Lessons from a 2 decade journey through customizing ablations and cornea biomechanics with CXL (CXL plus part I)

A. John Kanellopoulos, MD

President, the ISRS
Director, Laservision.gr Institute, Athens, Greece
Clinical Professor NYU Medical School, NY
Financial interests (D) consultant for:

AJKMD events
Alcon
Allergan
Avedro
KeraMed
i-Optics
ISP Surgical, LLC
Optovue
Zeiss

Topography - Guided University Courses 2016:

Become proficient interpreting in cornea diagnostics and designing expert topography guided laser treatments!

A. John Kanellopoulos, MD
For the things we have to learn before we can do, we learn by doing.

— Aristotle
CXL efficacy and safety
Decrease of UV-intensity
courtesy E. Spoel MD

<table>
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<th>depth in µm</th>
<th>3 mW/cm²</th>
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<tbody>
<tr>
<td>0</td>
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<td></td>
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<tr>
<td>100</td>
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<td>300</td>
<td>12%</td>
<td></td>
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<tr>
<td>400</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>500</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>600</td>
<td>2%</td>
<td></td>
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- 3.00 mW/cm²
- 1.49 mW/cm²
- 0.74 mW/cm²
- 0.36 mW/cm²
- 0.18 mW/cm²
- 0.09 mW/cm²
Our Athens team’s CXL contributions:

- Applying topo-guided PRK in CXLed ectatic corneas **2004**
- Combining same-day CXL with topo-guided reshaping of irregular corneas Athens Protocol: **2005**
- Higher fluence: **2006 (6mW, 10mW)**
- Intra-stromal treatments through femto-pocket: **2007**
- LASIK+CXL( Xtra ): **2008 (ESCRS)**
- LASIK Xtra for hyperopia: **2011 (ASCRS)**
- PiXL CXL corneal differentials: **2013 (AAO)**
- CXL in Boston Kpro (Cornea resistance to melt)
- Athens Protocol with PiXL CXL **2015**
- **TMR**: Topography-modified refraction **2016**
• LASIK combined with CXL
• CXL or bullus keratopathy
• In-pocket CXL
• The Athens Protocol
introduced: Higher fluence CXL: 6, 7, 9, 10 and 12mW/cm²

AAO 2008: CXL for 15 minutes utilizing 7mW/cm² fluence
2007: Introduction of riboflavin in a femto-pocket

Collagen Cross-linking in Early Keratoconus With Riboflavin in a Femtosecond Laser-created Pocket: Initial Clinical Results

Anastasios John Kanellopoulos, MD

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

Anastasios John Kanellopoulos 1,2
George Asimellis 1
Costas Karabatsas 1
1LaserVision.gr Clinical and Research Eye Institute, Athens, Greece; 2New York University Medical School, New York, NY, USA

Purpose: To compare 1-year results: safety, efficacy, refractive and keratometric stability, of femtosecond myopic laser-assisted in situ keratomileusis (LASIK) with and without concurrent prophylactic high-fluence cross-linking (CXL) (LASIK-CXL).

Methods: We studied a total of 155 consecutive eyes planned for LASIK myopic correction. Group A represented 73 eyes that were treated additionally with concurrent prophylactic high-fluence CXL; group B included 82 eyes subjected to the stand-alone LASIK procedure. The following parameters were evaluated preoperatively and up to 1-year postoperatively: manifest refractive spherical equivalent (MRSE), refractive astigmatism, visual acuity, corneal keratometric readings (D).

Figure 8: Stability of corneal keratometry for (A) the LASIK-CXL group and (B) the stand-alone LASIK group, expressed in diopters (D), up to 1-year postoperatively. Abbreviations: CXL, cross-linking; LASIK, laser-assisted in situ keratomileusis.
Athens Protocol: Topo-guided partial PRK + CXL

1-Topolyzer: Placido disc topography
2-Pentacam (Oculyzer)
3-Pentacam HD (Oculyzer II)-Refractive suite
4-Vario (placido disc + pupil sensor + iris recognition + limbal landmarks recognition)

WaveLight® Refractive Suite
Similar technologies: Zeiss, Schwind, Ivis
2004: Over the last 12 years we have introduced and treated over 3000 cases of KCN and ectasia with CXL combined with a topo-guided excimer normalization: the “Athens Protocol” now practiced globally!!!
The Athens Protocol 4 steps:
same day PTK > topoPRK > MMC > CXL (6mW/cm² x 15 min)

A. John Kanellopoulos, MD

Comparison of Sequential vs Same-day Simultaneous Collagen Cross-linking and Topography-guided PRK for Treatment of Keratoconus

Anastasios John Kanellopoulos, MD

ABSTRACT

Keratoconus is a bilateral, non-symmetric, noninflammatory progressive corneal degeneration that frequently manifests in post-pubescent young adults.

Sequential vs Simultaneous Topography-guided PRK and CXL/Kanellopoulos

Figure 2. Cornea optical coherence tomography demonstrates hyper-reflective interstrial "lines" at 2/3 depth corresponding with the clinical presence of the corneal collagen cross-linking (CXL) demarcation line in a patient from the simultaneous group 3 years following combined topography-guided photorefractive keratectomy and CXL procedure.
Kanellopoulos AJ: *JRS Sept 09*: 358 cases with over 2 year follow-up: 160 cases Sequential (left) Vs 198 cases same-day Combined (right)

<table>
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<tr>
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<th>PreOp</th>
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<tr>
<td><strong>UCVA LogMar</strong></td>
<td>0.9 ±0.3</td>
<td>0.49 ±0.25</td>
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<tr>
<td><strong>BSCVA LogMar</strong></td>
<td>0.41 ±0.25</td>
<td>0.16 ±0.22</td>
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<td><strong>Mean Decrease MRSE</strong></td>
<td>2.50±1.2</td>
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<td><strong>Mean K Decrease</strong></td>
<td>2.75±1.3</td>
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<td><strong>Mean Haze Score</strong></td>
<td>1.2±0.5</td>
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<tr>
<td><strong>Mean CCT</strong></td>
<td>465±45</td>
<td>395±25</td>
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<table>
<thead>
<tr>
<th></th>
<th>Pre-op</th>
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<tr>
<td><strong>UCVA LogMar</strong></td>
<td>0.96 ±0.2</td>
<td>0.3 ±0.2</td>
</tr>
<tr>
<td><strong>BSCVA LogMar</strong></td>
<td>0.39 ±0.3</td>
<td>0.11 ±0.16</td>
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<tr>
<td><strong>Mean Decrease MRSE</strong></td>
<td></td>
<td>3.2±1.4</td>
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<tr>
<td><strong>Mean K Decrease</strong></td>
<td></td>
<td>3.50±1.3</td>
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<tr>
<td><strong>Mean Haze Score</strong></td>
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<td>0.5±0.3</td>
</tr>
<tr>
<td><strong>Mean CCT</strong></td>
<td>475±55</td>
<td>405±35</td>
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</tbody>
</table>
Management of Corneal Ectasia After LASIK
With Combined, Same-day, Topography-guided Partial Transepithelial PRK and Collagen Cross-linking: The Athens Protocol

Anastasios John Kanellopoulos, MD; Perry S. Binder, MS, MD

Figure 2. Case 2. Topography on the left shows marked inferior steepening before topography-guided PRK/CXL treatment. The topography on the right shows the same cornea 18 months after topography-guided PRK/CXL with marked flattening of the corneal ectasia and normalization of the curves.

Figure 3. Case 3. Clinical course of the right eye. A) Topography 3 years after LASIK demonstrates irregular astigmatism and marked inferior corneal steepening. Uncorrected distance visual acuity was 20/40 with refraction of -1.50 - 2.00 x 68. B) Topography 3 months after topography-guided PRK/CXL procedure demonstrates a flatter and normalized cornea. Uncorrected distance visual acuity was 20/15. C) Topographic reproduction of the topography-guided PRK treatment plan with the WaveLight platform. This platform plans to achieve tissue in an irregular fashion to normalize the corneal ectasia seen in Figure 2A. D) Comparison map, derived from subtracting image B from A, represents the topographic difference in this case 3 months after the combined treatment. The para-central flattening is self-explanatory, as the PRK and CXL have flattened the cone apex. The superior nasal arcuate flattening represents the actual part-hyperopic correction, which the topography-guided treatment has achieved, to accomplish steepening in the area central to the arc.

He presented to our institution in September 2007, 3 years after LASIK. Uncorrected distance visual acuity was 20/40 in the right eye and 20/15 in the left eye. Manifest refraction was +1.50 - 2.00 x 35 (20/20) in the right eye and plano (20/15) in the left eye. Kera- tometry was 41.75/42.12@10 in the right eye and 41.75/42.12@10 in the left eye. Central ultrasound pachymetry was 476 µm in the right eye and 490 µm in the left eye.

On September 13, 2007, 39 months after LASIK, ectasia and was offered Intacs (Addition Technology Inc, Des Plaines, Illinois) or a corneal transplant.
The Athens Protocol 4 steps:

1- topo-guided PRK
2- PTK
3- 30" MMC
4- CXL

same day partialPRK > PTK > MMC > CXL (6mW/cm² x 15 min)
Surgical Procedure

1. Partial topography-guided excimer-laser ablation, employing photorefractive keratectomy (PRK) in combination with the T-CAT procedure. Optical zone 5.00 to 5.50 mm.

2. Excimer-laser ablation (uniform 50 µm over a 7.00 mm zone), employing the PTK mode.

3. CXL with UV-A irradiance of 6 mW/cm², applied for 15' employing the KXL I or II system (Avedro Inc., Waltham, MA).
Step 4: attempted Rx to 0, OZ to 5 or 5.5mm, cyl axis to match topo axis not refractive axis
Post LASIK ectasia: 26y/o pilot, from UCVA 20/60 to 20/15
Novel Placido-derived Topography-guided Excimer Corneal Normalization With Cyclorotation Adjustment: Enhanced Athens Protocol for Keratoconus

Anastasios John Kanellopoulos, MD; George Asimellis, PhD

ABSTRACT

PURPOSE: To comparatively investigate the efficacy of the enhanced Athens Protocol procedure guided by novel Placido-derived topography with cyclorotation adjustment against similar cases guided by Scheimpflug-derived topography without cyclorotation compensation (the non-cyclorotation adjusted group).

METHODS: Two groups were evaluated: the cyclorotation adjusted group (n = 110 eyes) and the non-cyclorotation adjusted group (n = 110 eyes). Analysis was based on digital processing of Scheimpflug imaging data using the ATLAS 9 software (Heidelberg Engineering, Heidelberg, Germany). Follow-up was conducted at 3 months postoperatively. The vector r (i) corresponding to the steepest corneal point center on the preoperative surgical planning map (r, i) and on the curvature difference map (r, i) were compared. The difference between the peak topographic angular data (Δθ = |θi – θf|) and weighted angular difference (Wθ = Δθ – Δθ) were calculated.

RESULTS: For the cyclorotation adjusted group, Δθ was 14.50° ± 12.65° (range: 0.00° to 80.56°) and Wθ was 10.23 ± 15.15 mm (range: 0.00 to 21.41 mm). For the non-cyclorotation adjusted group, Δθ was 3.43° ± 1.89° (range: 0.00° to 49°) and Wθ was 3.67 ± 4.76 mm (range: 0.00 to 21.41 mm). The cyclorotation adjusted group appeared superior to the non-cyclorotation adjusted group in both the smaller average angular difference (Δθ: P = .0058; Wθ: P = .015) and statistically significant margin (Δθ: P < .0001; Wθ: P < .0001).

CONCLUSIONS: This study suggests that employment of the novel Placido-derived topographic data of highly irregular corneas, similar cases guided by Scheimpflug-derived topography without cyclorotation compensation leads to markedly improved corneal normalization.


Figure B. The ‘compare 2 exams’ output from the Scheimpflug imaging device. (Left) The preoperative sagittal curvature map, (middle) the postoperative sagittal curvature map, and (right) the difference of the two maps.
Average K from 48.5 to 44
Refraction -2.5-4.5@155 (20/70) to -1-1.5@10 (20/20)
Caution: marked refractive effect with the 3mW protocols
Corneal Refractive Power and Symmetry Changes Following Normalization of Ectasias Treated With Partial Topography-Guided PTK Combined With Higher-Fluence CXL (The Athens Protocol)

Anastasios John Kanellopoulos, MD; George Asimolis, PhD

Keratoconus assessment employs indicators such as keratometric values, inferior-superior index, skew percentage, astigmatism, and the K/B/C index. Acceptable quantitative keratometric criteria include central corneal refractive power larger than 47.2 degrees (E), inferior–superior dioptric asymmetry larger than 1.2 D, and simulated astigmatism, expressed as the difference between steep and flat keratometric values greater than 3.5 D. The steep and flat志愿 keratometric values correspond to the smaller and larger anterior corneal curvature radius, respectively.

Corneal cross-linking (CXL) is an in vivo intrastromal photo-oxidative technique with riboflavin and ultraviolet-A light aiming to address the advancing central ectasia and, consequently, the keratoconus progression. With CXL, additional collagen bonding between stromal collagen can be achieved, which stabilizes the collagen framework. The remodeling effects of CXL on the cornea can be described by the reduction of mean anterior surface keratometric values. Few studies have been published on the quantitative link between anterior and posterior keratometric values in keratoconic eyes or particularly on the postoperative effects of CXL on the anterior cornea.

This study aims to investigate the distribution and relationship between anterior and posterior keratometric values and simulated anterior and posterior astigmatism on a large group of clinically diagnosed, untreated keratoconic eyes, and the 1-year postoperative effects on both anterior and posterior keratometric values and astigmatism included in a combined procedure known as the Athens Protocol, which intends to arrest the keratoconus progression and normalize the anterior corneal surface.

RESULTS: Mean visual acuity improved from 20/40 at baseline to 20/30 at 1 year. Decrease in keratometric values was observed at 1 year postoperatively compared with preoperatively. The comparison between anterior and posterior keratometric values and astigmatism showed significant differences throughout the study period. The reduction in keratometric values was observed to be gradual, with a slight increase in astigmatism.

CONCLUSIONS: The Athens Protocol offers a novel approach to the management of keratoconus by combining CXL with the surgery to improve vision and minimize progression.

Keratoconus Management: Long-Term Stability of Topography-Guided Normalization Combined With High-Fluence CXL Stabilization (The Athens Protocol)

Anastasios John Kanellopoulos, MD; George Asimolis, PhD

Keratoconus is a degenerative bilateral, noninflammatory disorder characterized by ectasia, thinning, and irregular corneal topography. The disorder usually has onset at puberty and often progresses until the third decade of life, may manifest asymmetrically in the two eyes of the same patient, and can present with unpredictable visual acuity, particularly in relation to corneal irregularities. One of the acceptable options for progressive keratoconus management is corneal collagen cross-linking (CXL) with riboflavin and ultraviolet-A.

To further improve the topographic and refractive outcomes, CXL can be combined with customized anterior surface normalization. Our team has developed a protocol involving sequential excimer laser epithelial keratectomy (50 μm), partial topography-guided excimer laser stromal ablation, and high-fluence ultraviolet-A irradiation (10 mW/cm²) accelerated (180 or modified) CXL. Early results and anterior segment optical coherence tomography quantitative findings are indicative of the long-term stability of the procedure.

Detailed studies on postoperative visual rehabilitation and anterior surface topographic changes by such combined CXL procedures are rare. Particularly, those reporting results longer than 1 year. This study aims to investigate safety and efficacy of the Athens Protocol procedure by analysis of long-term (3-year) refractive, topographic, and visual rehabilitation changes on clinical keratoconus management with the Athens Protocol in a large number of cases.

PATIENTS AND METHODS

This clinical study protocol was approved by the Ethics Committee of our institution and adhered to the tenets of the Declaration
Conclusions

- The Athens Protocol (partial topo-guided PTK combined with CXL) appears to be safe and effective in ectasia stabilization, and visual rehab over 12 years later.
- Alternative treatments are CXL alone
- Contact lenses: RGPs and/or Scleral lenses
  - ICRS
- Lamellar keratoplasty
- Penetrating keratoplasty
Athens Protocol: improved anterior corneal profile, but what about the posterior?
Variable Fluence, topo-customized pattern CXL
KXL II device (Avedro, Waltham, MA, USA)  CE marked 2013
The Athens Protocol evolution
topo-guided PTK+variable fluence topo-customized CXL
The Athens Protocol evolution
topo-guided PTK+variable fluence topo-customized CXL
The Athens Protocol evolution
Minimal cone ablation
4.8. Efficacy Outcomes  
Changes In Manifest Refraction, Refractive Stability, Vector Analyses, Changes In UCVA, Patient-Reported Outcomes  
A summary of key efficacy variables at each of the postoperative visits is provided below in Table 16 for the myopia cohort treated with Topo-guided (T-CAT) LASIK.

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<th>EFFICACY VARIABLES</th>
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<th>Month 9</th>
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<td>MRSE ± 0.50 D</td>
<td>220/248</td>
<td>227/247</td>
<td>222/244</td>
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<td>88.71%</td>
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<td>247/247</td>
<td>243/244</td>
<td>235/237</td>
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<td>(%)</td>
<td>98.39%</td>
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<td>(96.5, 99.7)</td>
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<td>(97.0, 99.9)</td>
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<td>MRSE ± 2.00 D</td>
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<td>243/244</td>
<td>237/237</td>
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<td>(%)</td>
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<td>99.59%</td>
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<td>UCVA 20/20 or better</td>
<td>217/248</td>
<td>229/247</td>
<td>217/244</td>
<td>212/237</td>
<td>213/230</td>
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<td>(%)</td>
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<td>(84.3, 92.6)</td>
<td>(84.8, 93.1)</td>
<td>(88.4, 95.6)</td>
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<td>UCVA 20/40 or better if BCVA 20/20 or better preop</td>
<td>239/242</td>
<td>239/241</td>
<td>235/238</td>
<td>231/232</td>
<td>224/225</td>
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<td>(%)</td>
<td>98.76%</td>
<td>99.17%</td>
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<td>(97.0, 99.9)</td>
<td>(97.6,100.0)</td>
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Table 16: Summary Of Key Efficacy Parameters After Topo-guided (T-CAT) LASIK  

http://www.accessdata.fda.gov/cdrh_docs/pdf2/P020050S012b.pdf
TMR: Topography-modified refraction
Astigmatism adjustment
decreased cyl
TMR: Topography-modified refraction
Astigmatism adjustment: decreased cyl
TMR: Topography-Modified refraction
Astigmatism adjustment
increased cyl
TMR : Topography-Modified refraction
Astigmatism adjustment: increased cyl
Research Article

Title: TMR: Topography-Modified Refraction

Abstract

Purpose: To evaluate the safety, efficacy, and clinical evaluation in a comparison of topography-guided LASIK, with different refraction adjustment strategies.

Setting: Patients with refractive error of ≥±0.25 diopters (D) were randomized into two groups. Group A was treated with one eye with the standard clinical refraction, and the contralateral eye with the topography-estimated treatment. Group B was treated with one eye with the standard clinical refraction, and the contralateral eye with the topography-modified treatment. The follow-up period was at least 12 months.

Results: Mean refractive error was ±0.50 D of astigmatism in both groups. The residual percentage of eyes with gain/loss in Snellen lines was 36.3% and 38.6% for group A and B, respectively. The mean postoperative CDVA was 20/20 and 20/13.5; 1 line of vision gained was 27.8% and 55.6%; and 2 lines of vision gained was 0%. The residual percentage of eyes with gain/loss in Snellen lines was 36.3% and 38.6% for group A and B, respectively. The mean postoperative CDVA was 20/20 and 20/13.5; 1 line of vision gained was 27.8% and 55.6%; and 2 lines of vision gained was 0%.

Conclusions: Topography-guided refraction (TMR: Topography-Adjusted Refraction) is a safe and effective treatment for myopic LASIK.

Keywords: LASIK, Refractive Error, Astigmatism, Corneal Topography, Clinical Ophthalmology.

Introduction

LASIK has been a popular treatment for the past 2 decades as a safe and effective treatment for myopic LASIK. However, with the advancements in laser technology, the need for a more personalized treatment has arisen.

A. John Kanellopoulos, MD
Topography - Guided University Courses 2016:

Become proficient interpreting in cornea diagnostics and designing expert topography guided laser treatments!

The course will be limited to 30 participants.

Advanced registration and information: http://www.topo-guided.com/

www.topo-guided.com

A. John Kanellopoulos, MD

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2016 Course’s Mutual Outline
(Copenhagen and Chicago)

8:00
breakfast - Registration

8:30-11:30
• Introduction to current cornea diagnostics and their relative differences: Placido Topography, Scheimpflug Topography, Anterior segment OCT, LED color reflection topography.
• Corneal epithelial mapping and its clinical relevance in diagnosis and treatment.
• Basic principles in employing topography data (Scheimpflug based and Placido-based) in the customization of an excimer corneal ablation.
• Topography customization, decentered and angle kappa considerations for possible revision of the clinical refraction used in each ablation.

11:30-12:30
Discussion lunch

12:30-15:30
• Topography customized methodology for irregular corneas (previously treated: RK, decentered and/or irregular ablations, as well as irregular and ectasia cases)
• Corneal epithelial mapping and its clinical relevance in diagnosis and treatment.
• Anticipating asphericity and sphere compensatory nomograms for better spherical correction and emmetropia.
• Participants will join access to an online database with over 100 cases examples (pre-op data, treatment design, treatment video, postop data and overview of what went well and what potentially went off-target)
• Complications assessment and management.

Each participant will have the chance to design several treatments on site!

Friday, September 9th, 2016 (pre-ESCRS)
8:00 AM to 15:30 PM
At the Crowne Plaza Copenhagen Towers
2300 København S, Denmark
Tel: +45 8877 6655
Fax: +45 8877 6611

Topography - Guided University Courses 2016:

Become proficient interpreting in cornea diagnostics and designing expert topography guided laser treatments!

Copenhagen ’16 course logistics

Course Director: A. John Kanellopoulos, MD

www.topo-guided.com

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Thursday, October 13th, 2016 (pre-AAO)
8:00 AM to 15:30 PM
At the Hyatt Regency McCormick Place
2225 S Martin Luther King Dr, Chicago, 60616, IL, USA
Tel: +1 312 567 1234

Disclaimers:

Information and data are current as of November 2015. Contact information is subject to change. For the most up-to-date and accurate information, please visit the respective course’s website or contact the course director directly.

A. John Kanellopoulos, MD

www.topo-guided.com

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www.topo-guided.com

A. John Kanellopoulos, MD

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Courses 2016:

• Pre-ESCRS
• Outline and 2016 locations
• Pre-AAO

Become proficient interpreting in cornea topography guided laser treatments!

Copenhagen'16 course logistics

Course Director: A. John Kanellopoulos, MD

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Become proficient interpreting in cornea topography guided laser treatments!

Copenhagen’16 course logistics

Course Director: A. John Kanellopoulos, MD

www.topo-guided.com

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Become proficient interpreting in cornea topography guided laser treatments!
Customized CXL for KCN!

A. John Kanellopoulos, MD
Epithelial remodeling after partial topography-guided normalization and high-fluence short-duration crosslinking (Athens protocol): Results up to 1 year

Anastasios John Kanellopoulos, MD, Georgo Asimellis, PhD

ARTICLE

The findings in the current study agree with those in our previous study: that is, although an overall thicker epithelium with large variations can be observed clinically and topographically in eyes with keratoconus, in eyes treated with CXL, the variability in epithelium thickness and topographic thickness decreased by a statistically significant margin and was more uniform. We have theorized that epithelial hyperplasia in biomechanically unstable corneas (ie, increased epithelial regrowth activity) might be associated with a more elastic cornea.

In conclusion, we present the results in a comprehensive study of the postoperative development of corneal epithelial thickness distribution after keratoconus management using combined anterior corneal normalization by topography-guided excimer ablation and accelerated CXL. The epithelial healing processes can be monitored by AS-OCT with ease in a clinical setting, expanding the clinical application of this technology. Our findings suggest less topographic variability and overall reduced epithelial thickness distribution in keratoconus eyes treated with CXL using the Athens protocol.

WHAT WAS KNOWN
- Postoperative epithelial remodeling after partial anterior surface normalization with an excimer laser and high-fluence CXL, assessed with high-frequency scanning UBM, results in reduced overall epithelial thickness and topographic variability.

WHAT THIS PAPER ADDS
- Detailed follow-up of Athens protocol–treated eyes up to 1 year confirmed previous ultrasound findings of the overall thinner and smoother epithelial thickness profiles compared with the profiles of untreated keratoconic eyes.

REFERENCES

Severe scar of the cornea
BCVA 20/200,
Lamellar or PK?
From 20/200 to 20/40!
Hyperopic LASIK
a drop of 0.1% riboflavin sodium phosphate solution, spread over the exposed stromal bed for 60”
Compelling stability evidence in the contralateral eye hyperopic LASIK + CXL group
Comparison of refractive and keratometric stability
Myopic LASIK vs LASIK+ CXL

Purpose: To compare 1-year postoperative safety, efficacy, refractive and keratometric stability, of Lasik and myopic LASIK+ collagen cross-linking (CXL) and without CXL, in eyes with myopic astigmatism.

Methods: We studied a total of 134 consecutive eyes (71 eyes for the LASIK, 63 eyes for the LASIK+CXL group) treated with the same excimer laser (Catalys, University of Southern California, Los Angeles, CA, USA). Twenty eyes were treated with CXL and 114 eyes with LASIK. The follow-up period was 12 months. The primary outcomes were postoperative best spectacle-corrected visual acuity (BCVA), manifest refraction, and keratometric readings. The secondary outcomes were patient satisfaction, patient-reported visual symptoms, and intraocular pressure.

Results: The mean postoperative BCVA was 0.03 ± 0.06 logMAR for the LASIK group and 0.03 ± 0.06 logMAR for the LASIK+CXL group. The mean manifest refraction was -0.25 ± 0.25 D for both groups. The mean keratometric readings were 43.2 ± 0.25 D for the LASIK group and 43.25 ± 0.25 D for the LASIK+CXL group.

Conclusions: The results of this study show that LASIK and LASIK+CXL are effective and safe procedures for correcting myopic astigmatism. The addition of CXL to LASIK does not significantly affect the refractive and keratometric outcomes.

Introduction
Lasik and LASIK+ CXL are among the most commonly performed refractive surgeries, offering predictable and stable refractive and visual outcomes. Specifically, in targeting moderate to high myopia (equal to or higher than -6.00 D) in the keratometric reading), there have been reports of the procedure showing significant long-term efficacy.

Comparison of keratometric stability compelling clinical evidence that LASIK+CXL works!

Does in situ CXL work? Ex-vivo evidence

Two-surface intra-lamellar bed corneal dissections were performed within a 5.5 mm optical zone. The lenticule was extracted through a 3.5 mm wide superior canal. High-fluence CXL was conducted in the pocket created.
2-dimensional biomechanical testing

<table>
<thead>
<tr>
<th>Stress units: kPa @ 10% strain</th>
<th>@ 20% strain</th>
<th>Young’s Shear Modulus units: MPa @ 10% strain</th>
<th>@ 20% strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>group-A (CXl study)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>305.04 ±23.30</td>
<td>1,284.79 ±34.20</td>
<td>6.98 ±1.12</td>
<td>11.46 ±0.75</td>
</tr>
<tr>
<td>group-B (control)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>147.39 ±10.72</td>
<td>874.38 ±29.40</td>
<td>4.04 ±0.85</td>
<td>8.80 ±0.72</td>
</tr>
<tr>
<td>Δ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>107%</td>
<td>47%</td>
<td>73%</td>
<td>30%</td>
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<tr>
<td>ρ</td>
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<tr>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>
Substantial (up to +100%) increase in biomechanical strength has been noted when using biaxial stress measurements.

Results

High-irradiance CXL combined with myopic LASIK: flap and residual stroma biomechanical properties studied ex-vivo
Longitudinal Postoperative LASIK Epithelial Thickness Profile Changes in Correlation With Degree of Myopia Correction

Anastasios John Kanellopoulos, MD; George Asimellis, PhD

Figure 1. Detail from the analysis and report software main report, showing corneal and epithelial three-dimensional pachymetry maps over the 6-mm corneal diameter in a postoperative LASIK examination. The patient (left eye) received treatment for -4.75 diopters of sphere and -0.75 diopters of astigmatism, and was imaged 1 month postoperatively. * = thickness minimum (both corneal and epithelial maps); + = thickness maximum (epithelial map only).

Figure 2. The correlation of increase in epithelial thickness at the center (green dots), on the mean over the 6-mm diameter (blue), and on the 5-mm mid-peripheral zone (yellow) 1 month following myopic LASIK correction. There were 4 cases between -8 and -9 diopters (D), 7 cases between -7 and -8 D, 10 cases between -6 and -7 D, 8 cases between -5 and -6 D, 15 cases between -4 and -5 D, 13 cases between -3 and -4 D, and 6 cases between -2 and -3 D. Error bars indicate standard deviation.
Epithelial Remodeling After Femtosecond Laser–Assisted High Myopic LASIK: Comparison of Stand-alone With LASIK Combined With Prophylactic High-fluence Cross-linking

Anastasios J. Kanellopoulos, MD*† and George Asimellis, PhD*

Combined laser in situ keratomileusis and prophylactic high-fluence corneal collagen crosslinking for high myopia: Two-year safety and efficacy

Anastasios John Kanellopoulos, MD, George Asimellis, PhD
CXL of “vehicle” cornea in Boston Keratoprosthesis type I: J. Cornea 2014

A. John Kanellopoulos, MD
Is CXL a refractive procedure?

Most investigators speak of “disease reversal” when flattening occurs after CXL in ectasia. This is a simple 3mW CXL-alone case from 2005.

No scar developed, Now 2013 has Flattened 12D!!!
Novel myopic refractive correction with transepithelial very high-fluence collagen cross-linking applied in a customized pattern: early clinical results of a feasibility study

Background: The purpose of this study is to report the safety and efficacy of the novel application of collagen cross-linking using a novel device to achieve predictable refractive myopic changes in virgin corneas.

Methods: Four cases were treated with a novel device employing very high-fluence collagen cross-linking applied in a myopic pattern. Prior to treatment, riboflavin solution was applied to the intact epithelium. The collagen cross-linking device was then engaged for a total of 15.5s; to be applied transepithelially in a predetermined pattern. Cornea clarity, corneal keratometry, and corneal topography were evaluated by both Placido disc and Scheimpflug imaging, along with cornea anterior segment optical coherence tomography and endothelial cell counts.

Results: An average of 2.3 diopters was achieved in the first week in all four cases treated with the very high-fluence myopic collagen cross-linking intervention. There was a slight regression to 1.44 diopters at 1 month, which remained stable at 6 month follow-up. The mean keratometry change was from 44.90 diopters to 43.46 diopters. There was some mild change in epithelial thickness distribution, with the treated area showing a slight but homogeneous reduction in mean thickness from 5.2 μm to 4.9 μm.

Discussion: This report describes the novel application of very high-fluence collagen cross-linking with a predictable well-defined myopic refractive (flattening) corneal effect. This technique has the advantages of essentially no postoperative morbidity, immediate visual rehabilitation, and the potential for tapering until the desired result is achieved.

Conclusion: This report describes the novel application of very high-fluence collagen cross-linking with a predictable well-defined myopic refractive (flattening) corneal effect. This technique has the advantages of essentially no postoperative morbidity, immediate visual rehabilitation, and the potential for tapering until the desired result is achieved.

Keywords: refractive correction, high-fluence collagen cross-linking, clinical results.
Toric Topographically Customized Transepithelial, Pulsed, Very High-Fluence, Higher Energy and Higher Riboflavin Concentration Collagen Cross-Linking in Keratoconus

Anastasios John Kanellopoulos, MD
Laservision.gr Eye Institute, Athens, Greece; Department of Ophthalmology, NYU Medical School, New York, N.Y., Departments of Ophthalmology and Biomedical Engineering, Cleveland Clinic, C, Cole Eye Institute, Cleveland Clinic, and Department of Chemical and Biomedical Engineering, Cleveland State University, Cleveland, Ohio, USA

Key Words
Topography customizable cross-linking · High-fluence cross-linking
Transepithelial cross-linking · Toric cross-linking · Keratoconus · Photorefractive intrastromal cross-linking · KXL II

Abstract
Purpose: To report a novel application of toric topographically customizable transepithelial collagen cross-linking (CXL) aiming to achieve refractive astigmatic changes in a keratoconic cornea. Methods: Specially formulated riboflavin transepithelial administration and delivery of high-fluence UVA in a topographically customized pattern was applied in an eye with progressive keratoconus. Visual acuity, corneal clarity, keratometry, topography, and pachymetry with a multitude of modalities, as well as endothelial cell counts were evaluated for >6 months. Results: Uncorrected distance visual acuity changed from preoperative 20/40 to 20/25 at 6 months. A mean astigmatic reduction of 0.8 D, and significant cornea surface normalization was achieved 6 months postoperatively. There was some mild change in the epithelial distribution, with the treated area having a slight normalization in the average epithelial thickness. Conclusions: We introduce herein the novel application of a topograph-
“profile Hyperopic” oz 6-9mm
“hyperopic PTK” 6-9oz 30 microns
Placido topo data
Infectious Keratitis in a 38y/o F MD

A. John Kanellopoulos, MD
Customized infectious keratitis treatment

20mW/cm², 20 Joules continuous for 10’
RESULTS

The mean age of the patients was 67 ± 14 years. Six patients were female and 5 were male. The visual acuity assessed from postoperative light perception and/or hand motion showed a 6-month postoperative improvement. The average UDVA was 20/80 (range: 20/100-20/40), and the CDVA was 20/20 (range: 20/30-20/20).

These patients are still being followed up. After the first postoperative year, each patient is evaluated at least annually. During the long follow-up time that these patients have been continuously monitored (minimum 1 year, maximum 5 years), 2 of the patients required subsequent injection of triamcinolone and/or acyclovir and/or bevacizumab injection (Avastin, Genentech/Roche, San Francisco, CA) because of cystoid macular edema. Additionally, 1 patient needed yttrium aluminium garnet laser intervention for a retropseudo phakic lens that was quite dense and had resulted in a CDVA reduction from 20/60 to 20/40. After this procedure, the patient’s vision returned to 20/50.

CXL of “vehicle” cornea in Boston Keratoprosthesis type I: J. Cornea 2014

A. John Kanellopoulos, MD
Conclusions / Our current CXL protocols

1- Athens Protocol: topo partial PRK +15’x 6mw/cm²
   or combined with PiXL (4-20 Joules)

2- LASIK Xtra: 1’ soaking and 60” 30mW/cm² (1.8 Joules) for all hyperopes, 80” for myopes (2.4 Joules)

2- PRK Xtra: 1’ soaking 80” X 30mW/cm² (2.4 Joules)

5- Transepi CXL: 0.25% ribo + 30mW X 3’

6- Infection: 0.25% riboflavin + 20mW/cm² /20 Joules

7- PiXL 0.25% ribo + 30mW/cm² 7.2-20 Joules

Prospective randomized trials have yet to establish the comparative efficacy of the multitude of CXL technique available today
Topography - Guided University
Courses 2016:

Become proficient interpreting in cornea diagnostics and designing expert topography guided laser treatments!

Copenhagen '16 course logistics

Friday September 9th, 2016 (pre-ESCRS)
8:00 AM to 15:30 PM
At the Crowne Plaza
Copenhagen Towers
Orestads Boulevard 114 - 118
2300 København S, Denmark
Tel: +45 8877 6655
Fax: +45 8877 6611
info@cpcopenhagentowers.com

Chicago '16 course logistics

Thursday October 13th, 2016 (pre-AAO)
8:00 AM to 15:30 PM
At the Hyatt Regency McCormick Place
2225 S Martin Luther King Dr,
Chicago, 60616, IL, USA
Tel: +1 312 567 1234

A. John Kanellopoulos, MD
www.topo-guided.com

The course will be limited to 30 participants.
Advanced registration and information: http://www.topo-guided.com/

2016 Course's Mutual Outline

(Copenhagen and Chicago)

8:00
breakfast - Registration

8:30-11:30
Topography customized methodology for virgin myopic and hyperopic eyes

11:30-12:30
Discussion lunch

12:30-15:30
• Anticipating asphericity and sphere compensatory nomograms for better spherical correction and emmetropia
• Corneal epithelial mapping and its clinical relevance in diagnosis and treatment modifications with hands-on the design platforms and data present on-site.
• Participants will gain access to an online database with over 100 cases examples (pre-op data, treatment design, treatment video, postop data and overview of what went well and what potentially went off-target)

15:00-15:30
Complications assessment and management.

16:00-17:30
• Participants will have the chance to design several treatments on site!
• Each participant will have the chance to design several treatments on site!
• This vigorous didactic course and wet lab on topography will focus on multiple imaging assessment and interpretation, data interpretation and treatment modifications with hands on the design platforms and data present on-site.

Experienced Hands-on Course: How to adjust optical zone, transition zone, and account of the clinical refraction used in each ablation

Course Director: A. John Kanellopoulos, MD

The course will be limited to 30 participants.

Advanced registration and information: http://www.topo-guided.com/

Disclaimer:

Please note that your name and contact information will be shared with the course instructors and event organizers.
The course will be limited to 30 participants.

Our courses are solely instructional. Any medical procedure liaison is the responsibility of the participant, and the course does not provide CME credits.

Our courses will not include international travel information or visa services.

Courses will be held in Copenhagen and Chicago.

US course or within the EU for a European course, you would be responsible for obtaining the appropriate visas on your own.

Please be advised that if you are traveling from outside the US for a

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A. John Kanellopoulos, MD
Thank You!