ORIGINAL RESEARCH

Placido disc vs Scheimpflug image derived topography-guided excimer laser surface normalization used combined with CXL (the Athens Protocol) in 181 progressive keratoconus cases.

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Abstract

Purpose

To compare the efficacy of two alternative corneal topography data sources employed in the topography - guided excimer laser normalization, combined with CXL, in the management of keratoconus with the Athens Protocol (AP) procedure, namely a Placido-disk imaging device and a Scheimpflug imaging device.

Patients and methods

One hundred eighty-one (181) consecutive keratoconic cases subjected to the Athens Protocol procedure, between 2008 and 2011, were studied pre-operatively and 1, 3, 6, and 12-months postoperatively for visual acuity, keratometry, and anterior surface corneal indices. Two groups were formed, depending on the primary source for the topo-guided photoablation, namely a Placido disc, for group A (Placido), and a Scheimpflug rotating camera, for group B (Scheimpflug). The one-year changes in visual acuity, keratometric, and seven anterior-surface topometric indices were studied for both groups.

Results

The visual acuity changes, expressed as difference between post– minus the pre-operative corrected distance visual acuity were, for group A (Placido) +0.12 ± 0.20 (range +0.60 to -0.45), and for group B (Scheimpflug), +0.19 ± 0.20 (range +0.75 to –0.30), respectively. For group A, K1 (flat keratometry) changed from 45.202 ± 3.782 diopters (D) to 43.022 ± 3.819, or a flattening of -2.18 D, and K2 (steep keratometry) changed from 48.670 ± 4.066 D to 45.865 ± 4.794 D, or a flattening of -2.805 D. Respectively, for group B, K1 (flat keratometry) changed from 46.213 ± 4.082 D to 43.190 ± 4.398 D, or a flattening of -3.023 D,

and K2 (steep keratometry) changed from 50.774 ± 5.210 to 46.380 ± 5.006 D, or a flattening of -4.394 D.

For group A, the value of the index of surface variance (ISV) was reduced to -5.07% and the value of the index of height decentration (IHD) to -26.81%. For group B, the value of the index of surface variance was reduced to -18.35% and the value of the index of height decentration to -39.03%, respectively. These value reductions indicate that the corneal surface became less irregular (ISV) and the 'cone' flatter and more central (IHD) in the post-operative assessment.

Conclusions

Of the two sources of primary corneal data, the Scheimpflug rotating camera (Oculyzer) for topography-guided normalization treatments with the WaveLight excimer laser platform, appear to provide statistically significant better improvement when compared to the Placido disk topographer (Vario Topolyzer). Overally, the Athens Protocol procedure, aiming to both arrest the keratoconus ectasia progression, as well as to improve corneal topometry and visual performance, demonstrates safe and notable refractive, keratometric and topometric results. The observed visual acuity changes, as well as keratometric flattening and topometric improvement are suggestive of the overall postoperative improvements.

Keywords

Athens Protocol; anterior surface Pentacam indices; keratoconus; cross-linking; WaveLight /Alcon excimer laser, EX500 excimer laser, topography-guided surface excimer ablation

Introduction

Keratoconus (KCN) 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 is manifested asymmetrically between the two eyes of the same patient. [5,6]

Corneal collagen cross-linking (CXL) using riboflavin and ultraviolet-A (UVA) irradiation has become acceptable as a treatment option for eyes with progressive keratoconus. [7]

Laboratory data suggest that CXL employing riboflavin and UVA irradiation increases stromal collagen fibril diameter resulting in increased corneal biomechanical strength. [8] Several clinical reports indicate that CXL treatment results in arrest of ectasia progression, [7,9] in improvement of corneal keratometry, refraction and visual acuity, and in reduction of higher-order aberrations; the post-operative complications are infrequent. [7] Our team has introduced several variations and applications with CXL. [10,11]

We have also introduced and reported in extent, in conjunction with the CXL treatment, sequential partial topography-guided photorefractive keratectomy (PRK), [12] which provides a promising approach for further improvement of the topometric and refractive outcomes [13] with good long-term stability. [14,15] Further, we introduced and have extensively reported [16-20] the combination of (a) excimer-laser removal of the top 50 μm of the epithelium, (b) partial topography-guided excimer ablation, limited to maximum of 50 μm stromal tissue removal, followed in the same session by (c) immediate high-fluence UVA radiation (5,6 and 10 mW/cm^2), short duration (18, 15, 10΄) CXL, in a procedure known as the Athens Protocol (AP). [21, 22] The surgical technique of the Athens Protocol has been described with detail previously. [23]

This study aims to compare the efficacy of two alternative corneal topography data sources employed in the topography - guided part of the procedure with the WaveLight/Alcon excimer laser platform (Alcon, Ft. Worth, TX), specifically, a Placido-disk imaging device and a Scheimpflug imaging device, by analysis of long term refractive, topometric and visual rehabilitation changes.

Materials and methods

This clinical series study received approval by the Ethics Committee of our Institution, adherent to the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject at the time of the Athens Protocol intervention or the first clinical visit. The study was conducted in our clinical practice on patients before the AP procedure and/or scheduled clinical visits.

Patient inclusion criteria

The study group consisted of one hundred eighty-one (181) consecutive keratoconic cases subjected to the Athens Protocol procedure, between 2008 and 2011. In all procedures - performed by the same surgeon (AJK)- the epithelial excimer-laser removal, as well as the topography-guided excimer-laser ablation was provided by the Alcon/WaveLight 400 Hz Eye-Q [24] or the 500 Hz EX500 excimer lasers. [25,26]

For a patient to be considered for the AP procedure, the following criteria were met: clinical diagnosis of progressive keratoconus, minimum age of 18 years, and minimum corneal thickness of 300 μm. No patient with systemic disease, previous corneal surgery, history of chemical injury or delayed epithelial healing, and pregnancy or lactation (for the female patients) were considered for the procedure. All patients included in the study completed an uneventful Athens Protocol procedure using the KXL CXL device (Avedro, Waltham, MA), and were presented to our institution for at least one-year follow-up monitoring.

Depending on the imaging source for the topography-guided partial photoablation, the following two groups were formed: Group A (nA = 54 eyes), in which the primary topography data were provided by a Placido-disk imaging device, and Group B (nB = 127 eyes), in which the primary topography data were provided by a Scheimpflug imaging device.

Imaging and measurement

The Placido-disk diagnostic device employed was the Alcon/WaveLight® Allegro Topolyzer™ Vario™ (WaveLight AG, Erlagen, Germany). The Topolyzer is a wide-cone corneal topographic Placido system with 22 concentric rings for the 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. An automatic measuring release ensures that the image centration has a peripheral standard deviation (StDev) of ± 4 μm. The embedded pupil-recognition software can measure pupil centroid shift, allowing centration of the 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, 'Placido' in which for each eye, eight acquisitions averaged for consistency, are employed.

The Scheimpflug diagnostic device employed 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) is thus referred to as 'Scheimpflug-guided', or simply 'Scheimpflug', in which for each eye, four acquisitions, averaged for consistency, are employed.

Post-operative follow-up assessment was performed by means of subjective refraction, best spectacle Corrected Distance Visual Acuity (CDVA) measurement with this refraction, and slit-lamp biomicroscopy, as well as anterior segment optical coherence tomography (OCT) imaging for clinical signs of corneal CXL. [15]

Anterior-surface topographic indices

To measure and monitor the induced topographic changes in keratometric refraction and topographic geometry, quantitative post-operative assessment (measured both pre-operatively and at 1, 3, 6, and 12 months postoperatively) was performed by the Oculyzer II, obtained and processed via the Oculyzer Examination Software (Version 1.17r47). For each eye, four consecutive measurements were obtained and processed to test for data repeatability (including topographic, tomographic, and pachymetric mapping). [21]

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

These indices are the following: index of surface variance (ISV), an expression of corneal surface curvature irregularity; the index of vertical asymmetry (IVA), a measure of the difference between superior and inferior corneal curvature; the keratoconus index (KI); the central keratoconus index (CKI); the index of height asymmetry (IHA), a measurement similar to the IVA 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 (Rmin), a measurement of the smallest radius of curvature of the cornea (ie, the maximum corneal steepness). [37] In the present work, the 12-month post-operative data were studied in comparison of the pre-operative respective data.

Linear regression analysis was performed to seek possible correlations between changes of these indices as well as 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). Paired analysis p-values less than 0.05 were considered indication of statistically significant results.

Results

Subjects' ages for group A at the time of the AP operation was (average ± standard deviation) 31.5 ± 7.9 years, (min 19, max 57), while for group B, 33.3 ± 7.3 years (min 21, max 57). Gender specifics for group A were 16 female and 38 male patients, while for group B, 42 female and 85 male. There is a preponderance towards male population, 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 left.

Visual Acuity Changes

Preoperative average CDVA (expressed decimally) was, for group A: (average ± standard deviation) 0.65 ± 0.23, range (max-min 1.00 to 0.10), and for group B: 0.63 ± 0.24 (range 1.00 to 0.10) (Table 1). The visual acuity changes, expressed as difference between post– minus the pre-operative CDVA were, for group A, +0.12 ± 0.20 (range +0.60 to -0.45), and for group B, +0.19 ± 0.20 (range +0.75 to –0.30), respectively.

Figures 1 illustrate the above data in the form of box plots, showing median level (indicated by ⊗), average symbol (⊕), 95% median confidence range box, and interquartile intervals range box. As shown in Figure 1b, the 95% median confidence range box shows that in both groups, 95% the eyes had positive change (stable or better) in visual acuity.

Keratometric and topographic indices distribution

Average, standard deviation (StDev), maximum (Max) and minimum (Min) anterior and posterior corneal surface keratometry and topometric indices, as measured in the 8 mm zone for both groups, pre- and 12-months post-operatively are presented in Table 2. Box plot describing induced changes (comparison pre- to post-operative values) for anterior K1 flat (top) and steep K2 (bottom) keratometry (in diopters, D) for group A and B are presented in Figures 2a and b, respectively. The resulting induced changes for all seven anterior surface indices for the two groups are reported in Table 3.

The anterior-surface keratometry had the following averaged changes (defined as the post-average operative value with regard to the respective preoperative value, from the data in table 2): for group A, K1 (flat) changed from 45.202 ± 3.782 diopters (D) to 43.022 ± 3.819, or a change of -2.18 D, and K2 (steep) changed from 48.670 ± 4.066 D to 45.865 ± 4.794 D, or a change of -2.805 D. Respectively, for group B, K1 (flat) changed from 46.213 ± 4.082 D to 43.190 ± 4.398 D, or a change of -3.023 D, and K2 (steep) changed from 50.774 ± 5.210 to 46.380 ± 5.006 D, or a change of -4.394 D.

Anterior-surface topographic index and keratoconus stages correlation

All eyes in both groups were pre-operatively classified by the Oculus software to keratoconus Amsler & Krumeich severity index stages (-, KC1, KC1-2, KC2, KC2-3, KC3, KC3-4, and KC4).

We pursued 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 illustrated in the form of box plots in Figures 3. The result was that the best correlates with the keratoconus stage classification were the ISV (with the exception of the highest stage KC4, all other P-values were < 0.001, as

seen in Table 4), and by the IHD (with the exception of the lowest stage KC1, all other P-values were < 0.001).

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

Anterior-surface topographic index post-operative changes

Based on the above mentioned results, we thus chose to follow these two indices, ISV and IHD, as reliable indicators of anterior-surface changes induced by the AP procedure. By their respective definitions, a change towards a lower value (negative change) is indicative of a trend towards a more normal corneal keratometry and topography. [31]

The AP-induced changes, expressed as difference of the 12-month post-operative minus the respective pre-operative values are illustrated in figures 4 (ISV changes) and figures 5 (IHD changes). The indices ISV and IHD had the following relative changes (defined as % of the change of the parameter with regard to the respective preoperative value), as shown in table 3: for group A, ISV was reduced to -5.07% and IHD to -26.81%, and for group B, ISV was reduced to -18.35% and IHD to -39.03%, respectively. This negative change is indicative of corneal surface becoming less irregular (ISV) and the 'cone' becoming more central (IHD) in the post-operative assessment.

Comparison of Placido-disk and Scheimpflug camera imaging for the topo-guided ablation

The above data, ie the changes in visual acuity, keratometry, as well as the anterior surface topometric indices, indicate that there exists a differential in the outcomes when comparing the two groups, group A (Placido disk) and group B (Scheimpflug camera).

To further expand our investigation we formed two subgroups within each group, based on the criterion of pre-operative value of IHD. The distinction was made by arbitrarily defining 'low IHD' if less or equal to 0.09, referring to a more centered keratoconus cone, and 'high IHD' if larger than 0.09, referring to a more decentered cone. Then, the following subgroups were formed: group A1, Placido Low, consisting of nAL = 30 eyes; group A2, Placido High, consisting of nAH = 24 eyes; group B1, Scheimpflug Low, consisting of nBL = 65 eyes; and group B2, Scheimpflug High, consisting of nBH = 64 eyes. Consequently we investigated within each such subgroup the induced AP changes in the IHD index. For group A1, the relative (%) change in ISV was -4.61% and in IHD -22.10% and for group A2, the relative (%) change in ISV was -5.35% and in IHD -29.05%. For group B1, the relative (%) change in ISV was -13.54% and in IHD -32.82% and for group B2, the relative (%) change in ISV was -20.36% and in IHD -41.19%. The results are presented in the form of box plots in Figure 6, and are tabulated in Table 5.

Discussion

For the clinical assessment and evaluation of keratoconus and the monitoring of induced postoperative potential improvement due to CXL procedures, the current options of the clinical investigator includes a multitude of diagnostic devices. Corneal pachymetry [39,40] and cornea biomechanical properties analysis [41] can also be very significant in the keratoconus assessment, although the long-standing standard for evaluating keratoconus and treatment results has been anterior surface topometry and topography. [42]

It has been known that CXL alone results in a change in corneal pachymetry, which may not be accurately depicted by the Scheimpflug imaging due to the principle of operation, namely densitometry. In addition the –partial- photoablation part of the AP procedure reduces corneal thickness, and thus any classification criteria scheme which includes corneal pachymetry may be insufficient for the post-operative assessment. Particularly after

treatment (eg CXL), changes in the anterior surface may provide a more pertinent analysis of the 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-month period) 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 call 'postoperative data'. In this study thus, we evaluated the one-year postoperative changes induced by the AP procedure in visual acuity, keratometry, and seven anterior surface topographic indices, and investigated associations with visual acuity outcomes.

Our results indicate that the Rmin (minimum radius of curvature), which is defined as the inverse of corneal steepness, was increased postoperatively in agreement with the decrease of anterior surface keratometry [47,48] (Table 2). As such, the improved observed one-year improvement in CDVA (Table 1 and Figure 1) can be justified, as the anterior corneal surface attains a more optically manageable refractive shape. In all other six topographic indices, their values were reduced in comparison to the respective preoperative values, indicating corneal surface improvement. The noted postoperative reduction of some of these indices has been reported only recently. [31] These changes are all indicative of corneal topography improvement, (ie reduction of irregularity, cone becoming less steep and more central) in agreement with other studies. [31, 41] It appears thus that the option to quantitatively assess CXL postoperative changes with the ISV and IHD topometric indices may be proven very helpful in the clinical practice.

Topography-guided ablation for keratoconus: which is the best image source for guidance?

Our study indicates that the outcomes of the Athens Protocol employed for keratoconus stabilization and visual rehabilitation appear to be better when using the Scheimpflug driven topography data. Based on our analysis, the group B, whose primary topographic data were provided by the Oculyzer II, a Scheimpflug rotating camera, when compared to the group A, whose primary topographic data were provided by the Vario Topolyzer, a Placido topographer, presented a more drastic reduction in keratometry, as well as the two anterior-surface topographic indices with the strongest correlation with keratoconus grading, namely the indices ISV and IHD.

This study evaluates a very large number of cases over an extended amount of time, when compared to the current peer-reviewed literature. The difference in absolute numbers between group A (Placido-disc guided) of 54 cases, and group B (Scheimpflug tomography-guided) of 127 is due to the early results suggesting that group B was of higher efficacy and thus, discontinuing recruitment of group A patients. Although different, these numbers and follow-up is still quite large and permits sensitive statistical analysis with confident conclusion of the differential in post-operative efficacy.

This change is more pronounced in the pre-operative more irregular and more decentrated anterior surfaces (subgroups A2 and B2), reaching up to a -41% reduction in the index of height decentration for group B2.

The above findings may be explained by the principles of operation of the corresponding diagnostic devices. Specifically, the Placido-disk imaging devices, despite providing a single, snap-shot measurement, are more suitable for peripheral cornea measurements, and have lower information reliability at the corneal center, in addition to being susceptible to error

due to abrupt corneal height changes. Specifically, Placido disc imaging cannot clearly differentiate between abrupt flattening to abrupt steepening changes, just measures curvature changes. This potential bias of measurement may be one, or the main, reason of the clinical efficacy difference in our data. On the other hand, the Scheimpflug imaging camera rotating measurement process, despite being sequential, captures images with a fine meshed dot matrix in the center, providing high-resolution data of absolute elevation from the large corneal area imaged. The potential bias here is the eyelid and eyelash interference in the image quality, as well as the potential bias of thickness measurement attributed to arcus senilis changes of the peripheral cornea. All Scheimpflug images used in our treatments are carefully screened in order to exclude these potential biases.

Conclusions

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

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Tables

Table 1

Best spectacle corrected distance visual acuity (CDVA) data, expressed decimally: Pre-operative, 12-month post-operative, and change (gain/loss), expressed as the difference of post minus the pre-operative CDVA.

	Pre-Operative		Post-Operative		Change (gain/loss)	
	Group A (Placido)	Group B (Scheimpflug)	Group A (Placido)	Group B (Scheimpflug)	Group A (Placido)	Group B (Scheimpflug)
average	0.65	0.63	0.77	0.82	0.12	0.19
StDev	± 0.23	± 0.24	± 0.19	± 0.19	± 0.20	± 0.20
Max	1.00	1.00	1.10	1.20	0.60	0.75
Min	0.00	0.00	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

Table 2

Average, standard deviation (StDev), maximum (Max) and minimum (Min) anterior and posterior corneal keratometry and topometric indices, as measured in the 8 mm zone for both groups, pre- and 12-months post-operatively. 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.

Group A	**Placido**	**Pre-Op**					**Post-Op**			
		average	stdev	max	min		average	stdev	max	min
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	ISV	91.33	± 42.59	187	14		86.70	± 43.91	190	14
(in 8mm zone)	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**	**Pre-Op**					**Post-Op**			
		average	stdev	max	min		average	stdev	max	min
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	ISV	98.14	± 45.32	208	18		80.13	± 35.98	169	15
(in 8mm zone)	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

Table 3

Induced changes for the seven anterior-surface indices for the two groups. Average change is defined as post-operative minus the pre-operative value). Relative change is defined as % of the average change of the parameter with regard to the respective preoperative value.

	ISV	IVA	KI	CKI	IHA	IHD	Rmin (mm)
	Group A (Placido)						
relative change	-5.07%	-5.65%	-3.20%	-1.42%	-15.24%	-26.81%	2.18%
average change	-4.630	-0.060	-0.040	-0.015	-3.991	-0.023	0.139
stdev	± 16.617	± 0.225	± 0.066	± 0.055	± 21.003	± 0.027	± 0.263
max	29	0.45	0.07	0.06	40.6	0.023	1.31
min	-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%
average change	-18.016	-0.175	-0.079	-0.034	-7.150	-0.035	0.585
stdev	± 20.687	± 0.253	± 0.073	± 0.042	± 17.087	± 0.036	± 0.409
max	38	0.42	0.08	0.06	37.7	0.017	1.93
min	-83	-0.95	-0.43	-0.22	-65.1	-0.213	-0.22

Table 4

Two-sample t-test results, not assuming equal variances, between the keratoconus grading subgroups (KC1, KC1-2, KC2, KC2-3, KC3, KC3-4, KC4) for the ISV and IHD topometric indices as measured pre-operatively. Abbreviations: ISV, index of surface variance; IHD, index of height decentration; CI, Confidence interval.

ISV	Estimate for difference:	95% CI for difference:	P-Value
K1 vs K1-2	10.31	(7.35, 13.27)	<0.001
K1-2 vs K2	21.84	(17.87, 25.82)	<0.001
K2 vs K2-3	21.02	(17.02, 25.03)	<0.001
K2-3 vs K3	20.3	(16.88, 23.72)	<0.001
K3 vs K3-4	43.7	(37.79, 49.62)	<0.001
K3-4 vs K4	61	(14.1, 107.8)	0.026

IHD	Estimate for difference:	95% CI for difference:	P-Value
K1 vs K1-2	0.01255	(0.00474, 0.02035)	0.003
K1-2 vs K2	0.02411	(0.01522, 0.03300)	<0.001
K2 vs K2-3	0.02012	(0.01038, 0.02985)	<0.001
K2-3 vs K3	0.01856	(0.00836, 0.02876)	0.001
K3 vs K3-4	0.04487	(0.03165, 0.05808)	<0.001
K3-4 vs K4	0.0888	(0.0610, 0.1166)	<0.001

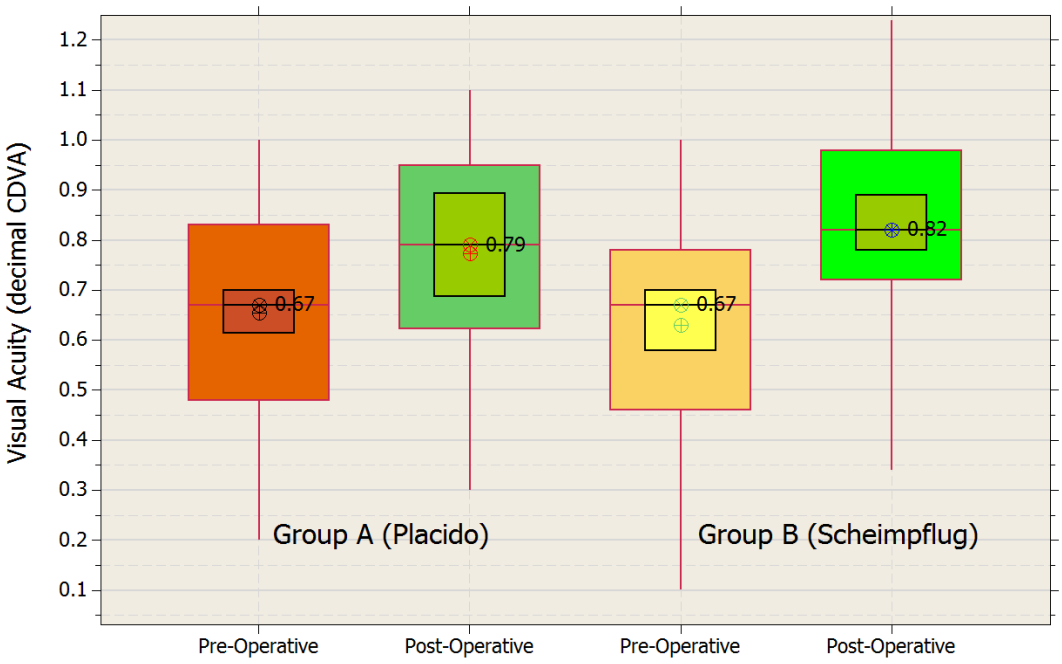
Table 5

Induced changes for the ISV and IHD indices for the four sub groups. Average change is derived from the post-operative minus the pre-operative value in each case. Relative change is defined as % of the average change of the parameter with regard to the respective preoperative value. Abbreviations: ISV, index of surface variance; IHD, index of height decentration

	ISV	IHD		ISV	IHD
	Group A1 – Placido Low			**Group A2 – Placido High**	
relative	-4.61%	-22.10%		-5.35%	-29.05%
average	-2.900	-0.011		-6.792	-0.038
stdev	± 17.010	± 0.020		± 16.208	± 0.026
max	29	0.023		23	0.013
min	-50	-0.054		-36	-0.102
	Group B1 – Scheimpflug Low			**Group B2 – Scheimpflug High**	
relative	-13.54%	-32.82%		-20.36%	-41.19%
average	-8.908	-0.016		-26.750	-0.054
stdev	± 18.339	± 0.020		± 18.968	± 0.037
max	38	0.014		13	0.017
min	-48	-0.074		-83	-0.213

Figures Figure 1

Box plots of CDVA (expressed decimally): (Top) Pre-operative, and post-operative values for both groups. (Bottom) Gain/loss expressed as difference between post- minus pre-operative CDVA. 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).



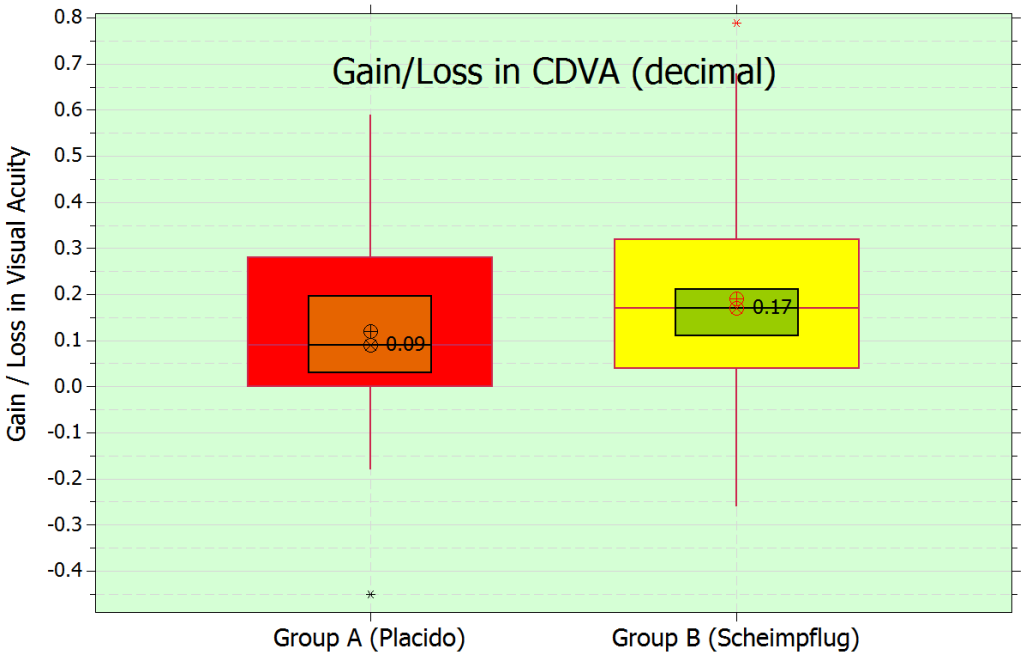
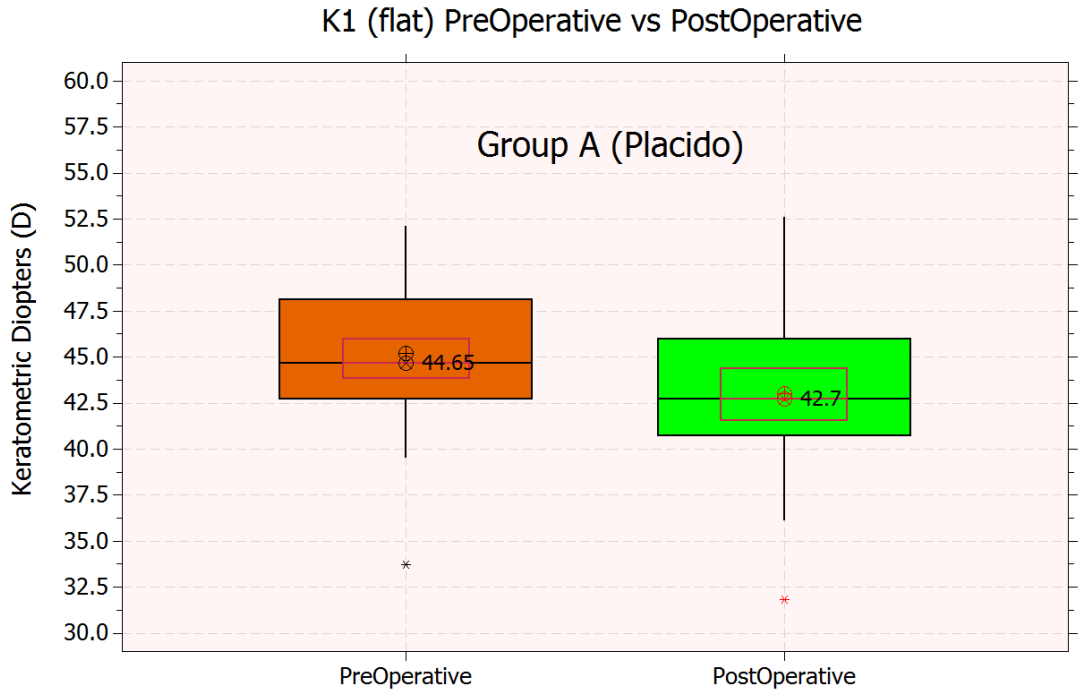


Figure 2a

Box plot describing induced changes (comparison pre- to post-operative values) for anterior flat (top) and steep (bottom) keratometry (in diopters, D) for group A (Placido). 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.



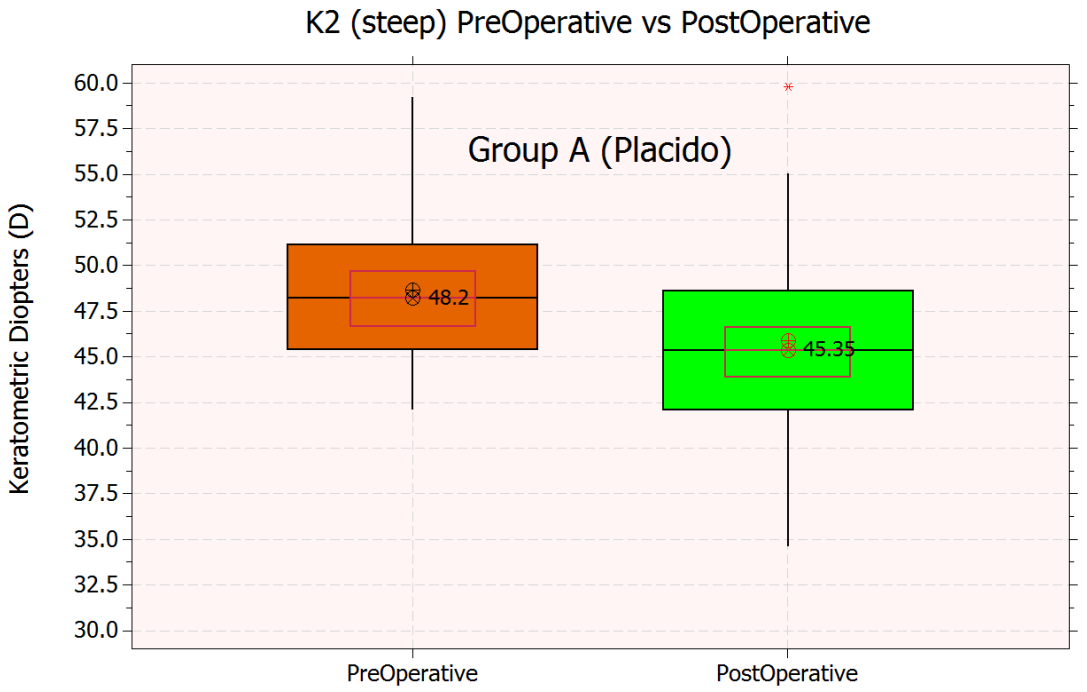
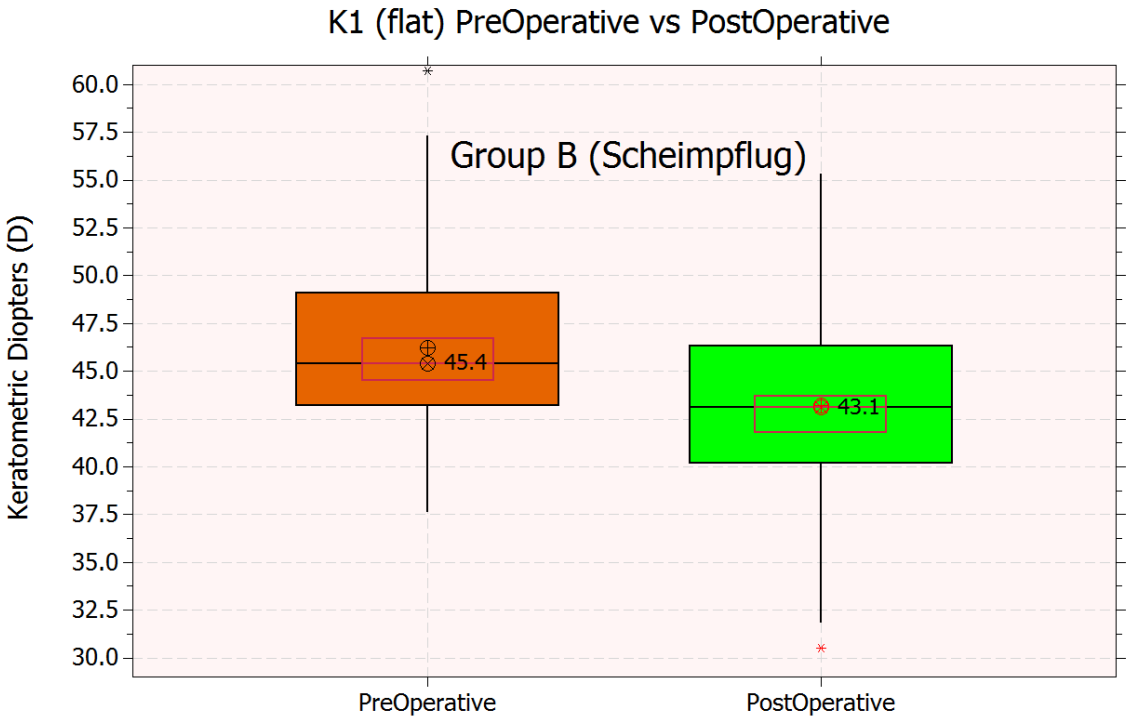


Figure 2b

Box plot describing induced changes (comparison pre- to post-operative values) for anterior flat (top) and steep (bottom) keratometry (in diopters, D) for group B (Scheimpflug). 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.



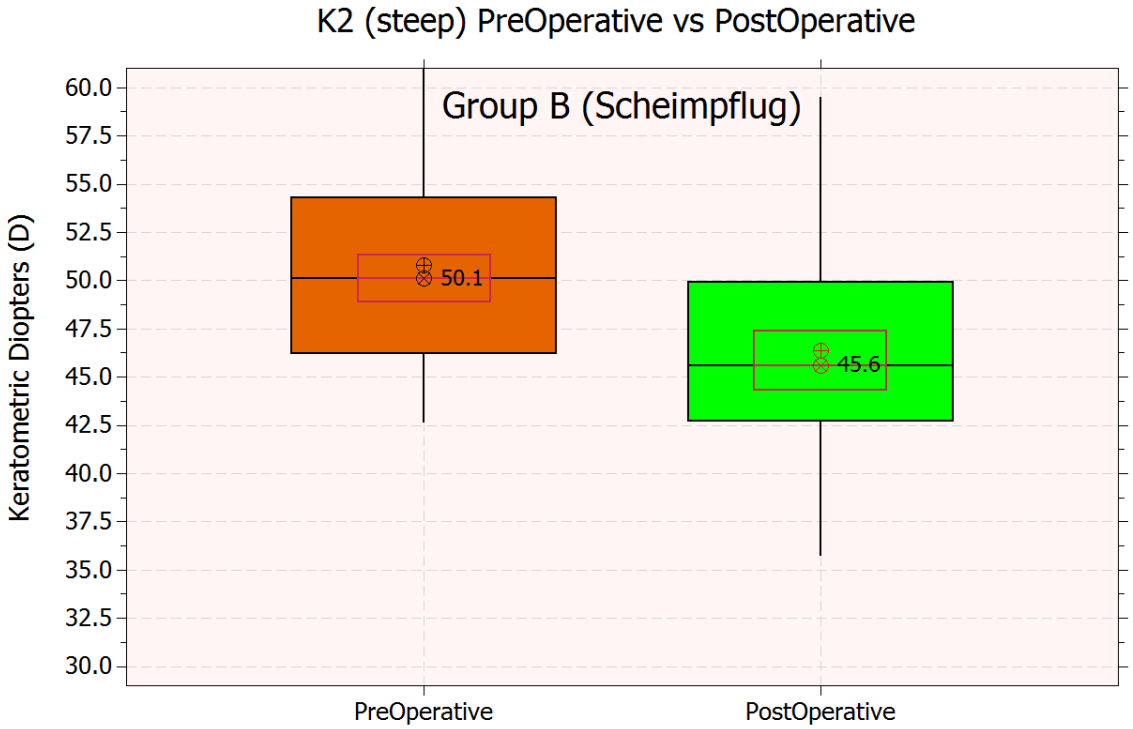


Figure 3

Top, box plot of pre-operative ISV (Index of Surface Variance) and bottom, preoperative IHD (Index of Height Decentration) vs keratoconus grading, as produced by the Oculyzer software. 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.

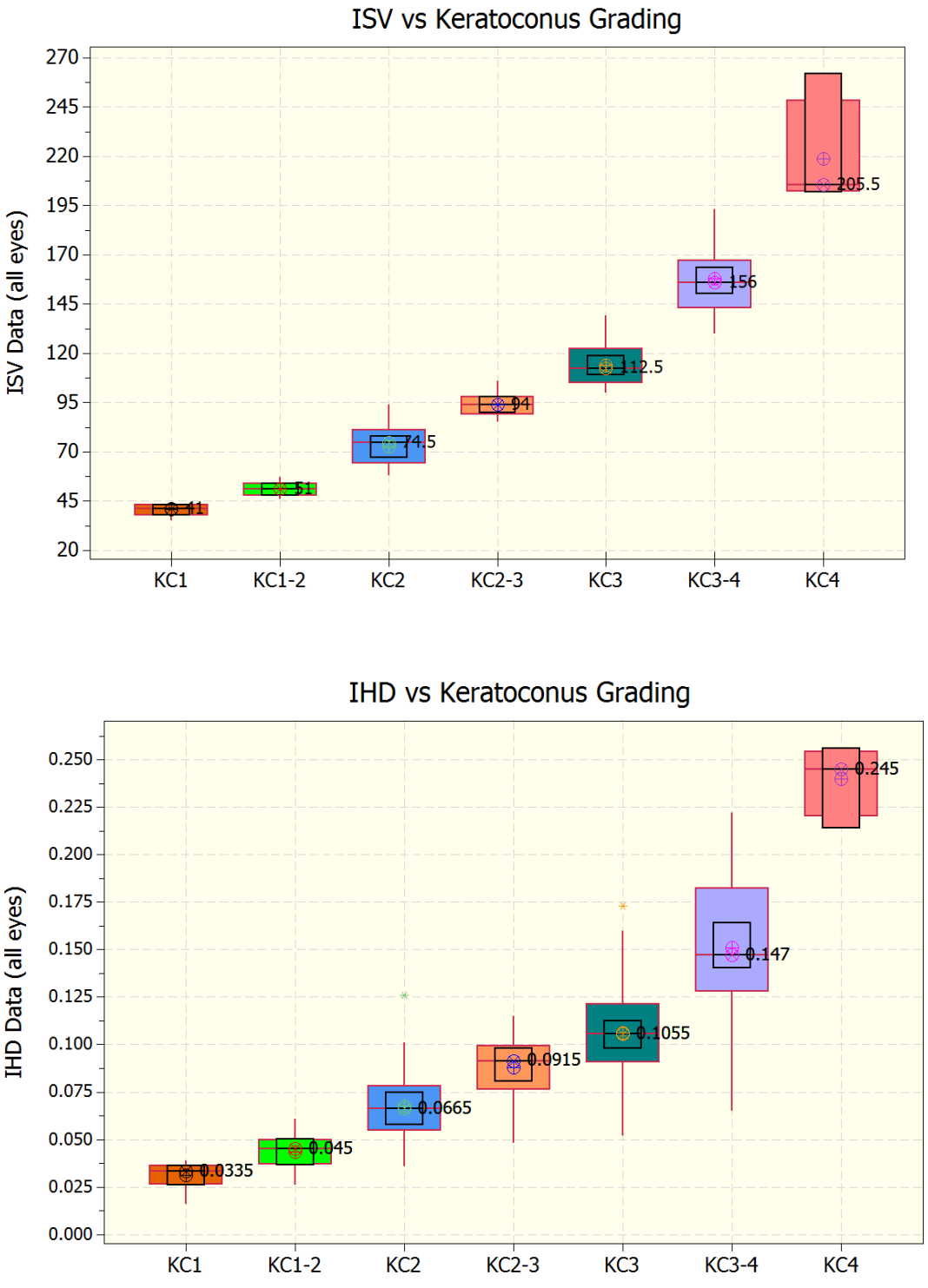


Figure 4

Box plot describing induced changes (comparison of pre to post-operative values) for the index of surface variance (ISV) for the two groups: top, group A, Placido, and bottom, group B, Scheimpflug. 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.

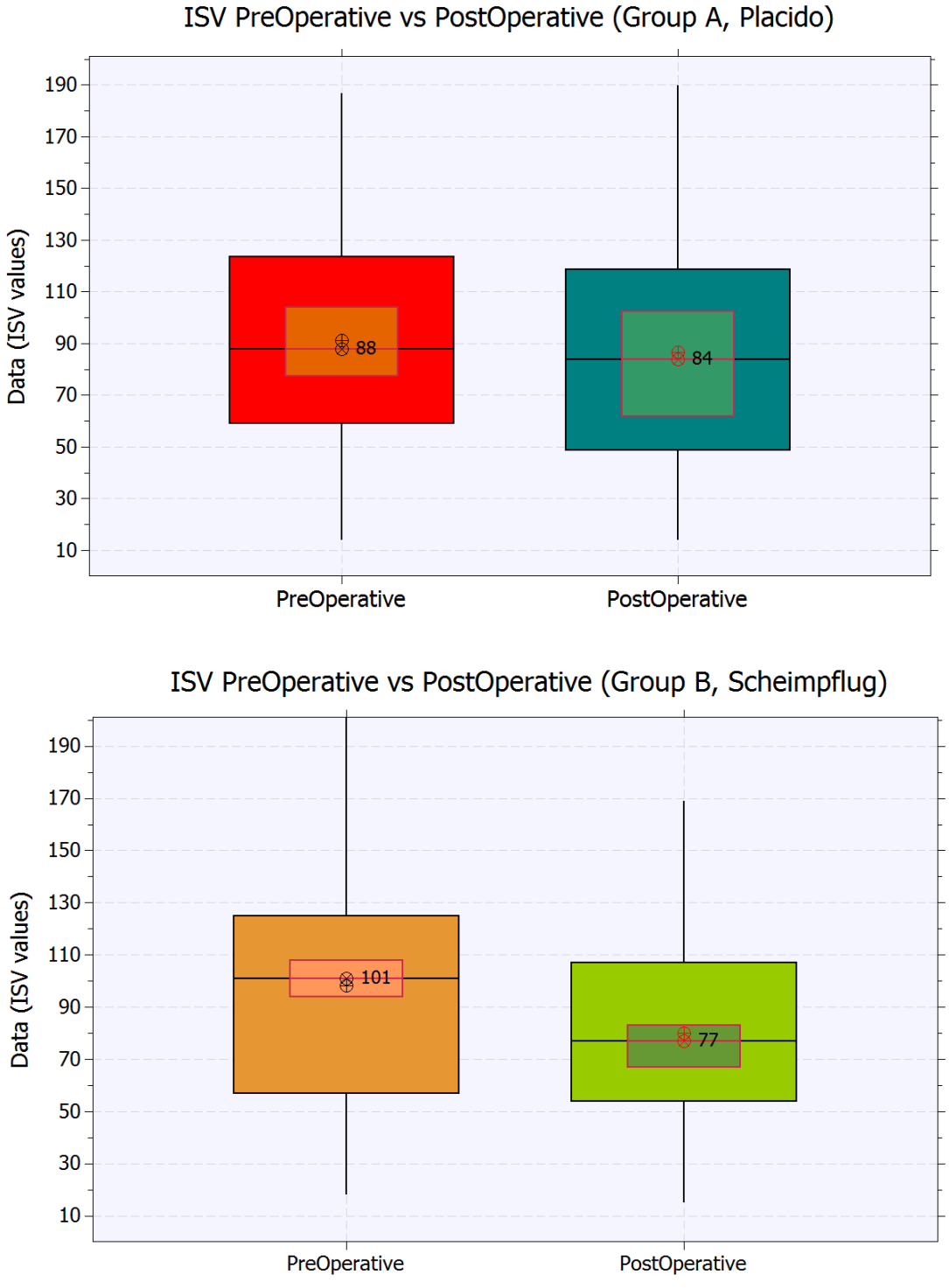
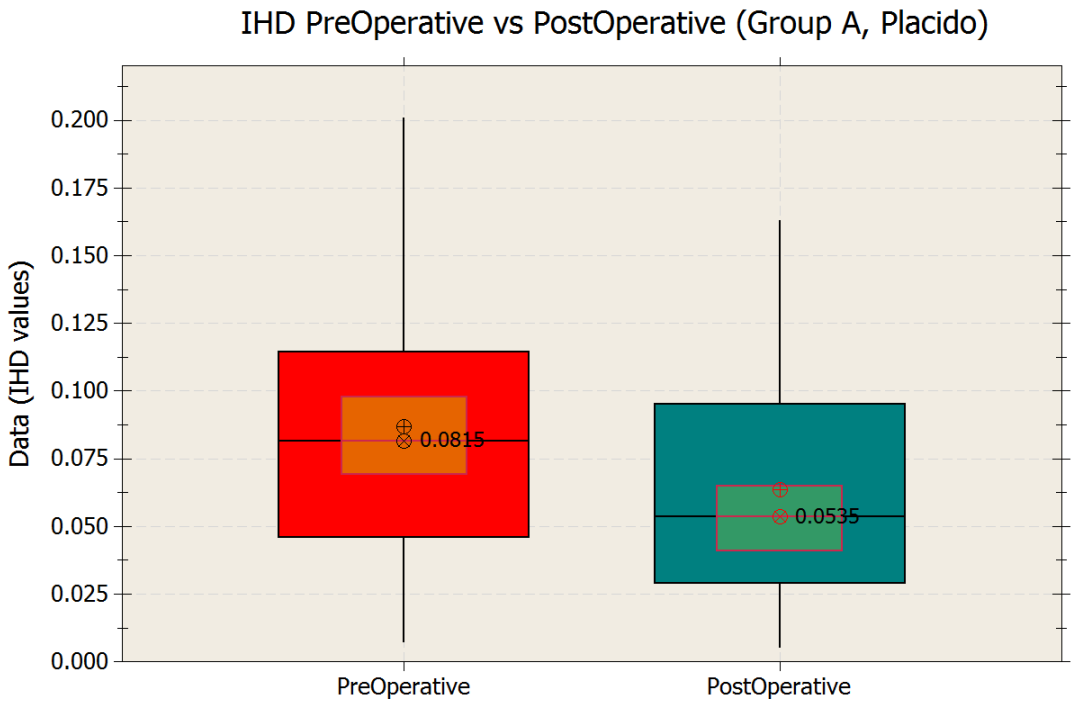


Figure 5

Box plot describing induced changes (comparison of pre to post-operative values) for the index of height decentration (IHD) for the two groups: top, group A, Placido, and bottom, group B, Scheimpflug. 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.



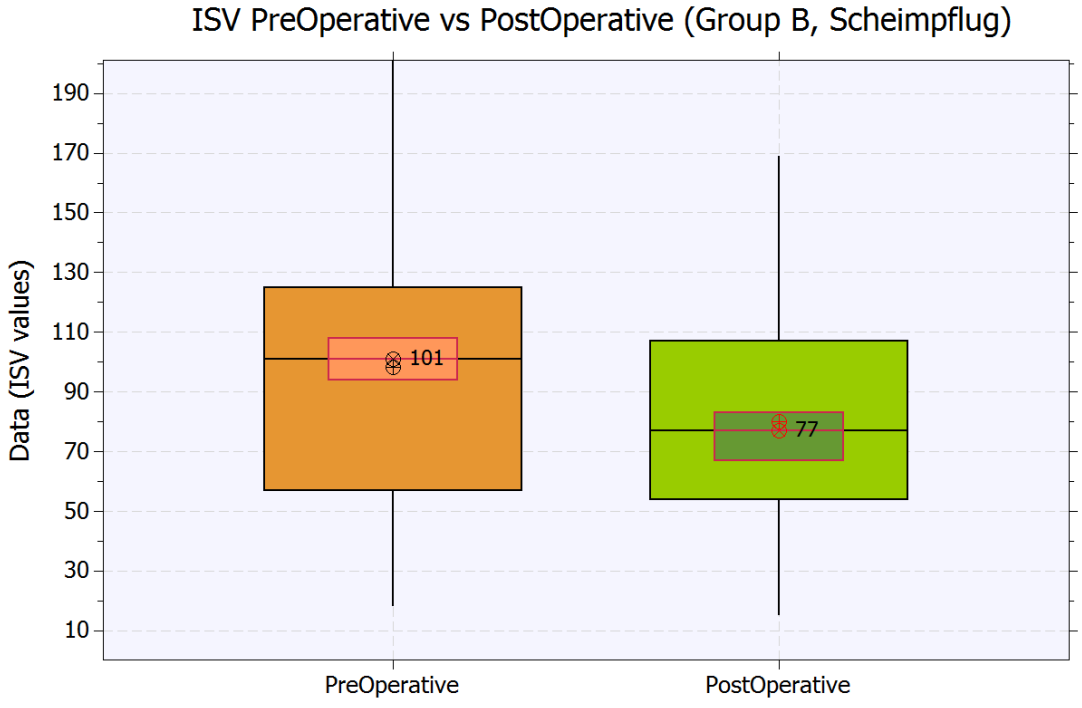


Figure 6a

Box plot describing induced changes (comparison of pre to post-operative values) for the index of height decentration (IHD) for the subgroups: top, group A1 – Placido Low, indicating less affected keratoconic eyes, and bottom, group A2 – Placido High, indicating more affected keratoconic eyes.

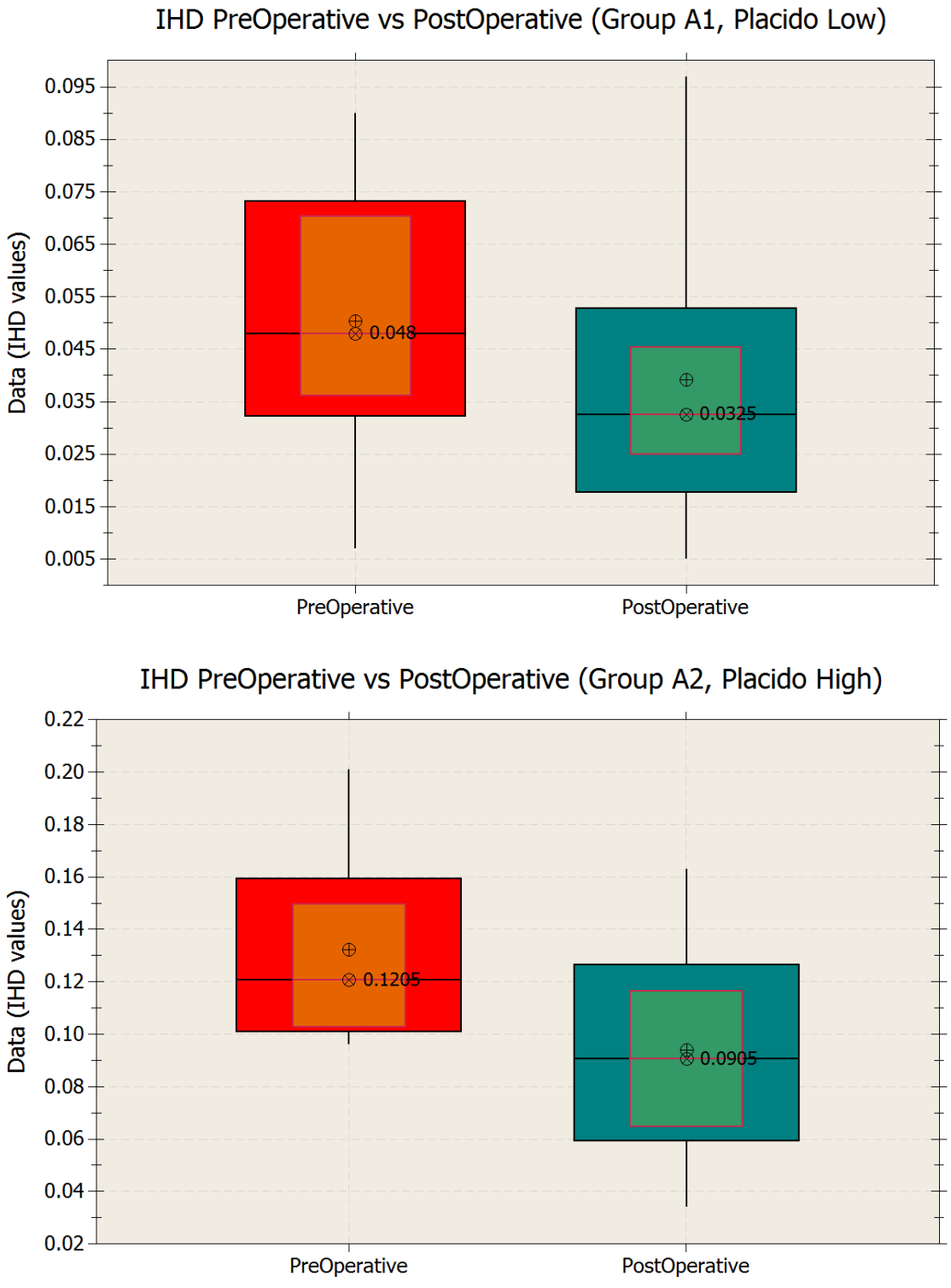
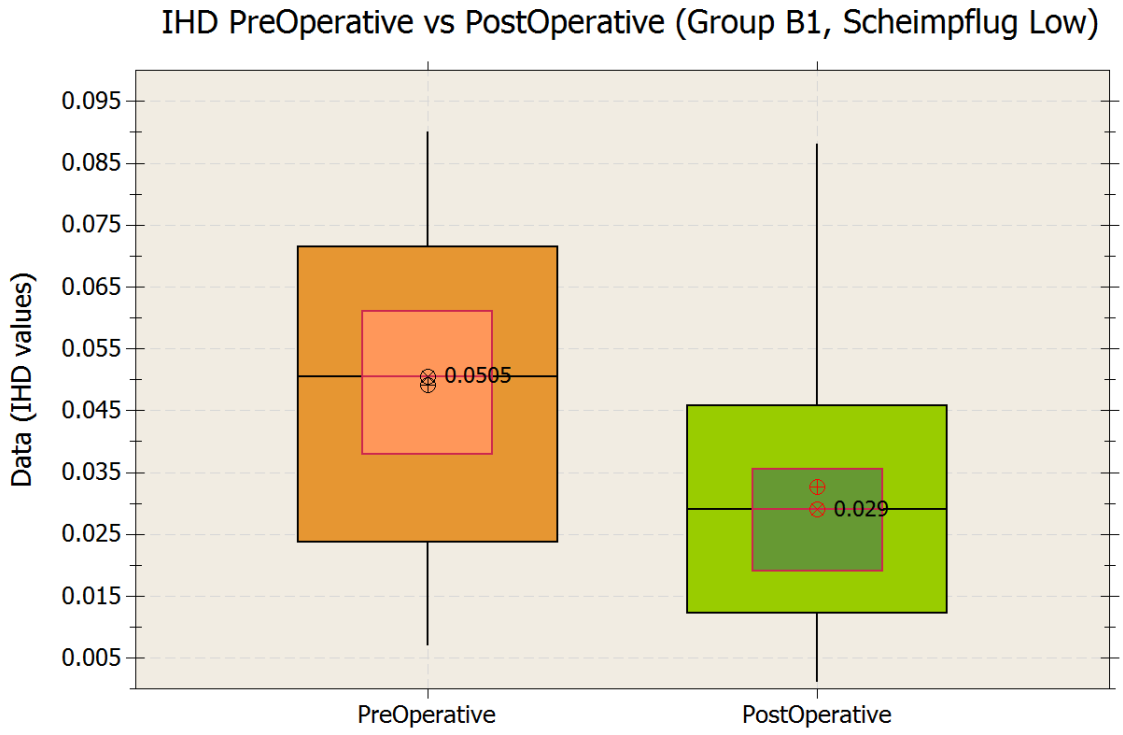
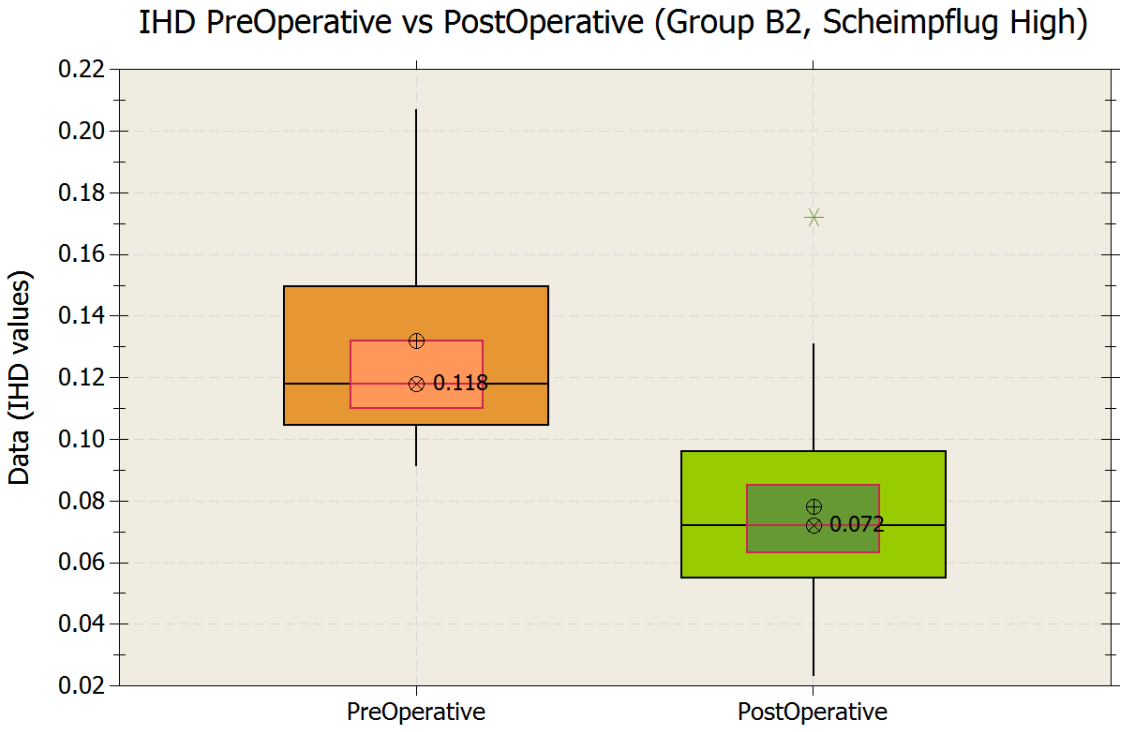


Figure 6b

Box plot describing induced changes (comparison of pre to post-operative values) for the index of height decentration (IHD) for the subgroups: top, group B1 – Scheimpflug Low, indicating less affected keratoconic eyes, and bottom, group B2 – Scheimpflug High, indicating more affected keratoconic eyes.





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