

**International**  
**CXU** **2021**  
**Experts' Meeting**

**Abstracts**



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## CXL for ectasia, keratoconus

### A Next Generation OCT in Collagen Imaging in Keratoconus and Cross-linking

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#### Abstract

**Purpose:** To study changes in corneal fibrillar distribution following corneal cross-linking (CXL) of keratoconus (KC) eyes using polarization sensitive optical coherence tomography (PS-OCT)

**Methods:** 25 eyes of KC, 25 eyes pre and post-CXL were imaged with PS-OCT at 1,3,6 months. Scan of 11 mm diameter were captured, and corneal fibril distribution images was generated using phase retardation (PR) maps. Eyes were imaged 3 times for repeatability.

**Results:** Enface maps of KC eyes showed an abrupt change in preferential arrangement of collagen fibril structures. Binding of collagen fibrils appeared to be weak in KC eyes. This weak binding of collagen fibrils strengthened at 3 months post CXL and stabilized at 6 months with a relatively stronger binding as compared to preoperative arrangements.

**Conclusion:** The binding of collagen fibrils improved and strengthened the cornea post CXL. Posterior corneal PR maps can be used to track ultrastructure changes in collagen fibrils aiding in analysing effect of CXL procedure

#### Topic Areas

CXL for ectasia, keratoconus

### A systemic bioinformatic analysis of the RNA-Seq data to understand the factors influencing progression of keratoconus

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#### Abstract

**Purpose:** Keratoconus (KC) is a noninflammatory, bilateral degenerative disorder of the cornea with poorly understood etiology. Many RNA-Seq studies were performed using samples collected from KC patients to find differentially expressed genes and their role in KC. However, the findings of each study vary greatly without any uniformity in the results obtained. The present study aimed to identify common factors that are responsible for KC progression through a systemic bioinformatic approach using the available RNA-Seq data.

**Materials & Methods:** RNA-Seq data submitted to the Gene Expression Omnibus database and differential gene expression (DEG) data submitted as the supplementary information was collected from 6 recent different studies. The raw RNA-Seq data was collected, cleaned, and processed using different bioinformatic tools to generate DEG data. All the collected data from each dataset was analysed using ShinyGO v0.66: Gene

Ontology Enrichment Analysis, a graphical gene-set enrichment tool, to find the common signaling events (KEGG pathways) that are severely downregulated during KC.

**Results:** We observed downregulation of MAPK, Hippo, TNF, AGE-RAGE, IL-17, PI3K-Akt, NF-kB, HIF1, neurotrophin, C-type lectin receptor, FoxO, adipocytokine, TGF- $\beta$ , and Wnt signaling pathways in different studies. Along with these signaling events, we also observed downregulation of axon guidance, autophagy, mitophagy, cell adhesion molecules, focal adhesion, apoptosis, cellular senescence, ferroptosis, and tight junction pathways. In addition, we also observed the manifestation of pathways related to neurodegeneration, Alzheimer's disease during our meta-analysis. Upon further comparison analysis with the available omics-data of neurodegeneration, we identified that the same factors contributing to neurodegeneration (mitochondrial dysfunction, cytoskeleton, stress response, autophagy, apoptosis, cell adhesion, extracellular matrix, signal transduction, aging, neurotrophic factors) are also deregulated during KC. The enriched biological processes involved in neurodegeneration (response to hypoxia, positive regulation of cytokines, positive regulation of angiogenesis, and RNA catabolic process) are also detected in our KC RNA-Seq data meta-analysis.

**Conclusions:** Through systemic bioinformatic analysis of the RNA-Seq data, we could identify common signaling events and pathways that are downregulated during KC. Further, our analysis also highlights the possible connection between neurodegeneration and KC progression. Since the cornea is highly innervated tissue with free nerve endings at the epithelial surface, and corneal nerves also degenerate during KC, it is important to focus also on corneal nerves

to understand the factors influencing KC progression.

### Topic Areas

CXL for ectasia, keratoconus

## Acanthamoeba Keratitis after Corneal Crosslinking for Keratoconus

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### Abstract

**Purpose:** To report a successfully treated case of acanthamoeba keratitis diagnosed two days after corneal crosslinking in a keratoconus patient.

**Materials & Methods:** A 28-year-old male patient with visual acuity cc 20/25 OS was treated with epi-off Riboflavin/Hydroxypropyl methylcellulose corneal crosslinking (CXL) for progressive keratoconus on his left eye. Two days later, he presented with multifocal epithelial and stromal infiltrates. After corneal scraping for immunohistochemistry and cultures, antibiotic therapy with fluoroquinolones and aminoglycosides was initiated. Corneal scraping, however, was positive for bacteria and acanthamoeba cysts on the following day. Acanthamoeba cysts could also be visualized via confocal microscopy. Taking into account these findings and recent literature reporting

resistance in 85% against fourth generation fluoroquinolones in bacterial infections following CXL, treatment was changed to polyhexanide 0.02%, propamidine 0.1% and gentamicin.

**Results:** Over the next five months, antiseptics were continuously tapered and corticosteroid eye drops were additionally initiated. At last follow-up five months later, the patient presented with stable scars, visual acuity cc 20/25 and no signs of keratoconus progression on the left eye.

**Conclusions:** As far as we know, only one report of acanthamoeba keratitis after CXL has been published so far. However, that case led to corneal perforation requiring keratoplasty. As the case presented herein shows, close follow-up after CXL is necessary to diagnose and treat microbial infections, also potentially including acanthamoeba, as early as possible.

### Topic Areas

CXL for ectasia, keratoconus

## Accelerated corneal crosslinking to arrest progression of corneal ectasia: a prospective multicenter study

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### Abstract

**Purpose:** To report results of two different epithelium-off accelerated corneal collagen crosslinking (ACXL) protocols in patients with progressive keratoconus.

**Methods:** Prospective, non-randomized, non-comparative, interventional and multicenter clinical study including all consecutive patients with topographic evidence of progressing keratoconus who underwent ACXL, either continuous (c-ACXL; 9 mW/cm<sup>2</sup>, 10', 5.4 J/cm<sup>2</sup>) at Royal Victoria Infirmary (RVI) or pulsed (p-ACXL; 2"ON/1"OFF, 30 mW/cm<sup>2</sup>, 4.5', 5.4 J/cm<sup>2</sup>) at Centro de Oftalmología Barraquer (COB) between January 2014 and May 2017. Best-corrected visual acuity (BCVA), sphere, cylinder, spherical equivalent (SE), and topographical keratometry were collected preoperatively and at 1, 3, 6, 12, 18 and 24 months postoperatively.

**Results:** 78 patients (96 eyes; RVI: 55 patients, 64 eyes; COB: 23 patients, 32 eyes) were included. Mean age was 20.8±4.4 years (14-33) for c-ACXL and 26.7±7.7 years (12-37) for p-ACXL. Mean follow-up time was 14.6±6.5 months (3-34) for c-ACXL and 16.4±6.9 months (2-30) for p-ACXL. Mean BCVA was 0.4±0.4 for c-ACXL and 0.01±0.1 for p-ACXL preoperatively, and 0.3±0.3 (p=0.0014) and 0.01±0.1 (p=0.1554) respectively at last follow-

up. Subjective sphere and SE did not show statistically significant differences between timepoints ( $p > 0.05$ ). Subjective cylinder showed differences ( $p = 0.0013$  for c-ACXL;  $p = 0.0358$  for p-ACXL). However, keratometric values ( $K_{steep}$ ,  $K_{flat}$ , SimK) remained stable, with no statistically significant differences ( $p > 0.05$ ); only SimK showed a statistically significant decrease after c-ACXL ( $p < 0.0001$ ). No major complications were noted.

**Conclusions:** Both c-ACXL and p-ACXL are equally safe and effective ACXL protocols in stabilizing progression of keratoconus and can be considered as alternatives to the conventional Dresden protocol.

### Topic Areas

CXL for ectasia, keratoconus

## Accelerated Cross-Linking Associated with Topography-Guided PRK in Keratoconus with and without Intraströmial Corneal Ring

### Authors

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### Abstract

**Purpose:** To compare visual acuity and keratoconus stabilization after treatment with accelerated cross-linking (CXL) associated with topography-guided photorefractive keratectomy (TG-PRK) preceded or not by the implantation of intraströmial corneal ring segments (ICRS).

**Methods:** Prospective non-randomized interventional study carried out in 20 eyes of 17 patients with keratoconus. The participants in this study were subdivided into 2 groups: the first group contained 10 eyes with indication for implantation of ICRS, which were submitted to this procedure and, one year later, the accelerated CXL (9 mW/cm<sup>2</sup>, 10 minutes) associated with TG-PRK surgical technique (group 1 – G1). The second group consisted of 10 eyes with no ICRS which were submitted to the accelerated CXL associated with TG-PRK (group 2 – G2). Both groups had periodic outpatient follow-up with the last evaluation being after 12 months of the combined procedure.

**Results:** Mean spherical equivalent (SE) improved in both groups after combined treatment. However, best evolution occurred in G1. Mean preop SE was  $-3.48 \pm 2.44$  (-4.75 to +2.00) diopters (D) (G1) and  $-3.65 \pm 1.65$  (-4.25 to +0.25) D (G2) ( $P = 0.9999$ ); in post-op, mean SE was  $-1.00 \pm 2.10$  (-3.50 to +4.75) D (G1) and  $-1.45 \pm 3.02$  (-6.50 to +5.25) D (G2) ( $P = 0.9999$ ). In both groups there was an improvement in corrected-distance visual acuity (CDVA). Mean preop CDVA (in logMAR) was  $0.40 \pm 0.14$  (G1) and  $0.23 \pm 0.09$  (G2) ( $P = 0.0026$ ); in postop, mean CDVA was  $0.19 \pm 0.12$  (G1) and  $0.12 \pm 0.06$  (G2) ( $P = 0.3176$ ). There was no progression of keratoconus during the follow-up.

**Conclusion:** Simultaneous treatment with accelerated CXL and TG-PRK was satisfactory to improve CDVA and to reduce the SE in eyes with keratoconus with and without ICRS. Eyes with ICRS showed a better final refractive result to the combined treatment.

### Topic Areas

CXL for ectasia, keratoconus



## Accelerated CXL Versus Accelerated Contact Lens–Assisted CXL for Progressive Keratoconus in Adults

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### Abstract

**Purpose:** To compare the clinical and tomographic properties of adult patients with keratoconus treated with accelerated corneal cross-linking (A-CXL) versus accelerated contact lens-assisted corneal cross-linking (A-CACXL).

**Methods:** Patients who underwent A-CXL and A-CACXL due to progressive keratoconus were enrolled from January 2015 to January 2018 in this retrospective case-control study. The treatment group (minimum corneal thickness of less than 400  $\mu\text{m}$  after epithelium removal; 30 patients, 30 eyes) was treated with A-CACXL; the control group (minimum corneal thickness of 400  $\mu\text{m}$  or greater, 32 patients,

32 eyes) was treated with A-CXL. Assessments occurred before treatment and 12 months postoperatively. Demographic, clinical, and tomographic data were obtained from outpatient clinic reports.

**Results:** Significant improvement in visual acuity was evident at 12-month follow-up for the control group in uncorrected distance visual acuity ( $0.62 \pm 0.42$  vs  $0.43 \pm 0.31$  LogMAR,  $P=0.01$ ) and the treatment group in corrected distance visual acuity ( $0.51 \pm 0.30$  vs  $0.40 \pm 0.49$  LogMAR,  $P=0.03$ ). Progression of keratoconus was halted at similar rates for both groups (76.7% treatment, 84.4% control,  $P=.21$ ). Mean minimum corneal thickness showed minor but significant thinning at the 12-month follow-up visit compared to baseline (control group= $463 \pm 31$  vs  $450 \pm 35$   $\mu\text{m}$ ,  $P>0.01$ ; treatment group= $398 \pm 32$  vs  $388 \pm 41$   $\mu\text{m}$ ,  $P=0.02$ ).

**Conclusions:** A-CACXL halted keratoconus progression in 76.7% of eyes and achieved regression in 33.3% of eyes, with rates comparable to A-CXL. Visual outcomes improved for both groups, with similar keratometry changes. A-CACXL is an effective and safe option for patients with keratoconus and thin corneas, with results similar to A-CXL treatment in patients with a minimum corneal thickness of 400  $\mu\text{m}$  or greater.

### Topic Areas

CXL for ectasia, keratoconus

## Accelerated Pulsed High-Fluence Corneal Cross-Linking for Progressive keratoconus: 5-year survival analysis of a large, multi-ethnic population

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#### **Abstract**

**Purpose:** To report our experience with the accelerated pulsed high-fluence protocol with outcome data at yearly time points up to 5 years on patients treated in the Early Keratoconus Clinic at Moorfields Eye Hospital, following an earlier report of our 2-year outcomes. Additionally, we generated adaptive thresholds for our own data to enable a tailored definition of progression.

**Materials & Methods:** This was a retrospective cohort study of 9341 eyes from 5025 patients with suspected or confirmed keratoconus from Moorfields Eye Hospital, London. 3541 eyes received collagen crosslinking (CXL). When defining an adaptive threshold for keratometric progression, we generated V-shaped 95% Limits Of Agreement (LOA) using regression. We defined failure as progression by at least 2 metrics on at least 2 appointments compared to the baseline Pentacam scan.

**Results:** Using the new adaptive thresholds for (front\_k2, back\_k2, Kmax) we found 203 failures out of 4077 eyes (5%) at 5 years following CXL.

**Conclusions:** Our data is one of the largest datasets with 5-year follow-up and shows the effectiveness of CXL, even with the more stringent adaptive thresholds. Moreover, our method for adaptive threshold is a good illustration of how clinicians can assess their outcomes based on locally derived parameters for progression as individual machines will vary in their repeatability limits. Our results have meaningful implications for the planning of post-operative monitoring.

#### **Topic Areas**

CXL for ectasia, keratoconus

## **Accelerated versus Standard Corneal Cross-linking for Progressive Keratoconus in Syria**

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#### **Abstract**

**Background:** To compare and evaluate the outcomes of accelerated and standard corneal cross-linking in the treatment of progressive keratoconus.

**Method:** In this retrospective comparative study, sixty-three eyes of 40 patients with progressive keratoconus were divided into two groups; 27 eyes in group 1 were treated with an accelerated protocol (10 mW/cm<sup>2</sup>, 9 min), and 36 eyes in group 2 were treated with the standard method (3 mW/cm<sup>2</sup>, 30 min). The visual acuity, refraction, corneal topography, corneal tomography, the anterior and posterior corneal HOAs, were assessed preoperatively and 18-30 months postoperatively. The data was statistically analysed.

**Results:** The LogMAR uncorrected and corrected distance visual acuity values were improved in both groups, postoperatively. However, the improvement was significantly higher in group one (P <0.05, all). The

flattening in the anterior keratometry readings, flat K, steep K, and average K were significantly higher in group two ( $P < 0.001$ , all). The maximum anterior keratometry (AKf) values significantly decreased in both groups, whereas the maximum posterior keratometry (AKb) values increased. The reduction in the minimum corneal thickness (ThKmin) was significantly greater (36.49um) in group two, compared to (10.85um) in group one. There was a significant increase in the posterior average keratometry, and a significant decrease in the posterior astigmatism, along 3mm meridian in S-CXL ( $P=0.03$ ,  $P=0.008$ , respectively), while the corresponding values showed no statistical significance in group one ( $P>0.05$ ). The anterior corneal trefoil was significantly reduced in group one ( $P=0.002$ ), whereas anterior total HOAs and coma were significantly improved in group two ( $P < 0.0014$ , all). The posterior corneal spherical aberration decreased significantly in group one ( $P=0.02$ ), while group two revealed significant reduction in the posterior trefoil values ( $P=0.011$ ). The change in the anterior maximum keratometry was significantly and positively correlated to the preoperative maximum keratometry in group 2 ( $P=0.53$ ,  $P=0.003$ ).

**Conclusion:** An accelerated cross-linking protocol, using  $10 \text{ mW/cm}^2$  for 9 minutes, showed better visual improvement and less pachymetric reduction when compared to the standard protocol, but the anterior corneal flattening, the posterior corneal steepening and the change in the posterior astigmatism were significantly higher in standard protocols, while corneal HOAs were improved in both protocols.

### Topic Areas

CXL for ectasia, keratoconus

## Algorithmic Approach to plan Laser Based Corneal Collagen Cross Linking

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### Abstract

**Purpose:** Conventional keratoconus management protocols endeavour to arrest the progression of the disease, and enhance the biomechanical strength of the cornea. Correction of vision in these patients is challenging - their high irregular astigmatism may not be corrected with spectacles, and fitting a contact lens onto such irregular corneas is often cumbersome. A laser-based approach is a viable alternative to conventional methods of treatment in such eyes. These treatments were initially corneal wavefront-guided (CW), and have now advanced to more tissue-sparing techniques that are ocular wavefront-guided (OW). Topography-guided removal of epithelium in keratoconus (TREK) is a novel customised laser-based procedure involving simultaneous removal of epithelium and stroma, particularly in decentred cones. We attempt to delineate an algorithm to plan laser-based corrections in ectatic eyes, so as to select the right candidates for each treatment.

**Methods:** Based on our algorithm, 100 eyes underwent CW treatment, 100 eyes underwent OW treatment, and another 100 eyes underwent TREK. CW treatment was planned on the ORK-CAM module of the Schwind-Sirrus topographer, and OW treatment was planned on the Schwind-Peramis topo-aberrometer. TREK was planned using the PTK-CAM module on the Schwind-Sirrus topographer, wherein the maximum

and minimum diameter of the cone area were qualitatively assessed, such that the ablation zone included the steepest zone and extended beyond it by 1.5 to 2 mm. Then, the epithelium over the rest of the cornea up to 8 mm diameter was scraped manually. This was followed by accelerated collagen cross-linking with 0.1% riboflavin solution, using the Mosaic system. Their visual function, tomography and biomechanics were recorded at 1, 3 and 6 months post-operatively.

**Result:** In the CW and TREK groups, unaided and best corrected visual acuity, sphere, cylinder, spherical equivalent, keratometry, CCT, MCT, RMS LOA and HOA, defocus, coma 90° and spherical aberration reduced significantly after surgery ( $p < 0.05$ ). The percentage of eyes, which gained one Snellen line or more on UDVA, was 56.25% in TREK and 57% in CW group. The OW group eyes had greater decrease in keratometry, anterior defocus and spherical aberration ( $p < 0.001$ ) at the cost of greater ablation of tissue ( $p < 0.001$ ). The median MCT decreased by 27  $\mu\text{m}$  and 32.5  $\mu\text{m}$  in the TREK and OW eyes, respectively. Both TREK and OW groups had similar decreases in anterior root mean square of lower ( $p = 0.15$ ) and higher order aberrations ( $p = 0.17$ ).

**Conclusion:** Application of this algorithm showed promising results in the management of keratoconus. It can be used to customise treatment for each patient with corneal ectasia, thus enhancing outcomes and minimising complications.

#### Topic Areas

CXL for ectasia, keratoconus

## Appropriate scleral lens filled with transepithelial Riboflavin during corneal soaking before UV collagen corneal crosslinking

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#### Abstract

**Aim:** to evaluate the efficiency and the safety of corneal soaking using high vault scleral lens filled with transepithelial Riboflavin before collagen corneal crosslinking (CCC).

**Materials and method:** retrospective study of 70 eyes of 50 patients with corneal ectasia who underwent accelerated transepithelial CCC after 30 mn of wearing then removing appropriate scleral lens filled with transepithelial Riboflavin for corneal soaking. Sub 400 protocol was performed without removing the epithelium when necessary.

**Results:** after 30 mn of corneal soaking with this technic, Riboflavin diffuse to all the cornea and the anterior chamber when checked at slit lamp examination. Corneal OCT imaging when performed at 1 month, showed a demarcation line at 146 +/-27 microns above the corneal endothelium. 1 eye with cornea less than 400 micron, continue to progress after 1 year of follow up.

**Conclusion:** using scleral lens to deliver the B12 vitamin is an efficient, safe, economic, delegable way to soak the cornea with transepithelial Riboflavin before CCC.

**Key words:** transepithelial Riboflavin, scleral lens delivery, cross linking.

## Topic Areas

CXL for ectasia, keratoconus

## Changes in Visual acuity and Corneal Parameters after Corneal Cross-linking for Keratoconus: Long-term Follow-up

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Ms. Swanandi G - L V Prasad Eye Institute, Hyderabad, India

### Abstract

**Purpose:** To assess the long-term efficacy and safety of epithelium-off accelerated corneal cross-linking (9 mW/cm<sup>2</sup> for 10 minutes) protocol in patients with keratoconus.

**Methods:** A total of 1512 eyes of 761 patients with a mean age of 17.86 ± 06.26 years were included. At baseline and after 1, 3, 6, 12, 24, 36, 48, and more than 60 months after corneal cross-linking (CXL). All patients were assessed with LogMAR corrected distance visual acuity (CDVA) and corneal tomography with WaveLight® Oculyzer™ (WaveLight AG, Erlangen, Germany). Outcome measures were maximum keratometry(K-Max), mean keratometry (K-mean), thinnest corneal thickness (TCT).

**Results:** The K-Max increased from mean 62.74 ± 08.43D to 64.23 ± 08.19D at 1 month and then decreased to 61.35 ± 07.97D at the last visit. The mean LogMAR CDVA showed a minimal improved from 0.37 ± 0.30 to 0.28 ± 0.20 at final follow up. At the final follow-up there was a greater flattening in patients who had TCT <399 microns compared to those who had TCT 400 microns or more to start with. There was at least 2 lines improvement

in CDVA in patients who had TCT <399 microns compared to those who had TCT 400 microns or more. There was a greater amount of flattening and improvement in CDVA in eyes with severe form of keratoconus compared to those with mild disease.

**Conclusions:** Accelerated CXL is shown to be a safe and effective treatment for keratoconus inducing a significant flattening of the cornea.

## Topic Areas

CXL for ectasia, keratoconus

## Combined Phototherapeutic keratectomy, intracorneal ring implantation and corneal collagen cross linking in keratoconus management

Authors: Dr. Guillermo Rocha - Max Rady College of Medicine, University of Manitoba, MB, Canada, Dr. Tarek Ibrahim - Ocular Microsurgery & Laser Centre

### Abstract

**Purpose:** To evaluate the efficacy, predictability, and safety of combined corneal crosslinking (CXL), intracorneal ring segment (ICRS) implantation, and superficial photo therapeutic keratectomy (PTK) in patients with keratoconus.

**Methods:** Fifty-five eyes received ICRS implantation followed by CXL and PTK combination treatment. Patients were followed for 6 months. Primary outcomes included logMAR uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), sphere, cylinder, mean spherical equivalent, index of surface variance, index of vertical asymmetry, keratoconus index, central keratoconus index, index of height asymmetry, and index of

height decentration. Secondary outcomes were higher-order aberrations (HOA), including HOA total, coma, spherical, secondary astigmatism, and trefoil.

**Results:** At 6 months, there was a statistically significant improvement in UDVA, CDVA, sphere and cylinder compared with baseline ( $P < 0.001$ ). UDVA improved in 14% of eyes to 20/25 and 96% had at least 20/40 spectacle corrected vision. 30.9% of eyes were within  $\pm 0.5$  D, 45.5% within  $\pm 1.0$  D, and 74.5% within  $\pm 2.0$  D. For CDVA, one eye (2%) lost 3 lines (but gained UDVA), 11% lost 1 line, 38% showed no change, and 49% gained between 1 and 8 lines of vision. 88% of eyes had at least a 1 line of UDVA visual improvement, 79% improved by  $\geq 2$  lines, and 69% improved by  $\geq 3$  lines. HOA total, coma, spherical aberration, and secondary astigmatism showed improvements of  $-0.87$  ( $P < 0.001$ ),  $-0.84$  ( $P < 0.001$ ),  $-0.10$  ( $P = 0.002$ ), and  $-0.15$  ( $P = 0.035$ ), respectively.

**Conclusions:** A combined procedure of ICRS implantation, CXL, and PTK is effective, predictable, and safe for patients diagnosed with moderate keratoconus.

#### Topic Areas

CXL for ectasia, keratoconus

## Comparison of the Long-Term Efficacy and Safety of Bilateral Corneal CXL Treatment Performed In The Same or Separate Sessions

Authors: Prof. Nilufer Yesilirmak - Ankara Yildirim Beyazit University, Department of Ophthalmology, Dr. Ferhan Guler - Ankara Yildirim Beyazit University, Department of Ophthalmology, Prof. Ozge Sarac - Ankara Yildirim Beyazit University, Department of Ophthalmology

#### Abstract

**Purpose:** To compare the efficacy and safety results of the bilateral corneal collagen cross-linking (CXL) treatment in the same or separate sessions in patients diagnosed with bilateral progressive keratoconus.

**Materials & Methods:** Patients who underwent bilateral CXL treatment in the same (Group-1) or separate (Group-2) sessions for bilateral progressive keratoconus and had a 3-year postoperative follow-up were included in the study. Preoperative and postoperative corneal tomographic values (keratometry 1 (K1), K2, maximum keratometry (Kmax), topographic astigmatism (TA), posterior elevation (PE)), visual and refractive outcomes (corrected distance visual acuity (CDVA), uncorrected distance visual acuity (UDVA), manifest astigmatism (MA)) and complications were evaluated. In addition, the values at the time of the diagnosis of bilateral progressive keratoconus were compared with the postoperative values in and between the groups. Thus, waiting time effects between the operations are included to the comparison.  $K_{max} \geq 1D$  increase was considered as progression.

**Results:** A total of 134 eyes of 67 patients were included in this study (Group-1 included 76 eyes of 38 patients and Group-2 included 58 eyes of 29 patients). The mean waiting time in intermittent application was 7 (0.5-22) months. Preoperative demographic and tomographic parameters were similar between the groups ( $p > 0.05$ ). There were no intraoperative and postoperative complications in either group. Although a significant improvement was observed in the 3rd year mean K1, K2, Kmax, TA, PE, CDVA, UDVA, MA results in both groups compared with the preoperative level ( $p < 0.05$ ), when the changes were compared between the two groups, Kmax improvement was higher in the

eyes that underwent CXL in the same session ( $p=0.03$ ). As the waiting time between the first operation and the second operation increased in Group-2, the degree of preoperative progression of the second eye increased in correlation with this time ( $p<0.05$ ). When the waiting time is taken into account, K1, K2, Kmax, TA, PE, CDVA, UDVA, MA results were significantly improved in Group-1 compared to those in Group-2 ( $p<0.05$ ).

**Conclusions:** CXL results applied in the same or separate sessions in patients with bilateral progressive keratoconus show similar efficacy and safety in the long-term when compared pre and postoperatively. However, the untreated second eyes may progress in relation to the waiting time. When the waiting time is taken into account, performing CXL in same session for both eyes provides much better outcomes compared to treatments in separate session. Therefore, it is advised that in cases where the treatment time between the two eyes will be prolonged (especially in pandemic periods as COVID-19), bilateral CXL can be applied in the same session to prevent progression affecting the long-term outcomes.

#### Topic Areas

CXL for ectasia, keratoconus

## Corneal Cross-Linking for Paediatric Keratoconus: A Systematic Review and Meta-Analysis

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- Department of Ophthalmology, School of Medicine, University of Kitasato, Dr. Naoko Kato - Department of Ophthalmology, School of Medicine, Keio University, Prof. Jun Shimazaki - Department of Ophthalmology, Ichikawa General Hospital, Tokyo Dental College, Prof. Kazuo Tsubota - Tsubota Laboratory Inc.

#### Abstract

All corneal cross-linking techniques attenuated disease progression in patients with pediatric keratoconus for at least one year based on a meta-analysis. A standard and accelerated technique led to marked improvement in visual acuity. We determined the efficacy and safety of corneal cross-linking (CXL) in pediatric keratoconus by conducting a systematic review and meta-analysis. The PubMed and Cochrane databases were searched for relevant studies on the effects of standard, transepithelial, and/or accelerated CXL protocols in patients aged 18 years or younger. Standardized mean differences with 95% confidence intervals were calculated to compare the data collected at baseline and 12 months. The primary outcomes were maximum keratometry (Kmax) and uncorrected visual acuity (UCVA), and the secondary outcomes were the thinnest corneal thickness (TCT), best-corrected visual acuity (BCVA), and manifest refraction spherical equivalent or cylindrical refraction. Our search yielded 7913 publications, of which 26 were included in our systematic review and 21 were included in the meta-analysis. Standard CXL significantly improved the Kmax, UCVA, and BCVA, and significantly decreased the TCT. Accelerated CXL significantly improved UCVA and BCVA. In the transepithelial and accelerated-transepithelial CXL methods, each measurable parameter did not change after treatments. All CXL techniques attenuated disease progression in patients with pediatric keratoconus for at

least one year. Standard and accelerated CXL led to marked improvement in visual acuity.

#### **Topic Areas**

CXL for ectasia, keratoconus

## Corneal stiffness measurement using in-vivo Brillouin microscopy

Authors: Dr. Hongyuan Zhang - Cleveland Clinic, Dr. Lara Asroui - Cleveland Clinic, Dr. James Bradley Randleman - Cleveland Clinic

#### **Abstract**

**Purpose:** Demonstrate that in-vivo Brillouin microscopy can distinguish keratoconus, post-LASIK or post-PRK from the control based on the different distribution of Brillouin shifts.

**Methods:** Optical coherence tomography (OCT) and pupil tracking were combined with a traditional Brillouin microscope to reduce motion blur caused by patient movement during slow Brillouin scan. Positioning errors were corrected in 3 dimensions by combing axial information from OCT and radial information from pupil tracking. Tracking accuracy was verified in advance using porcine eyes. The whole setup sat on a slit lamp base. A chin rest and a bite bar were used to keep patients stable. During in-vivo measurement, 30 axial scans were applied to discrete points on the cornea. Each axial scan took 5 second with a step size of 15  $\mu\text{m}$ . 2-dimensional interpolation was used to connect the measured discrete points to generate a map of Brillouin shifts of the cornea.

**Results:** Data from tests on porcine eyes showed that axial positioning errors were within 5  $\mu\text{m}$  along a movement of 1 mm with a step size of 100  $\mu\text{m}$ . Meanwhile, lateral positioning errors were within 3  $\mu\text{m}$  over a 9 mm movement. In-vivo Brillouin results

showed that a normal cornea, a keratoconus, a post-LASIK and a post-PRK shared similar Brillouin shifts of around 5.7 GHz at the periphery. The difference mainly existed in the center region. The Brillouin shift at the center was about 5.69 GHz for the normal cornea, 5.67 GHz for the post-LASIK cornea and 5.66 GHz for the post-PRK cornea. For the keratoconus cornea, the Brillouin shift at the cone was about 5.62 GHz.

**Conclusions:** Patient movement can be tracked precisely by pupil tracking and OCT. Brillouin shifts at different depths can be reaccommodated properly after motion compensation. Maps of Brillouin shifts across the cornea can show weak regions and help keratoconus diagnosis.

#### **Topic Areas**

CXL for ectasia, keratoconus  
, CXL for Refractive

## Detecting Keratoconus in Spectral Domain Optical Coherence Tomography: Corneal and Epithelial Thickness Map Parameters and Patterns

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Ms. Anika Rost - Zentrum fur Refraktive Chirurgie Muenster, Prof. H. Burkhard Dick - Ruhr-University Bochum

#### **Abstract**

**Purpose:** To detect keratoconus by analyzing the corneal and epithelial map parameters and patterns in optical coherence tomography (OCT).

**Methods:** Corneal and epithelial thickness maps of normal, manifest keratoconic and



subclinical keratoconic eyes (according to the Belin-Ambrosio display, Pentacam, Oculus) were retrospectively evaluated by spectral domain OCT (Zeiss Cirrus 5000 HD). A two-step decision tree was developed based on previous studies with another OCT device. In the first step of the decision tree, if at least one of the four independent parameters (pachymetry minimum, pachymetry minimum-median, pachymetry superonasal-inferotemporal, epithelial superonasal-inferotemporal) overrun the cutoff values, the eye was suspicious for keratoconus. In the second step, if epithelial map showed concentric thinning and the thinnest point of the cornea and epithelium is coincident the eye was classified as keratoconic.

**Results:** The study included 172 manifest keratoconic eyes (108 patients), 21 subclinical keratoconic eyes (20 patients), and 172 normal eyes (90 age-matched participants). Step 1 identified 100% of manifest and subclinical keratoconic eyes. Step 2 ruled out all suspicious but normal cases and falsely, 2 subclinical keratoconic eyes. Our two-step decision tree reached 100% specificity, 100% sensitivity in manifest keratoconus and 90.4% sensitivity in subclinical keratoconus.

**Conclusion:** Pachymetric and epithelial map parameters and patterns in OCT can be used in the diagnosis of keratoconus, including subclinical cases, yielding a high level of agreement with the current gold standard, the Belin-Ambrosio display. Further improvements by refining our algorithm and including an automated evaluation in the software are desirable.

#### Topic Areas

CXL for ectasia, keratoconus

## Effect of Autologous Serum Eye Drops on Corneal Haze and Reepithelization Rates After Corneal Crosslinking

Authors: Dr. Ana Roldan - Department of Ophthalmology, Massachusetts Eye & Ear, Dr. Sofia De Arrigunaga - Massachusetts Eye and Ear, Dr. Joseph Ciolino - Department of Ophthalmology, Massachusetts Eye & Ear, Harvard Medical School

#### Abstract

**Purpose:** To compare the effect of autologous serum tears vs. preservative-free artificial tears on the prevention and resolution of post-crosslinking corneal haze and reepithelization rates.

**Methods:** A retrospective cohort study was conducted in a sample population from one surgeon at a tertiary eye center from 2016 to 2019. Seventy-six eyes of consecutive patients who underwent crosslinking were included. Records were reviewed for corneal Scheimpflug densitometry values and maximum keratometry ( $K_{max}$ ), epithelial healing time, and the use of either autologous serum tears or preservative-free artificial tears. Corneal densitometry values, expressed in standardized Grayscale Units (GSU), were recorded for the anterior 150  $\mu$ m corneal stroma and in the 0.0-2.0 mm and 2.0-6.0 mm zones.

**Results:** 44 eyes received autologous serum tears, while 32 eyes received preservative-free artificial tears. The baseline GSU of the anterior stromal 0-2 mm annulus and the 2-6 mm annulus did not significantly differ between groups ( $P=.5$  and  $P=.4$ , respectively). There was a statistically significant increase in mean GSU for both anterior 0-2 mm and 2-6 mm zones between baseline and 1 month ( $P<.001$ ) and 3 months ( $P<.001$ ). When

comparing the two groups, no statistically significant difference was found postoperatively between the mean GSU at one month for the anterior 0-2 mm ( $P=.38$ ) nor the 2-6 mm zone ( $P=.12$ ); or for the third month ( $P=.60$  and  $P=.44$ , respectively). In terms of reepithelization rates, the mean epithelial closure time was similar for both groups, with no statistically significant differences observed ( $P=.49$ ). The number of patients who had epithelial closure time at the 1-week follow-up (range 6-8 days) was 35 (79.6%) in the serum tears group and 30 (93.8%) in the artificial tears group ( $P=.11$ ).

**Conclusion:** Using Scheimpflug densitometry, we did not find a significant difference in the post-crosslinking corneal haze at 1 and 3 postoperative months nor a difference in reepithelization rates between patients that use autologous serum tears or preservative-free artificial tears.

#### Topic Areas

CXL for ectasia, keratoconus

## End-Stage Paediatric Keratoconus and Epi-off-lenticule-on Corneal Crosslinking: A Case Report

Authors: Dr. Ugnė Rumelaitienė - Department of Ophthalmology, Hospital of Lithuanian University of Health Sciences, Dr. Tomas Mickevicius - Department of Ophthalmology Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Prof. Dalia Žaliūnienė - Department of Ophthalmology Hospital of Lithuanian University of Health Sciences Kaunas Clinics

#### Abstract

To present a case of paediatric patient with end-stage progressive keratoconus, whose right eye underwent epi-off-lenticule-on

accelerated corneal collagen crosslinking (CXL).

#### Topic Areas

CXL for ectasia, keratoconus  
, CXL Plus (combination)

## Enhanced Transepithelial Crosslinking Using Femtosecond Laser Machined Epithelial Microchannels for Riboflavin Delivery

Authors: Dr. Samantha Bradford - University of California, Irvine, Mr. Rohan Joshi - University of California, Irvine, Dr. Yilu Xie - University of California, Irvine, Dr. Donald Brown - University of California, Irvine, Dr. Tibor Juhasz - University of California, Irvine, Dr. James Jester - University of California, Irvine

#### Abstract

**Purpose:** Ultraviolet light corneal collagen crosslinking (UVA-CXL) via photoactivation of riboflavin (Rf) is an effective treatment for Keratoconus that is also being developed as a refractive procedure. A major drawback of UVA-CXL is the need to remove the corneal epithelium to achieve adequate stromal Rf concentrations for CXL, leading to patient discomfort, delayed visual recovery, and risk of infection. Transepithelial (TE) CXL, even using chemical disruption of the corneal epithelial barrier, has been shown to have limited success in both increasing stromal Rf concentration and decreasing patient pain and delayed visual recovery. Additionally, an intact epithelium could act as a barrier to irradiation, preventing effective transepithelial UVA-CXL altogether. This study describes a femtosecond laser (FS) approach to machine corneal epithelial microchannels (MC) for enhanced stromal Rf penetration that when combined with nonlinear optical

(NLO) CXL avoids both epithelial damage and shielding of irradiation.

**Methods:** Using a 1030nm FS laser with 5µl pulse energy, the corneal epithelium of ex vivo rabbit eyes were machined to create 2µm diameter by 25µm long MC at a density of 100 MC/mm<sup>2</sup>. Stromal Rf penetration through the MC was then determined by applying 1% Rf in PBS with osmolarity ranging from 200-450 mOsm for 30 minutes followed by removal of the cornea and extraction from the central stromal button. Stromal Rf concentrations were then compared between osmolarity groups. Eyes treated with MC and UVA-CXL were also compared to eyes treated with BAK and UVA-CXL using blue collagen autofluorescence (CAF) to detect the efficacy of stromal CXL. CXL was performed both with and without continuing drops of Rf solution to determine the shielding effect of the solution on the surface of the eye.

**Results:** Stromal Rf levels were highest in MC eyes treated with 250 mOsm Rf solution, 1.4 times higher than 300 mOsm solution. No eyes treated with TE UVA CXL with continued Rf application produced measurable CAF. Eyes for which Rf application during CXL was discontinued showed strong CAF. Additionally, eyes receiving MC alone or MC and NLO CXL exhibited an intact epithelium 24 hours after treatment, while eyes receiving BAK alone, BAK UVA CXL, and MC UVA CXL treated corneas all showed extensive epithelial and stromal damage.

**Conclusion:** FS corneal micromachining to create MC greatly enhances stromal Rf penetration, and suggests that coupling MC with NLO CXL minimizes epithelial and stromal damage, leading to greater patient comfort, more rapid visual recovery and decreased risk of infection. We also note that there is significant shielding of Rf activation by the TE

UVA CXL and the continued application of Rf during UVA irradiation.

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### Topic Areas

CXL for ectasia, keratoconus

, CXL pre-clinical, translational, CXL for Refractive

## Independent-Effect Comparison of Seven Crosslinking Procedures for Progressive Keratoconus in a Chinese Population

Authors: Dr. Yu Liu - Aier School of Ophthalmology; Central South University

### Abstract

**Purpose:** To compare the 1-year outcomes of seven corneal crosslinking (CXL) procedures for progressive keratoconus in a Chinese population.

**Methods:** This prospective, longitudinal cohort study included 225 eyes of 162 patients with keratoconus who underwent CXL and were observed for 1 year. Seven CXL procedures were assessed, including accelerated transepithelial corneal-crosslinking (A-TE CXL), iontophoresis corneal-crosslinking (I-CXL) for 10 min, I-CXL for 5 min, hypoosmolar CXL, CXL plus phototherapeutic keratectomy (PTK), accelerated corneal crosslinking (A-CXL), and standard corneal cross-linking (S-CXL). Patients treated with S-CXL represented the reference group. Primary outcomes were the changes of visual acuity, spherical equivalence, and corneal topography 1-year postoperatively compared with baseline. Secondary outcomes were comparisons of corrected generalized

estimating equation from each procedure versus the S-CXL group for the same indexes.

**Results:** The CXL-plus-PTK group performed significantly better than the reference group as reflected by maximum keratometry ( $K_{max}$ ;  $\beta=-1.011$ ,  $P=0.043$ ) and keratoconus indices. The A-TE CXL group performed worse than S-CXL group with mean keratometry ( $K_{mean}$ ;  $\beta=0.95$ ,  $P<0.001$ ) and  $K_{max}$  ( $\beta=1.397$ ,  $P=0.025$ ). The two I-CXL groups ( $\beta=0.416$ ,  $P=0.041$ ; and  $\beta=0.727$ ,  $P=0.031$ ) also performed worse than the S-CXL group with the regard to  $K_{mean}$ . Forty-one eyes (18.22%) showed progression; most (36 eyes) were in transepithelial groups. The corneal capacity of five eyes from three pediatric patients who underwent A-CXL procedure was measured.

**Conclusions:** The CXL-plus-PTK procedure appeared to have better efficacy than the S-CXL procedure. The A-TE CXL procedure performed worse efficacy. Stronger protection of the cornea should be taken for pediatric patients who undergo the A-CXL procedure.

#### Topic Areas

CXL for ectasia, keratoconus

## Individualized topography-guided crosslinking for keratoconus – comparison of epi-on/high oxygen to epi-off room air protocols.

Authors: Prof. Anders Behndig - Dept of Clinical Sciences / Ophthalmology, Umeå University, Umeå, Dr. Anneli Fredriksson - Dept of Clinical Sciences / Ophthalmology, Dr. Sofie Näslund - Dept of Clinical

#### Abstract

**Purpose:** To compare the efficacy, safety and healing phase of two different crosslinking (CXL) protocols for keratoconus.

**Materials and Methods:** This ongoing single-masked, intra-individually comparing study so far involves 27 patients with bilateral progressive keratoconus at 12 month follow up treated with bilateral CXL; one eye with a high-oxygen epi-on protocol, the other eye with an epi-off protocol in room air, which was randomized. Uncorrected (UDVA) and corrected visual acuities (CDVA), low-contrast visual acuities, refractive spherical equivalents (SE), endothelial cell count (ECC) and adverse events were analyzed pre- and post-treatment. The discomfort symptoms during the healing phase for each eye was registered during the first week post-treatment.

**Results:** UDVA improved at 12 months ( $-0.25 \pm 0.29$  logMAR for epi-on;  $-0.18 \pm 0.17$  logMAR for epi-off, ( $p<0.01$ ), as did the CDVA ( $-0.11 \pm 0.13$ ,  $-0.11 \pm 0.12$ , respectively,  $p<0.01$ ), the  $K_{max}$  ( $-1.71 \pm 2.16$ ,  $-1.30 \pm 2.15$  D, respectively,  $p<0.01$ ) and 10% LCVA ( $-0.24 \pm 0.36$  and  $-0.15 \pm 0.14$ , respectively,  $p<0.01$ ). LCVA 2.5 % improved in epi-on ( $p=0.05$ ), but not in epi-off ( $-0.43 \pm 0.93$ ,  $-0.26 \pm 0.66$ , respectively). The epi-on eyes had less discomfort during the first week post-treatment. ECC was unchanged with both protocols at 12 months. No adverse events occurred.

**Conclusions:** Our 12-months results indicate that the novel individualized high-oxygen epi-on treatment protocol can be a promising alternative to an epi-off protocol. Our final (24-months) results are approaching.

#### Topic Areas

CXL for ectasia, keratoconus

## Intereye asymmetry in children with vernal keratoconjunctivitis

Authors: Dr. Sevil Karaman Erdur - Istanbul Medipol University, Dr. Funda Dikkaya - Istanbul Medipol University, Dr. Fatma Feyza Nur Keskin Perk - Istanbul Medipol University

### Abstract

#### Purpose

To report the intereye asymmetry in children with vernal keratoconjunctivitis and controls using Pentacam.

#### Setting/Venue

In a tertiary university hospital

#### Methods

This is a prospective study included 34 children with vernal keratoconjunctivitis and 30 sex age matched controls. Central corneal thickness (CCT), pachymetry at the thinnest point (TP), posterior elevation at the thinnest point of the cornea (PETP), distance, volume, and differential pachymetry were measured. Intereye asymmetry was determined by subtracting the lowest value from the highest value for each variable. The degree of asymmetry between each subject's eyes was calculated with intraclass correlation coefficients for all the variables.

#### Results

In the normal subjects, the mean intereye asymmetries in CCT, TP, and PETP were 9.31, 10.23, and 3.59  $\mu\text{m}$ , respectively. In the vernal keratoconjunctivitis patients, the mean intereye asymmetries in CCT, TP, and PETP were 14.24, 17.24, and 7.46  $\mu\text{m}$ , respectively. Control eyes demonstrated the smallest difference, compared with the vernal keratoconjunctivitis patients' eyes, in all of the variables analyzed ( $P < 0.05$ ).

### Conclusions

There is a greater intereye asymmetry in pachymetry and posterior corneal elevation variables in vernal keratoconjunctivitis patients than in controls.

### Topic Areas

CXL for ectasia, keratoconus

## Iontophoresis-assisted Corneal Cross-linking for Progressive Keratoconus: 3 Year Results

Authors: Dr. Yu Liu - Aier School of Ophthalmology; Central South University, Prof. Qing-yan Zeng - Aier School of Ophthalmology; Central South University

### Abstract

**Purpose:** To assess the 3-year safety and efficacy of corneal cross-linking assisted by iontophoresis (I-CXL) of riboflavin solution for 10 min in Chinese patients with progressive keratoconus.

**Methods:** This retrospective, non-randomized, self-controlled study included 26 eyes of 21 patients, of mean age  $18.48 \pm 4.2$  years (range: 11 to 24 years). All patients underwent stromal imbibition of riboflavin solution for iontophoresis for 10 min, followed by epithelium-on CXL. The uncorrected distance visual acuity (UDVA; in logarithm of the minimum angle of resolution [LogMAR] units), corrected distance visual acuity (CDVA; in LogMAR units), corneal tomography, corneal optical coherence tomography (OCT), and confocal microscopy were evaluated at baseline and postoperatively at 1, 3, 6, 12, 24, and 36 months. Subgroup analyses were conducted according to baseline age ( $< 18$  vs  $\geq 18$  years) and baseline maximum keratometry ( $< 58$  diopters, D vs  $\geq 58$ D).

**Results:** The demarcation line was detected in 19 eyes (73.08%) 1 month postoperatively, at a mean depth of  $234.49 \pm 55.98 \mu\text{m}$ . Average CDVA improved from  $0.26 \pm 0.18$  LogMAR at baseline to  $0.18 \pm 0.14$  LogMAR 3 years postoperatively ( $P < 0.05$ ), and average maximum keratometry ( $K_{\text{max}}$ ) decreased from  $59.35 \pm 9.22$  D at baseline to  $57.62 \pm 8.36$  D 3 years postoperatively (Delta:  $-1.73 \pm 3.24$  D,  $P < 0.05$ ). The average topographic indices also decreased significantly. Subgroup analysis showed there was no significant difference in topographic indices between age  $\geq 18$  years and  $< 18$  years at baseline and 3 years postoperatively and there was no significant difference in  $K_{\text{max}}$  reduction between the group with baseline  $K_{\text{max}} < 58$  D and that with  $K_{\text{max}} \geq 58$  D.

**Conclusions:** I-CXL for 10 min was safe and effective for the treatment of keratoconus patients over a 3-year follow-up period, even in those of young age and those with more severe keratoconus.

#### Topic Areas

CXL for ectasia, keratoconus

## Keratoconus progression to collagen cross-linking: creating personalised predictions at time of presentation

Authors: Mr. Howard Maile - UCL Institute of Ophthalmology, Dr. Olivia Li - Moorfields Eye Hospital, Dr. Mary Fortune - University of Cambridge, Mr. Marcello Leucci - Moorfields Eye Hospital, Prof. Patrick Royston - UCL, Prof. Stephen Tuft - Moorfields Eye Hospital, Dr. Nikolas Pontikos - UCL Institute of Ophthalmology, Dr. Daniel Gore - Moorfields Eye Hospital

#### Abstract

**Purpose:** To develop a prognostic model which can be used in the clinical setting to inform patients and clinicians of an individual's probability of progression to corneal collagen cross-linking over time. Crosslinking is a well-established treatment to halt the progression of keratoconus. Given though that there is a small risk of complications from the treatment, clinicians usually prefer to demonstrate progression before initiating treatment unless the disease is more advanced, and the patient is considered to be higher risk. There is a need to provide patients and clinicians with an early predictor of progression to allow for judicious and timely treatments, limiting appointments needed for monitoring and visual loss while awaiting to demonstrate progression. To address this unmet need, we set out to create an algorithm that generates a projected progression curve demonstrating the likelihood of progression or needing crosslinking based on data collected at presentation.

**Materials & Methods:** This was a retrospective cohort study of 9341 eyes from 5025 patients with suspected or confirmed keratoconus from Moorfields Eye Hospital, London. 3541 eyes received collagen crosslinking (CXL). Genetic data from 926 patients were included. The Royston-Parmar method on the proportional hazards scale was used to generate a prognostic model. Hazard Ratios (HR) for each significant covariate with explained variation and discrimination were calculated for the final model. Internal-external cross validation was performed by splitting the dataset into patient residential regions defined by their postcode and measuring the consistency in discrimination across different regions.

**Results:** The final dataset used for model fitting comprised 8701 eyes from 4823

patients of which 3232 eyes underwent CXL. Our model explained 33% of the variation in time-to-event with four significant covariates: age HR [95% confidence limits] 0.9 [0.90-0.91], Kmax 1.08 71 [1.07-1.09], Front K1 0.93 [0.91-0.94], and minimum corneal thickness 0.95 [0.93-0.96]. When performing internal-external cross validation, the predicted time-to-event curves generally followed the observed time-to-event curves and differences in discrimination between regions was low, suggesting the model maintained its predictive ability.

**Conclusions:** We have fitted a prognostic model for progression of keratoconus to CXL that could be used to aid clinical decision making. Age of presentation contributed most of the explained variation. It was trained and validated from a large dataset of 8701 eyes from ethnically diverse keratoconus patients from Moorfields Eye Hospital in London, followed up for over 5 years. We have identified key variables that contribute to the explained variation. Furthermore, and quite uniquely to our model, genomic risk loci associated with keratoconus for 926 patients were included and their contribution to the explained variation was assessed. We have also built a web application in order to demonstrate our predictive model in practice: <https://pontikoslab.com/kcprog>.

#### Topic Areas

CXL for ectasia, keratoconus

## Long term outcomes of accelerated corneal crosslinking in pediatric keratoconus patients with new progression indices

Authors: Dr. Pinar Kosekahya - Ulucanlar Eye Training and Research Hospital, Dr. Tugce Horozoglu - Ulucanlar Eye Training and

Research Hospital, Dr. Mustafa Koc - Special Ideal Eye Hospital

#### Abstract

**Purpose:** To evaluate the long term (5 years) outcomes of accelerated corneal crosslinking (CCL) with new progression parameters in pediatric keratoconus patients.

**Materials & Methods:** Forty eyes of 40 pediatric keratoconus (range; 9-17 years) patients were included to this retrospective study. CCL was performed under topical anesthesia with mechanical epithelial removal, 30 minutes riboflavin instillation, and 10 minutes 9 mW/cm<sup>2</sup> ultraviolet-A irradiation. Best corrected visual acuity (BCVA) and tomographical parameters from Pentacam Scheimpflug device were noted before and 1 and 5 years after CCL.

**Results:** Best corrected visual acuity, keratometry, front elevation, and asphericity values significantly improved 5 years after CCL ( $p < 0.001$  for all). Corneal densitometry values at total central and total 6-10, 10-12 zones significantly increased ( $p \leq 0.001$  for all). Five years progression was investigated with Belin ectasia progression software and regression in A value/anterior radius of curvature ( $p = 0.001$  and  $p = 0.001$ ); progression in B value/posterior radius of curvature ( $p = 0.04$  and  $p = 0.03$ ); progression in C value/thinnest corneal thickness ( $p < 0.001$  and  $p < 0.001$ ); regression in D value/best corrected visual acuity ( $p < 0.001$  and  $p < 0.001$ ). Multiple pachymetric indices indicated that corneal thickness significantly decreased after CCL ( $p < 0.01$  for all). Anterior corneal curvature was more flatter at 5 years compared to 1 year ( $p = 0.002$ ). Posterior corneal curvature, pachymetry, and BCVA values were similar to 1 year values at 5 years ( $p > 0.05$  for all).

**Conclusions:** Accelerated CCL was efficient and safe in halting the progression of pediatric

keratoconus at 5 years follow-up. The importance and how to interpret the Belin progression indices after CXL should be investigated further.

### Topic Areas

CXL for ectasia, keratoconus

## Morphological and immunohistochemical changes in the cornea after different UV crosslinking protocols

Authors: Dr. Usubov Emin - Ufa Eye Research Institute, Prof. Bikbov Mukharram M - Ufa Eye Research Institute

### Abstract

Purpose: to assess the dependence of oxidative and morphological changes in the cornea on the basis of immunohistochemical methods, confocal microscopy and optical coherence tomography after corneal crosslinking (CXL).

**Methods:** 33 patients (33 eyes) with stage I-III keratoconus (classification according to Amsler-Krumeich) underwent the study at the Ufa Research Institute of Eye Diseases, men - 21 (63.6%), women - 12 (36.4%). The S-CXL consisted of 20 patients (20 eyes), and the A-CXL-13 patients (13 eyes). The average age of the patients is  $28.7 \pm 5.6$  years. The local level of superoxide dismutase (SOD) and total antioxidant status (OSA) and their correlation with the keratocytes density and the depth of the DL were determined. The observation period - 3rd, 7th, 14th and 30th days after the procedure.

**Results:** In keratoconus there is a statistically significant low baseline TAAS level of  $1.68 \pm 0.21$  mmol/L with a significant decrease after S-CXL - on the 3rd day - to  $0.81 \pm 0.12$  mmol/L, on the 7th day -  $0.98 \pm 0.11$  mmol/L, 14th -  $1.19 \pm 0.15$  mmol/L and 30th -  $1.31 \pm 0.19$

mmol/L, respectively. After A-CXL, this indicator turned out to be slightly higher: 3rd -  $1.03 \pm 0.14$  mmol/L, 7th -  $1.15 \pm 0.15$  mmol/L, 14th -  $1.47 \pm 0.21$  mmol/L, and 30th -  $1.80 \pm 0.24$  mmol/L. The SOD level was  $96.7 \pm 11.3$  ng/ml, which decreased after S-CXL by the 3rd day - to  $9.1 \pm 8.5$  ng/ml, on the 7th -  $49.2 \pm 9.6$  ng/ml, on the 14th -  $58.7 \pm 16.7$  ng/ml with level restoration on the 30th - up to  $80.2 \pm 14.1$  ng/ml. After A-CXL, the dynamics were slightly better: on the 3rd day -  $60.5 \pm 11.2$  ng/ml, 7th -  $71.4 \pm 10.1$  ng/ml, 14th -  $93.5 \pm 3.2$  ng/ml and 30th -  $106.3 \pm 20.4$  ng/ml.

Oxidative stress showed a direct correlation with a decrease in the initial density of keratocytes on average from  $273 \pm 19$  c/mm<sup>2</sup> at a depth of up to 300  $\mu$ m: after S-CXL on the 3rd day - to  $202 \pm 11$  c/mm<sup>2</sup> and on the 30th day -  $212 \pm 18$  c/mm<sup>2</sup>, and after A-CXL the density of keratocytes was  $232 \pm 22$  c/mm<sup>2</sup> on the 3rd day and  $243 \pm 14$  c/mm<sup>2</sup> on the 30th day.

The depth of the DL after 30 days, in the center after S-CXL- $305.73 \pm 41.08$   $\mu$ m, while after A-CXL- $214.73 \pm 42.18$   $\mu$ m.

**Conclusions:** CXL in human keratoconus induces significant morphological changes as increased oxidative stress and keratocyte death. The severity of oxidative stress after S-CXL in comparison with A-CXL deserves higher. This was accompanied by a decrease in the density of keratocytes in the corneal stroma to a greater extent after S-CXL by 26% compared with 15% after A-CXL. This was accompanied by the formation of DL 29% deeper in S-CXL. The shown pathomorphological changes in the cornea can form the basis for choosing the optimal protocol for varying degrees of risk of disease progression in patients with keratoconus.

### Topic Areas

CXL for ectasia, keratoconus



## MyoRing and CXL in keratoconus treatment

Authors: Dr. Gyulli Kazakbaeva - Ufa Eye Research Institute, Prof. Bikbov Mukharram M - Ufa Eye Research Institute

### Abstract

**Purpose:** To evaluate functional results of complete corneal ring (MyoRing) implantation with corneal collagen crosslinking (CXL) in different combinations for progressive keratoconus.

**Design:** Retrospective cohort study.

**Methods:** MyoRing implantation with corneal CXL was performed in 135 eyes with progressive keratoconus of the II-III disease degree according to the Amsler classification. Implantation of a MyoRing in the corneal pocket was performed using a PocketMaker microkeratome and corneal intrastromal implantation system. Saturation of the cornea was performed with a solution of 0.1% riboflavin. Standard surface UV irradiation (370 nm, 3 mW/cm<sup>2</sup>) was carried out. The follow-up was 36 months.

**Results:** Significant improvements in uncorrected distance visual acuity and corrected distance visual acuity were observed. Corneal thickness decreased from baseline postoperatively, which corresponds with pachymetry reduction after conventional CXL. In all three subgroups, there was a significant decrease in Kav, as well as corneal astigmatism, the spherical equivalent of refraction. The effectiveness of combined operations in the three subgroups was comparable, cornea parameters remained stable.

**Conclusion:** Combination of CXL and MyoRing implantation was effective for keratoconus treatment. Combination of intrastromal ring

implantation with corneal crosslinking in patients with keratoconus provides a synergistic effect, contributing to the prevention of disease progression in 96.6% of cases by increasing the biomechanical stabilization of the tissue and flattening of the corneal surface.

### Topic Areas

CXL for ectasia, keratoconus

### Decision

Poster (4-minute pre-recorded video presentation, 6 slides max)

## Oxygen boosted transepithelial corneal collagen cross-linking: ultrastructural results

Authors: Prof. David Touboul - Bordeaux University and Hospital, National Reference Center for Keratoconus, Dr. Pierre Legout - Dr. Valentine Saunier - Bordeaux University and Hospital, National Reference Center for Keratoconus

Ms. Nathalie Thiery - Dr. Valentine Saunier - Bordeaux University and Hospital, National Reference Center for Keratoconus, Dr. Valentine Saunier - Bordeaux University and Hospital, National Reference Center for Keratoconus

### Abstract

**Introduction:** Corneal collagen cross-linking (CXL) treatment is an oxygen-dependent reaction, and the amount of singlet oxygen released in the stroma is dependent on both the UVA energy transfer from the activated riboflavin molecules and stromal oxygen concentration available. A new technique of transepithelial CXL using specially designed oxygen delivery goggles has been proposed to provide a high oxygen environment into the cornea.

**Material and methods:** This prospective, non-comparative, single-center, pilot cohort study was conducted at Bordeaux's French National Reference Center for Keratoconus. Patients with progressive KC were involved and transepithelial, pulsed, accelerated CXL in an oxygen-rich atmosphere was performed (Oxygen boosted CXL from Avedro - USA). We registered postoperatively the OCT demarcation line depth using an anterior segment optical coherence tomography (AS-OCT) (Cirrus, Zeiss, Germany) and a swept-source OCT-topography (SS-OCT) (CASIA2, Tomey, Japan) in between 3 and 6 months. Corneal innervation (sub basal nerve plexus) and keratocyte activation were subjectively evaluated with confocal microscopy (Heidelberg Engineering GmbH, Heidelberg, Germany). As well, endothelial cells count was assessed at each visit using a non-contact specular microscopy (Tomey, Japan) at each visit.

**Results:** Ten eyes of 10 patients were enrolled. The mean patient age was 23,8 (16-31). The mean preoperative Kmax was  $47,4 \pm 2,9$  D and the mean corneal thickness at the thinnest point was  $467 \mu\text{m} \pm 44$ . At 3 months, a posterior demarcation line was visible in 9 eyes (90%) with a mean depth of  $414 \mu\text{m} \pm 80,91$  with AS-OCT and  $397 \mu\text{m} \pm 148$  with SS-OCT (85,7 % of mean corneal full thickness). We also observed, more anteriorly, a hyperreflective band reaching the depth of  $213 \mu\text{m} \pm 42$  with AS-OCT. Compared to baseline, the corneal sub-basal nerve density had significantly decreased and superficially keratocytes apoptosis was observed at 3 months postoperatively. Indeed, there were no statistically significant differences between the mean endothelial cell counts before and 6 months after CXL. No intraoperative, neither postoperative complications were observed.

**Discussion:** Previous work suggests that the supplementary oxygen strategy might increase the aerobic type II reaction, enabling a potentially deeper and more effective CXL. The posterior demarcation line depth we found in our study, despite the absence of epithelial debridement, does confirm this hypothesis. We can assume that the hyperreflective anterior band we visualized was a change in corneal refractive index. Occurring in the strongest corneal part with closer collagen fibers and decreased in water content, we hypothesized the healing process could be amplified in that area. The posterior demarcation line remains probably the posterior limit of CXL biological interaction.

**Conclusion:** Transepithelial oxygen boosted CXL could provide a deep corneal photoreculation, avoiding the drawbacks of epithelium removal. Further complementary studies are necessary to confirm the long-term safety and efficacy.

#### Topic Areas

CXL for ectasia, keratoconus  
, CXL pre-clinical, translational

## Pilot Study of Transepithelial Corneal Crosslinking Using a Novel Ultraviolet Light-Emitting Contact Lens Device

Authors: Dr. Evan Dackowski - Albert Einstein College of Medicine, Bronx, New York, Dr. Juan Batlle Logroño - Cornea and Refractive Surgery Laser Center, Santo Domingo, Dr. Christina Rivera - Cornea and Refractive Surgery Laser Center, Santo Domingo

Ms. Najwa Taylor - TECLens, LLC, Mr. Patrick Lopath - TECLens, LLC, Stamford, Connecticut, Dr. Roy Chuck - Albert Einstein College of Medicine, Montefiore Medical Center, Department of Ophthalmology and Visual Sciences, New York

## Abstract

**Purpose:** To evaluate the feasibility of a novel, on-eye UVA light-emitting contact lens device driven by fiber optics for the corneal crosslinking (CXL) of patients with keratoconus.

**Methods:** In nine corneal transplant candidates with advanced keratoconus a scleral contact lens reservoir containing 0.007% benzalkonium chloride preserved with 0.25% riboflavin-monophosphate was placed on the eye for 30 minutes. The reservoir lens was removed and replaced with the CXLens UVA light-emitting contact lens. A 375-nm UVA light at 4 mW/cm<sup>2</sup> intensity was delivered for 30 minutes for a dose of 7.2 J/cm<sup>2</sup>. A one-sided paired *t*-test was used to evaluate mean differences in maximum keratometry, thinnest corneal thickness, and endothelial cell density between screening and 6 months after CXL. A two-sided paired *t*-test was used to evaluate differences in best-corrected distance visual acuity between screening and 6 months after CXL.

**Results:** All patients received the treatment as per protocol and adhered to follow-up testing. At 6 months after CXL, treated eyes had an average  $-1.0 \pm 1.6$  diopters decrease in the maximum keratometry ( $P=0.049$ ), a nonsignificant  $2.3 \pm 7.5$  letter improvement in best-corrected distance visual acuity ( $P=0.19$ ), a nonsignificant  $-17 \pm 14$   $\mu\text{m}$  decrease in thinnest corneal thickness ( $P < 0.01$ ), and a nonsignificant  $-86 \pm 266$  cells/mm<sup>2</sup> decrease in endothelial cell density ( $P=0.20$ ).

**Conclusions:** Our pilot study demonstrated the feasibility of the novel CXL device for the treatment of keratoconus and indicates the device is ready for larger scale studies with longer follow-up periods and offers the potential for efficient, high-throughput transepithelial corneal CXL.

## Topic Areas

CXL for ectasia, keratoconus

## Predicting factors for efficacy of corneal collagen cross-linking for pediatric keratoconus

Authors: Dr. Denise Wajnsztajn Vamos - Hadassah Medical Center - Hebrew University Hospital, Dr. Or Shmueli - Hadassah Medical Center - Hebrew University Hospital, Mr. Yehuda Tarnovsky - Hadassah Medical Center - Hebrew University Hospital, Prof. Joseph Frucht-Pery - Hadassah Medical Center - Hebrew University Hospital, Prof. Abraham Solomon - Hadassah Medical Center - Hebrew University Hospital

## Abstract

**Purpose:** To evaluate predicting factors of success of corneal collagen cross-linking (CXL) for pediatric keratoconus (KC) patients (18 years old or younger) in a single tertiary referral center.

**Materials & Methods:** Retrospective study based on a prospectively built database of pediatric patients who had CXL for KC. CXL was performed from 2007 to 2017 and included patients who had 1-year follow-up or more. We used univariate and multivariate analysis of the effects of CXL type (Accelerated or Non-Accelerated), demographics (age, gender, background of ocular allergy, ethnicity) and pre-operative LogMAR visual acuity, maximal corneal power (Kmax), pachymetry (CCT<sub>pre</sub>) and refractive cylinder as well as follow-up (FU) time on outcome measures. Outcome measures were the final change of Kmax ( $\Delta$  Kmax = Kmax<sub>last</sub> - Kmax<sub>pre</sub>) and the final change in LogMAR visual acuity ( $\Delta$ LogMAR = LogMAR<sub>last</sub> - LogMAR<sub>pre</sub>)

**Results:** 131 eyes from 110 children were included (mean age  $16 \pm 2$  years, range 10 to 18 years). Kmax and LogMAR significantly improved from baseline to last visit: from  $53.81 \text{ D} \pm 6.39 \text{ D}$  to  $52.31 \text{ D} \pm 6.06 \text{ D}$  ( $p < 0.001$ ) and from  $0.27 \pm 0.23$  LogMAR units to  $0.23 \pm 0.19$  LogMAR units ( $p = 0.005$ ), respectively. Negative  $\Delta K_{\text{max}}$  (cornea flattening) was associated with long FU, low  $\text{CCT}_{\text{pre}}$ , high  $K_{\text{max}_{\text{pre}}}$ , high  $\text{LogMAR}_{\text{pre}}$  and non-accelerated CXL in univariate analysis. Of those, high  $K_{\text{max}_{\text{pre}}}$  and non-accelerated CXL were associated with negative  $\Delta K_{\text{max}}$  in multivariate analysis. Negative  $\Delta \text{LogMAR}$  (vision improvement) was only associated with high  $\text{LogMAR}_{\text{pre}}$ .

**Conclusion:** CXL for pediatric KC patients is an effective treatment. Our results showed that the topographic CXL effect is time-dependent and that non-accelerated treatment is more effective than the accelerated protocol. Corneas with advanced disease had greater CXL effect.

#### Topic Areas

CXL for ectasia, keratoconus

## Progressive Ectatic Change Post Penetrating Keratoplasty for Keratoconus

#### Authors

Ms. Lynette Johns - Department of Ophthalmology, Massachusetts Eye & Ear, Harvard Medical School, Dr. Pia Easter Leon - Department of Ophthalmology, Massachusetts Eye & Ear, Harvard Medical School, Dr. Paola Cortez - Department of Ophthalmology, Massachusetts Eye & Ear, Harvard Medical School, Dr. Mehenaz Hanbazazh - Mass, Dr. Thaddeus Dryja - Department of Ophthalmology, Massachusetts Eye & Ear, Dr. Joseph Ciolino -

Department of Ophthalmology, Massachusetts Eye & Ear, Harvard Medical School

#### Abstract

**Purpose:** To evaluate postoperative Scheimpflug imaging changes during the first five years following penetrating keratoplasty (PK) in patients with keratoconus (KC).

**Methods:** This retrospective, interventional case series includes 31 consecutive eyes that underwent their first PK with a history of KC. Post-operative Scheimpflug imaging was performed 3 months after removal of the last suture (baseline) and then repeated 3 and 5 years following the PK. Demographic data, donor and host trephination diameter, and Scheimpflug imaging (Pentacam HR, Oculus, Germany) parameters indicative of ectasia were analyzed to evaluate postoperative graft changes that occur following PK.

**Results:** The maximal keratometry (Kmax) progressed significantly between baseline ( $53.5 \pm 6.1 \text{ D}$ ) and postoperative year 3 and year 5 ( $56.5 \pm 6.1 \text{ D}$  and  $58.8 \pm 7.9 \text{ D}$ ,  $p < 0.001$ ). Significant changes were also observed for the anterior best-fit-sphere and posterior best-fit-sphere ( $p < 0.001$  for 3 and 5 years compared to baseline). Kmax increased by at least 2 diopters for 74.2% of patients and up to 7 diopters or more 25.8% of the patients. A significant inverse correlation was observed for host trephine size and progression of Kmax ( $r = -0.52$ ,  $p = 0.01$ ), which indicated that larger host trephination size was associated with a smaller increase in postoperative Kmax.

**Conclusions:** Tomographic graft changes indicative of ectasia were observed within 3 to 5 years following PK in KC patients. These changes were observed more frequently and sooner following corneal transplants than previously reported.

**Key words:** Keratoconus, Recurrence, Ectasia, Tomography, Keratoplasty.

#### **Topic Areas**

CXL for ectasia, keratoconus

## Quantitative comparison of corneal surface areas in keratoconus and normal eyes

Authors: Prof. Damien Gatinel - Fondation Rothschild, Paris, Dr. François-Xavier Crahay - Fondation Rothschild, Paris, Dr. Guillaume Debellemanière - Fondation Rothschild, Paris

#### **Abstract**

Keratoconus is a highly prevalent corneal disorder characterized by progressive corneal thinning, steepening and irregular astigmatism. To date, pathophysiology of keratoconus development and progression remains debated. In this study, we retrospectively analyzed topographic elevation maps from 3227 eyes of 3227 patients (969 keratoconus and 2258 normal eyes) to calculate anterior and posterior corneal surface area. We compared results from normal eyes and keratoconus eyes using the Mann-Whitney U test. The Kruskal-Wallis test was used to compare keratoconus stages according to the Amsler-Krumeich classification. Anterior and posterior surface areas were calculated at the central 4.0 mm and 8.0 mm diameter from raw elevation data. Anterior and posterior surfaces areas from 8.0 mm to the limbus were extrapolated using a best fitting curve method. Distributions showed wide overlap between normal and keratoconus values. Keratoconus eyes were shown to have statistically significantly larger corneal surface areas, measured at the central 4.0 mm and 8.0 mm, and total corneal diameter. However, the differences were small (less than 1%) and no significant increase in corneal surface area

was seen with increasing severity of keratoconus. We suggest that these results indicate redistribution, rather than increase, of the corneal surface area with keratoconus severity.

#### **Topic Areas**

CXL for ectasia, keratoconus

## Refractive Lenticule Assisted Crosslinking of Ultrathin Corneas

Authors: Dr. Mahipal Sachdev - Centre for Sight Eye Hospital, Delhi, India, Dr. Tulika Chauhan - Centre for Sight Eye Hospital, Delhi, India, Dr. Raghav Malik - Centre for Sight Eye Hospital, Delhi, India, Dr. KANIKA BHARDWAJ - Centre for Sight Eye Hospital, Delhi, India, Dr. Krishna Boggarapu - Centre for Sight Eye Hospital, Delhi, India, Dr. Yuganki Kush - Centre for Sight Eye Hospital, Delhi, India

#### **Abstract**

**Purpose:** To evaluate the safety and efficacy of Crosslinking in thin corneas (less than 400 microns) following intraoperative stromal expansion using allogenic refractive lenticules obtained from Small Incision Lenticule Extraction (SMILE)

**Materials and methods:** In this prospective, interventional case series, allogenic corneal lenticules extracted from patients undergoing small incision lenticule extraction procedure were used as a method for stromal expansion in cases of keratoconus with ultrathin corneas (<400  $\mu\text{m}$ ). After scraping the epithelium, the extracted lenticule is placed with its thickest dimension above the thinnest part of cone, hence increasing thickness of the apex. An augmented stromal thickness of more than 400 microns is confirmed using intraoperative pachymetry. Remaining procedure of crosslinking is carried out according to the

accelerated protocol. At the end of the procedure the lenticule is peeled off the surface and bandage contact lens are applied.

**Result:** No intra-operative or postoperative complications, topography demonstrated corneal stability at 12 months post-operative period, anterior segment OCT showed demarcation line in all patients post operatively. All patients demonstrated BSCVA of 20/30 or more, with no deterioration in endothelial cell counts.

**Conclusion:** Refractive lenticule assisted corneal crosslinking is a safe, effective, and most physiological procedure for ultrathin corneas.

#### **Topic Areas**

CXL for ectasia, keratoconus

## **Riboflavin impregnation of 10 minutes during epi-off cross-linking is safe and efficient**

Authors: Prof. Arie Marcovich - Department of Ophthalmology, Kaplan Medical Center, Rehovot and Hadassa Faculty of Medicine, Hebrew University, Jerusalem

#### **Abstract**

**Purpose:** To demonstrate by literature search and experimentally that 10 minutes of riboflavin (RF) impregnation time before epi-off corneal crosslinking is safe and efficient.

**Setting:** Department of Ophthalmology, Kaplan Medical Center, Rehovot, Israel & Weizmann Institute of Science, Rehovot, Israel.

**Methods:** Analysis of clinical reports on safety and efficacy of corneal epi-off cross-linking with shortened RF impregnation time and experimental studies of RF corneal

penetration and UVA absorption and endothelial toxicity.

**Results:** Several clinical reports of corneal cross-linking with 5 to 10 minutes of RF impregnation showed safety and long-term efficacy. Experimental studies demonstrated that sufficient UVA blocking RF concentration is reached after 10 minutes, and endothelial toxicity is not increased compared to 30 minutes of impregnation.

**Conclusions:** RF impregnation time before epi-off corneal cross linking can be minimized to 10 minutes, reducing procedure duration without compromising safety and efficacy.

#### **Topic Areas**

CXL for ectasia, keratoconus

## **Safety and efficacy of Repeated Corneal Collagen Cross-linking in progressive Keratoconus**

Authors: Dr. Ofri Vorobichik Berar - Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel, Dr. Michael Rotenberg - Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel, Dr. Yoav Berger - Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel, Dr. Adham Matani - Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel, Dr. Noa Avni-Zauberman - Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel, Prof. Irit Barequet - Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel

## Abstract

**Purpose:** Progressive keratoconus may lead to severe visual disability. Although corneal collagen crosslinking (CXL) halts the progression of keratoconus in most cases, recurrence of progression, described in up to 8%, poses a therapeutic challenge. Our study evaluates the outcomes of repeated CXL in eyes that developed progression keratoconus after CXL.

**Material and Methods:** This retrospective study included all CXL-treated eyes that required CXL-retreatment due to progression between 2011 and 2020. All procedures were epi-off with a standard protocol of accelerated treatment. Data was retrieved on demographic, clinical, refractive, and topographic parameters.

**Results:** Ten consecutive eyes of 9 patients that developed progressive keratoconus after CXL were identified. The mean age at diagnosis of keratoconus was  $20.2 \pm 6.0$  years (range, 10.8-26.5 years) and the mean time from diagnosis to CXL-1 was  $2.7 \pm 2.0$  years (range, 0.3-6.6 years). Five (50%) patients reported atopic background and eye rubbing. The mean follow-up time from first to last visit was  $6.5 \pm 2.3$  years (range, 1.8-9.2 years) and after CXL-2 was  $2.1 \pm 1.3$  years, (range 0.6-4.8 years). The average Kmax was  $60.4 \pm 3.6$  D at indication for CXL-2. The average progression rate ( $\Delta K_1$ ), measured as the subtraction of K max values in the last 2 visits prior to referral to CXL-2, was  $2.84 \pm 2.30$  D. K max values have significantly progressed before the second CXL ( $P=0.005$ ). After CXL-2, Kmax was significantly lower at 6m, 12m and 24m comparing pre-CXL-2 ( $p=0.046$ ,  $p=0.018$ ,  $0.046$  respectively). Average progression rate ( $\Delta K_2$ ), measured as the subtraction of K max values prior to referral to CXL-2 and on the last post CXL-2 visit was  $-1.7 \pm 2.0$  D. Eight eyes (80%) showed stable or better corrected visual

acuity. No significant adverse effects were recorded post-CXL-2.

**Conclusion:** Repeated CXL is a safe and effective treatment when failure of the initial CXL is diagnosed in this relatively young group of patients. This procedure may prevent further vision deterioration and need for keratoplasty.

## Topic Areas

CXL for ectasia, keratoconus

## Ten years of corneal crosslinking follow-up

Authors: Prof. Madelyn Jareño - Cuban Society of Ophthalmology, Prof. Zaadia Pérez - Cuban Society of Ophthalmology, Prof. Alexeide Castillo - Cuban Society of Ophthalmology

## Abstract

A study with a quasi-experimental design was carried out to evaluate the treatment with corneal crosslinking in progressive keratoconus. Corneal crosslinking, the Dresden conventional method, was performed between 2008 and 2010. The operated eye was compared with the contralateral eye in 68 patients with a 10-year follow-up. Visual acuity slightly improved in more than 50% of the patients, as refractive parameters improved, as well as corneal surface regularity indices. we obtained a progressive flattening in 4 patients, and one of them exaggerated with hyperopic change. moderate permanent corneal Haze was found in two patients at ten years. We found no complications related to corneal, lens or retina endothelium. Corneal Crosslinking is an effective and safe long-term treatment.

## Topic Areas

CXL for ectasia, keratoconus

## The Impact of Previous Corneal Cross-Linking on Intrastromal Corneal Ring Segments Effect in Keratoconus Eyes: A Multi-Parameter Exact-Match Comparison to Virgin Eyes

Authors: Prof. Shady Awwad - American University of Beirut Medical Center, Dr. Karim Kozhaya - American University of Beirut Medical Center, Dr. Jad F. Assaf - American University of Beirut Medical Center, Dr. Anais Salloukh - American University of Beirut Medical Center

### Abstract

**Purpose:** To retrospectively evaluate the visual, refractive, and tomographic results of intracorneal ring segments (ICRS) insertion in keratoconus eyes with a previous history of corneal cross-linking (CXL), compared to virgin eyes.

**Methods:** A retrospective analysis of eyes with mild to moderate keratoconus that underwent ICRS was conducted from January 2017 to December 2018. 168 eyes were identified, of which 31 eyes had undergone previous CXL. Multi-parameter matching was performed on the virgin eyes to match the smaller post-CXL eyes group, based on ICRS size, type and arc-length, age, SimK, Kmax, pachymetry, topographic and manifest astigmatism, and manifest spherical equivalent refraction. Coarsened Exact Matching (CEM) was performed using 1:1 ratio, run twice on the remaining unmatched strata to yield a 2:1 ratio. The final comparison groups had 62 virgin keratoconus eyes and 31 post-CXL keratoconus eyes. Primary outcome measures preoperatively, and at 1, 3, and 6 months postoperatively, included uncorrected and distance-corrected visual acuity (UCVA and DCVA), manifest

sphere and cylinder, SimK and Kmax, and corneal higher order aberrations.

**Results:** The LogMAR UCVA for the ICRS and ICRS-CXL groups improved from  $0.74 \pm 0.23$  to  $0.37 \pm 0.27$ , and  $0.61 \pm 0.27$  to  $0.41 \pm 0.29$  respectively, while LogMAR CDVA improved from  $0.43 \pm 0.20$  to  $0.15 \pm 0.19$ , and  $0.31 \pm 0.16$  to  $0.10 \pm 0.12$  respectively, ( $P < 0.01$ ), and Kmax improved from  $53.57 \pm 4.16$  D to  $49.64 \pm 4.06$  D and  $53.59 \pm 4.85$  D to  $49.09 \pm 5.23$  D, respectively ( $P < 0.01$ ). Manifest cylinder improved from  $3.31 \pm 1.50$  D to  $1.56 \pm 1.33$ , and  $3.76 \pm 1.28$  D to  $1.01 \pm 0.87$  D, respectively ( $P < 0.01$ ). SimK changed from  $45.88 \pm 1.96$  D to  $44.46 \pm 2.28$  D, and  $45.5 \pm 3.08$  D to  $44.21 \pm 3.09$  D. Corneal total higher order aberrations and coma improved from  $1.87 \pm 0.85$  D to  $1.33 \pm 0.73$  D and  $1.53 \pm 0.58$  D to  $1.05 \pm 0.75$  D, respectively for the ICRS eyes, and  $1.96 \pm 0.83$  D to  $1.33 \pm 0.59$  D and  $1.62 \pm 0.80$  to  $1.02 \pm 0.44$  D, respectively, for the ICRS-post CXL eyes ( $P < 0.01$ ). No statistical difference was observed in the change from pre to postoperative values between the two groups in any category. No clinically relevant intraoperative or postoperative complications were observed during the follow up period in either group.

**Conclusions:** Corneal ring segments insertion in keratoconus eyes with previous corneal cross-linking have similar visual, refractive, and topographical results as virgin keratoconus eyes.

### Topic Areas

CXL for ectasia, keratoconus

## Transepithelial Accelerated Corneal Collagen Cross-Linking: Two-Year Results

Authors: Dr. Ana Maria Cunha - Department of Ophthalmology, Centro Hospitalar de São João, Dr. Tiago Sardinha - Faculty of Medicine,



University of Porto, Porto, Portugal, Dr. Luís Torráo - Department of Ophthalmology, Centro Hospitalar de São João, Dr. Raúl Moreira - Department of Ophthalmology, Centro Hospitalar de São João, Prof. Fernando Falcão-Reis - Department of Ophthalmology, Centro Hospitalar de São João; Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Dr. João Pinheiro-Costa - Department of Ophthalmology, Centro Hospitalar de São João; Department of Biomedicine, Faculty of Medicine of University of Porto

### Abstract

**Purpose:** To report 2-year outcomes of trans-epithelial accelerated corneal collagen crosslinking (TE-ACXL) procedure in the treatment of progressive keratoconus patients.

**Methods:** Twenty-four eyes from 24 patients who underwent TE-ACXL (6mW/cm<sup>2</sup> for 15 minutes) were included in this retrospective interventional study. Best corrected visual acuity (BCVA), keratometry values, thinnest corneal thickness (PachyMin) and topometric indexes were analysed preoperatively and at 6-month, 12-month, 18-month and 24-month postoperative. Progression was assessed by increase  $\geq 1.00D$  in maximum keratometry (Kmax); increase  $\geq 1.00D$  in corneal astigmatism; decrease  $\geq 2\%$  in PachyMin; increase  $\geq 0.42$  in D-index.

**Results:** There were no complications during or after TE-ACXL. No significant differences ( $\Delta$ ) were observed between baseline and 12-month or 24-month postoperative:  $\Delta BCVA$  ( $-0.08 \pm 0.25$ ,  $p=0.190$ ;  $-0.04 \pm 0.17$ ,  $p=0.588$ ),  $\Delta Kmax$  ( $-0.08 \pm 1.32$ ,  $p=0.792$ ;  $-1.04 \pm 1.89$ ,  $p=0.135$ ),  $\Delta Astigmatism$  ( $-0.15 \pm 0.89$ ,  $p=0.485$ ;  $-0.24 \pm 1.38$ ,  $p=0.609$ ),  $\Delta PachyMin$  ( $-0.56 \pm 15.70$ ,  $p=0.882$ ;  $0.56 \pm 18.74$ ,  $p=0.931$ ),  $\Delta Index Surface Variation (\Delta ISV)$  ( $-2.11 \pm 10.27$ ,  $p=0.395$ ;  $-4.67 \pm 17.32$ ,

$p=0.442$ ),  $\Delta Index Vertical Asymmetry (\Delta IVA)$  ( $-0.05 \pm 0.17$ ,  $p=0.208$ ;  $-0.08 \pm 0.26$ ,  $p=0.397$ ),  $\Delta Index Height Decentration (\Delta IHD)$  ( $0.00 \pm 0.02$ ,  $p=0.368$ ;  $-0.01 \pm 0.04$ ,  $p=0.484$ ),  $\Delta KI$  ( $0.00 \pm 0.05$ ,  $p=0.851$ ;  $0.01 \pm 0.06$ ,  $p=0.877$ ) and  $\Delta D$ -index ( $0.15 \pm 1.14$ ,  $p=0.572$ ;  $0.06 \pm 1.36$ ,  $p=0.892$ ). Eleven to 33% of patients had disease progression at 24-month postoperative according to the parameters used to determine progression.

**Conclusion:** Although some patients maintain disease progression, TE-ACXL seems to be a safe and effective treatment for keratoconus over the 2-year follow-up period. Studies with longer follow-up periods and larger patient cohorts are recommended.

### Topic Areas

CXL for ectasia, keratoconus

## Visual rehabilitation post corneal collagen crosslinking- Large Diameter Gas Permeable Contact Lenses

Authors: Dr. Tulika Chauhan - Centre For Sight Eye Hospital, Delhi, Dr. Mahipal Sachdev - Centre For Sight Eye Hospital, Delhi

### Abstract

**Purpose:** To elucidate on superior role of large diameter gas permeable contact lenses in visual rehabilitation after corneal collagen cross linking (CXL) in Mild to Advanced cases of ectasia.

Large diameter gas permeable contact lenses are one of the most underutilized therapeutic adjuncts in the management of corneal diseases. Irregular corneas with high astigmatism, severe ectasia and scarring limit patients to achieving full visual potential with spectacles alone. This comes from a lack of understanding of the mechanisms in which

contact lenses help these patients as well as difficulty of access to new and special types contact lenses

While the role of RGP lenses has been reiterated multiple times in literature, the advantages of other specialty contact lenses such as Scleral, mini scleral lenses and newer hybrid lenses remains untapped. Although the fitting of contact lenses is typically managed by optometrists, it is important for ophthalmologists to understand the potential role for scleral lenses, particularly in corneal ectasia and ocular surface disease. We present a case series of 20 patients of corneal disorders presenting to our clinic which were rehabilitated using large diameter gas permeable contact lenses and gained good visual outcome (improvement in Snellen acuity of two lines and more). These included 10 cases of advanced keratoconus with apical scarring and status post C3R, 3 cases of advanced keratoconus with history of corneal hydrops, 5 cases of corneal ectasia following previous Keratorefractive surgery and 2 cases of Pellucid Marginal Degeneration. All these cases showed significant improvement in visual acuity and improved quality of life. Giving various examples from our practice, we emphasize on proper utilization and promotion of use of specialty contact lenses in regular clinical practice in ophthalmology clinics in Indian scenario to provide a superior vision quality and symptomatic relief to such patients.

#### **Topic Areas**

CXL for ectasia, keratoconus  
, CXL Plus (combination), CXL for Refractive

## CXL for Refractive

### Determining the Utility of Epithelial Thickness Mapping in Refractive Surgery Evaluations

Authors: Dr. Lara Asroui - Cleveland Clinic, Dr. William Dupps - Cleveland Clinic, Dr. J. Bradley Randleman - Cleveland Clinic

#### Abstract

**Purpose:** To determine the impact of corneal epithelial thickness maps on screening for refractive surgery candidacy.

**Materials and Methods:** 100 consecutive patients who presented for refractive surgery screening were re-evaluated. For each patient, screening based on Scheimpflug tomography, clinical data, and patient history was done and a decision on eligibility for LASIK, PRK, and SMILE was independently made by two masked examiners. Examiners were then shown patients' epithelial thickness maps derived from OCT and were asked to reconsider their decisions. The percentage of screenings that changed after evaluating the epithelial thickness maps, with regards to candidacy for surgery and ranking of surgical procedures from most favorable to least favorable, was determined.

**Results:** Candidacy for corneal refractive surgery changed in 16% of patients after evaluation of the epithelial thickness maps, with 10% of patients screened in and 6% screened out. Surgery of choice changed for 16% of patients, and the ranking of surgical procedures from most to least favorable changed for 25% of patients. 11% of patients gained eligibility for LASIK while 8% lost eligibility for LASIK. No significant difference

was found between the evaluations of the two examiners.

**Conclusions:** Epithelial thickness mapping derived from OCT imaging of the cornea alters candidacy for corneal refractive surgery, as well as choice of surgery, in a substantial percentage of patients, and is thus a valuable tool for screening evaluations. Overall, the use of epithelial thickness maps results in screening in a slightly larger percentage of patients for corneal refractive surgery.

#### Topic Areas

CXL for Refractive

### Use of Corneal Collagen Cross-Linking with a new customized treatment scheme, for the reduction of hyperopic shift and visual fluctuations in a patient previously operated on for myopic radial keratotomy: a case report.

Authors: Dr. Alfonso Anania - Ophthalmology Villa Valeria, Rome Italy

#### Abstract

Radial keratotomy was the first refractive surgery technique used since the 1970s and used until the arrival of PRK in the mid-1990s, worldwide. One of the most frequent complications of this technique is the "hyperopic shift" that is the accentuation of the flattening effect of the central area of the cornea, with an overcorrection that tends to become accentuated over the years.

In addition, corneal instability leads to annoying visual fluctuations throughout the day. Up to now, the solutions for this complication have been the continuous use of pilocarpine eye drops, The Grene encircling

sutures, PRK and its variants, LASIK, intraLasik, phakic IOL, and refractive lens exchange.

All of these methods have not been shown to be completely effective and not free from complications, and also do not solve the problem of visual fluctuations during the day. For this reason, a less invasive method was sought, characterized by lower risks of complications and easily repeatable.

**Case presentation:** This report describes a case of a patient, a 50-year-old male, operated in 1995 with radial keratotomy with 10 incisions and an optical zone of 3.0 mm for a myopia of -8.00 D. At the time of surgery, he presented a hyperopic shift of + 4.25 sf +0.75 cyl (50), with anisometropia and strong visual fluctuations during the day.

The main goal was to stabilize visual fluctuations. The Dresden protocol was used for UV irradiation but customizing the removal of the epithelium and the treatment areas. Three-month postoperative examinations demonstrated an increase in central corneal dioptric power of 1.75 D, a reduction in corneal aberrations, a better UCVA, a better BCVA, a reduction in hypermetropic defect, and a marked reduction in patient-reported diurnal visual fluctuation.

**Conclusions:** Until now, the solutions proposed for the treatment of hyperopic shift as a complication of KTR were invasive and ineffective, with conflicting results, reported in the literature.

We propose a new treatment modality with customized- CXL, to stabilize the corneal tectonics and reduce the hyperopic defect.

The result of this case is encouraging, but it will be necessary to evaluate the results on a greater number of patients and in the longer

term, to better value the usefulness and effectiveness of this treatment.

### **Topic Areas**

CXL for Refractive

## CXL Plus (combination)

### Comparison of Corneal Thickness Changes during Corneal Collagen Crosslinking and Surgical Efficiency Using Different Rose Bengal Formulations

Authors: Dr. Jinhai Huang - Eye & ENT Hospital, Dr. Rongrong Gao - School of Ophthalmology and Optometry and Eye Hospital, Dr. Mengdi Yan - Wenzhou Medical University, Dr. Ming Chen - Wenzhou Medical University, Dr. Sally Hayes - Cardiff University, Dr. Keith M. Meek - Cardiff University, Prof. Qinmei Wang - School of Ophthalmology and Optometry and Eye Hospital

#### Abstract

**Purpose:** To compare the central corneal thickness (CCT) changes during in vivo rose bengal-green light corneal collagen cross linking (RGX) and surgical efficiency using different rose bengal (Rb) formulations in rabbit corneas.

**Methods:** The rabbits were divided into 10 groups according to Rb solution formulas and infiltration time. After epithelium removal, five Rb solutions were immersed in rabbit cornea in vivo, then the Rb fluorescence distribution in corneal stroma was analyzed by confocal fluorescence detection. During the in vivo RGX process, the CCT was measured at the following 7 time points: before and after epithelium removal, after Rb solution infiltration, after irradiation for 200 seconds, 400 seconds, 600 seconds, and after irrigation. Corneal enzymatic resistance test and corneal biomechanics test were performed to compare the RGX effect among different groups.

**Results:** During RGX, the CCT increased significantly after infiltration, then decreased significantly in the first 200seconds of green light irradiation but decreased slowly for the next 600 seconds. CCT of 20minute groups was significantly higher than that of 2 min groups ( $P < 0.0001$ ). RGX both improved the anti-solubility and biomechanical properties of corneas, and the effect of 20 min groups was better than that of 2 min groups. Hydroxypropyl methylcellulose (HPMC) help to maintain CCT during the process of light exposure, while did not affect the infiltration of Rb into the corneal stroma and the effect of RGX.

**Conclusions:** HPMC in Rb formulation helped maintaining the CCT during green light irradiation and improved the safety of RGX surgery. HPMC-Rb formulation infiltrating for 20 minutes achieved an ideal RGX effect. It has a great application prospect in clinical corneal collagen cross-linking.

#### Topic Areas

CXL Plus (combination)

### Comparison of outcomes of Bowman Stromal Inlay (combined Bowman layer and anterior stroma) with corneal collagen cross linking in progressive keratoconus.

Authors: Dr. Yatri Pandya - L J Eye Institute , Ambala , Haryana, Dr. Debapriya Chatterjee - L J Eye Institute , Ambala , Haryana, Dr. Vikas Mittal - L J Eye Institute , Ambala , Haryana

#### Abstract

**Purpose:** To report outcomes of bowman stromal inlay and corneal collagen cross linking performed in either eye of five patients with progressive bilateral keratectasia.

**Methods:** This is a prospective non randomized study including five patients of bilateral progressive keratoconus wherein each patient underwent cross linking in one eye and was operated with BS Inlay in the other eye. The eye which had minimal 400 microns thickness at thinnest point were taken up for corneal collagen cross linking with riboflavin and UV light. The eyes not amenable for such treatment underwent a novel kind of stromal augmentation in the form of bowman stromal inlay (BS Inlay) fashioned using femtosecond laser from donor eyes and implanted with simple IOL injector in femto created recipient stromal pocket. Serial refractive and tomographic outcomes were recorded and analyzed.

**Results:** Mean follow up of all cases was 14.4 months (minimum 6, maximum 24) in terms of clinical refraction, retinoscopy, slit lamp examination and tomographic assessment. In all five patients halt of progression was noted with both the techniques. The change in Kmax was 0.6 +- 1.81 D and 1.04+-9.08 D in CXL and BS Inlay eyes respectively. There was decrease in Kmax in 3 cases. Similarly, Kmean of anterior corneal surface showed change of 0.34+-0.21 D in CXL eyes and 0.74+-4.32 D in BS Inlay eyes. Pachymetry at thinnest point was increased in all cases of BS Inlay with average increase of 96.2+-32.77  $\mu$ . CXL eyes, pachymetry was decreased in almost all cases ( -19.4+-33.05  $\mu$ ). All BS Inlay eyes, corneas became more oblate or less prolate after the surgery whereas Q value in CXL eyes remained same as pre-operative level.

**Conclusion:** We report a comparative study of two techniques for progressive keratoconus. Both have comparable results in terms of halting the progression of ectasia. The BS Inlay technique additionally achieved increase in pachymetry which may provide opportunity for future topo guided laser surgery.

## Topic Areas

CXL Plus (combination)

## Difference between anterior and stromal topography in keratoconus - Treatment implications for combined CXL with topo-guided ablation

Authors: Prof. Aleksandar Stojanovic - University Hospital North Norway, Tromsø

### Abstract

A didactic presentation will cover in depth the mechanisms and rules of epithelial remodelling, the differences between the anterior corneal and stromal surface optical characteristics in keratoconus and the impact of those differences on regularizing topography-guided treatments, often used within a combined procedure with CXL.

**Methods:** Anterior corneal- and stromal surface topographies and epithelial thickness maps were analyzed in 12 keratoconus eyes. On one of the eyes, three different surface ablations techniques were simulated: 1. Conventional topography guided photo-refractive keratectomy (PRK), 2. Trans-epithelial topography guided PRK in combination with photo-therapeutic keratectomy (PTK) and 3. Stromal topography guided PRK.

**Results:** Stromal surface topographies showed higher K-values, astigmatism, asphericity and corneal higher-order aberrations compared to topographies of anterior corneas covered by epithelium. Topography guided PRK combined with trans-epithelial PTK, delivered on intact epithelium and stromal topography guided PRK, delivered after epithelial removal, both resulted in regularization of corneal surface, while anterior topography guided PRK delivered after epithelial removal, resulted in residual irregularities.

**Conclusion:** The difference in optical landscapes between the stromal and the anterior surfaces represent a source of error when anterior topography guided treatments are delivered on the de-epithelialized stroma, as in traditional PRK. Hence, anterior corneal topography guided ablations should be performed as trans-epithelial PRK, stromal topography guided ablations should be delivered after epithelial removal. Our conclusion is that one should always ablate the same surface from which the topography data originate.

#### **Topic Areas**

CXL Plus (combination)

## Prospective, Randomized, Multicenter, Double-Masked, Clinical Trial Evaluating Corneal Crosslinking of Keratoprosthesis Carrier Tissue

Authors: Dr. Sofia De Arrigunaga - Massachusetts Eye and Ear, Dr. David Zurakowski - Boston Children's Hospital, Dr. Esen Akpek - Wilmer Eye Institute, Johns Hopkins, Dr. Anthony Aldave - UCLA Stein Eye Institute, Dr. Shahzad Mian - Kellogg Eye Center, University of Michigan, Dr. Joseph Ciolino - Department of Ophthalmology, Massachusetts Eye & Ear, Harvard Medical School

#### **Abstract**

**Purpose:** Evaluate the safety and efficacy of donor collagen crosslinked corneas as carriers for Boston Keratoprosthesis (KPro) in patients with high risk of corneal melt after keratoprosthesis.

**Methods:** Candidates for KPro at increased risk for sterile cornea ulceration were randomized to either crosslinked or non-crosslinked donor corneas as carrier tissue for

KPro. There was a 52-week follow-up period followed by standard of care for three years every six months or until study closure. Main efficacy measure was KPro retention. Safety measures include incidence of delayed epithelial healing at day 30, time from surgery to retroprosthetic membrane treatment and occurrence of vitritis. Unmasked survival analysis of efficacy and safety measures will be presented in detail. A multivariable Cox proportional hazards regression model will be used to assess the effect of crosslinking in preventing corneal melts and increasing KPro retention time independent of patient covariates and adjusting for center.

**Results:** Data collection has been completed. Sixty-eight Kpros were implanted in 68 eyes (56 with previous sterile corneal ulceration) in 68 patients (15 with autoimmune disease) between 2017 - 2020 across 13 sites. The average age at the time of surgery was 62 [24-89] years and 42 (62%) subjects were male. The mean follow-up time was 91 weeks (SD=47.6). A total of 20 KPros were removed with an average survival time of 70 [6-160] weeks.

Eighteen (90%) KPros were removed because of corneal melts, 1 because of a retinal detachment and 1 because of endophthalmitis.

**Conclusion:** We will present unmasked safety and efficacy data on the use of crosslinked carrier tissue for Kpros.

#### **Topic Areas**

CXL Plus (combination)

## Simultaneous surface ablation and accelerated high-fluence corneal cross-linking for subclinical keratoconus

Authors: Dr. Juan Arbelaez - Muscat eye Laser Center

### Abstract

**Purpose:** To determine the safety and efficacy of transepithelial photorefractive keratectomy (Trans-PRK) combined with simultaneous accelerated high-fluence corneal cross-linking (A-CXL) in patients with subclinical keratoconus.

**Setting:** Muscat Eye Laser Center, Muscat, Sultanate of Oman.

**Methods:** This single-center, retrospective, observational study evaluated the clinical outcomes of Trans-PRK with the Amaris 1050RS (SCHWIND eye-tech-solutions, Kleinostheim, Germany), and simultaneous A-CXL (30\*1'16", 2.3) (Avedro) on patients with subclinical keratoconus. Patients with at least one year of Follow-up were included.

**Results:** This study included 633 eyes of mean age 27 years. At 1 year of follow up there was a significant improvement in UCVA  $p < 0.05$ , mean manifest refractive spherical equivalent (MRSE)  $p < 0.05$ , sphere  $p < 0.05$  and cylinder  $p < 0.05$ . Although mean BCVA improved the difference was not statistically significant.

**Conclusions:** Trans-PRK plus accelerated high-fluence corneal cross-linking (Trans-PRK xtra) provides excellent visual outcomes in subclinical keratoconus patients. Long-term stability of these results will need to be confirmed with longer follow up.

Financial Disclosure: None.

### Topic Areas

CXL Plus (combination)

## Ten-year follow-up of corneal cross-linking and refractive surface ablation in patients with asymmetric corneal topography

Authors: Mr. Bernardo Moscovici - Unifesp, Mr. Pablo Rodrigues - Unifesp, Mr. Felipe Taguchi - Unifesp, Mr. Mauro Campos - Unifesp

### Abstract

**Purpose:** Compare the safety and efficacy of wavefront-guided PRK combined or not with CXL for refractive correction in patients with bilateral asymmetric corneal topography.

**Setting:** Outpatient Surgical Optics, Department of Ophthalmology and Visual Sciences, Federal University of São Paulo, Brazil.

**Design:** Prospective randomized clinical trial

**Methods:** Sixteen patients (32 eyes) were enrolled in this study. CXL with subsequent PRK after 6 months was performed in one eye, and PRK alone was performed in contralateral eyes. Patients were followed for 10 years. We analyzed visual outcomes, Scheimpflug tomography and corneal haze evaluation.

**Results:** Overall, control eyes showed better results than eyes in the CXL + PRK group. Mean CDVA was 0.044 (SD, 0.073) in the PRK group and 0.1 (SD, 0.21) in the CXL + PRK group, mean sphere was 0.21 (SD, 0.6) D in the PRK group and 0.87 (SD, 2.3) D in the CXL + PRK group, and mean SE was -0.35 (SD, 0.65) D in the PRK group and 0.62 (SD, 2.32) D in the CXL + PRK group. In one patient, a steepening of 2.5 D and a thinning of 17  $\mu\text{m}$  occurred in the control eye (PRK alone). Two patients in the CXL + PRK group presented corneal haze. The overall complication rate was 18,75%.



**Conclusion:** Non-simultaneous CXL and PRK procedures yielded good refractive results, but worse than those obtained with PRK alone. Although one patient in the PRK group developed corneal ectasia, the CXL + PRK group had a higher rate of loss vision lines, indicating less safety. Due to the high percentage of complications, refractive surgery in patients with asymmetric corneas should be carefully analyzed, probably avoided, but studies with a larger sample may contribute to this area of study.

#### Topic Areas

CXL Plus (combination)

## Visual and Refractive outcomes and Aberrations of Simultaneous Wavefront Guided Photorefractive Keratectomy and Corneal Cross-Linking in Early Keratoconus.

Authors: Dr. Seyed Javad Hashemian - Iran University of Medical Science

#### Abstract

**Purpose:** To evaluate the safety, efficacy and aberration changes of simultaneous wavefront guided photorefractive keratectomy (WFG-PRK) and accelerated corneal cross-linking (ACXL) in early keratoconus and low myopic astigmatism.

**Setting;** Eye Research Center, The Five Senses Institute, Rassoul Akram Hospital, Iran University of Medical Sciences and Iranian Eye Clinic, Tehran, Iran.

**Design;** Prospective, interventional, non-randomized, case series

**Methods:** Fifty eyes of 29 patients (mean age: 30.76y) with mild, non-progressive (stages 1) keratoconus and low myopic astigmatism were enrolled. Uncorrected (UDVA) and

corrected distance visual acuity (CDVA), refraction, steep and flat keratometry readings, aberrometry and adverse events were evaluated, over 6.0 months of follow-up.

**Results:** All study parameters showed a statistically significant improvement at 6 months over baseline values. The mean follow-up time was 10.24±4.9mo (range: 6-24mo). Patients showed a significant improvement in UDVA from 1.2±0.29 logMAR prior to procedure to 0.10±0.14 logMAR postoperatively. CDVA significantly increased from 0.08±0.10 logMAR preoperatively to 0.02±0.06 postoperatively. A significant decrease in the mean spherical equivalent (SE) refraction was observed from -2.40±1.13 to -0.13±0.50 diopters (D) ( $P=0.00$ ), and the manifest sphere decreased from -1.34±0.99 to -0.19±0.57 D ( $P=0.00$ ). The manifest cylinder significantly decreased from -1.73±0.86 to -0.66±0.59 D postoperatively ( $P=0.00$ ). The mean steep keratometry and mean steepest keratometry (Kmax) was 45.60±1.68, 46.44±1.6D preoperatively reduced significantly to 43.01±1.71, 44.09±1.77D respectively ( $P<0.05$ ). Thirty-three (46%) eyes gained 1-3 line of CDVA. The total high order aberrations were decreased from 0.61±0.41  $\mu\text{m}$  to 0.58±0.24 ( $p=0.586$ ). Ten eyes developed mild haze that responded well to a short course of topical steroids.

**Conclusion:** Combined WFG-PRK with accelerated CXL is an effective and safe option for correcting mild refractive error and improving visual function in patients with early stable Keratoconus.

#### Topic Areas

CXL Plus (combination)

## CXL pre-clinical, translational

### A novel Pathfinder to predict postoperative corneal stiffness after refractive surgery which will aid in preventing postoperative ectasia

Authors: Dr. SAVITRI KUMARI - Narayana Nethralaya, Dr. Rohit Shetty - Narayana Nethralaya, Dr. Abhijit Sinha Roy - Narayana Nethralaya, Mr. Mathew Francis - Narayana Nethralaya, Dr. Pooja Khamar - Narayana Nethralaya, Dr. Sailie Shirodkar - Narayana Nethralaya

#### Abstract

**Purpose:** The purpose of our study is to develop a novel pathfinder software for predicting the postoperative corneal stiffness (Kcmean) after laser vision correction (LVC) surgery. Additionally, we aim to demonstrate its accuracy in predicting the risk of developing ectasia postoperatively.

**Materials and Methods:** A retrospective, observational, randomized study was conducted at three different tertiary eye care hospitals. The study included 529 eyes of 529 patients from three different tertiary level eye care health facilities (Narayana Nethralaya Eye Hospital, India; Sankara Nethralaya, India; Humanitas Clinical and Research Center, Italy). Also, 7 eyes that had developed ectasia after LVC were evaluated and analyzed in detail. Pathfinder software (called AcuSimX™) is a predictive tool based on finite element method (FEM) and artificial intelligence (AI) model (Orange AI, University of Ljubljana, Slovenia). It used the preoperative Pentacam tomography (OCULUS Optikgeräte GmbH, Germany) and Corvis-ST parameters to build a biomechanically functional virtual cornea. The virtual cornea mimicked in vivo corneal

biomechanical response. The software computed the postoperative Kcmean after factoring the surgical parameters and postoperative measurement uncertainties on the virtual cornea. We further tested the applicability of the software in depth by testing it on 7 eyes which had developed ectasia after LVC. Based on all the above analysis, a nomogram was then built which will help in the risk assessment of ectasia preoperatively. The predictability of developing ectasia was calculated from the mean absolute error and intraclass correlation coefficient (ICC) between the measured in vivo and software computed postoperative Kcmean.

**Results:** In the training set consisting of 60% of the data, the ICC between measured & predicted postoperative Kcmean was found to be 0.84 [0.80-0.84] (median and 95% confidence interval), along with a mean absolute error value of 6.24 N/m. Likewise, in the test cohort consisting of 40% of the data, these values were 0.84 [0.78-0.89] and 6.47 N/m respectively. The measured in vivo and software computed Kcmean of the 7 ectatic eyes were found to be statistically similar ( $p > 0.05$ ). Also, the nomogram which was developed for the ectasia risk assessment was able to detect all of these 7 eyes. The prediction took about 20 keystrokes and an average run time of 1.72 [1.66, 1.79] hours on a regular desktop computer.

**Conclusion:** Overall, excellent ICC (0.84) demonstrated the accuracy of predicting the postoperative corneal stiffness. Additionally, an effective nomogram was created that will help in the preoperative identification and screening of eyes who are at risk for developing ectasia. This pathfinder software has an easy user interface and can be a part of our day-to-day refractive practice.

## Topic Areas

CXL pre-clinical, translational

## AI KC Demographics – “Using Artificial Intelligence in predicting keratoconus progressors” - A novel insight

Authors: Dr. Tulasi Meda - Narayana Nethralaya, Dr. Rohit Shetty - Narayana Nethralaya, Dr. Pooja Khamar - Narayana Nethralaya, Dr. Gairik Kundu - Narayana Nethralaya

### Abstract

**Purpose:** To identify and analyse the high risk factors and demographic factors influencing the progression of keratoconus using an Artificial intelligence (AI) model.

**Materials and Methods:** 500 eyes of 500 patients of keratoconus with at least 2 visits were included. Changes in the anterior corneal curvature (Kmax) between 2 visits at least 6 months apart were looked at. We used the Random Forest (RF) classifier model from our previous study that evaluated longitudinal changes in tomographic parameters to predict “progression” and “no progression” to classify these patients. Demographic data and risk factors assessment was done through a questionnaire which included eye rubbing, IgE, Vit D and Vit B12 levels, duration of indoor activity, usage of lubricants and immunomodulator topical medications, duration of computer use, hormonal disturbances, use of hand sanitisers. An AI model was built to look at these risk factors. The area under the curve (AUC), sensitivity (se), specificity (sp) and accuracy (ac) along with other metrics were evaluated.

**Results:** 2 AI models were used – tomographic AI model to classify eyes as “progression” and as “no progression”. The second AI model was

built to evaluate the clinical risk factors in each group. About 76% of the cases that were classified as “progression” (from tomographic changes) were correctly predicted as “progression” and 65% of cases that were classified as “no progression” were predicted as “no progression” based on changes in clinical risk factors. IgE levels had the highest information gain, followed by presence of systemic allergies, Vitamin D levels and eye rubbing. The clinical risk factors model had accuracy, sensitivity, specificity of, 71.3%, 83% and 87 %, respectively.

**Conclusions:** This demonstrates the importance of use of AI for risk stratification and profiling patients which could impact disease progression in keratoconus and thereby help us identify and manage them better.

## Topic Areas

CXL pre-clinical, translational

## Cone Shape Change with Keratoconus Progression

Authors: Dr. Ashkan Eliasy - University of Liverpool, Dr. Prema Padmanabhan - Sankara Nethralaya, Dr. Bernardo Lopes - University of Liverpool, Dr. Haixia Zhang - Capital Medical University, Dr. Ahmed Abass - University of Liverpool, Prof. Ahmed Elsheikh - University of Liverpool

### Abstract

**Purpose:** To evaluate the cone shape change with keratoconus (KC) progression using a new and validated method.

**Methods:** In this retrospective record review, the preoperative of progressive KC cases that were submitted to corneal cross-linking were evaluated. All cases were examined with

Pentacam HR (Oculus, Wetzlar, Germany). Significant progression was based on the Pentacam's ABCD system. Progression was established when there was a significant change (above the CI 95%) towards kc deterioration in corneal thickness and anterior and posterior surfaces. On the first and last visit before the procedure, cone features including centre location, height and area were assessed.

**Results:** A total of 49 eyes were included in the study. The mean time between the two examinations was  $35.9 \pm 29.8$  months. A significant increase in cone height was observed in both corneal surfaces with the posterior ( $36 \pm 27 \mu\text{m}$ ) being higher than the anterior ( $20 \pm 17 \mu\text{m}$ ,  $p < 0.001$ ). A non-statistically significant increase was observed in cone area (anterior:  $0.09 \pm 1.24 \text{ mm}^2$ ,  $p=0.921$ ; posterior:  $0.08 \pm 1.12 \text{ mm}^2$ ,  $p=0.465$ ). A small shift of the cone centre towards the corneal apex was recorded on both surfaces. There was high correlation between the change in cone height and maximum anterior curvature (anterior:  $p=0.74$ , posterior:  $p=0.72$ ,  $p < 0.001$ ) and between the change in cone height and minimum thickness (anterior:  $p=-0.72$ , posterior:  $p=-0.52$ ,  $p < 0.001$ ).

**Conclusions:** Cone morphological changes were described in a longitudinal study. There was a significant increase in cone height especially in the posterior surface with small alterations in the cone area. The cone centre also shifted towards the apex with disease progression.

#### Topic Areas

CXL pre-clinical, translational

## Corneal biomechanical deterioration with keratoconus progression assessed by the Stress-Strain Index

Authors: Dr. Bernardo Lopes - University of Liverpool, Dr. Prema Padmanabhan - Sankara Nethralaya, Dr. Ashkan Eliasy - University of Liverpool, Dr. Haixia Zhang - Capital Medical University, Dr. Ahmed Abass - University of Liverpool, Prof. Ahmed Elsheikh - University of Liverpool

#### Abstract

**Purpose:** To evaluate the corneal biomechanical deterioration with keratoconus (KC) progression as measured by the stress-strain index (SSI).

**Methods:** In this retrospective record review, the preoperative of progressive KC cases that were submitted to corneal cross-linking were evaluated. All cases were examined with Pentacam HR and the Corvis ST (Oculus, Wetzlar, Germany). Significant progression was based on the Pentacam's ABCD system. Progression was established when there was a significant change (above the CI 95%) towards kc deterioration in corneal thickness and anterior and posterior surfaces. On the first and last visit before the procedure, the biomechanically corrected intraocular pressure (bIOP), the SSI, the integrated inverse radius (IIR), the stiffness parameter at the first applanation (SP-A1), the maximum corneal apex displacement in the Z direction (DA), the deformation amplitude ratio over 2mm (DA Ratio), were assessed.

**Results:** A total of 32 eyes fulfilled the inclusion criteria. The mean age at the last exam before the CXL procedure was  $22.0 \pm 7.7$  years (10 – 43). The mean time between the two examinations was  $41.4 \pm 40.9$  months (4 – 145). A spectrum of disease stages was

observed at the first examination with Kmax of  $54.41 \pm 4.34$  D (44.5 – 64.4) and minimum thickness of  $466.72 \pm 28.48$   $\mu$ m (414 – 520). While the bIOP showed non-significant change between the exams ( $-0.05 \pm 1.21$  mmHg, range: -2.0 to 2.3,  $p=0.731$ ), the biomechanical parameters changed between the two time points towards tissue softening. There was significant reduction in the SSI ( $-0.10 \pm 0.06$ , range: -0.2 to 0.0,  $p<0.001$ ) and increase in IIR ( $0.95 \pm 1.04$  mm<sup>-1</sup>, range: -2.34  $\pm$  2.69,  $p<0.001$ ). In the same direction towards corneal softening were observed a barely significant increase in DA ( $0.04 \pm 0.13$  mm, range: -0.22 to 0.53,  $p=0.056$ ), a significant increase in central 2mm DA ratio ( $0.23 \pm 0.58$ , range: -1.31 to 1.49,  $p=0.034$ ) and a significant decrease in SP-A1 ( $-6.1 \pm 12.0$  mmHg/mm, range: -31.8 to 18.9,  $p=0.011$ ), however in these last three measures, there was a substantial overlap between the two time points.

**Conclusions:** It has been observed corneal biomechanical deterioration measured in vivo with KC progression. The SSI and the IIR have been shown to be suitable biomechanical biomarkers of the disease progression.

#### Topic Areas

CXL pre-clinical, translational

## Estimate Corneal Remodelling in Response to Intracorneal Ring Segments

Authors: Dr. Ahmed Abass - University of Liverpool, Dr. Bernardo Lopes - University of Liverpool, Dr. Ashkan Eliasy - University of Liverpool, Prof. Ahmed Elsheikh - University of Liverpool

#### Abstract

**Purpose:** To present a robust finite element (FE) modelling based method that can predict

the performance of intracorneal ring segments (ICRSs) on the eye and predict the corneal remodelling.

**Methods:** The study utilises a record of 38 clinical cases of ICRS fittings. Records of Pentacam tomography data from Brazilian participants aged  $65.4 \pm 15.2$  were retrospectively assessed pre and one month post the ICRS implementation. The Pentacam raw elevation data was analysed using a custom-built MATLAB master code that is capable of constructing and operating Abaqus software FE models. The code is using the principle of fire-and-forget as it automatically modifies the simulation strategy according to the Abaqus stability performance without user intervention. This advanced approach to build a custom-built fully automated computer code allowed for the full completion of the FE modelling successfully. Consequently, the code triggers a set of scripted Python codes to extract the analyses outcomes and process them in an autonomous validation process.

**Results:** Each of the clinical cases' postoperative data were used to validate the relevant model by comparing the tangential curvature within the central 4 mm diameter. The minimum error recorded was  $0.01 \pm 0.91$  mm and the maximum was  $0.72 \pm 0.92$  mm. Validation error between the FE model and the clinical record did not strongly correlate to Pentacam pre and postoperative clinical parameters in cases fitted with one ICRS. Validation error strongly correlated with postoperative corneal horizontal radius ( $R=0.73$ ) and preoperative asphericity Q ( $R=0.78$ ) and CCT (0.7) in cases fitted with two ICRSs.

**Conclusions:** The presented method allows clinicians to predict the outcome of ICRS procedures without performing the surgery, therefore, allowing them to adjust their plans

in order to get the best outcome. The method is simulation-based and has zero risks on the patient as it utilises the usual clinical measurements taken from the subject before the surgery such as topography and intraocular pressure with no additional measurements. The achieved results open the door to further future research that could replace ICRS nomograms with reliable methods.

#### **Topic Areas**

CXL pre-clinical, translational

## **Keratoconus screening in Basic School Children using keratoconus suspect criteria in Aljaded Althawra (Aljazeera State) November 2014 to April 2015**

Authors: Dr. Diana Mohammed, Dr. Elnazir Adam

#### **Abstract**

**Objectives:** Keratoconus screening in Basic Children School using Keratoconus suspect criteria & to detect specificity and sensitivity of each criteria in Aljaded Althawra. Also to identify the risk factors of keratoconus.

**Method:** This study is a community based cross sectional analytical study conducted in Aljaded Althawra–Alkamleen locality– Aljazeera state – between Nov 2014 April 2015 . Four hundred students (800 eyes), age between 5 - 15 years old were examined 58.2% were males, and 41.8% were females. Visual acuity, slit lamp, fundus examination were taken. KC was detected from study sample according to keratoconus suspect criteria & corneal topography done to detect KC.

**Results:** 45 (11.25%) 90 eyes had keratoconus suspect Criteria. Male 68.9 %, female were 31.1 %. Peak's age group was 9-12 years old (48,9%). VKC 76 eyes (84.4%), CVA less than normal (6/6 – 6/9) 21 eyes (23.3%) , real cylinder (– 4.0) or more 8eyes (8.9%), KC in fellow eye 14(15.6%) and family history of KC & frequent change of glasses 0.0%. The risk factor associated with KC, rubbing eye 71.1% , history of wearing glasses 31.1% & FHx of refractive error 31.1%.14 eyes (15.5%) were KC, males (57.1%) & females 42.9%. 11 eyes (14.5%) had VKC,7 eyes (33.3%) had CVA less than normal (6/6 - 6/9), 6 eyes (75.0%) had real cylinder (– 4.0) or more,4 eyes (28.6%) had KC in fellow eye,0 eyes (0.0%) had family history of KC & frequent change of glasses.

**Conclusion:** Results of this study suggested strong association between KC and high cylinder (– 4.0) or more in autorefractometer reading & CVA less than normal (6/9 - 6/9) and KC in fellow eye according to p value and sensitivity & specificity but there is no relation to VKC. Keratoconus was more related to rubbing eyes, Hx of wearing glasses and FHx of refractive errors. Screening of KC with corneal topography allows early detection and management.

#### **Topic Areas**

CXL pre-clinical, translational

## **Pain protocol in PRK and CXL: Cold to the rescue**

Authors: Dr. Sailie Shirodkar - Narayana Nethralaya, Dr. Rohit Shetty - Narayana Nethralaya, Dr. Arkasubhra Ghosh - Narayana Nethralaya, Dr. Swaminathan Sethu - Narayana Nethralaya, Dr. Pooja Khamar - Narayana Nethralaya, Mr. Nikhil Ashok - Narayana Nethralaya

## Abstract

**Purpose:** To compare post-operative analgesic effects rendered by the use of cold and room temperature (RT) bandage contact lenses (BCLs), with or without 0.4% ketorolac tromethamine, post photorefractive keratectomy (PRK) and crosslinking (CXL), and to identify molecular factors associated with the differences in pain scores.

**Materials and Methods:** Patients diagnosed with keratoconus, who were advised topography-guided PRK (Group 1), and those undergoing PRK surgery for refractive correction (Group 2), were further randomly divided into four sub groups: Conventional (subjects receiving BCL soaked in balanced salt solution - BSS maintained at room temperature – RT, 24°C prior to use), Conventional+KT (subjects receiving BCL soaked in BSS containing 0.4% ketorolac tromethamine maintained at RT prior to use), Cold (subjects receiving BCL soaked in BSS maintained at 4°C in a refrigerator for 3 hours prior to use) and Cold+KT (subjects receiving BCL soaked in BSS containing 0.4% ketorolac tromethamine maintained at 4°C in a refrigerator for 3 hours prior to use). The status of post-operative pain was assessed on the basis of Wong-Baker (WB) scoring on the first post-operative day. Molecular profiling in tear samples and BCLs was also performed using multiplex ELISA and qPCR, respectively. Statistical analyses include Kruskal-Wallis test, followed by Dunn’s Multiple Comparison Test.

**Results:** Cold (WB Score, Mean±SD: 3.08±2.1) and Cold+KT (2.28±2.4) groups had significantly ( $P<0.0001$ ) low pain scores compared to Conventional (7.28±1.8) and Conventional+KT (5.32±2.7) in CXL patients. Cold (WB Score, Mean±SD: 3.4±2.9) and Cold+KT (2.7±2.6) groups also had significantly ( $P<0.0001$ ) low pain scores compared to Conventional group (7.43±1.6) but not compared to Conventional+KT (4.76±2.65). No

difference in epithelial healing pattern was observed on slit lamp examination among the four study groups. Differences in expression of nociception related transient receptor potential ion channels (TRPV1, TRPA1 and TRPM8), Pro-inflammatory cytokine (IL6) and cyclo-oxygenase enzyme (COX-2) were observed among patients who demonstrated low and high scores.

**Conclusions:** Acceptance of these procedures amongst patients and surgeons alike is limited, considerably due to significant post-operative pain. This simple and economical approach can potentially control post-operative pain and increase patient comfort with no delay in epithelial healing. It thereby aims to increase acceptance of these highly beneficial procedures.

## Topic Areas

CXL pre-clinical, translational

## Regional variation of corneal stiffness with Keratoconus progression assessed by the Stress-Strain Maps

Authors: Prof. Ahmed Elsheikh - University of Liverpool, Dr. Bernardo Lopes - University of Liverpool, Dr. Ashkan Eliasy - University of Liverpool, Dr. Haixia Zhang - Capital Medical University, Dr. Ahmed Abass - University of Liverpool, Dr. Prema Padmanabhan - Sankara Nethralaya

## Abstract

**Purpose:** To evaluate the regional corneal biomechanical deterioration with keratoconus (KC) progression as measured by the stress-strain maps (SSI).

**Methods:** In this retrospective record review, the preoperative of progressive KC cases that were submitted to corneal cross-linking were evaluated. All cases were examined with

Pentacam HR and the Corvis ST (Oculus, Wetzlar, Germany). Significant progression was based on the Pentacam's ABCD system. The SSI Maps were built on the first and last visits using numerical modelling based on the finite element method. Through inverse analysis of patient-specific corneas, the regional variation of mechanical stiffness across the corneal surface was determined.

**Results:** A total of 29 eyes were included. The cases presented the disease in different stages with maximum anterior curvature (KMax) of  $54.37 \pm 4.55$  D (44.5 – 64.4) and minimum thickness of  $468.55 \pm 27.74$   $\mu$ m (414 – 520). The mean age at the last exam before the CXL procedure was  $20.1 \pm 7.0$  years (9 – 40). The mean time between the two examinations was  $17.1 \pm 17.1$  months (1.4 – 58.4). The bIOP showed minimum non-significant alteration between the two exams ( $-0.08 \pm 1.21$  mmHg, range: -2.0 to 2.3,  $p=0.584$ ). The overall corneal stiffness as measured by SSI value in 8mm diameter presented slightly, but significant reduction from the first to the last exam ( $-0.02 \pm 0.02$ , range: -0.09 to 0,  $p<0.001$ ). The regional reduction in stiffness was concentrated in the area inside the cone. The SSI values inside the cone were significant lower in the last exam ( $-0.15 \pm 0.09$ , range: -0.42 to -0.01,  $p<0.001$ ), while the SSI outside the cone presented minimum non-significant difference ( $0 \pm 0.01$ , range: -0.04 to 0.01,  $p=0.999$ ).

**Conclusions:** It has been observed through the SSI maps that the regional deterioration in stiffness was concerted inside the cone area, while only mild non-significant alteration was observed outside the diseased area.

#### Topic Areas

CXL pre-clinical, translational

## Rose Bengal Photodynamic Therapy: A Novel Treatment for Corneal Cross-linking

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#### Abstract

**Purpose:** The purpose of this study was to evaluate elasticity in the anterior and middle stromal regions of the cornea after cross linking with two different protocols using atomic force microscopy (AFM) through microindentation.

**Materials & Methods:** Experiments were conducted on 27 pairs of human cadaver eyes (age: 36-90 years). The corneal epithelium was removed using a cotton-tipped applicator, and whole globes were placed in 20% dextran overnight at 4°C to restore corneal thickness to physiological levels (500-600mm). The left eyes (OS) were left as control for all pairs. The right eyes (OD) of all pairs were pretreated with 0.1% rose bengal solution in saline for 30 minutes: one drop of rose bengal solution was applied to the cornea every 3 minutes. After this, 12 corneas were included in the low intensity group ( $6\text{mW}/\text{cm}^2$  of green light at 525nm for 15 minutes) and 15 corneas were included in the high intensity group ( $12\text{mW}/\text{cm}^2$  of green light at 525nm for 7.5 minutes). After irradiation, Young's modulus of elasticity was assessed using a custom Atomic Force Microscopy system that has been used extensively to characterize corneas post-crosslinking. The corneas were cut with a



microkeratome at 50mm (anterior stroma) and then at 250mm (middle stroma), with mechanical properties measured at each of these depths. The thickness was measured with a pachymeter after each cut with the microkeratome.

**Results:** For corneas in the low intensity group, Young's modulus for the anterior stromal region was  $42.2 \pm 29.7$  kPa for treated and  $38.5 \pm 17.8$  kPa for control; Young's modulus for the middle stromal region was  $2.8 \pm 1.8$  kPa for treated and  $6.5 \pm 5.9$  kPa for control. For corneas in the high intensity group, Young's modulus for the anterior stromal region was  $46.1 \pm 11.2$  kPa for treated and  $32.0 \pm 19.8$  kPa for control; Young's modulus for the middle stromal region was  $3.4 \pm 1.9$  kPa for treated and  $3.4 \pm 2.2$  kPa for control. Corneas crosslinked with the high intensity protocol were significantly stiffer than controls ( $p < 0.05$ ) in the anterior region only. The stiffening effect (treated/control Young's modulus) was significantly greater ( $p < 0.05$ ) with the high intensity protocol than with the low intensity protocol. Finally, when analyzing Young's modulus of elasticity as a function of depth in the stroma, the corneas in the high intensity group were stiffer deeper in the stroma ( $\sim 150$ mm) compared to those in the low intensity group ( $\sim 50$ mm).

**Conclusions:** The effects of Rose Bengal PDAT cross-linking seem to be limited to the anterior corneal stroma and do not extend to the deeper stromal region. Additionally, the higher intensity protocol produces a stiffer anterior corneal stroma when compared to the low intensity protocol.

### **Topic Areas**

CXL pre-clinical, translational

## PACK-CXL for keratitis

### Antimicrobial efficacy of genipin in rabbit models of *Staphylococcus aureus* and *Pseudomonas aeruginosa* keratitis

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#### Abstract

Purpose: Infectious keratitis is a severe sight-threatening ocular condition and is considered one of the leading causes of monocular blindness. In bacterial keratitis, the

most common causative agents are *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). If treatment is not adequate, corneal infection and host inflammatory response may lead to ulceration, melting and perforation. The increasing emergence of antimicrobial resistance has significantly made the management of keratitis more complicated and consequently, there is an urgent need for the development of alternative therapeutic approaches. Recently, using an ex vivo model of corneal keratitis we demonstrated that genipin exerts antimicrobial action against *S. aureus* and *P. aeruginosa*. The purpose of this study was to evaluate the antimicrobial effects of genipin in rabbit models of *S. aureus* and *P. aeruginosa* keratitis.

Materials & Methods: *S. aureus* (ATCC 25923) or *P. aeruginosa* (ATCC 27853) strains were intrastromally injected to one eye of 20 rabbits. The rabbits were equally divided into four treatment groups: *S. aureus* + vehicle (group 1), *S. aureus* + genipin (group 2), *P. aeruginosa* + vehicle (group 3) and *P. aeruginosa* + genipin (group 4). Uninfected, untreated eyes were served as healthy, control group (group 5). Eyes received two doses of genipin, at 6 hours and 24 hours post inoculation. Clinical ocular evaluation was performed following bacterial inoculation, before and after each treatment. Corneal homogenates were cultured to determine bacterial survival and expressed as the log number of colony forming units (log CFU) per cornea. Transcription of selected pro- and anti-inflammatory cytokines, growth factors and matrix metalloproteinases (MMPs) was assayed by quantitative gene expression analysis.

Results: All vehicle-treated eyes had a higher clinical score on corneal opacity, ulceration and chemosis. Corneal perforation occurred in one out of five vehicle-treated eyes of the *S.*

*aureus* keratitis model and in two out of five vehicle-treated eyes in the *P. aeruginosa* model. None of the genipin-treated eyes progressed to corneal perforation. In the *S. aureus* keratitis model, genipin treatment significantly reduced the bacterial load compared to the vehicle treated group (mean log  $3.42 \pm 0.65$  versus  $5.64 \pm 0.93$  CFU, respectively;  $p=0.0142$ ). There were no statistically significant differences in the CFU between vehicle and genipin treatment groups in the *P. aeruginosa* model (mean log  $3.42 \pm 0.55$  versus  $3.01 \pm 0.68$  CFU, respectively). With regards to the inflammatory response, genipin treatment resulted in significantly decreased levels of MMP9, IL1B, IL8, IL15 and IL1RA in both models. However, in the *S. aureus* model, genipin treatment further demonstrated significant reduction in the levels of MMP2, IL6, TNF $\alpha$ , TGF $\beta$  and IFN $\gamma$ .

Conclusions: The potential application of genipin for the management of infectious keratitis deserves further examination, especially for the *S. aureus* keratitis

#### Topic Areas

PACK-CXL for keratitis

## Evaluation of Rose Bengal Mediated Photodynamic Therapy for In Vitro Growth Inhibition of Bacterial, Rapidly Growing Mycobacteria, Fungi and Parasites

Authors: Dr. Talita Rocchetti - Unifesp, Mr. Wirley Mendonca - Unifesp

Ms. Larissa Fagundes - Unifesp, Dr. Jarbas Caiado de Castro Neto - USP, Dr. Viviane Sant'Ana - Unifesp, Prof. Maria Cecilia Yu - Unifesp, Dr. Denise de Freitas - Unifesp, Dr. Ana Luiza Hofling Lima - Unifesp

#### Abstract

**Purpose:** The purpose of this study was to evaluate the in vitro efficacy of rose bengal mediated photodynamic therapy for inhibition of bacteria, Rapid Growing Mycobacteria, Fungi and Parasites.

**Methods:** Twelve corneal clinical isolates: Methicilin Resistan *Staphylococcus aureus* (MRSA), *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Moraxella* spp., *Fusarium solani*, *Purpureocillium lilacinum*, *Candida parapsilosis*, *Scedosporium* spp., *Curvularia geniculata*, *Mycobacterium chelonae*, *Mycobacterium abscessus* and *Acanthamoeba* spp. were used in the experiments. Microorganisms were grown and incubated at specific conditions and prepared in suspension to concentrations adjusts. Tested in triplicate, groups included: Group I, control, no treatment; Group II, microorganism suspension treated with 0.1% rose bengal and exposed to the dark for 30min; Group III, microorganism suspension exposed with a 7.15 mW/cm<sup>2</sup> custom-made green LED source for 30 minutes (12.87 J/cm<sup>2</sup>) and Group IV, microorganism suspension treated with 0.1% rose bengal and exposed with a 7.15 mW/cm<sup>2</sup> custom-made green LED source for 30 minutes (12.87 J/cm<sup>2</sup>). Final work concentration was 10<sup>4</sup> cells per mL. Plates were incubated at specific conditions and photographed after growth.

**Results:** Complete growth inhibition of all bacteria, Rapid Growing Mycobacteria, *Fusarium solani*, *Purpureocillium lilacinum* and *Candida parapsilosis* were demonstrated after treatment with 0.1% rose bengal under green LED irradiation for 30 minutes. *Acanthamoeba* spp. showed an 85% decrease in cell viability after treatment with 0.1% rose bengal under green LED irradiation for 30 minutes. *S. aureus* and *S. epidermidis* treated with 0.1% rose bengal and exposed to the dark also showed complete growth inhibition.

*Scedosporum* spp., *Curvularia geniculata* growths were not inhibited after treatment with 0.1% rose bengal under green LED irradiation for 30 minutes.

**Conclusion:** Rose bengal mediated photodynamic therapy demonstrated an expressive inhibition to 10 of 12 microorganisms tested. Clinical treatment may offer an alternate adjunct therapy for eye infection.

#### Topic Areas

PACK-CXL for keratitis

## Evaluation of Rose Bengal Photodynamic Antimicrobial Therapy as an adjunctive treatment for severe infectious keratitis

Authors: Mr. Wirley Mendonca - Unifesp, Dr. Talita Rocchetti - Unifesp, Dr. Denise de Freitas - Unifesp, Dr. Ana Luiza Hofling Lima - Unifesp, Dr. Jarbas Caiado de Castro Neto - USP

#### Abstract

**Purpose:** To evaluate adjunctive rose bengal photodynamic antimicrobial therapy (RB-PDAT) for treatment of patients with severe infectious keratitis.

**Methods:** Eight patients presenting severe infectious keratitis: Methicillin-Resistant *Staphylococcus aureus* (MRSA), Methicillin-Susceptible *Staphylococcus aureus* (MSSA), *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Moraxella* spp., *Pseudomonas aeruginosa*, *Fusarium solani* and *Fusarium delphinoides*, not responsive to standard medical care, were treated with RB-PDAT. The areas of epithelial defect were 95, 90, 3, 52, 24.44, 14, 1 and 6 mm<sup>2</sup> while the stromal opacification areas were 95, 64, 4, 52, 24.44,

14, 6 and 12.25 mm<sup>2</sup>, respectively. The length of standard medical treatment prior to procedure was 7, 1, 15, 15, 18, 15, 21 and 6 days, respectively. RB-PDAT was performed by applying a solution of rose bengal (0.1% in balanced salt solution) to the de-epithelialized cornea for 30 minutes, followed by irradiation with a 7.15 mW/cm<sup>2</sup> custom-made green LED source for 15 minutes (6.43 J/cm<sup>2</sup>). Results: The eyes had clinical resolution of infection in 40 (MRSA), 16 (MSSA), 7 *S. epidermidis*, 59 *S. pneumoniae*, 102 (*Moraxella* spp), 20 *P. aeruginosa*, 67 *Fusarium solani*) and 31 *F. delphinoides* days after RB-PDAT. Patients presenting *Moraxella* spp. and *F. solani* keratitis required to be treated twice. Patient with MSSA infection had a small corneal perforation 9 days after procedure, managed with cyanoacrylate glue. None of the cases needed therapeutic keratoplasty.

**Conclusion:** RB-PDAT can be considered as an adjunctive therapy in cases of severe and progressive infectious keratitis despite of standard medical care, especially in order to avoid therapeutic keratoplasty.

#### Topic Areas

PACK-CXL for keratitis

## Photo-activated chromophore for keratitis (PACK-CXL) window absorption (WA) alone versus combined PACK-CXL window absorption and standard antimicrobial therapy (SAT) for treatment of infectious keratitis: a prospective study

Authors: Dr. Mohammed M. Mahdy Tawfeek - Faculty of Medicine - Zagazig University

#### Abstract

**Objective:** The aim of this study was to compare the outcome of photo-activated

chromophore for keratitis cross-linking (PACK-CXL) window absorption (WA) alone with combined PACK-CXL WA and standard antimicrobial therapy (SAT) for treatment of infectious keratitis.

**Patients and methods:** This is a randomized prospective comparative clinical trial that enrolled 30 eyes with clinically suspected infectious keratitis. They were randomly assigned into 2 equal groups of 15 eyes each: Group A was treated by PACK-CXL WA alone and group B was treated by PACK-CXL WA combined with SAT. Identification of organisms was done by laboratory study before treatment. Corneal healing was evaluated by corneal examination and anterior segment OCT (AS-OCT).

**Results:** Complete healing and resolution (successful treatment) was observed in 10 eyes (66.7%) of group A and in 14 eyes

(93.3%) of group B, a statistically significant difference ( $P=0.042$ ). Complications were absent in 12 eyes (80%) in group A and in 14 eyes (93.3%) of group B. However, perforation and impending perforation were found in 3 patients of group A and in only 1 patient of group B, a statistically insignificant difference ( $P=0.123$ ).

**Conclusion:** PACK-CXL is a promising, non-invasive treatment option for superficial infectious keratitis, especially when performed with WA technique, either alone or combined with SAT. However, combined PACK-CXL WA with SAT was more effective for treatment of infectious keratitis than PACK-CXL WA alone with shorter resolution period.

**Keywords:** corneal cross linking, infectious keratitis, PACK-CXL, window absorption

#### **Topic Areas**

PACK-CXL for keratitis