Brillouin Microscopic Imaging to Detect Biomechanical Changes after LASIK Combined with Rapid Corneal Cross-Linking

J. Bradley Randleman, MD
Professor, Department of Ophthalmology, Keck School of Medicine of USC
Director, Cornea & Refractive Surgery Service
USC Roski Eye Institute, Los Angeles, CA, USA
Editor-in-Chief, Journal of Refractive Surgery

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Collaborators

- Giuliano Scarcelli, PhD
- Johnny P. Su, PhD
- Fischell Department of Bioengineering, University of Maryland, College Park, MD, USA
LASIK Combined with Cross-Linking

CONCEPT

• Provide cross-linking:
  • Sufficient to improve corneal strength
  • Insufficient to induce conceal flattening
  • “Just Right” amount needed
LASIK Combined with Cross-Linking

GOALS

• Reduce ectasia risk in at risk eyes

• Reduce regression risk
  • Myopic surgery
  • Hyperopic surgery

• Conflicting results in literature
LASIK Combined with Cross-Linking

Topography-guided Hyperopic LASIK With and Without High Irradiance Collagen Cross-linking: Initial Comparative Clinical Findings in a Contralateral Eye Study of 34 Consecutive Patients

Anastasios John Kanellopoulos, MD; Jonathan Kahn, MD

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Figure 1. Riboflavin is instilled on the bare stromal bed. Care is taken to avoid contact with the folded LASIK flap.

Figure 2. Repositioned LASIK flap. The yellow tinge seen within the corneal stroma is the riboflavin.
Topography-guided Hyperopic LASIK With and Without High Irradiance Collagen Cross-linking: Initial Comparative Clinical Findings in a Contralateral Eye Study of 34 Consecutive Patients

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[Graph showing Keratometry over time for Lasik Xtra and Std Lasik]
Comparison of prophylactic higher fluence corneal cross-linking to control, in myopic LASIK, one year results

Anastasios John Kanellopoulos¹,²
George Asimellis¹
Costas Karabatsas¹

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Comparison of prophylactic higher fluence corneal cross-linking to control, in myopic LASIK, one year results.

A

B

USC Roski Eye Institute
Keck Medicine of USC
Superficial corneal crosslinking during laser in situ keratomileusis

Theo G. Seiler, MD, Isaak Fischinger, MD, Tobias Koller, MD, Viktor Derhartunian, MD, Theo Seiler, MD, PhD

J Cataract Refract Surg 2015; 41:2165–2170

CXL eyes

Worse 1 month
Loss 1 line CDVA
DLK stage 1
DLK stage 2
Erosions
Consecutive laser in situ keratomileusis and accelerated corneal crosslinking in highly myopic patients: preliminary results.

Tan J, Lytle GE, Marshall J.

Abstract

PURPOSE: To report the preliminary results of an evaluation of the safety and predictability of Lasik Xtra, a technique combining laser in situ keratomileusis (LASIK) and accelerated corneal crosslinking, in highly myopic patients.

METHODS: In this consecutive comparative case series, 70 consecutive eyes undergoing LASIK for correction of high myopia (-8.00 D to -19.00 D manifest refractive spherical equivalent) were prospectively recruited and treated with Lasik Xtra and compared with a retrospective consecutive control group of 64 eyes who had undergone LASIK alone for correction of high myopia. The follow-up was 3 months. Outcome measures included uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), and refraction.

RESULTS: A total of 61% of LASIK only eyes achieved UDVA of 20/25 or better, compared to 98% of Lasik Xtra eyes (p<0.001) at 3 months. A greater percentage of eyes were within ±0.50 of the intended correction in the Lasik Xtra group (88%) than in the LASIK only group (65%) at 3 months (p = 0.005). Linear regression of the scatterplot of attempted versus achieved correction reveals a coefficient of determination of 0.83 in the LASIK only group vs 0.99 in the Lasik Xtra group. A trend (p = 0.051) towards greater refractive drift in the LASIK group (-0.13 D) vs the Lasik Xtra group (-0.04 D) was observed. No adverse events were observed in either group.

CONCLUSIONS: Lasik Xtra did not reduce the refractive accuracy of the LASIK procedure. The addition of crosslinking may induce early stabilization of the cornea after LASIK, improving the predictability of refractive outcomes in highly myopic subjects.
Short-term Variance of Refractive Outcomes After Simultaneous LASIK and High-Fluence Cross-linking in High Myopic Correction

Tommy C. Y. Chan, FRCS; Marco C. Y. Yu, PhD; Alex L. K. Ng, MRCS; George P. M. Cheng, FRCS; Jiamei Zhang, MD; Yan Wang, MD; Vishal Jhanji, MD, FRCOphth

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High-irradiance CXL combined with myopic LASIK: flap and residual stroma biomechanical properties studied ex-vivo

Anastasios John Kanellopoulos,¹,² George Asimellis,¹ Borja Salvador-Culla,³ James Chodosh,³ Joseph B Ciolino³

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### Table 2  Biomechanical comparative measurements between the two groups

<table>
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<th>Young's shear modulus</th>
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<td>@ 10% strain</td>
<td>@ 20% strain</td>
<td></td>
<td>@ 10% strain</td>
<td>@ 20% strain</td>
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<tr>
<td>Group A (control)</td>
<td>158.3 ±16.8</td>
<td>1566.6 ±45.9</td>
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<td>5.9 ±3.9</td>
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<td>Group B (CXL)</td>
<td>182.8 ±20.8</td>
<td>1534.5 ±134.8</td>
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<td>6.5 ±3.2</td>
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<tr>
<td>Δ</td>
<td>15%</td>
<td>–2%</td>
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</table>

Δ, relative (%) difference between metrics; p, Student t test p value; t, Student t test t value. Results from flap specimens.
Brillouin Microscopy can Measure Corneal Biomechanics
Fig. 3: Brillouin microscopy. (a) Back-scattered light acquires a frequency shift due to interaction of incident light with phonons in the sample. (b) The scattered light is collected by a confocal microscope and analyzed by a home-built high-resolution spectrometer. (c) CCD spectrometer output shows Brillouin spectrum of corneal stroma. (d) Analysis of the Brillouin spectrum (red) with Lorentzian curve fit (gray). (e) Log-log correlation between Brillouin and shear modulus of corneal tissue.
Depth-dependent Cohesive Tensile Strength in Human Donor Corneas: Implications for Refractive Surgery

J. Bradley Randleman, MD; Daniel G. Dawson, MD; Hans E. Grossniklaus, MD; Bernard E. McCarey, PhD; Henry F. Edelhauser, PhD
Mathematical Model to Compare the Relative Tensile Strength of the Cornea After PRK, LASIK, and Small Incision Lenticule Extraction

Dan Z. Reinstein, MD, MA(Cantab), FRCPht; Timothy J. Archer, MA(Oxon), DipCompSci(Cantab); J. Bradley Randleman, MD

J Refract Surg. 2013:454-460

Scarcelli G, Pineda R, Yun SH. IOVS 2012:185-190
Brillouin can measure differences before & after CXL and between different CXL techniques.
Purpose

• To determine the impact of an accelerated corneal cross-linking protocol on corneal biomechanics as measured by Brillouin microscopy in porcine eyes.
Methods

• Ten porcine eyes had LASIK flaps created using the Amadeus II mechanical microkeratome and then subjected to accelerated corneal cross-linking (A-CXL)
  • Ultraviolet-A (UVA) fluence of 30 mW/cm²
  • 80 seconds (total energy 2.4 J/cm²)
  • VibeX Xtra riboflavin solution (Avedro, Inc.)
    • 0.22% riboflavin, isotonic

• Brillouin microscopy was performed before and after flap creation and after A-CXL
Results

Figure 1. Brillouin shift characterization of the standard Flap-CXL procedure. (A) Representative cross-sectional Brillouin image of virgin porcine cornea. (B) Brillouin image of cornea after flap creation with mechanical microkeratome. (C) Brillouin image of cornea after standard CXL. (D) Brillouin depth profiles of the virgin (red line), flap only (green only) and after flap and rapid cross-linking (blue line).
Results

Significant reduction after flap creation
No significant difference with A-CXL
Figure A
Significant reduction after flap creation in anterior and central stroma only

Figure B
no significant change after A-CXL in any region
Conclusions

• Flap creation significantly reduces corneal stiffness in the anterior third of the porcine cornea.

• Accelerated CXL did not have any significant biomechanical impact on the porcine cornea at any depth.
Thank You