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ORIGINAL RESEARCH

Comparison of Placido disc and Scheimpflug image-derived topography-guided excimer laser surface normalization combined with higher fluence CXL: the Athens Protocol, in progressive keratoconus

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Anastasios John Kanellopoulos[1,2]
George Asimellis[1]

[1]Laservision.gr Eye Institute, Athens, Greece; [2]New York University School of Medicine, Department of Opthalmology, NY, NY, USA

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Correspondence: A John Kanellopoulos
Laservision.gr Institute, 17 Tsocha Str, 11521, Athens, Greece
Tel +30 210 747 2777
Fax +30 210 747 2789
Email ajk@brilliantvision.com

Background: The purpose of this study was to compare the safety and efficacy of two alternative corneal topography data sources used in topography-guided excimer laser normalization, combined with corneal collagen cross-linking in the management of keratoconus using the Athens protocol, ie, a Placido disc imaging device and a Scheimpflug imaging device.

Methods: A total of 181 consecutive patients with keratoconus who underwent the Athens protocol between 2008 and 2011 were studied preoperatively and at months 1, 3, 6, and 12 postoperatively for visual acuity, keratometry, and anterior surface corneal irregularity indices. Two groups were formed, depending on the primary source used for topoguided photoablation, ie, group A (Placido disc) and group B (Scheimpflug rotating camera). One-year changes in visual acuity, keratometry, and seven anterior surface corneal irregularity indices were studied in each group.

Results: Changes in visual acuity, expressed as the difference between postoperative and preoperative corrected distance visual acuity were +0.12 ± 0.20 (range +0.60 to –0.45) for group A and +0.19 ± 0.20 (range +0.75 to –0.30) for group B. In group A, K1 (flat keratometry) changed from 45.202 ± 3.782 D to 43.022 ± 3.819 D, indicating a flattening of –2.18 D, and K2 (steep keratometry) changed from 48.670 ± 4.066 D to 45.865 ± 4.794 D, indicating a flattening of –2.805 D. In group B, K1 (flat keratometry) changed from 46.213 ± 4.082 D to 43.190 ± 4.398 D, indicating a flattening of –3.023 D, and K2 (steep keratometry) changed from 50.774 ± 5.210 D to 46.380 ± 5.006 D, indicating a flattening of –4.394 D. For group A, the index of surface variance decreased to –5.07% and the index of height decentration to –26.81%. In group B, the index of surface variance decreased to –18.35% and the index of height decentration to –39.03%. These reductions indicate that the corneal surface became less irregular (index of surface variance) and the "cone" flatter and more central (index of height decentration) postoperatively.

Conclusion: Of the two sources of primary corneal data, the Scheimpflug rotating camera (Oculyzer™) for topography-guided normalization treatment with the WaveLight excimer laser platform appeared to provide more statistically significant improvement than the Placido disc topographer (Topolyzer™). Overall, the Athens protocol, aiming both to halt progression of keratoconic ectasia and to improve corneal topometry and visual performance, produced safe and satisfactory refractive, keratometric, and topometric results. The observed changes in visual acuity, along with keratometric flattening and topometric improvement, are suggestive of overall postoperative improvement.

Keywords: Athens protocol, anterior Pentacam indices, keratoconus, cross-linking, WaveLight/Alcon excimer laser, EX500 excimer laser, higher fluence collagen cross-linking

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Introduction

Keratoconus is a degenerative bilateral, progressive, noninflammatory disorder characterized by ectasia, thinning, and irregular topography.[1,2] It is associated with loss of visual acuity particularly in relation to corneal irregularity,[3,4] and usually manifests asymmetrically between two eyes in the same patient.[5,6]

Corneal collagen cross-linking (CXL) using riboflavin and ultraviolet A irradiation is an acceptable treatment option for eyes with progressive keratoconus.[7] Laboratory data suggest that CXL using riboflavin and ultraviolet A irradiation increases stromal collagen fibril diameter, resulting in increased corneal biomechanical strength.[8] Several clinical reports indicate that CXL halts progression of ectasia,[7,9] improves corneal keratometry, refraction and reduces higher-order aberrations. Postoperative complications are infrequent.[7] Our team has introduced several variations and applications of CXL.[10,11]

We have also reported on sequential partial topography-guided photorefractive keratectomy in conjunction with the CXL treatment,[12] which is a promising approach to improve topometric and refractive outcomes,[13] with good long-term stability.[14,15] Furthermore, we have introduced and extensively reported[16–20] the combination of excimer-laser debridement of the top 50 μm of the epithelium, partial topography-guided excimer ablation limited to removal of a maximum of 50 μm stromal tissue, followed in the same session by immediate high-fluence ultraviolet A radiation (5, 6, and 10 mW/cm^2) and short-duration (18, 15, and 10 seconds) CXL in a procedure known as the Athens protocol.[21,22] This technique has already been described in detail.[23]

This study compared the efficacy of two alternative corneal topography data sources used in the topography-guided part of this procedure with the WaveLight®/Alcon excimer laser platform (Alcon, Fort Worth, TX, USA), specifically, a Placido disc imaging device and a Scheimpflug imaging device, by analysis of long-term refractive, topometric, and visual rehabilitation changes.

Materials and methods

This study was approved by the ethics committee at our institution, adhered with the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject at the time of intervention using the Athens protocol or at the first clinical visit. The study was conducted in patients visiting our clinical practice before the procedure and attending scheduled post-operative visits.

Patient inclusion criteria

The study group consisted of 181 consecutive patients with keratoconus who underwent the Athens protocol between 2008 and 2011. In all procedures, performed by the same surgeon (AJK), epithelial excimer-laser debridement and topography-guided excimer-laser ablation was performed employing the Alcon/WaveLight 400 Hz Eye-Q laser[24] or the 500 Hz EX500 excimer laser.[25,26]

To be considered for the Athens protocol, the patient had to meet the following criteria: clinical diagnosis of progressive keratoconus, minimum age 18 years, and minimum corneal thickness of 300 μm. Patients with systemic disease, previous corneal surgery, history of chemical injury or delayed epithelial healing, pregnancy, or lactation were not considered for the procedure. All patients included in the study underwent an uneventful Athens protocol using the KXL CXL device (Avedro Inc, Waltham, MA, USA), with higher fluence of 6 mW/cm^2 for 15 minutes after a five-minute soak in 0.1% riboflavin solution (Avedro) and were able to attend our institution for at least one-year of follow-up monitoring.

The consecutive cases were assigned randomly to receive one or the other treatment. Depending on the imaging source used for topography-guided partial photoablation, the following two groups were formed: group A ($n = 54$ eyes), in which the primary topography data were provided by the Placido disc imaging device, and group B ($n = 127$ eyes) in which the primary topography data were provided by a Scheimpflug imaging device.

Imaging and measurement

The diagnostic Placido disc device used was the Alcon/WaveLight Allegro Topolyzer™ (WaveLight AG, Erlagen, Germany). The Topolyzer is a wide-cone corneal topographic Placido system with 22 concentric rings for detection of up to 22,000 elevation points. The Placido ring image is referenced to the corneal apex and locates the pupil center and the limbus. Automatic measuring release ensures that the image centration has a peripheral standard deviation of ±4 μm. The embedded pupil recognition software can measure pupil centroid shift, allowing centration of subsequent laser ablation according to the patient's visual needs. The Athens protocol based on topographic data from the Topolyzer (group A) is thus referred to as Placido disc-guided, or simply as "Placido", in which eight acquisitions averaged for consistency are used for each eye.

The Scheimpflug diagnostic device used was the Alcon/WaveLight Oculyzer™ II. The Oculyzer is a high-resolution Pentacam camera (Oculus Optikgeräte

GmbH, Wetzlar, Germany)[27] which is incorporated into the Alcon/WaveLight Refractive Suite.[25] The integrated rotating Scheimpflug camera acquires up to 50 images in real-time measurement. The Athens protocol was based on data from the Oculyzer (group B), so is referred to as Scheimpflug-guided, or simply "Scheimpflug", in which four acquisitions averaged for consistency are used for each eye.

Postoperative follow-up assessment was performed by subjective refraction, best spectacle-corrected distance visual acuity measurement with this refraction, and slit-lamp biomicroscopy, as well as anterior segment optical coherence tomography imaging for clinical signs of corneal CXL.[15]

Anterior surface topographic indices

To measure and monitor topographic changes in keratometric refraction and topographic geometry, quantitative postoperative assessment (measured preoperatively and at months 1, 3, 6, and 12 postoperatively) was performed using the Oculyzer II, obtained and processed via the Oculyzer examination software (Version 1.17 release 47). For each eye, four consecutive measurements were obtained and processed to test for data repeatability (including topographic, tomographic, and pachymetric mapping).[21]

To this end, in addition to keratometric measurements, specific anterior surface indices were studied when used in conjunction with Pentacam camera analysis, developed for grading and classification based on the Amsler–Krumeich stages of keratoconus,[29] as well as the postoperative assessment.[30–36]

These indices include the following: index of surface variance (ISV), an expression of corneal surface curvature irregularity; the index of vertical asymmetry, a measure of the difference between superior and inferior corneal curvature; the keratoconus index; the central keratoconus index; the index of height asymmetry, a measurement similar to the index of vertical asymmetry but based on corneal elevation; the index of height decentration (IHD), calculated with Fourier analysis of corneal height to quantify the degree of vertical decentration; and the minimum radius of curvature, a measurement of the smallest radius of curvature of the cornea (ie, the maximum corneal steepness).[37] In the present work, 12-month postoperative data were compared with the respective preoperative data.

Linear regression analysis was done to seek possible correlations between changes in these indices and visual rehabilitation. Descriptive and comparative statistics, analysis of variance between keratoconus stage subgroups, and linear regression were performed with statistics tools provided by Minitab version 1.6.1 (MiniTab Ltd, Coventry, UK) and Origin Lab version 9 (OriginLab Corp, Northampton, MA, USA). Paired analysis P values < 0.05 were considered to be statistically significant.

Results

The mean ± standard deviation subject age in group A at the time of the Athens protocol was 31.5 ± 7.9 (19–57) years and for group B was 33.3 ± 7.3 (21–57) years. Group A included 16 women and 38 men and group B included 42 women and 85 men. There was a preponderance of males, which is consistent with our clinical experience[15] and keratoconus incidence studies.[38] In group A, 25 eyes were right (OD) and 29 left (OS), while in group B, 69 eyes were right and 58 were left.

Changes in visual acuity

Mean preoperative corrected distance visual acuity in group A was 0.65 ± 0.23 (1.00–0.10) and for group B was 0.63 ± 0.24 (1.00–0.10, Table 1). Changes in visual acuity, expressed as the difference between postoperative and preoperative corrected distance visual acuity, for group A were +0.12 ± 0.20 (+0.60 to –0.45) and for group B were +0.19 ± 0.20 (+0.75 to –0.30).

Figure 1 shows the above data in the form of box plots, showing median and mean values with 95% confidence

Table 1 Preoperative, 12-month postoperative, and change (gain/loss) in best spectacle-corrected distance visual acuity data, expressed as the difference between postoperative and preoperative corrected distance visual acuity

	Preoperative		Postoperative		Change (gain/loss)	
	Group A (Placido)	Group B (Scheimpflug)	Group A (Placido)	Group B (Scheimpflug)	Group A (Placido)	Group B (Scheimpflug)
Mean	0.65	0.63	0.77	0.82	0.12	0.19
Standard deviation	±0.23	±0.24	±0.19	±0.19	±0.20	±0.20
Maximum	1.00	1.00	1.10	1.20	0.60	0.75
Minimum	0.01	0.01	0.30	0.30	–0.45	–0.30
Shapiro–Wilk normality test *P* value	>0.100	0.049	>0.100	<0.010	>0.100	0.054

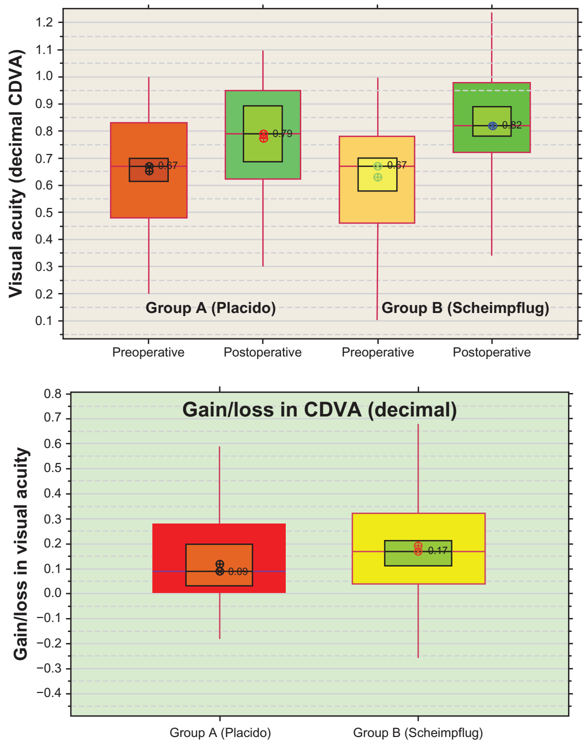

Figure 1 Box plots of corrected distance visual acuity, expressed as decimals. Top, preoperative and postoperative values for both groups. Bottom, gain/loss expressed as difference between postoperative minus preoperative corrected distance visual acuity.
Notes: Box plots are showing median level indicated by ⊗, average symbol ⊕, 95% median confidence range box (black borderline boxes), and interquartile intervals range box (red borderline boxes).
Abbreviation: CDVA, corrected distance visual acuity.

intervals and interquartile ranges. As shown in Figure 1B, the 95% median confidence interval indicates that 95% of eyes in each group had a positive change (stable or better) in visual acuity.

Distribution of keratometric and topographic indices

Average, standard deviation, maximum, and minimum anterior and posterior corneal surface keratometric and topometric indices, as measured preoperatively and 12 months postoperatively in the 8 mm zone, are presented for both groups in Table 2. Box plots of changes (preoperative versus postoperative values) induced for anterior K1 flat (top) and steep K2 (bottom) keratometry (in diopters, D) for groups A and B are shown in Figure 2A and B, respectively. The changes induced for the seven anterior surface indices are reported for the two groups in Table 3.

Anterior surface keratometry showed the following mean changes (defined as mean postoperative versus respective preoperative values from the data in Table 2). In group A, K1 (flat) changed from 45.202 ± 3.782 D to 43.022 ± 3.819 D, indicating a change of –2.18 D, and K2 (steep) changed from 48.670 ± 4.066 D to 45.865 ± 4.794 D, indicating a change of –2.805 D. In group B, K1 (flat) changed from 46.213 ± 4.082 D to 43.190 ± 4.398 D, indicating a change of –3.023 D, and K2 (steep) changed from 50.774 ± 5.210 to 46.380 ± 5.006 D, indicating a change of –4.394 D.

Correlation between anterior surface topographic index and stages of keratoconus

All eyes in each group were classified preoperatively according to the Amsler–Krumeich keratoconus severity index (nil, KC1, KC1–2, KC2, KC2–3, KC3, KC3–4, and KC4) using the Oculus software. We sought correlations between all of the seven anterior surface topographic images with the above grading stages. The correlation between the derived keratoconus severity index and the seven anterior surface topographic indices is shown as box plots in Figure 3. The best correlates with keratoconus stage classification were the index of surface variance (with the exception of the highest stage, KC4, all other P values < 0.001, as seen in Table 4) and index of height decentration (with the exception of the lowest stage, KC1, all other P values < 0.001).

We also conducted an index repeatability measurement study, and expressed the measured repeatability as the relative percentage change between four consecutive measurements from the same eye (lower values indicating better repeatability). The results indicate that the indices of surface variance and height decentration were among the best performers, having an average repeatability of 2.77% ± 1.32% for index of surface variance and 4.67% ± 1.62% for index of height decentration index.

Postoperative changes in anterior surface topographic index

Based on the abovementioned results, we followed these two indices, ie, index of surface variance and index of height decentration, as reliable indicators of anterior surface changes induced by the Athens protocol. By their respective definitions, a change towards a lower value (negative change) is indicative of a trend towards more normal corneal keratometry and topography.[31]

The changes induced by the Athens protocol, expressed as the difference between the 12-month postoperative values minus the respective preoperative values are shown in Figure 4 (changes in index of surface variance) and in Figure 5 (changes in index of height decentration). Relative changes in indices of surface variance and height

Table 2 Anterior and posterior corneal keratometry and topometric indices, as measured in the 8 mm zone for both groups, preoperatively and 12 months postoperatively

	Preoperative			Postoperative		
	Mean ± SD	Max	Min	Mean ± SD	Max	Min
Group A (Placido)						
Anterior surface						
K1 flat, D	45.20 ± 3.78	52.1	33.7	43.02 ± 3.82	52.6	31.8
K2 steep, D	48.67 ± 4.07	59.2	42.1	45.86 ± 4.79	59.8	34.6
Km mean, D	46.88 ± 3.60	54.6	41.3	44.37 ± 4.14	54.5	33.1
Posterior surface						
K1 flat, D	−6.44 ± 0.78	−4.6	−8.0	−6.39 ± 0.86	−4.8	−8.5
K2 steep, D	−7.28 ± 0.84	−5.9	−9.4	−7.40 ± 0.91	−5.8	−10.1
Km mean, D	−6.82 ± 0.74	−5.5	−8.6	−6.85 ± 0.82	−5.6	−9.2
Anterior surface indices (in 8 mm zone)						
ISV	91.33 ± 42.59	187	14	86.70 ± 43.91	190	14
IVA	1.06 ± 0.54	2.52	0.09	1.00 ± 0.59	2.69	0.13
KI	1.25 ± 0.15	1.72	1.02	1.21 ± 0.17	1.66	0.93
CKI	1.05 ± 0.05	1.30	0.98	1.04 ± 0.06	1.16	0.86
IHA	26.19 ± 19.80	84	0.60	22.20 ± 18.37	75.1	3.3
IHD	0.087 ± 0.051	0.201	0.007	0.064 ± 0.043	0.163	0.005
Rmin (mm)	6.35 ± 0.70	7.73	5.03	6.69 ± 0.71	7.93	4.96
Group B (Scheimpflug)						
Anterior surface						
K1 flat, D	46.21 ± 4.08	60.7	37.6	43.19 ± 4.40	55.3	30.5
K2 steep, D	50.77 ± 5.21	71.7	42.6	46.38 ± 5.01	59.5	35.7
Km mean, D	48.36 ± 4.44	65.7	40.7	44.71 ± 4.58	57.3	32.9
Posterior surface						
K1 flat, D	−6.58 ± 0.83	−4.6	−9.0	−6.52 ± 0.96	−3.3	−9.8
K2 steep, D	−7.66 ± 1.08	−5.8	−10.9	−7.68 ± 1.13	−5.6	−11
Km mean, D	−7.07 ± 0.90	−5.1	−9.8	−7.04 ± 0.98	−4.6	−10.3
Anterior surface indices (in 8 mm zone)						
ISV	98.14 ± 45.32	208	18	80.13 ± 35.98	169	15
IVA	1.05 ± 0.51	2.45	0.17	0.87 ± 0.46	2.42	0.1
KI	1.27 ± 0.16	1.80	0.97	1.19 ± 0.15	1.56	0.86
CKI	1.05 ± 0.06	1.30	0.90	1.02 ± 0.05	1.16	0.87
IHA	30.95 ± 20.88	88.7	0.3	23.80 ± 17.36	96.3	0.1
IHD	0.09 ± 0.05	0.26	0.01	0.06 ± 0.03	0.172	0.001
Rmin (mm)	6.07 ± 0.79	7.61	4.20	6.65 ± 0.66	7.88	5.12

Abbreviations: ISV, index of surface variance; IVA, index of vertical asymmetry; KI, keratoconus index; CKI, central keratoconus index; IHA, index of height asymmetry; IHD, index of height decentration; Rmin, smallest sagittal curvature; SD, standard deviation; D, diopter K1, flat keratometry; K2, steep keratometry; Km, median keratometry.

decentration (defined as percentage change in the parameter with regard to respective preoperative value) are shown in Table 3. In group A, the index of surface variance was reduced to −5.07% and the index of height decentration to −26.81%; in group B, the index of surface variance was reduced to −18.35% and the index of height decentration to −39.03%, respectively. This negative change is indicative of the corneal surface becoming less irregular (index of surface variance) and the "cone" becoming more central (index of height decentration) at the postoperative assessment.

Placido disc versus Scheimpflug camera imaging for topoguided ablation

The above data, ie, changes in visual acuity, keratometry, and anterior surface topometric indices, indicate that there was a difference in outcomes when comparing group A (Placido disc) and group B (Scheimpflug camera).

To expand our investigation further, we formed two subgroups within each group, based on preoperative index of height decentration. The distinction was made by arbitrarily defining this as "low" if IHD $\leq$ 0.09, referring to a more centered keratoconus cone, and "high" if IHD $>$ 0.09, referring to a more decentered cone. The following subgroups were formed: group A1 (Placido low, n = 30 eyes), group A2 (Placido high, n = 24 eyes), group B1 (Scheimpflug low, n = 65 eyes), and group B2 (Scheimpflug high, n = 64 eyes). We then investigated the changes induced by the Athens protocol in index of height decentration within each subgroup. For group A1, the relative percentage change in index of surface variance was –4.61% and in index of height decentration was –22.10%; for group A2,

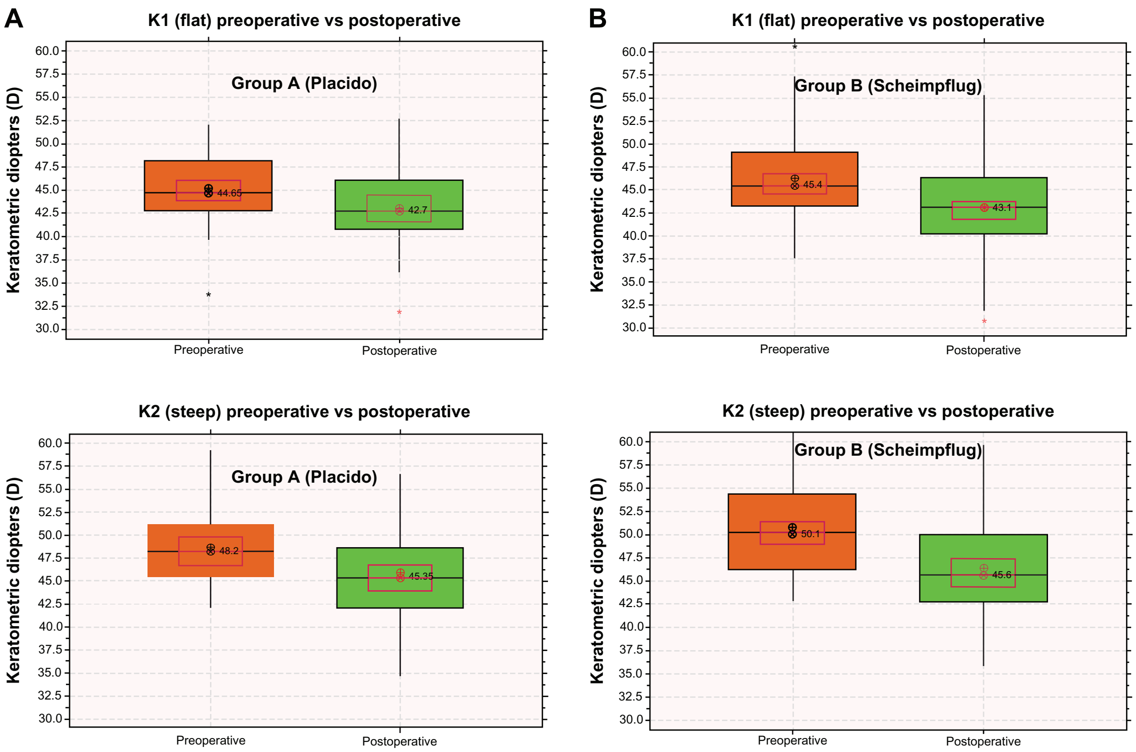

Figure 2 (**A**) Box plot describing induced changes (preoperative versus postoperative values) for anterior flat (top) and steep (bottom) keratometry (in diopters, D) for group A (Placido). (**B**) Box plot describing induced changes (preoperative versus postoperative values) for anterior flat (top) and steep (bottom) keratometry (in diopters, D) for group B (Scheimpflug).

Notes: Median level is indicated by ⊗, average by ⊕, the 95% median confidence range box by the red borderline, and the interquartile intervals range box by the black borderline.

the relative percentage change in index of surface variance was –5.35% and in index of height decentration was –29.05%. For group B1, the relative percentage change in index of surface variance was –13.54% and in index of height decentration was –32.82%; for group B2, the relative percentage change in index of surface variance was –20.36% and in index of height decentration was –41.19%. The results are presented in the form of box plots in Figure 6, and are tabulated in Table 5.

Discussion

The options available to clinical investigators for clinical assessment and evaluation of keratoconus and monitoring of induced postoperative improvement due to CXL procedures include a multitude of diagnostic devices. Corneal pachymetry[39,40] and analysis of cornea biomechanical properties[41] can also be very significant in the keratoconus assessment, although the long-standing standard for

Table 3 Changes induced in seven anterior surface indices for the two groups

	ISV	IVA(mm)	KI	CKI	IHA(μm)	IHD(μm)	Rmin (mm)
Group A (Placido)							
Relative change	–5.07%	–5.65%	–3.20%	–1.42%	–15.24%	–26.81%	2.18%
Mean change	–4.630	–0.060	–0.040	–0.015	–3.991	–0.023	0.139
SD	±16.617	±0.225	±0.066	±0.055	±21.003	±0.027	±0.263
Maximum	29	0.45	0.07	0.06	40.6	0.023	1.31
Minimum	–50	–0.74	–0.23	–0.27	–57.5	–0.102	–0.28
Group B (Scheimpflug)							
Relative change	–18.36%	–16.64%	–6.24%	–3.24%	–23.10%	–39.03%	9.64%
Mean change	–18.016	–0.175	–0.079	–0.034	–7.150	–0.035	0.585
SD	±20.687	±0.253	±0.073	±0.042	±17.087	±0.036	±0.409
Maximum	38	0.42	0.08	0.06	37.7	0.017	1.93
Minimum	–83	–0.95	–0.43	–0.22	–65.1	–0.213	–0.22

Notes: Average change is defined as the postoperative value minus the preoperative value. Relative change is defined as the percentage mean change in each parameter with regard to the respective preoperative value.

Abbreviations: ISV, index of surface variance; IVA, index of vertical asymmetry; KI, keratoconus index; CKI, central keratoconus index; IHA, index of height asymmetry; IHD, index of height decentration; Rmin, smallest sagittal curvature; SD, standard deviation.

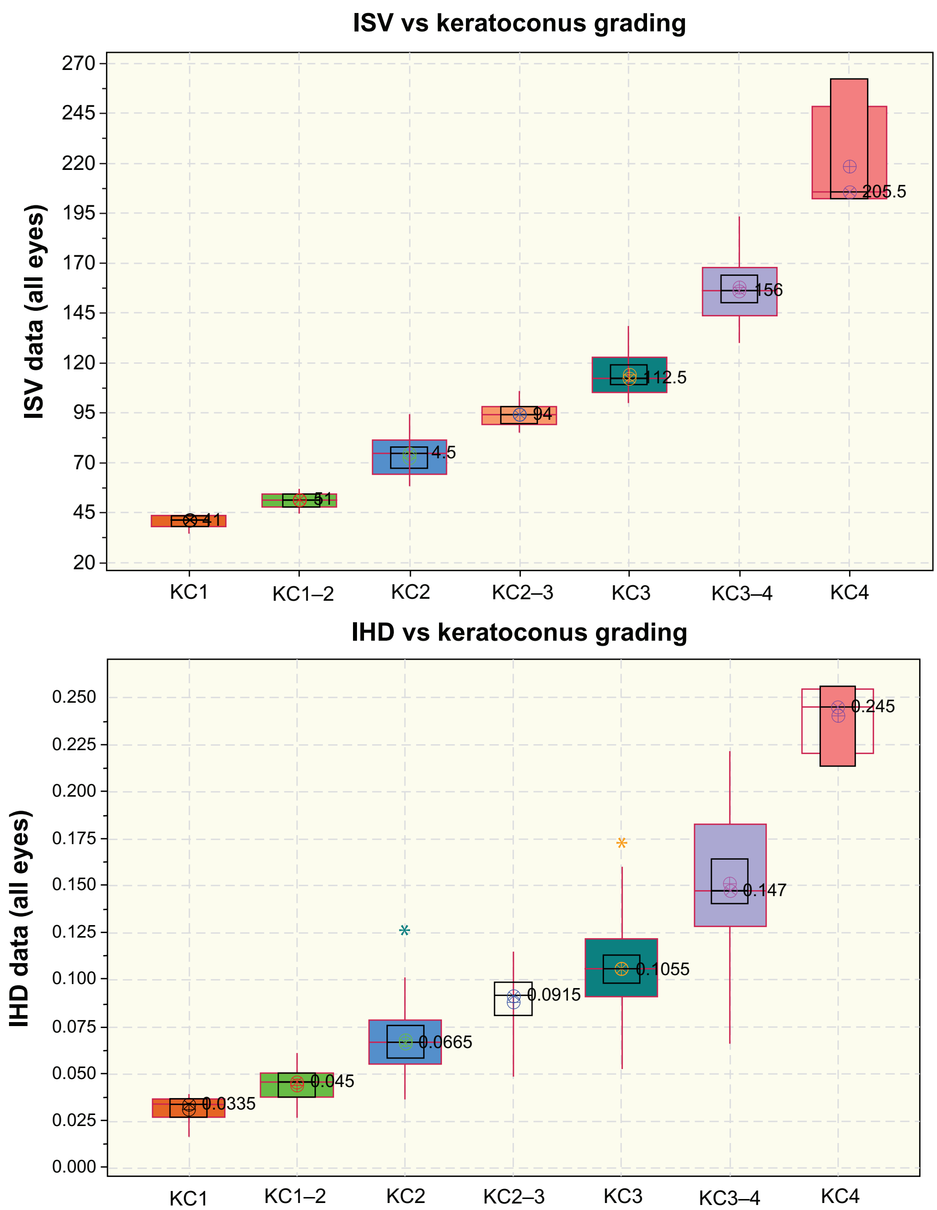

Figure 3 Top, box plot of preoperative ISV, and bottom, preoperative IHD versus keratoconus grading, as produced by the Oculyzer software.
Notes: Median level is indicated by ⊗, average by ⊕, the 95% median confidence range box by the lack borderline, and the interquartile intervals range box by the red borderline.
Abbreviations: IHD, index of height decentration; ISV, index of surface variance.

evaluating keratoconus and the results of treatment has been anterior surface topometry and topography.[42]

It is known that CXL alone results in a change in corneal pachymetry, which may not be accurately depicted by Scheimpflug imaging because of the procedure used, ie, densitometry. In addition, the partial photoablation aspect of the Athens protocol reduces corneal thickness, so any classification scheme which includes corneal pachymetry may be insufficient for postoperative assessment. Particularly after treatment (eg, with CXL), changes in the anterior surface may provide a more pertinent reflection of changes induced by the procedure.[43,44]

Our clinical observation, which is also confirmed by other researchers,[45] has been that postoperatively, the short-term (particularly during the first 6 months) refractive, topometric, and pachymetric results[46] can be described as being "in continuous change", with progressive improvement towards the one-year assessment, and possibly further on. Because of this, we chose to select and analyze the one-year interval results as a common reference to what we subsequently refer to as "postoperative" data. In this study, we evaluated the one-year postoperative changes in visual acuity, keratometry, and seven anterior surface topographic indices induced by

Table 4 Two-sample *t*-test results, not assuming equal variance, between the keratoconus grading subgroups (KC1, KC1–2, KC2, KC2–3, KC3, KC3–4, and KC4) for the topometric indices of ISV and IHD as measured preoperatively

	Estimate for difference	95% CI for difference	*P* value
ISV			
K1 versus K1–2	10.31	(7.35, 13.27)	<0.001
K1–2 versus K2	21.84	(17.87, 25.82)	<0.001
K2 versus K2–3	21.02	(17.02, 25.03)	<0.001
K2–3 versus K3	20.3	(16.88, 23.72)	<0.001
K3 versus K3–4	43.7	(37.79, 49.62)	<0.001
K3–4 versus K4	61	(14.1, 107.8)	0.026
IHD			
K1 versus K1–2	0.01255	(0.00474, 0.02035)	0.003
K1–2 versus K2	0.02411	(0.01522, 0.03300)	<0.001
K2 versus K2–3	0.02012	(0.01038, 0.02985)	<0.001
K2–3 versus K3	0.01856	(0.00836, 0.02876)	0.001
K3 versus K3–4	0.04487	(0.03165, 0.05808)	<0.001
K3–4 versus K4	0.0888	(0.0610, 0.1166)	<0.001

Abbreviations: ISV index of surface variance; IHD, index of height decentration; CI, confidence interval.

the Athens protocol, and investigated for associations with visual acuity outcomes.

Our results indicate that the minimum radius of curvature, defined as the inverse of corneal steepness, was increased postoperatively in agreement with the decrease in anterior surface keratometry[47,48] (Table 2). As such, the improved one-year improvement observed for corrected distance visual acuity (Table 1 and Figure 1) can be justified, because the anterior corneal surface attains a more optically manageable refractive shape. The values of all other six topographic indices were reduced in comparison with the respective preoperative values, indicating corneal surface improvement. The postoperative reduction noted in some of these indices has been reported only recently.[31] These changes are all indicative of improved corneal topography (ie, reduction of irregularity, cone becoming less steep and more central) in agreement with other studies.[31,41] Therefore, it appears that quantitative assessment of

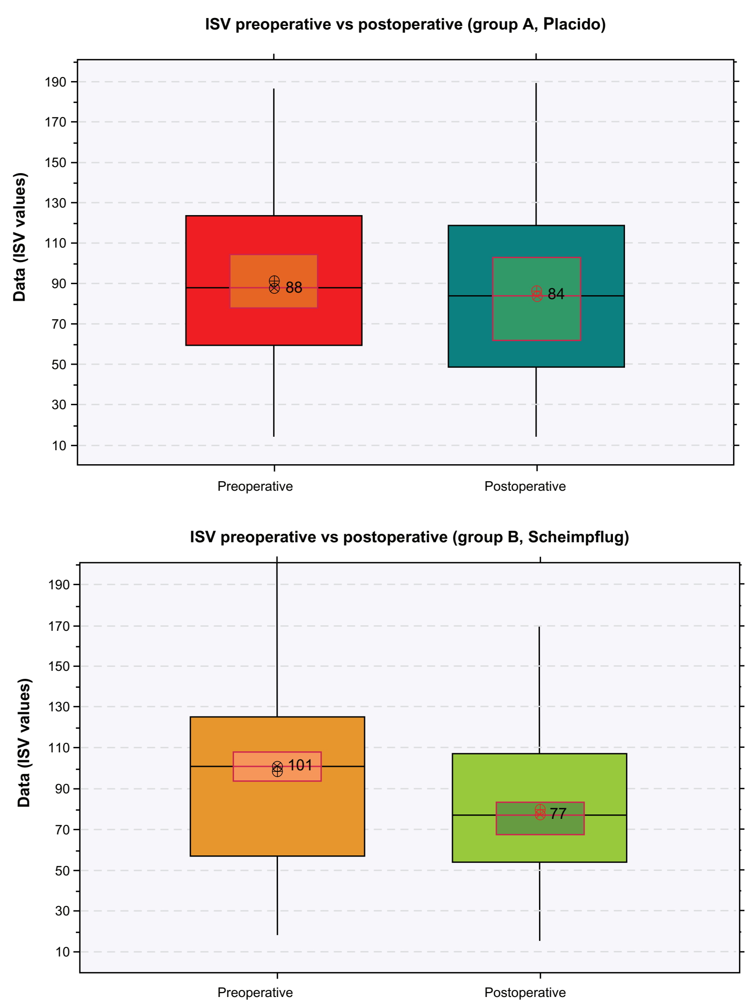

Figure 4 Box plot describing changes (preoperative versus postoperative values) induced for ISV in the two groups: top, group A, Placido; bottom, group B, Scheimpflug.
Notes: ⊗, median level; ⊕, average; red borderline, 95% median confidence range box; black borderline, interquartile intervals range box.
Abbreviation: ISV, index of surface variance.

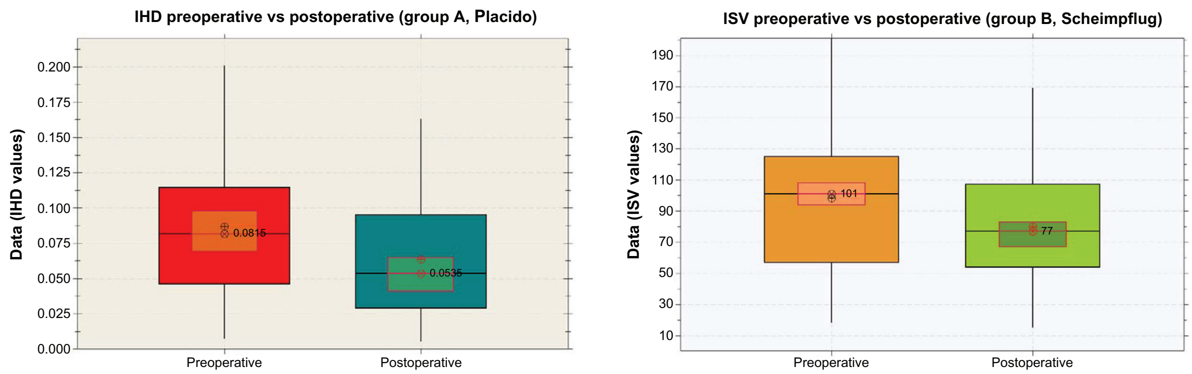

Figure 5 Box plot describing changes (preoperative versus postoperative values) induced for IHD for the two groups: top, group A, Placido; bottom, group B, Scheimpflug.

Notes: ⊗, median level; ⊕, average; red borderline, 95% median confidence range box; black borderline, interquartile intervals range box.

Abbreviations: IHD, the index of height decentration; ISV, index of surface variance.

postoperative changes in CXL using the topometric indices of surface variance and height decentration may prove very helpful in clinical practice.

Our study indicates that the outcomes of the Athens protocol used for keratoconus stabilization and visual rehabilitation appear to be better when using Scheimpflug-driven topography data. Based on our analysis, group B, for which primary topographic data were provided by the Oculyzer II, a Scheimpflug rotating camera, when compared with group A, the primary topographic data for which were provided by the Vario Topolyzer, a Placido topographer, showed a greater reduction in keratometry, as well as the two anterior surface

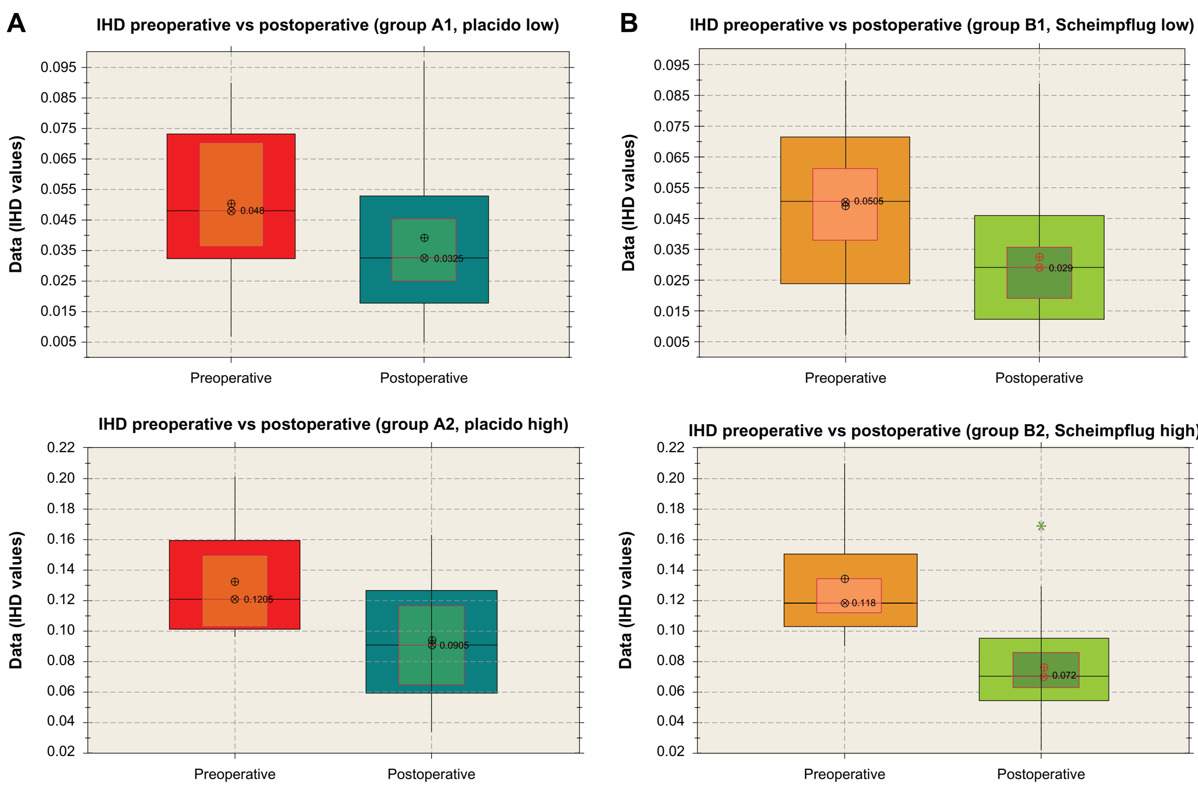

Figure 6 (**A**) Box plot describing preoperative versus postoperative changes in IHD induced for the subgroups. Top, group A1 (Placido low) indicating less affected keratoconic eyes; bottom, group A2 (Placido high) indicating more affected keratoconic eyes. (**B**) Box plot describing preoperative versus postoperative changes in IHD induced for the subgroups. Top, group B1 (Scheimpflug low) indicating less affected keratoconic eyes; bottom, group B2 (Scheimpflug high) indicating more affected keratoconic eyes.

Notes: ⊗, median level; ⊕, average; red borderline, 95% median confidence range box; black borderline, interquartile intervals range box.

Abbreviation: IHD, index of height decentration.

Table 5 Changes in ISV and IHD induced in the four subgroups

	ISV	IHD
Group A1 (Placido low)		
Relative	–4.61%	–22.10%
Mean	–2.900	–0.011
SD	±17.010	±0.020
Maximum	29	0.023
Minimum	–50	–0.054
Group A2 (Placido high)		
Relative	–5.35%	–29.05%
Mean	–6.792	–0.038
SD	±16.208	±0.026
Maximum	23	0.013
Minimum	–36	–0.102
Group B1 (Scheimpflug low)		
Relative	–13.54%	–32.82%
Mean	–8.908	–0.016
SD	±18.339	±0.020
Maximum	38	0.014
Minimum	–48	–0.074
Group B2 (Scheimpflug high)		
Relative	–20.36%	–41.19%
Mean	–26.750	–0.054
SD	±18.968	±0.037
Maximum	13	0.017
Minimum	–83	–0.213

Notes: Mean change is derived from the postoperative minus the preoperative value in each case. Relative change is defined as percentage mean change in the parameter with regard to respective preoperative value.
Abbreviations: ISV, index of surface variance; IHD, index of height decentration; SD, standard deviation.

topographic indices having the strongest correlation with keratoconus grading, ie, the indices of surface variance and height decentration.

This study evaluated a very large number of cases over an extended period of time, when compared with the current peer-reviewed literature. The difference in absolute numbers between group A (Placido disc-guided, 54 cases) and group B (Scheimpflug tomography-guided, 127 cases) is due to early results suggesting that the procedure used in group B demonstrated higher efficacy, leading to discontinuation of recruitment for group A. Although different, these numbers and the duration of follow-up are still quite substantial and permit sensitive statistical analysis and a confident conclusion regarding the differential in postoperative efficacy. This change is more pronounced in the more irregular and more decentrated anterior surfaces preoperatively (subgroups A2 and B2), reaching up to a –41% reduction in index of height decentration for group B2.

The above findings may be explained by the procedures used with the corresponding diagnostic devices. The Placido disc imaging devices, despite providing a single, snapshot measurement, are more suitable for measurements at the peripheral cornea, and have lower reliability for information at the corneal center, in addition to being susceptible to error due to abrupt changes in corneal height. Placido disc imaging cannot clearly differentiate between abrupt flattening and abrupt steepening changes, and simply measures changes in curvature. This potential bias of measurement may be one, or the main, reason for the difference in clinical efficacy seen in our study. On the other hand, the rotating measurement process used by the Scheimpflug imaging camera, despite being sequential, captures images with a fine meshed dot matrix in the center, providing high-resolution data for absolute elevation from the large corneal area imaged. The potential bias here is interference of the eyelid and eyelashes with the image quality, as well as potential bias in thickness measurement attributed to arcus senilis in the peripheral cornea. All Scheimpflug images used in our treatments are carefully screened in order to exclude these potential biases.

Conclusion

Topography-guided normalization of extreme cornea irregularity, such as keratoconus, coupled with higher fluence CXL appears to be achieved with significantly greater efficacy when the Scheimpflug rotating camera (Oculyzer) is used with the WaveLight excimer laser platform. It appears to provide significantly better improvement in refractive, topometric, and visual rehabilitation when compared with Placido disc (Topolyzer) topography-driven normalization and CXL treatments. This Athens protocol, aiming to both halt progression of keratoconic ectasia and improve anterior corneal normality, topometry, and visual performance, demonstrates a good safety record with either platform and very effective refractive, keratometric, and topometric results.

Disclosure

AJK is a consultant for Alcon/Wavelight and Avedro. GA is a consultant for Alcon/Wavelight. The authors report no conflicts of interest in this work.

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