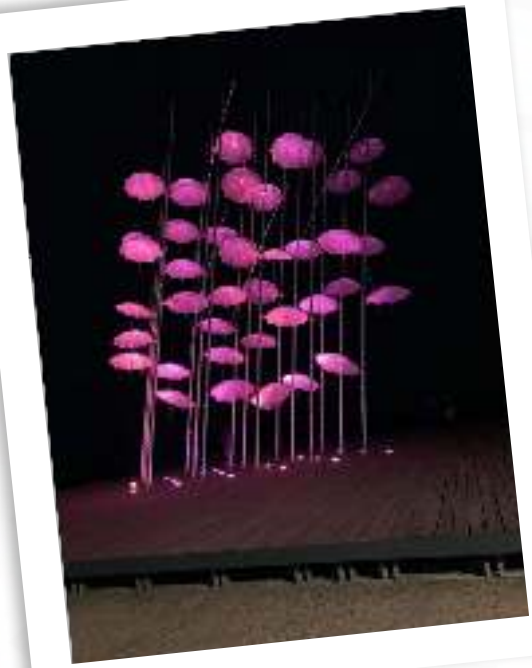
Miltos Balidis PhD, FEBOphth, ICOphth

Lessons learned in PRK CXL



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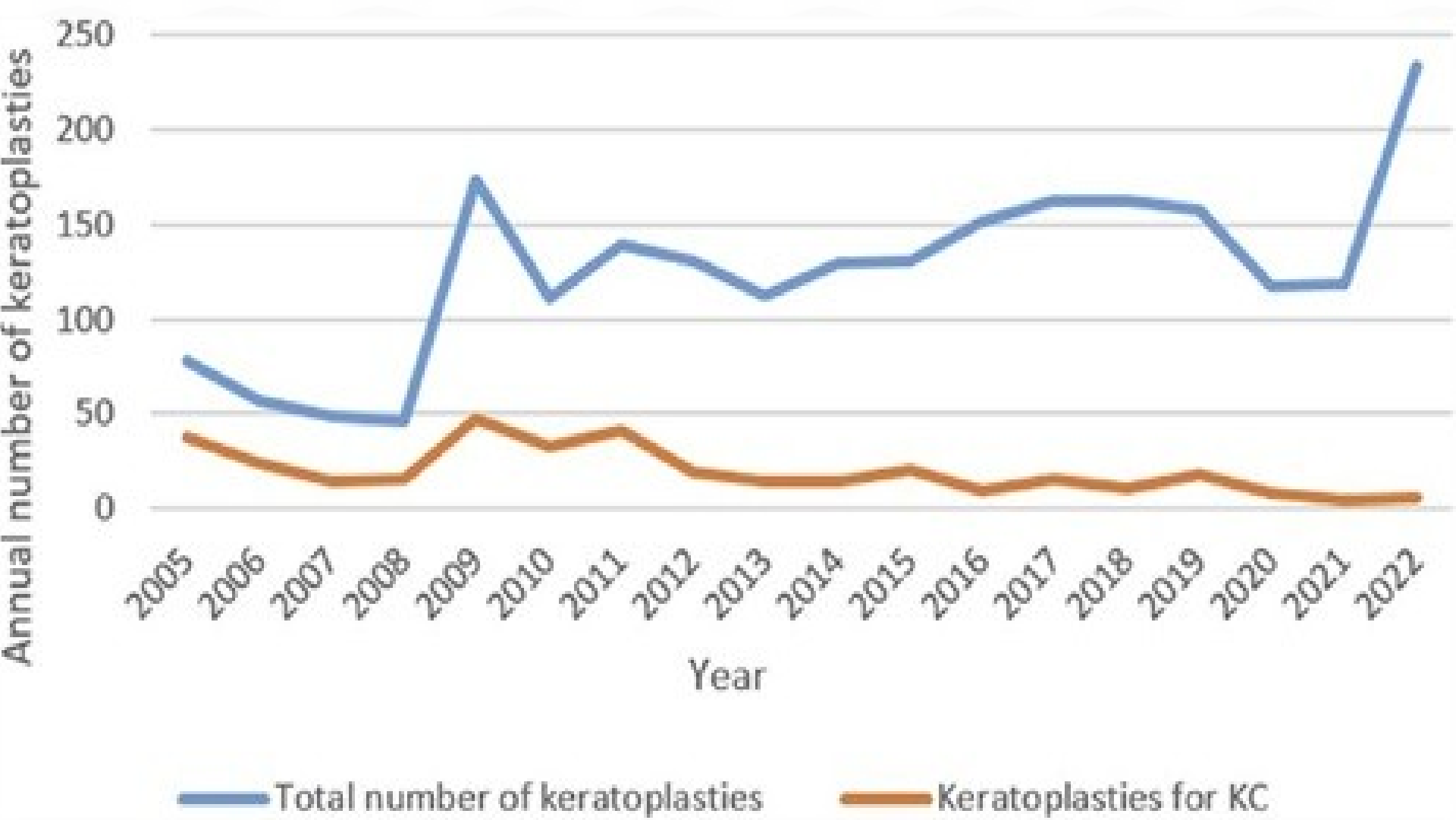

Annual number of keratoplasties
250
200
150
100
50
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
Total number of keratoplasties
Keratoplasties for KC

Cochrane Library

Comparison of different protocols	Parameter	Number of studies	Sample size A	Sample size B	Model (fixed versus random effect)	MD/SMD (95% CI)	P	Heterogeneity χ^2/df	Heterogeneity P	Heterogeneity I² (%)
CXL (A) versus control/ placebo (B)	Kmax at 6 months[1,2]	2	141	142	Fixed	−1.87 (−3.89-0.16)	0.07	0.31/1	0.58	0
	ΔThinnest corneal thickness at 1 year	2	71	63	Random	−4.23 (−32.33-23.87)	0.77	11.51/1	0.0007	91
TE-CXL (using chemical enhancer, A) versus C-CXL (B)	Kmax at 6 months[3,4]	2	55	46	Fixed	−0.83 (−3.04-1.38)	0.46	0.06/1	0.80	0
	BCVA at 6 months[3-6]	4	115	106	Fixed	0.02 (−0.01-0.04)	0.13	2.81/3	0.42	0
	CCT at 6 months[3-6]	4	115	106	Fixed	3.47 (−1.76-8.70)	0.19	3.53/3	0.32	15
	SE at 6 months[3-6]	4	75	66	Fixed	−2.87 (−10.50-4.77)	0.46	213.69/2	<0.00001	99
	SE at 1-year[3-5,7]	4	105	96	Random	0.34 (−1.05-1.74)	0.63	11/3	0.01	73
	CCT at 1-year[3-5,7]	4	105	96	Fixed	0.98 (−4.39-6.35)	0.72	0.55/3	0.91	0
T-Ionto (enhanced using T-Ionto, A) versus C-CXL (B)	BCVA at 6 month[8,9]	2	98	95	Random	−0.03 (−0.12-0.05)	0.43	2.44/1	0.12	59
	CCT at 6 month[8,9]	2	98	95	Fixed	−5.51 (−16.46-5.45)	0.32	0.36/1	0.55	0
	BCVA at 1-year[8,9]	2	98	85	Fixed	−0.02 (−0.07-0.03)	0.90	0.6/1	0.51	0
	CCT at 1-year[8,9]	2	98	85	Fixed	0.75 (−11.09-12.59)	0.94	0.01/1	0.94	0
	BCVA at 2 year[8,10]	2	98	85	Fixed	0.00 (−0.07-0.06)	0.98	0.38/1	0.54	0
	CCT at 2 year[8,10]	2	98	85	Fixed	−1.36 (−10.09-7.38)	0.76	0.88/1	0.35	0
A-CXL (A) versus C-CXL	BCVA at 6 month[11-15]	5	153	151	Fixed	0.01 (−0.04-0.06)	0.76	7.18/4	0.13	44
	SE at 6 months[11,12,15]	3	62	64	Fixed	0.05 (−0.98-1.08)	0.93	1.11/2	0.58	0
	Kmax at 6 months[11,13-15]	5	153	151	Random	0.09 (−1.35-1.53)	0.90	12.82/4	0.01	69
	CCT at 6 months[14,15]	2	43	40	Fixed	16.20 (4.20-28.20)	0.008	0.53/1	0.047	0
	Δthinnest corneal thickness[11,17]	2	46	51	Random	0.09 (−1.35-1.53)	0.90	12.82/1	0.01	69
	BCVA at 1 year[13,14,16]	3	106	102	Fixed	−0.03 (−0.08-0.03)	0.33	0.37/2	0.83	0
	CCT at 1 year[14,16]	2	29	26	Fixed	14.22 (−0.99-29.43)	0.07	0.61/1	0.44	0

Kmax=Maximum keratometry, ECD=Endothelial cell density, BCVA=Best-corrected visual acuity, SE=Spherical equivalence, CCT=Central corneal thickness, MD=Mean difference, CI=Confidence interval, CXL=Corneal collagen cross-linking, TE-CXL=Transepithelial CXL, C-CXL=Conventional CXL, A-CXL=Accelerated CXL, T-Ionto=Iontophoresis, SMD=Standard mean difference P<0.005 indicate statistically significant difference, Δindicate change from baseline

Comparative outcomes of different corneal collagen cross-linking protocols in patients with progressive keratoconus

Reshaping the conic cornea

TREK Rohit Shetty

M Rechichi STARX

Bruce Allan

WG PRK CXL

G. Kymionis

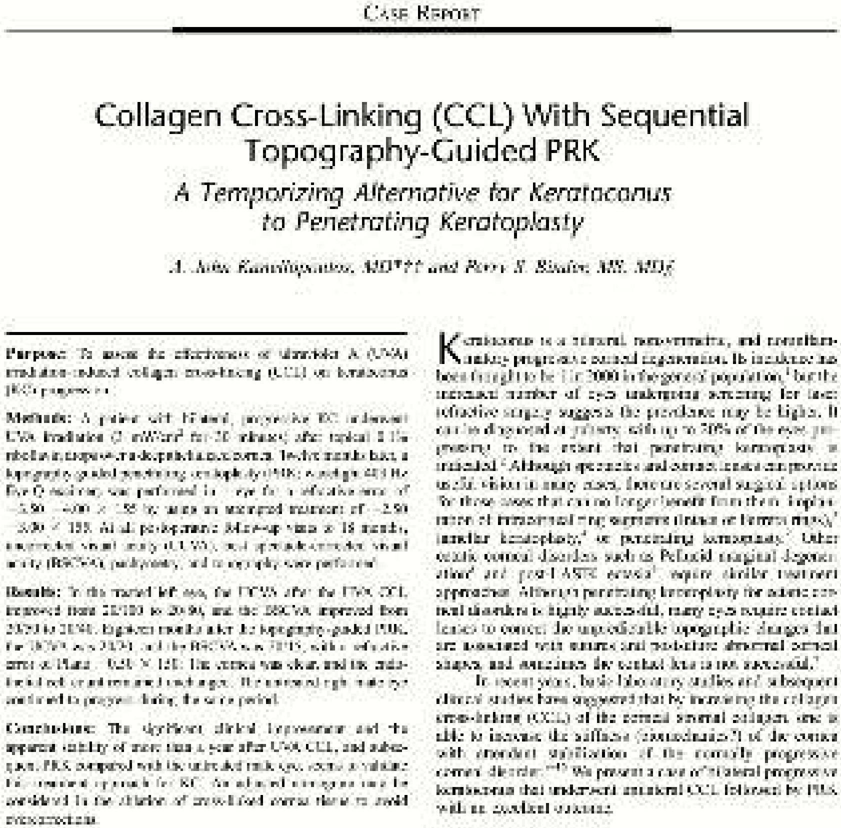
Cretan Protocol

J Kanellopoulos Athens protocol

Newborn method?

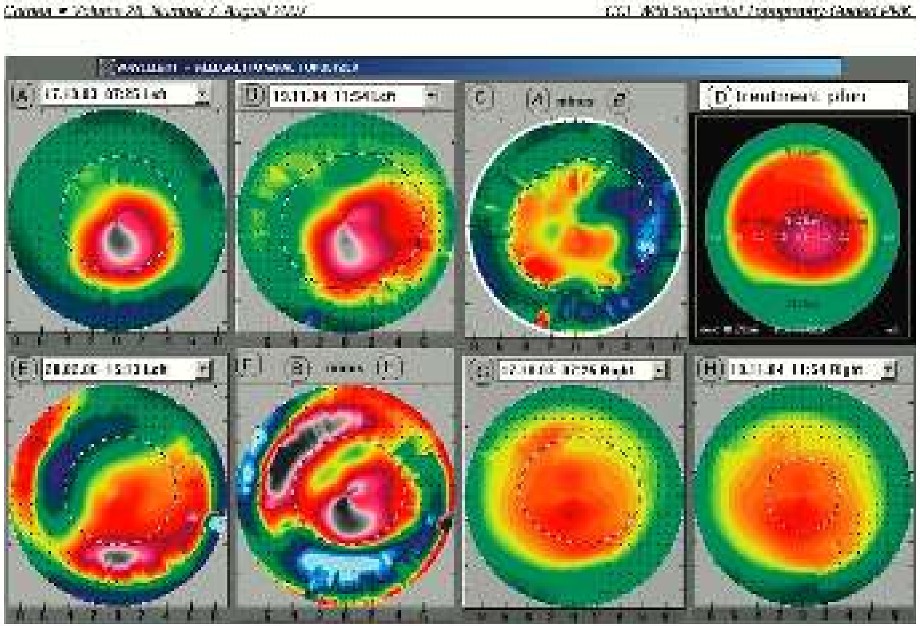
- Refractive outcome
- Pain
- Healing time
- Haze

- TG-**PRK** (max 50µm) then high-fluence CXL (Athens protocol)
- **tPTK** then **PRK+CXL** (Cretan **Plus** protocol)
- Selective transepithelial TG-PRK with simultaneous accelerated CXL (STARE-X)
- Cornea **Ray tracing** PRK with CXL



'Effective optical zone diameter to 5.5 mm from our standard routine of 6.5 mm and partially treated the sphere to not exceed 50mm in planned stromal removal '

Cornea Volume26,Number7,August2007

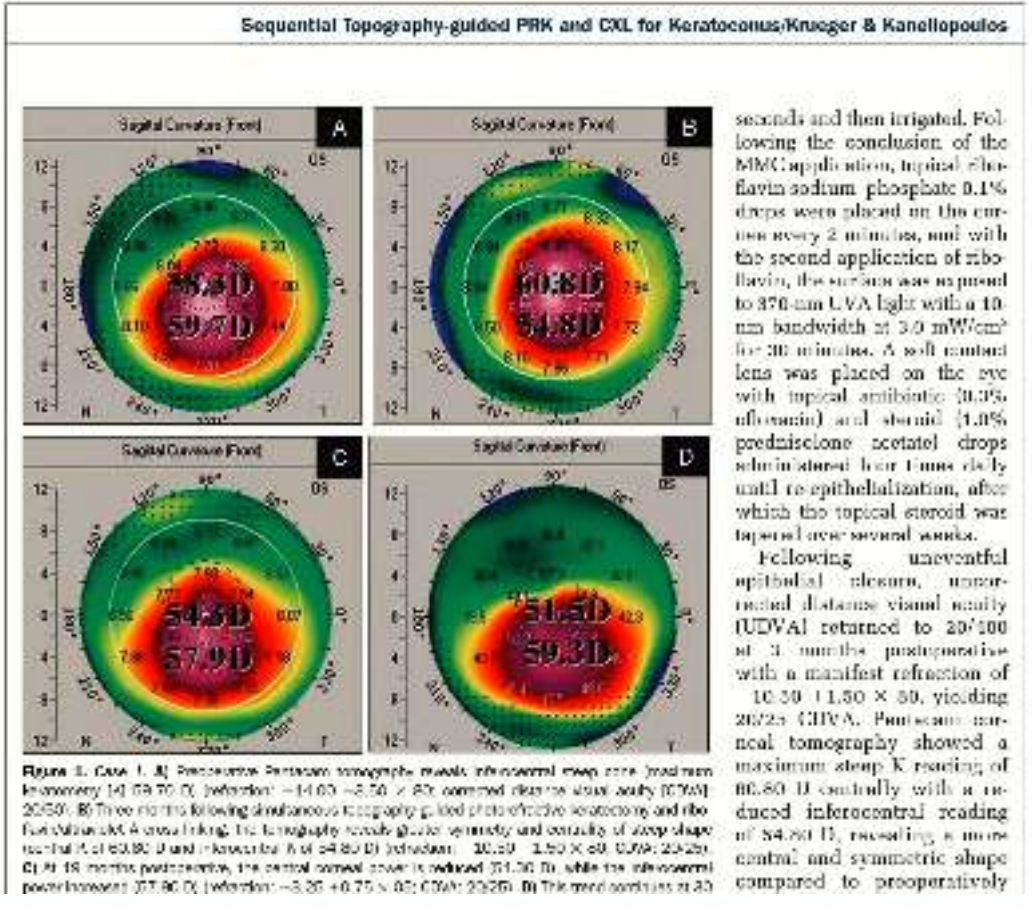


Stability of Simultaneous Topography-guided Photorefractive Keratectomy and Riboflavin/UVA Cross-linking for Progressive Keratoconus: Case Reports

Daniel G. Krueger MD, MSE | A. John Kanellopoulos MD

Athen's protocol

- Effective optical zone diameter to 5.5 mm
- ~70% treatment of cylinder and sphere (up to 70%), so as not to exceed 50 µm of **Maximum ablation depth**
- **MMC 0.01% application for 30 sec**



Sequential Topography-guided PRK and CXL for Keratoconus/Krueger & Kanellopoulos

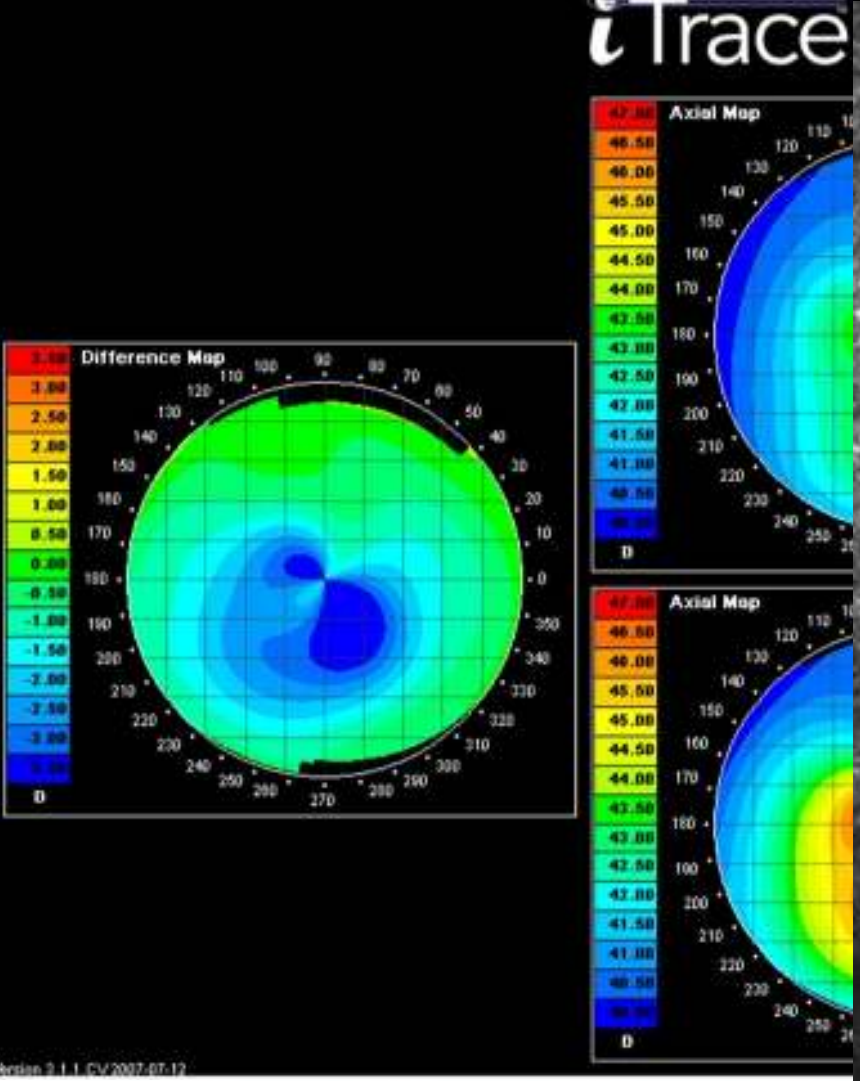
seconds and then irrigated. Following the conclusion of the MMC application, topical riboflavin sodium phosphate 0.1% drops were placed on the cornea every 2 minutes, and with the second application of riboflavin, the cornea was exposed to 370-nm UVA light with a 10-nm bandwidth at 3.0 mW/cm² for 30 minutes. A soft contact lens was placed on the eye with topical antibiotic (0.3% ofloxacin) and steroid (1.0% prednisolone acetate) drops administered four times daily until re-epithelialization, after which the topical steroid was tapered over several weeks.

Following uneventful epithelial closure, uncorrected distance visual acuity (UDVA) returned to 20/100 at 3 months postoperative with a manifest refraction of −0.50 −1.50 × 50, yielding 20/25 (UDVA). Pentacam corneal tomography showed a maximum steep K reading of 60.80 D centrally with a reduced inferocentral reading of 54.80 D, revealing a more central and symmetric shape compared to preoperatively

Table 1 Outcomes of combined PRK and CXL in treatment of corneal ectatic disorders

Author & year	Study design & number of eyes	Techniques	Follow-up	Outcomes	Complications
Kymionis *et al* (2009)[20]	Prospective study; 14 eyes	Simultaneous topography-guided PRK followed by CXL	10.69±5.95mo (range 3 to 16mo)	Improvement in visual parameters (UDVA, CDVA) and keratometry readings substantially.	No complications
Kanellopoulos (2009)[21]	Retrospective comparative study; 127 eyes (sequential) and 198 (simultaneous)	Sequential (>6mo following CXL) and simultaneous topography-guided PRK followed by CXL on the same day	36±18mo (range 24 to 68mo)	Improvement in visual parameters (UDVA, CDVA) and keratometric readings much higher in the simultaneous group compared to a sequential group.	19 eyes showed the development of corneal haze. No eyes lost lines of UCVA or BSCVA
Kymionis *et al* (2011)[22]	Case report; 1 eye	Simultaneous topography-guided PRK followed by CXL	12mo	UDVA and CDVA showed significant improvement. topographic findings showed improvement of astigmatic patterns.	No complication was reported
Spadea & Parolo (2012)[23]	Prospective, non-comparative case series;14 eyes	Customized PRK combined with CXL	15±6.5mo (range 6-24mo)	Improvement in CDVA, topographic parameters.	None of the eyes developed corneal haze
Siqueira *et al* (2013)[24]	Case report; 2 eyes	Custom topography-guided surface ablation followed by riboflavin-UVA CXL in the same day	5y	Regularization of the corneal surface and improvement in the BCVA	No complication was reported
Padmanabhan *et al* (2014)[25]	Prospective, non-randomized single-center study; 66 eyes (40 eyes with CXL alone and 26 eyes with the combination technique)	Topography-guided customized ablation treatment followed by CXL in one group CXL alone in another group	7.7±1.3mo (3-16.5mo)	Combined CXL and PRK is an effective and safe method to provide stability to the cornea and corneal contour, as well as refractive, topography, and abberometric outcomes than CXL alone	No complication was reported
Shah *et al* (2016)[26]	Prospective nonrandomized study; 39 eyes	Simultaneous topography-guided PRK followed by CXL	6mo	Mean UCVA and BCVA improved. Keratometry readings decreased significantly, better vision quality	No complication was reported
Pawirorama *et al* (2017)[27]	Case report; 4 eyes	Sequential CXL followed by PRK after 1mo	3mo	Following CXL the corneal rigidity is increased, which amplify PRK results	No side effects and complications reported
Althomali (2018)[28]	Retrospective study; 140 eyes	Combined PRK with accelerated corneal CXL simultaneously	1y	Statistically significant improvement of refractive and keratometric outcomes	Development of corneal haze in 10 eyes and corneal ectasia in 1 eye
Al-Amri (2018)[29]	Prospective non-randomized and non-controlled case-series; 60 eyes	Simultaneous non-topography guided PRK and CXL	5y (68±4.71mo with a range of 60-106mo)	Significant improvement in UDVA, CDVA, significant reduction in mean spherical equivalent and keratometry. Visual acuity and refraction improved considerably.	No serious complications were reported

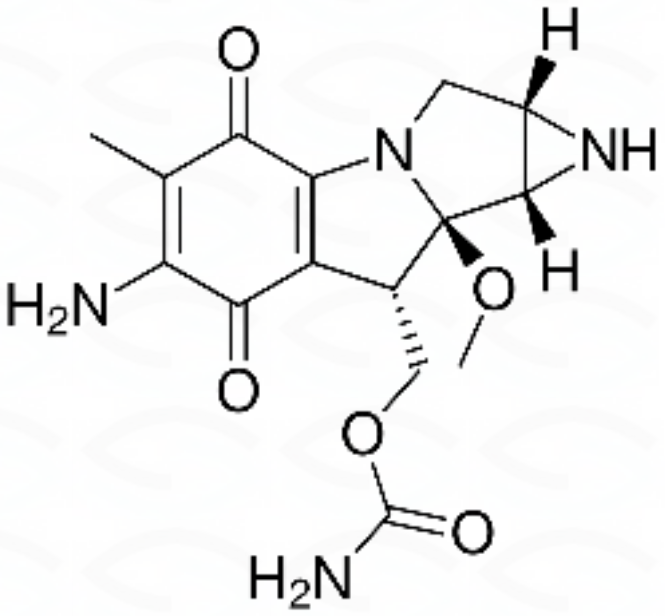
CXL: Collagen cross-linking; PRK: Photorefractive keratectomy; UDVA: Uncorrected distance visual acuity; CDVA: Corrected distance visual acuity; BCVA: Best corrected visual acuity; BSCVA: Best-spectacle corrected visual acuity.


iTrace
Axial Map
Axial Map
Difference Map


Lessons
Learned

PRK CXL

- Laser platform
- Diagnostic equipment
- Ablation properties
  - Depth
  - Pattern
  - Refractive correction percentage



MMC

TABLE 4

Percentage of Haze Reflectivity in Each Corneal Region After Conventional CXL and CXL+MMC[a]

	Anterior Stroma		Middle Stroma		Posterior Stroma	
Time	**CXL**	**CXL+MMC**	**CXL**	**CXL+MMC**	**CXL**	**CXL+MMC**
Baseline	16.66 ± 5.59 (7.78 to 27.68)	16.30 ± 5.12 (7.78 to 27.65)	18.82 ± 6.68 (7.01 to 35.89)	18.61 ± 6.85 (7.01 to 35.89)	19.18 ± 7.60 (9.30 to 42.40)	18.06 ± 6.00 (9.30 to 27.65)
P	.852		.916		.595	
1 month	23.15 ± 5.91 (13.97 to 42.27)	33.14 ± 16.58 (6.54 to 69.73)	21.51 ± 6.09 (11.42 to 39.88)	28.45 ± 14.09 (5.54 to 59.45)	20.60 ± 7.54 (8.14 to 41.06)	27.07 ± 16.92 (0.00 to 58.51)
P	.005[b]		.021[b]		.105	
3 months	24.18 ± 6.66 (14.97 to 37.31)	34.09 ± 19.30 (13.02 to 64.18)	20.67 ± 7.85 (9.53 to 39.69)	30.05 ± 17.47 (9.58 to 68.62)	20.37 ± 7.77 (4.47 to 34.50)	24.55 ± 16.69 (10.60 to 58.51)
P	.014[b]		.020[b]		.316	
6 months	22.56 ± 6.16 (10.79 to 35.56)	28.13 ± 12.52 (6.63 to 48.14)	20.92 ± 6.48 (9.57 to 38.10)	25.55 ± 12.96 (5.69 to 48.18)	21.03 ± 7.11 (7.82 to 38.12)	22.93 ± 11.55 (6.18 to 43.39)
P	.074		.141		.592	
12 months	20.58 ± 7.88 (2.90 to 38.22)	27.14 ± 12.80 (7.09 to 49.28)	22.93 ± 12.16 (2.87 to 50.30)	24.95 ± 12.72 (7.00 to 51.04)	22.31 ± 12.88 (3.14 to 47.99)	25.17 ± 12.61 (6.70 to 45.15)
P	.049[b]		.562		.492	

CXL = corneal cross-linking; MMC = mitomycin C

[a]*Values are presented as mean ± standard deviation (range).*

[b]*Statistically significant.*

Mitomycin C Application After Corneal Cross-linking for Keratoconus Increases Stromal Haze

Shady T. Awwad, MD; Lily M. Chacra, MD; Chadi Helwe, MSc; Ahmad B. Dhaini, PhD; Talar Telvizian, MD; Julien Torbey, MD; Maamoun Abdul Fattah, MD; Emilio A. Torres-Netto, MD; Farhad Hafezi, MD, PhD; Rohit Shetty, MD, PhD

Instead of reducing postoperative haze as in its use after PRK, the application of MMC following CXL induced more postoperative haze, and therefore should be avoided. Based on the results of this study, we also recommend caution in using MMC in combined PRK and CXL procedures.

Tomography or topography

Simultaneous Topography-guided PRK Followed by Corneal Collagen Cross-linking for Keratoconus

George D. Kymionis, MD, PhD; Georgios A. Kontadakis, MD, MSc; George A. Kounis, PhD; Dimitra M. Portaliou, MD; Alexandra E. Karavitaki, MD; Michael Magarakis, MD; Sonia Yoo, MD; Ioannis G. Pallikaris, MD, PhD

TABLE 1

Attempted Correction and Maximum Ablation Depth[a] in 14 Eyes That Underwent Topography-guided PRK and Cross-linking

Patient No.	Attempted Correction (D)	Ablation Depth (µm)
1	[illegible]	[illegible]
2	1.75	[illegible]
3 (OD)	[illegible]	[illegible]
3 (OS)	[illegible]	[illegible]
4 (OD)	[illegible]	[illegible]
4 (OS)	[illegible]	[illegible]
5	[illegible]	[illegible]
6	[illegible]	[illegible]
7	[illegible]	[illegible]
8	[illegible]	[illegible]
9	[illegible]	[illegible]
10	[illegible]	[illegible]
11	[illegible]	[illegible]
12	[illegible]	[illegible]

[illegible]

PATIENTS AND METHODS

[illegible]

CLINICAL EVALUATION

[illegible]

SURGICAL PROCEDURE

[illegible] Attempted correction and maximum ablation depth are shown in Table 1.

[illegible]

RESULTS

[illegible]

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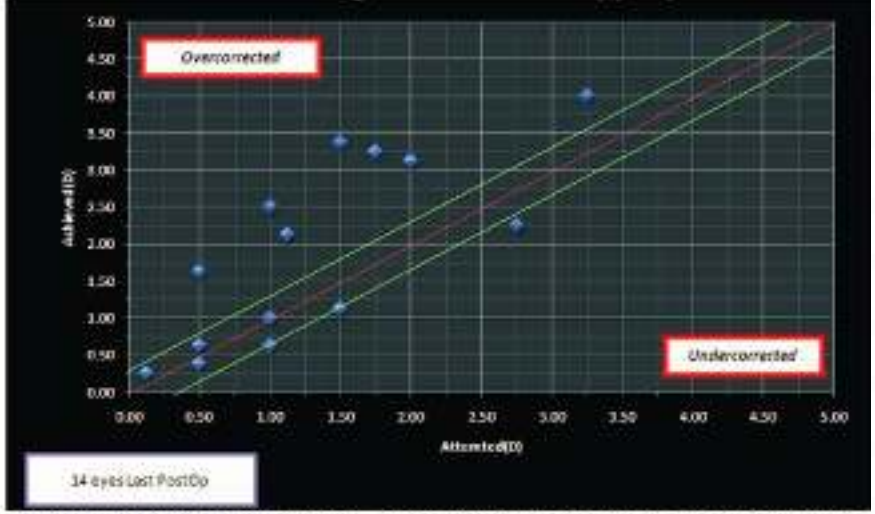


Figure 3. Scattergram of attempted versus achieved refraction following topography-guided photorefractive keratectomy and corneal cross-linking.

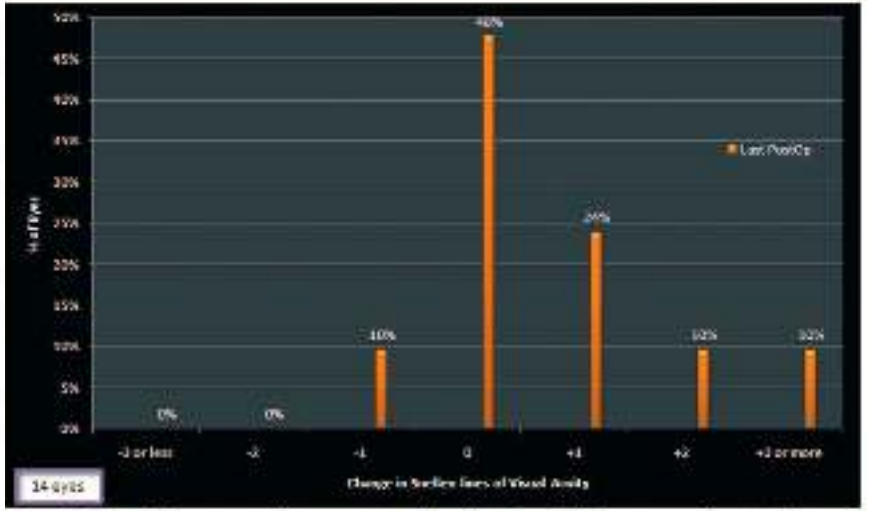
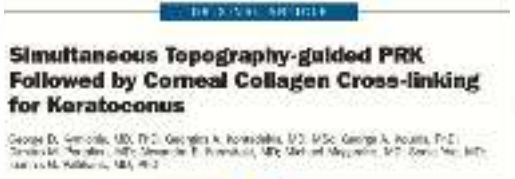


Figure 2. Change in best spectacle-corrected visual acuity (letters) following topography-guided photorefractive keratectomy and corneal cross-linking.

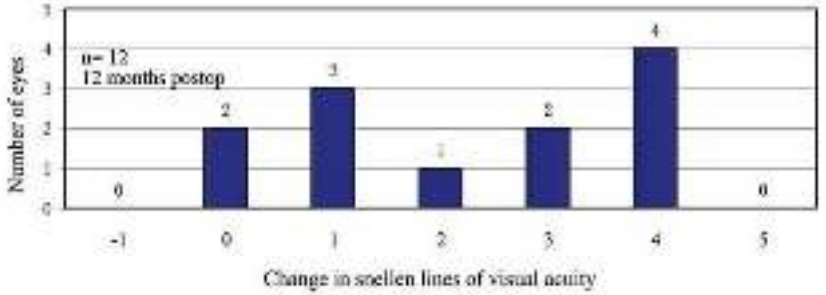
- Corneal topography iTrace, PRK Solid-state 1064 Pulzar Z1; CustomVis).
- Customization was based on the corneal higher order aberrations. Use of a percentage of customization from 0% to 100%.
  - *0% would be a conventional laser treatment and 100% a full customized treatment. Maximum ablation depth was 50 µm.*
- Topography-guided PRK immediately followed by CXL


Simultaneous Topography-guided PRK Followed by Corneal Collagen Cross-linking for Keratoconus

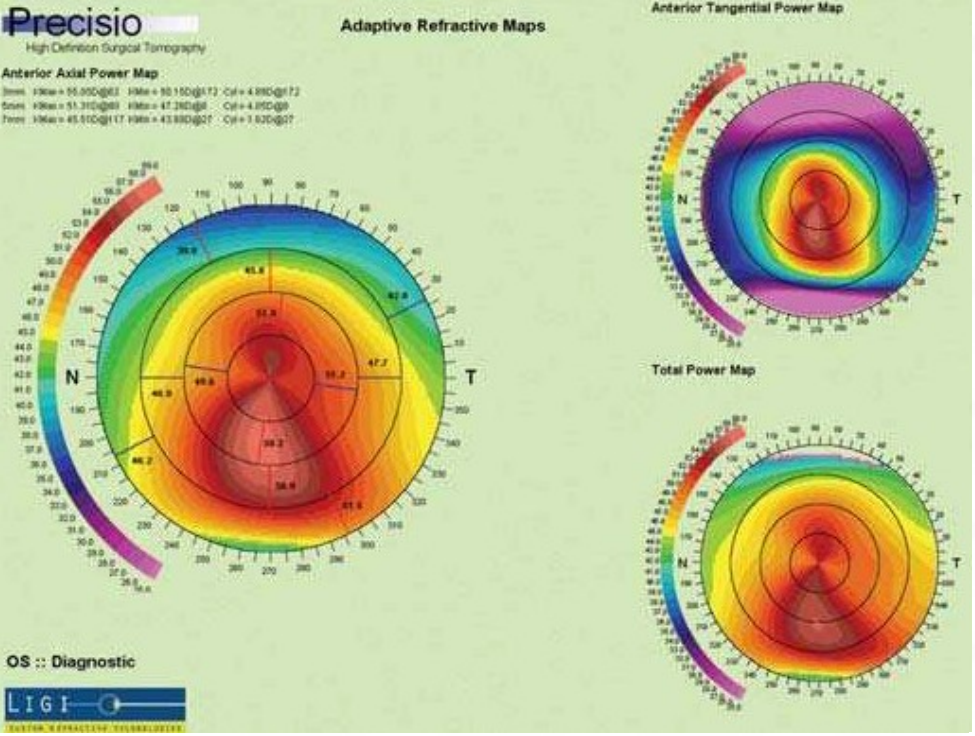
NEW TECHNIQUE

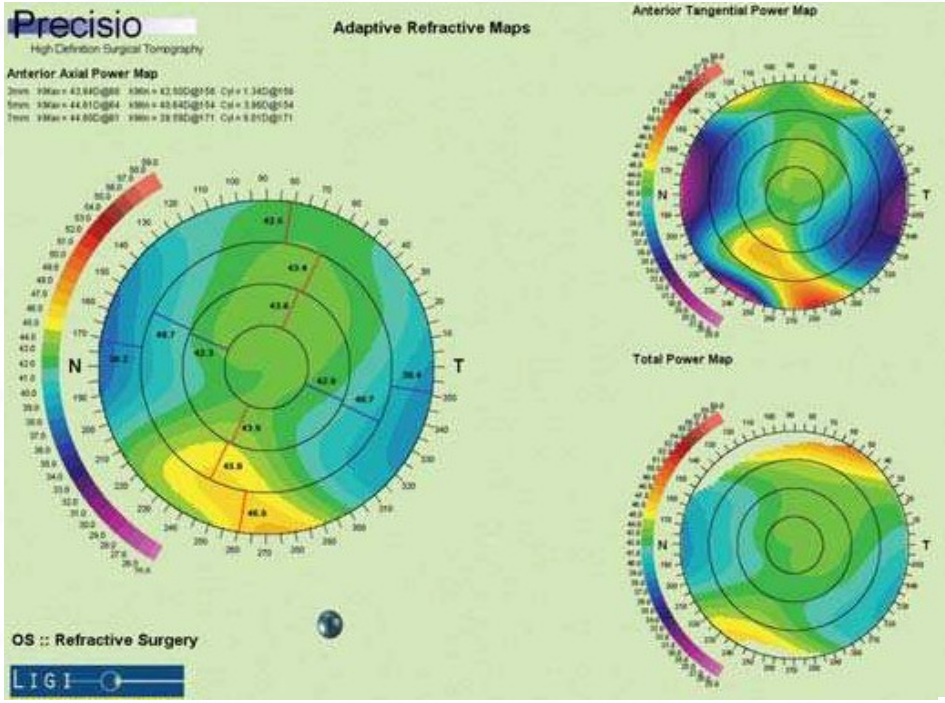
Topography-guided Transepithelial Surface Ablation Followed by Corneal Collagen Cross-linking Performed in a Single Combined Procedure for the Treatment of Keratoconus and Pellucid Marginal Degeneration

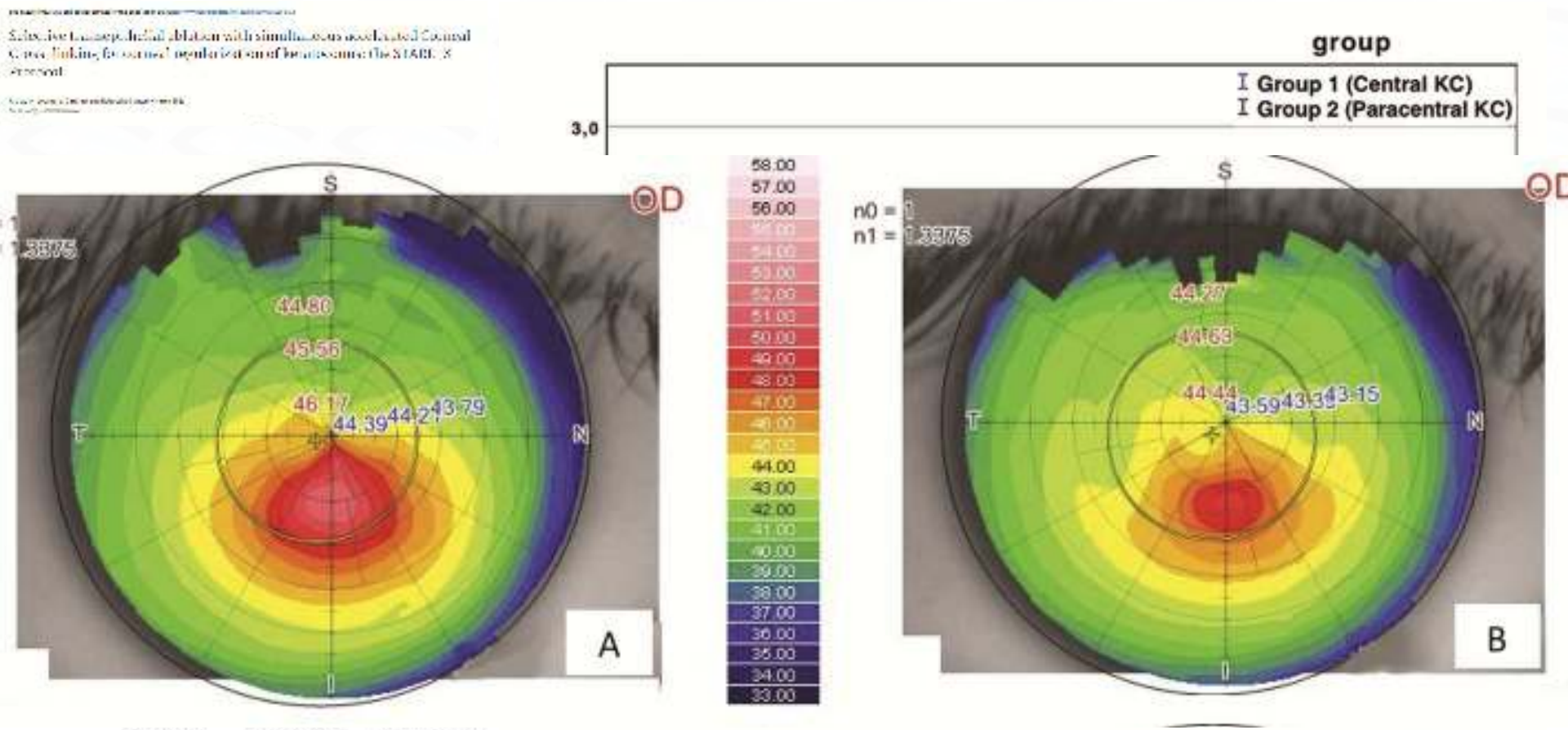
Aleksandar Stojanovic, MD; Jia Zhang, MD; Xiangjun Chen, MD; Tore A. Nitter, MD, PhD; Shihao Chen, MD; Qinmei Wang, MD



- **IVIS topography-guided**
- CIPTA software custom ablation system, refraction, corneal elevation data, and pupillometry data
- Ablation that transforms the actual corneal shape into a regularized aspheric shape
- Minimal ablation strategy, maximal reduction of the irregularities with the least possible amount of tissue consumption


Precisio
High Definition Surgical Tomography
Adaptive Refractive Maps
Anterior Axial Power Map
Anterior Tangential Power Map
Total Power Map
N
T
OS :: Diagnostic
LIGI


Precisio
High Definition Surgical Tomography
Adaptive Refractive Maps
Anterior Axial Power Map
Anterior Tangential Power Map
Total Power Map
N
T
OS :: Refractive Surgery
LIGI



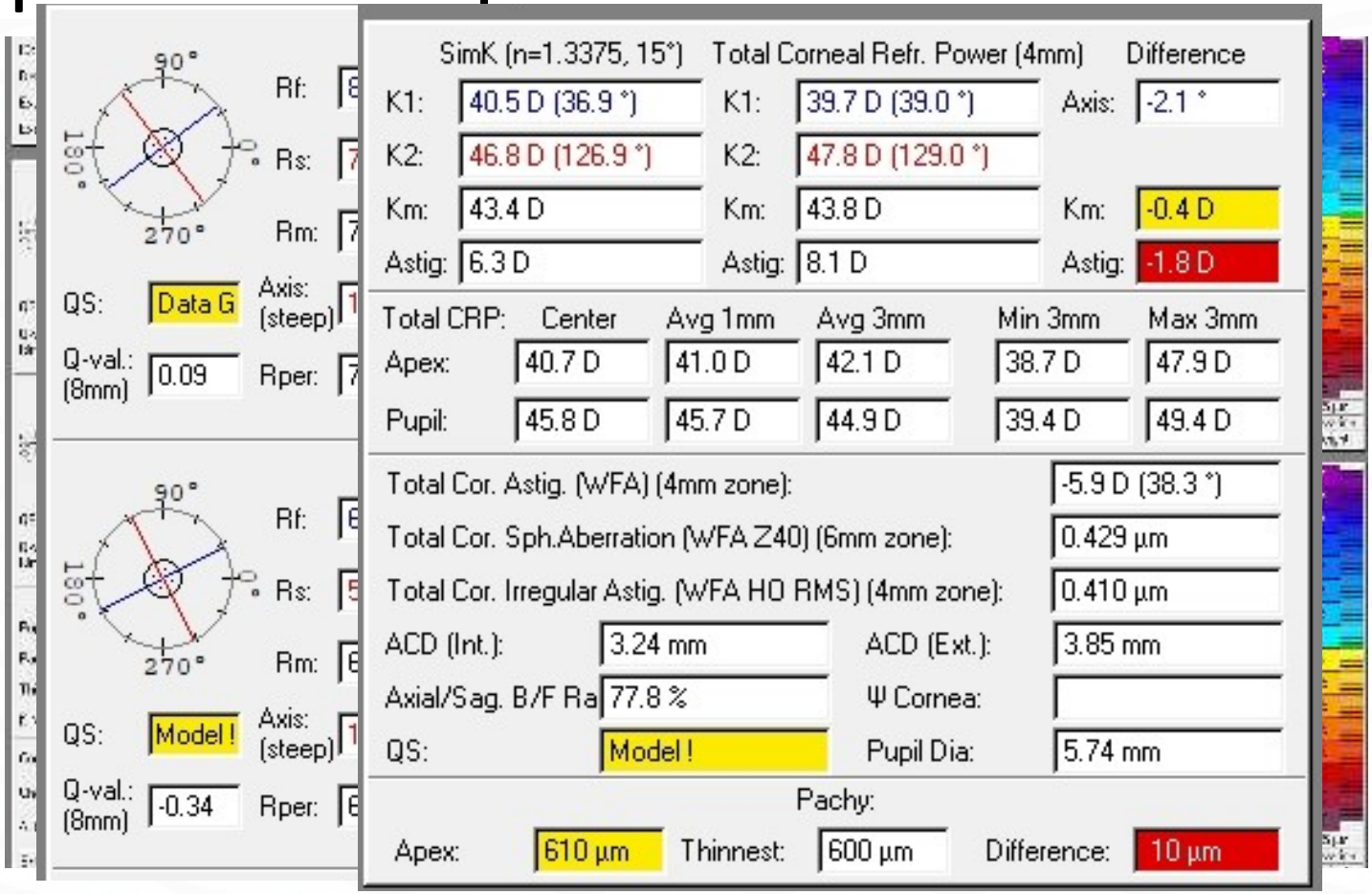
UDVA (LogMAR)

CDVA (LogMAR)

STAR X

- Simultaneous tomography-guided trans-epithelial PRK
- OZ of 7 mm for central cone
- 6.5 mm OZ for peripheral cone.
- Epithelium removal of 55 to 65 µm, stromal ablation 50 µm,
- maximum correction of coma aberration, limiting spherical and cylinder correction
- Second Step: customized energy pulsed accelerated collagen crosslinking.

The importance of posterior curvature

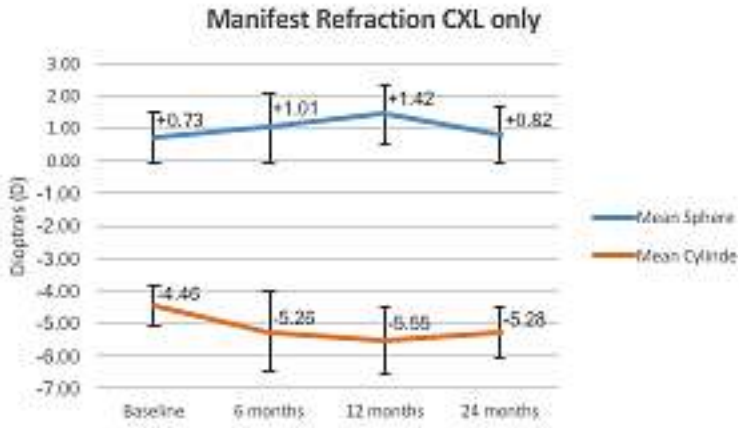


Tomography or Ocular Wavefront

Fig 4f

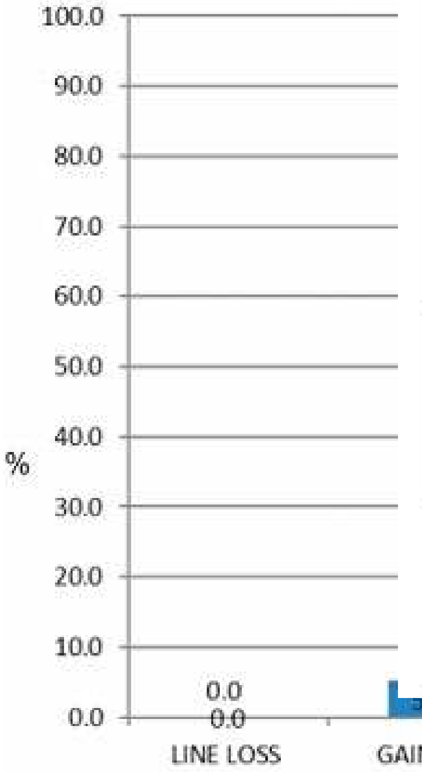

Manifest Refraction TransPRK/CXL
Dioptres (D)
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
-6.00
-7.00
+0.39
-1.66
-1.80
-1.76
-3.22
-3.25
-3.16
-5.26
Baseline
6 months
12 months
24 months
Mean Sphere
Mean Cylinder

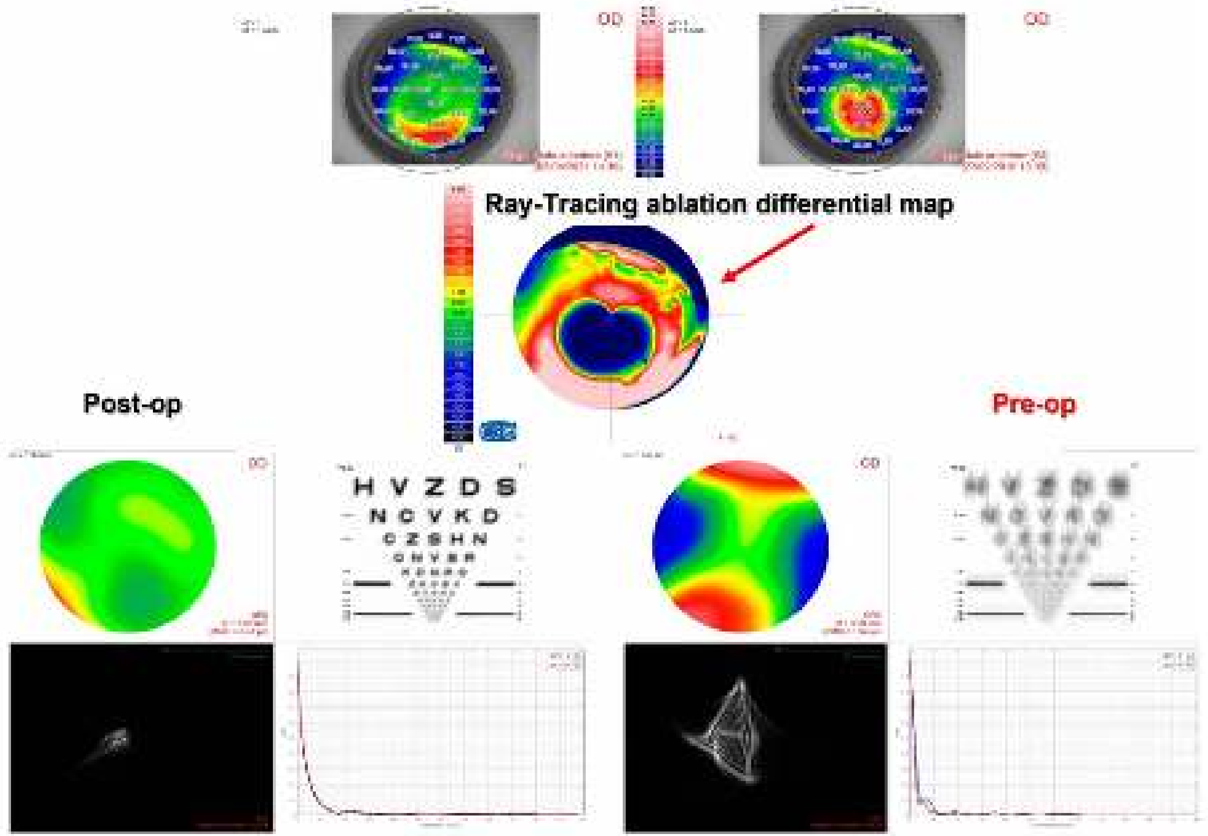
Fig 4g


Manifest Refraction CXL only
Dioptres (D)
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
-6.00
-7.00
+0.73
+1.01
+1.42
+0.82
-4.46
-5.25
-5.66
-5.28
Baseline
6 months
12 months
24 months
Mean Sphere
Mean Cylinde

OPEN

Ray-Tracing Transepithelial Excimer Laser Central Co Remodeling Plus Pachymetry-Guided Accelerated Co Crosslinking for Keratoconus





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Simultaneous or Sequential

PRK CXL
Simultaneous vs Sequential

Simultaneous PRK CXL

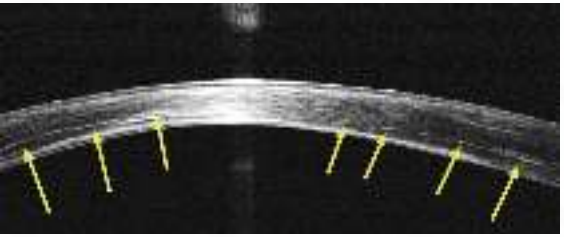
- More treated area
- One procedure , less risk of complications

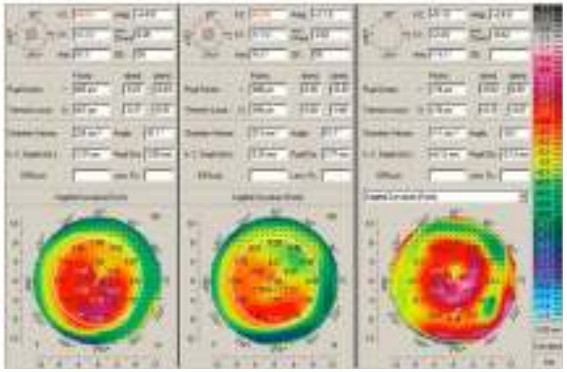
Sequential treatment

- Removal of crosslinked tissue
- Avoids undercorrection and scarring
- Better HOA correction?

AIM = minimum depth required for regularization

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

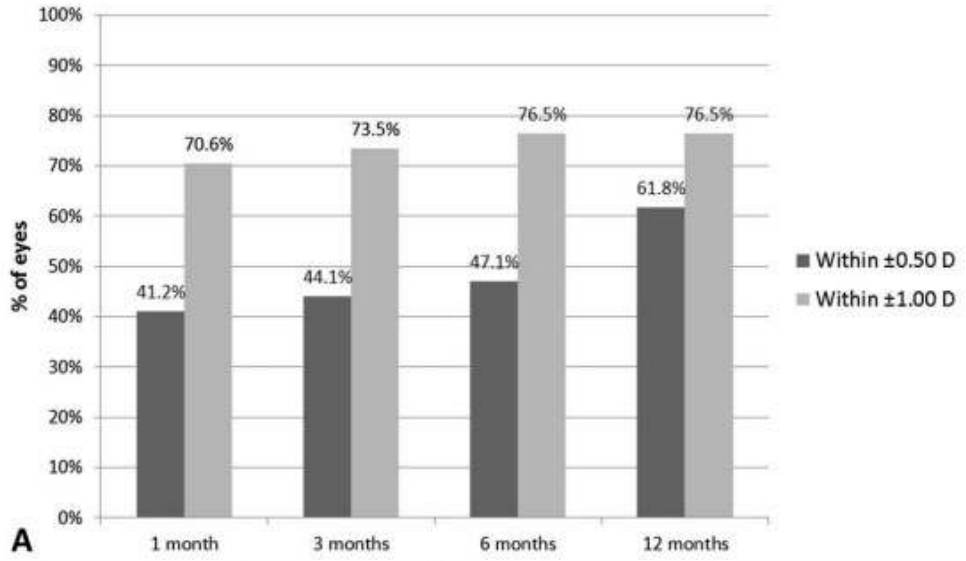


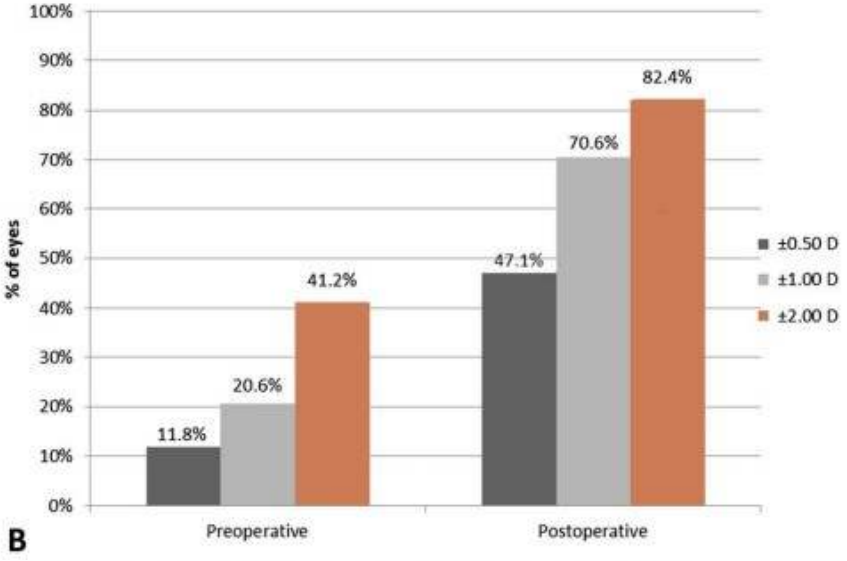


- **WaveLight** customized platform (Topolyzer).
- Athens protocol
- Mean **haze score** was 1.2+/- 0.5. Mean CCT decreased from 465 µm preoperatively to 395 µm postoperatively.
- UCVA improved 0.96 logMAR to 0.3. postoperatively
- BSCVA from 0.39 logMAR to 0.11 logMAR.
- **The simultaneous group performed superiorly** with a better BSCVA. spherical equivalent reduction, mean K reduction and corneal haze score

Wave Front–Guided Photorefractive Keratectomy Using a High-Resolution Aberrometer After Corneal Collagen Cross-Linking in Keratoconus

Mohamed Shafik Shalaby, MD, PhD,* Ahmed Shalaby Bardan, MB, MRCSED,* David P. Piñero, PhD,†‡ Dani Ezzeldin, MD,§ Mohamed El Kateb, MD, PhD,* Hany Goleby, MD,* and Mounir A. Khalifa, MD, PhD*






Outcomes of Simultaneous and Sequential Cross-linking With Excimer Laser Surface Ablation in Keratoconus

- The sequential group showed greater improvement in CDVA, SE, and refractive astigmatism.
- Corneal haze was frequently reported in all protocols.
- Safety and efficacy indices were highest when CXL was performed before excimer laser


PROBLEMS
AHEAD
CAUTION

Continued Long-term Flattening After Corneal Cross-linking for Keratoconus

Inger Heleen Noor, MD; Theo G. Seiler, MD; Kai Noor, MD; Theo Seiler, MD, PhD

ABSTRACT

PURPOSE: To report 3 cases with continued long-term flattening after corneal cross-linking (CXL) for keratoconus and to determine its prevalence.

METHODS: Case series.

RESULTS: Three eyes of three patients presented with an ongoing corneal flattening over 10 years after CXL in the absence of corneal opacities. Of the initial 433 eyes treated with CXL between 2005 to 2007, only 45 eyes completed the 10-year follow-up period, indicating a prevalence of 6.7%.

CONCLUSIONS: Besides continuous flattening due to scars and intense early flattening, a third entity of continuous flattening can be observed after CXL. Continuous long-term flattening after CXL

Corneal cross-linking (CXL) tries to reverse this softening effect by inducing new chemical bonds within the extracellular matrix.[9] The clinically accepted procedure includes ultraviolet light and riboflavin as a photomediator and results in halting keratoconus progression in more than 90% of the cases[10] with a low rate of complications.[11] In a minority of treated eyes, corneal flattening occurs as a side effect[12,13] within the first years after CXL, stabilizing after 1 to 3 years.[14,15]

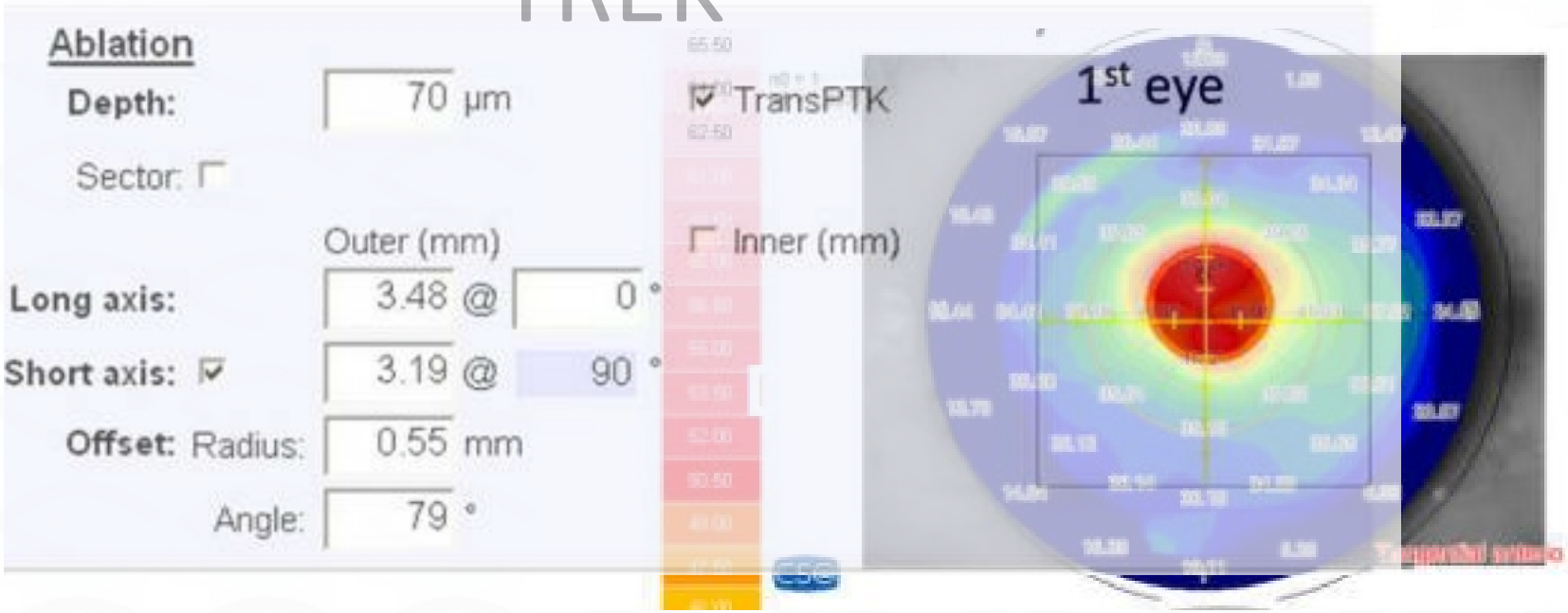
In this series, we present 3 cases with continuous flattening of the cornea during follow-up of up to 12 years after CXL.

CASE REPORTS

Between 2005 and 2007, 433 eyes with documented progressive keratoconus were treated with CXL at the Institut für Refraktive und Ophthalmo-Chirurgie (IROC, Zürich, Switzerland) and the Silmalaser Eye Clinic (Tallinn, Estonia). Inclusion criteria for the current study were a follow-up period of 10 years or more, no additional corneal operations such as additional CXL or refractive surgeries, and no complications of CXL such as scarring or infection. At that time, the CXL procedure

Customised PTK

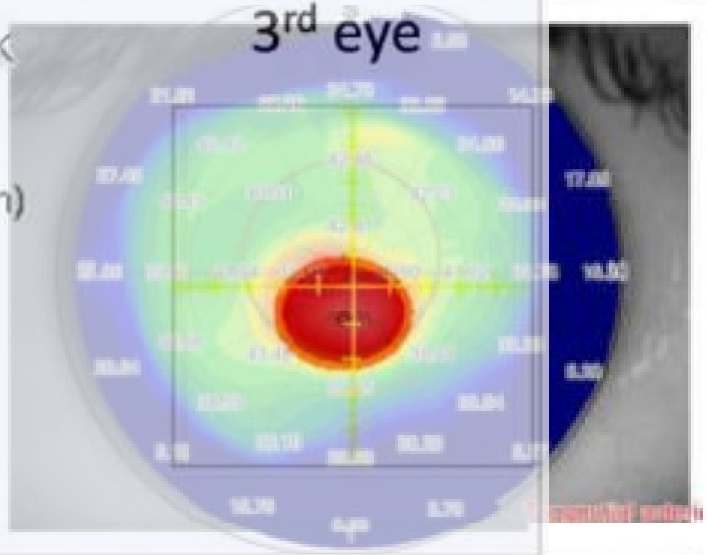
TREK




Topoguided Removal of corneal Epithelium for Keratoconus (TREK): a novel and customized technique

Ablation

Depth:	61 µm	☑ TransPTK	
Sector: ☐			
	Outer (mm)	☐ Inner (mm)	
Long axis:	3.50 @	0 °	
Short axis: ☑	2.78 @	90 °	
Offset: Radius:	0.83 mm		
Angle:	250 °		



- PACE stands for ‘PTK-assisted customized epi-on corneal cross-linking
  - Trea ure, in whic e top of the c
  - Precisely remove just the epithelium (and not the stroma) over the cone region by performing an epithelial map-driven PTK with the excimer laser (not a normal PTK).

EPI OFF PROCEDURE

SIMILAR TO TREK

Personal Approach

- Treat according to
  - Coma
  - Spectacle Correct VA
  - 50µm stromal ablation
- Aim to improve Spectacle Correct VA

Pyramidal wavefront sensing

Peramis diagnostic workstation – Schwind Eye Tech Solutions GmbH

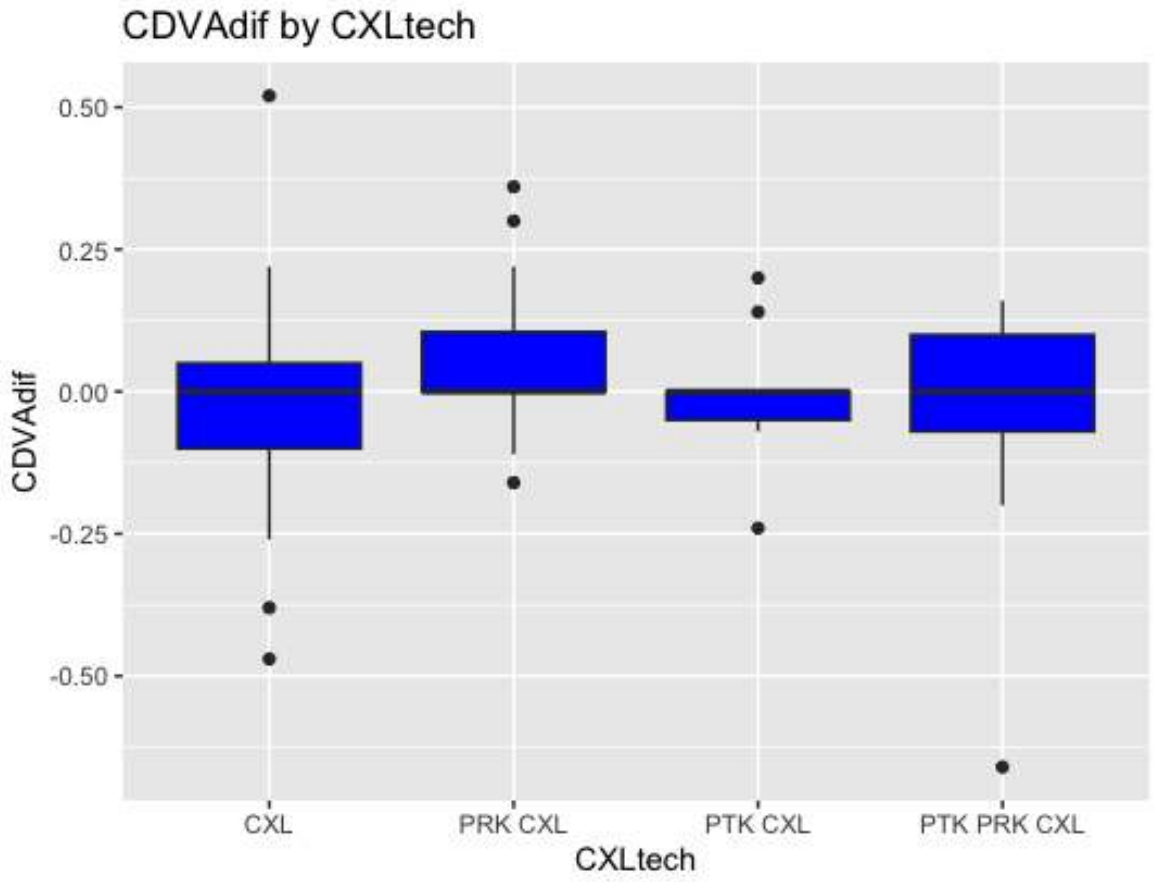
- Male 45

Female 90

Mean follow up 4.2 years

Click to add Title

	1-year post-op	Final follow-up	Change	p-value
Kmax				
Mean±SD	49.3±4.8	48.7±4.7	-0.6±1.7	
Median, IQR	48.9, 5.8	48.3, 5.8	-0.4, 1.4	<0.001
Kmin				
Mean±SD	37.3±4.4	36.8±4.6	-0.46±1.9	
Median, IQR	38, 4.8	37.5, 4.95	-0.4, 1.5	<0.001
Thinnest				
Mean±SD	**436.4±50.2**	430.9±58.4	-5.5±20.0	
Median, IQR	440, 67.5	440, 78.5	-4, 17.5	<0.001


CDVAdif by CXLtech
0.50
0.25
0.00
-0.25
-0.50
CDVAdif
CXL
PRK CXL
PTK CXL
PTK PRK CXL
CXLtech

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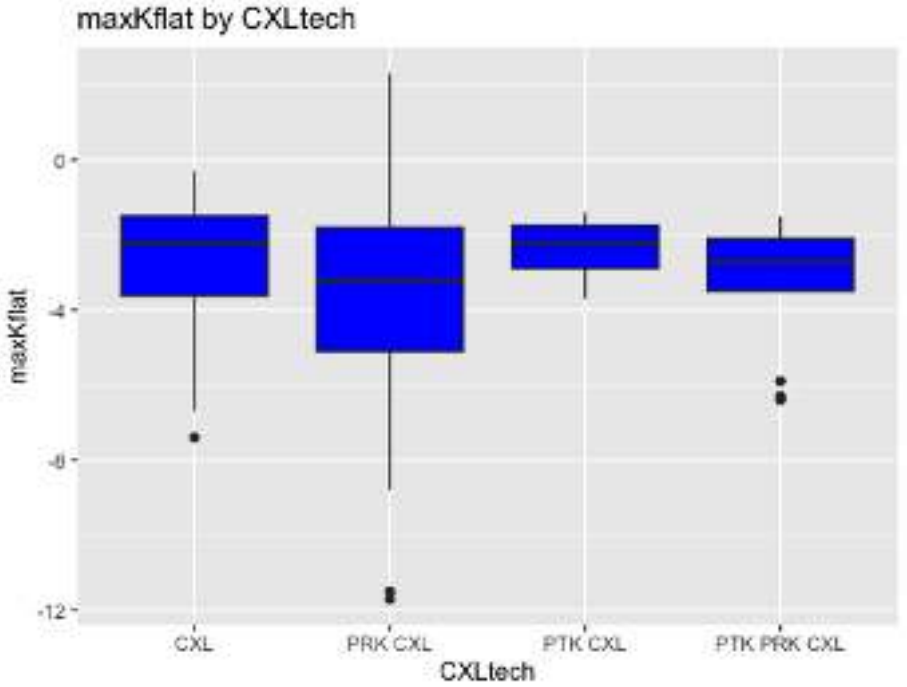
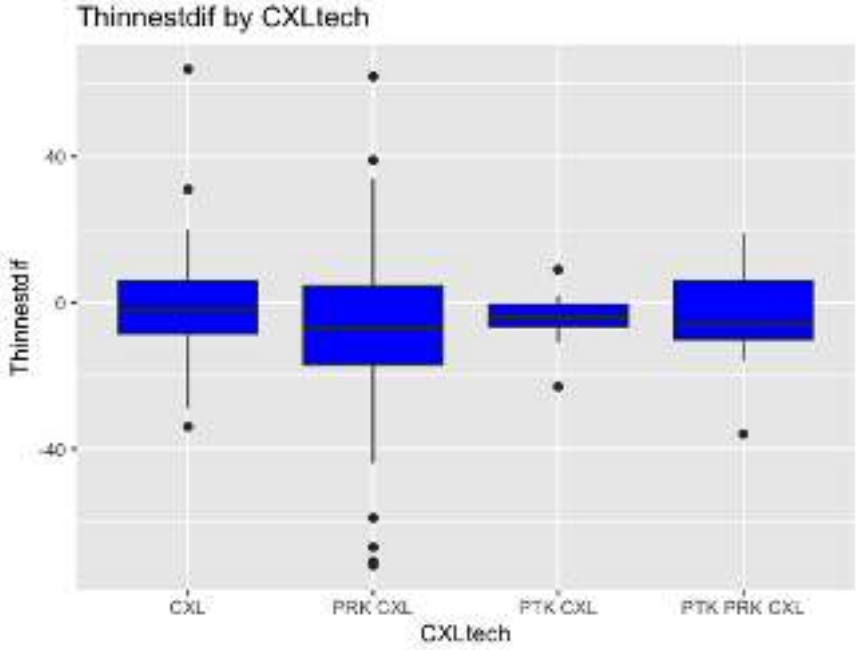
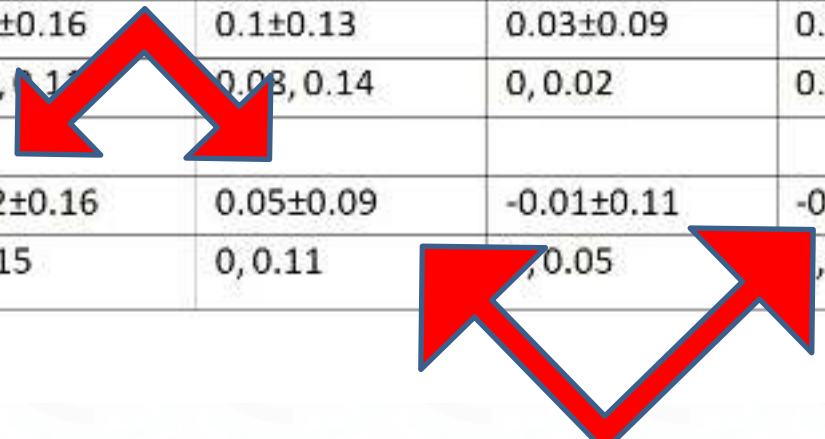




CDVAdif
Kruskal Wallis
P=0.0098
CXL vs PRK CXL p=0.011
Other p>0.05

	CXL	PRK+CXL	PTK+CXL	PTK+PRK+CXL
CDVA1				
Mean±SD	0.14±0.19	0.05±0.1	0.04±0.07	0.1±0.21
Median, IQR	0.1, 0.1	0, 0.075	0, 0.04	0, 0.1
CDVA2				
Mean±SD	0.12±0.16	0.1±0.13	0.03±0.09	0.06±0.08
Median, IQR	0.09, [illegible]	[illegible], 0.14	0, 0.02	0.04, 0.14
CDVA change				
Mean±SD	-0.02±0.16	0.05±0.09	-0.01±0.11	-0.04±0.21
Median, IQR	0, 0.15	0, 0.11	[illegible], 0.05	[illegible], 0.17



RIO (

Kmaxdif

Kruskal Wallis

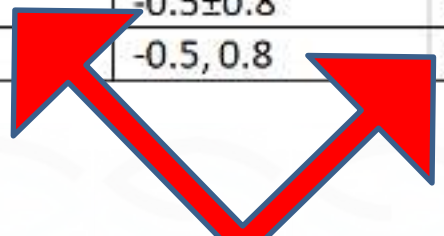
P=0.06

Dunn Test Bonferroni method

PRK CXL vs PTK PRK CXL p=0.044

Others p>0.05

	CXL	PRK+CXL	PTK+CXL	PTK+PRK+CXL
Kmax1				
Mean±SD	51.5±5.3	48.6±4.1	48.4±3.5	46.7±5.2
Median, IQR	50.6, 5.5	47.9, 5.8	48.2, 3.8	46.3, 7.3
Kmax2				
Mean±SD	50.7±5.2	47.8±4.1	47.9±3.7	47.4±4.5
Median, IQR	49.9, 4.9	47.4, 4.7	47.8, 3.9	46.2, 6.7
Kmax Change				
Mean±SD	-0.7±1.6	-0.8±1.7	-0.5±0.8	0.7±2.2
Median, IQR	-0.5, 1.0	-0.5, 1.8	-0.5, 0.8	0.1, 0.5



- **Kmin1**
- Kruskal Walllis
- P<0.01
- Dunn Test Bonferroni method
- CXL vs PRK CXL p=0.0015
- CXL vs PTK PRK CXL p<0.001
- Other p>0.05

- **Kmin2**
- Kruskal Walllis
- P<0.001
- Dunn Test Bonferroni method
- CXL vs PRK+CXL p=0.0032
- CXL vs PTK PRK CXL p<0.001
- Other p>0.05

	CXL	PRK+CXL	PTK+CXL	PTK+PRK+CXL
Thinnest1				
Mean±SD	458±45.7	426±46	464±31.4	395±57.8
Median, IQR	458, 59.5	414, 66	470, 22	399, 72
Thinnest2				
Mean±SD	456±52.1	418±57.5	459±29.2	391±60.4
Median, IQR	456, 52.2	424, 70.5	469, 26	389, 67
Thinnest change				
Mean±SD	-1.5±16.1	-8.5±24.1	-4.5±8.1	-4.1±13.6
Median, IQR	-2, 14.5	-7, 21.5	-4, 6	-6, 16

	CXL		PRK CXL		PTK CXL		PTK PRK CXL
	Mean±SD	Median,IQR	Mean±SD	Median,IQR	Mean±SD	Median,IQR	Mean±SD
CDVA1	0.14±0.19	0.1, 0.1	0.05±0.1	0, 0.08	0.04±0.07	0, 0.4	0.1±0.21
CDVA2	0.12±0.15	0.095, 0.11	0.1±0.12	0.08, 0.14	0.03±0.09	0, 0.02	0.04, 0.14
p		0.265		<0.001		0.66	1
Thinnest1	457.6±45.7	457.5, 59.5	426.0±46.0	414, 66	463.8±31.4	470, 22	395.1±57.8
Thinnest2	456.1±52.1	455.5, 52.3	417.5±57.5	424, 70.5	459.4±29.2	469, 26	391.0±60.4
p		0.281	0.0051			0.07	0.3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