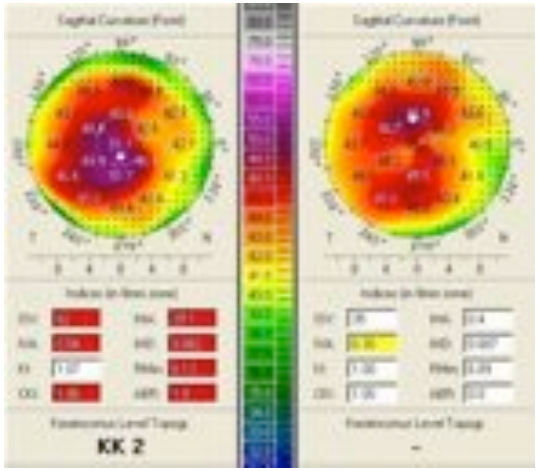
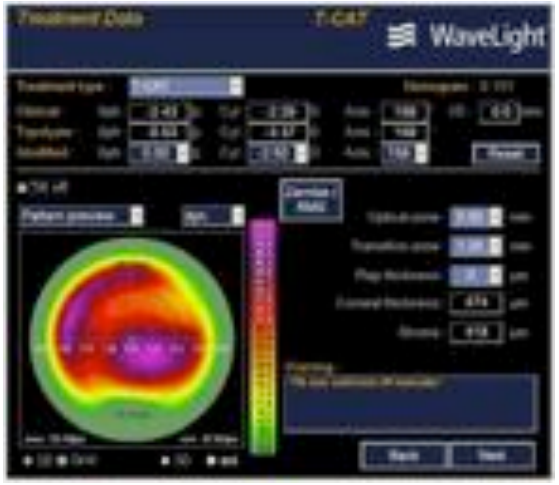
Keratoconus





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Clinical Ophthalmology

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ORIGINAL RESEARCH

Revisiting keratoconus diagnosis and progression classification based on evaluation of corneal asymmetry indices, derived from Scheimpflug imaging in keratoconic and suspect cases

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

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

Purpose: To survey the standard keratoconus grading scale (Pentacam®-derived Amsler–Krumeich stages) compared to corneal irregularity indices and best spectacle-corrected distance visual acuity (CDVA).

Patients and methods: Two-hundred and twelve keratoconus cases were evaluated for keratoconus grading, anterior surface irregularity indices (measured by Pentacam imaging), and subjective refraction (measured by CDVA). The correlations between CDVA, keratometry, and the Scheimpflug keratoconus grading and the seven anterior surface Pentacam-derived topometric indices – index of surface variance, index of vertical asymmetry, keratoconus index, central keratoconus index, index of height asymmetry, index of height decentration, and index of minimum radius of curvature – were analyzed using paired two-tailed *t*-tests, coefficient of determination (r^2), and trendline linearity.

Results: The average ± standard deviation CDVA (expressed decimally) was 0.626 ± 0.244 for all eyes (range 0.10–1.00). The average flat meridian keratometry was (K1) 46.7 ± 5.89 D; the average steep keratometry (K2) was 51.05 ± 6.59 D. The index of surface variance and the index of height decentration had the strongest correlation with topographic keratoconus grading ($P < 0.001$). CDVA and keratometry correlated poorly with keratoconus severity.

Conclusion: It is reported here for the first time that the index of surface variance and the index of height decentration may be the most sensitive and specific criteria in the diagnosis, progression, and surgical follow-up of keratoconus. The classification proposed herein may present a novel benchmark in clinical work and future studies.

Keywords: diagnosis and classification, Pentacam topometric indices, Amsler–Krumeich keratoconus grading, surface variance, vertical asymmetry, keratoconus index, central keratoconus index, height asymmetry, height decentration, minimum radius of curvature

Video abstract

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Introduction

Keratoconus is described as a degenerative bilateral, progressive, noninflammatory corneal disorder characterized by ectasia, thinning, and increased curvature.[1,2] It is associated with loss of visual acuity particularly in relation to progressive cornea irregularity,[3,4] and usually is manifested asymmetrically between the two eyes of the same patient.[5,6] Occasionally, the patient may present with symptoms of photophobia, glare, and monocular diplopia.

The problem of specificity and sensitivity of keratoconus assessment, particularly the diagnosis of early signs of ectasia and/or subclinical keratoconus, and for monitoring the progression of the disease, has been extensively studied.[7] The commonly used

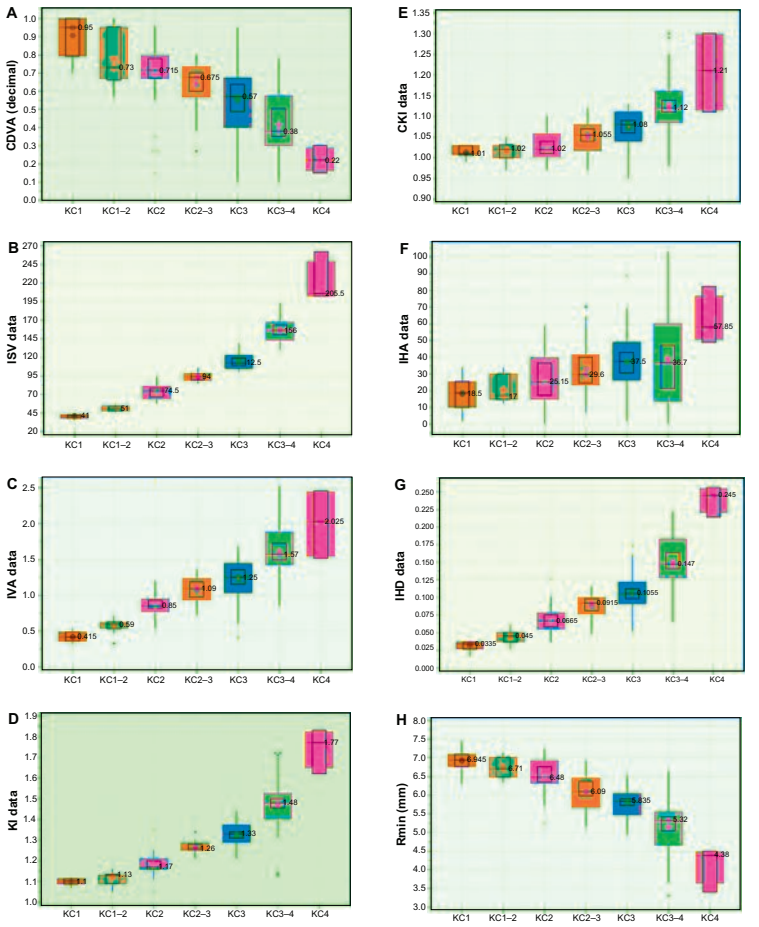


Figure 2 Box plots of measured parameters versus keratoconus grading, as produced by the Oculyzer™ software, showing median level (indicated by □), average symbol (□), 95% median confidence range box (black line boxes), and interquartile intervals range box (red line boxes). (**A**) CDVA versus keratoconus grading. (**B**) ISV versus keratoconus grading. (**C**) IVA versus keratoconus grading. (**D**) KI versus keratoconus grading. (**E**) CKI versus keratoconus. (**F**) IHA versus keratoconus grading. (**G**) IHD versus keratoconus grading. (**H**) Rmin versus keratoconus grading.

Abbreviations: CDVA, best spectacle-corrected distance visual acuity; CKI, central keratoconus index; IHA, index of height asymmetry; IHD, index of height decentration; ISV, index of surface variance; IVA, index of vertical asymmetry; KC1, keratoconus grading Stage I; KC1–2, keratoconus grading Stage I–II; KC2, keratoconus grading Stage II, KC2–3, keratoconus grading Stage II–III; KC3, keratoconus grading Stage III; KC3–4, keratoconus grading Stage III–IV; KC4, keratoconus grading Stage IV; KI, keratoconus index; PI, prediction interval; Rmin, minimum radius of curvature.

Methods

212 cases were evaluated for keratoconus grading, anterior surface irregularity indices (measured by Pentacam imaging), and subjective refraction (measured by CDVA). The correlations between CDVA, keratometry, and the Scheimpflug keratoconus grading and the seven anterior surface Pentacam-derived topometric indices – index of surface variance, index of vertical asymmetry, keratoconus index, central keratoconus index, index of height asymmetry, index of height decentration, and index of minimum radius of curvature – were analyzed using paired two-tailed *t*-tests, coefficient of determination (r2), and trendline linearity.

Results

- The average ± standard deviation CDVA (expressed decimally) was 0.626 ± 0.244 for all eyes (range 0.10–1.00). The average flat meridian keratometry was (K1) 46.7 ± 5.89 D; the average steep keratometry (K2) was 51.05 ± 6.59 D.
- The index of surface variance and the index of height decentration had the strongest correlation with topographic keratoconus grading (*P* , 0.001). CDVA and keratometry correlated poorly with keratoconus severity.

Table 1 Collective average, standard deviation, maximum, and minimum anterior keratometry and topometric indices, as measured in the 8 mm zone

	Average	SD	Max	Min
Anterior cornea				
K1 – flat (D)	46.78	±5.89	78.50	33.70
K2 – steep (D)	51.05	±6.59	80.70	42.10
Km – mean (D)	48.80	±6.05	78.80	40.60
Astigmatism (D)	−2.10	±6.05	+11.30	−12.40
Anterior surface topometric indices				
ISV	98.99	±47.43	262	14
IVA (mm)	1.05	±0.52	2.52	0.09
KI	1.28	±0.17	1.83	0.97
CKI	1.06	±0.07	1.30	0.90
IHA (μm)	30.60	±22.21	103.00	0.20
IHD (μm)	0.091	±0.054	0.256	0.005
Rmin (mm)	6.07	±0.88	7.73	3.30
CDVA				
Decimal	0.63	±0.25	1.00	0.10

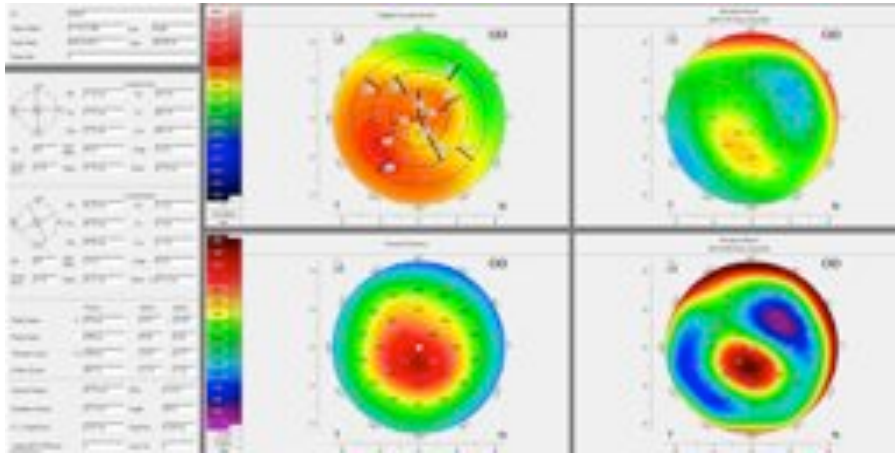
Abbreviations: CDVA, best spectacle-corrected distance visual acuity; CKI, central keratoconus index; IHA, index of height asymmetry; IHD, index of height decentration; ISV, index of surface variance; IVA, index of vertical asymmetry; KI, keratoconus index; Max, maximum; Min, minimum; Rmin, minimum radius of curvature; SD, standard deviation.

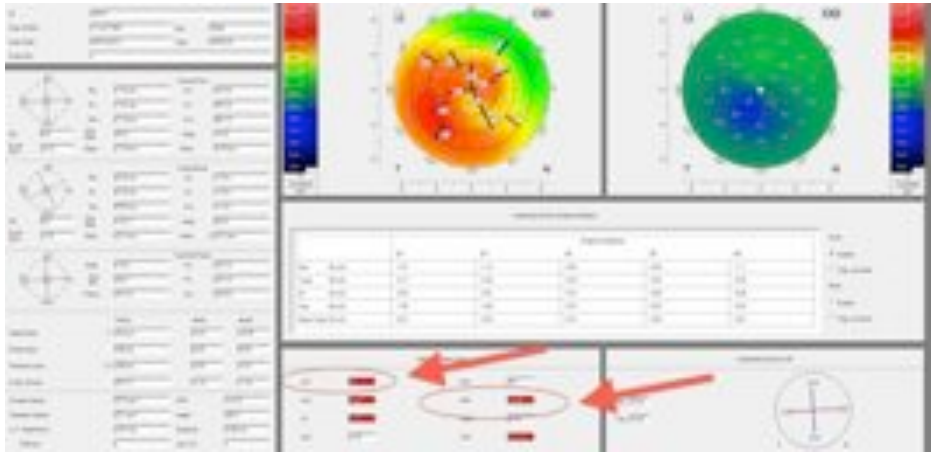
- **ISV**: the unitless standard deviation of individual corneal sagittal radii from the mean curvature. ISV is thus an expression of the corneal surface irregularity.
- **IHD:** the value of the decentration of elevation data in the vertical direction (expressed in μm), and is calculated from a Fourier analysis. This index provides the degree of decentration in the vertical direction, calculated on a ring with radius 3 mm. An IHD value larger than 0.014 is considered abnormal, and larger than 0.016 is pathological.
-


Revisiting the Diagnosis and Progression criteria of Keratoconus

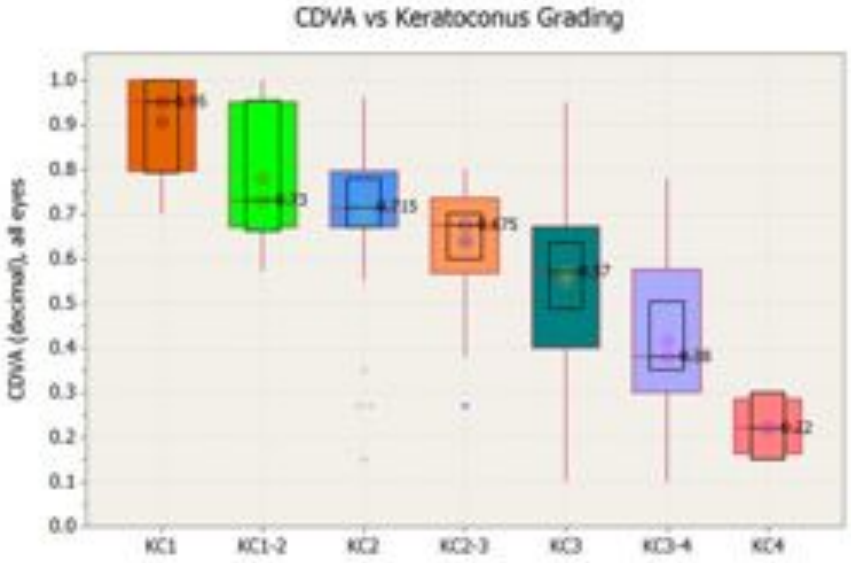
Traditionally:

- Visual acuity
- Refraction
- Pachymetry
- Keratometry
- Anterior inferior asymmetry

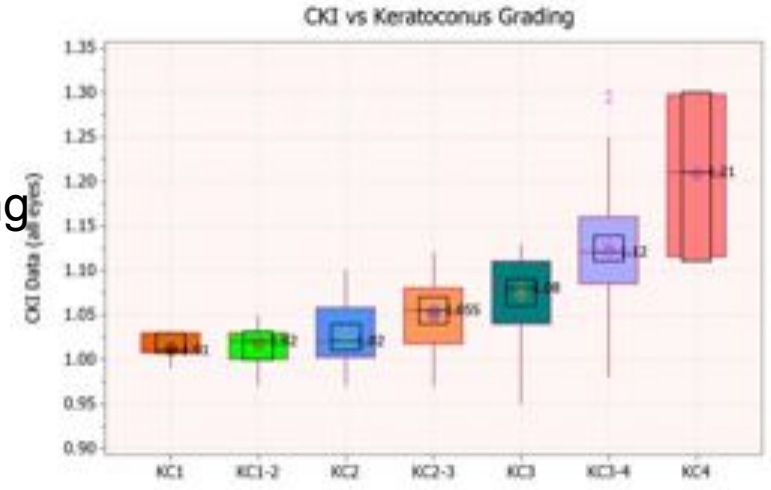


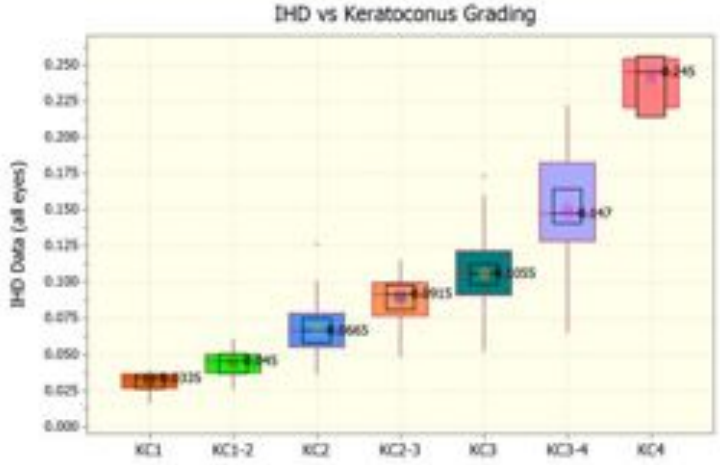


Vision, Ks, pach=irrelavant in 700 KCN cases test ISV and IHD!

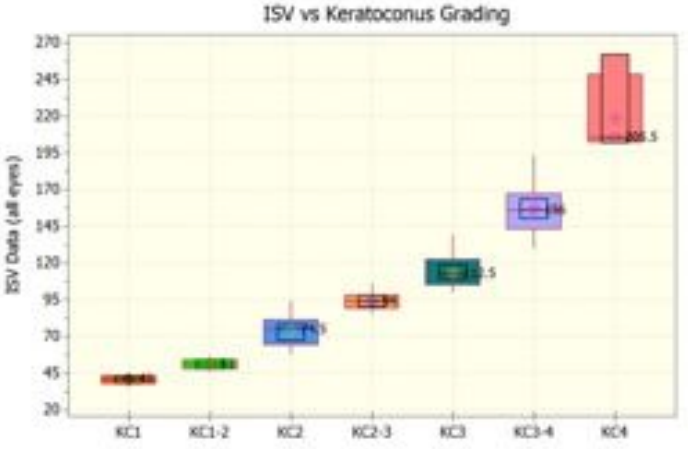


overlapping

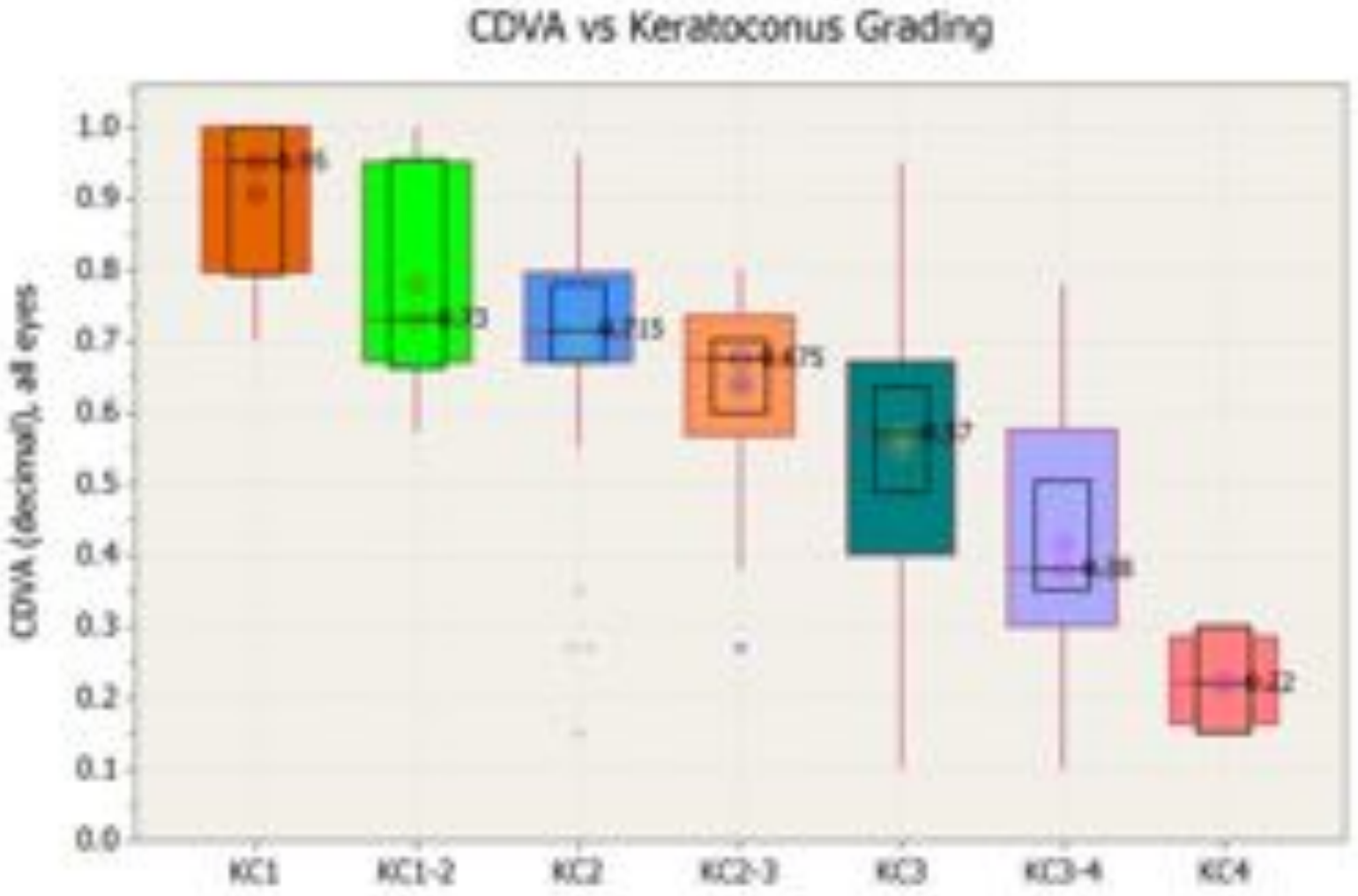


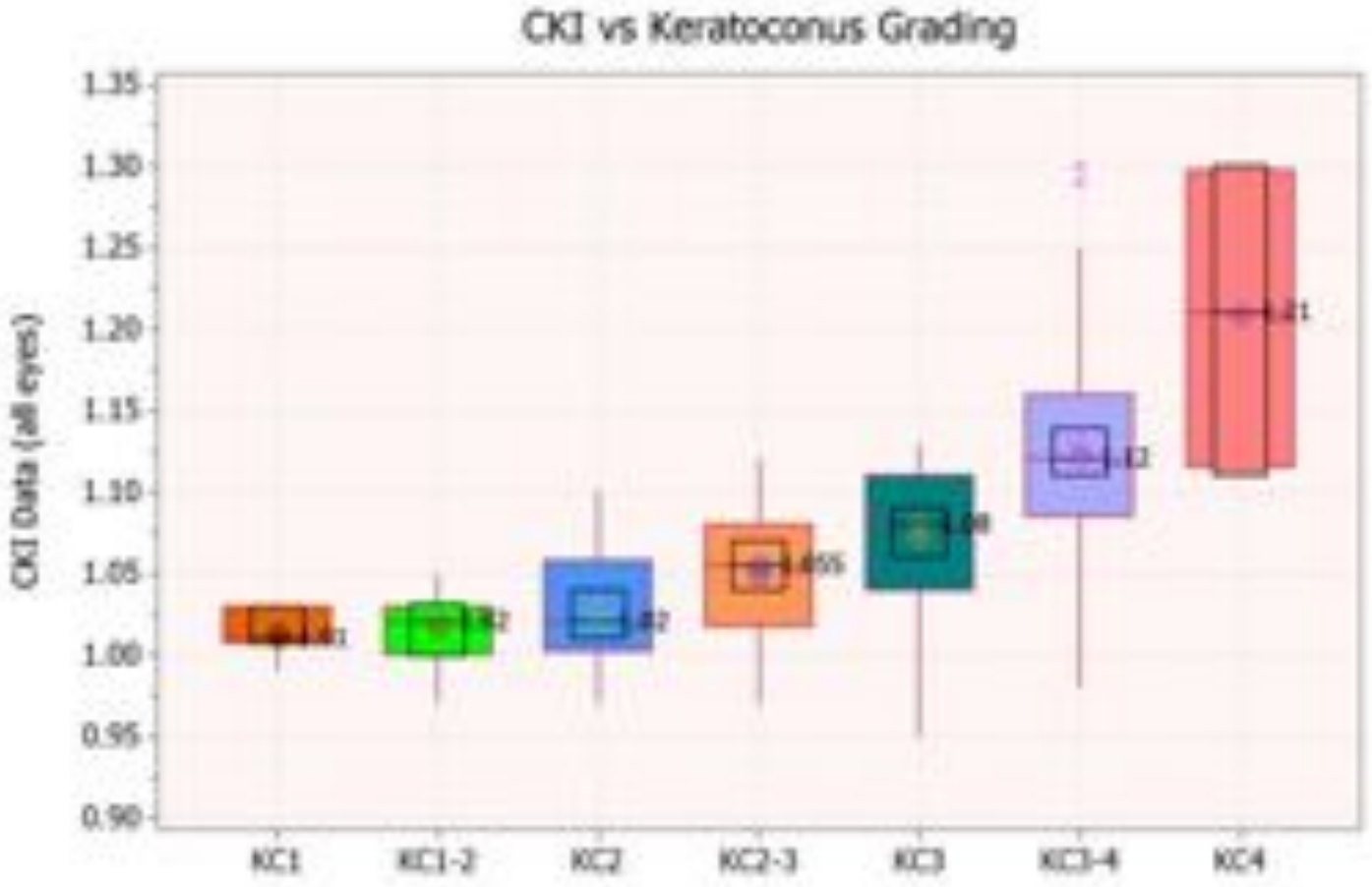


Stratification
Of severity

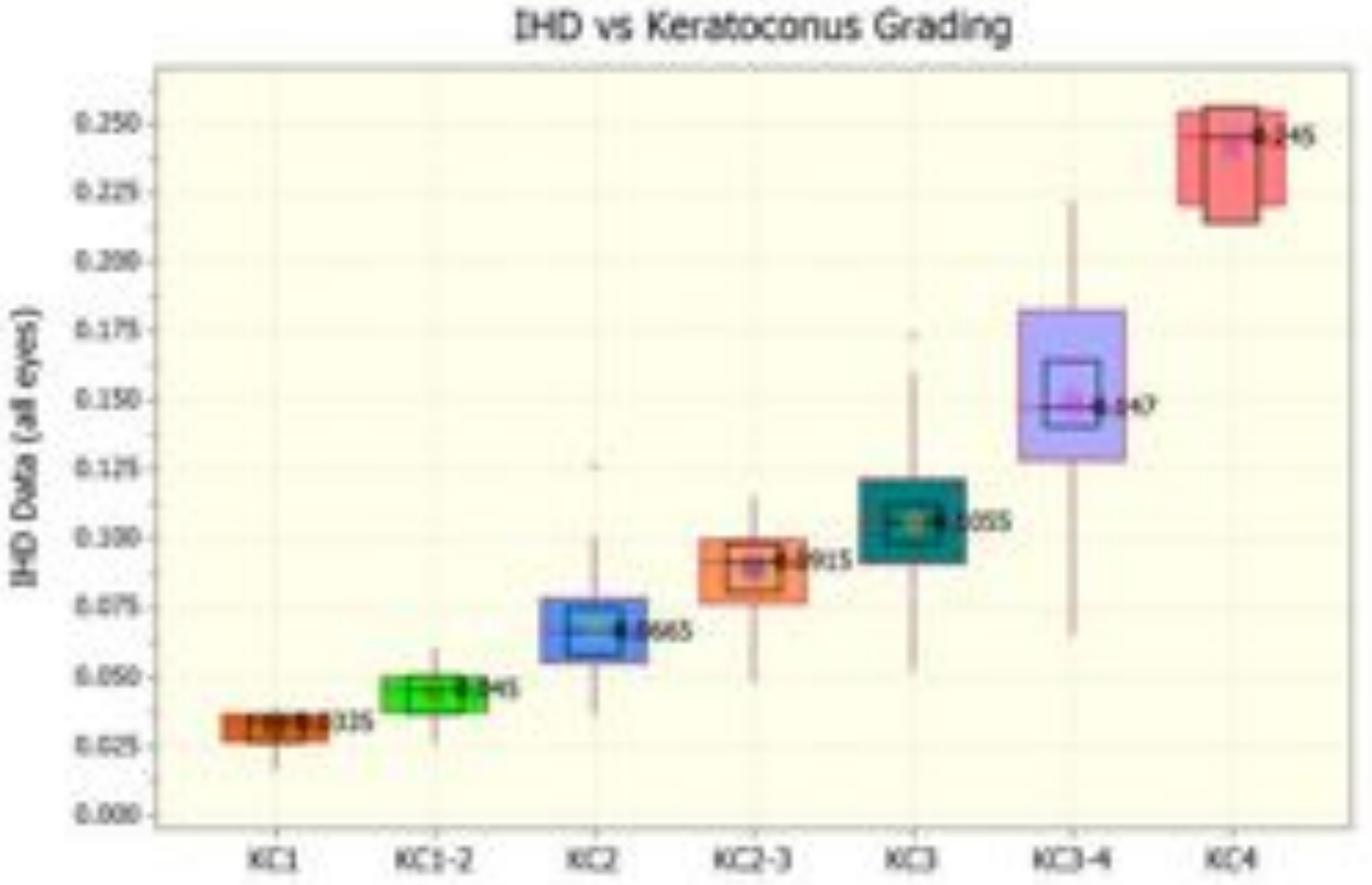


CDVA correlation with Amsler-Krumeich Criteria

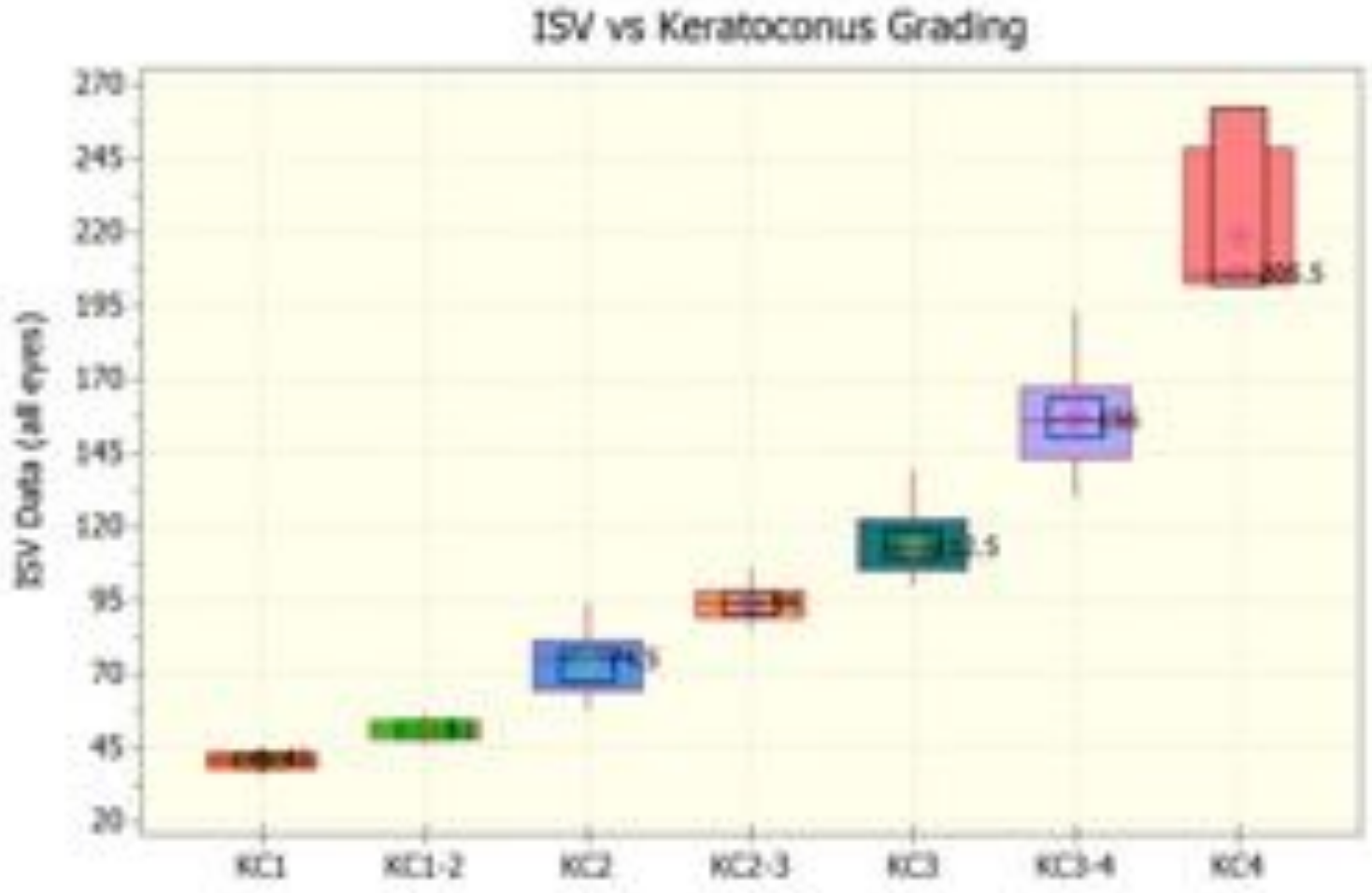


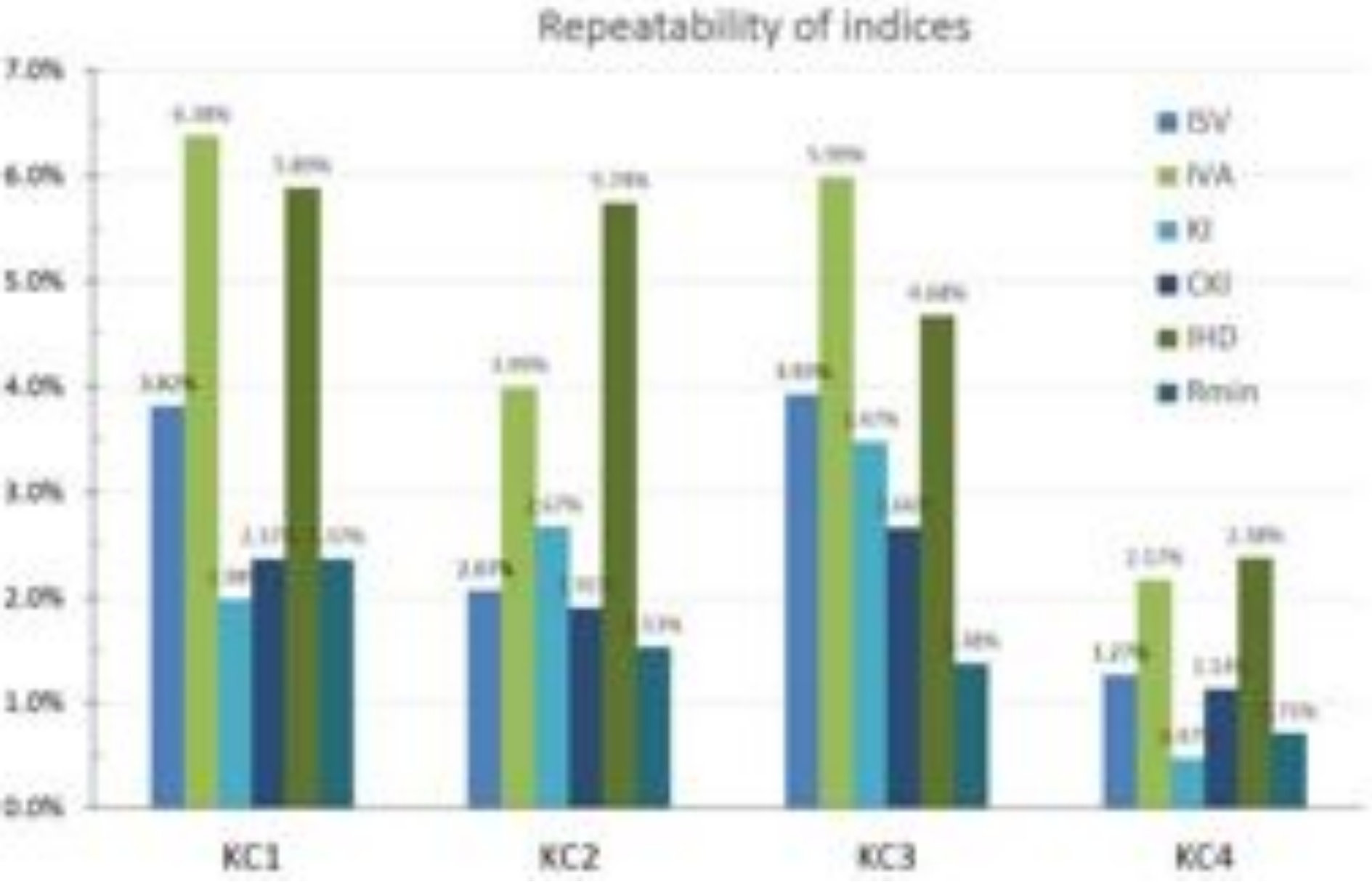

CKI vs Keratoconus Grading
CKI Data (all eyes)
1.35
1.30
1.25
1.20
1.15
1.10
1.05
1.00
0.95
0.90
KC1
KC1-2
KC2
KC2-3
KC3
KC3-4
KC4

Index of Height Decentration



Index of Surface Variance





New York University School of Medicine

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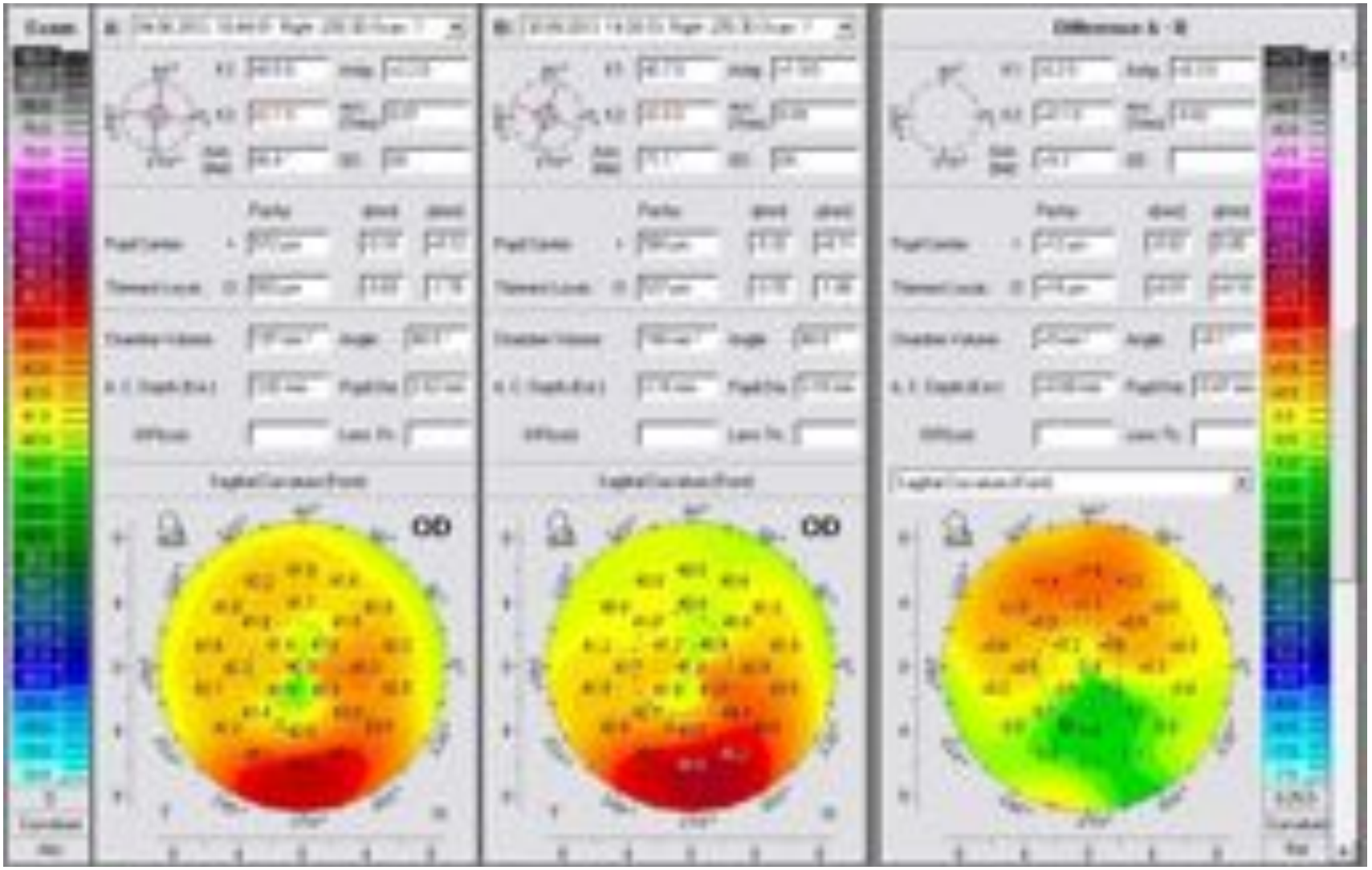
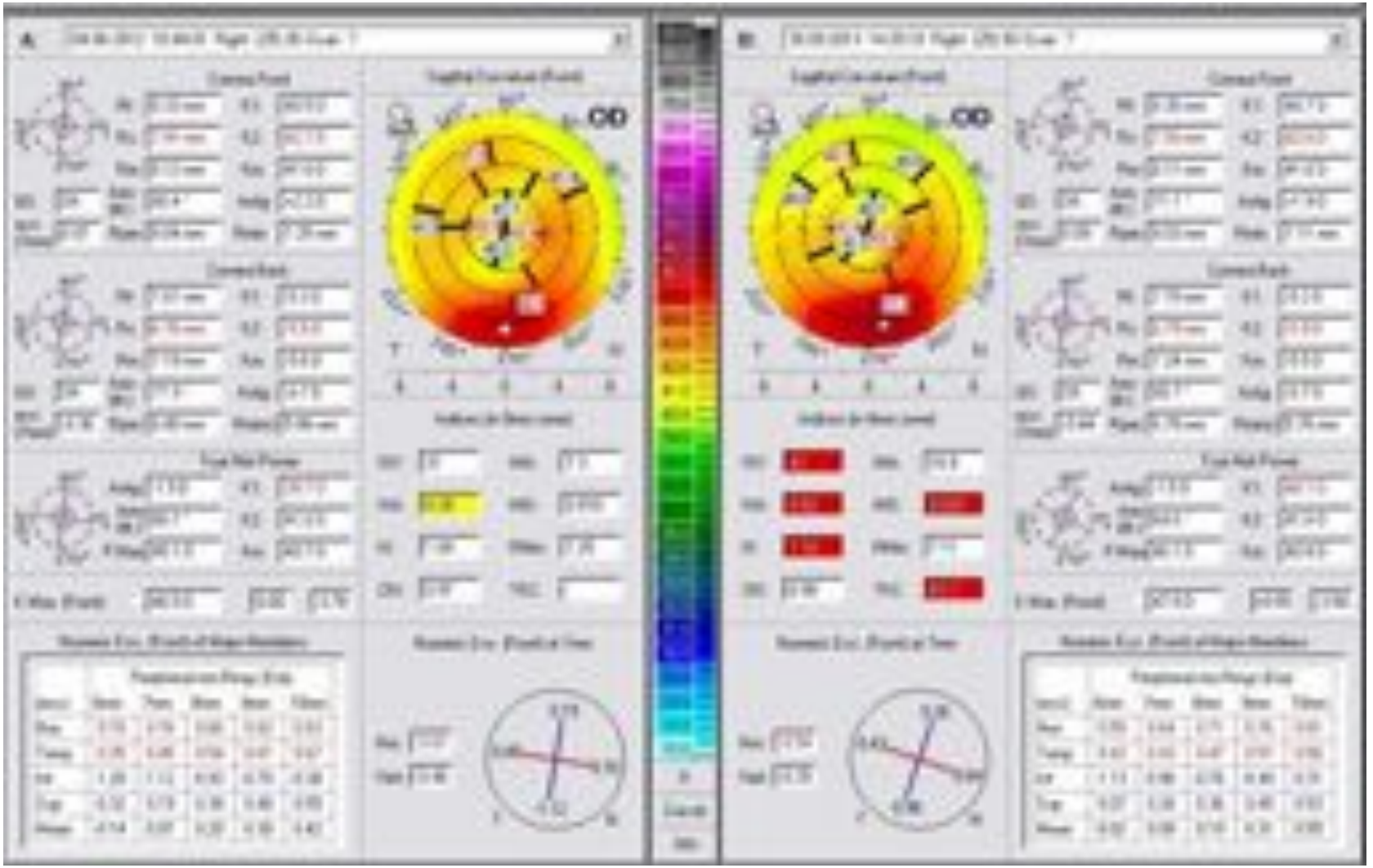
Conclusions

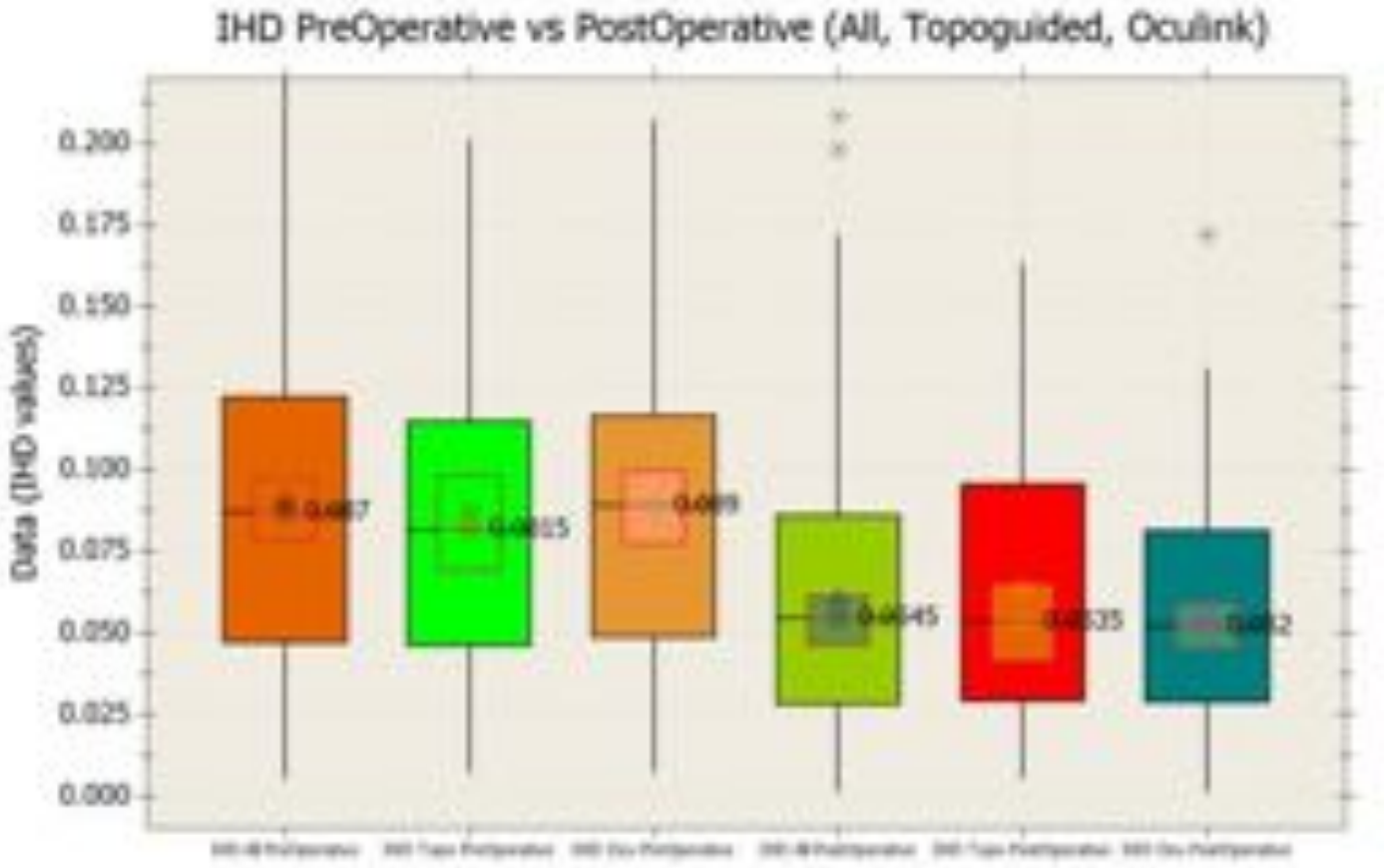
- ISV The index of surface variance and the
- IHD index of height decentration had the **strongest correlation with topographic keratoconus grading** (*P* , 0.001).
- CDVA and keratometry **correlated poorly** with keratoconus severity.



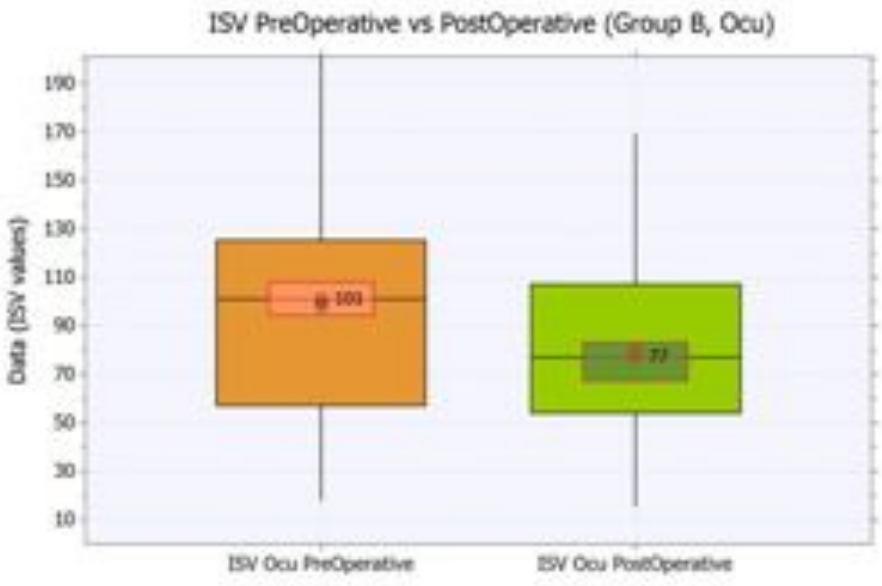


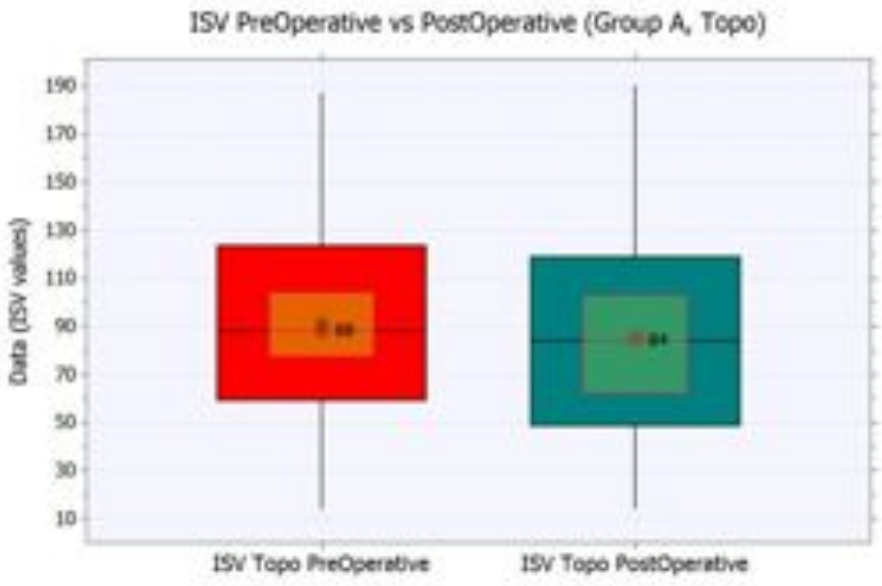
Comparison of Placido disc Vs Scheimpflug

image-derived topography-guided excimer laser surface normalization used combined with CXL (the Athens Protocol) in progressive keratoconus cases (500!).



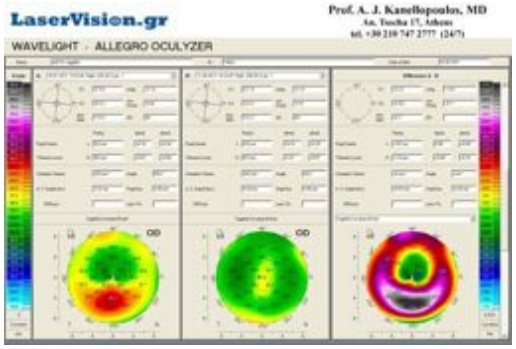
Oculink Vs Topolink in Athens Protocol

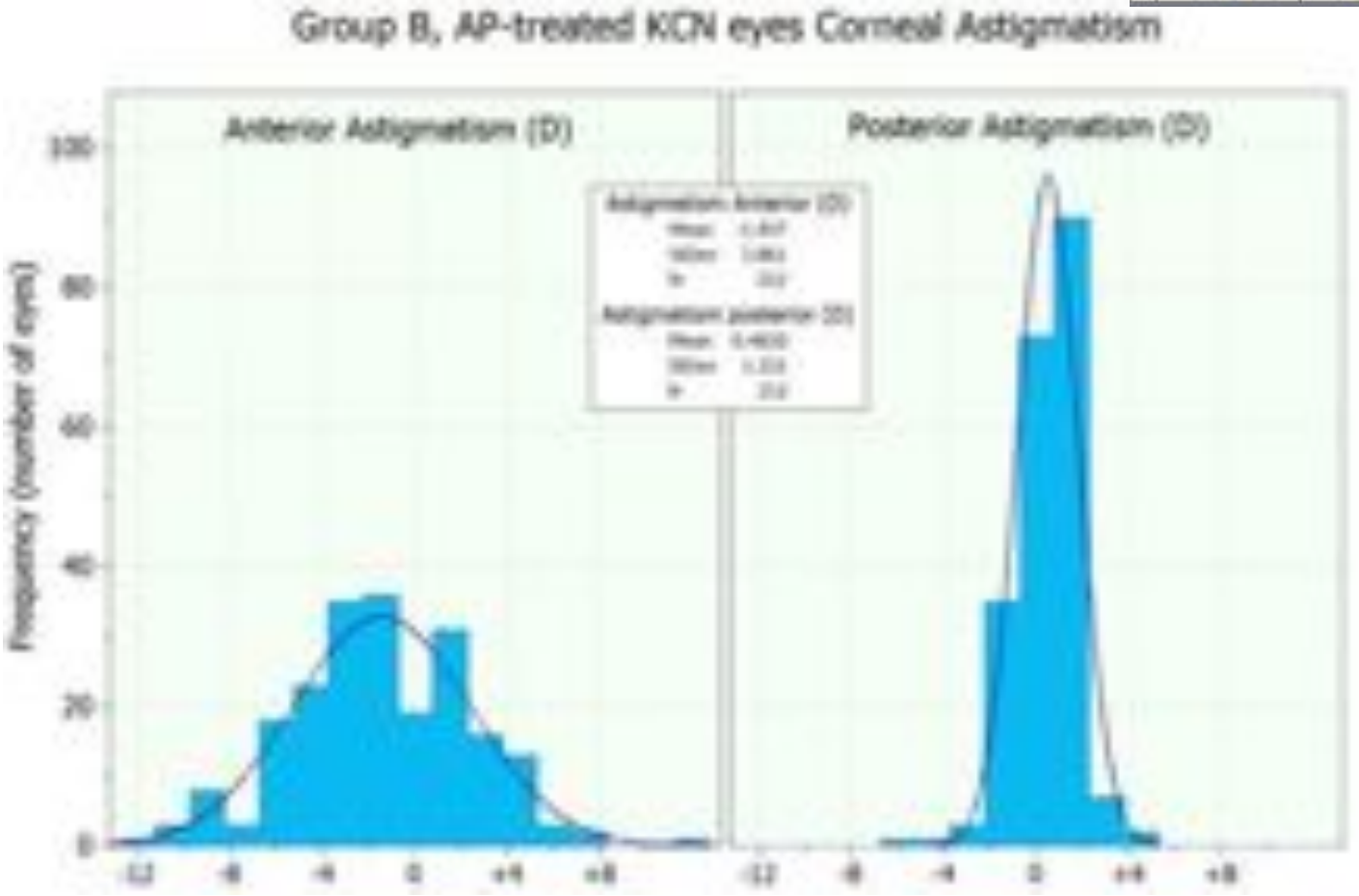




Oculink (Pentacam driven) appears more effective!

Athens Protocol: improved anterior corneal profile, but what about the posterior?





Athens Protocol Vs. ICRS+CXL in a contralateral eye study

Dr Sharif BADDAR of Cairo, Egypt

Preliminary data suggest that the Athens Protocol eyes have more predicatable improvement in BSCVA, quality of vision, less glare than ICRS+CXL eyes although a longer recovery

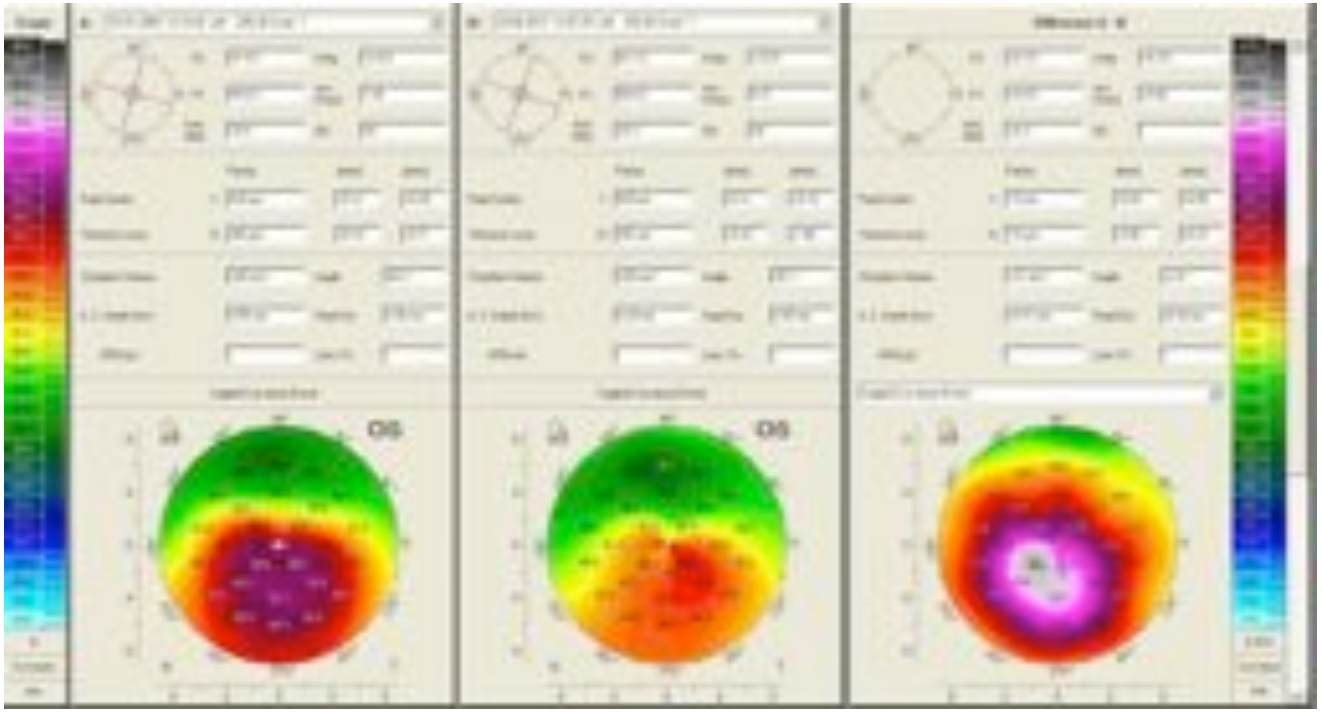
Same patient

← Athens Protocol

ICRS+CXL-->

Why not to combine?

- Unpredictable refractive change with CXL
- Additional cornea thinning with the ablation
- Potential for scarring that will flatten the cornea unpredictably
- This is a simple 3mW CXL-alone case from 2005 Flattened 12D!!!



Conclusions: why better to combine

- Combined treatment offers a more stable biomechanically cornea
- More homogenous CXL (deeper-wider)
- Bypass the difficulty of an ablation nomogram for CXL'ed stroma

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ORIGINAL RESEARCH

Correlation between epithelial thickness in normal corneas, untreated ectatic corneas, and ectatic corneas previously treated with CXL; is overall epithelial thickness a very early ectasia prognostic factor?

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Ioannis M Aslanides[3]
George Asimellis[1]

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Video abstract

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Purpose: To determine and correlate epithelial corneal thickness (pachymetric) measurements taken with a digital arc scanning very high frequency ultrasound biomicroscopy (HF UBM) imaging system (Artemis-II), and compare mean and central epithelial thickness among normal eyes, untreated keratoconic eyes, and keratoconic eyes previously treated with collagen crosslinking (CXL).

Methods: Epithelial pachymetry measurements (topographic mapping) were conducted on 100 subjects via HF UBM. Three groups of patients were included: patients with normal eyes (controls), patients with untreated keratoconic eyes, and patients with keratoconic eyes treated with CXL. Central, mean, and peripheral corneal epithelial thickness was examined for each group, and a statistical study was conducted.

Results: Mean, central, and peripheral corneal epithelial thickness was compared between the three groups of patients. Epithelium thickness varied substantially in the keratoconic group, and in some cases there was a difference of up to 20 µm between various points of the same eye, and often a thinner epithelium coincided with a thinner cornea. However, on average, data from the keratoconic group suggested an overall thickening of the epithelium, particularly over the pupil center of the order of +3 µm, while the mean epithelium thickness was on average +1.1 µm, compared to the control population ($P = 0.005$). This overall thickening was more pronounced in younger patients in the keratoconic group. Keratoconic eyes previously treated with CXL showed, on average, virtually the same average epithelium thickness (mean −0.7 µm, −0.2 µm over the pupil center, −0.9 µm over the peripheral zone) as the control group. This finding further reinforces our novel theory of the "reactive" component of epithelial thickening in corneas that are biomechanically unstable, becoming stable when biomechanical rigidity is accomplished despite persistence of cornea topographic irregularity.

Conclusion: A highly irregular epithelium may be suggestive of an ectatic cornea. Our results indicate that the epithelium is thinner over the keratoconic protrusion, but to a much lesser extent than anticipated, and on average epithelium is thicker in this group of patients. This difference appears to be clinically significant and may become a screening tool for eyes suspected for ectasia.

Keywords: corneal pachymetry, ectasia, keratoconus screening, cornea epithelial thickness

Introduction

Importance of corneal epithelium imaging

The contribution of the corneal epithelium to the refractive power of the cornea, and thus ocular refraction, cannot be ignored. Studies have shown that epithelial refractive

http://dx.doi.org/10.2147/OPTH.S31524

- CXLed corneas has thinner epi
- KCN corneas had OVERAL thicker epi
- Even suspect KCN corneas had THICKER epi

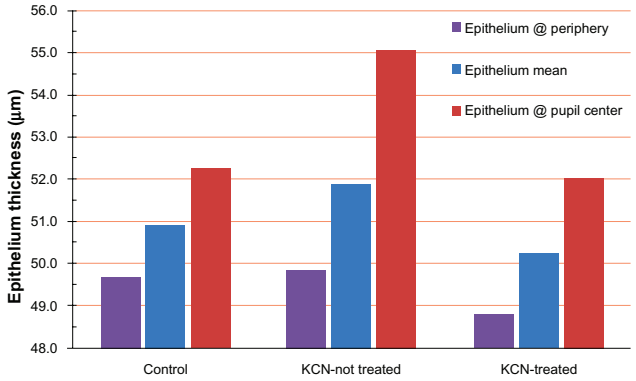

Figure 7 Epithelium thickness across the three study groups, at the periphery, mean, and pupil center.
Abbreviation: KCN, keratoconus.

surprise that while the epithelial center was, on average, thicker by only 1.3 µm compared to the mean, on several occasions it was thicker compared to the nasal, temporal, inferior, or superior points by up to 10 µm. This conclusion is also supported by the fact that the periphery epithelium thickness value of 49.7 µm was closer to the mean (50.9 µm) than to the pupil center (52.3 µm).

We note that the standard deviation of the measurements (±3–4 µm) is comparable to the accuracy and precision of the instrument, as established by our investigation, and thus epithelial thickness variations of ±4–4 µm, as it is the case, might be observed differently even on the same eye. An example of a control patient who demonstrated a thicker epithelium at the pupil center is shown in Figure 6. In one instance the central epithelium was elevated by 9 µm (51 µm–42 µm), while in a subsequent examination of the same eye, the difference between the same points was recorded as only 6 µm (54 µm–48 µm).

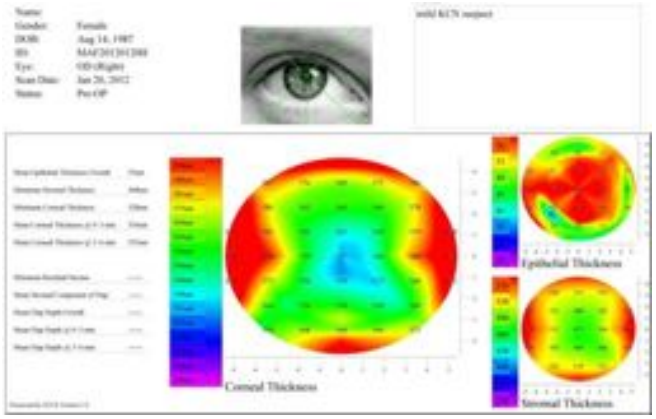

Figure 8 Corneal and epithelial thickness maps of a KCN patient.
Note: A significantly thicker epithelium over the pupil center is observed.
Abbreviation: KCN, keratoconus.

Case Reports in Ophthalmology

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Anterior Segment Optical Coherence Tomography: Assisted Topographic Corneal Epithelial Thickness Distribution Imaging of a Keratoconus Patient

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[a]Laservision.gr Eye Institute, Athens, Greece; [b]NYU Medical School, New York, N.Y., USA

Key Words
Anterior segment optical coherence tomography · Keratoconus · Epithelial imaging · Pentacam HR

Abstract
Purpose: To evaluate safety, efficacy and ease of measurement of epithelial thickness in a keratoconic patient based on anterior segment optical coherence tomography (AS-OCT). ***Methods:*** A 25-year-old male patient, previously diagnosed with keratoconus, with highly asymmetric manifestation among the two eyes, was subjected to AS-OCT corneal epithelial imaging. We investigated epithelial thickness and epithelial topographic thickness distribution. ***Results:*** Mean epithelial thickness was 51.97 ± 0.70 for the less affected right eye (OD), and 55.65 ± 1.22 for the more affected left eye (OS). Topographic epithelial thickness variability for the OD was 1.53 ± 0.21 µm, while for the OS it was 9.80 ± 0.41 µm. ***Conclusions:*** This case further supports our previous findings with high-frequency ultrasound measurements of the increase in overall epithelial thickness in keratoconic eyes in comparison with normal eyes. AS-OCT further offers ease of use and possibly higher predictability of measurement. This case report, based on AS-OCT imaging, verifies increased overall epithelial thickness in keratoconic eyes, as introduced by a previous study [Kanellopoulos et al.: Clin Ophthalmol 2012;6:789–800], based on high-frequency scanning ultrasound biomicroscopy imaging.

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KARGER

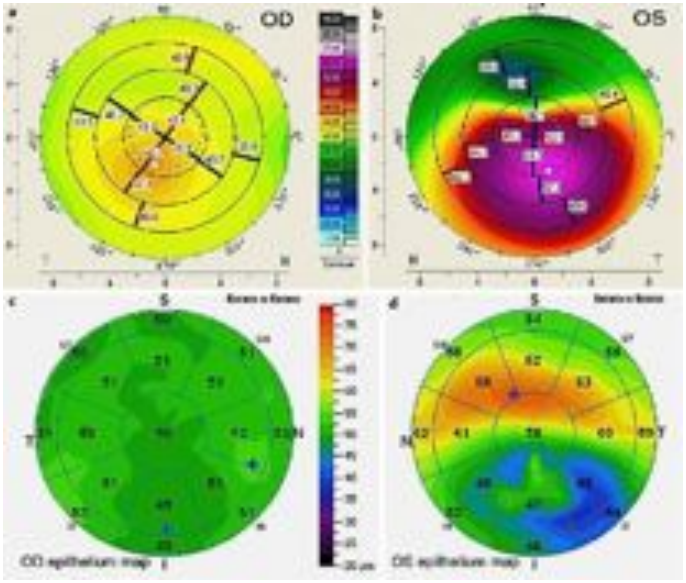


Fig. 1. **a** Tomographic anterior corneal sagittal curvature map for OD. **b** Tomographic anterior corneal sagittal curvature map for OS. **c** AS-OCT epithelial thickness map for OD. **d** AS-OCT epithelial thickness map for OS.

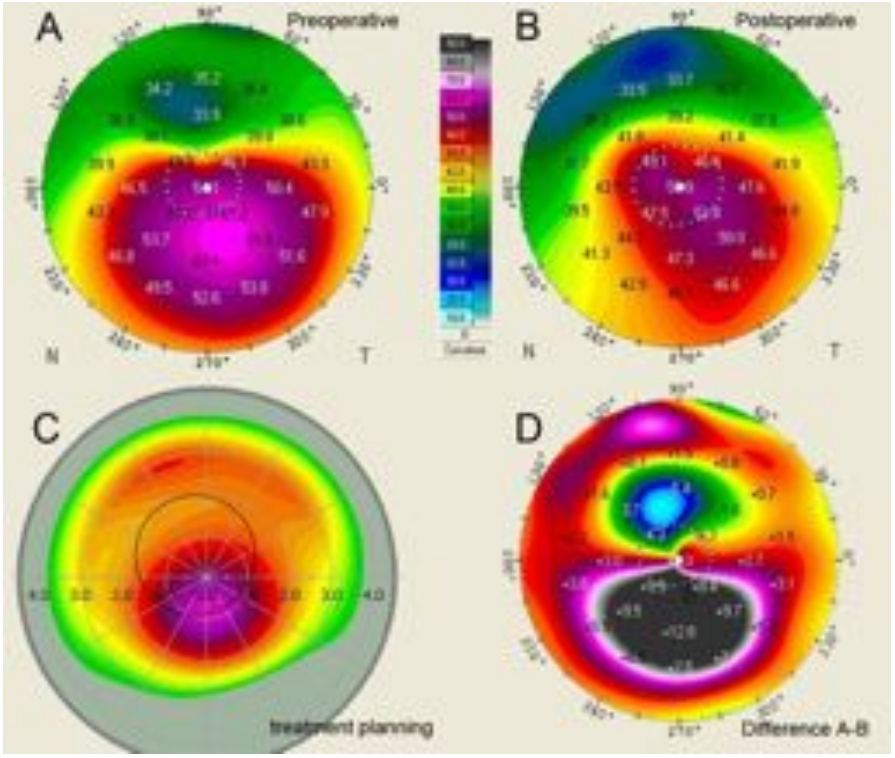
Epithelial thickness profile changes after partial topography-guided ablation and high-fluence, short duration cross-linking with riboflavin

In press AJO

The epithelium thickness showed an overall six month post-operative reduction.

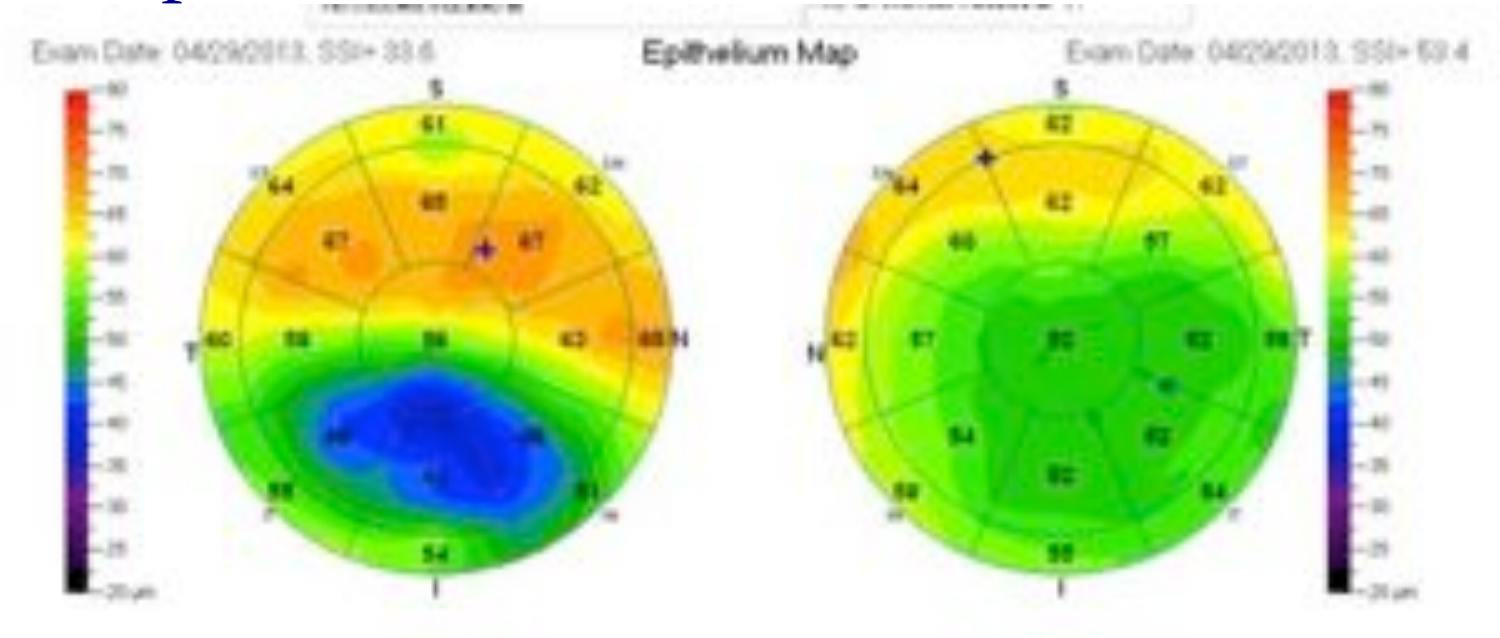
Specifically, mean thickness was preoperatively 55.65 ± 1.22 µm, and postoperatively, 40.60 ± 1.22 µm.

Topographic epithelial thickness variability was also reduced, from 9.80 ± 0.41 µm, preoperatively to 5.37 ± 0.40 µm postoperatively.

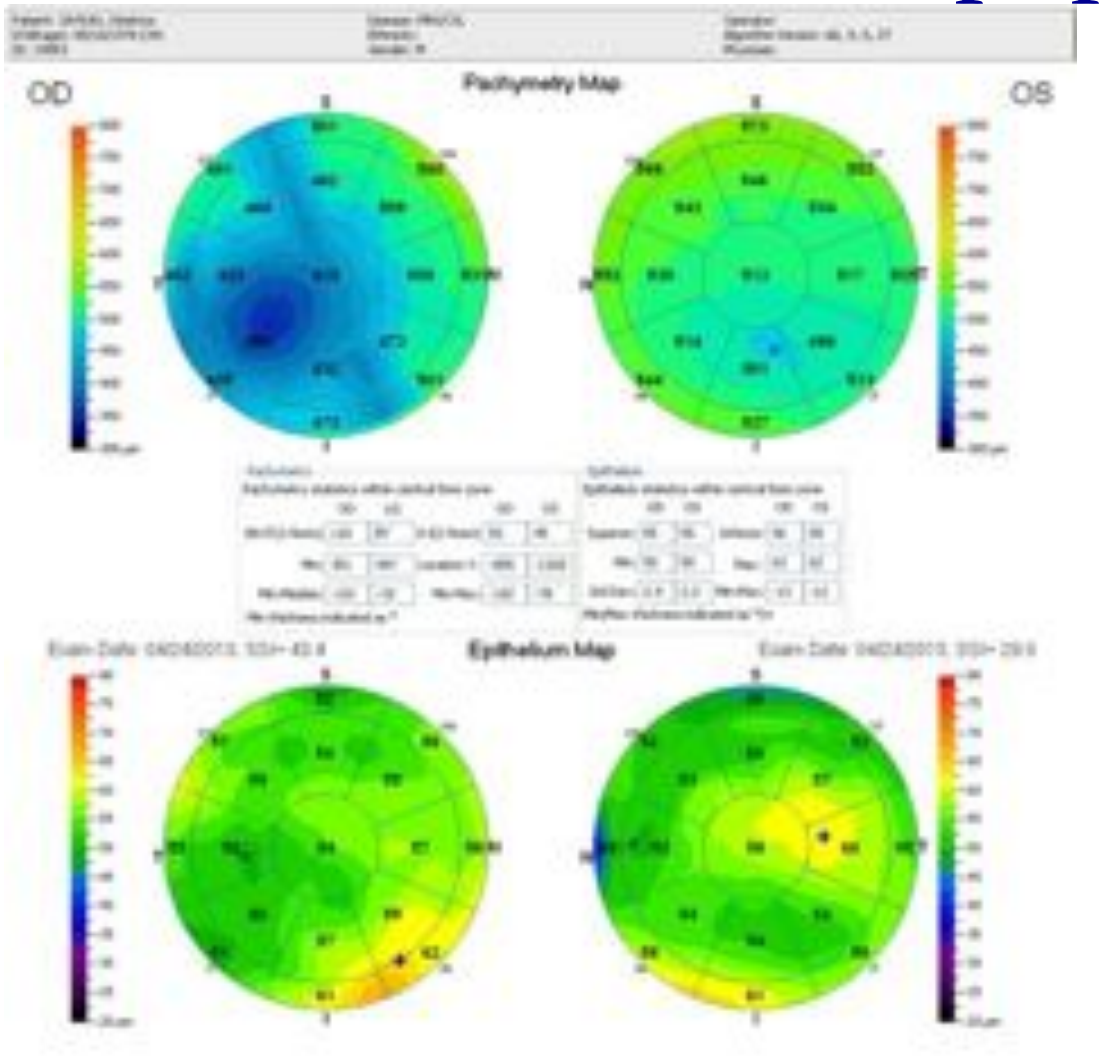


Conclusions: why better to combine

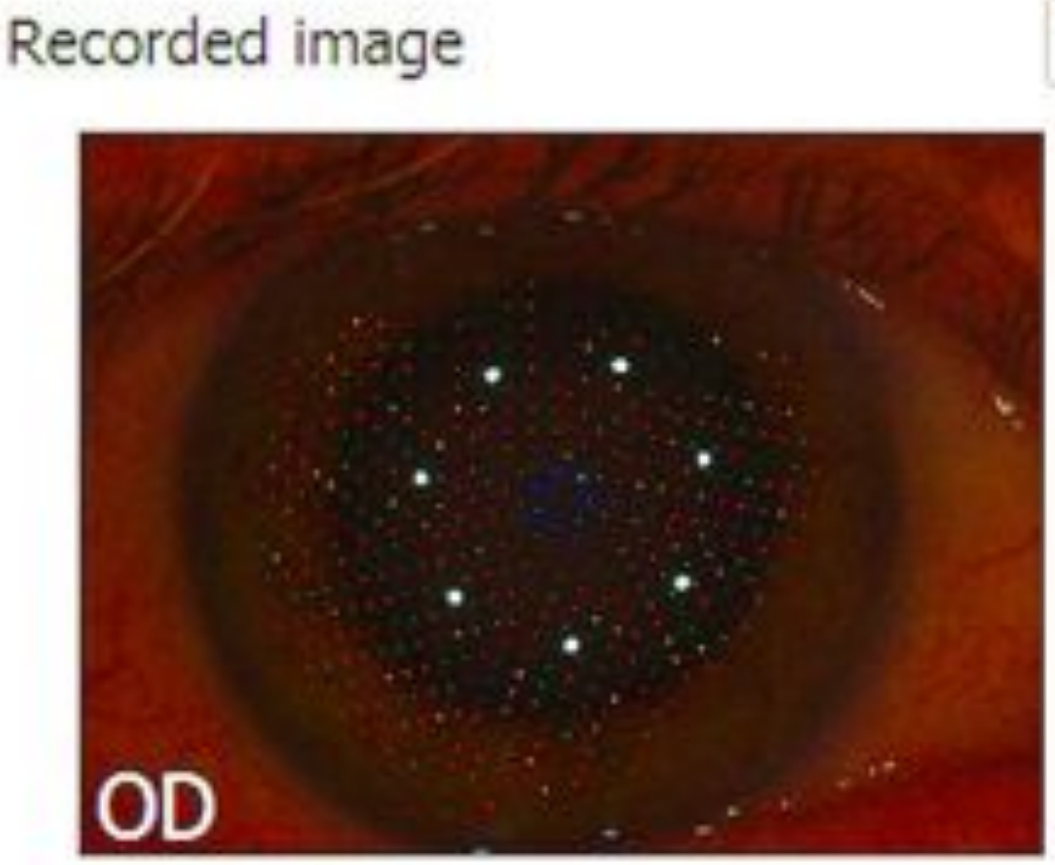
- No need to remove CXLed tissue
- Less scarring predictable epithelial profile
- This is not a refractive procedure, but rather therapeutic



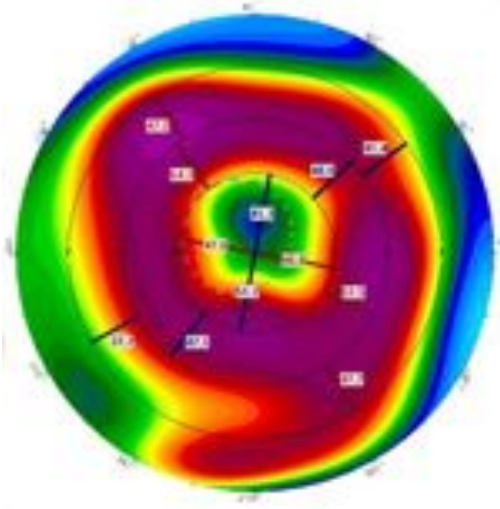
Bilateral Athens Protocol epi profiles

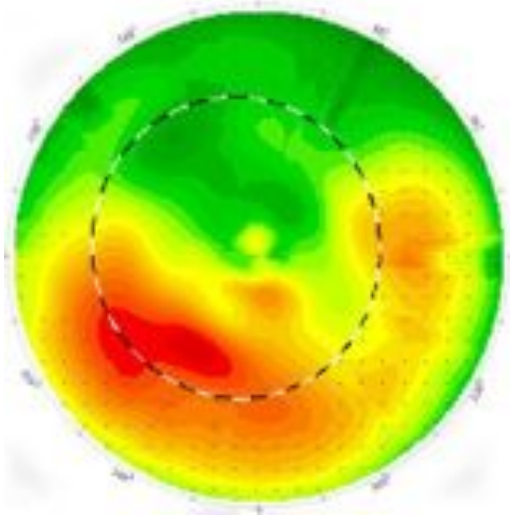


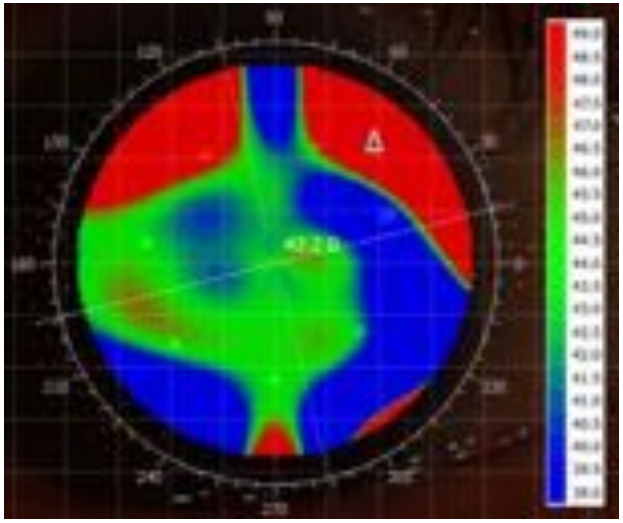
Cassini

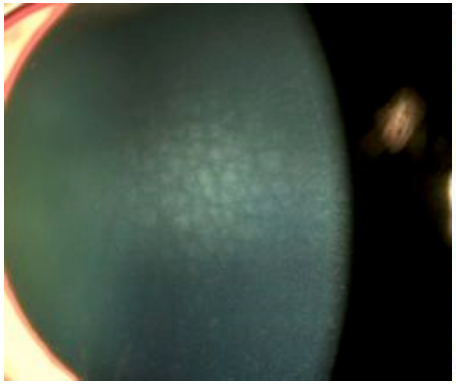


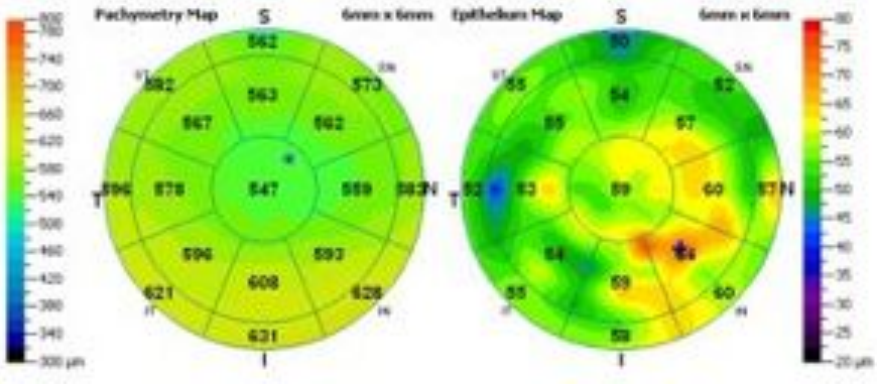
Central Cloudy

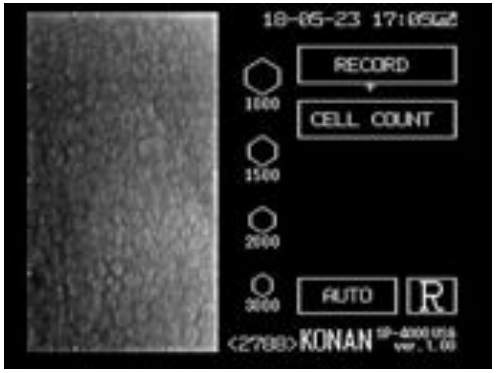












Athens, September 14th, 2013 next year October 4th, 2014

New York University School of Medicine Kanellopoulos,MD

LaserVision.gr Institute for laser


Thank you