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Very High-Fluence CXL (cCXL), Combined with Simulation of Femtosecond Laser-Assisted Myopic Refractive Lens Extraction (FSME). Study of a Novel Procedure ex-Vivo

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Purpose

To evaluate biomechanical differences induced by intra-stromal corneal cross-linking through a stromal pocket-delivered high-concentration riboflavin and irradiated superficially by high-fluence, high-energy, UV-A.

Methods

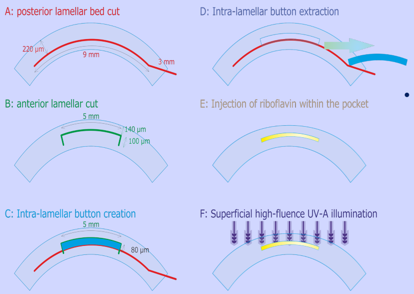
- Human donor corneas (Eye Bank for Sight Restoration, NY),
- Lamellar Cuts: Femtosecond laser (FS200, Alcon/WaveLight),
- In-situ Cross Linking: High-fluence device (KXL, Avedro),
- Keratometry: Scheimpflug imaging (Pentacam, Oculus),
- Pachymetry: Anterior-Segment OCT (AS-OCT, RtVue100, Optovue),
- Biaxial load cell-based analysis: BioTester 5000, CellScale Testing, Canada).

Surgical Procedure

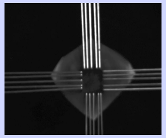
A-C: Two-surface intra-lamellar bed corneal dissections were performed within a 5.5-mm optical zone.

D: The lenticule was extracted through a 3.5-mm wide superior canal.

E: High-fluence CXL was conducted in the pocket created.



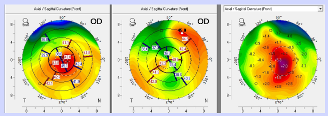
Testing

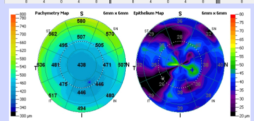


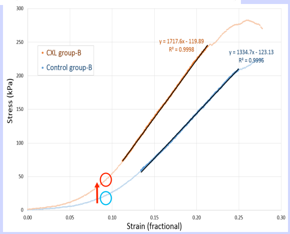
Biotester provides via a biaxial load cell-based analysis the simultaneous recording of x- and y-axis displacement, applied force, and time. An integrated CCD camera records images at a 1280×960 pixel resolution, and analyzes by embedded custom software. May be considered superior to corneal strip extensiometry utilized in past experiments, taking into account the non-uniform topographic distribution of the corneal strength profile.

Results

- "Lenticule" creation simulation and secondary extraction through the superior canal was efficient when employing the FS200 laser. "Lenticule" central thickness was 50 µm.
- OCT-derived corneal thickness differences, as well as Scheimpflug imaging-derived topographic differences were consistent with a myopic change. Both modalities highlighted the inter-lamellar CXL effect.
- Substantial (up to +100%) increase in biomechanical strength has been noted.







	Stress units: kPa				Young's Shear Modulus units: MPa			
	@ 10% strain		@ 20% strain		@ 10% strain		@ 20% strain	
group-A (CXL study)	305.04	±23.30	1,284.79	±34.20	6.98	±1.12	11.46	±0.75
group-B (control)	$\boxed{147.39}$	±10.72	874.38	±29.40	$\boxed{4.04}$	±0.85	8.80	±0.72
Δ	107%		47%		73%		30%	
p	< 0.05		< 0.05		< 0.05		< 0.05	

Discussion

Standard Dresden CXL protocol: Epithelial removal, riboflavin (0.1%) instillation, and UV-A dosage of 5.4 J/cm². Postoperative pain, unstable Visual Acuity, Potential of complications.

Epithelium-on CXL:

Challenges: Epithelial permeability to riboflavin application. May not effectively halt the progression of keratoconus. A significantly weaker biomechanical effect is attributed mainly to the insufficient and inhomogeneous transepithelial riboflavin diffusion into the corneal stroma.

Challenges: Delivery of UV-A through the cornea. Epithelial absorption/filtering of the UV-A that could potentially lead to lesser energy (about 1/3) delivered to the stroma. This has been stated as an argument against the use of epithelium-on CXL.

In-situ Riboflavin application:

Naturally overcomes challenge of riboflavin penetration through the intact epithelium and in acting as a 'blocking' agent against the UV-A exposure. The effectiveness of such techniques may warrant investigation. Some in-situ CXL applications evaluated ex-vivo, in porcine corneas (no Bowman's membrane) indicate that the biomechanical strengthening effect of CXL using a femtosecond laser pocket technique is about 50% less in comparison to standard CXL.

Our Findings:

After the creation of an intrastromal 'button' we tested the changes in corneal strength employing objective biaxial stress-strain measurements. The orientation of the cornea specimens during the tensile strength measurements was intentionally random, exactly to address the fact that the shear modulus should naturally vary along different meridians of the cornea because of the known anisotropic differences of collagen.

In our study we demonstrated that the effective CXL corneal rigidity increase, as measured in the central 3.5-mm section, in comparison to the non-CXL corneas that otherwise received the same treatment, was of the order of +100% at the 10% strain point. The depth-dependence of transverse shear modulus of the cornea (stronger at the anterior third), indicates that tissue removal from this upper third may affect corneal rigidity the most.

The findings in this work provide substantial ex-vivo evidence that significant corneal strengthening takes place even when UV-A light is projected through the intact cornel epithelium, Bowman's membrane and anterior stroma, to reach underlying riboflavin-soaked stroma in order to conduct CXL.

These data offer support to our previous clinical findings in vivo of intracorneal refractive stability in high-myopic LASIK cases treated with prophylactic CXL, as well as the compelling refractive effect found in hyperopic LASIK cases treated with prophylactic in-situ CXL.

Conclusions

- This ex-vivo laboratory study simulates refractive lens extraction with the FS200 femtosecond laser, using the venting channel instead of a "smile" incision.
- The aim of the in-situ CXL application was to provide prophylactic corneal stiffening to counter weakening due to tissue removal, and thus potential long-term stability. The almost + 100% increase of corneal strengthening effect is a very important finding.
- In-pocket adjunct cross-linking may facilitate, stabilize the postoperative recovery, and may potentially be employed to induce asphericity and correct small residual spherocylindrical refractive errors.

Commercial Relationship(s) Disclosure:
A.John KanellopoulosConsultant for Alcon, Avedro, OptoVue, i-Optics
G. Asimellis: none

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