Advanced Cross-Linking Techniques: Epi-On and Customized Protocols with Supplemental Oxygen

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Objectives

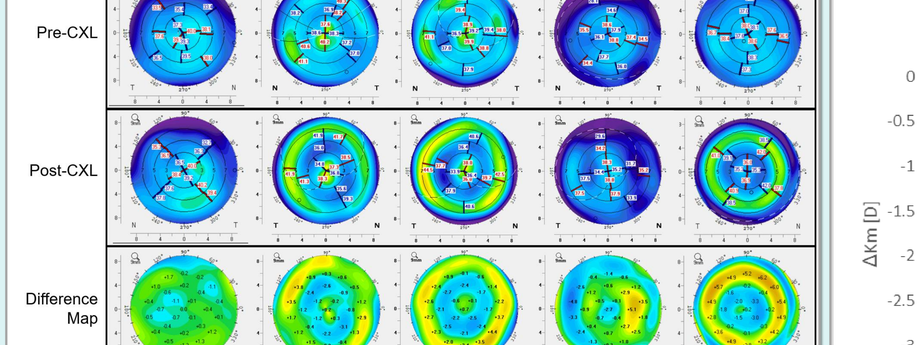
Cross-Linking with Supplemental Oxygen

Corneal collagen cross-linking photochemistry is strongly dependent on stromal oxygen levels in combination with UV delivery parameters and photosensitizer formulation. Stromal oxygen can be modulated by providing oxygen gas around the ocular surface. This laboratory study aimed to evaluate a series of normoxic and hyperoxic epi-on cross-linking protocols that have recently been translated into clinical use by:

1. Invasive measurement of stromal oxygen concentrations before, during, and after UV irradiation
2. Analysis of induced acute anterior surface flattening via Scheimpflug tomography and bulk material stiffening via biaxial extensiometry
3. Comparison of all results to positive (epi-off Dresden protocol) and negative (no cross-linking) control samples

Methods - Measurement Apparatus and CXL Protocols

Environmental Chamber (a), Invasive Oxygen Probe (b), and Protocols



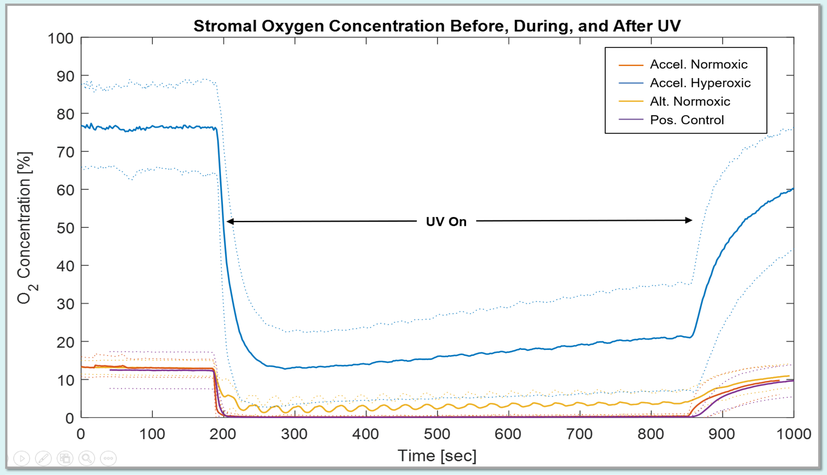
Test Group	Epi	O_2 Conc.	Drug	Irradiance [mW/cm^2]	Pulsing [sec on:off]	Dose [J/cm^2]	UV Time [min]
Neg. Control	On	21%	-	-	-	-	-
Accel. Hyperoxic	On	>90%	Pt 1: 0.25% ribo + BAC Pt 2: 0.22% ribo + saline	30	1:1	10	11.1
Accel. Normoxic	On	21%	Pt 1: 0.25% ribo + BAC Pt 2: 0.22% ribo + saline	30	1:1	10	11.1
Alt. Normoxic	On	21%	0.50% ribo + NaI	4	15:15	4.1	34.2
Pos. Control	Off	21%	0.10% ribo + HPMC	3	-	5.4	30.0

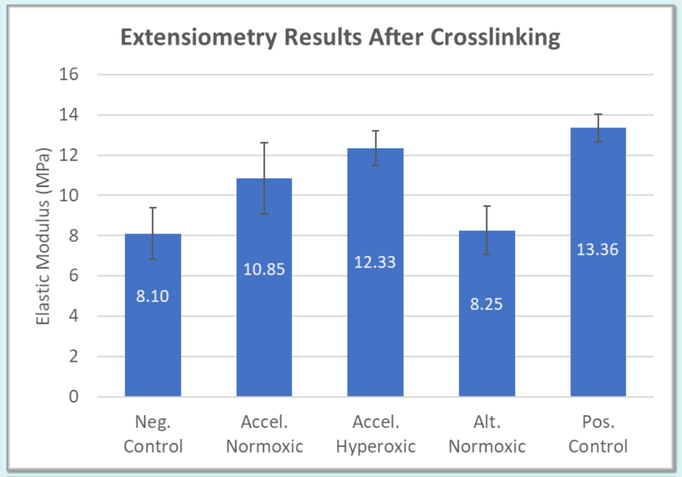
Notes

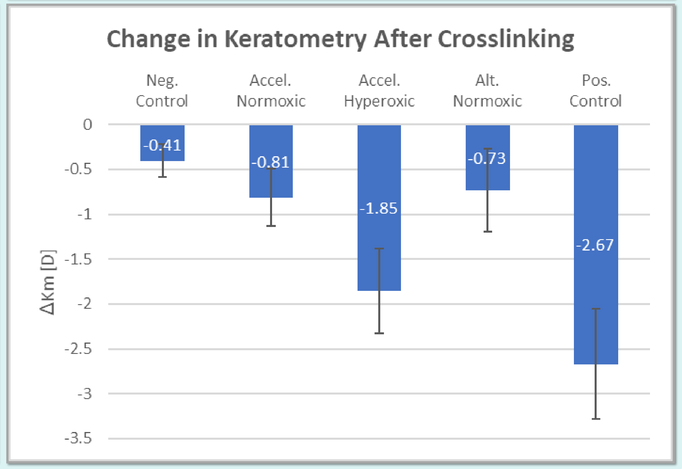
- Continuous control of ambient oxygen, temperature, IOP, humidity, hydration / drug administration
- Window interfaces to UV device (vertical) and Pentacam HR (horizontal)
- Fresh, whole porcine eyes used for all experiments <24 hours from enucleation
- Eyes inspected for epithelial / stromal defects prior to use

Results

Intrastromal Oxygen Levels, Extensiometry, and Tomography







Findings & Conclusions

Supplemental Oxygen Drives Increased Corneal Stiffness and Flattening

Intrastromal Oxygen Levels and Extensiometry

- Supplemental oxygen enables aerobic conditions to be maintained in mid-stroma during high-irradiance epi-on cross-linking
- Extensiometry shows statistically significant ($p < 0.05$) increase in stiffness with accel. hyperoxic protocol vs. other epi-on protocols
- No significant difference ($p > 0.05$) between accel. hyperoxic epi-on protocol and epi-off Dresden positive control
- *Extensiometer results correlate to findings from novel flattening assay*

Tomography

- Statistically significant ($p < 0.05$) increase in anterior surface flattening with accel. hyperoxic protocol vs. other epi-on protocols
- No significant difference ($p > 0.05$) between accel. hyperoxic epi-on protocol and epi-off Dresden control
- *Supplemental oxygen drives increased epi-on flattening effect compared to normoxic protocols*
- *Flattening results correlate to biomechanical changes from extensiometry assay*

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