE DO NOTHING


ANY KID WOULD BEG FOR THEIR 10-YEAR OLD VISION BACK



FACTS ABOUT CROSSLINKING AND THE CORNEA


FLEXIBLE ELASTIC & NOT CROSSLINKED	NOT FLEXIBLE, RIGID & CROSSLINKED
	

How Do We Know UV Ages the Body?



The young have to flexible and elastic That's why they grow from this

GUESS WHO THIS IS?




TO THIS...

DAMIAN LEWIS FROM HOMELAND

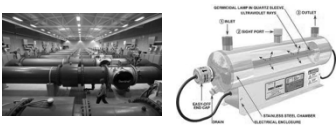


CXL Is Everywhere

We see Collagen Cross Linking **EVERYWHERE** in our world but **NEVER** pay attention to it




Our Water Supply is UV Treated



Camelback Water Bottle



Tanning (cross-linking) leather has been around for over 6000 years.



This woman is 6000 years old. CXL Works!



Safe enough for a child




Ever Get A Manicure?



What's The Technique?

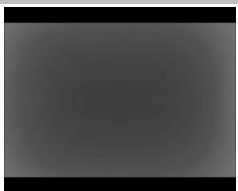
How do you do it?

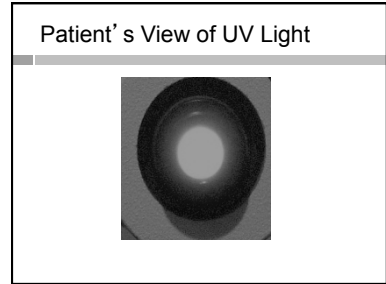
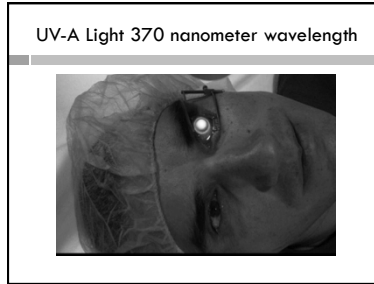
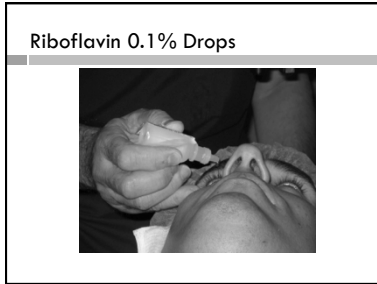
"Dresden" Technique



- Anesthetic drops
- Prepare cornea
- Riboflavin drops for 30 mins
- UV light for 30 mins
- Bandage contact lens
- Postop Course: Similar to PRK

Daya Epithelial Disrupter





Let the cookies bake at 350

For 20-30 minutes until golden brown and delicious

**So We Know it is Safe
But How Does it Work?**

- The collagen in our cornea has links between the layers
- UV light stimulates strengthening between the bonds
 - ▣ Takes decades to do it naturally
- We are using UV light activated by riboflavin to stimulate the creation of more cross links

New CXL study came out 3 days ago

- Academy blast email
- **Cross-linking for keratoconus improves long-term visual acuity, refraction, topography** *Br J Ophthalmol. 2013;97(4):433-437.*
- Corneal collagen cross-linking successfully halted the progression of keratoconus for up to 4 years or more

New Study Cont.

- Investigators analyzed 30 patients with early to moderate keratoconus who underwent unilateral CXL with Riboflavin and UV-A 4-6 yrs previously.
- Mean Age was 26.3 years.
- Mean Interval between CXL and evaluation was 53.3 months.

New Study Cont.

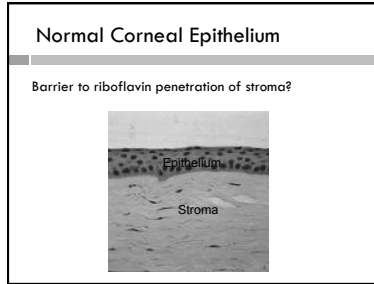
- From before treatment out to 4 years to 6 years, mean spherical equivalent refractive error and corrected distance visual acuity improved significantly; mean simulated keratometry, cone apex power, root mean square, coma, secondary astigmatism and pentafoil decreased significantly.
- From 1-year results out to 4 years to 6 years, mean simulated keratometry, cone apex power, root mean square, coma and secondary astigmatism decreased significantly; central pachymetry increased significantly.

New Study Cont.

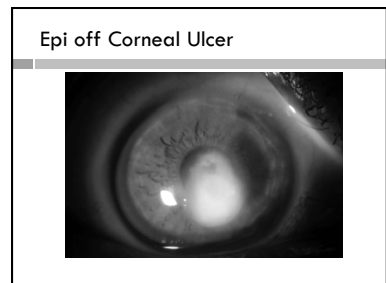
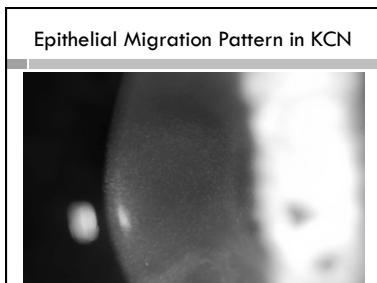
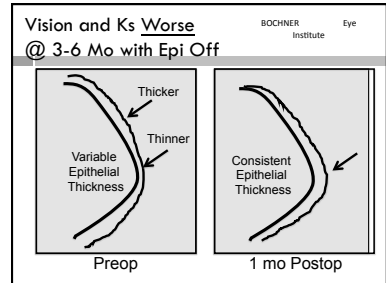
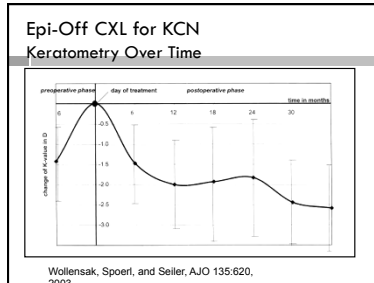
- No treated eyes had progression of keratoconus and none lost more than one line of corrected distance visual acuity; keratoconus progressed in seven untreated fellow eyes.

Epi on vs. Epi Off

<u>Epi-On</u>	<u>Epi-Off</u>
<ul style="list-style-type: none"> □ Longer "load time" □ Late stage technique □ More ribo needed □ No epi defect □ Less chance of infection and haze □ No reported complications 	<ul style="list-style-type: none"> □ Shorter "load time" □ Early adopted technique □ Less ribo needed □ Large Epi defect □ Slower recovery □ Higher risk of infection and haze □ Reported Complications



- ### Typical Epi Off CXL
- Worse vision for 3-6 months
 - Steeper Ks
 - More compact corneas
 - Some haze
 - SPÉs, pseudodendrites if epi-off



So all Thin Corneas are Weaker, Right???

Not Really...
 Corneal Biomechanics is fast becoming the most important variable

Corneal Biomechanics

- New way to determine the keratoconic/ectatic status of the cornea
- Not dependent on curvature or thickness but the strength of the cornea.
- A cornea may be thin but biomechanically strong
- A cornea may be thick but structurally weak
- Think of how rebar makes a difference in construction of a building.

Oculus Corvis Device

- Measures biomechanical properties of the cornea
- Uses an air puff to first deform the cornea
- Watches for the time to deform and the rebound
- Measures the dampening and floppiness of the cornea
- Objective tool to determine if a cornea is structurally weak and at risk for keratoconus or ectasia

Corvis by Oculus

Images from Cynthia Roberts Ph.D.

- The Ohio State University
- Professor of Ophthalmology and Biomedical Engineering

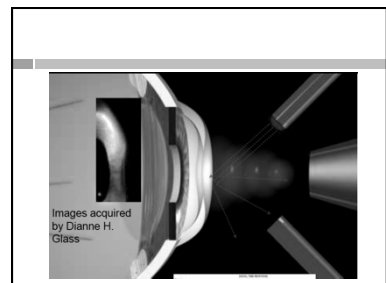
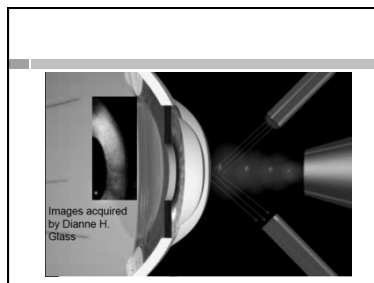
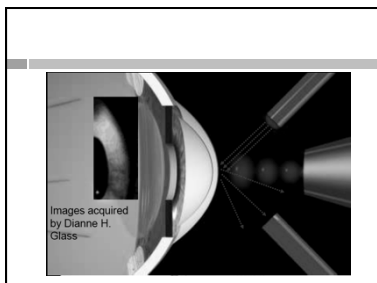
Weakening of Cornea from LASIK

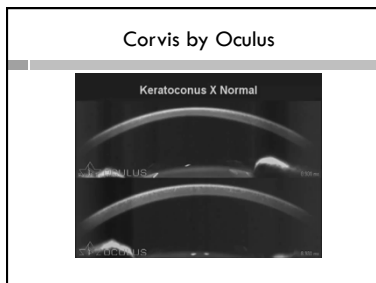
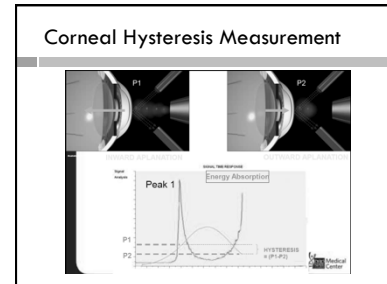
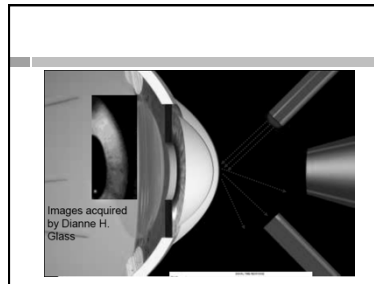
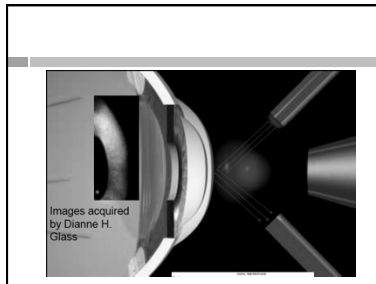
A Mechanical Model of Keratectomy-Induced Flattening

- Crosslinks (x):
 - antero-peripheral distribution
 - interlamellar cohesion
 - couple PST & central curvature
- Stroma = fibers vs matrix
- Ablation => **flattening** and peripheral stromal thickening

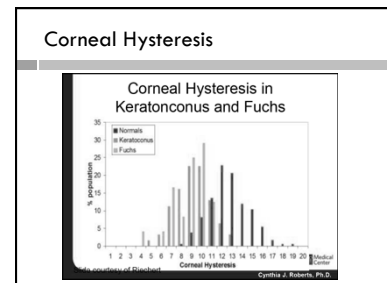
Figure 11. Roberts C.J. "Mechanical Model of Keratectomy-Induced Flattening" presented at the American Society of Biomechanics, Annual Meeting, Denver, CO, 2010.

Biomedical Engineering & Mechanics
 Cynthia J. Roberts, Ph.D.





- ### Corneal Hysteresis
- Soft Cornea is associated with
 - Keratoconus and Post LASIK ectasia
 - Stiff Cornea is associated with
 - Older (aged) cornea
 - High IOP



- ### Morgensterns Rule to LASIK Candidacy Other than RFX and PMHX
- Check to see if your residual bed is greater than 300
 - Check to see if your K's are steeper than 37 and/or flatter than 48 on a primary procedure
 - Check to see if your HOA value is less than .60
 - Check the biomechanical properties of the cornea to make sure that they fall within 1.5sd of normal
 - Pentacam posterior float centered and less than 15 microns and anterior float centered and less than 10
 - No family history of keratoconus/PKP/ectasia/PMD
 - Always think of other options & potential complications

- ### Other Applications of CXL: The Universal Dreams
- LASIK and CXL
 - PRK and CXL
 - Post RK Fluctuations
 - Cornea-Plastics
 - Scleral CXL
 - Optic Nerve Head CXL
 - Infection
 - Intacs - Which currently do the following:
 - Increased K flattening
 - Increased BCVA
 - Increased UCVA

- ### Diabetes and CXL
- Diabetics typically do not get keratoconus
 - 1999 in The Journal of Refractive Surgery
 - Spoerl and Seiler
 - Aldehyde sugars in diabetics form natural cross-links but only after prolonged time

Who Is The Best Candidate?

- Mild to Moderate Phase of Keratoconus
 - Little to no corneal scarring
 - BCVA better than 20/40 with best optical device
 - Young
 - Typically the younger and earlier in the disease, the better
- Post RK refractive fluctuations
- Post LASIK ectasia with refractive fluctuations

I've heard that Vitamin C cant be used before CXL?



Vitamin C Supplements

- Vitamin C naturally strengthens collagen
- Scurvy is a disease where the lack of Vitamin C leads to an enzymatic breakdown of collagen
- A surplus will possibly be an extra building block for collagen
- Vitamin C therefore will have a synergistic effect
- Many studies do not want their data affected by the addition of Vitamin C
- It is advisable to have your KCN patients that do not have CXL to take daily Vit C

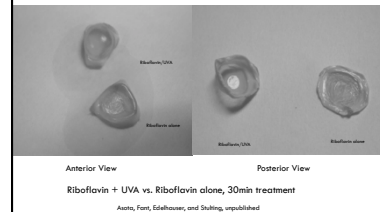
Contraindications

- Corneal Thickness
 - Variable but never less than 300-350
 - Minimum pachy different from study to study
- Prior herpetic infection
 - Reactivation Issues
- Pregnancy or Nursing
 - Absolute
- Severe Scarring
 - No benefit, better with partial of full thickness graft
- Poor wound healing
- Autoimmune disease
 - Relative contraindication

Complications

- Infection
 - Epi-off only reported
- Corneal Haze and Scarring
 - Epi-Off only reported
- Progression of disease
- Intra-Ocular Inflammation
- Worsening of refraction
- Inability to tolerate contact lenses
- Need for PKP

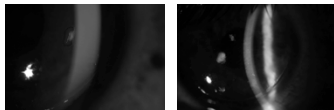
"Moving Pictures" of CXL Riboflavin + UVA Effect



"Moving Pictures" of CXL

LASIK AND CXL

LASIK AND CXL



"Moving Pictures" of CXL

CXL AND INTACS

CXL WITH OK CORNEAPLASTICS



"Moving Pictures" of CXL

RK FROM COLOMBIA c. 1988

FELLOW EYE POST GRAFT

