Customized corneal crosslinking using different UVA beam profiles

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A new era of cross linking
Research Question

W I L L T H I S W O R K?

Biomechanics & newer insights

Information from cell biology

Cross linking current lacunae

Application

Future
The Biomechanical profile is ‘differential’ in keratoconus.
Research Question

W I L L T H I S W O R K?

Information from cell biology
Inflammation Driving Keratoconus
Possible structural molecules affected by disease process!
Observations in our Molecular biology Lab

Epithelium over cone

Epithelium over non-ectatic area

Biorepository
Differential Molecular Expression of Extracellular Matrix and Inflammatory Genes at the Corneal Cone Apex Drives Focal Weakening in Keratoconus


- LOX ↓
- TIMP-1 ↓
- Col I A1 ↓
- Col IV A1 ↓
- MMP9 ↑
- IL6 ↑
- TNFα ↑
Observations in Clinic

KC Grade I

KC Grade II

KC Grade III

KC Grade IV

Localised disease
Research Question

W I L L
T H I S
W O R K?

Cross linking
current lacunae

Application

Cross linking
current lacunae

Future

Information from

Biomechanics &
newer insights

ROHIT SHETTY, NATASHA KISHORE PAHUJA, RUDY M.M.A. NUIJTS, AMRITA AJANI, CHAITRA JAYADEV, CHETNA SHARMA, AND HARSHA NAGARAJA

• CONCLUSION: Conventional CXL (Group I) and accelerated CXL with irradiations of 9 mW/cm² (Group II) and 18 mW/cm² (Group III) showed better visual, refractive, and tomographic improvements at the end of 12 months. (Am J Ophthalmol 2015;■:■–■. © 2015 by Elsevier Inc. All rights reserved.)
But still....

Complication and failure rates after corneal crosslinking

Tobias Koller, MD, Michael Mrochen, PhD, Theo Seiler, MD, PhD

Parasurgical therapy for keratoconus by riboflavin–ultraviolet type A rays induced cross-linking of corneal collagen

Preliminary refractive results in an Italian study

Aldo Caporossi, MD, Stefano Ballocchi, MD, Cosimo Mazzotta, MD, Claudio Traversi, MD, Tomaso Caporossi, MD

Corneal collagen crosslinking with riboflavin and ultraviolet-A light in progressive keratoconus: Ten-year results

Frederik Raiskup, MD, PhD, FEBO, Anja Theuring, MD, Lutz E. Pillunat, MD, Eberhard Spoerl, PhD

4.6. Treatment Failure

CXL failure is largely defined as keratoconic progression following treatment. One study of 117 eyes from 99 patients who underwent CXL documented a failure rate of 7.6% at one-year follow up. The results also
Research Question

W I L L T H I S W O R K?
Localised disease

Uniform UVA irradiation?

Programmable beam pattern with differential surface dose?
Beam Profiles

- Rings beam
- Axial Map

- Rings beam
- Tangential Map

- Sectoral beam
- Axial Map

- Uniform beam
<table>
<thead>
<tr>
<th></th>
<th>Ring Axial Map</th>
<th>Ring Tangential Map</th>
<th>Sector Axial Map</th>
<th>Uniform</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔK1 (D)</td>
<td>0.114±0.214</td>
<td>0.492±0.205</td>
<td>0.25±0.188</td>
<td>0.357±0.250</td>
<td>0.74</td>
</tr>
<tr>
<td>ΔK2 (D)</td>
<td>-0.029±0.182</td>
<td>0.525±0.192</td>
<td>0.483±0.154</td>
<td>0.979±0.312</td>
<td>0.07</td>
</tr>
<tr>
<td>ΔKm (D)</td>
<td>0.043±0.119</td>
<td>0.5±0.178</td>
<td>0.383±0.167</td>
<td>0.636±0.274</td>
<td>0.38</td>
</tr>
<tr>
<td>ΔKmax (D)</td>
<td>0.443±0.232</td>
<td>1.308±0.333</td>
<td>1.508±0.255</td>
<td>1.707±0.347</td>
<td>0.09</td>
</tr>
<tr>
<td>ΔTangential Kmax (D)</td>
<td>0.586±0.239</td>
<td>1.475±0.384</td>
<td>1.625±0.288</td>
<td>1.657±0.499</td>
<td>0.37</td>
</tr>
<tr>
<td>ΔAnterior Surface Q</td>
<td>0.020±0.009</td>
<td>-0.027±0.025</td>
<td>-0.062±0.014</td>
<td>-0.081±0.042</td>
<td>0.19</td>
</tr>
<tr>
<td>ΔPosterior Surface Q</td>
<td>-0.011±0.016</td>
<td>-0.059±0.04</td>
<td>-0.024±0.014</td>
<td>-0.051±0.026</td>
<td>0.68</td>
</tr>
<tr>
<td>ΔMinimum corneal thickness (μm)</td>
<td>0.857±3.019</td>
<td>6.083±3.432</td>
<td>7.333±4.164</td>
<td>2.455±3.135</td>
<td>0.37</td>
</tr>
<tr>
<td>ΔCentral corneal thickness (μm)</td>
<td>0.0±3.155</td>
<td>3.667±2.813</td>
<td>5.909±4.254</td>
<td>0.818±3.110</td>
<td>0.39</td>
</tr>
<tr>
<td>ΔBAD-D</td>
<td>-0.01±0.208</td>
<td>0.074±0.214</td>
<td>-0.292±0.273</td>
<td>-0.669±0.318</td>
<td>0.21</td>
</tr>
<tr>
<td>ΔAxial CLMI of anterior surface (D)</td>
<td>-0.143±0.639</td>
<td>0.312±0.416</td>
<td>0.86±0.35</td>
<td>0.895±0.740</td>
<td>0.62</td>
</tr>
<tr>
<td>ΔTangential CLMI of anterior surface (D)</td>
<td>-1.206±1.828</td>
<td>0.448±0.279</td>
<td>0.934±0.268</td>
<td>0.700±0.833</td>
<td>0.37</td>
</tr>
<tr>
<td>ΔAxial CLMI of posterior surface (D)</td>
<td>-0.019±0.147</td>
<td>0.134±0.086</td>
<td>-0.078±0.128</td>
<td>0.143±0.138</td>
<td>0.51</td>
</tr>
<tr>
<td>ΔTangential CLMI of posterior surface (D)</td>
<td>-0.019±0.110</td>
<td>0.109±0.097</td>
<td>-0.107±0.143</td>
<td>0.090±0.103</td>
<td>0.51</td>
</tr>
</tbody>
</table>
Case examples

Difference map

Difference map

Difference map

Difference map

Difference map

Difference map
<table>
<thead>
<tr>
<th></th>
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<th>Uniform</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average energy density (J/cm²)</td>
<td>8.316±0.392</td>
<td>2.424±0.068</td>
<td>8.260±0.309</td>
<td>5.40±0.00</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Peak energy density (J/cm²)</td>
<td>13.571±0.922</td>
<td>10.8±0.00</td>
<td>14.375±0.625</td>
<td>5.40±0.00</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Treated area (cm²)</td>
<td>32.964±2.231</td>
<td>50.017±2.077</td>
<td>32.699±3.554</td>
<td>63.63±0.00</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>ΔΔK1 (D. cm²/J)</td>
<td>0.016±0.027</td>
<td>0.205±0.117</td>
<td>0.013±0.024</td>
<td>0.043±0.043</td>
<td>0.046*</td>
</tr>
<tr>
<td>ΔΔK2 (D. cm²/J)</td>
<td>-0.003±0.021</td>
<td>0.227±0.095</td>
<td>0.043±0.019</td>
<td>0.148±0.051</td>
<td>0.045*</td>
</tr>
<tr>
<td>ΔΔKm (D. cm²/J)</td>
<td>0.007±0.015</td>
<td>0.214±0.094</td>
<td>0.030±0.021</td>
<td>0.090±0.050</td>
<td>0.040*</td>
</tr>
<tr>
<td>ΔΔKmax (D. cm²/J)</td>
<td>0.053±0.028</td>
<td>0.625±0.187</td>
<td>0.172±0.039</td>
<td>0.305±0.068</td>
<td>0.01*</td>
</tr>
<tr>
<td>ΔΔTangential Kmax (D. cm²/J)</td>
<td>0.071±0.029</td>
<td>0.698±0.209</td>
<td>0.189±0.046</td>
<td>0.291±0.098</td>
<td>0.01*</td>
</tr>
<tr>
<td>ΔΔAnterior surface Q</td>
<td>0.002±0.001</td>
<td>-0.013±0.015</td>
<td>-0.006±0.002</td>
<td>-0.010±0.007</td>
<td>0.70</td>
</tr>
<tr>
<td>ΔΔPosterior surface Q</td>
<td>-0.002±0.002</td>
<td>-0.023±0.023</td>
<td>-0.004±0.002</td>
<td>-0.013±0.036</td>
<td>0.62</td>
</tr>
<tr>
<td>ΔΔMinimum corneal thickness (µm. cm²/J)</td>
<td>0.139±0.388</td>
<td>2.396±1.617</td>
<td>0.652±0.655</td>
<td>1.880±1.129</td>
<td>0.55</td>
</tr>
<tr>
<td>ΔΔCentral corneal thickness (µm. cm²/J)</td>
<td>0.011±0.391</td>
<td>0.992±1.383</td>
<td>0.286±0.623</td>
<td>1.467±1.039</td>
<td>0.75</td>
</tr>
<tr>
<td>ΔΔABAD-D</td>
<td>0.001±0.024</td>
<td>0.062±0.097</td>
<td>-0.027±0.039</td>
<td>-0.085±0.047</td>
<td>0.35</td>
</tr>
<tr>
<td>ΔΔAxial CLMI of anterior surface (D. cm²/J)</td>
<td>-0.011±0.069</td>
<td>0.323±0.151</td>
<td>0.128±0.045</td>
<td>0.174±0.148</td>
<td>0.046*</td>
</tr>
<tr>
<td>ΔΔTangential CLMI of anterior surface (D. cm²/J)</td>
<td>-0.112±0.197</td>
<td>0.286±0.139</td>
<td>0.122±0.028</td>
<td>0.103±0.164</td>
<td>0.048*</td>
</tr>
<tr>
<td>ΔΔAxial CLMI of posterior surface (D.cm²/J)</td>
<td>0.003±0.019</td>
<td>0.067±0.043</td>
<td>0.001±0.016</td>
<td>0.041±0.023</td>
<td>0.35</td>
</tr>
<tr>
<td>ΔΔTangential CLMI of posterior surface (D.cm²/J)</td>
<td>-0.001±0.012</td>
<td>0.074±0.041</td>
<td>-0.005±0.018</td>
<td>0.024±0.019</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>Pre-op</td>
<td>Post op 12 months</td>
<td>p value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>----------</td>
<td>-------------------</td>
<td>---------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deformation amplitude</td>
<td>1.3 ±0.1</td>
<td>1.2 ± 0.1</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specular CD</td>
<td>2704±359</td>
<td>2658 ± 430</td>
<td>0.69</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Corneal biomechanics: Safe
Specular microscopy
We studied the epithelium of the cone area in these eyes collected during the surgery. Eyes were categorized into good prognosis (Kmax difference post-op minus pre-op ≥ 0) and bad prognosis if its < 0).

Trend shows increased expression of LOX in patients with good outcomes as compared to the patients with bad outcomes.

Whereas TNFα expression is less in patients with good outcomes as compared to the patients with bad outcomes.
Research Question

W I L L T H I S W O R K?

Future
Future

Masking

Diagram showing layers of the cornea:
- Bowman's Layer
- Stroma
- Descemet's membrane
- Endothelium
OCT based Topography

Pentacam Anterior Surface

OCT Anterior Surface

OCT Bowman’s Interface Surface
Pentacam

OCT Air-Epithelium Interface

OCT Epithelium-Bowman’s Interface

Kmax ~ 55.5D

Kmax ~ 58.5D

Kmax ~ 60.5D
Programmable beam pattern with differential surface dose?
Thank you
Clinicians Scientists
Basic Scientists
Dr. Rohit Shetty
Dr. Abhijit Sinha Roy
Mathew Francis
Dr. Arkasubhra Ghosh
Grace Lytle
Fellow colleagues