CXL Updates

Tarek El-Naggar, MD, FRCS (Glasg)

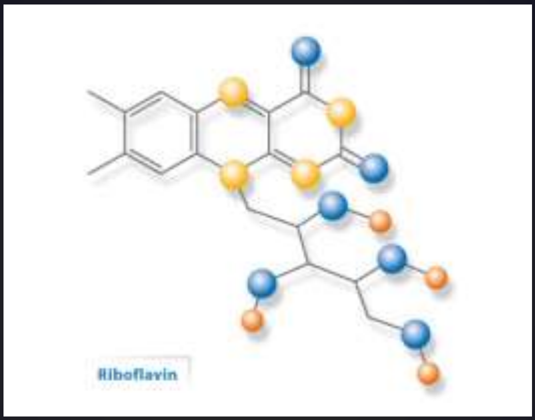
Research Institute of Ophthalmology (RIO)

The Speaker Has No Financial Interest

Options for treatment

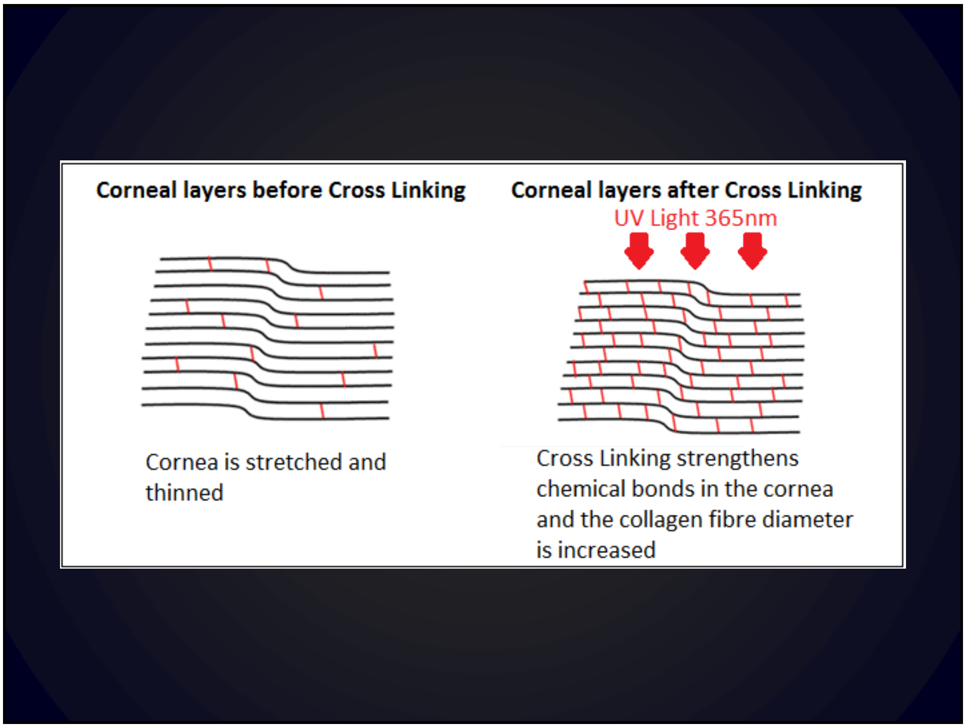
- Lower intraocular pressure
- RGP lens
- Collagen cross-linking
- Intracorneal ring segments
- Phakic IOLs/CLE
- Deep lamellar keratoplasty
- PKP
- Combinations

CXL: BASICS



Hydrophilic VS lipophilic epithelium.

Electrostatic repulsion between the anionic riboflavin-5-phosphate and the negatively charged surface of the cornea

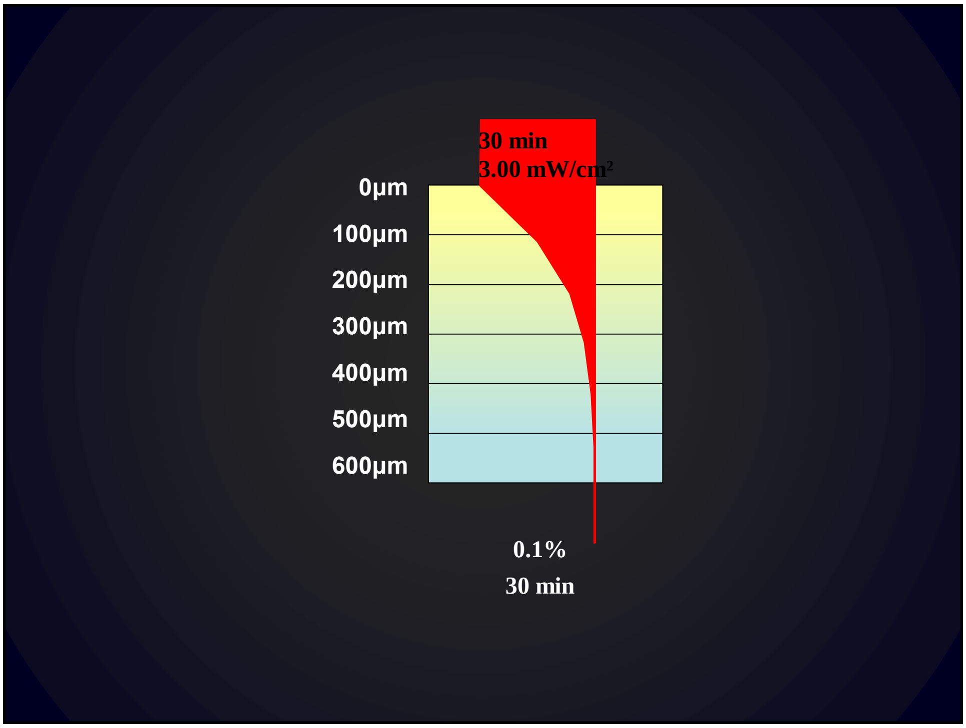


Corneal layers before Cross Linking

Corneal layers after Cross Linking

Cornea is stretched and thinned

Cross Linking strengthens chemical bonds in the cornea and the collagen fibre diameter is increased



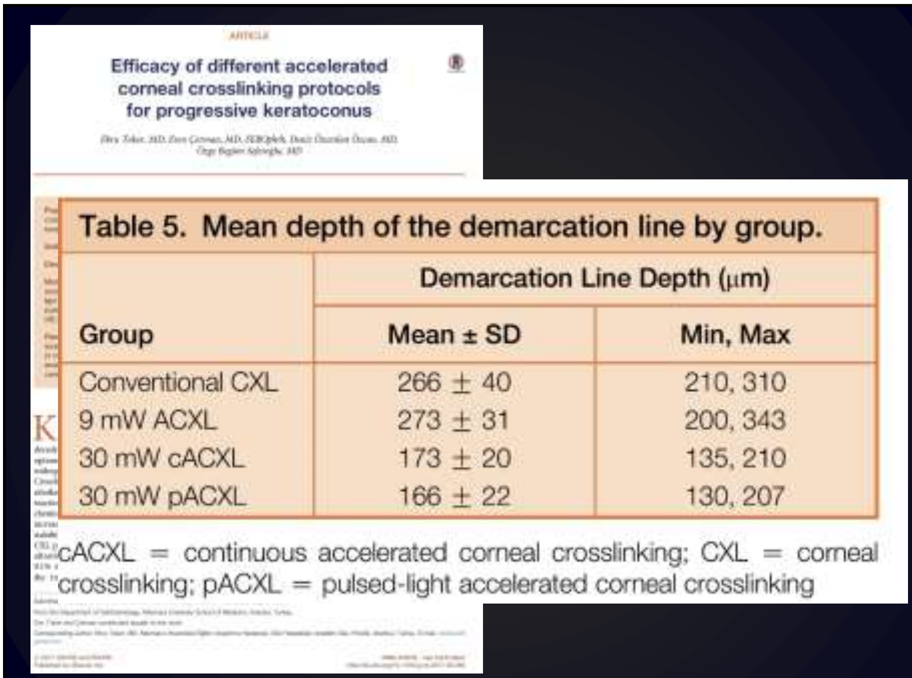
The Protocol
CXL: Power x Time

- The standard Dresden protocol:
  - 3 mW/cm^2 x 30 min = 5.4 J/cm^2
- Accelerated Cxl:
  - 9 mW/cm^2 x 10 min = 5.4 J/cm^2
  - 10 mW/cm^2 x 9 min = 5.4 J/cm^2
  - 18 mW/cm^2 x 5 min = 5.4 J/cm^2
  - 30 mW/cm^2 x 3 min = 5.4 J/cm^2
  - 45 mW/cm^2 x 2 min = 5.4 J/cm^2

Continuous Vs Pulsed

- Rapid oxygen depletion with accelerated protocols leads to a reduced efficacy
- 1S On 1S Off

CXL-depth 250 to 330 µm



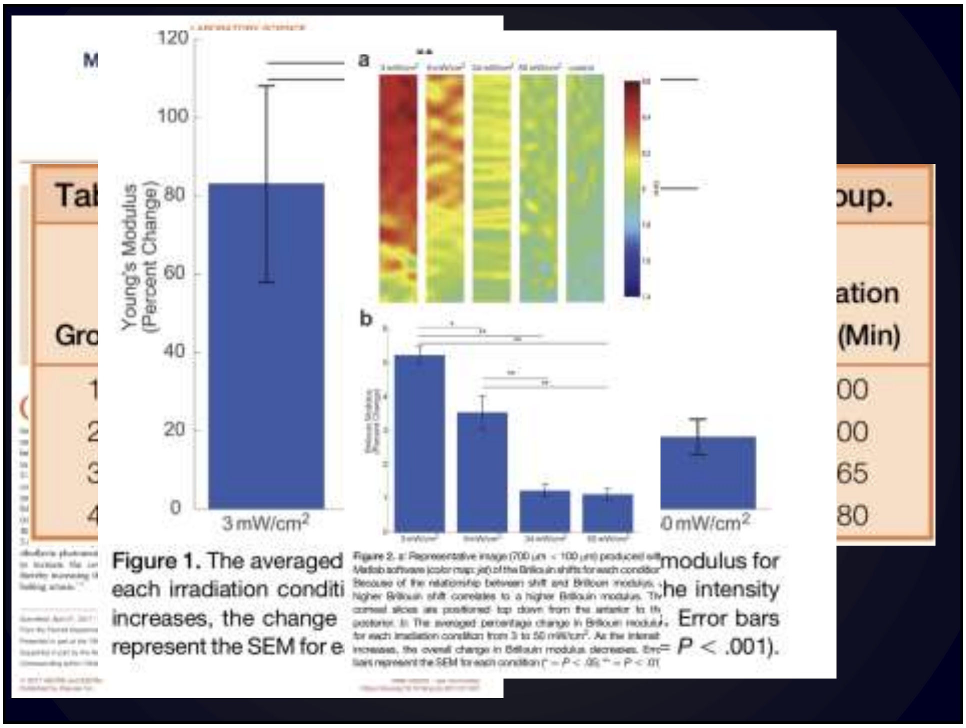
ARTICLE

Efficacy of different accelerated corneal crosslinking protocols for progressive keratoconus

Table 5. Mean depth of the demarcation line by group.

Group	Demarcation Line Depth (µm)	
	Mean ± SD	**Min, Max**
Conventional CXL	266 ± 40	210, 310
9 mW ACXL	273 ± 31	200, 343
30 mW cACXL	173 ± 20	135, 210
30 mW pACXL	166 ± 22	130, 207

cACXL = continuous accelerated corneal crosslinking; CXL = corneal crosslinking; pACXL = pulsed-light accelerated corneal crosslinking



The Solution

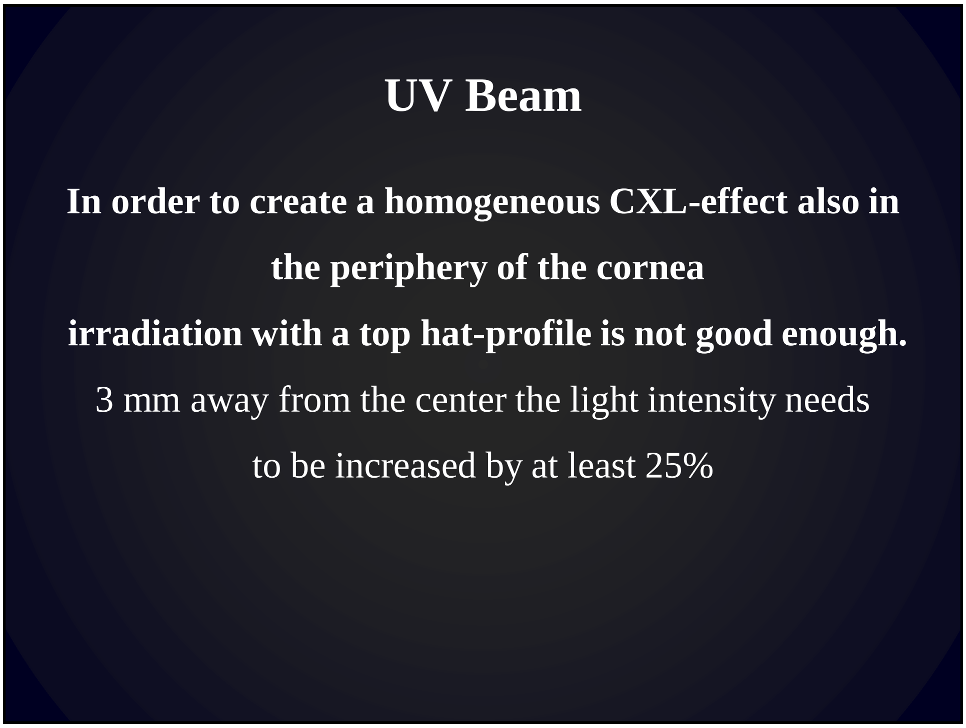
Riboflavin Type	Commercially available brands
Isotonic Riboflavin 0.1% (with 20% Dextran)	Mediocross-D, Vibex , Ricrolin
Riboflavin 0.1% in HPMC (without Dextran)	Mediocross-M, Vibex Rapid
Hypotonic Riboflavin (0.1% Riboflavin with buffered salt solution)	Mediocross-H, InnoCross-R Hypotonic
TransEpithelial Riboflavin 0.25% with HPMC+BAK/EDTA/Tromethamine	Mediocross TE, Ricrolin TE, ParaCel
Riboflavin 0.25% in NaCl (saline)	FreshK, Vibex Xtra

The LAMP

TABLE. SPECIFICATIONS OF CXL LAMPS

Manufacturer	**IROC Innocross AG**	**Sooft Italia S.p.A.**	**Opto Global Pty Ltd.**	**Avedro, Inc.**	**Peschke Meditrade GmbH**	**IROC Innocross AG**	**Appasamy**	**Avedro, Inc.**
Name of device	UV-X 1000	Vega	Opto XLink	KXL I System	[illegible]	UV-X 2000	CL-UVR	KXL II System
Country of origin	Switzerland	Italy	Brazil	United States	Switzerland	Switzerland	India	United States
Wavelength, nm	365	370	365	365	365	365	365	365
Intensity of illumination, mW/cm²	3.0	3.0	[illegible]	[illegible]	[illegible]	Up to 12	3.0	3 to more than 90
Variable intensity?	No	No	Yes	Yes	No	No	No	Yes
Duration of CXL treatment, min	30	30	30	5	5	10	30	[illegible]
Working distance, mm	50	50	50	NS	[illegible]	[illegible]	NS	NS
Light emission	Continuous	NS	NS	Continuous	Continuous	Continuous	NS	NS
Beam profile	Homogenous	Homogenous	Homogenous	Homogenous	Homogenous	Optimized	NS	Programmable illumination
Beam diameter, mm	[illegible]	[illegible]	[illegible]	[illegible]	7-11	7-11	NS	[illegible]
Weight, kg	[illegible]	NS	NS	NS	[illegible]	[illegible]	NS	NS
CE Mark	Yes	Yes	Yes	Yes	Yes	Yes	NS	Expected in late 2012
No. of treated eyes reported in the literature	[illegible]	[illegible]	[illegible]	NS	NS	NS	NS	[illegible]

Abbreviations: CXL, corneal collagen cross-linking; NS, not specified.

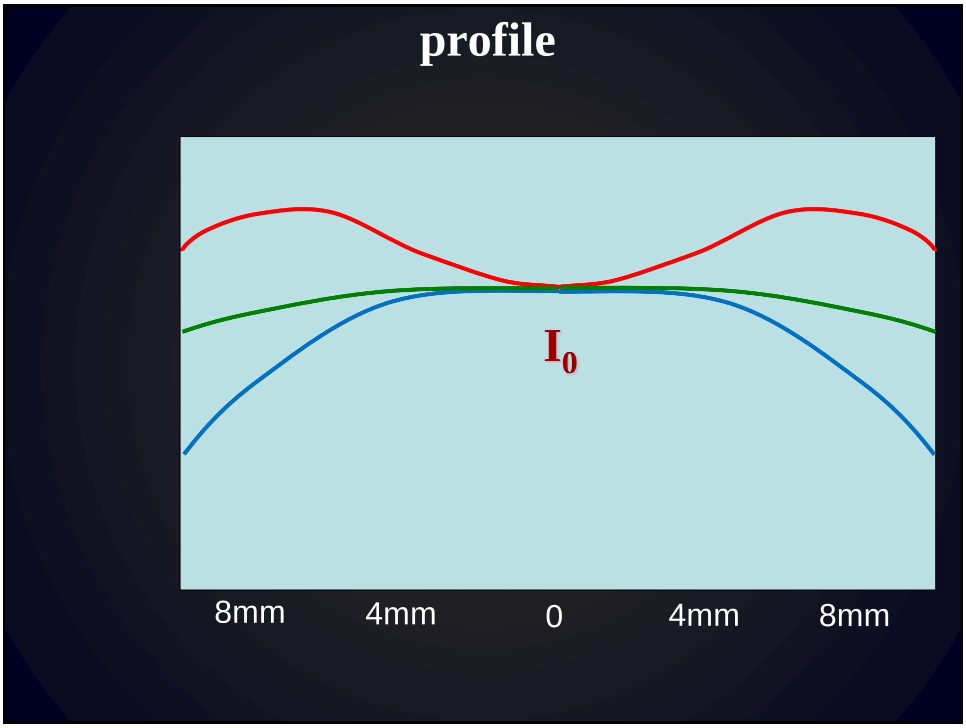


UV Beam

In order to create a homogeneous CXL-effect also in the periphery of the cornea

irradiation with a top hat-profile is not good enough.

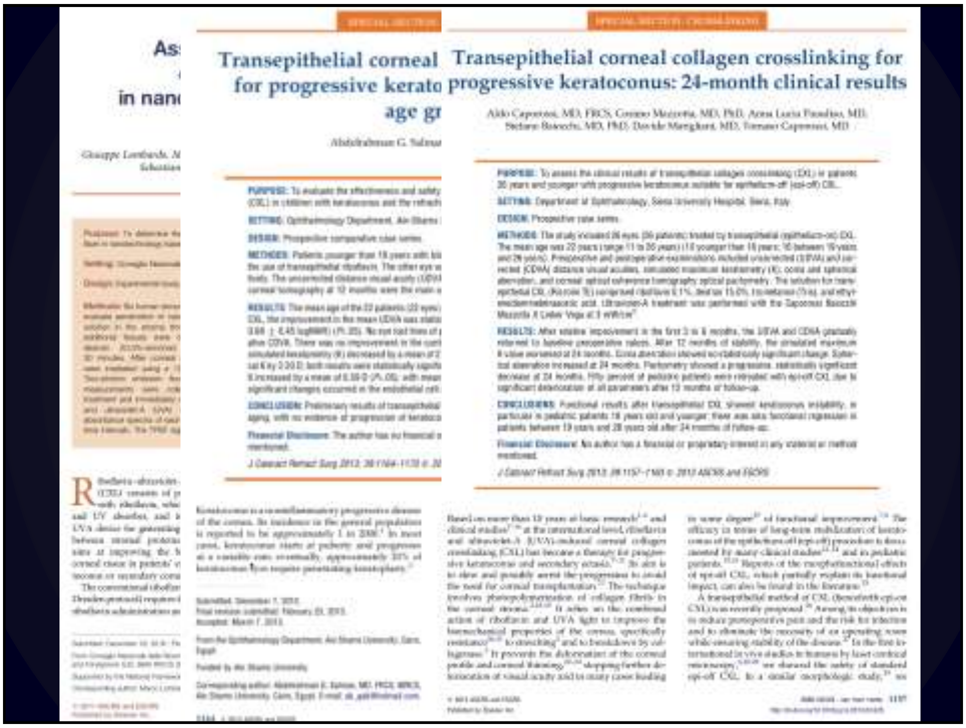
3 mm away from the center the light intensity needs to be increased by at least 25%



profile

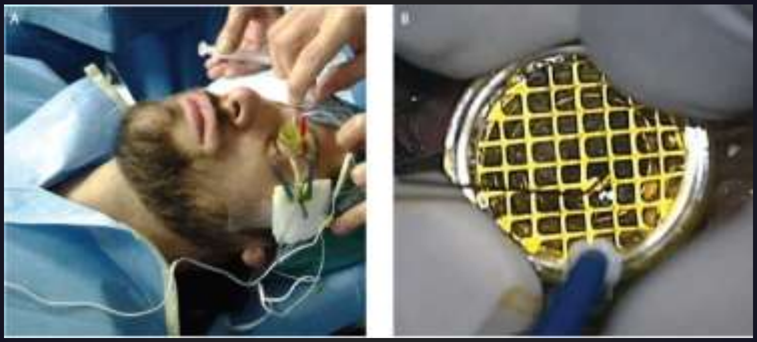
Transepithelial Cross-linking

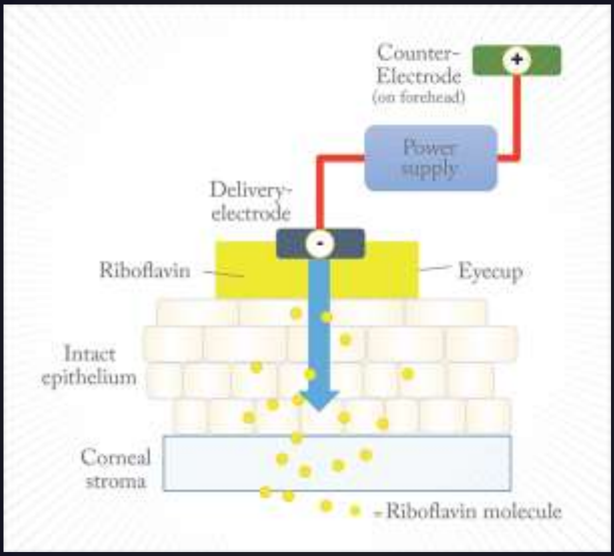
- To avoid Postoperative pain, haze, and infection.
- Techniques:
  - ➞Pharmacological cleavage of epithelial tight junctions
  - ➞Application via intrastromal pocket/channels.
  - ➞Iontophoresis-assisted CXL (I-CXL)
- Efficacy was lower as compared to conventional treatment particularly in stabilizing or improving keratometry.



Transepithelial corneal collagen crosslinking for progressive keratoconus: 24-month clinical results

Iontophoresis-assisted CXL (I-CXL)





THE PROBLEM WITH EPI-ON TECHNIQUES

Successful CXL requires three components:

1. **Adequate, homogeneous stromal loading of riboflavin.**
2. **Adequate, unblocked transmission of UV-A light energy through the epithelium.**
3. **Adequate oxygen, the rate-limiting reagent for the photochemical reaction that causes cross-linking when both Nos. 1 and 2 are present**

Cross-linking in Thin Corneas

- Hypoosmolar cross-linking with instillation of hypotonic riboflavin
- Transepithelial crosslinking
- Customized pachymetry-guided epithelial debridement
- Contact lens-assisted collagen crosslinking (CACXL)
- Stromal thickness augmentation using refractive lenticule
- New protocols according to CT
- Riboflavin with HPMC

LABORATORY SCIENCE

Biomechanical stiffening: Slow low-irradiance corneal crosslinking versus the standard Dresden protocol

Sabine Kling, PhD, Farhad Hafezi, MD, PhD

PiXL: Photorefractive Intrastromal Cross-linking

Oculus Pentacam Tomography

Avedro Mosaic Treatment Design

Customized UVA Pattern

LASIK Xtra

- A higher concentration 0.25% riboflavin is applied on the stromal bed subsequent to excimer laser ablation with a soak time of 90 s. The interface is washed thoroughly and the flap is repositioned.
- UV-A: 30 mW/cm^2 for 90 s = 2.7J/cm^2

REPORT

Corneal Ectasia After LASIK Combined With Prophylactic Corneal Cross-linking

Suphi Taneri, MD; Saskia Kiessler, Dipl-Ing; Anika Rost, MSc; H. Burkhard Dick, MD

ABSTRACT

(J Refract Surg. 2017;33(1):50-52.)

CASE REPORT

CXL: Corneal infection

C-Eye© device

Take home message

- Revise your Riboflavin
- Revise your protocol
- Be cautious with Epi On
- Other options are still for research purposes

Thank you