Preparing and performing LASIK in 2015

Basic Steps for effective Informed Consent and Customized Refractive Error Correction

XXXIII Congress of the ESCRS

BARCELONA 2015

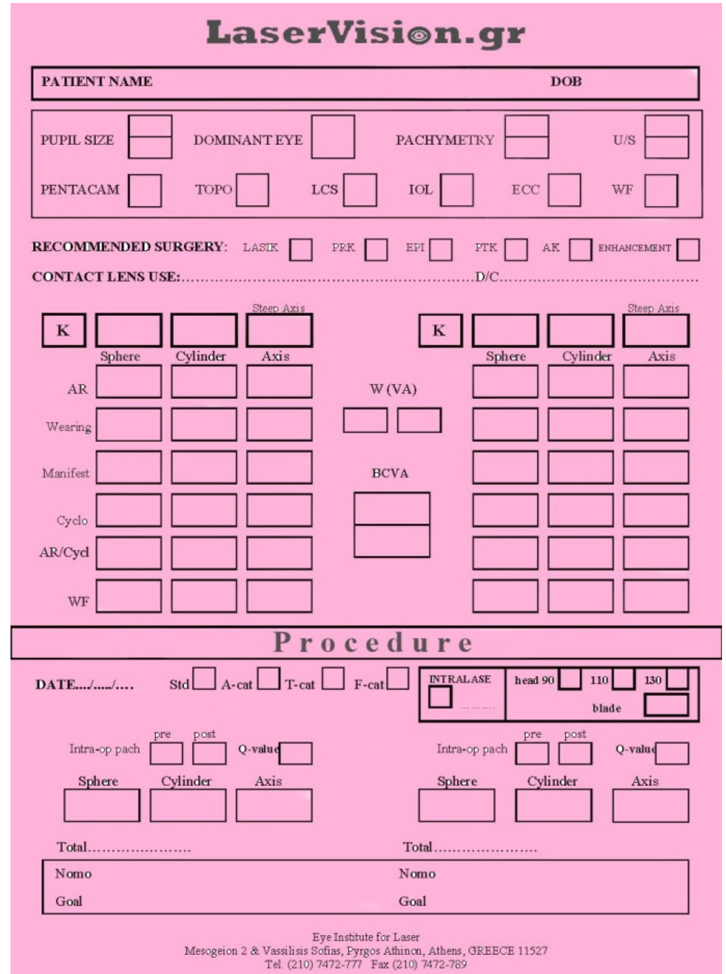
New York University School of Medicine

Kanellopoulos, MD
www.brilliantvision.com

Eye Institute
Laser Vision
Your Vision Our Mission


Purpose:

To present our screening protocol, along with the intraoperative and postoperative care protocols for Femtosecond Excimer Refractive Surgery



LaserVision.gr

PATIENT NAME DOB

PUPIL SIZE DOMINANT EYE PACHYMETRY U/S

PENTACAM TOPO LCS IOL ECC WF

RECOMMENDED SURGERY: LASIK PRK EPI PTK AK ENHANCEMENT

CONTACT LENS USE:...D/C...

			Steep Axis					Steep Axis
K					K			
	Sphere	Cylinder	Axis			Sphere	Cylinder	Axis
AR				W (VA)				
Wearing								
Manifest				BCVA				
Cyclo								
AR/Cycl								
WF								

Procedure

DATE..../...../.... Std A-cat T-cat F-cat INTRALASE .... head 90 110 130 blade

Intra-op pach pre post Q-value Intra-op pach pre post Q-value

Sphere Cylinder Axis Sphere Cylinder Axis

Total...................... Total......................

Nomo Nomo

Goal Goal

Eye Institute for Laser
Mesogeion 2 & Vassilisis Sofias, Pyrgos Athinon, Athens, GREECE 11527
Tel. (210) 7472-777 Fax (210) 7472-789

Telephone call - Appointment – The First Contact!

- Reception identifies the patient's interested in refractive surgery
- Attempt to make an appointment as soon as possible
- No price discussion over the phone
- Identification Data
- Explain that initial exam will entail multiple measurements of spectacles, topographies and preferably a dilated fundus exam (1-2 hours)

Telephone call - Appointment – The First Contact!

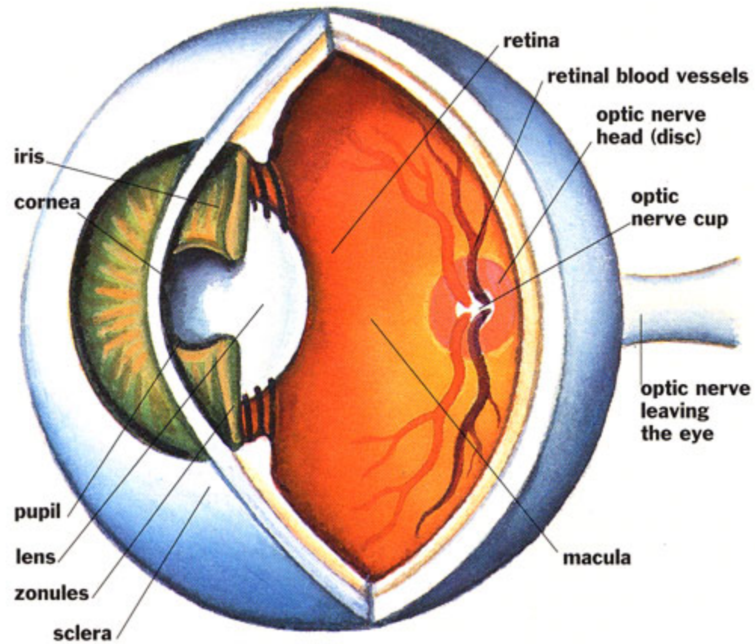
- Determine contact lens use and encourage the discontinuation of their use for at least a week, so in our evaluation we can perform the final measurements and avoid several visits that may inconvenience the patient

- If our protocol appears inconvenient, we encourage a short visit with the surgeon were the prescription and Pentacam will be discussed

Complete Eye Examination

- Reception explains the evaluations that will take place
- The patient fills-out a data questionnaire
- Full medical history
- Contact Lenses / Glasses
- Endothelial Corneal Cell Count
- Laser Interferometry

  (IOL Master and/ or Biograph)
- IOP measurement

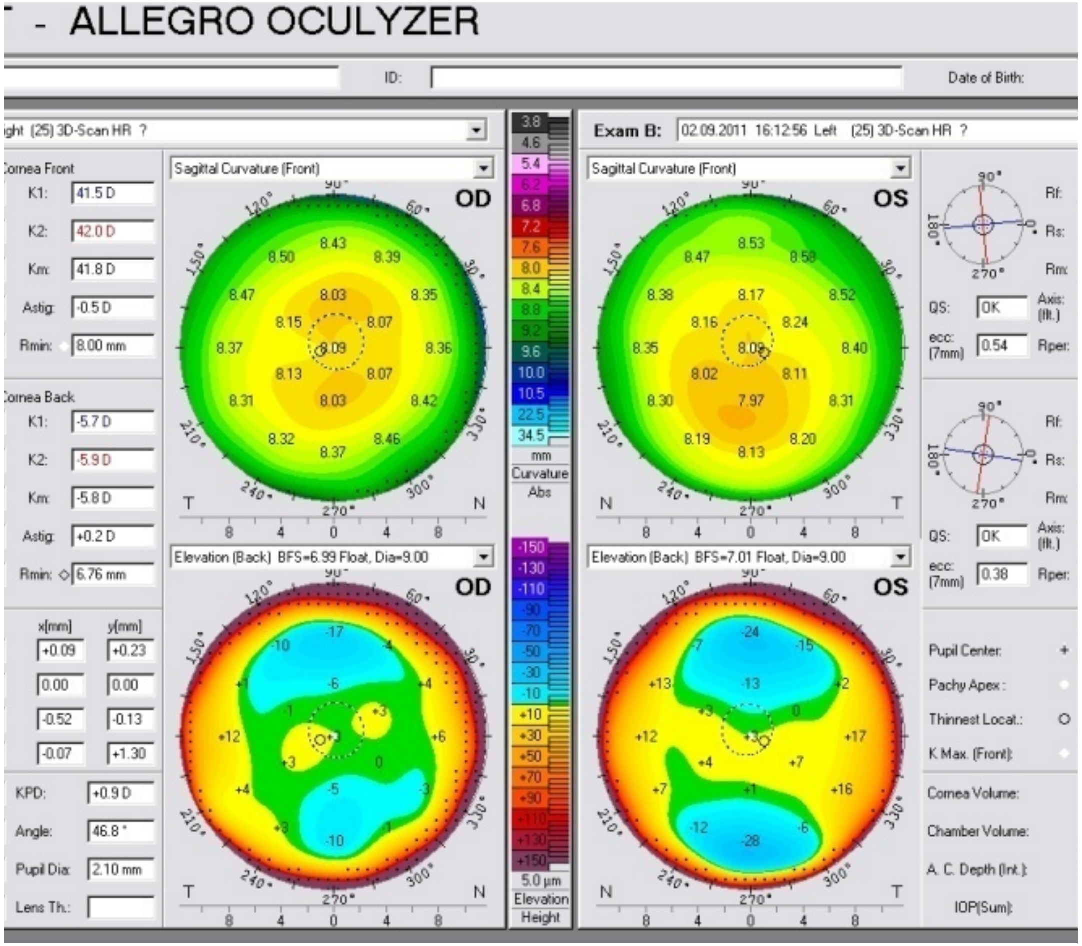


Complete Eye Examination

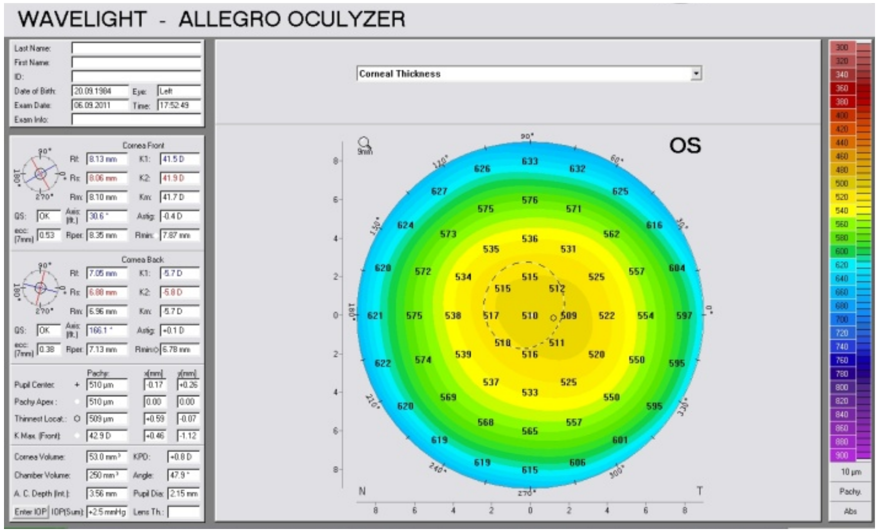
Corneal Tomography

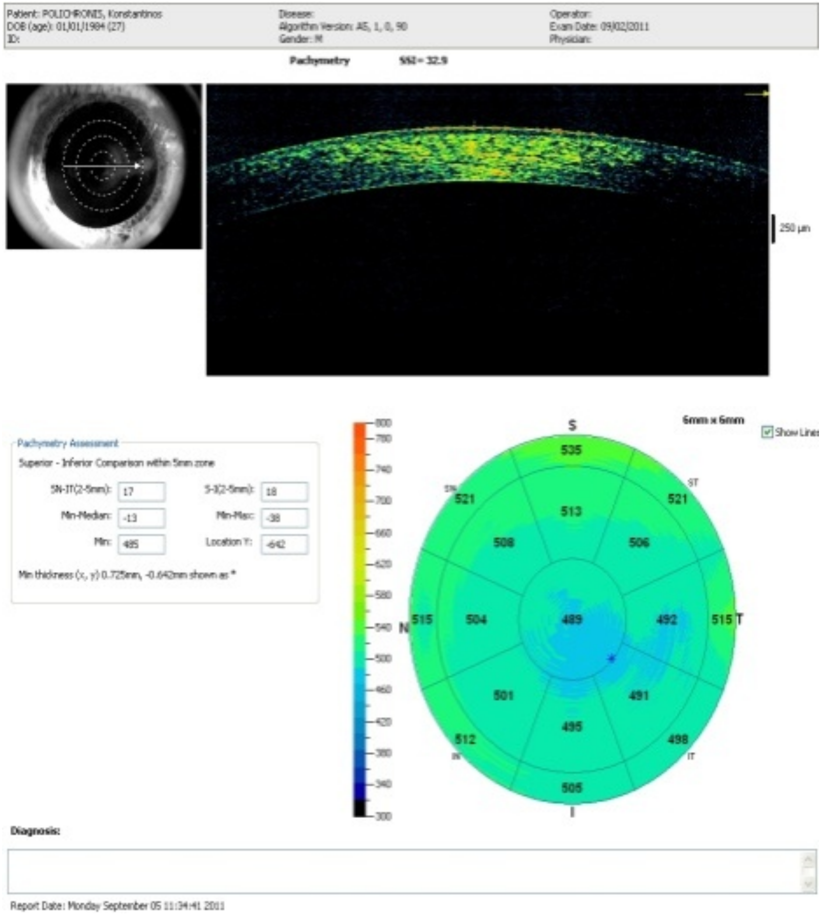
Oculyzer (Pentacam) reveals:

- Posterior curvature parameters
- Corneal thickness



Complete Eye Examination





Large Color Map, Oculyzer

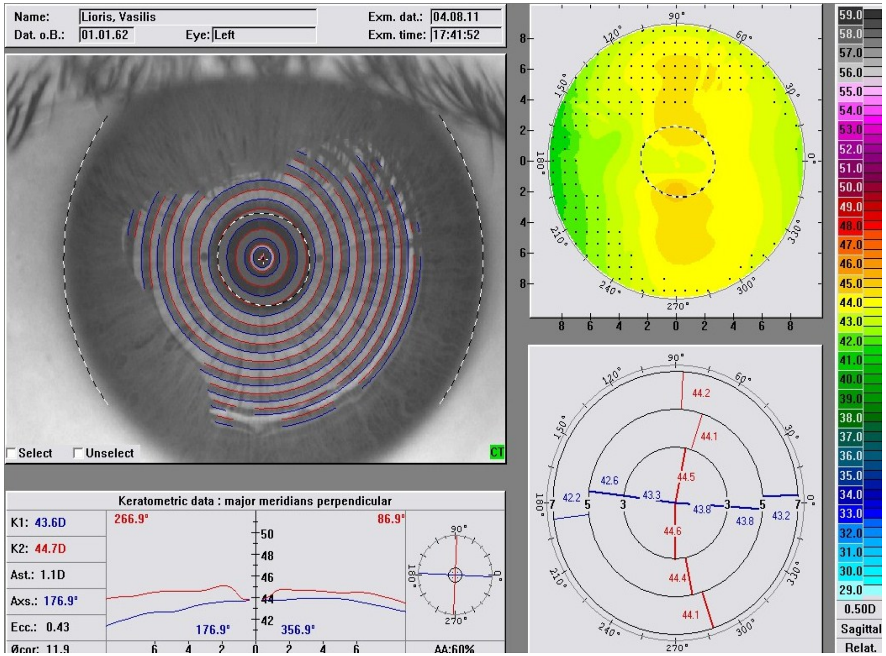
Pachymetry, OCT image

Complete Eye Examination

Corneal Topography

Topolyzer reveals:

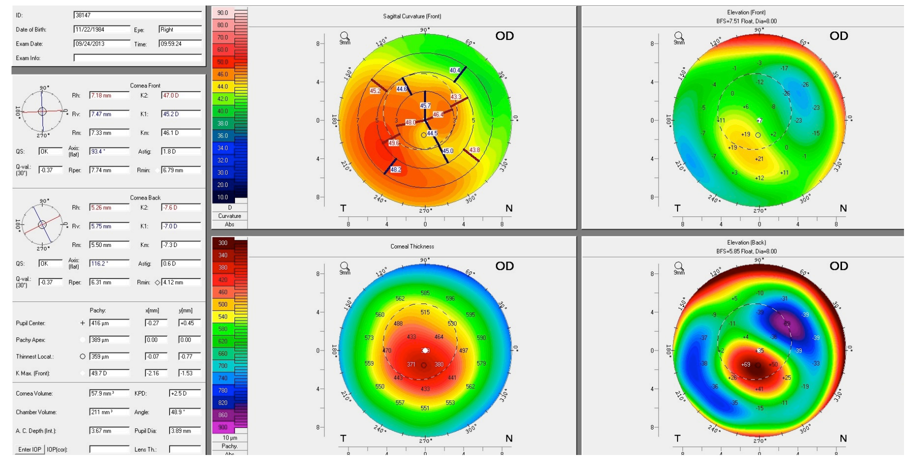
- Irregular Astigmatism
- Keratoconus
- Topographical irregularities in CL Pt
- Irregularities due to Dry Eye Disease
- Provides asphericity and pupil centroid shift data

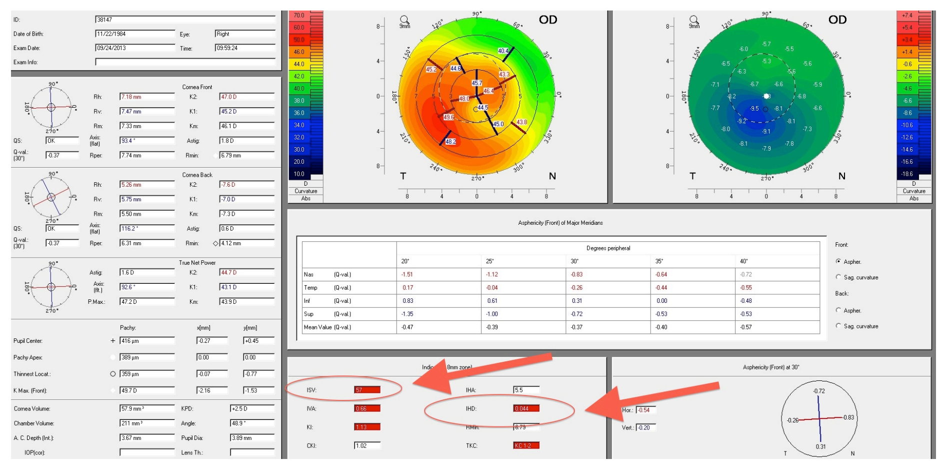


Revisiting the Diagnosis and Progression criteria of Keratoconus

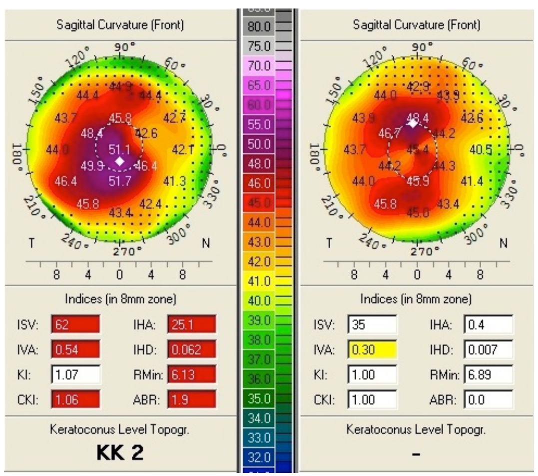
Traditionally:

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





What parameters I use to evaluate Dx and progression of keratoconus



A. John Kanellopoulos, MD
Director, Laservision.gr Institute, Athens, Greece
Clinical Professor NYU Medical School, NY

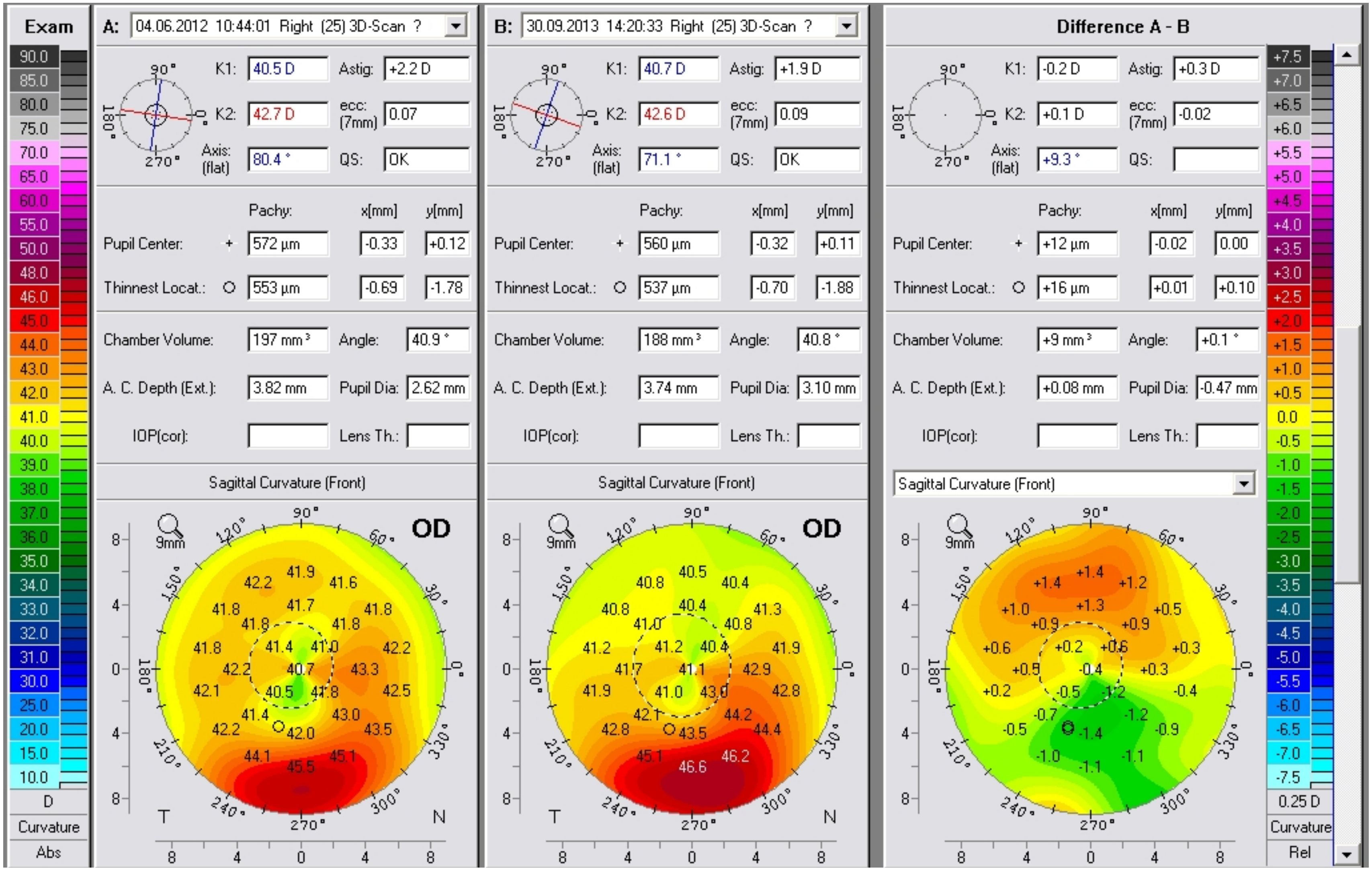
www.laservision.gr

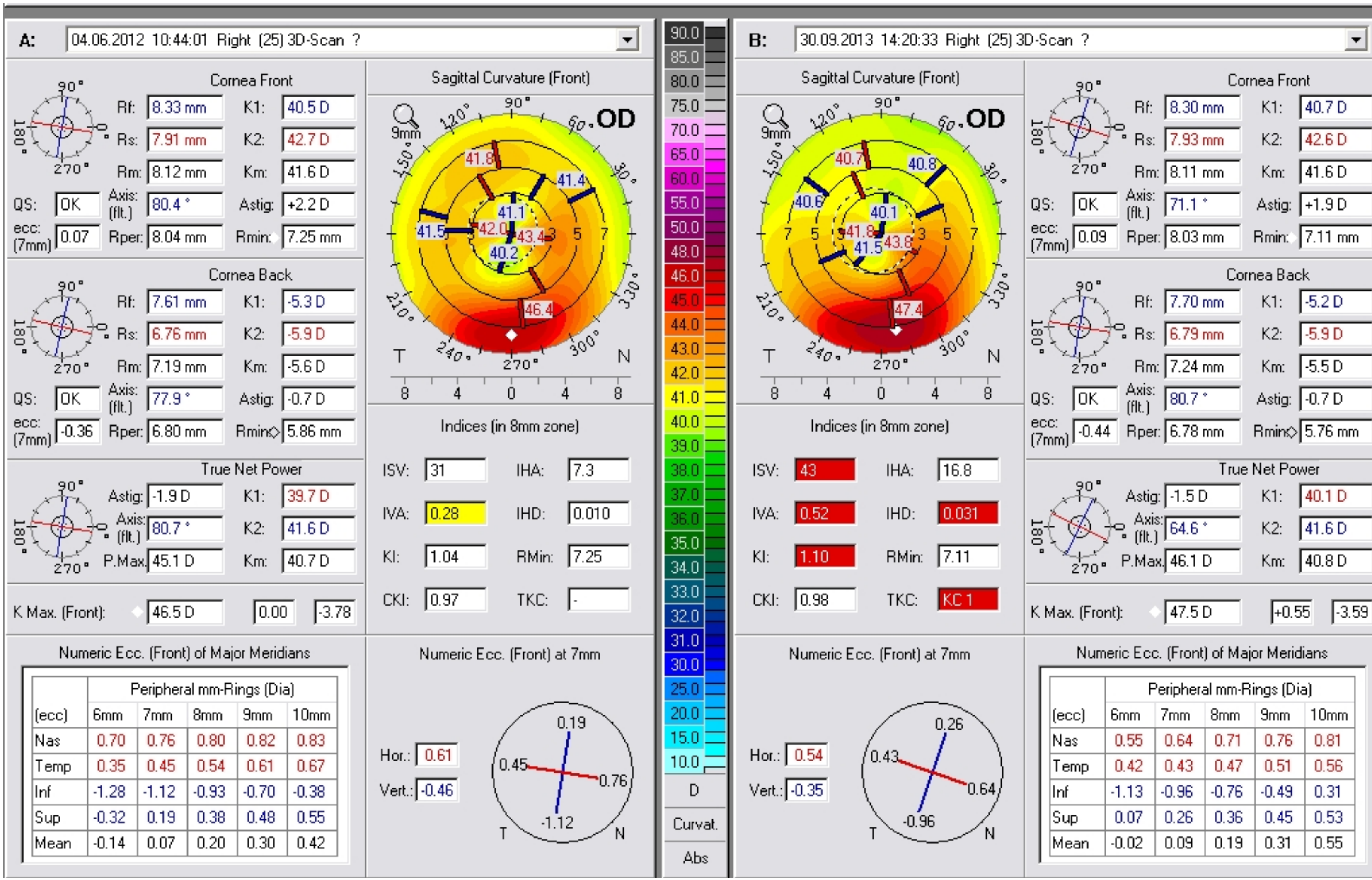
“Currently sensitive criteria”

- Topometric asymmetry indices IHD and ISV
- Pachymetric asymmetry; Scheimpflug, OCT
- ART-Max=TP/PPI-Max (essentially “steep” cornea pachymetry change)
- Epithelial profiles
- Biomechanical measurements-Brillouin

My Clinical practice

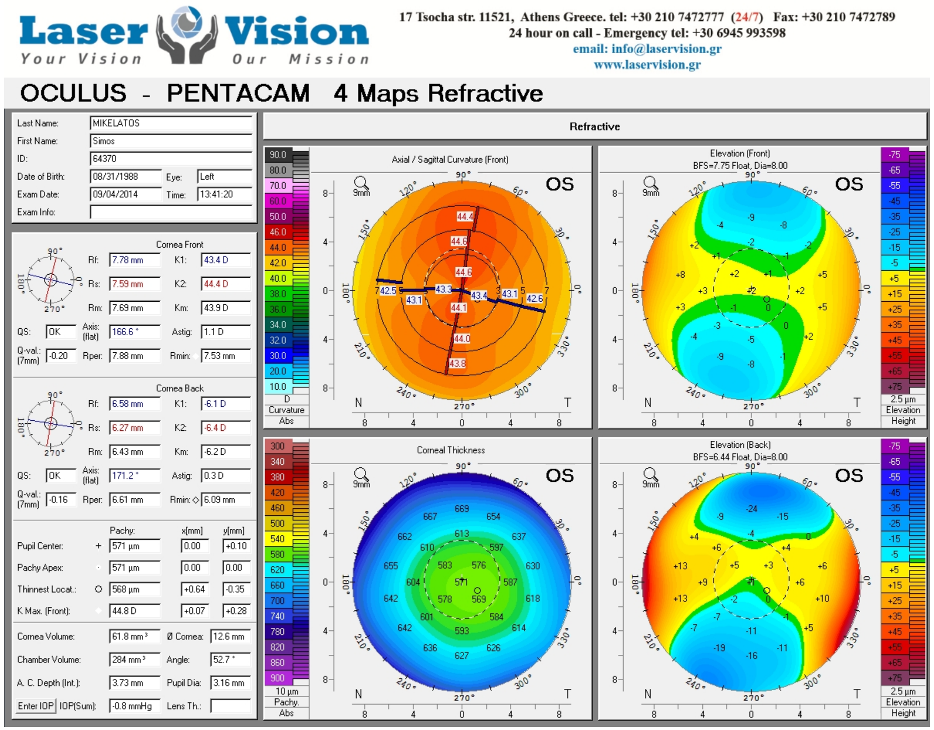
- Asymmetry indices
- Topometric indices IHD, ISV
- Pachymetric norms and asymmetry changes
- Epithelial remodeling
- Biomechanical measurements?
- View all topos in correlation with Biomicroscopy!
- Family topos important!!!

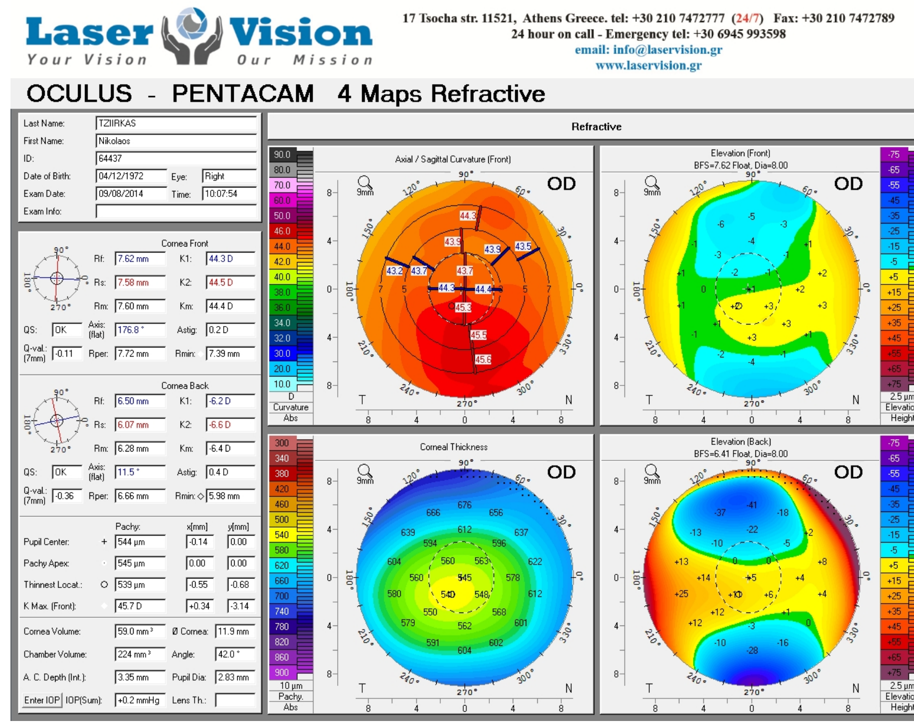

Exam
A: 04.06.2012 10:44:01 Right (25) 3D-Scan ?
K1: 40.5 D
Astig: +2.2 D
K2: 42.7 D
ecc: (7mm) 0.07
Axis: (flat) 80.4 °
QS: OK
Pachy:
x[mm]
y[mm]
Pupil Center: 572 µm -0.33 +0.12
Thinnest Locat.: 553 µm -0.69 -1.78
Chamber Volume: 197 mm³
Angle: 40.9 °
A. C. Depth (Ext.): 3.82 mm
Pupil Dia: 2.62 mm
IOP(cor):
Lens Th.:
Sagittal Curvature (Front)
OD
B: 30.09.2013 14:20:33 Right (25) 3D-Scan ?
K1: 40.7 D
Astig: +1.9 D
K2: 42.6 D
ecc: (7mm) 0.09
Axis: (flat) 71.1 °
QS: OK
Pupil Center: 560 µm -0.32 +0.11
Thinnest Locat.: 537 µm -0.70 -1.88
Chamber Volume: 188 mm³
Angle: 40.8 °
A. C. Depth (Ext.): 3.74 mm
Pupil Dia: 3.10 mm
IOP(cor):
Lens Th.:
Sagittal Curvature (Front)
OD
Difference A - B
K1: -0.2 D
Astig: +0.3 D
K2: +0.1 D
ecc: (7mm) -0.02
Axis: (flat) +9.3 °
QS:
Pupil Center: +12 µm -0.02 0.00
Thinnest Locat.: +16 µm +0.01 +0.10
Chamber Volume: +9 mm³
Angle: +0.1 °
A. C. Depth (Ext.): +0.08 mm
Pupil Dia: -0.47 mm
IOP(cor):
Lens Th.:
Sagittal Curvature (Front)
D
Curvature
Abs
0.25 D
Curvature
Rel
T
N
9mm



A: 04.06.2012 10:44:01 Right (25) 3D-Scan ?
Cornea Front
Rf: 8.33 mm K1: 40.5 D
Rs: 7.91 mm K2: 42.7 D
Rm: 8.12 mm Km: 41.6 D
QS: OK Axis: (flt.) 80.4 ° Astig: +2.2 D
ecc: (7mm) 0.07 Rper: 8.04 mm Rmin: 7.25 mm
Cornea Back
Rf: 7.61 mm K1: -5.3 D
Rs: 6.76 mm K2: -5.9 D
Rm: 7.19 mm Km: -5.6 D
QS: OK Axis: (flt.) 77.9 ° Astig: -0.7 D
ecc: (7mm) -0.36 Rper: 6.80 mm Rmin: 5.86 mm
True Net Power
Astig: -1.9 D K1: 39.7 D
Axis: (flt.) 80.7 ° K2: 41.6 D
P.Max 45.1 D Km: 40.7 D
K Max. (Front): 46.5 D 0.00 -3.78
Sagittal Curvature (Front)
OD
9mm
41.8 41.4 41.1 41.5 42.0 43.4 40.2 46.4
T N
Indices (in 8mm zone)
ISV: 31 IHA: 7.3
IVA: 0.28 IHD: 0.010
KI: 1.04 RMin: 7.25
CKI: 0.97 TKC: -
Numeric Ecc. (Front) of Major Meridians
Peripheral mm-Rings (Dia)
(ecc) 6mm 7mm 8mm 9mm 10mm
Nas 0.70 0.76 0.80 0.82 0.83
Temp 0.35 0.45 0.54 0.61 0.67
Inf -1.28 -1.12 -0.93 -0.70 -0.38
Sup -0.32 0.19 0.38 0.48 0.55
Mean -0.14 0.07 0.20 0.30 0.42
Numeric Ecc. (Front) at 7mm
Hor.: 0.61
Vert.: -0.46
0.19 0.45 0.76 -1.12 T N
90.0 85.0 80.0 75.0 70.0 65.0 60.0 55.0 50.0 48.0 46.0 45.0 44.0 43.0 42.0 41.0 40.0 39.0 38.0 37.0 36.0 35.0 34.0 33.0 32.0 31.0 30.0 25.0 20.0 15.0 10.0
D
Curvat.
Abs
B: 30.09.2013 14:20:33 Right (25) 3D-Scan ?
Sagittal Curvature (Front)
OD
9mm
40.7 40.8 40.6 40.1 41.8 41.5 43.8 47.4
T N
Indices (in 8mm zone)
ISV: 43 IHA: 16.8
IVA: 0.52 IHD: 0.031
KI: 1.10 RMin: 7.11
CKI: 0.98 TKC: KC 1
Numeric Ecc. (Front) at 7mm
Hor.: 0.54
Vert.: -0.35
0.26 0.43 0.64 -0.96 T N
Cornea Front
Rf: 8.30 mm K1: 40.7 D
Rs: 7.93 mm K2: 42.6 D
Rm: 8.11 mm Km: 41.6 D
QS: OK Axis: (flt.) 71.1 ° Astig: +1.9 D
ecc: (7mm) 0.09 Rper: 8.03 mm Rmin: 7.11 mm
Cornea Back
Rf: 7.70 mm K1: -5.2 D
Rs: 6.79 mm K2: -5.9 D
Rm: 7.24 mm Km: -5.5 D
QS: OK Axis: (flt.) 80.7 ° Astig: -0.7 D
ecc: (7mm) -0.44 Rper: 6.78 mm Rmin: 5.76 mm
True Net Power
Astig: -1.5 D K1: 40.1 D
Axis: (flt.) 64.6 ° K2: 41.6 D
P.Max 46.1 D Km: 40.8 D
K Max. (Front): 47.5 D +0.55 -3.59
Numeric Ecc. (Front) of Major Meridians
Peripheral mm-Rings (Dia)
(ecc) 6mm 7mm 8mm 9mm 10mm
Nas 0.55 0.64 0.71 0.76 0.81
Temp 0.42 0.43 0.47 0.51 0.56
Inf -1.13 -0.96 -0.76 -0.49 0.31
Sup 0.07 0.26 0.36 0.45 0.53
Mean -0.02 0.09 0.19 0.31 0.55

Qualitative pachymetry changes





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

Point your SmartPhone at the code above. If you have a QR code reader the video abstract will appear. Or use: http://dvpr.es/11vcPjX

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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

http://dx.doi.org/10.2147/OPTH.S44741

Clinical Ophthalmology 2013:7 1539–1548

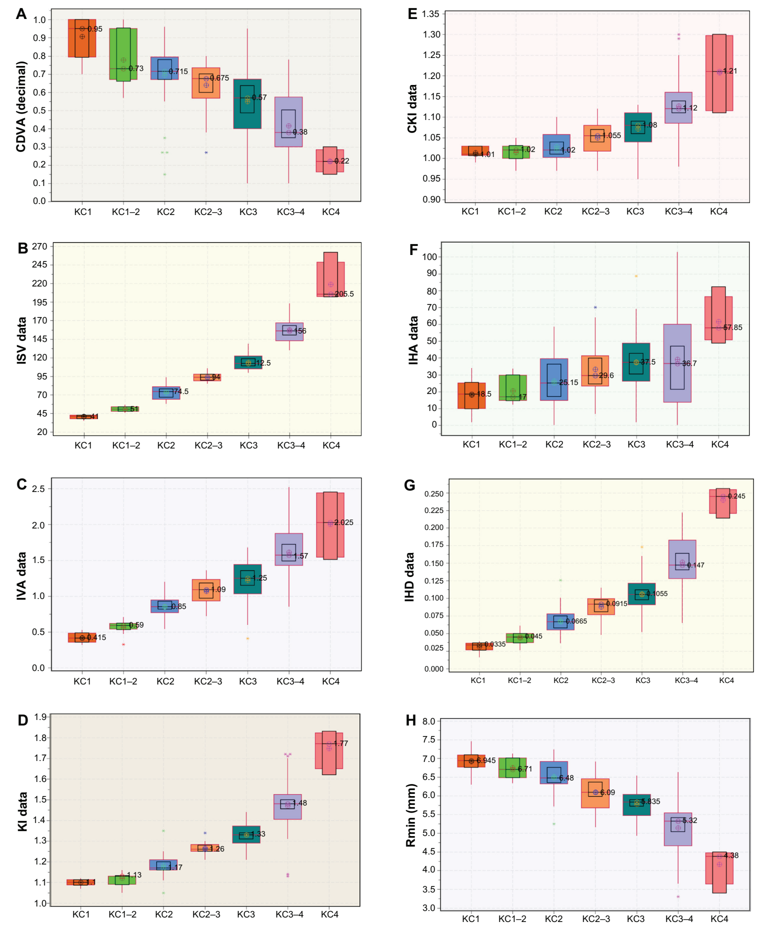

Figure 2 Box plots of measured parameters versus keratoconus grading, as produced by the Oculyzer™ software, showing median level (indicated by □), average symbol (□), 95% median confidence range box (black line boxes), and interquartile intervals range box (red line boxes). (**A**) CDVA versus keratoconus 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.

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

IJKECD

10.5005/jp-journals-10025-1060

ORIGINAL ARTICLE

Evaluation of Visual Acuity, Pachymetry and Anterior-Surface Irregularity in Keratoconus and Crosslinking Intervention Follow-up in 737 Cases

Anastasios John Kanellopoulos, Vasiliki Moustou, George Asimellis

ABSTRACT

Purpose: To investigate visual acuity, corneal pachymetry, and anterior-surface irregularity indices correlation with keratoconus severity in a very large pool of clinically-diagnosed untreated keratoconic eyes, and in keratoconic eyes subjected to cross-linking intervention.

Materials and methods: Total of 737 keratoconic (KCN) cases were evaluated. Group A was formed from 362 untreated keratoconic eyes, and group B from 375 keratoconic eyes subjected to partial normalization via topography-guided excimer laser ablation and high-fluence collagen crosslinking. A control group C of 145 healthy eyes was employed for comparison. We investigated distance visual acuity, uncorrected (UDVA), best-spectacle corrected (CDVA), and Scheimpflug-derived keratometry, pachymetry (central corneal thickness, CCT and thinnest, TCT), and two anterior-surface irregularity indices, the index of surface variance (ISV) and the index of height decentration (IHD). The correlations between these parameters *vs* topographic keratoconus classification (TKC) were investigated.

Results: Keratometry for group A was K1 (flat) 46.67 ± 3.80 D and K2 (steep) 50.76 ± 5.02 D; for group B K1 44.03 ± 3.64 D and K2 46.87 ± 4.61 D; for group C, K1 42.89 ± 1.45 D and K2 44.18 ± 1.88 D. Visual acuity for group A was UDVA 0.12 ± 0.18 and CDVA 0.59 ± 0.25 (decimal), for group B, 0.51 ± 0.28 and 0.77 ± 0.22, and for group C, 0.81 ± 0.31 and 0.87 ± 0.12.

Correlation between ISV and TKC (r^2) was for group A 0.853, and for group-B 0.886. Correlation between IHD and TKC was for group A r^2 = 0.731, and for group B 0.701. The ROC analysis 'area under the curve' was for CDVA 0.550, TCT 0.596, ISV 0.876 and IHD 0.887.

Conclusion: Our study indicates that the traditionally employed metrics of visual acuity and corneal thickness may not be robust indicators nor provide accurate assessment on either keratoconus severity or postoperative evaluation. Two anterior surface irregularity indices, derived by Scheimpflug-imaging, ISV and IHD, may be more sensitive and specific tools.

Précis: Visual acuity, Scheimpflug-derived pachymetry and anterior-surface irregularity correlation to keratoconus severity in untreated cases (A), treated with crosslinking (B), and in a control group (C) reveals that visual acuity and pachymetry do not correlate well with keratoconus severity.

Keywords: Athens Protocol, Combined topography guided PRK and higher fluence CXL, Visual rehabilitation in keratoconus, Severity criteria, Keratoconus progression, Keratoconus classification, Pentacam, Keratoconic Scheimpflug topometric indices, Visual acuity, Keratoconus, Grading anterior surface Pentacam indices, Keratoconus Amsler and Krumeich grading, Corneal pachymetry, Receiver operating characteristic ROC analysis.

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Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

Keratoconus (KCN), derived from the Greek words κερατοειδής: cornea; κώνος: cone, meaning cone-shaped protrusion, is a corneal disorder, defined as a noninflammatory degenerative axial thinning of an ectatic cornea.[1] Vision is affected by increased myopia due to the cone protrusion, and irregular astigmatism due to substantial corneal asymmetry.[2-4]

Our long clinical experience with keratoconic screening and rehabilitation[5-7] indicates that neither corneal pachymetry nor visual acuity (uncorrected distance visual acuity, UDVA, and best-spectacle corrected distance visual acuity, CDVA) can be reliable indicators of ectasia and/or keratoconus progression assessment.[8] One may expect that the presence of large amounts of corneal irregularities might hamper sufficient spectacle-correction of visual acuity. However, at least in our experience, often enough keratoconic patients present with surprisingly high CDVA, even near 20/20, despite severe topographic irregularity and/or pachymetric thinning present. This makes keratoconus diagnosis a difficult and potentially dangerous process, as most early, many advanced and even some severe cases can be missed with traditional screening methods. We have also encountered cases with progressive keratoconus with no clinically significant reduction in visual acuity.

To the best of our knowledge, the subject of quantitative correlation of visual acuity with keratoconus grading[9-11] has been reported only in very few peer-review publications.

This study aims to investigate the possible correlations of visual acuity (UDVA and CDVA), corneal pachymetry, and specific Scheimpflug-imaging derived anterior-surface topographic irregularity indices with keratoconus severity, in a large pool of clinically-diagnosed keratoconic eyes, and in a group of keratoconic eyes subjected to cross-linking and anterior-surface normalization intervention, and examine the applicability of these indicators in keratoconus screening,

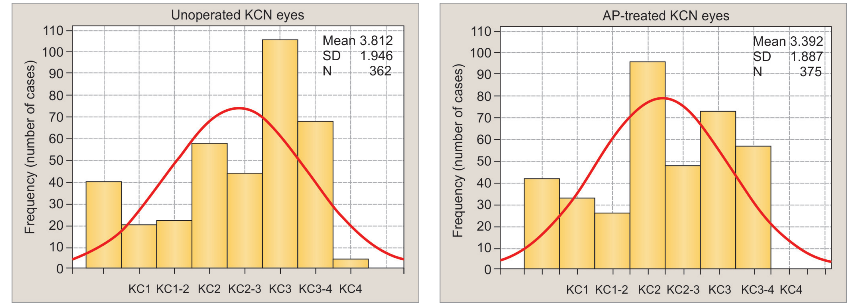


Fig. 1: Histograms of keratoconus classification for the two groups under study. Left — group A, unoperated KCN eyes and, right — group B, Athens-protocol (AP) treated KCN eyes

Table 2: Coefficient of determination (r^2) and pearson correlation coefficient for the two groups in the study between UDVA and TKC, CDVA and TKC, TCT and TKC, ISV TKC, IHD and TKC

	Coefficient of determination (r^2)	Pearson correlation coefficient
UDVA vs TKC		
Group A, unoperated KCN eyes	0.071	– 2.931
Group B, AP-treated KCN eyes	0.263	– 3.367
CDVA vs TKC		
Group A, unoperated KCN eyes	0.292	– 4.285
Group B, AP-treated KCN eyes	0.175	– 3.549
TCT vs TKC		
Group A, unoperated KCN eyes	0.236	– 0.0245
Group B, AP-treated KCN eyes	0.176	– 0.0131
ISV vs TKC		
Group A, unoperated KCN eyes	0.853	0.0415
Group B, AP-treated KCN eyes	0.886	0.0485
IHD vs TKC		
Group A, unoperated KCN eyes	0.731	31.9
Group B, AP-treated KCN eyes	0.701	43.1

KCN: keratoconus; UDVA: uncorrected distance visual acuity (decimal); TKC: topographic keratoconus classification; CDVA: best-spectacle corrected distance visual acuity (units, decimal); TCT: thinnest corneal thickness (units, μm); ISV: index of surface variance; IHD: index of height decentration; AP: Athens-protocol

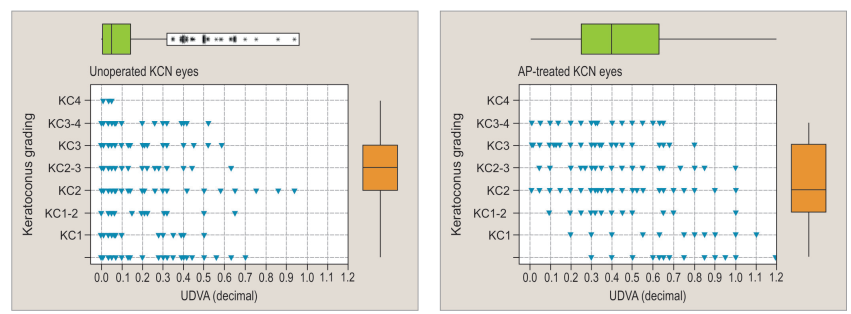
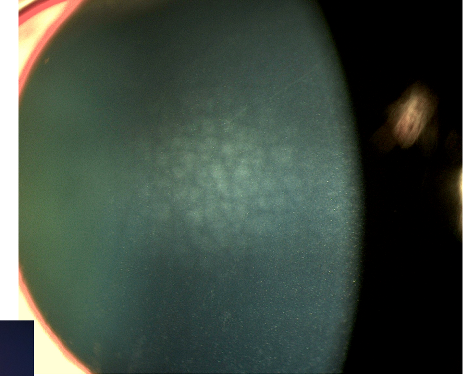
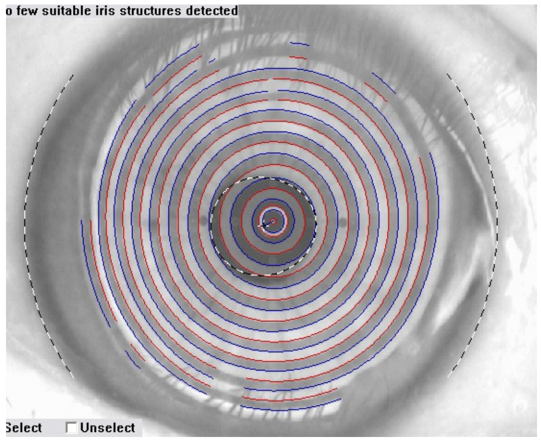


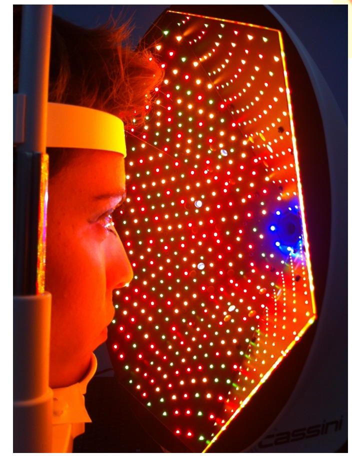
Fig. 2: Marginal plot of UDVA (expressed decimally) and TKC grading with overlying box plots showing mean levels and outliers. Left — group A, unoperated KCN eyes and, right — group B, Athens-protocol (AP) treated KCN eyes

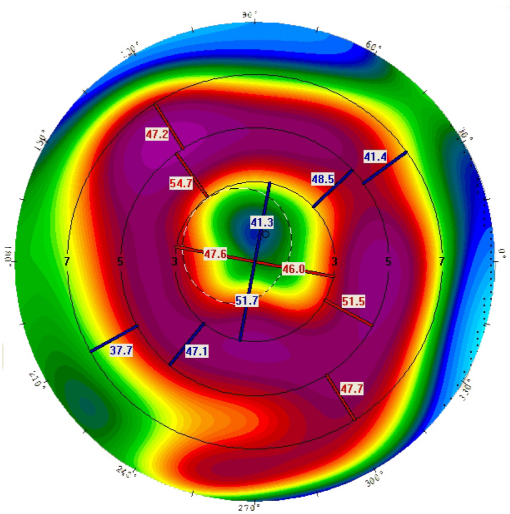
A simple case of Central Cloudy dystrophy (Francois) illustrates the possible discrepancy between different imaging modalities

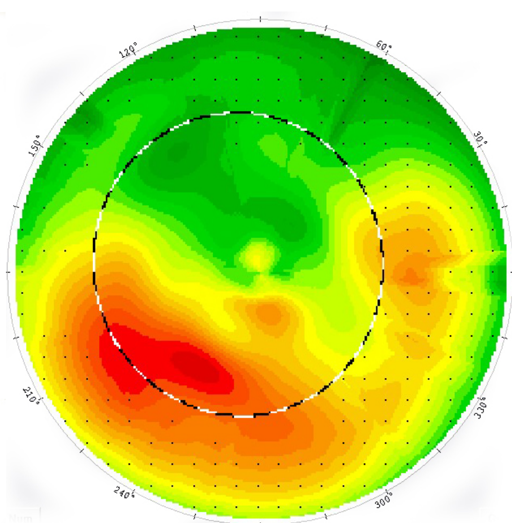
Kanellopoulos AJ, Asimellis G CRO 2013

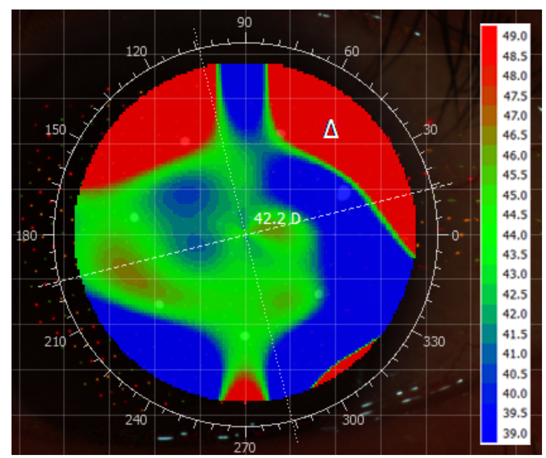




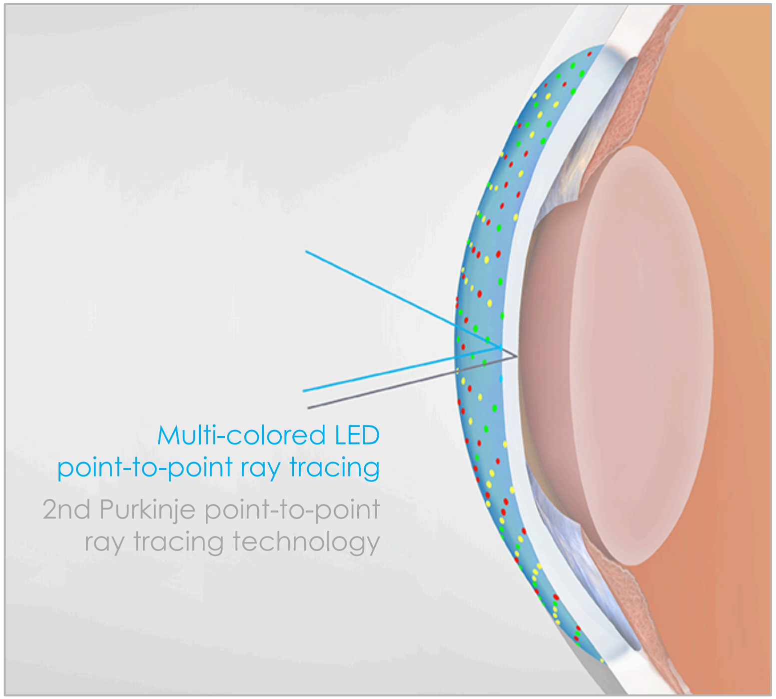








Total Corneal Astigmatism



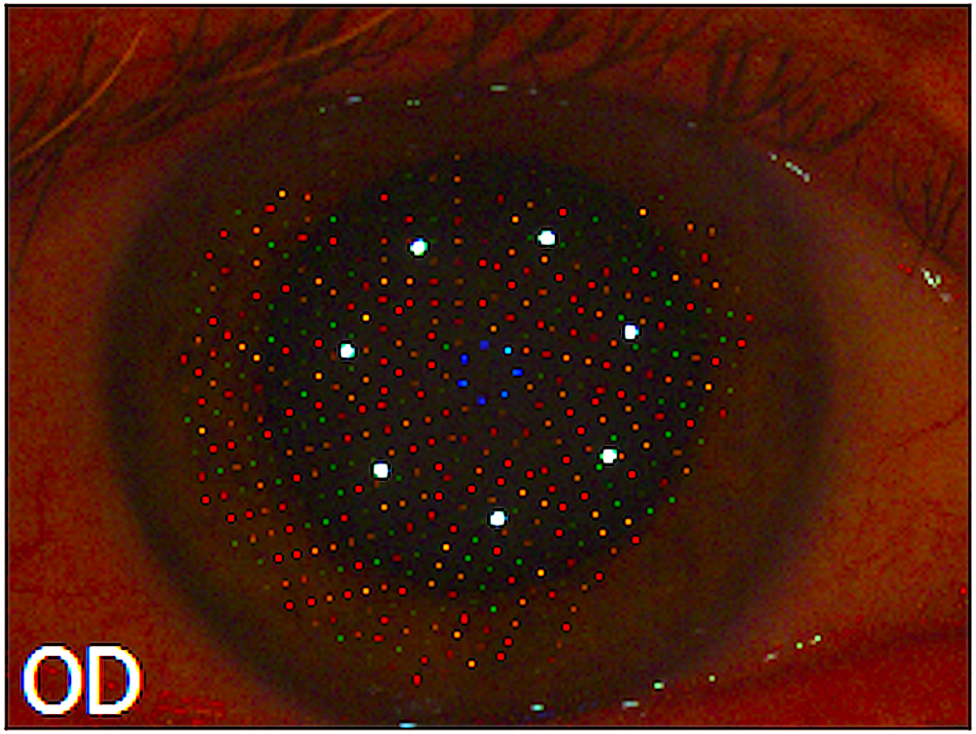
Cassini uses patented multi-colored LED point-to-point ray tracing to provide a GPS-like analysis of the cornea along with high-resolution images utilized for surgical guidance.
The unique measuring principle enables highly accurate and repeatable measurements of the Total Corneal Astigmatism.

Cassini provides critical information to properly select the power and position of Toric intraocular lenses

Cassini users meeting;
Saturday Sep 13th
6PM-Sunborn Yacht Excel London

Cassini

Recorded image



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Laservision Eye Institute
Athens, Greece

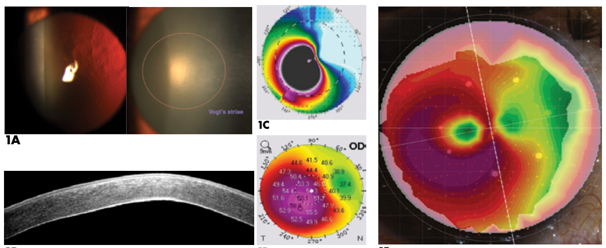
Accurate Central Cornea Measurement

Superior in central corneal measurement to Placido and to Scheimpflug if opacity, haze or high irregularity is present.

Case 1

42 year old Keratoconus patient, surprisingly has additional posterior polymorphous corneal dystrophy which shows clearly in slit lamp **(1A)** and anterior segment OCT **(1B)**.

For corneal topographies: Both Placido **(1C)** and Scheimpflug **(1D)** showed the inferior temple cone but no sign of anything special in the central cornea part. The axial curvature image of Cassini **(1E)** shows clearly the influence of the posterior polymorphous corneal dystrophy part to the anterior cornea curvature.



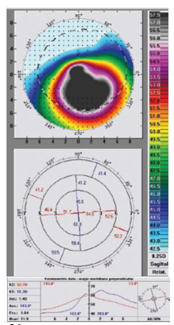
1A 1B 1C 1D 1E

Case 2

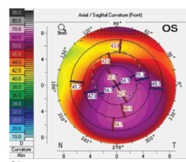
38 year old severe Keratoconus patient, in Placido **(2A)** shows a unreasonable 45.6D and 61.8D along the meridian of the inferior temporal cone in the central 3mm zone. The overall astigmatism was only 1.4D and the flat meridian at 103.8° along the cone direction.

While the flat meridian from Pentacam **(2B)** was 27.8° and Cassini **(2C)** was 20°. Furthermore, Pentacam generates 62.9D and 52.3D along the cone meridian with more than 10D difference in the central 3mm zone which is not reliable as well.

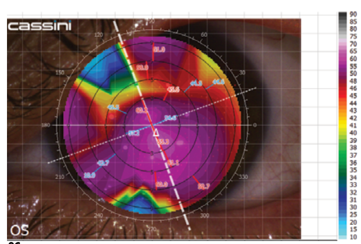
Cassini **(2C)** on the other hand, performs well on this kind of irregular cornea especially in central cornea part. Within 3mm zone the data showed 65.3D/60.2D and 57.2D/54.6D parallel the cone meridian and vertical the cone meridian, respectively. Overall general keratometric was 61.74D@110° and 54.32D@20° in this case.



2A



2B

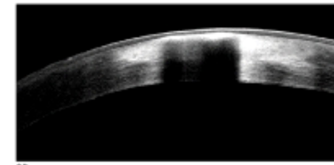


2C

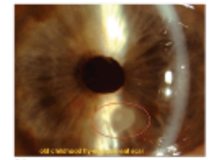
Data Courtesy of
A. John kanellopoulos, M.D. Clinical Professor of Ophthalmology New York University Medical School, NY United States; Medical Director at LaserVision Eye Institute, Athens, Greece

Case 3

72 year old monocular female cataract candidate with old scar (flying injury) shows clearly in slit lamp **(3A)** and anterior segment OCT **(3B)**. The measurements were inconsistent among Placido, Lenstar and Cassini **(3C)**. Cassini keratometry was selected as the best fit for the Toric IOL calculation and postoperative UCVA was 20/20.



3B



3A

	K1 (D)	K2 (D)	Astigmatism (D)	Axis°
Placido	47.8	44.1	2.9	9.2
Optical Biometer	49.0	43.8	5.2	97
Cassini	**45.0**	**40.7**	**4.3**	**2.5**

3C

Data Courtesy of
A. John kanellopoulos, M.D. Clinical Professor of Ophthalmology New York University Medical School, NY United States; Medical Director at LaserVision Eye Institute, Athens, Greece

Cassini Specifications

True Axis

- Multicolor LED imaging technology combined with 2nd Purkinje imaging technology
- Axis repeatability within 3 degrees

True Magnitude

- Diopter range 4.00D – 171.00D
- Display K-values per zone 3/5/7/9mm
- Keratometric indices display in D (diopters) or mm (millimeters)

True Capture

- Auto Capture with joystick positioning
- Measurement Quality Factor parameter
- Auto pupil detection
- Topographic indices - E (shape factor), e (eccentricity), Q (asphericity), p (form factor)
- Keratoconus indices - SAI (Surface Asymmetry Index), SRI (Surface Regularity Index)

True Accuracy

- Submicron accuracy due to color LED triangulation technology < 0.8μm

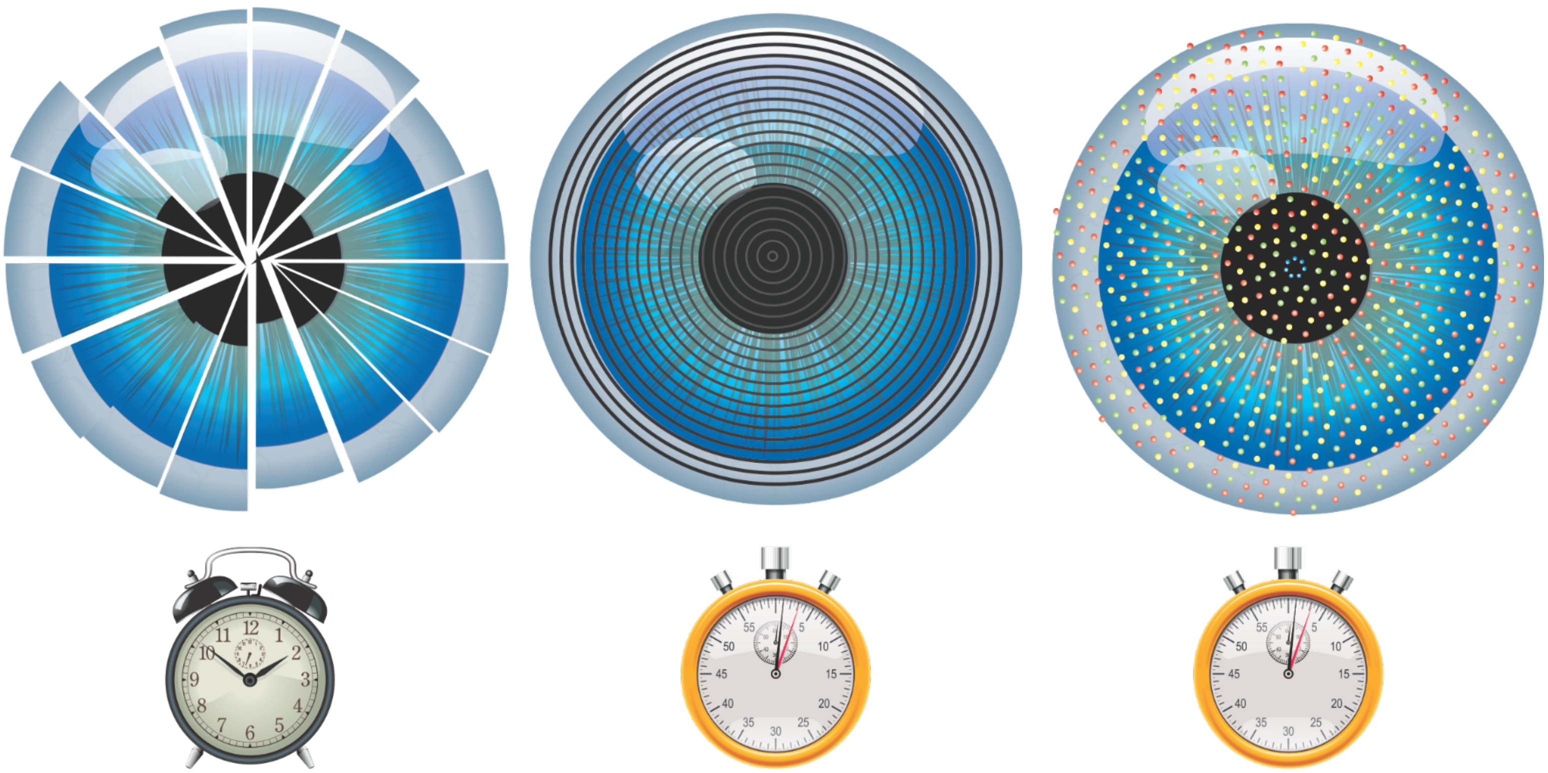
True Technology

- External Ocular Photography
- Topographic maps - Axial, Refractive, Tangential, Elevation, Corneal Aberrations, Recorded color HD external ocular photography
- Multiple color spectrum options
- Incorporated patient management program
- USB, Direct print, PDF, JPG, 3rd party output connectivity
- Mesopic and photopic pupillometry

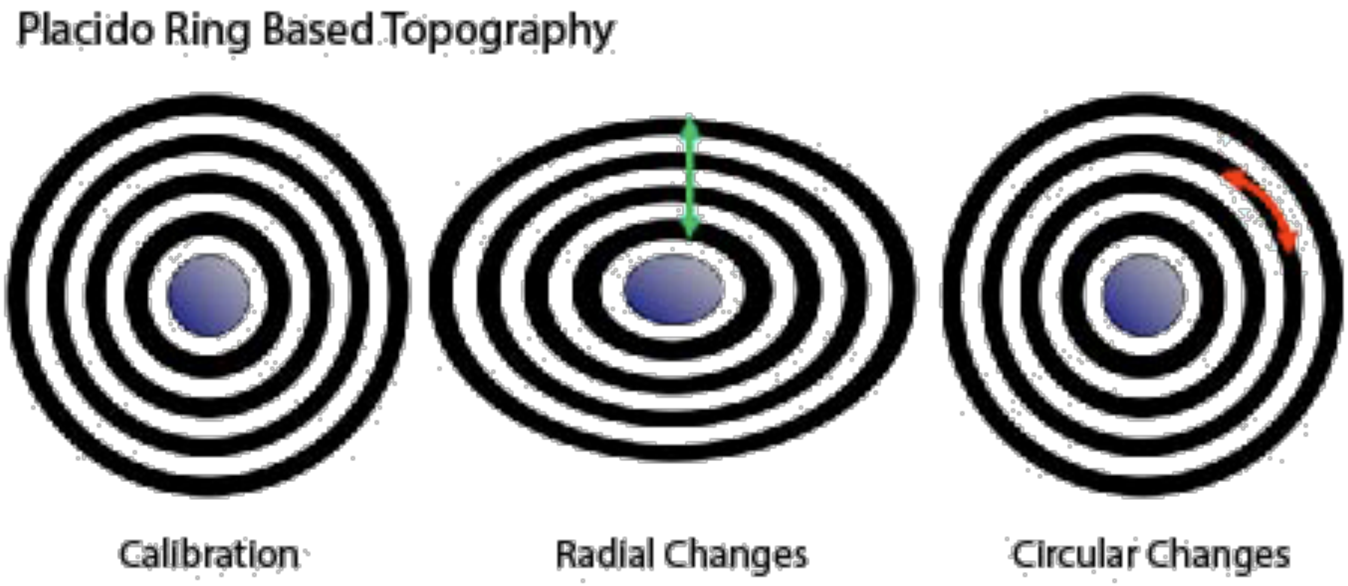
i-optics

For more information:
i-Optics USA • usa@i-optics.com • +1 888 660 6965
i-Optics International • info@i-optics.com • www.i-optics.com

Single-shot Acquisition



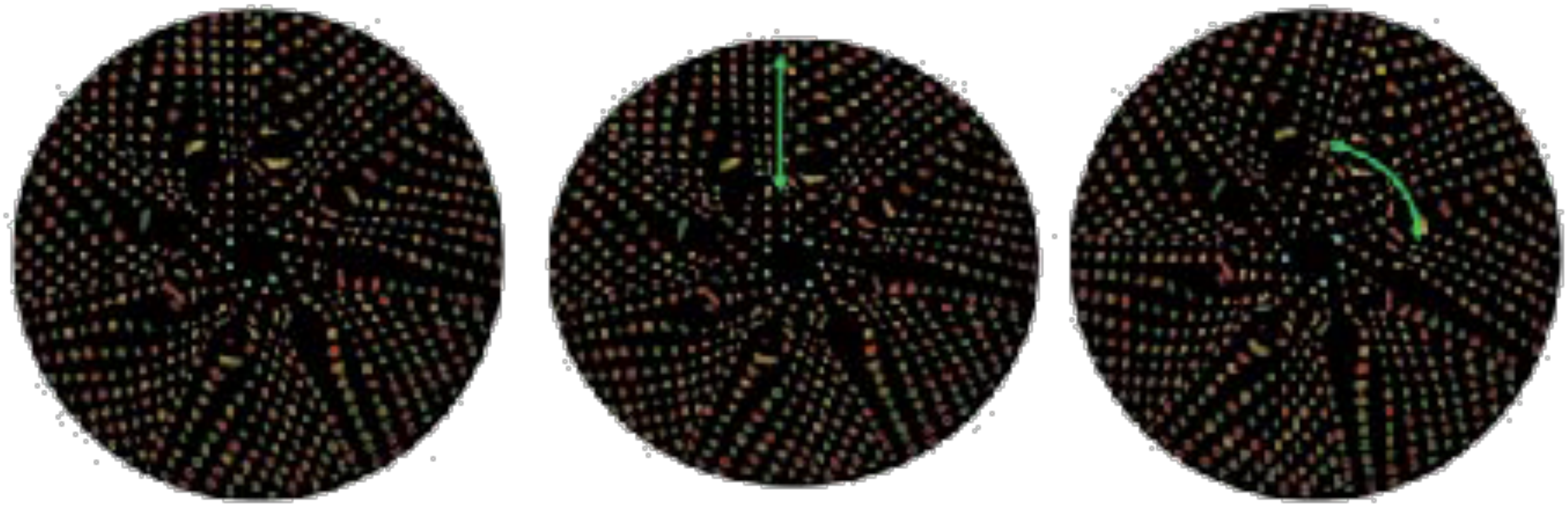
Cassini vs Placido



Ring pattern may not discern feature changes along the tangential direction.

Cassini vs Placido

Cassini Color Led Technology

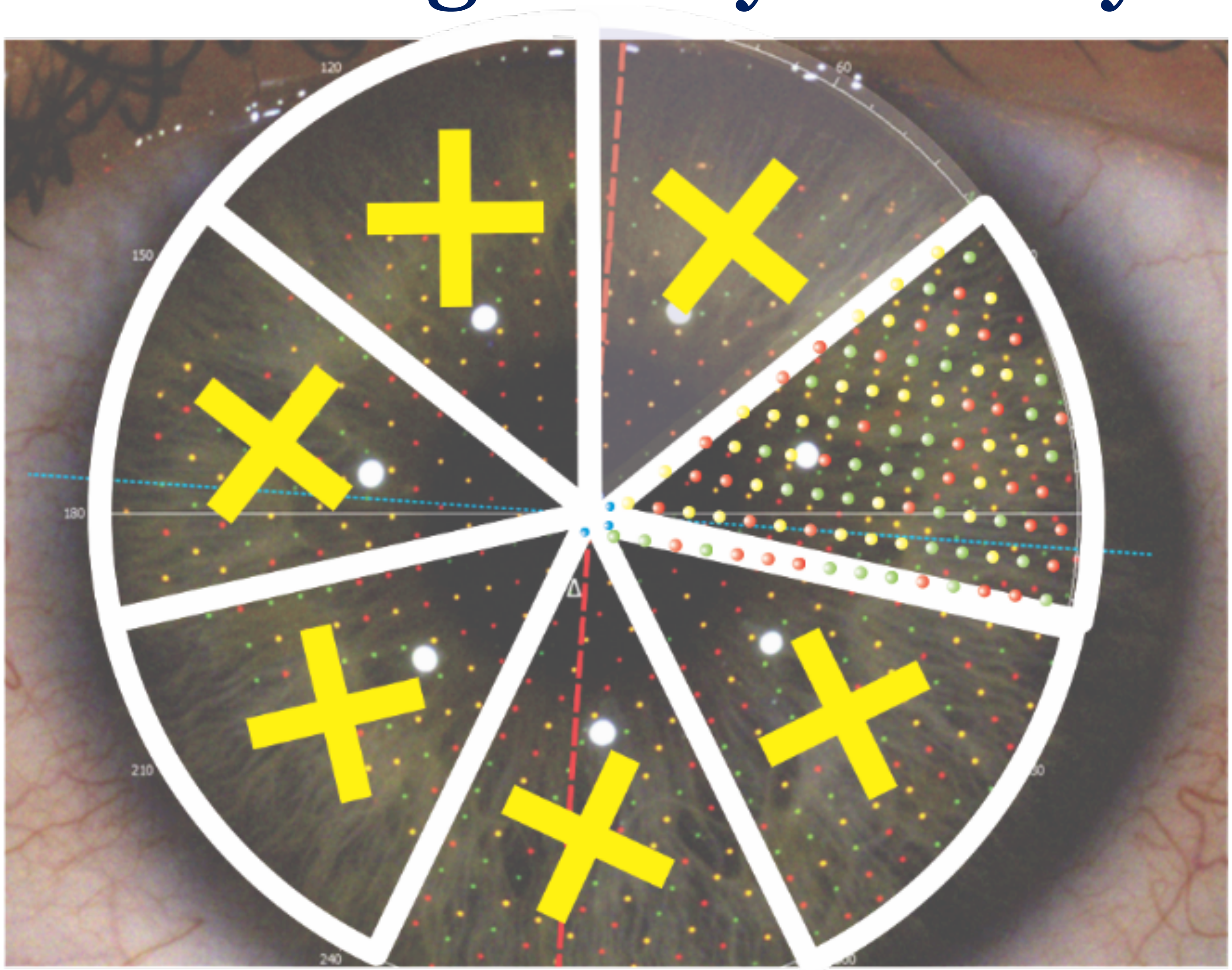


Cassini

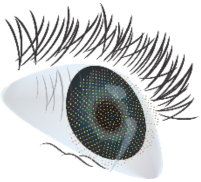
Radial Circular Changes

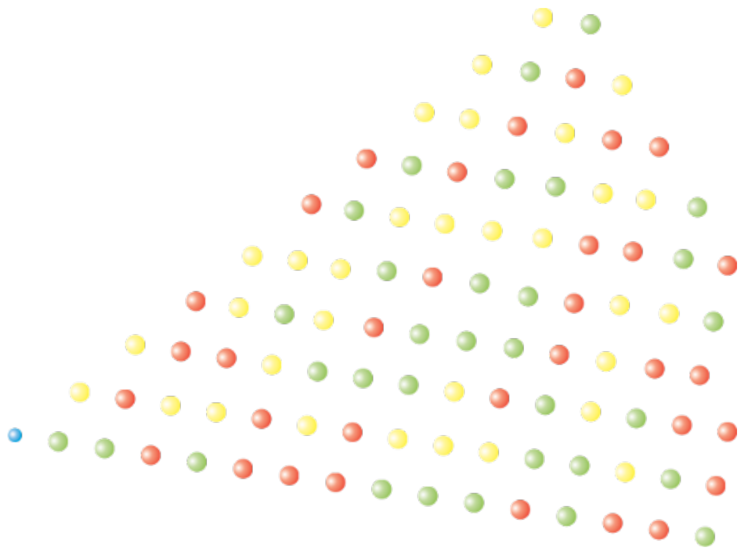
Radial effects can be wel measured as well

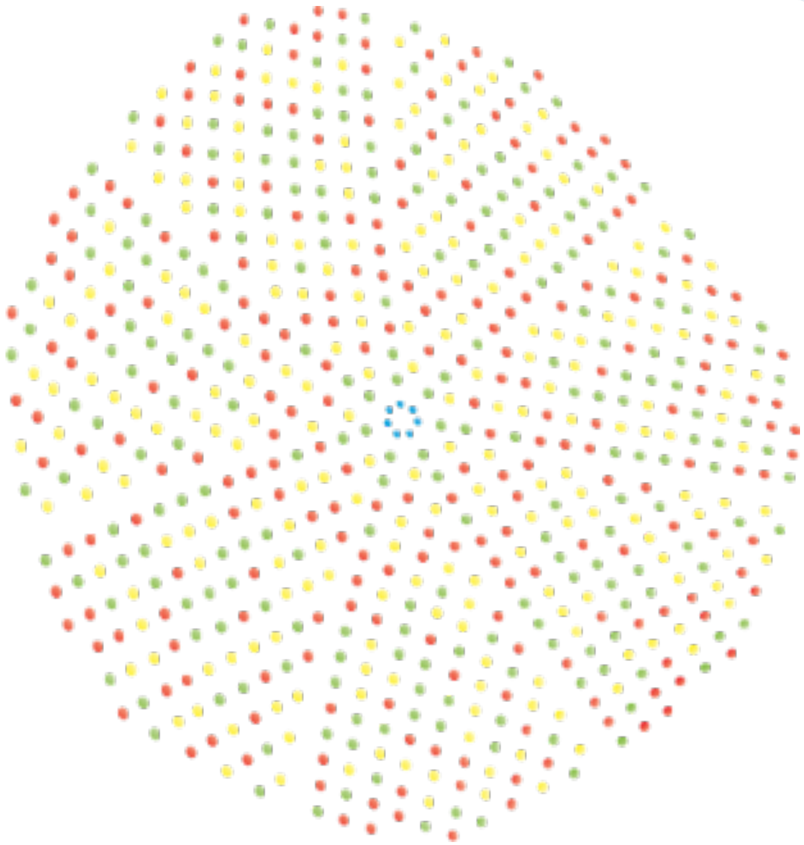
Breaking the Symmetry



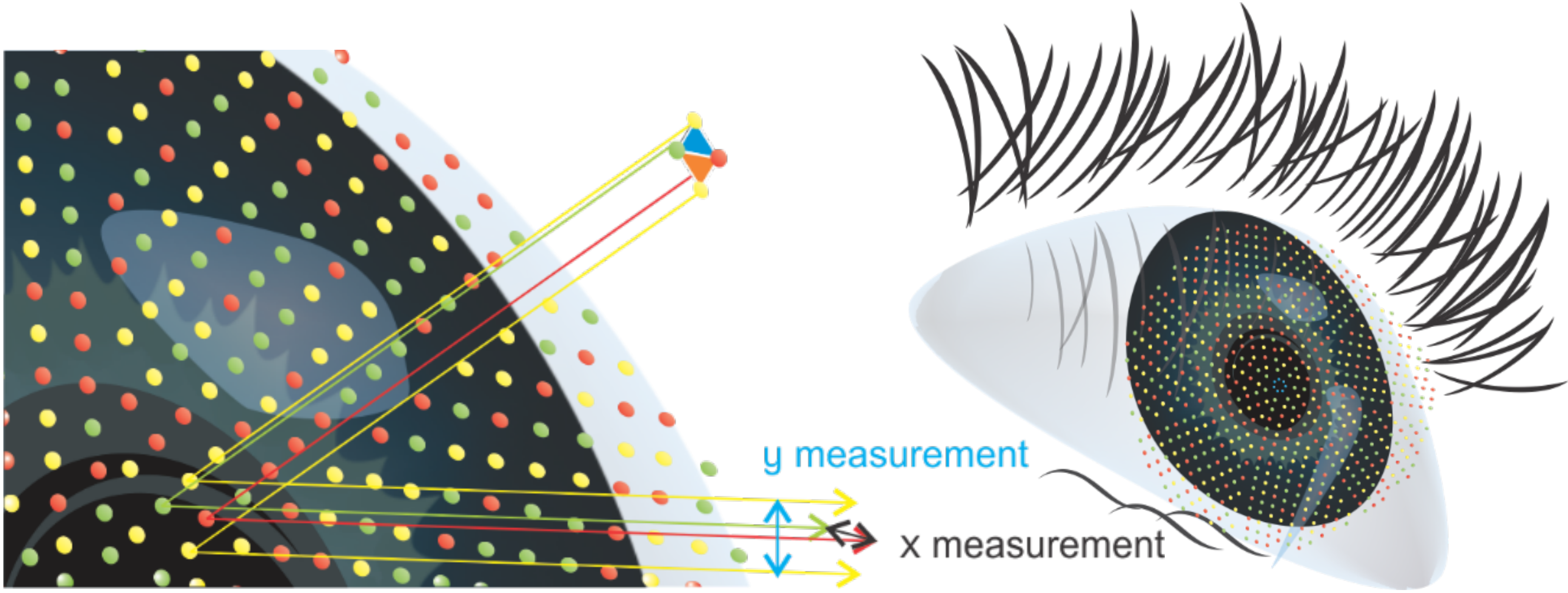
Color – coded Point-Source Analysis





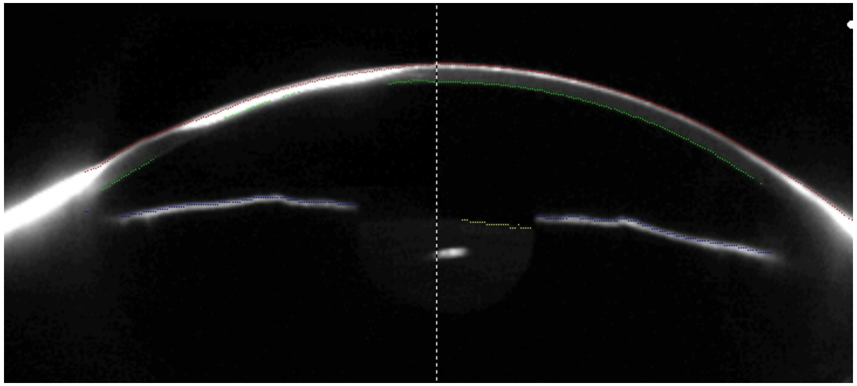


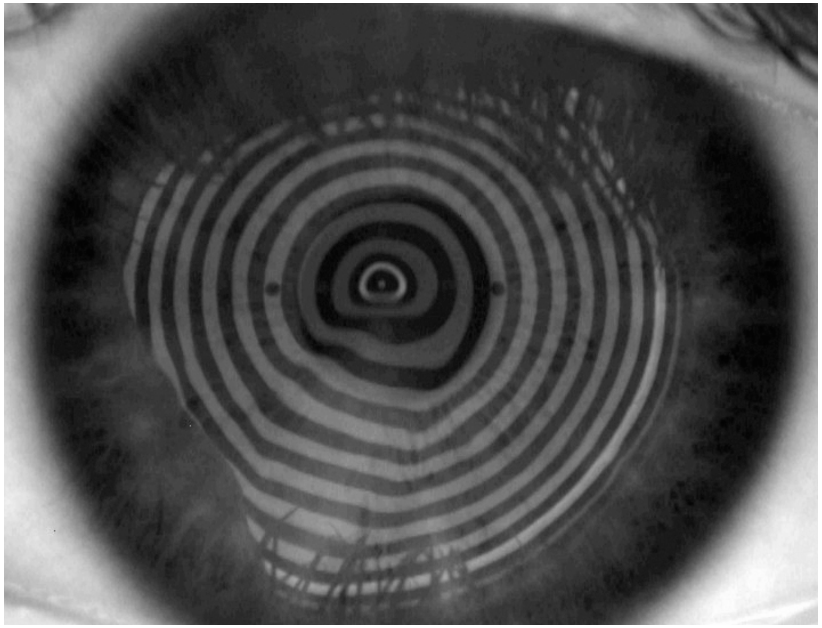
Color – coded Point-Source Analysis



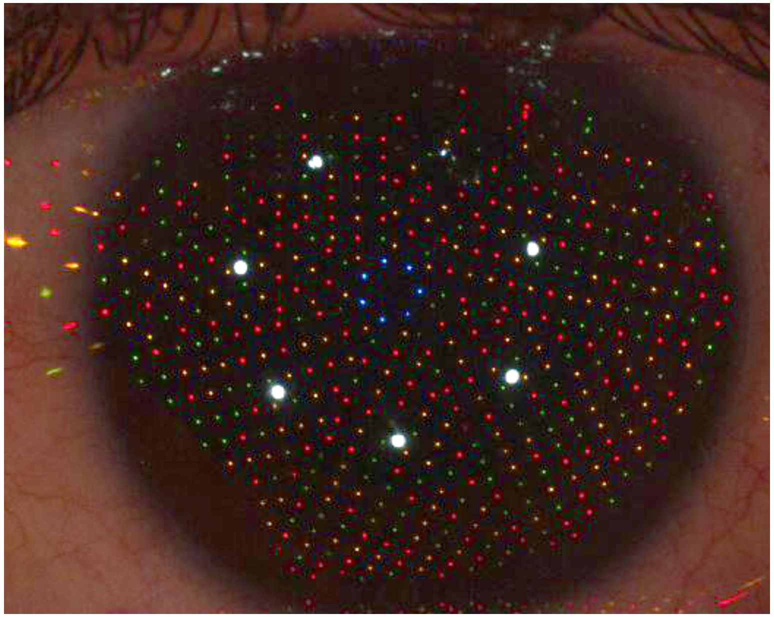
Point-pattern provides information in both coordinates

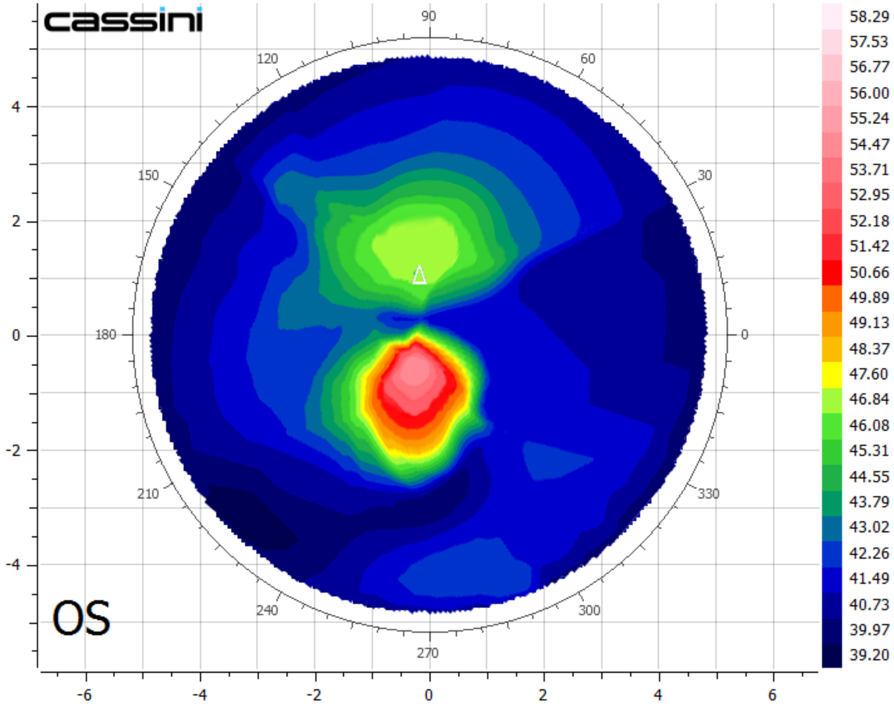
Corneal Scarring (HSV Keratitis)





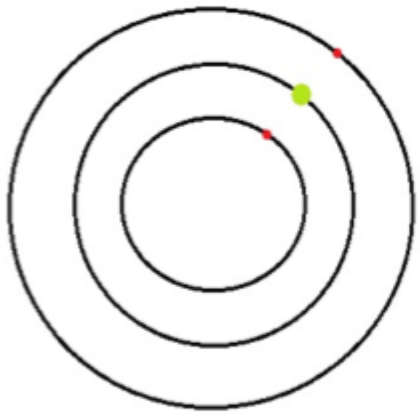
Corneal Scarring (HSV Keratitis)



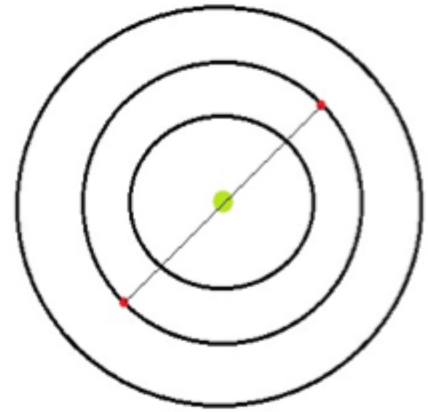


Keratoconus Indices

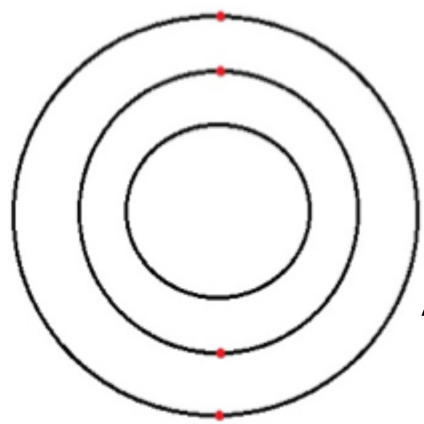
Index	Value
Keratometric indices (3)	
Steep K	42.88 D @ 99º
Flat K	38.32 D @ 9º
Astigmatism	4.56 D
Topographic indices (4)	
p	6.615
Q	5.615
e	-2.370
E	-5.615
Measurements (1)	
W2W/HVID	N/A
Image Quality (4)	
QF	71 %
Coverage	84 %
Align. Ax.	60 %
Align. Lat.	60 %
Keratoconus indices (2)	
SRI	2.930
SAI	13.939



Surface Regularity Index (SRI)

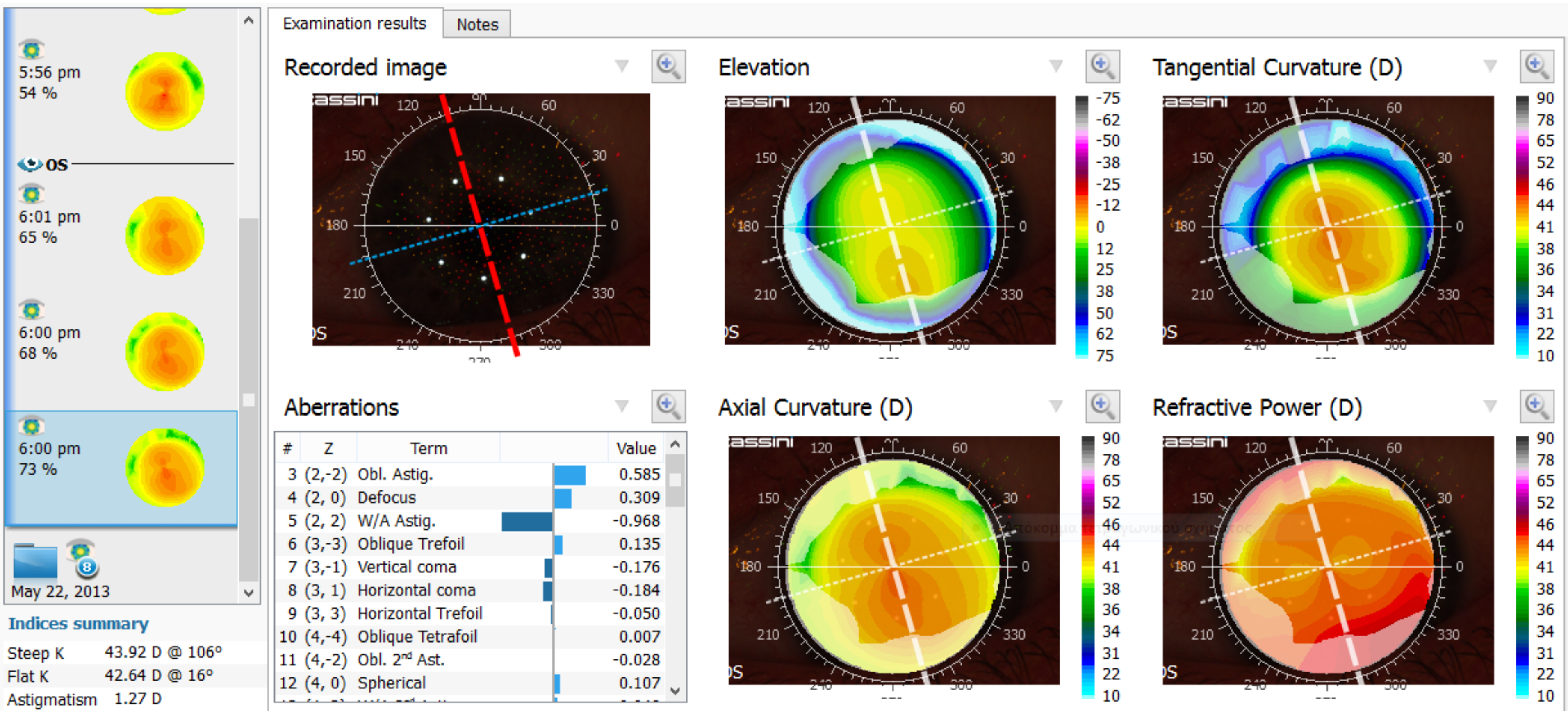


Surface Asymmetry Index (SAI)

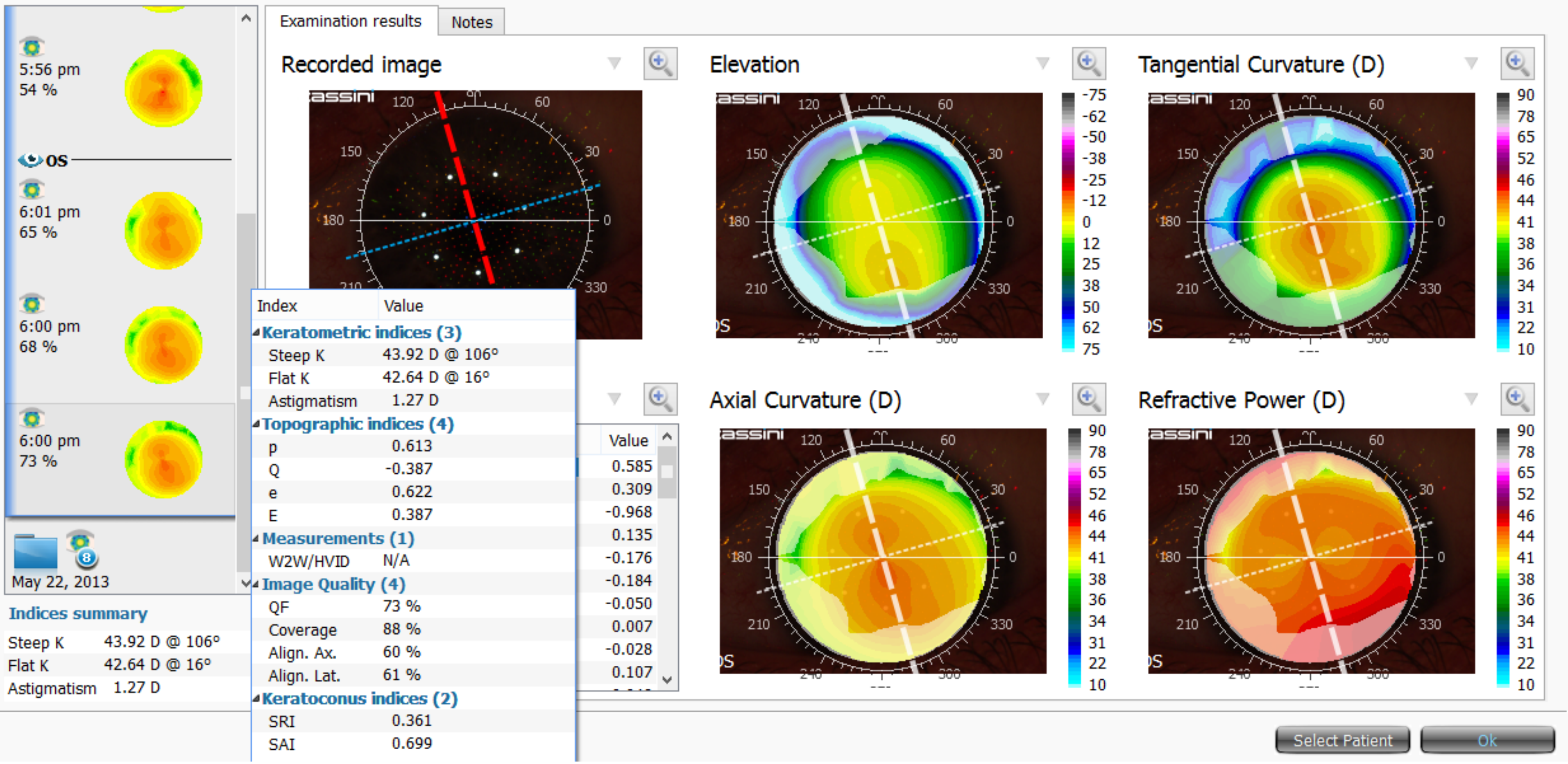


Inferior-Superior Asymmetry (I-S)

Keratometry in D, shape factors and Keratoconic Indices



Keratometry in D, shape factors and Keratoconic Indices



Forme Fruste Keratoconus

Case Reports in Ophthalmology

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Published online: October 25, 2013

Forme Fruste Keratoconus Imaging and Validation via Novel Multi-Spot Reflection Topography

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

Key Words
Light-emitting diode Cassini · Light-emitting diode topography · Diagnosis of keratoconus · Forme fruste keratoconus · Point-source topography · Pentacam HR · Placido topography · Surface Asymmetry Index · Surface Regularity Index · Index of Surface Variance · Index of Height Decentration · Differential topography · Color-point topography

Abstract
Background/Aims: This case report aims to evaluate safety, efficacy and applicability of anterior surface imaging in a patient with forme fruste keratoconus (FFKC) based on a novel multi-spot, multicolor light-emitting-diode (LED) tear film-reflection imaging technology ***Case Description:*** A 45-year-old male patient, clinically diagnosed with FFKC, with highly asymmetric manifestation between his eyes, was subjected to the multicolor-spot reflection topography. We investigated elevation and sagittal curvature maps comparatively with the multicolor-spot reflection topographer, a Placido topographer and a Scheimpflug imaging system. For the right eye, steep and flat keratometry values were 41.92 and 41.05 D with the multicolor spot-reflection topographer, 42.30 and 42.08 D with the Placido, and 41.95 and 41.19 D with the Scheimpflug system. For the left eye, steep and flat keratometry values were 41.86 and 41.19 D with the multicolor spot-reflection topographer, 42.06 and 41.66 D with the Placido topographer, and 41.96 and 41.66 D with the Scheimpflug camera. Average repeatability of the keratometry measurements was ±0.35 D for the multicolor spot-reflection topographer, ±0.30 D for the Placido, and ±0.25 D for the Scheimpflug camera. Very good agreement between the instruments was demonstrated on the elevation and curvature maps. ***Conclusion:*** The ease of use and the comparable results offered by the multicolor spot-reflection topographer, in comparison to established Placido and Scheimpflug imaging, as well as the increased predictability that may be offered by the multicolor spot-reflection topographer, may hold promise for wider clinical application, such as screening of young

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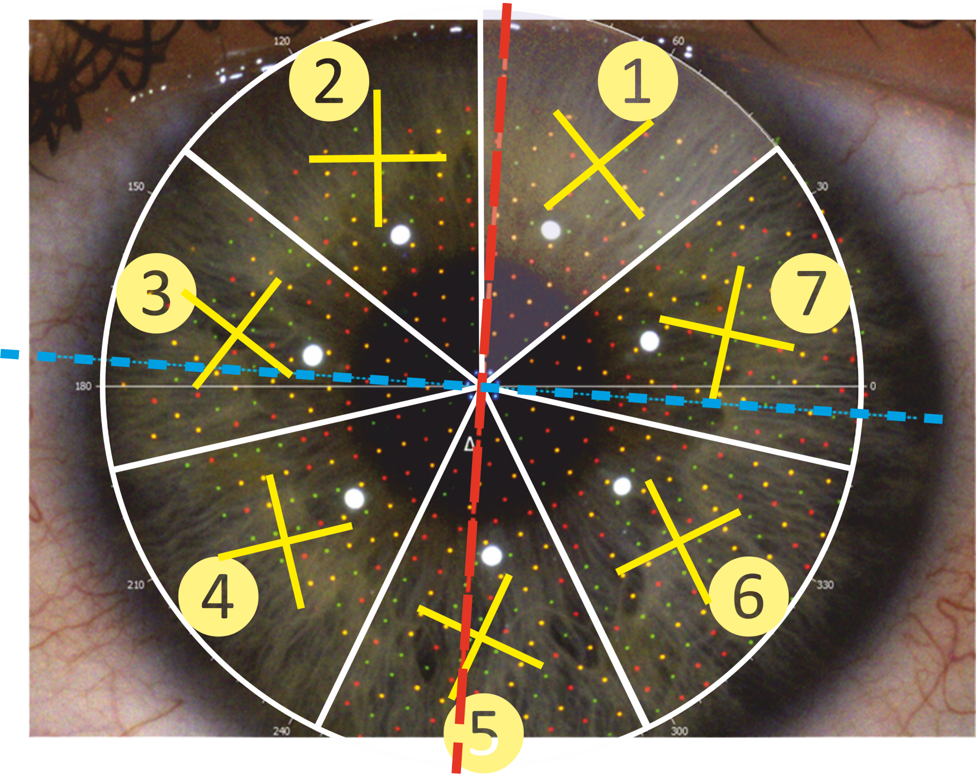
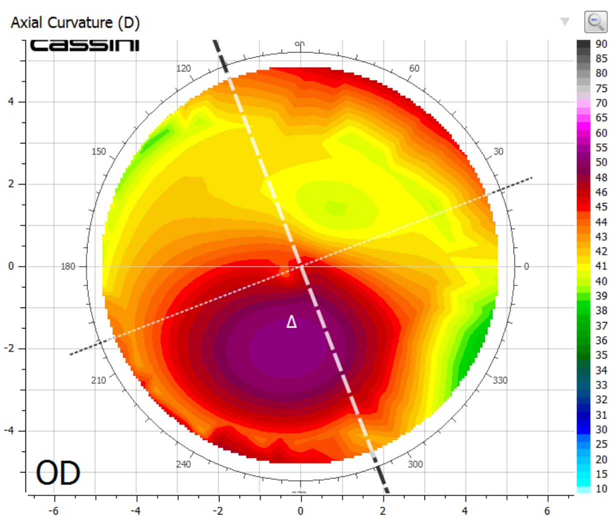
Table 3. Descriptive statistics for corneal elevation data, as obtained by both the Cassini and the Pentacam systems

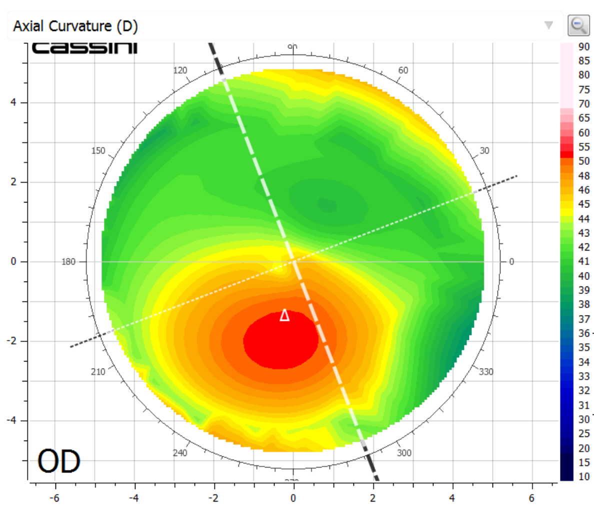
Cassini		
OD		
Average	10.50	–10.50
StDev	1.29	1.73
Min	9.00	–13.00
Max	12.00	–9.00
OS		
Average	7.50	–4.75
StDev	0.58	0.96
Min	7	–6
Max	8	–4
Pentacam		
OD		
Average	9.50	–11.50
StDev	0.58	1.29
Min	9.00	–13.00
Max	10.00	–10.00
OS		
Average	7.25	–5.75
StDev	0.50	1.71
Min	7.00	–8.00
Max	8.00	–4.00

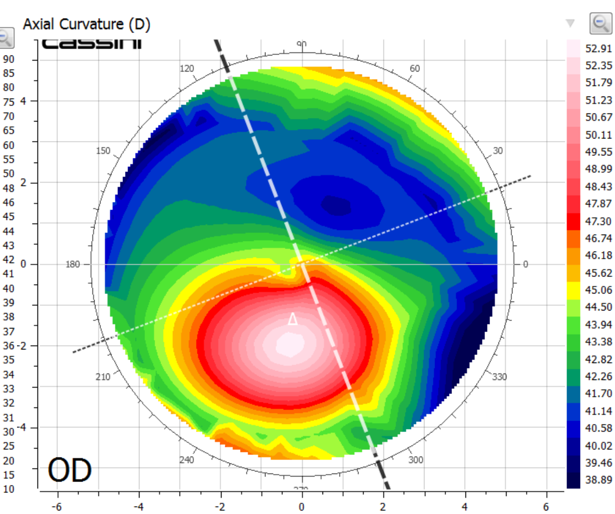
All units are expressed in micrometer.

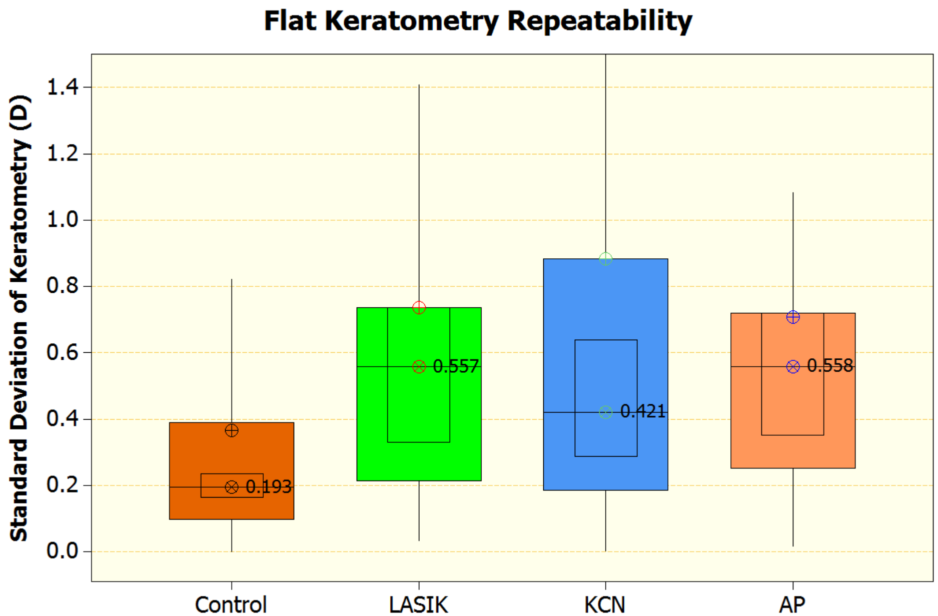


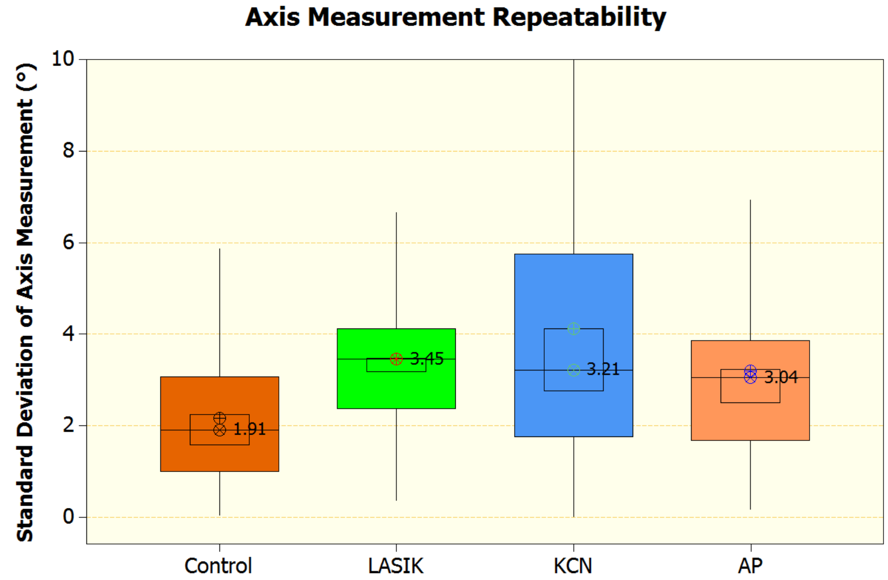
Astigmatic Axis Repeatability in Normal, Keratoconic, Collagen cross-linked and LASIK-treated Eyes with Novel Multi-Colored Spot Reflection Topography

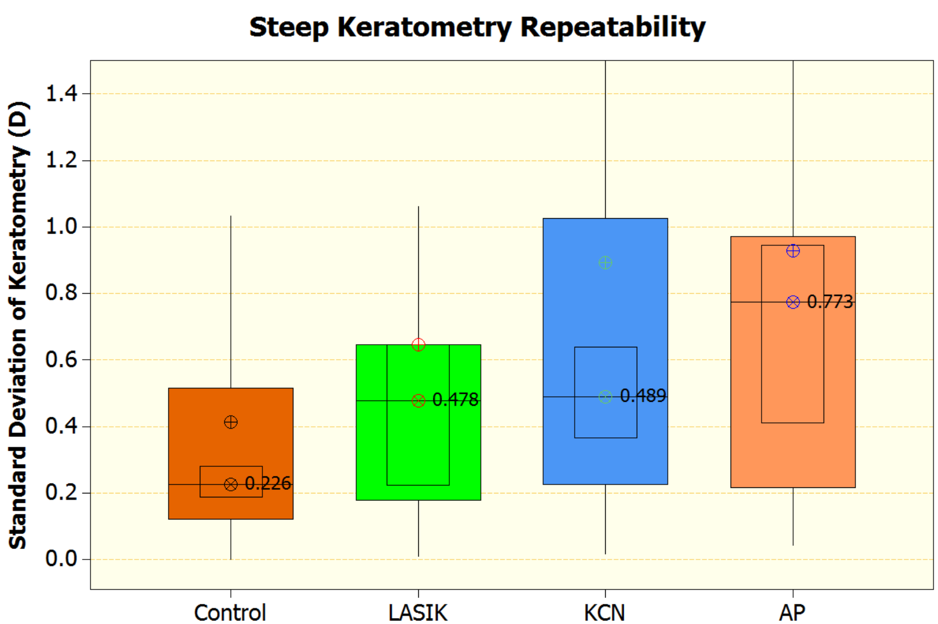


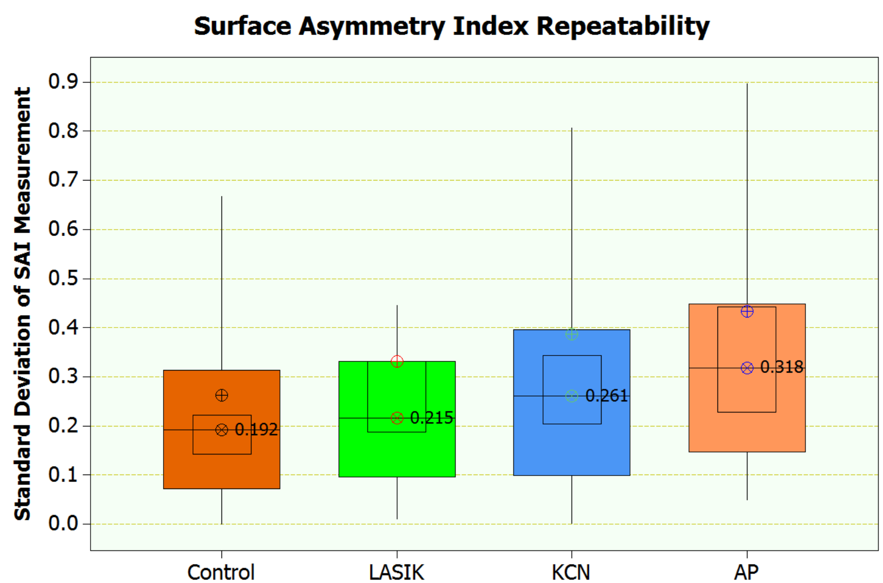





Flat Keratometry Repeatability
Standard Deviation of Keratometry (D)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
0.193
0.557
0.421
0.558
Control
LASIK
KCN
AP


Axis Measurement Repeatability
Standard Deviation of Axis Measurement (°)
0
2
4
6
8
10
1.91
3.45
3.21
3.04
Control
LASIK
KCN
AP


Steep Keratometry Repeatability
Standard Deviation of Keratometry (D)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
0.226
0.478
0.489
0.773
Control
LASIK
KCN
AP


Surface Asymmetry Index Repeatability
Standard Deviation of SAI Measurement
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
0.192
0.215
0.261
0.318
Control
LASIK
KCN
AP

MS NO: ICO202744

In Vivo Three-Dimensional Corneal Epithelium Imaging in Normal Eyes by Anterior-Segment Optical Coherence Tomography: A Clinical Reference Study

Anastasios John Kanellopoulos, MD,† and George Asimellis, PhD**

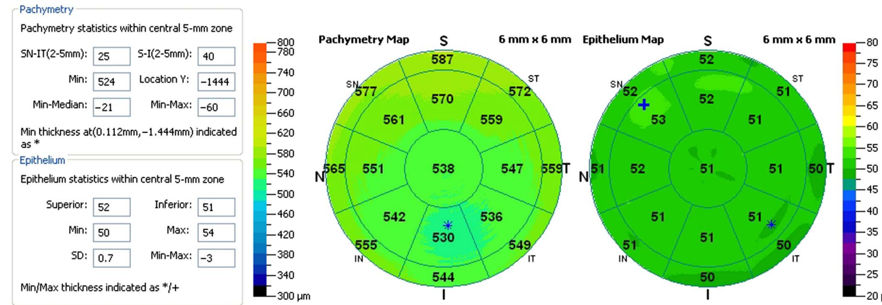


FIGURE 1. Details from the analysis software main report, showing corneal and epithelial 3-dimensional pachymetry maps over the 6-mm corneal diameter. The symbol * indicates the thickness minimum (both corneal and epithelial maps), and the symbol + indicates the thickness maximum (epithelial map only).

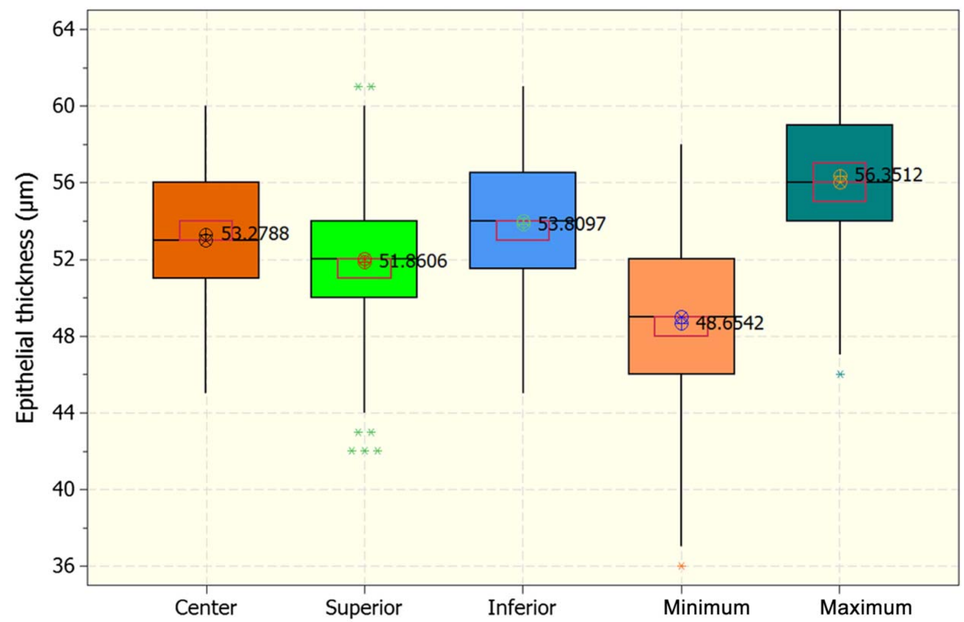


FIGURE 2. Box plot describing central, superior, inferior, minimum, and maximum epithelial thickness for all 373 cases. The median level is displayed numerically and indicated by ⊗, average by ⊕, the 95% median confidence range box by the red borderline, and the interquartile intervals range box by the black borderline. All units are in micrometers.

In Vivo 3-Dimensional Corneal Epithelial Thickness Mapping as an Indicator of Dry Eye: Preliminary Clinical Assessment

ANASTASIOS JOHN KANELLOPOULOS AND GEORGE ASIMELLIS

• PURPOSE: To evaluate in vivo epithelial thickness in dry eye by anterior segment optical coherence tomography.

• DESIGN: Observational, retrospective case-control study.

• METHODS: Two age-matched groups of female subjects, 70 eyes each, age ≈ 55 years, were studied in clinical practice setting: a control (unoperated, no ocular pathology) and a dry eye group (clinically confirmed dry eye, unoperated and no other ocular pathology). Corneal epithelium over the entire cornea was topographically imaged via a novel anterior segment optical coherence tomography (AS-OCT) system. Average, central, and peripheral epithelial thickness as well as topographic epithelial thickness variability were measured.

• RESULTS: For the control group, central epithelial thickness was 53.0 ± 2.7 μm (45-59 μm). Average epithelium thickness was 53.3 ± 2.7 μm (46.7-59.6 μm). Topographic thickness variability was 1.9 ± 1.1 μm (0.7-6.1 μm). For the dry eye group, central epithelial thickness was 59.5 ± 4.2 μm (50-72 μm) and average thickness was 59.3 ± 3.4 μm (51.4-70.5 μm). Topographic thickness variability was 2.5 ± 1.5 μm (0.9-6.9 μm). All pair tests of respective epithelium thickness metrics between the control and dry eye group show statistically significant difference ($P < .05$).

• CONCLUSIONS: This study, based on very user-friendly, novel AS-OCT imaging, indicates increased epithelial thickness in dry eyes. The ease of use and the improved predictability offered by AS-OCT epithelial imaging may be a significant clinical advantage. Augmented epithelial thickness in the suspect cases may be employed as an objective clinical indicator of dry eye. (Am J Ophthalmol 2014;157:63–68. © 2014 by Elsevier Inc. All rights reserved.)

DRY EYE IS A MULTIFACTORIAL DISEASE OF THE tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.[1]

Dry eye is responsible for significant population morbidity and is a common clinical problem for eye clinicians. Besides the significant symptoms and toll on quality of life, it may present significant challenges in refractive surgery patient assessment.[2] As reported in the peer-review literature,[3–7] its manifestations may range from episodic and mild condition to chronic and severe disease: the disorder can be presented with any or many symptoms of visual disturbance and blurred vision, eye discomfort, irritation, foreign body sensation, ocular surface damage, redness, excess tearing, and photosensitivity.

Epidemiologic review studies estimate the prevalence of dry eye disease between 4% and 33%, largely depending, among other factors, on the diagnosis mode, the geographic locale,[8,9] age, and sex, being most prominent in the middle-aged (over age 45 years) female populace.[10–12]

Several clinically available modalities may facilitate in vivo measurement of corneal epithelium, including high-frequency scanning ultrasound biomicroscopy (HF-UBM),[13] anterior segment optical coherence tomography (AS-OCT),[14] and confocal microscopy through focusing (CMTF).[15,16] In the clinical practice, epithelial evaluation is limited by the resolution and the variability of the ocular surface tests.[17]

In pursuit of an objective, repeatable, and quantitative clinical test that may aid in the differential diagnosis of dry eye, we introduce the concept of corneal epithelial thickness as a possible tool in dry eye assessment. We report herein initial clinical results regarding 3-dimensional corneal epithelial thickness mapping in dry eye corneas with a newly commercially available anterior segment optical coherence tomography system.

MATERIALS AND METHODS

THIS OBSERVATIONAL, RETROSPECTIVE CASE-CONTROL study received approval by the Ethics Committee of our Institution (LaserVision.gr Eye Institute), and was adherent to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each subject

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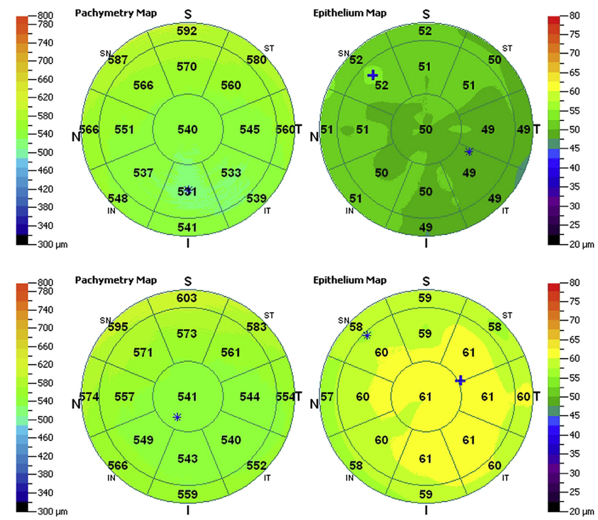

FIGURE 1. Representative corneal total thickness maps (left) and corneal epithelium thickness maps (right) of (Top) a "normal" patient from Group A and (Bottom) a dry eye patient from Group B, as provided by the optical coherence tomography system report.

DISCUSSION

THE CHALLENGE OF OBJECTIVE DRY EYE ASSESSMENT HAS been argued in length. The current options of the clinical investigator includes slit-lamp observations, osmolarity test, tear-film breakup time measurement, Schirmer lacrimation test, corneal and conjunctival staining, meibomian grading, and Ocular Surface Disease Index.[10] Research evidence suggests that clinical dry eye symptoms alone may be insufficient for the diagnosis and management of dry eye, and there is argument for a consensus of newer metrics that may better reflect the differential discrimination of the disease.[18]

One such possible element in diagnosis is overall epithelial thickness, as well as the topographic distribution of epithelial thickness. For example, atopic keratoconjunctivitis has been associated with significant alterations of the basal epithelium and subbasal and stromal corneal nerves, related to the changes in tear functions and corneal sensitivity.[19]

Very little is reported, however, in the peer-review literature on the subject matter of entire corneal area in vivo measurement of epithelial thickness, particularly in relationship with dry eye. This can be justified by the fact that neither HF-UBM nor AS-OCT nor CMTF techniques have been fully applicable and/or with a commercially available mode for this use, as well as the fact that some (eg, HF-UBM) employ instrument or fluid interface contact with the epithelium. We have not identified, for example, reported correlation of dry eye and HF-UBM measurements. CMTF has been restricted in this application because of the degraded precision by eye movement during the long acquisition time; in addition, other available clinical evaluation techniques for the corneal epithelium either are invasive or require contact between the probe and the ocular surface, and thus cannot provide precise in vivo measurement of the epithelial thickness.[20] In a confocal laser scanning microscopy study in dry eye,[21] the mean superficial and intermediate epithelial cell densities in the central cornea in the dry eye groups were significantly lower than in normal participants. Dry eye corneas showed significant alterations, presumably attributable to increased desquamation of the superficial cell layer.

Reports on entire corneal epithelium imaging via AS-OCT, a novel entity, have been also few. In most of these studies, investigator-modified software/hardware[22–24] or caliper software measurement techniques[25,26] have been employed (for example, by manually placing cursors to measure epithelial thickness in each location).

The recent availability of full-cornea corneal epithelial thickness imaging by AS-OCT potentially presents a practical clinical tool for qualitative (by examination of the

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?

Anastasios John Kanellopoulos[1,2]
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

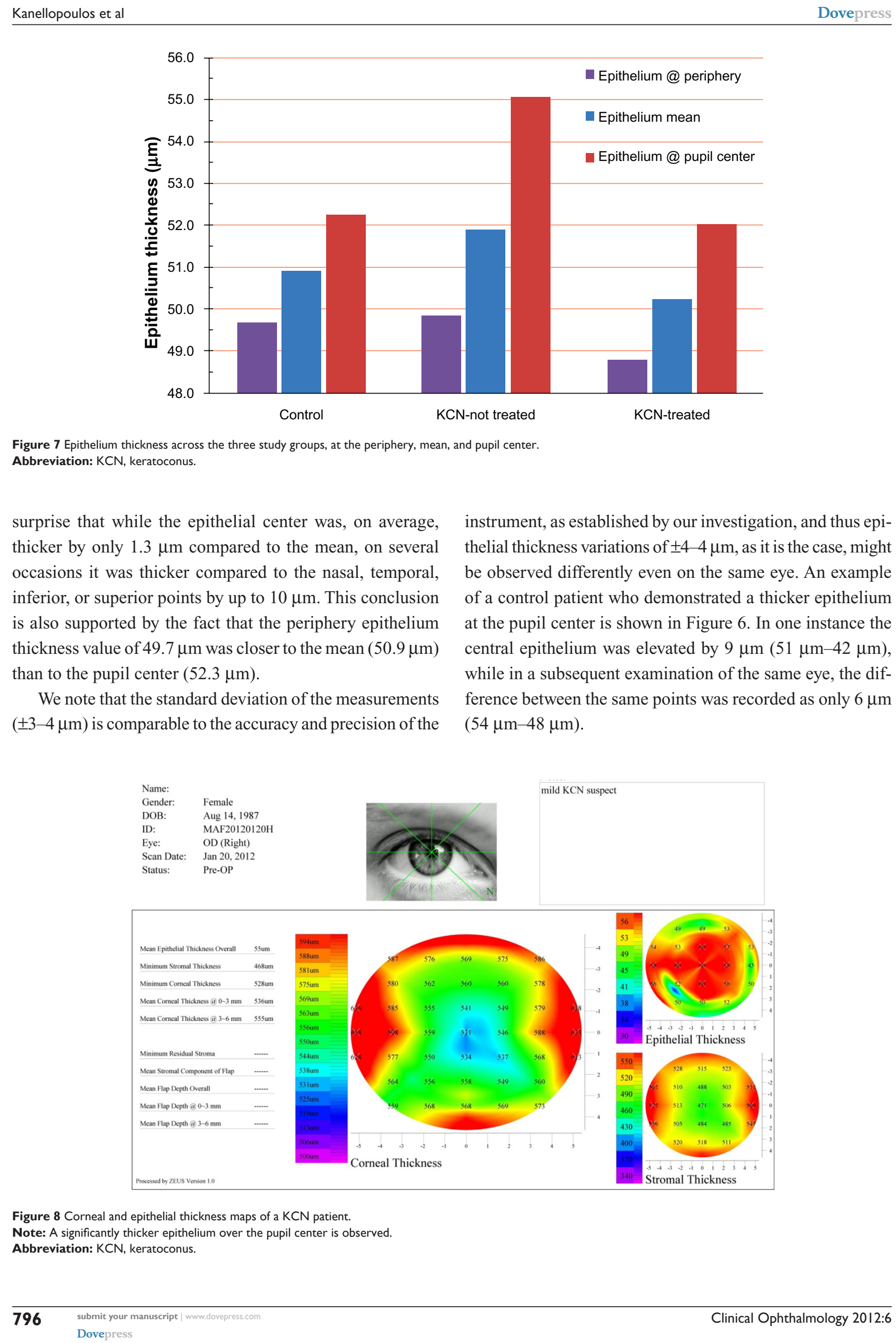
Kanellopoulos et al Dovepress

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.

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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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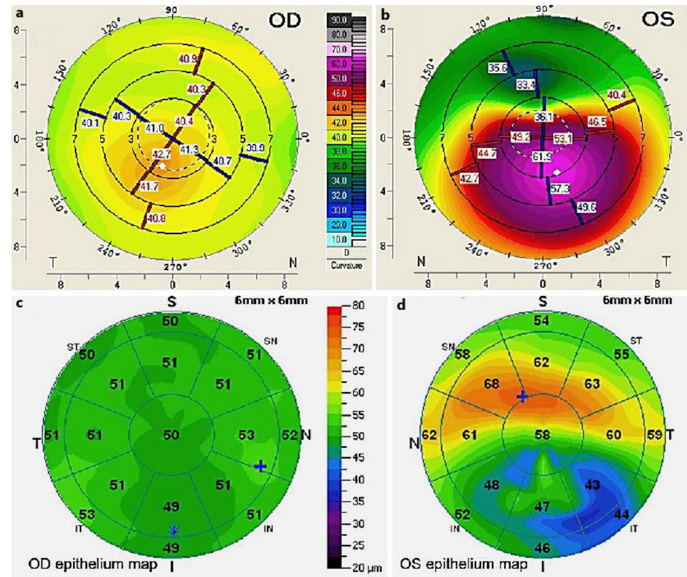

Fig. 1. **a** Tomographic anterior corneal sagittal curvature map for OD. **b** Tomographic anterior corneal sagittal curvature map for OS. **c** AS-OCT epithelial thickness map for OD. **d** AS-OCT epithelial thickness map for OS.

ARTICLE

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

Anastasios John Kanellopoulos, MD, George Asimellis, PhD

ARTICLE

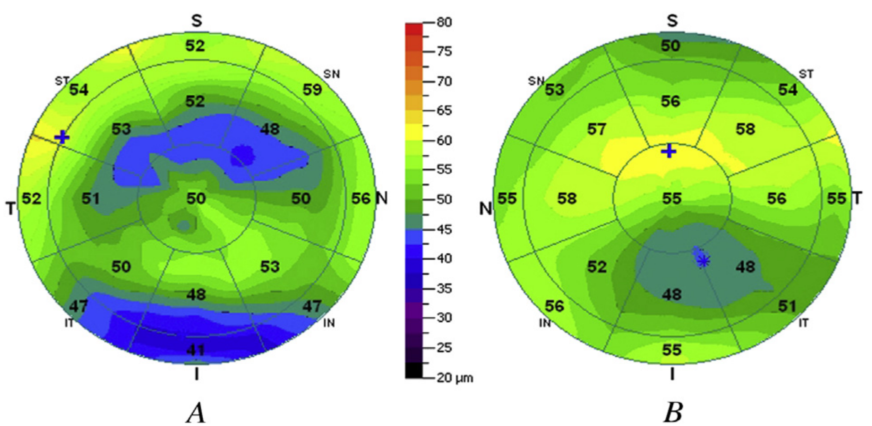

Figure 2. Comparative AS-OCT epithelial thickness (µm) 3-D maps shows an *image* from Group A taken 1 year postoperatively and an image from Group B (I = inferior; IN = inferior–nasal; IT = inferior–temporal; N = nasal; S = superior; SN = superior–nasal; ST = superior–temporal; T = temporal).

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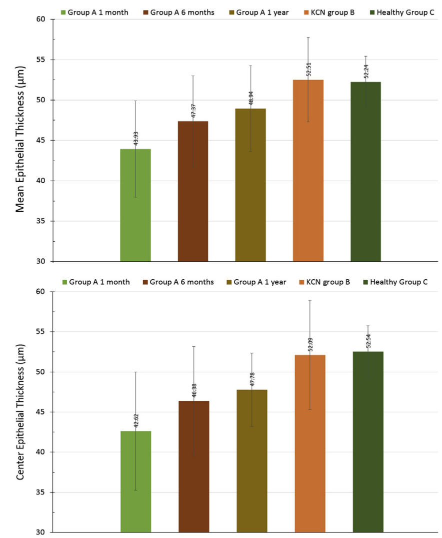

Figure 3. Mean and center epithelial thicknesses in the 3 groups. Error bars correspond to the SD (KCN = keratoconus, no treatment).

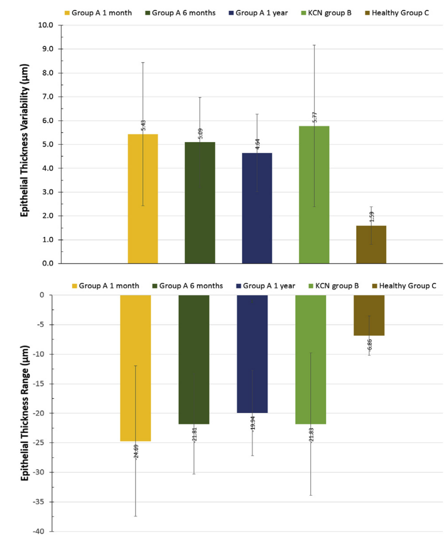

Figure 4. Epithelial thickness variability and range in the 3 groups. Error bars correspond to the SD (KCN = keratoconus, no treatment).

The findings in the current study agree with those in our previous study[1]; that is, although an overall thicker epithelium with large variations can be observed clinically and topographically in eyes with keratoconus, in eyes treated with CXL the variability in epithelium thickness and topographic thickness decreased by a statistically significant margin and was more uniform. We have theorized that epithelial hyperplasia in biomechanically unstable corneas (ie, increased epithelial regrowth activity) might be associated with a more elastic cornea.[1] The laboratory and clinical findings of increased corneal rigidity after CXL are widely accepted,[23–25] including in studies of accelerated high-fluence CXL.[26]

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

WHAT WAS KNOWN

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

WHAT THIS PAPER ADDS

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

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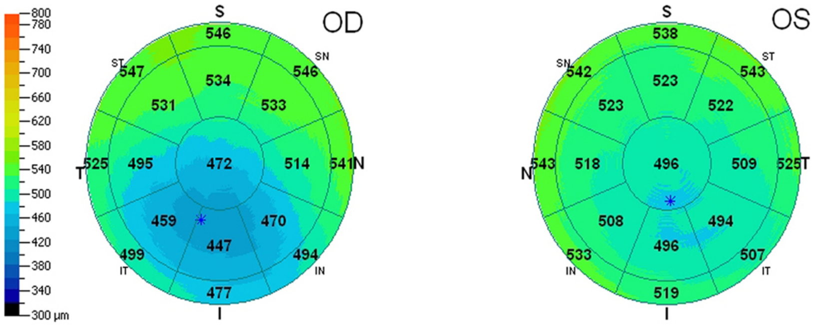
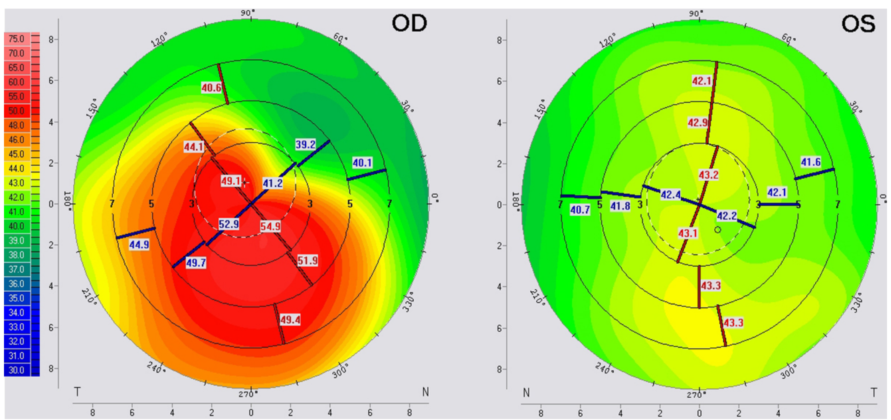
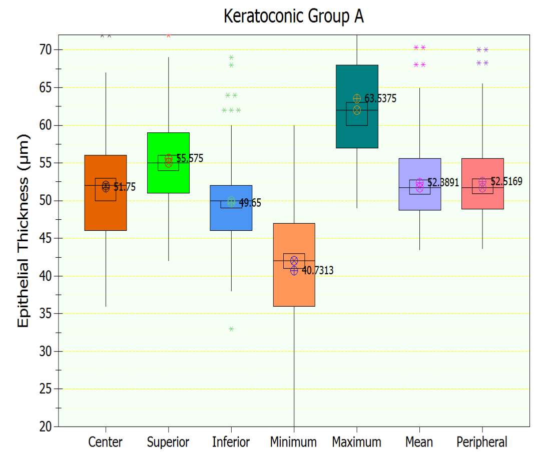
2. Kanellopoulos AJ. Long term results of a prospective randomized bilateral eye comparison trial of higher fluence, shorter duration ultraviolet A radiation, and riboflavin collagen cross

160 Normal Vs. 160 KCN epi distribution

Box plots of epithelial thickness (showing center, superior, inferior, minimum, maximum, mean, and peripheral) showing median level (indicated by ⊗), average symbol (⊕), 95% median confidence and interquartile intervals range boxes. Top, keratoconic group-A, bottom, control group-B.







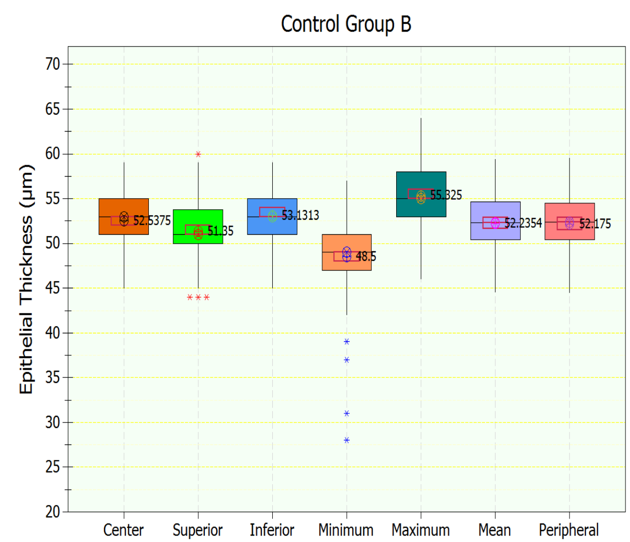


Figure 3

Box plots of epithelial thickness topographic variability (top) and range, defined as minimum minus maximum (bottom) for the two groups. Graphs include median level (indicated by ⊗), average symbol (⊕), 95% median confidence and interquartile intervals range boxes.

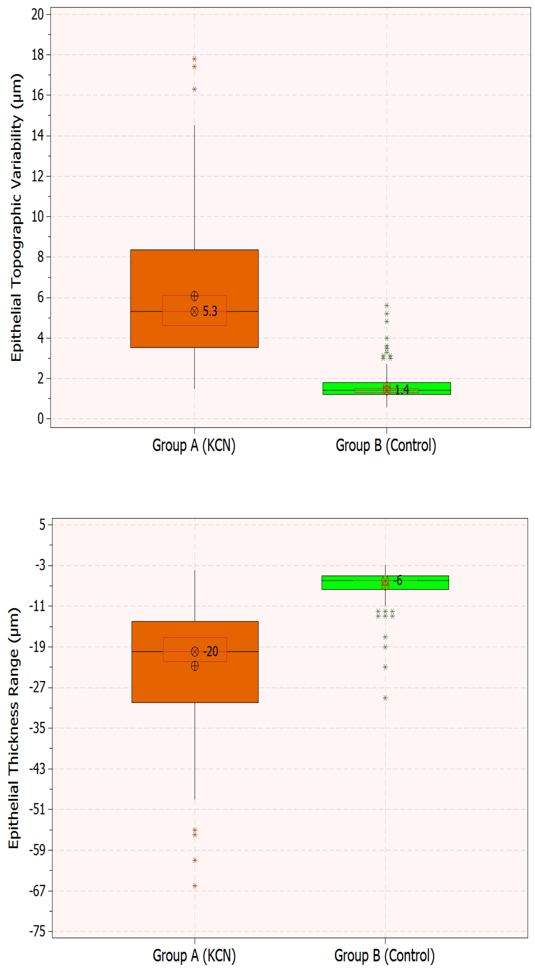
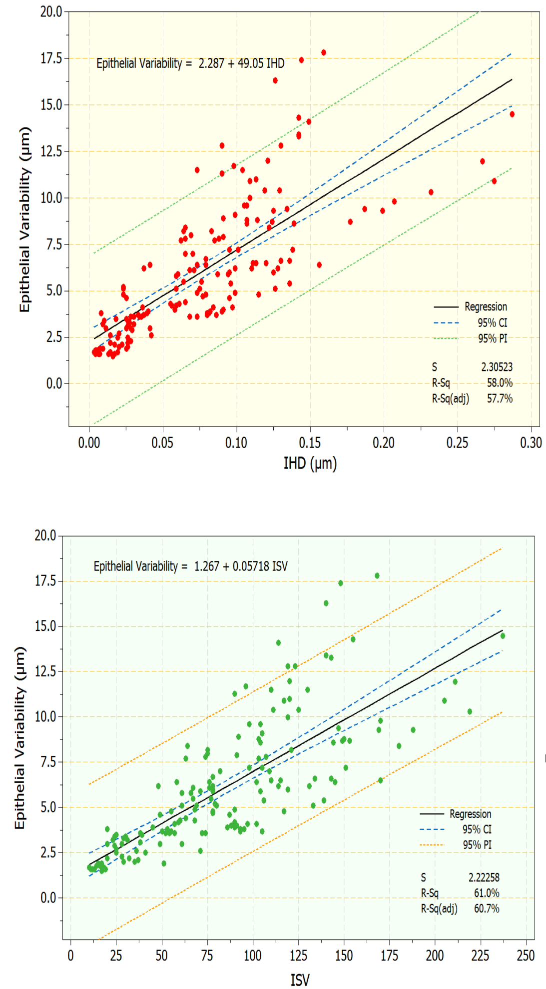


Figure 4

Scatter and Fitted Line Plot of topographic epithelial thickness variability vs index of height decentration (IHD), top, and index of surface variance (ISV), bottom. Graphs include regression, 95% confidence intervals (CI) and 95% prediction intervals (PI) lines.



ARTICLE

Optical coherence tomography–derived corneal thickness asymmetry indices: Clinical reference study of normal eyes

Anastasios John Kanellopoulos, MD, Marianthi Chiridou, OD, George Asimellis, PhD

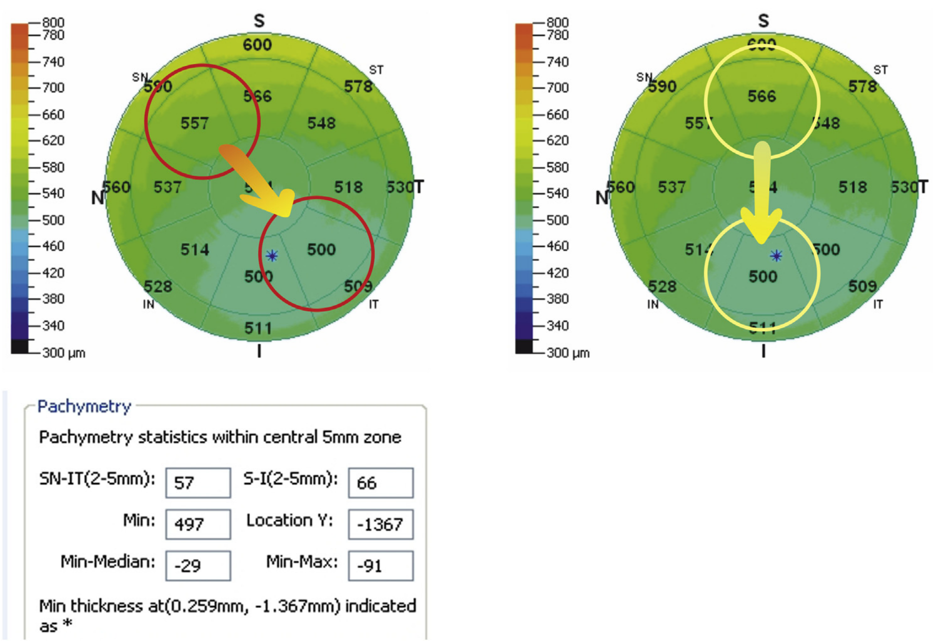


Figure 1. Definitions of SN–IT and S–I corneal asymmetry indices obtained by AS-OCT corneal 3-D pachymetry maps (6.0 mm diameter) (I = inferior; IN = inferonasal; IT = inferotemporal; Min-Max = thickness range, or global thinning, defined as the minimum corneal thickness minus the maximum corneal thickness; Min-Median = focal thinning, defined as the minimum corneal thickness minus the median corneal thickness; S = superior; S-I = superior–inferior; SN-IT = superonasal–inferotemporal; ST = superotemporal; T = temporal).

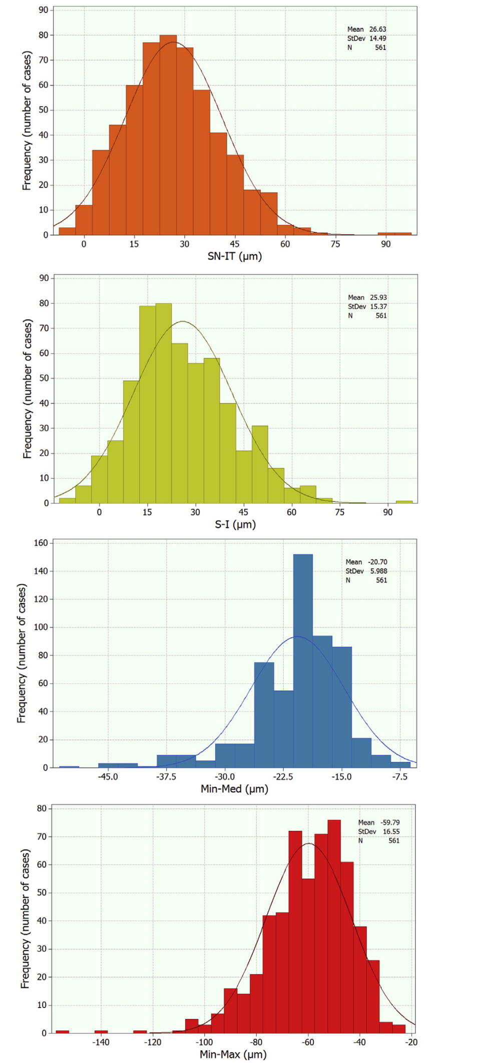
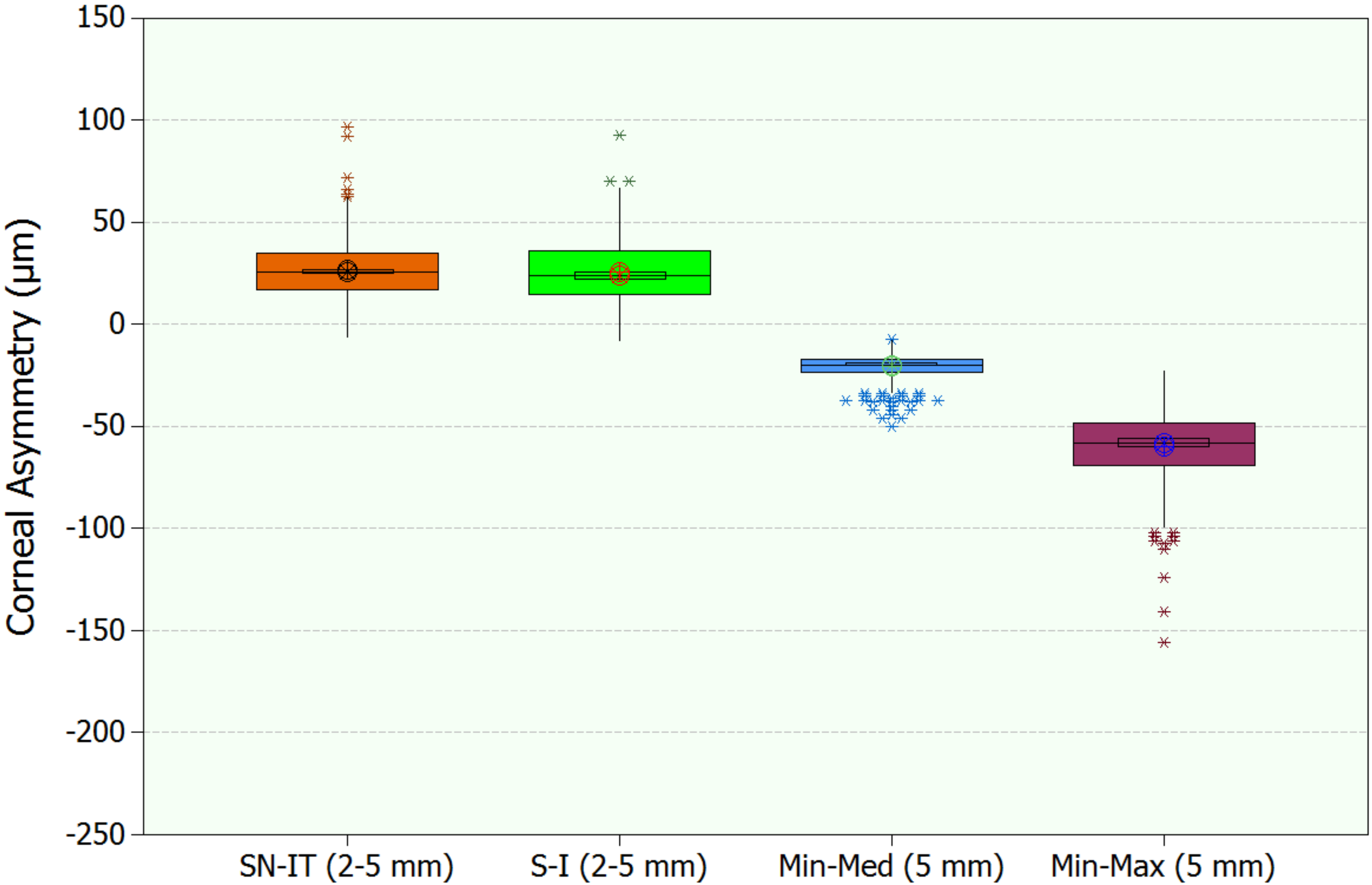


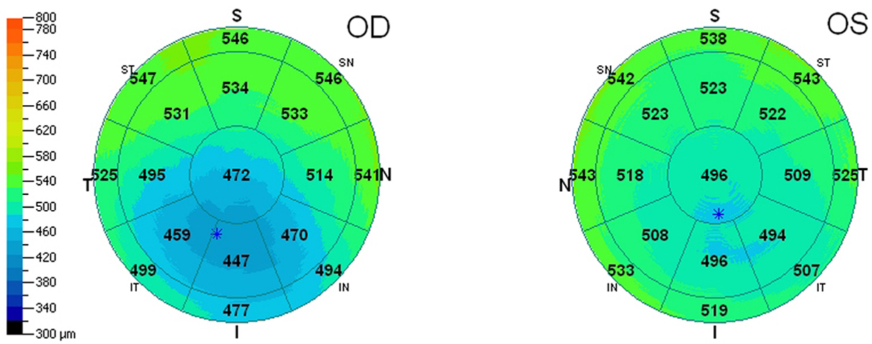
Figure 3. Optical coherence tomography–derived corneal asymmetry and thinning indices for the 561 cases (Min-Max = thickness range, or global thinning, defined as the minimum corneal thickness minus the maximum corneal thickness; Min-Med = focal thinning, defined as the minimum corneal thickness minus the median corneal thickness; S-I = superior–inferior; SN-IT = superonasal–inferotemporal).

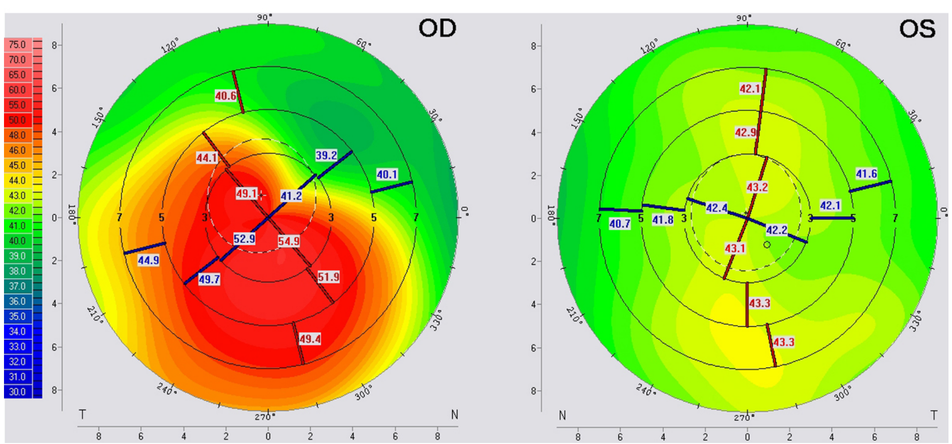


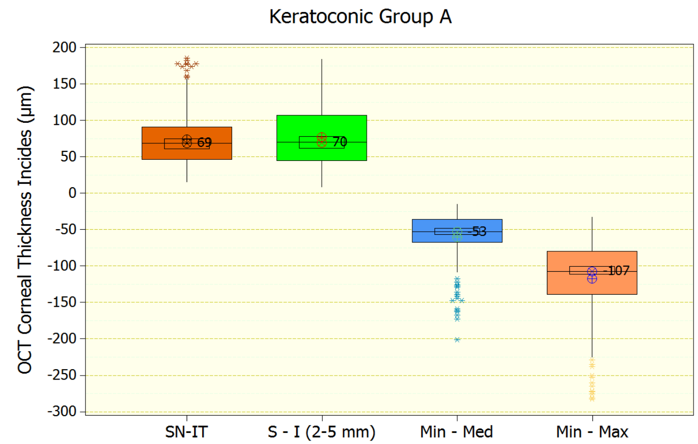
150
100
50
0
-50
-100
-150
-200
-250
Corneal Asymmetry (µm)
SN-IT (2-5 mm)
S-I (2-5 mm)
Min-Med (5 mm)
Min-Max (5 mm)

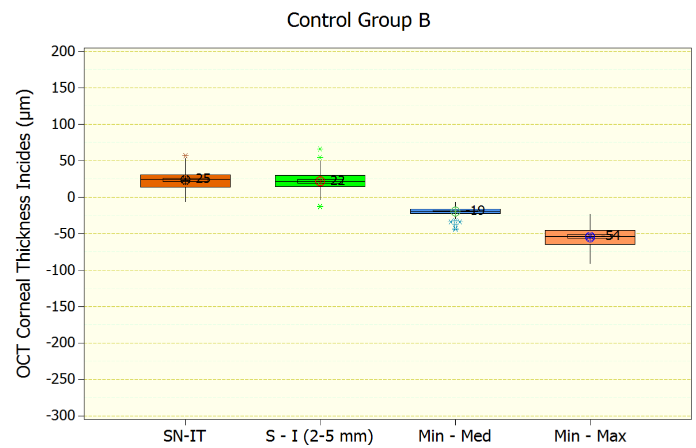
OCT-derived Comparison of Corneal Thickness Distribution and Asymmetry Differences between Normal(175) and Keratoconic Eyes(175)

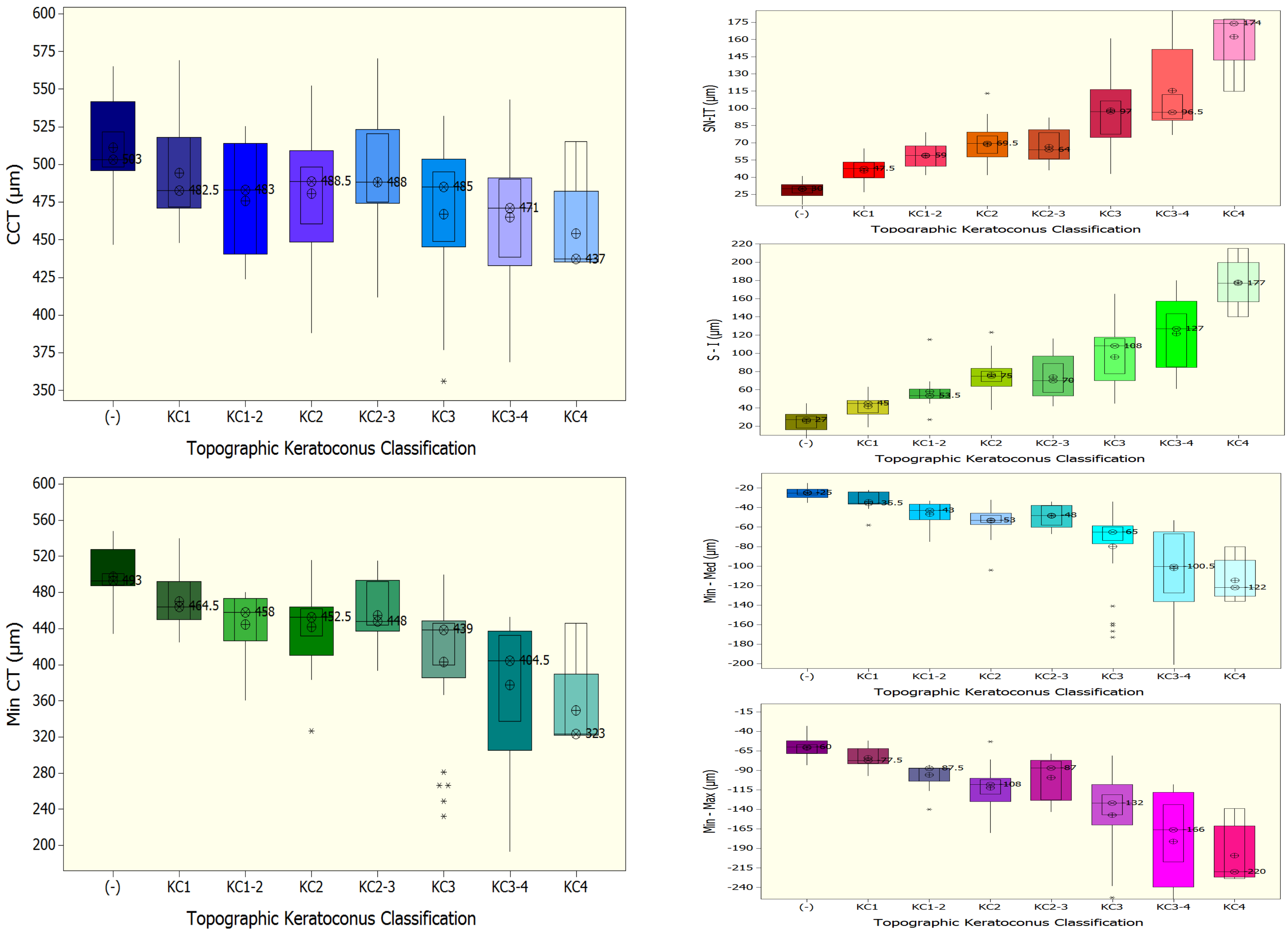
Kanellopoulos et al in press J Cornea 2014









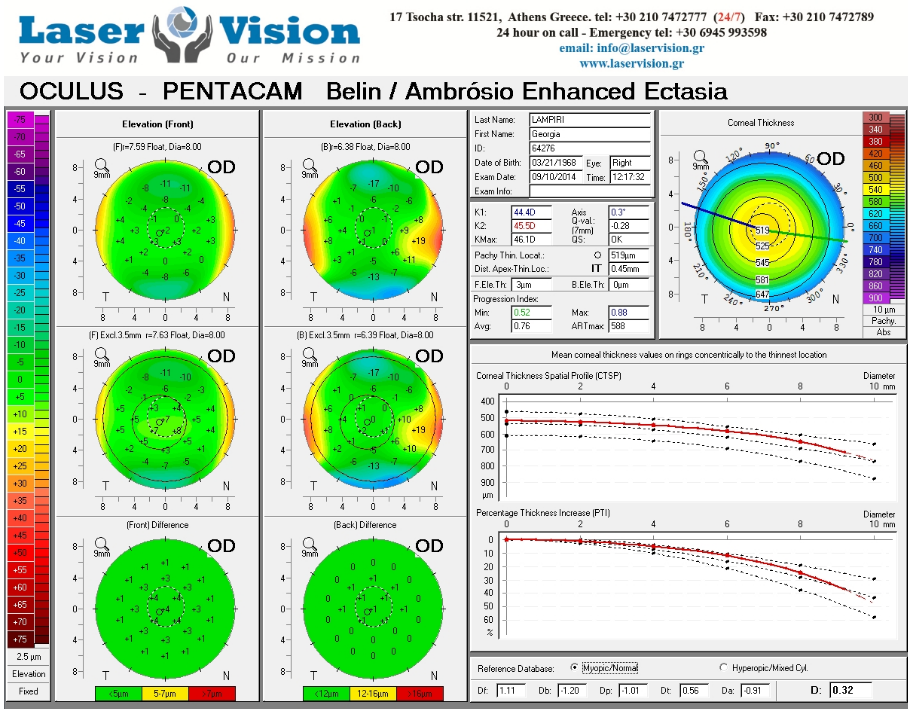


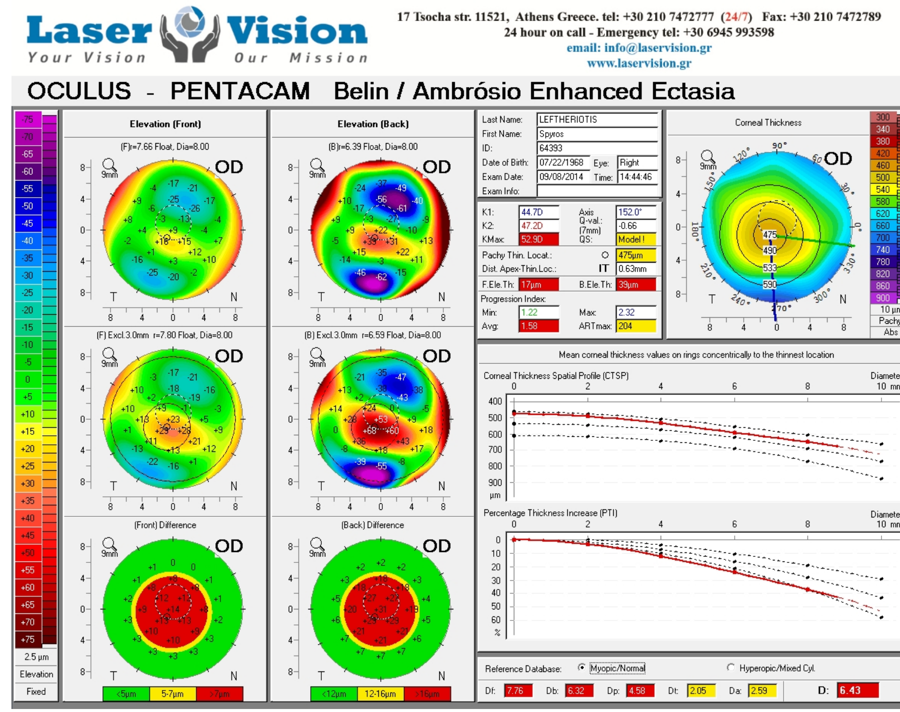
CCT (µm)
503
482.5
483
488.5
488
485
471
437
(-)
KC1
KC1-2
KC2
KC2-3
KC3
KC3-4
KC4
Topographic Keratoconus Classification
Min CT (µm)
493
464.5
458
452.5
448
439
404.5
323
SN-IT (µm)
S - I (µm)
Min - Med (µm)
Min - Max (µm)

Results:

Increased overall epithelial thickness in keratoconic eyes, in comparison to normal, was documented, with potential particular clinical importance in relation to milder and/or suspect stages of keratoconus. Increased topographic thickness variability and range was found to be in tight correlation with keratoconus severity.

Pachymetric maps





ART Max = Thinnest / pachymetric index of progression

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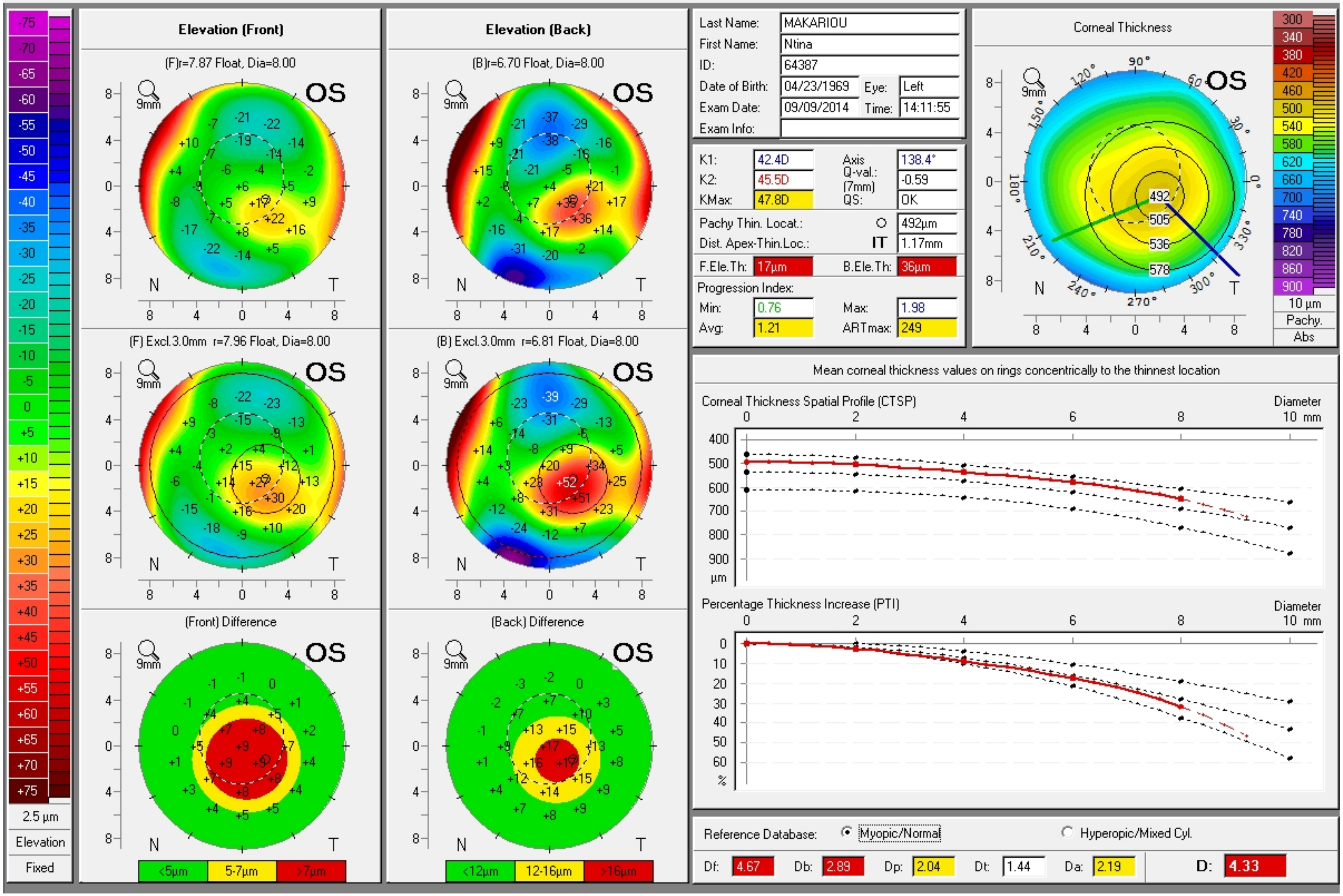
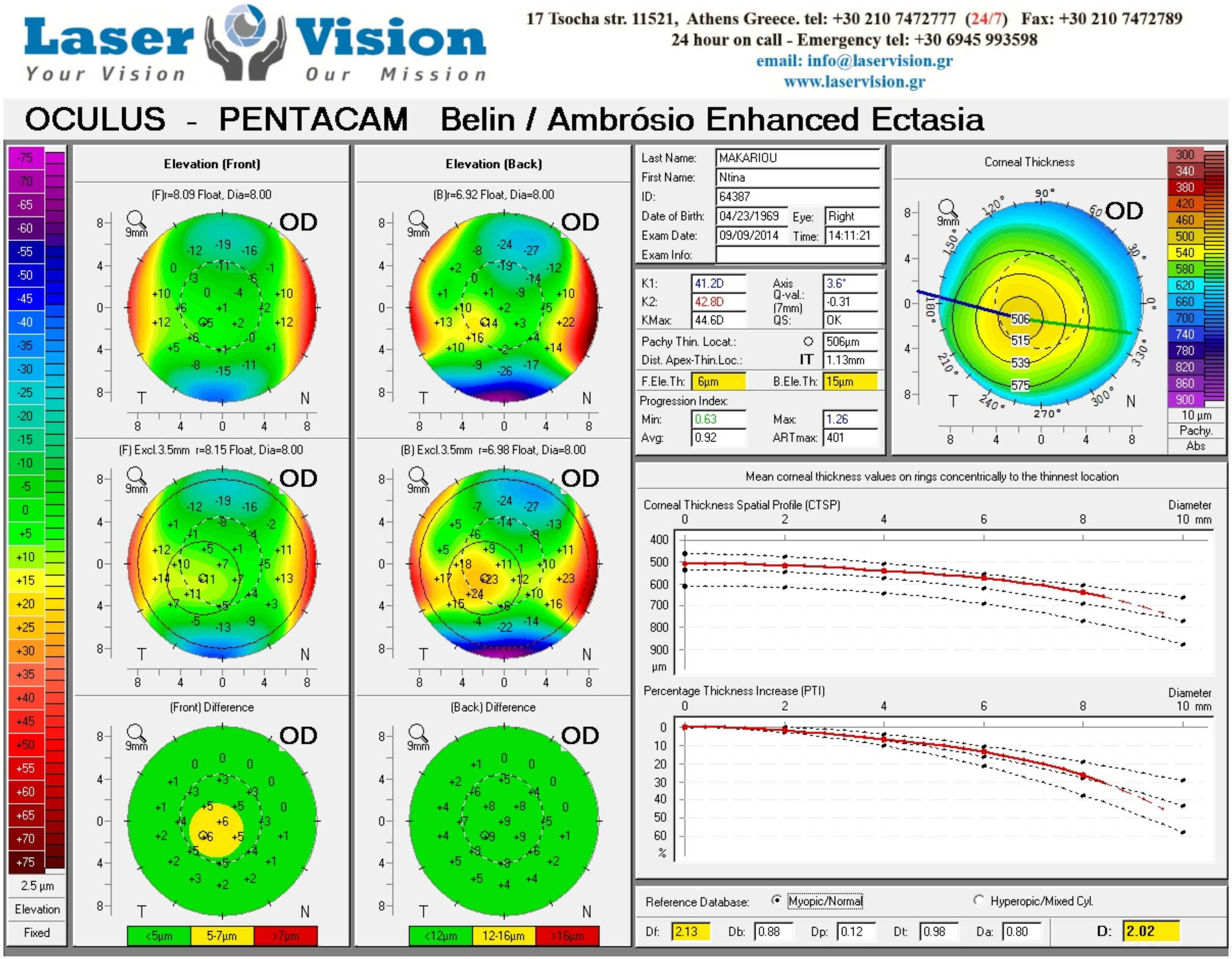
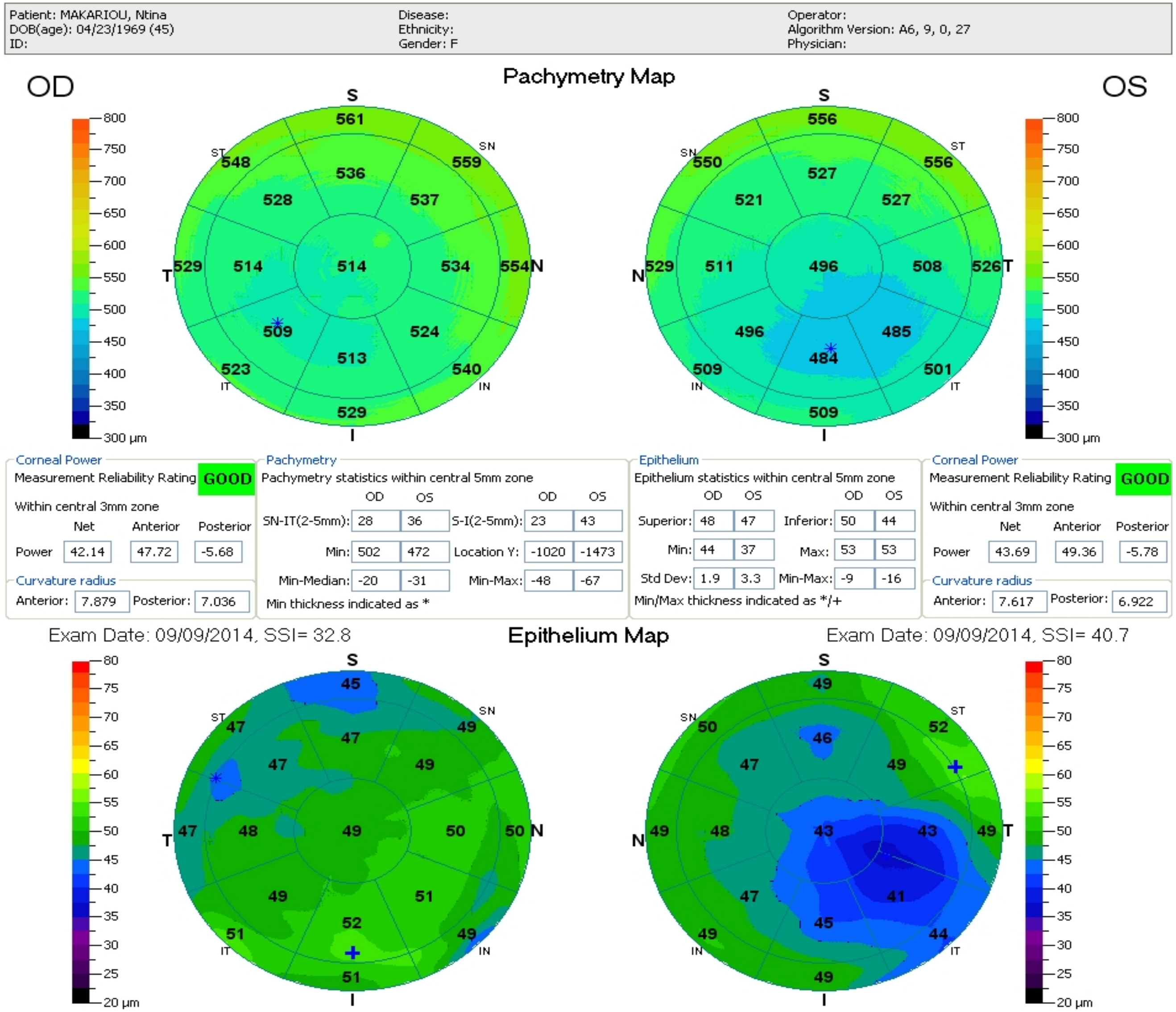


The other eye!



Does the epithelium tell the story here?



Cornea

Brillouin Microscopy of Collagen Crosslinking: Noncontact Depth-Dependent Analysis of Corneal Elastic Modulus

Giuliano Scarcelli,[1,2] *Sabine Kling,*[3] *Elena Quijano,*[1] *Roberto Pineda,*[4] *Susana Marcos,*[3] *and Seok Hyun Yun*[1,2,5]

Purpose. Corneal collagen crosslinking (CXL) is designed to halt the progression of keratoconus and corneal ectasia by inducing corneal stiffening. However, it currently is difficult to monitor and evaluate CXL outcome objectively due to the lack of suitable methods to characterize corneal mechanical properties. We validated noncontact Brillouin microscopy to quantify corneal mechanical properties before and after CXL.

Methods. CXL was performed on fresh porcine eyes using various presoaking times and light doses, with or without epithelial debridement. From Brillouin maps of corneal elastic modulus, stiffness and average modulus of anterior, middle, and posterior stroma were analyzed. Corneal stiffening index (CSI) was introduced as a metric to compare the mechanical efficacy of a given CXL protocol with respect to the standard protocol (30-minute riboflavin presoak, 3 mW/cm^2 ultraviolet illumination for 30 minutes).

Results. Brillouin corneal stiffness increased significantly ($P <$ 0.001) by epi-off and epi-on CXL. The increase of Brillouin modulus was depth-dependent, indicating that anterior stromal stiffening contributes the most to mechanical outcome. The increase of anterior Brillouin modulus was linearly proportional to the light dose ($R^2 > 0.98$). Compared to the standard epi-off procedure, a typical epi-on procedure resulted in a third of stiffness increase in porcine corneas (CSI = 33).

Conclusions. Brillouin microscopy allowed imaging and quantifying CXL-induced mechanical changes without contact in a depth-dependent manner at high spatial resolution. This technique may be useful to evaluate the mechanical outcomes of CXL procedures, to compare different crosslinking agents, and for real-time monitoring of CXL in clinical and experimental settings. (*Invest Ophthalmol Vis Sci.* 2013;54:1418–1425) DOI:10.1167/iovs.12-11387

From the [1]Wellman Center for Photomedicine, Massachusetts General Hospital, Cambridge, Massachusetts; the [2]Department of Dermatology, Harvard Medical School, Boston, Massachusetts; the [3]Instituto de Optica, Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain; the [4]Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts; and [5]Harvard-MIT Health Sciences and Technology, Cambridge, Massachusetts.

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Disclosure: **G. Scarcelli**, P; **S. Kling**, None; **E. Quijano**, None; **R. Pineda**, None; **S. Marcos**, None; **S.H. Yun**, P

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The decrease of corneal mechanical stability has a critical role in the onset and progression of keratoconus and post-LASIK ectasia.[1] Corneal collagen crosslinking (CXL) is a promising treatment that aims at stopping the progression of ectasia by increasing corneal stiffness.[2] CXL induces the formation of covalent bonds between collagen fibers in the corneal stroma by photoactivation of a photosensitizer, such as riboflavin. The increased number of the crosslinks increases the elastic modulus of the corneal tissue. CXL has been approved in Europe and is under clinical trials in the United States. The majority of CXL procedures follow the original "Dresden" protocol described by Wollensak et al.[3] Over the past decade, studies following the long-term clinical outcome of the treatment have shown that the CXL procedure effectively stops progression of ectasia in the majority of patients.[4–6] Recently, however, a great deal of interest has been placed towards devising new CXL protocols to minimize the damage to keratocytes and to reduce the recovery time post intervention.[7–10] In this respect, a central role is played by the epithelium: because the epithelium represents a major barrier for the diffusion of photosensitizers into the stroma, the standard Dresden protocol involves the removal of the epithelium, which results in delayed recovery and increased risks of infections; novel CXL procedures try to solve this issue by chemically loosening epithelial junctions,[7,10] or by custom epithelial debridement.[9]

Despite the advance in CXL, it has been difficult to measure, monitor, and optimize the defining feature that drives the clinical outcome of the different CXL protocols, that is corneal mechanical stiffening, due to the lack of noninvasive mechanical characterization tools able to assess the performance of different protocols in vivo.

Mechanical measurements traditionally are macroscopic and destructive.[11] Recently, a widespread effort to achieve a noninvasive test of corneal mechanical properties has been put forward. An ocular response analyzer measures corneal hysteresis.[12] Corneal hysteresis has been shown to correlate with CXL and advanced keratoconus,[13,14] but its clinical usefulness remains questionable.[15,16] Anterior segment imaging combined with an air puff has allowed dynamic measurements of corneal deformation, showing different deformation parameters in untreated corneas and crosslinked corneas.[17] This technique allows for in vivo measurements, but it remains challenging to determine the corneal biomechanical properties from the deformation images due to the contributions of the corneal geometry and intraocular pressure among other factors.[17] (Roberts CJ, et al. *IOVS* 2011;52:ARVO E-Abstract 4384). Other techniques based on

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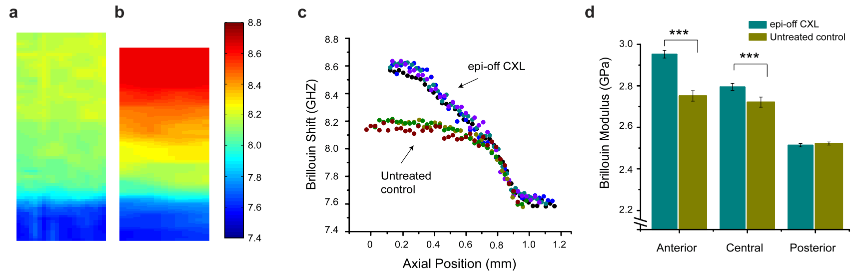


Figure 1. Brillouin mechanical characterization of standard epi-off CXL procedure. (**a**) A representative cross-sectional Brillouin image of normal porcine cornea. (**b**) A Brillouin image of the cornea after the standard CXL. The *horizontal* and *vertical* span is 0.05 mm (x) by 1.2 mm (z) in (**a**, **b**). (**c**) Brillouin depth profiles of crosslinked and untreated corneas. (**d**) Mean Brillouin modulus of the anterior, mid, and posterior regions for the crosslinked ($N = 6$) versus untreated corneas ($N = 3$). $^{***}P < 0.005$.

quasi-static rheology. This measurement showed that epi-on CXL induced stiffening of approximately 39% (i.e., CSI = 39), consistent with the Brillouin-based measurement. As the experiments were performed ex vivo immediately after the CXL procedure, this estimation includes the mechanical effect of the notably different hydration states of the cornea in the epi-on versus epi-off procedure.

Sham Controls

Sham control experiments were performed to evaluate the effects of different parameters (e.g., timing, soaking, evaporation) within the CXL procedure. UV light was administered to only a half of the eye after riboflavin soaking, whereas the other half of the eye was blocked during UV illumination. Figures 5a and 5b show the results for the epi-off protocol and the epi-on protocol, respectively. The Brillouin profiles of the UV-illuminated region and unilluminated (sham) region of the eye are shown, along with the average Brillouin profile of untreated controls before soaking. As expected, the epi-off CXL profile in Figure 5a and the epi-on CXL profile in Figure 5b are consistent with the ones in Figure 1c and Figure 4c, respectively. Importantly, the Brillouin moduli for the sham regions in Figure 5a and Figure 5b are equivalent to the results obtained with the controls used in Figures 1 to 3 and Figure 4, respectively. These control data were obtained with different

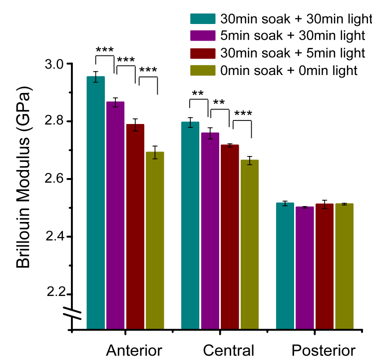


Figure 2. The effects of the varying soaking time and light exposure time on the mean Brillouin modulus of the anterior, mid, and posterior cornea. $^{**}P < 0.01$, $^{***}P < 0.005$.

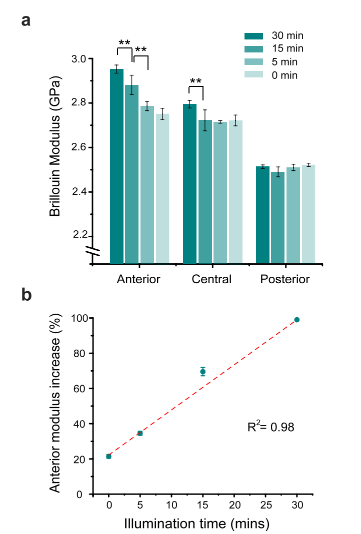


Figure 3. Mechanical outcome dependence on the light exposure time. (**a**) Mean Brillouin modulus of the anterior, mid, and posterior regions in the corneas treated with a presoaking time of 30 minutes, and various UV exposure times of 0, 5, 15, and 30 minutes, respectively. $^{**}P < 0.01$. (**b**) The increase of mean Brillouin modulus in the anterior region as a function of exposure time. *Circles*: data. *Error bars*: standard deviations. *Line*: linear curve fit.

“Currently sensitive criteria”

- Topometric asymmetry indices IHD and ISV
- Pachymetric asymmetry; Scheimpflug, OCT
- ART-Max=TP/PPI-Max (essentially “steep” cornea pachymetry change)
- Epithelial profiles
- Biomechanical measurements-Brillouin

Complete Eye Examination

Refractive Error Measurements

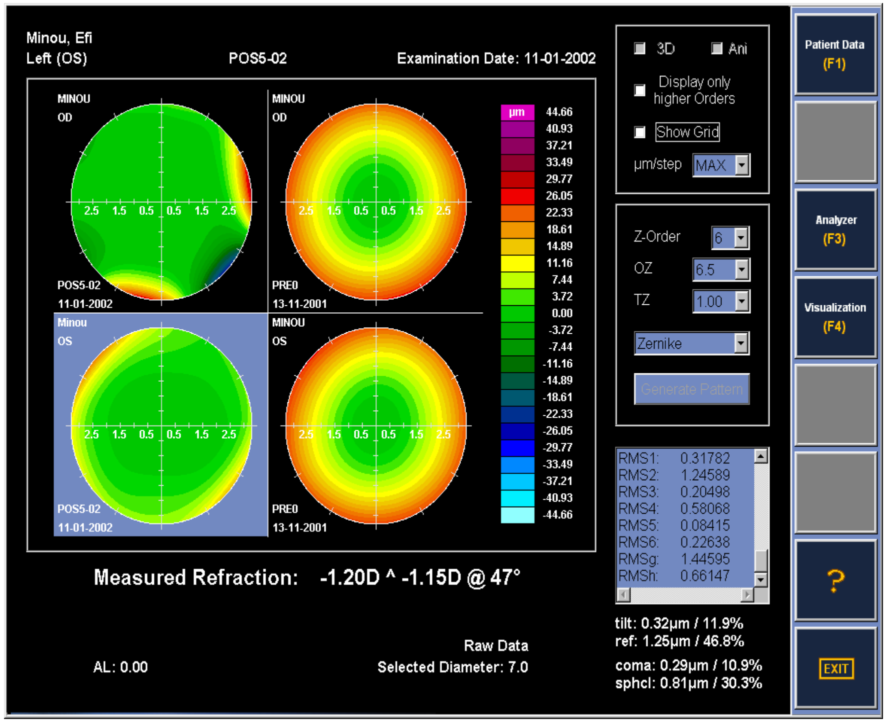
- VA (CC/SC)
- Autorefractor
- BCVA
- Soft Contact Lens Test
  - Monovision
  - Presbyopia
  - Scotopic Symptoms
- Refraction
- Dilated Refraction (1 drop Tropicamide

(0.5%)

Complete Eye Examination

Wavefront measurements

- Accurate measurements of refractive errors and visual aberrations
- Evaluation of the Eye as an “Optical System”
- Scanning of high order aberrations
- Aims not simply to “Corrected Vision”, but to vision > 10/10



More accurate measurements for more accurate result

Topo – guided LASIK

- Improved results of refractive surgery

- Minimization of complications of refractive surgery

- Hyperopia – Angle Kappa

- Minimization of Hyper and Hypo corrections

Patient Selection

- Over 18 with stable refraction
- Free of certain eye diseases, eye viruses & health problems
- Slit lamp exam and conversation with the surgeon is recorded on a DVD
- All incidental findings are discussed (lens opacities, retina abnormalities, cup/disc ratio)
- Medication in use or any allergies especially in medications
- Pregnancy and nursing = contraindications!

Day of procedure

- Staff member appointed to each patient
- Make patient comfortable
- Last questions
- Family / friend is asked to observe
- Talk to him/her ALL the time
- Diazepam (5mg) pill
- No make up

Informed Consent

- Patient education and information
- Benefits vs know and unknown risks
- Patient accepts a certain degree of risk and responsibility during both:
    - The procedure
    - The heeling process

Pt signs under two statements:

- ✓ I understand that "there are risks and no guarantees"
- ✓ I understand that "I may still need to wear glasses"

WaveLight®

Refractive Suite

After the procedure

- Bandage contact lens
- Explain meds to pt and family
- Give detailed instructions and brochure with LARGE pictures
    - ➢ Eye drops provided antibiotics and steroids for 1 week
    - ➢ For 1 week no eye scrubbing/wiping, avoid water, use plastic eye shields while sleeping
- Provide all material (shields, tape, sunglasses, tears etc)
- Surgeon evaluates the patient 15 to 30 minutes after the procedure
- Same day call the pt and check for the eye drops, remind the doctor' s 24h availability

Post-Op Follow up

1st day Post-Op	Flap check
1st week	Visual Acuity Check
1st month	Assessment of necessity for enhancement procedures
3rd month	If needed, enhancement procedure takes place
6th month	Visual Acuity Check
12th month	Final Check

Our intention is not to frighten!!

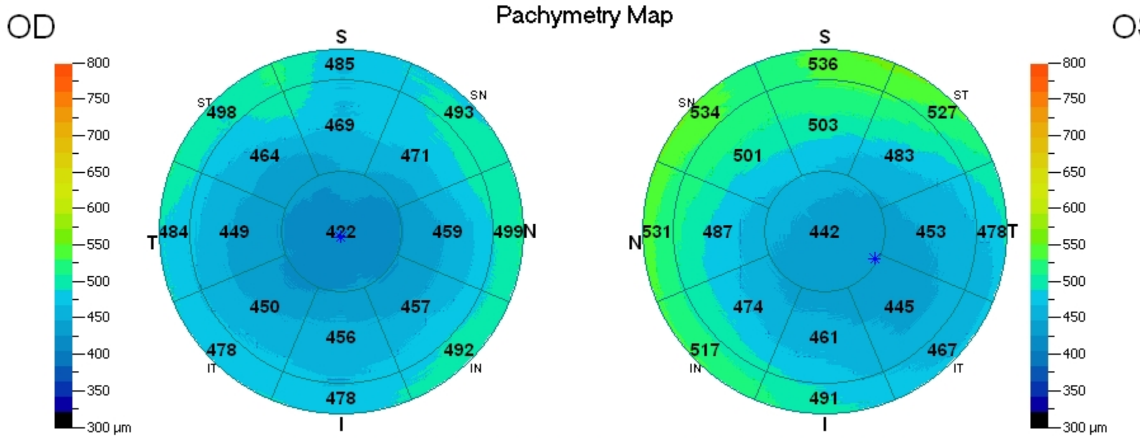
- Most of pts never encounter any serious complications

- Vast majority is thrilled with the gross improvement in vision

- Intention:
    - to accurately outline the risks to all candidates so that they may either select not to accept these risks or be better prepared to deal with them if they arise

Background

Patient: KATERIS, Polidefkis	Disease: LASIK	Operator:
DOB(age): 01/01/1991 (22)	Ethnicity:	Algorithm Version: A6, 9, 0, 27
ID:	Gender: M	Physician:



Pachymetry
Pachymetry statistics within central 5mm zone

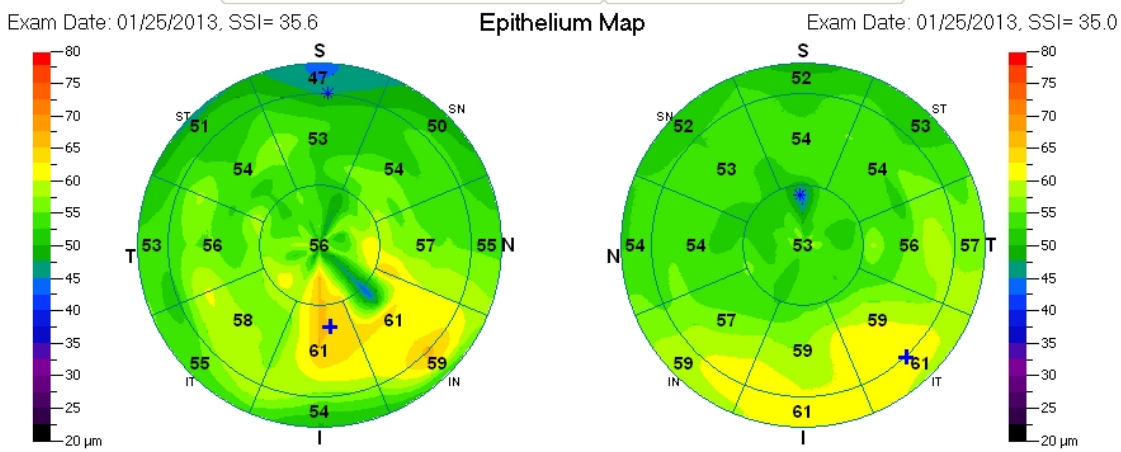
	OD	OS		OD	OS
SN-IT(2-5mm):	21	56	S-I(2-5mm):	13	42
Min:	414	430	Location Y:	-88	-430
Min-Median:	-38	-41	Min-Max:	-84	-98

Min thickness indicated as *

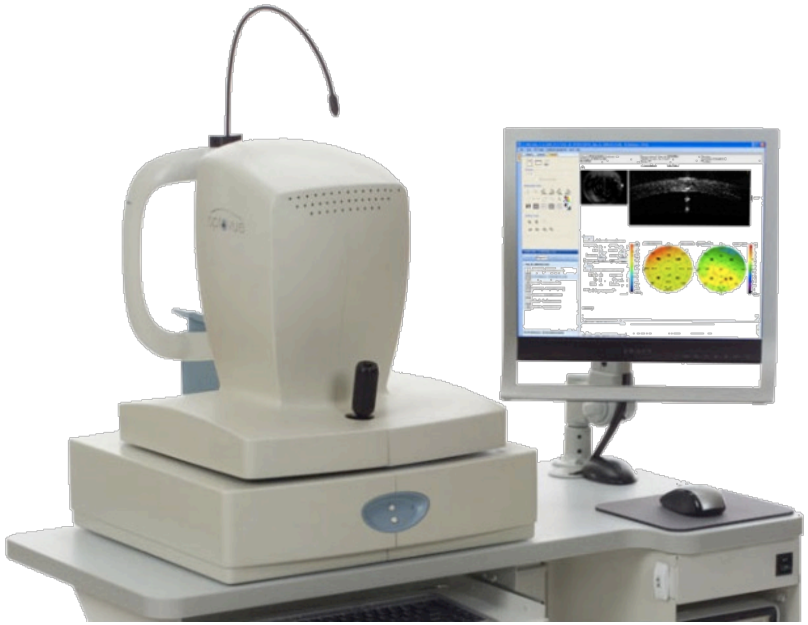
Epithelium
Epithelium statistics within central 5mm zone

	OD	OS		OD	OS
Superior:	54	54	Inferior:	59	58
Min:	50	49	Max:	65	62
Std Dev:	3.8	2.9	Min-Max:	-15	-14

Min/Max thickness indicated as */+



Materials

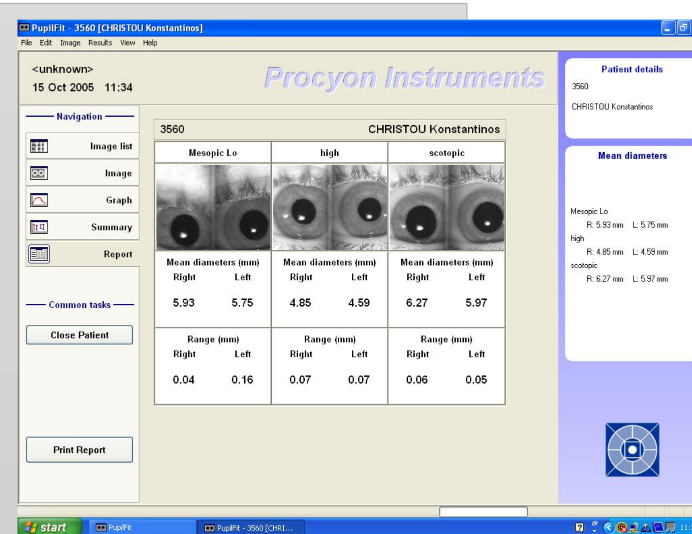


Parameter	Optovue RTVue (Frequency)
Wavelength	830 nm
Penetration Depth	2.3 mm
Axial Resolution	5 µm
Transverse Resolution	5 - 10 µm
A-Scans/Line	1024
A-Scans/Second	26,000
Acquisition Time	0.31 sec (5 scans per meridian)
Scan Diameter	4 - 6 mm
Scan Alignment	Corneal vertex
System Design	Hybrid Anterior/Posterior Segment

RtVue-100 (OptoVue Inc., Fremont, CA)

Define customised in 2015?

- Wavefront guided?
- Topography guided?
- Wavefront-optimised?
- Asphericity adjustment?
- Ray tracing?
- Adjustment to pupil size?
- Adjustment to angle kappa?
- Customised flap (femto lasers)?
- Customizing cornea biomechanics with CXL?



Summary:
Some of the key elements to customized planning I will discuss today

- Cornea curvature imaging
- Corneal epithelium
- Wavefront
- Topographic variability (Cornea wavefront)
- Flap may affect topography, epithelium and HOAs
- Angle kappa
- Biomechanical stability (hyperopia, ectasias)
- Topography-guided customized ablations

New York University
School of Medicine

Kanellopoulos, MD
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Refractive surgery today offers impressive precision, safety and stability

ORIGINAL ARTICLE

Refractive and Keratometric Stability in High Myopic LASIK With High-Frequency Femtosecond and Excimer Lasers

Anastasios John Kanellopoulos, MD; George Asimellis, PhD

ABSTRACT

PURPOSE: To evaluate safety, efficacy, ergonomy, and refractive and keratometric stability in high myopia LASIK procedures using a novel femtosecond and excimer laser surgery platform.

METHODS: One hundred sixteen eyes in consecutive cases of high myopic LASIK (⩾ -6.00 diopters [D]) with the Alcon-WaveLight FS200 femtosecond and EX500 excimer lasers (Alcon Laboratories, Fort Worth, TX) were evaluated preoperatively and postoperatively for the following parameters: refractive error, corrected distance visual acuity, uncorrected distance visual acuity, spherical equivalent correction, keratometry (with Placido topography and Scheimpflug tomography), and refractive astigmatism. Average follow-up time was 6.2 months (range: 3 to 12 months).

RESULTS: Postoperative average refractive error was -0.37, -0.43, and -0.25 D for the 3-, 6-, and 12-month period, compared to -7.67 ± 1.55 D preoperatively. At 3, 6, and 12 months postoperatively 94%, 96.3%, and 100% of eyes, respectively, were within 1.0 D defocus equivalent. Postoperative refractive astigmatism was -0.21, -0.21, -0.13 D for the 3-, 6-, and 12-month period compared to -1.07 ± 1.91 D preoperatively. The proportion of eyes with postoperative astigmatism within 0.25 D was 85.3%, 81.5%, and 100%, for the 3-, 6-, and 12-month visit, respectively. Keratometric stability was within 0.22 D after the 12-month visit. There was no epithelial ingrowth or diffuse lamellar keratitis in any case.

CONCLUSIONS: Clinical outcomes with this technique and technology appear to be promising in high level uncorrected visual rehabilitation of high myopia. There was small regression potential in the sample evaluated.

[*J Refract Surg*. 2013;29(12):832-837.]

Both excimer and femtosecond laser platforms have evolved significantly over the past 10 years. Today's excimer lasers for refractive surgery have high pulse repetition (more than 400 Hz),[1,2] operate with scanning spot,[3] and can provide customized ablation, including aspheric ablation profiles[4] and wavefront-guided[5,6] or topography-guided[7,8] treatments. These improvements have further advanced the applications of the LASIK procedure[9,10] in correcting not just the spherocylindrical refractive error, but also the higher-order aberrations.[1,11,12]

The Alcon-WaveLight EX500 excimer laser and the FS200 femtosecond laser[13] constitute the Alcon-WaveLight Refractive Suite (Alcon Laboratories, Fort Worth, TX). The Refractive Suite operates on its own Ethernet network and allows the importation of diagnostic data from several networked screening devices (including Vario Placido topography, Oculyzer II Scheimpflug tomography, Tscherning wavefront analysis, and the OB820 interferometric biometry system[14]) into the planning software tools of both lasers.

Specifically for high myopia (refractive error ⩾ -6.00 diopters [D] in the least minus meridian), although LASIK provides reliable outcomes,[15] there are reports indicating that significant regression develops in the long term.[16,17] This matter has been discussed in the past[18,19] and gained new interest with the advent of femtosecond laser-assisted LASIK.[20] Due to the large ablation depths required for the correction of high refractive error, obvious potential limitations of high myopic LASIK are risk for reduced accuracy, higher risk of ectasia, and potential for increased postoperative spherical aberration. To allow for thicker residual stroma, a thinner flap is preferable.

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Dr. Kanellopoulos is a consultant to WaveLight. The remaining authors have no financial or proprietary interest in the materials presented herein.

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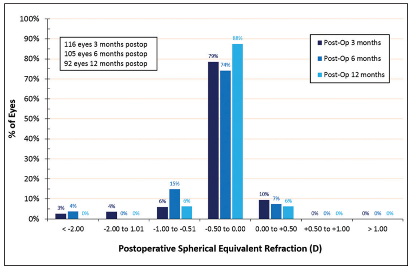

Figure 1. Spherical equivalent correction at the 3-, 6-, and 12-month postoperative visit, respectively. UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity

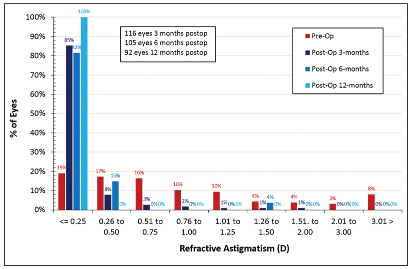

Figure 2. Refractive astigmatism preoperatively and at 3-, 6-, and 12-month postoperative visits. Percentage of eyes (vertical axis) versus refractive astigmatism (diopters [D]) (horizontal axis).

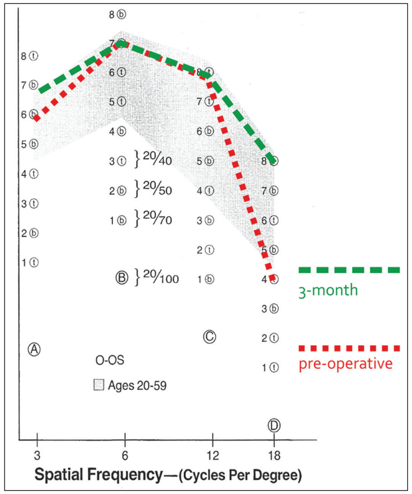

Figure 3. Contrast sensitivity (average comparison between postoperative (average) and 3-month postoperative visit (average) on the CSV-100 Contrast Sensitivity Chart.

Figure 2 displays the postoperative refractive astigmatism within intervals of 0.50 D. Average preoperative and postoperative contrast sensitivity results are illustrated in **Figure 3**.

Tscherning aberrometry was attempted preoperatively and postoperatively in all cases. None of the cases was successfully measured preoperatively with the specific aberrometer due to inherent limitations of this architecture for high defocus such as the over -6 D in our sample. In the specific Tscherning aberrometry, only real retina data from 169 laser spots projected onto the retina are imaged and analyzed. By design, this process does not image well in high myopia, or even after successful correction due to projection distortion. Nevertheless, all patients were evaluated at the 3- and 12-month visit with the above aberrometer. We were able to image 54 of the 116 eyes with mean aberrometric measurement of 0.38 ± 0.25 µm.

Uncorrected Visual Acuity Outcome and Stability

The uncorrected visual acuity (distance monocular) outcome and stability for the first 3 months (**Figure 4**) shows that 90.50% of the eyes had postoperative uncorrected visual acuity better than 1.0 (20/20), whereas 92.20% had better than 0.8 (20/25). **Figure 4** also displays the preoperative corrected distance visual acuity for the same group of patients.

Efficacy of Corrected Visual Acuity

As shown in **Figure 5**, the changes in corrected distance visual acuity at 3 months compared to preoperative corrected distance visual acuity and postoperative uncorrected distance visual acuity indicate that 30.4% of the eyes were unchanged, whereas 55.6% of the eyes gained one Snellen line and 12.2% gained two or more Snellen lines. Only 1.7% (2 eyes) lost one line. Even better results occurred at the 6- and 12-month visits, at which no eye had lost any Snellen line (also shown in **Figure 5**).

Refractive Stability and Predictability

The refractive stability is demonstrated by the spherical equivalent correction over the 12-month postoperative visit (**Figure 6**). Defocus equivalent results are presented in **Figure 7**. At the 3-, 6-, and 12-month visit,

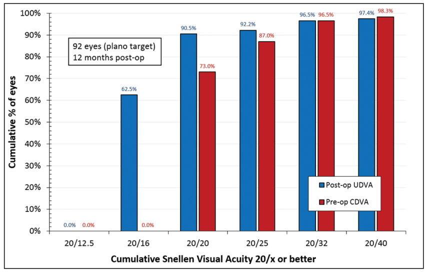

Figure 4. Postoperative uncorrected distance visual acuity (UDVA) (blue columns) at 3 months versus preoperative corrected distance visual acuity (CDVA) (orange line).

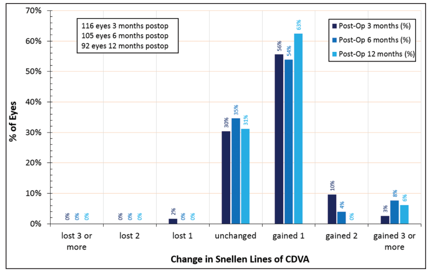

Figure 5. Percentage of eyes with gain/loss in Snellen lines of corrected distance visual acuity (CDVA), at the 3-, 6-, and 12-month visit, respectively. SE = spherical equivalent

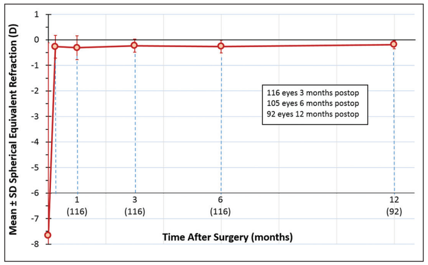

Figure 6. Stability of spherical equivalent, expressed in diopters (D) at the 3-, 6-, and 12-month visit, respectively.

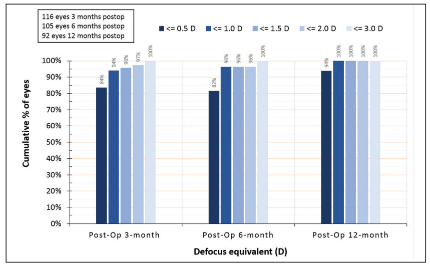

Figure 7. Defocus equivalent results, at the 3-, 6-, and 12-month visit, respectively. D = diopters

94.0%, 96.3%, and 100% of eyes, respectively, were within 1.0 D defocus equivalent.

Predictability results are illustrated in **Figure 8**, where the achieved spherical equivalent versus attempted spherical equivalent (in diopters) at the 12-month visit is plotted. Of the 116 eyes at the 3-month visit, 92 were available for the 12-month visit; 3 eyes (3.2%) indicate slight overcorrection, 86 eyes (93.5%) are marked with green (indicating individual outcomes where the achieved spherical correction was within 0.5 D of the attempted correction), and 3 eyes (3.2%) indicate slight undercorrection. The data shown, corresponding to the 12-month visit, have a linearity of coefficient 0.95. These results are in agreement with the spherical equivalent manifest refraction results (**Figure 1**), where spherical equivalent correction results recorded during the 3-, 6-, and 12-month postoperative follow-up visits are illustrated.

Keratometric and Astigmatic Changes and Stability

The comparison between postoperative and preoperative refractive astigmatism is demonstrated by the percentage of eyes within 0.25 D of postoperative refractive astigmatism. **Figure 2** presents the 3-, 6-, and 12-month refractive astigmatism. Astigmatism was within 0.5 D in 85.3% of the eyes at 3 months, 81.5% of the eyes at 6 months, and 100% of the eyes at 12 months postoperatively.

The keratometric changes and stability are demonstrated by the K-flat and K-steep average values as followed during the 1-, 3-, 6-, and 12-month postoperative visits (**Figure 9**.)

DISCUSSION

In our study of 116 cases, the 1-year high myopic LASIK evaluation of the the WaveLight Refractive Suite shows impressive refractive outcome, predictability, and stability. Regarding efficacy, the refractive results expressed in terms of spherical equivalent refraction, in agreement with the defocus equivalent results, indicate that 83% and 93% of eyes were within 0.5 D at the 3- and 12-month visits, respectively (**Figure 7**).

In terms of visual rehabilitation, 90.5% of the eyes achieved postoperative uncorrected distance visual

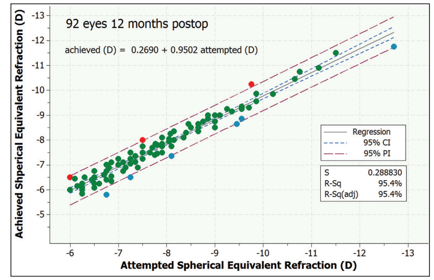

Figure 8. Predictability of spherical equivalent correction, measured at the 12-month visit, showing achieved spherical equivalent (SE) (vertical axis, in diopters [D]) versus attempted SE (horizontal axis, in D): green dots = postoperative SE within 0.50 D of target; red dots = cases overcorrected by or over 0.50 D; blue dots = cases undercorrected by or over 0.50 D

acuity better than 1.00 (20/20) (**Figure 4**) and a significant percentage (53.5%) of the cases achieved better than 1.25 (20/16). This compares to only 72.5% of the eyes having corrected distance visual acuity of 1.00 (20/20) preoperatively.

In terms of gained or lost Snellen lines, only 1.7% (2 cases) had a loss in Snellen lines and most gained at least one line. These visual outcomes are satisfactory.

The predictability of the outcome was extremely accurate. As shown in **Figure 8**, only 3 of the 116 eyes (3%) were overcorrected. Regarding the cylinder correction (**Figure 2**), 85.3%, 81.50%, and 100% of eyes had residual cylinder power less than 0.25 D at the 3-, 6-, and 12-month visits, respectively, compared to 81% of the eyes preoperatively.

The stability of the outcome is evidenced by the strength of the spherical equivalent over the course of 12 months, as shown in **Figure 1** and **Figure 6**. The percentage of eyes achieving postoperative manifest refraction spherical equivalent in the -0.50 to 0.00 D range of emmetropia was more than 87.5% after the 12-month visit (**Figure 1**). The cumulative percentage of eyes within ±1.0 D of emmetropia was 94% for 3 months, 96.3% for 6 months, and 100% for 12 months postoperatively. These results compare favorably to other studies,[24] in which the cumulative percentages were 98% within ±1.0 D[25] and 84.3% of eyes had a postoperative spherical equivalent within ±0.50 D of emmetropia. More importantly, no cases in our study had hyperopic manifest refraction spherical equivalent more than +0.50 D.

The slight positive slope in the keratometric readings, similar for both the flat and the steep meridian, as illustrated in **Figure 9**, might indicate a mild pro-

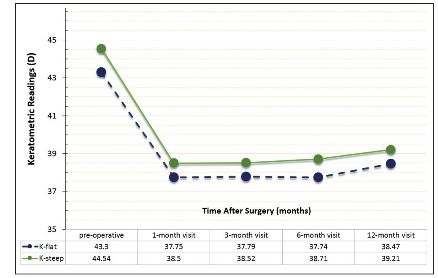

Figure 9. Keratometric (K) readings at the 3-, 6-, and 12-month visit, respectively.

gressive corneal steepening. The recorded changes correspond to +0.68 D for the flat meridian and +0.69 D for the steep meridian. This is an indication that corneal stiffening might be required for all LASIK cases, in the form of cross-linking applied at the corneal stroma prior to repositioning of the flap.[26] The data clearly show a trend toward mild corneal steepening in the longer postoperative period, confirming our clinical observations of the potential need of a stabilizing adjunct procedure such as high fluence, short duration corneal cross-linking. We have introduced[27] and reported[28] using the employment of a high-fluence corneal cross-linking within the high myopic LASIK procedure as a possible means to achieve better long-term stability.

A slight hyperopic shift of the total refractive error was observed comparing the 3- and 12-month postoperative results, which was on average from -0.31 to -0.19 D, or a change of 0.12 D. In correlation with the finding of slight steepening of K-readings over the same postoperative interval (+0.68 D), there is a slight contradiction that might be explained by the subjective nature of refractive error measurement (manifest refraction) versus an objective (Scheimpflug imaging) measurement of the keratometry. Perhaps further study of epithelial behavior and/or dry eye related to the LASIK flaps and a possible change in the biomechanical behavior of the cornea may explain this small discrepancy.

Steepening of the K-reading (or regression of the myopic ablation) should manifest as myopic shift postoperatively and not a hyperopic shift. The long-term trend as noted in this study is toward a myopic shift. It is possible that the transient early hyperopic shift represents a build-in factor created by our nomogram for high myopia developed over 20 years of LASIK experience. The long-term steepening of most cases studied herein is significant in our opinion and needs to be reported.

All flaps are not same topographically even when comparing femtos!

Clinical Ophthalmology

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ORIGINAL RESEARCH

Three-dimensional LASIK flap thickness variability: topographic central, paracentral and peripheral assessment, in flaps created by a mechanical microkeratome (M2) and two different femtosecond lasers (FS60 and FS200)

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

[1]Laservision.gr Institute, Athens, Greece; [2]NYU Medical School, New York, USA

Purpose: To evaluate programmed versus achieved laser-assisted in situ keratomileusis (LASIK) flap central thickness and investigate topographic flap thickness variability, as well as the effect of potential epithelial remodeling interference on flap thickness variability.

Patients and methods: Flap thickness was investigated in 110 eyes that had had bilateral myopic LASIK several years ago (average 4.5 ± 2.7 years; range 2–7 years). Three age-matched study groups were formed, based on the method of primary flap creation: Group A (flaps made by the Moria Surgical M2 microkeratome [Antony, France]), Group B (flaps made by the Abbott Medical Optics IntraLase™ FS60 femtosecond laser [Santa Ana, CA, USA]), and Group C (flaps made by the Alcon WaveLight® FS200 femtosecond laser [Fort Worth, TX, USA]). Whole-cornea topographic maps of flap and epithelial thickness were obtained by scanning high-frequency ultrasound biomicroscopy. On each eye, topographic flap and epithelial thickness variability was computed by the standard deviation of thickness corresponding to 21 equally spaced points over the entire corneal area imaged.

Results: The average central flap thickness for each group was 138.33 ± 12.38 µm (mean ± standard deviation) in Group A, 128.46 ± 5.72 µm in Group B, and 122.00 ± 5.64 µm in Group C. Topographic flap thickness variability was 9.73 ± 4.93 µm for Group A, 8.48 ± 4.23 µm for Group B, and 4.84 ± 1.88 µm for Group C. The smaller topographic flap thickness variability of Group C (FS200) was statistically significant compared with that of Group A (M2) ($P = 0.004$), indicating improved topographic flap thickness consistency – that is, improved precision – over the entire flap area affected.

Conclusions: The two femtosecond lasers produced a smaller flap thickness and reduced variability than the mechanical microkeratome. In addition, our study suggests that there may be a significant difference in topographic flap thickness variability between the results achieved by the two femtosecond lasers examined.

Keywords: Moria M2, IntraLase FS60, WaveLight® FS200, Allegretto Wave® Eye-Q, 400 Hz excimer, ultrasound biomicroscopy

Video abstract

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Introduction

We have previously reported, in agreement with many others, on the safety and accuracy of flap making with mechanical keratomes for correction of myopia and myopic astigmatism[1] as well as hyperopia.[2]

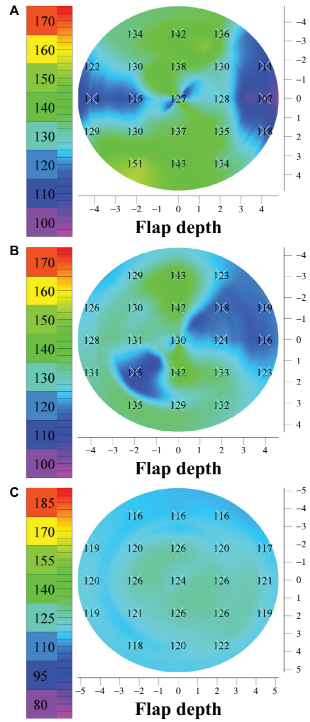

Figure 3 Three representative flap thickness maps (8 mm diameter) from flaps created with the modalities studied in this paper: **(A)** M2 microkeratome (Moria Surgical, Antony, France), **(B)** Intralase™ FS60 femtosecond laser (Abbott Medical Optics, Santa Ana, CA, USA), **(C)** WaveLight® FS200 femtosecond laser (Alcon, Fort Worth, TX, USA).
Note: The values over the 21 points are those used for the flap thickness mean and topographic flap thickness variability study.

the epithelium contribute to the flap thickness homogeneity differences found between the three groups.

Discussion

The importance of flap thickness

Flap parameter accuracy and homogeneity have been studied and debated at length by refractive surgeons globally over the last 10 years. There appear to be variable differences reported in the basic surgical outcomes when comparing procedures with flaps created either with a mechanical microkeratome or a femtosecond laser.[16] For example, a study in hyperopic patients showed significantly better refractive results with femtosecond laser flaps than with microkeratome flaps.[17] Another study showed that clinically significant epithelial ingrowth after femtosecond LASIK is an infrequent complication, the incidence being less than reported for microkeratome LASIK.[18]

Table 1 Flap thickness measurements, range, and topographic flap thickness variability statistics for the three groups examined

	0–6 mm	0–3 mm	3–6 mm	Flap thickness variability
Group A	**M2**			
Average	138.83	138.33	140.58	9.73
Maximum	159.00	159.00	159.00	17.05
Minimum	114.00	115.00	114.00	3.37
SD	12.38	12.85	12.09	4.93
Group B	**FS60**			
Average	128.46	130.31	128.15	8.48
Maximum	137.00	142.00	136.00	17.16
Minimum	119.00	120.00	119.00	2.94
SD	5.72	6.80	5.49	4.23
Group C	**FS200**			
Average	122.00	122.20	122.53	4.84
Maximum	135.00	137.00	136.00	7.96
Minimum	94.00	90.00	97.00	1.68
SD	5.64	6.11	5.47	1.88

Note: All values are expressed in micrometers (µm).
Abbreviation: SD, standard deviation.

Despite the fact that multiple generations of femtosecond lasers for refractive surgery have been introduced so far, and while the "perfect LASIK flap" is becoming increasingly tangible, the field continues to welcome research on the comparative characteristics of the femtosecond laser versus mechanical microkeratome flap, including that on morphology, cut accuracy, flap thickness reproducibility, flap-edge quality, stromal-bed surface roughness, and histopathology.[19–25]

The femtosecond laser continues to be preferred for flap creation over the bladed mechanical microkeratome due to the increased safety, precision, and regularity this modality offers.[26,27]

Flap thickness is considered an important indicator of LASIK safety due to the critical importance of adequate residual stromal preservation, not only at the center of the cornea, but also for the overall area of the cornea affected. To ensure a thicker residual stroma, a thin flap is preferable in myopic treatments. A further benefit of a thin flap (in

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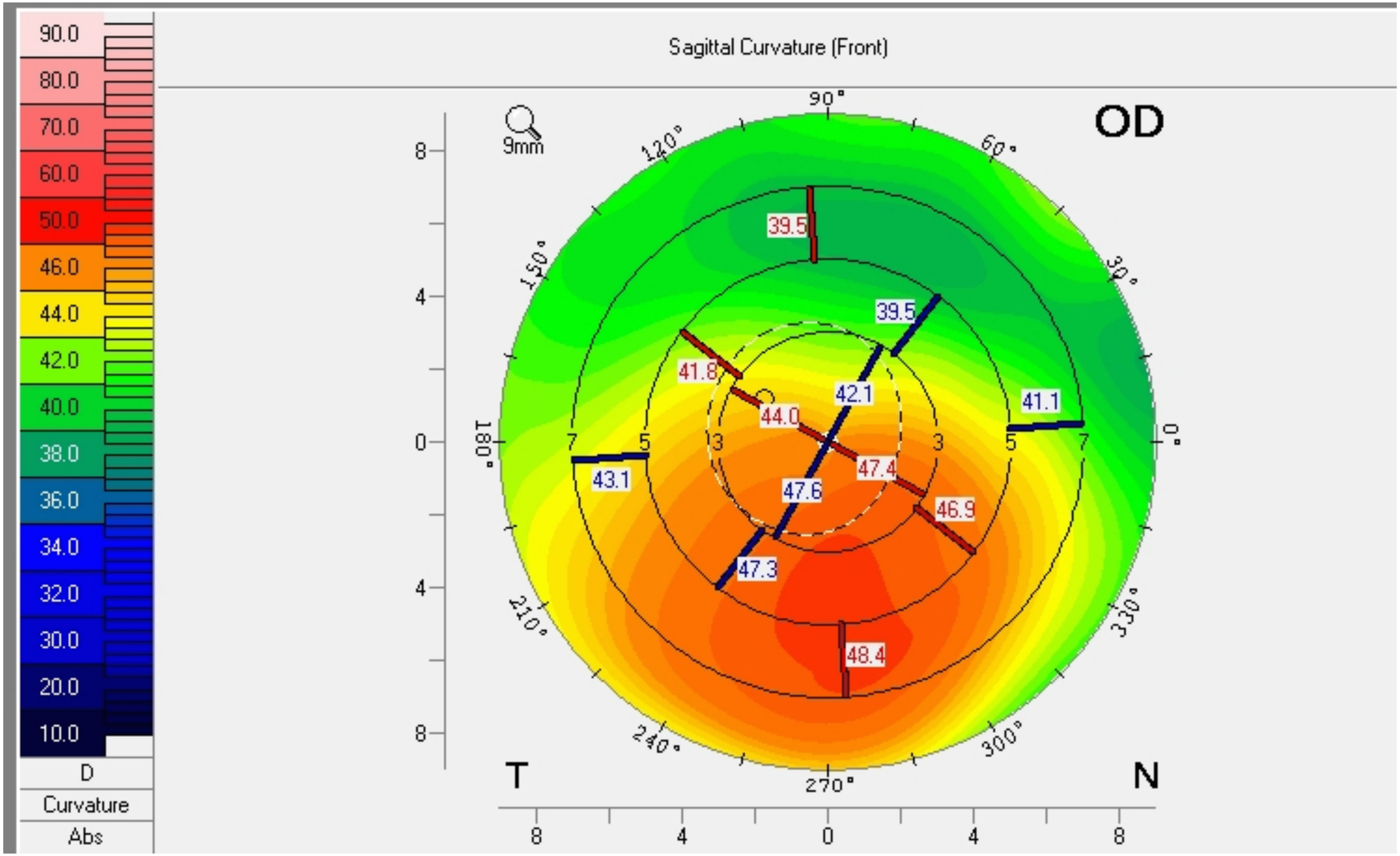
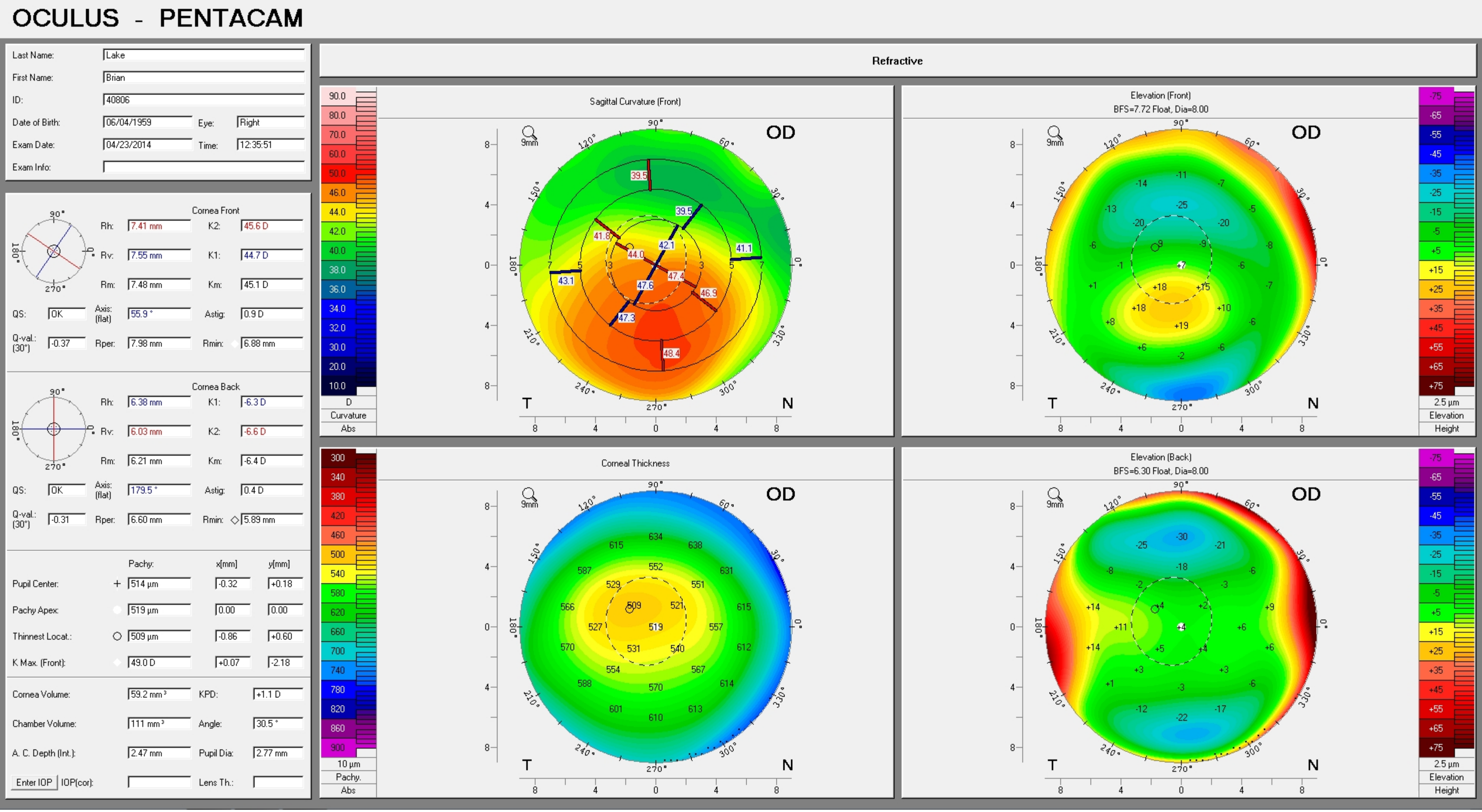
Most feared LASIK complication: ectasia?



Not Post-LASIK ectasia, just a decentered hyperopic ablation



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10.5005/jp-journals-10025-1060
ORIGINAL ARTICLE

Evaluation of Visual Acuity, Pachymetry and Anterior-Surface Irregularity in Keratoconus and Crosslinking Intervention Follow-up in 737 Cases

Anastasios John Kanellopoulos, Vasiliki Moustou, George Asimellis

ABSTRACT

Purpose: To investigate visual acuity, corneal pachymetry, and anterior-surface irregularity indices correlation with keratoconus severity in a very large pool of clinically-diagnosed untreated keratoconic eyes, and in keratoconic eyes subjected to cross-linking intervention.

Materials and methods: Total of 737 keratoconic (KCN) cases were evaluated. Group A was formed from 362 untreated keratoconic eyes, and group B from 375 keratoconic eyes subjected to partial normalization via topography-guided excimer laser ablation and high-fluence collagen crosslinking. A control group C of 145 healthy eyes was employed for comparison. We investigated distance visual acuity, uncorrected (UDVA), best-spectacle corrected (CDVA), and Scheimpflug-derived keratometry, pachymetry (central corneal thickness, CCT and thinnest, TCT), and two anterior-surface irregularity indices, the index of surface variance (ISV) and the index of height decentration (IHD). The correlations between these parameters *vs* topographic keratoconus classification (TKC) were investigated.

Results: Keratometry for group A was K1 (flat) 46.67 ± 3.80 D and K2 (steep) 50.76 ± 5.02 D; for group B K1 44.03 ± 3.64 D and K2 46.87 ± 4.61 D; for group C, K1 42.89 ± 1.45 D and K2 44.18 ± 1.88 D. Visual acuity for group A was UDVA 0.12 ± 0.18 and CDVA 0.59 ± 0.25 (decimal), for group B, 0.51 ± 0.28 and 0.77 ± 0.22, and for group C, 0.81 ± 0.31 and 0.87 ± 0.12.

Correlation between ISV and TKC (r^2) was for group A 0.853, and for group-B 0.886. Correlation between IHD and TKC was for group A r^2 = 0.731, and for group B 0.701. The ROC analysis 'area under the curve' was for CDVA 0.550, TCT 0.596, ISV 0.876 and IHD 0.887.

Conclusion: Our study indicates that the traditionally employed metrics of visual acuity and corneal thickness may not be robust indicators nor provide accurate assessment on either keratoconus severity or postoperative evaluation. Two anterior surface irregularity indices, derived by Scheimpflug-imaging, ISV and IHD, may be more sensitive and specific tools.

Précis: Visual acuity, Scheimpflug-derived pachymetry and anterior-surface irregularity correlation to keratoconus severity in untreated cases (A), treated with crosslinking (B), and in a control group (C) reveals that visual acuity and pachymetry do not correlate well with keratoconus severity.

Keywords: Athens Protocol, Combined topography guided PRK and higher fluence CXL, Visual rehabilitation in keratoconus, Severity criteria, Keratoconus progression, Keratoconus classification, Pentacam, Keratoconic Scheimpflug topometric indices, Visual acuity, Keratoconus, Grading anterior surface Pentacam indices, Keratoconus Amsler and Krumeich grading, Corneal pachymetry, Receiver operating characteristic ROC analysis.

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Conflict of interest: None declared

INTRODUCTION

Keratoconus (KCN), derived from the Greek words κερατοειδής: cornea; κώνος: cone, meaning cone-shaped protrusion, is a corneal disorder, defined as a noninflammatory degenerative axial thinning of an ectatic cornea.[1] Vision is affected by increased myopia due to the cone protrusion, and irregular astigmatism due to substantial corneal asymmetry.[2-4]

Our long clinical experience with keratoconic screening and rehabilitation[5-7] indicates that neither corneal pachymetry nor visual acuity (uncorrected distance visual acuity, UDVA, and best-spectacle corrected distance visual acuity, CDVA) can be reliable indicators of ectasia and/or keratoconus progression assessment.[8] One may expect that the presence of large amounts of corneal irregularities might hamper sufficient spectacle-correction of visual acuity. However, at least in our experience, often enough keratoconic patients present with surprisingly high CDVA, even near 20/20, despite severe topographic irregularity and/or pachymetric thinning present. This makes keratoconus diagnosis a difficult and potentially dangerous process, as most early, many advanced and even some severe cases can be missed with traditional screening methods. We have also encountered cases with progressive keratoconus with no clinically significant reduction in visual acuity.

To the best of our knowledge, the subject of quantitative correlation of visual acuity with keratoconus grading[9-11] has been reported only in very few peer-review publications.

This study aims to investigate the possible correlations of visual acuity (UDVA and CDVA), corneal pachymetry, and specific Scheimpflug-imaging derived anterior-surface topographic irregularity indices with keratoconus severity, in a large pool of clinically-diagnosed keratoconic eyes, and in a group of keratoconic eyes subjected to cross-linking and anterior-surface normalization intervention, and examine the applicability of these indicators in keratoconus screening,

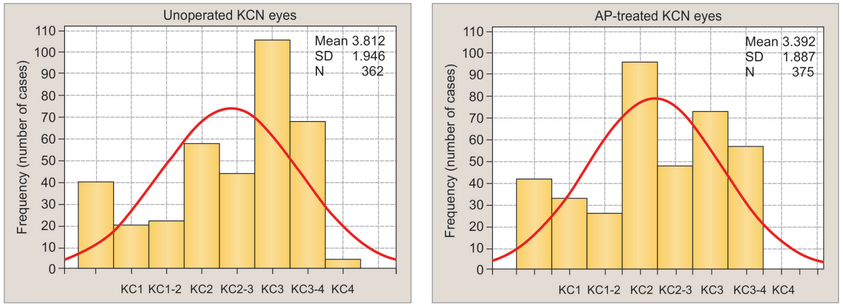

Fig. 1: Histograms of keratoconus classification for the two groups under study. Left — group A, unoperated KCN eyes and, right — group B, Athens-protocol (AP) treated KCN eyes

Table 2: Coefficient of determination (r^2) and pearson correlation coefficient for the two groups in the study between UDVA and TKC, CDVA and TKC, TCT and TKC, ISV TKC, IHD and TKC

	Coefficient of determination (r^2)	*Pearson correlation coefficient*
UDVA vs TKC		
Group A, unoperated KCN eyes	0.071	– 2.931
Group B, AP-treated KCN eyes	0.263	– 3.367
CDVA vs TKC		
Group A, unoperated KCN eyes	0.292	– 4.285
Group B, AP-treated KCN eyes	0.175	– 3.549
TCT vs TKC		
Group A, unoperated KCN eyes	0.236	– 0.0245
Group B, AP-treated KCN eyes	0.176	– 0.0131
ISV vs TKC		
Group A, unoperated KCN eyes	0.853	0.0415
Group B, AP-treated KCN eyes	0.886	0.0485
IHD vs TKC		
Group A, unoperated KCN eyes	0.731	31.9
Group B, AP-treated KCN eyes	0.701	43.1

KCN: keratoconus; UDVA: uncorrected distance visual acuity (decimal); TKC: topographic keratoconus classification; CDVA: best-spectacle corrected distance visual acuity (units, decimal); TCT: thinnest corneal thickness (units, μm); ISV: index of surface variance; IHD: index of height decentration; AP: Athens-protocol

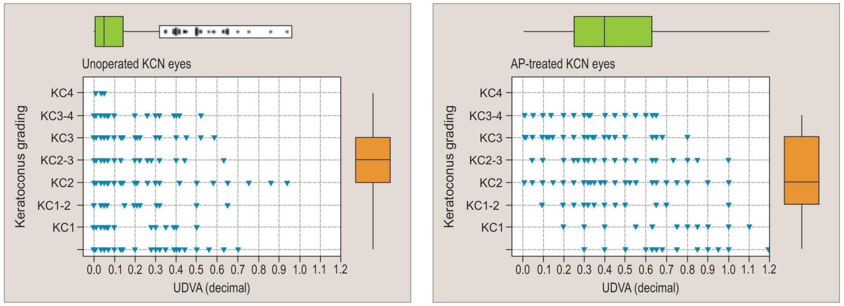

Fig. 2: Marginal plot of UDVA (expressed decimally) and TKC grading with overlying box plots showing mean levels and outliers. Left — group A, unoperated KCN eyes and, right — group B, Athens-protocol (AP) treated KCN eyes

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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

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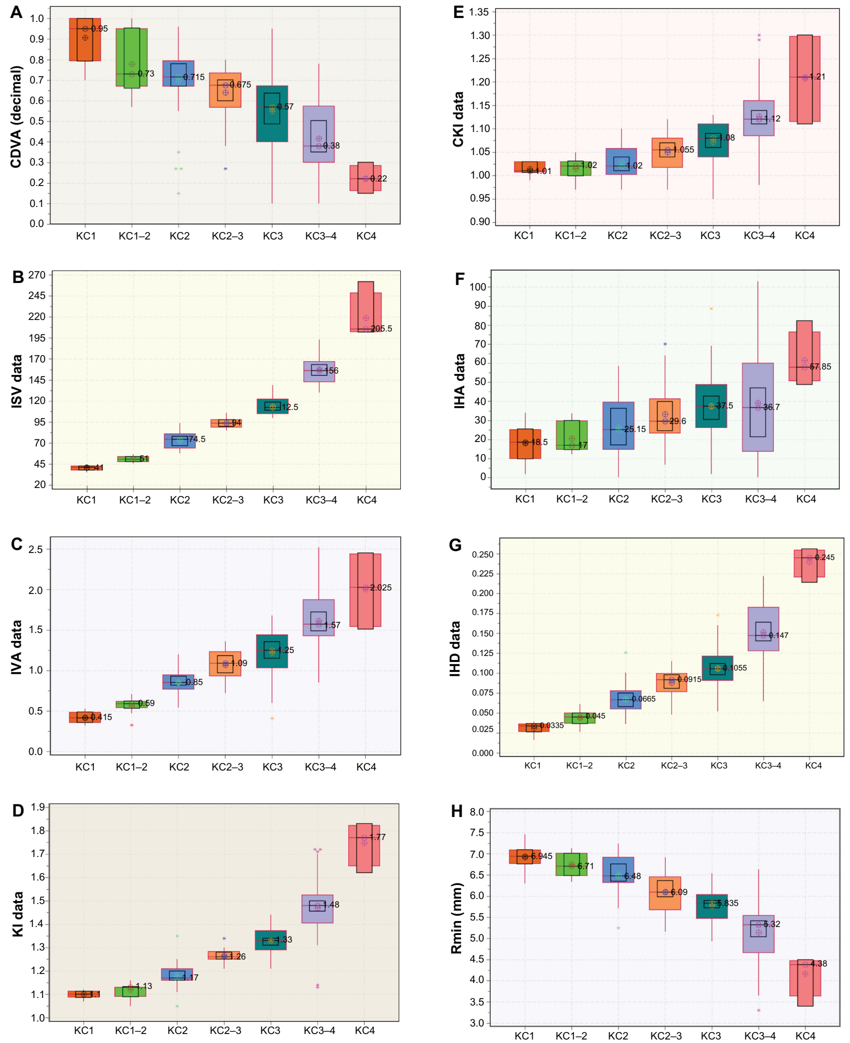
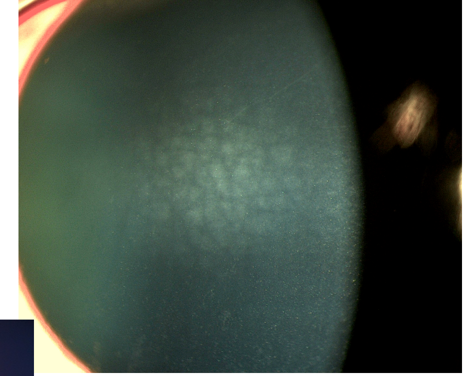


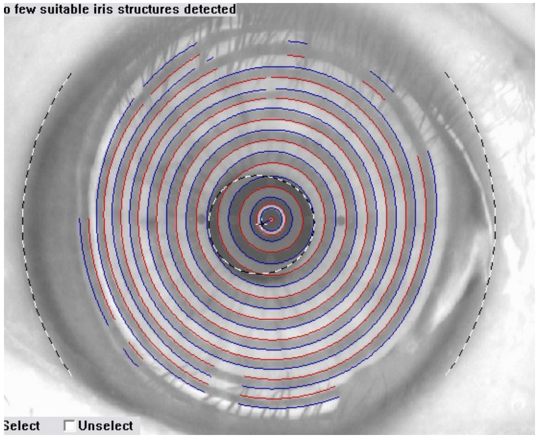
Figure 2 Box plots of measured parameters versus keratoconus grading, as produced by the Oculyzer™ software, showing median level (indicated by ☐), average symbol (☐), 95% median confidence range box (black line boxes), and interquartile intervals range box (red line boxes). **(A)** CDVA versus keratoconus 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.

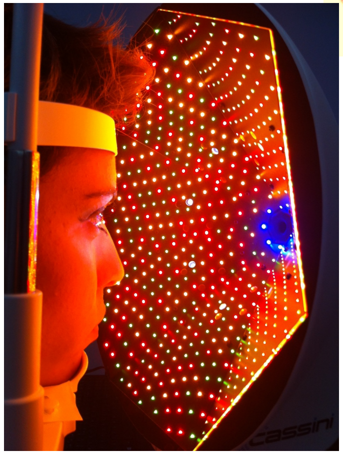
Abbreviations: CDVA, best spectacle-corrected distance visual acuity; CKI, central keratoconus index; IHA, index of height asymmetry; IHD, index of height decentration; ISV, index of surface variance; IVA, index of vertical asymmetry; KC1, keratoconus grading Stage I; KC1–2, keratoconus grading Stage 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.

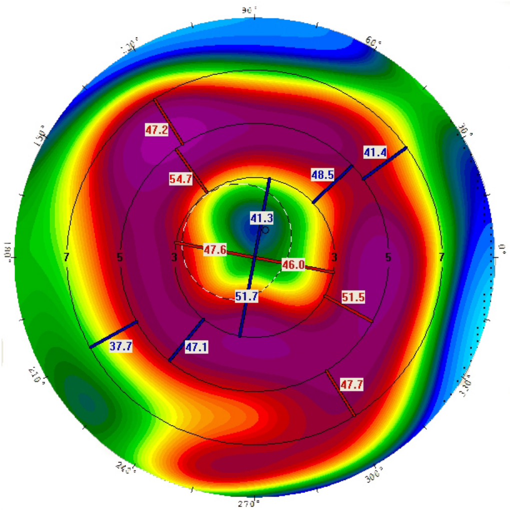
A simple case of Central Cloudy dystrophy (Francois) illustrates the possible discrepancy between different imaging modalities

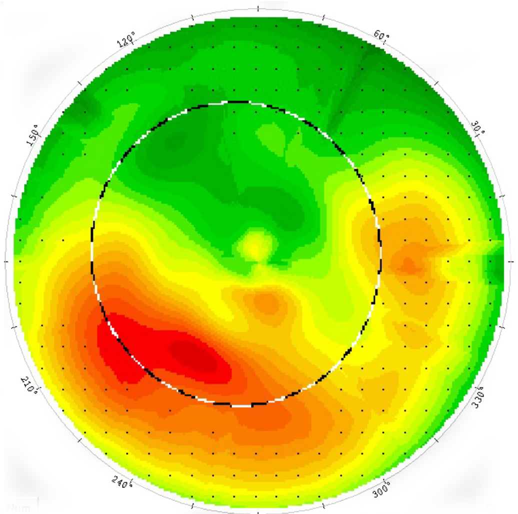
Kanellopoulos AJ, Asimellis G CRO 2013

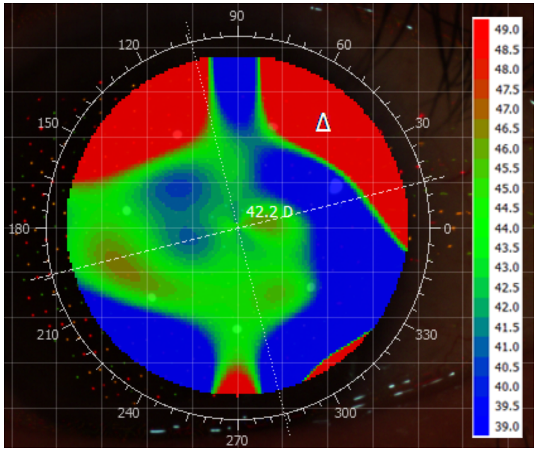












MS NO: ICO202744

In Vivo Three-Dimensional Corneal Epithelium Imaging in Normal Eyes by Anterior-Segment Optical Coherence Tomography: A Clinical Reference Study

Anastasios John Kanellopoulos, MD,† and George Asimellis, PhD**

Purpose: To evaluate the safety and efficacy of real-time measurement of corneal epithelial thickness and investigate the distribution characteristics in a large normal-eye population using a clinically available spectral-domain anterior-segment optical coherence tomography (AS OCT) system.

Methods: Corneal epithelial thickness distribution and topographic thickness variability were clinically investigated using AS OCT imaging in 373 patients with normal, healthy eyes. Descriptive statistics investigated 3 sets of subgroups, male (n = 171) and female (n = 202), younger (n = 194) and older (n = 179), right eyes (n = 195) and left eyes (n = 197).

Results: Pupil center epithelial thickness repeatability was an average 0.88 ± 0.71 μm; a similar repeatability was noted for the superior, inferior, maximum, and minimum epithelial thickness. On average, the pupil center epithelial thickness was 53.28 ± 3.34 μm, superior 51.86 ± 3.78 μm, inferior 53.81 ± 3.44 μm, minimum 48.65 ± 4.54 μm, maximum 56.35 ± 3.80 μm, and topographic variability was 1.78 ± 0.78 μm. Small differences were noted between male (average center 54.10 ± 3.34 μm) and female (52.58 ± 3.19 μm) subjects. The topographic thickness variability seems to increase with age: younger group, 1.65 ± 0.83 μm; older group, 1.93 ± 0.90 μm ($P = 0.173$).

Conclusions: We present a comprehensive investigation of corneal epithelial thickness distribution characteristics in a healthy, untreated human eye population by using in vivo, clinically available Fourier-domain AS OCT. The 3-dimensional epithelial maps reveal epithelial nonuniformity and provide a novel benchmark for future and comparative studies.

Key Words: anterior-segment optical coherence tomography, epithelium imaging, epithelial thickness distribution, epithelial layer thickness topography

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The authors have no funding or conflicts of interest to disclose.

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The distribution of the corneal epithelial layer thickness can be very useful in clinical[1] and in basic research.[2,3] Epithelial thickness maps may be valuable in making close-call clinical decisions and can aid in a safer screening of excimer-laser corneal refractive surgery candidates. The reason for this is the epithelial average thickness differences, and the topographic thickness irregularities,[4] which may contribute unevenly to the total corneal refractive power.

Several clinically available modalities may facilitate in vivo corneal epithelial thickness measurement, including scanning high-frequency ultrasound (HF-UBM),[1] confocal microscopy,[5,6] and anterior-segment optical coherence tomography (AS OCT),[7,8] complementing corneal cross-sectional imaging[9,10] and pachymetry.[11,12] The recent availability of corneal epithelial imaging by AS OCT presents a practical tool for clinical in vivo epithelial mapping, with the speed of optical imaging and ease of use due to the noncontact nature.[13–15]

This study evaluates the clinical quantitative and qualitative 3-dimensional imaging of the corneal epithelial layer in a large number of normal eyes by means of AS OCT. We report here clinical results regarding epithelial thickness mapping in normal corneas with a commercially available AS OCT system. This study aims to investigate the accuracy and precision of the epithelial thickness distribution in a large pool of healthy eyes, and investigate gender and age specifics.

MATERIALS AND METHODS

This prospective study received the approval of the Ethics Committee of our Institution, adherent to the tenets of the Declaration of Helsinki. Informed written consent was obtained from each subject at the time of the first clinical visit.

The study group (n = 373 different cases) consisted of patients with unoperated, normal eyes with no current or past ocular pathology other than refractive error, no previous surgery, and no present irritation or dry eye disorder, all confirmed by a complete ophthalmologic evaluation. Contact lens wearers were excluded. To avoid potential artifacts (eg, because of possible drop instillation), OCT imaging preceded the ocular clinical examination.

The Fourier-domain AS OCT system RTVue-100 (Optovue Inc, Fremont, CA), running on analysis and report software version A6 (9.0.27), was used in the study. Data output included total corneal and epithelial thickness maps corresponding to a 6-mm diameter area. The settings were L-Cam lens, 8 meridional B-scans per acquisition, consisting

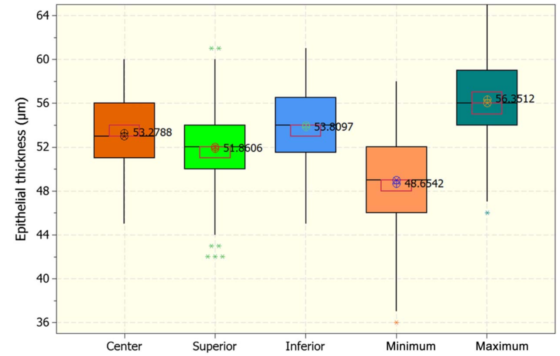

FIGURE 2. Box plot describing central, superior, inferior, minimum, and maximum epithelial thickness for all 373 cases. The median level is displayed numerically and indicated by ⊗, average by ⊕, the 95% median confidence range box by the red borderline, and the interquartile intervals range box by the black borderline. All units are in micrometers.

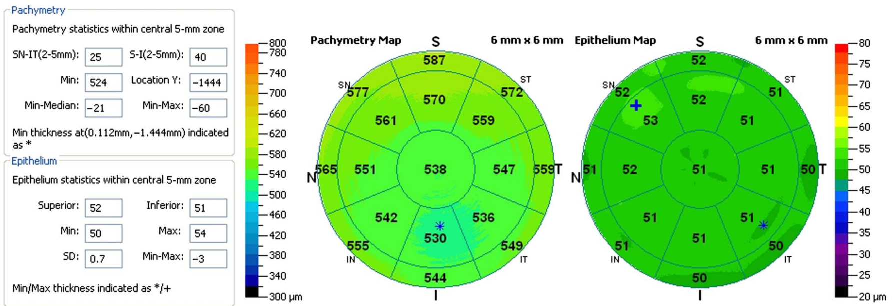

FIGURE 1. Details from the analysis software main report, showing corneal and epithelial 3-dimensional pachymetry maps over the 6-mm corneal diameter. The symbol * indicates the thickness minimum (both corneal and epithelial maps), and the symbol + indicates the thickness maximum (epithelial map only).

In Vivo 3-Dimensional Corneal Epithelial Thickness Mapping as an Indicator of Dry Eye: Preliminary Clinical Assessment

ANASTASIOS JOHN KANELLOPOULOS AND GEORGE ASIMELLIS

• PURPOSE: **To evaluate in vivo epithelial thickness in dry eye by anterior segment optical coherence tomography.**
• DESIGN: **Observational, retrospective case-control study.**
• METHODS: **Two age-matched groups of female subjects, 70 eyes each, age ≈ 55 years, were studied in clinical practice setting: a control (unoperated, no ocular pathology) and a dry eye group (clinically confirmed dry eye, unoperated and no other ocular pathology). Corneal epithelium over the entire cornea was topographically imaged via a novel anterior segment optical coherence tomography (AS-OCT) system. Average, central, and peripheral epithelial thickness as well as topographic epithelial thickness variability were measured.**
• RESULTS: **For the control group, central epithelial thickness was 53.0 ± 2.7 μm (45-59 μm). Average epithelium thickness was 53.3 ± 2.7 μm (46.7-59.6 μm). Topographic thickness variability was 1.9 ± 1.1 μm (0.7-6.1 μm). For the dry eye group, central epithelial thickness was 59.5 ± 4.2 μm (50-72 μm) and average thickness was 59.3 ± 3.4 μm (51.4-70.5 μm). Topographic thickness variability was 2.5 ± 1.5 μm (0.9-6.9 μm). All pair tests of respective epithelium thickness metrics between the control and dry eye group show statistically significant difference ($P < .05$).**
• CONCLUSIONS: **This study, based on very user-friendly, novel AS-OCT imaging, indicates increased epithelial thickness in dry eyes. The ease of use and the improved predictability offered by AS-OCT epithelial imaging may be a significant clinical advantage. Augmented epithelial thickness in the suspect cases may be employed as an objective clinical indicator of dry eye. (Am J Ophthalmol 2014;157:63–68. © 2014 by Elsevier Inc. All rights reserved.)**

DRY EYE IS A MULTIFACTORIAL DISEASE OF THE tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.[1]

Dry eye is responsible for significant population morbidity and is a common clinical problem for eye clinicians. Besides the significant symptoms and toll on quality of life, it may present significant challenges in refractive surgery patient assessment.[2] As reported in the peer-review literature,[3–7] its manifestations may range from episodic and mild condition to chronic and severe disease: the disorder can be presented with any or many symptoms of visual disturbance and blurred vision, eye discomfort, irritation, foreign body sensation, ocular surface damage, redness, excess tearing, and photosensitivity.

Epidemiologic review studies estimate the prevalence of dry eye disease between 4% and 33%, largely depending, among other factors, on the diagnosis mode, the geographic locale,[8,9] age, and sex, being most prominent in the middle-aged (over age 45 years) female populace.[10–12]

Several clinically available modalities may facilitate in vivo measurement of corneal epithelium, including high-frequency scanning ultrasound biomicroscopy (HF-UBM),[13] anterior segment optical coherence tomography (AS-OCT),[14] and confocal microscopy through focusing (CMTF).[15,16] In the clinical practice, epithelial evaluation is limited by the resolution and the variability of the ocular surface tests.[17]

In pursuit of an objective, repeatable, and quantitative clinical test that may aid in the differential diagnosis of dry eye, we introduce the concept of corneal epithelial thickness as a possible tool in dry eye assessment. We report herein initial clinical results regarding 3-dimensional corneal epithelial thickness mapping in dry eye corneas with a newly commercially available anterior segment optical coherence tomography system.

MATERIALS AND METHODS

THIS OBSERVATIONAL, RETROSPECTIVE CASE-CONTROL study received approval by the Ethics Committee of our Institution (LaserVision.gr Eye Institute), and was adherent to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each subject

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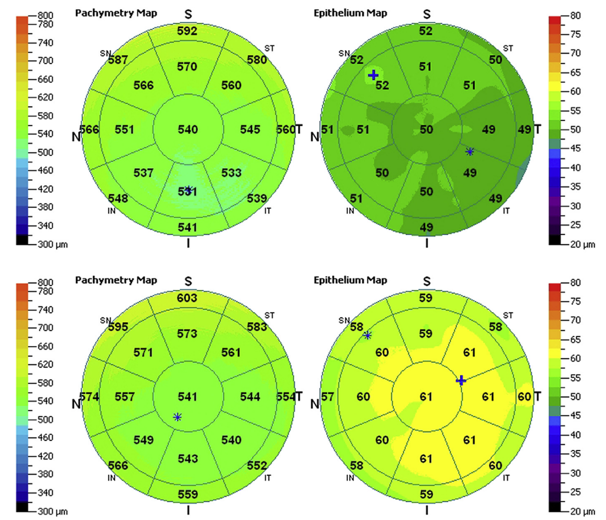

FIGURE 1. Representative corneal total thickness maps (left) and corneal epithelium thickness maps (right) of (Top) a "normal" patient from Group A and (Bottom) a dry eye patient from Group B, as provided by the optical coherence tomography system report.

DISCUSSION

THE CHALLENGE OF OBJECTIVE DRY EYE ASSESSMENT HAS been argued in length. The current options of the clinical investigator includes slit-lamp observations, osmolarity test, tear-film breakup time measurement, Schirmer lacrimation test, corneal and conjunctival staining, meibomian grading, and Ocular Surface Disease Index.[10] Research evidence suggests that clinical dry eye symptoms alone may be insufficient for the diagnosis and management of dry eye, and there is argument for a consensus of newer metrics that may better reflect the differential discrimination of the disease.[18]

One such possible element in diagnosis is overall epithelial thickness, as well as the topographic distribution of epithelial thickness. For example, atopic keratoconjunctivitis has been associated with significant alterations of the basal epithelium and subbasal and stromal corneal nerves, related to the changes in tear functions and corneal sensitivity.[19]

Very little is reported, however, in the peer-review literature on the subject matter of entire corneal area in vivo measurement of epithelial thickness, particularly in relationship with dry eye. This can be justified by the fact that neither HF-UBM nor AS-OCT nor CMTF techniques have been fully applicable and/or with a commercially available mode for this use, as well as the fact that some (eg, HF-UBM) employ instrument or fluid interface contact with the epithelium. We have not identified, for example, reported correlation of dry eye and HF-UBM measurements. CMTF has been restricted in this application because of the degraded precision by eye movement during the long acquisition time; in addition, other available clinical evaluation techniques for the corneal epithelium either are invasive or require contact between the probe and the ocular surface, and thus cannot provide precise in vivo measurement of the epithelial thickness.[20] In a confocal laser scanning microscopy study in dry eye,[21] the mean superficial and intermediate epithelial cell densities in the central cornea in the dry eye groups were significantly lower than in normal participants. Dry eye corneas showed significant alterations, presumably attributable to increased desquamation of the superficial cell layer.

Reports on entire corneal epithelium imaging via AS-OCT, a novel entity, have been also few. In most of these studies, investigator-modified software/hardware[22–24] or caliper software measurement techniques[25,26] have been employed (for example, by manually placing cursors to measure epithelial thickness in each location).

The recent availability of full-cornea corneal epithelial thickness imaging by AS-OCT potentially presents a practical clinical tool for qualitative (by examination of the

ORIGINAL ARTICLE

Corneal Epithelial Remodeling Following Cataract Surgery: Three-Dimensional Investigation With Anterior-Segment Optical Coherence Tomography

Anastasios John Kanellopoulos, MD; George Asimellis, PhD

ABSTRACT

PURPOSE: To map corneal and epithelial layer thickness changes following cataract removal surgery employing a spectral-domain anterior-segment optical coherence tomography system.

METHODS: Corneal and epithelial thickness three-dimensional profile distribution was clinically imaged preoperatively and up to 3 months postoperatively with anterior-segment optical coherence tomography in 116 consecutive cases. Descriptive statistics investigated central corneal thickness, minimum corneal thickness, and epithelial thickness at the central 2-mm area, the mean over the 6-mm area, and mid-peripherally at 5-mm ring.

RESULTS: In comparison to preoperative, the center, mean, and mid-peripheral epithelial thickness at the first postoperative day increased by +2.84, +2.35, and +2.25 μm, respectively (P < .001, < .001, and = .0014). One week postoperatively, the epithelial thickness differences were -1.91, -2.62, and -2.76 μm, respectively (P < .001, < .001, and < .001). Four weeks postoperatively, the differences of -0.20, -0.59, and -0.66 μm for the center, mean, and mid-periphery were not statistically significant (P = .6449, .1512, and .11097). Three months postoperatively, the differences were -0.05, -0.28, and -0.09 μm, respectively (P = .8722, .2341, and .6431).

CONCLUSIONS: Qualitative and quantitative assessment of epithelial remodeling following cataract removal indicated that the early (1 day and 1 week) corneal and epithelial thickness returned to the preoperative baseline 4 weeks postoperatively. This in vivo epithelial and corneal screening with optical coherence tomography can be valuable for the postoperative assessment and follow-up.

[*J Refract Surg*. 2014;30(5):348-353.]

One of the most recent applications of anterior-segment optical coherence tomography (AS-OCT) is clinical in vivo epithelial layer thickness three-dimensional mapping.[1,2] Clinical epithelial imaging and evaluation is a novel application, with ramifications that are still being explored. Currently, there is a limited number of commercially available AS-OCT systems[3] that offer three-dimensional epithelial thickness imaging over the cornea, such as the RTVue-100 (Optovue Inc., Fremont, CA).[1]

The question of near-term corneal and epithelial layer thickness recovery following cataract surgery is related to the postoperative rehabilitation of the affected eye, reflecting the corneal structure changes after the surgery. Little has been published in the literature on this matter.[4-6] To the best of our knowledge, there is no study evaluating epithelial layer thickness changes following cataract surgery.

This study employs clinical spectral-domain AS-OCT imaging in the evaluation of quantitative and qualitative three-dimensional corneal and epithelial layer thickness changes in a large number of cases undergoing cataract surgery by clear corneal phacoemulsification with implantation of an intracapsular intraocular lens. The study aims to investigate longitudinal near-term postoperative changes in corneal and epithelial thickness, and the possible association of these thickness changes with gender and age of patients at the time of the sugery.

PATIENTS AND METHODS

This observational, prospective longitudinal study received approval from the ethics committee of our institution and adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained from all patients at the time of the first clinical visit or prior to the surgery.

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Dr. Kanellopoulos is a consultant of Alcon/WaveLight, Avedro, and i-Optics. Dr. Asimellis has no financial or proprietary interest in the materials presented herein.

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Inclusion–Exclusion Criteria

The study group consisted of unoperated, normal eyes with no current or past ocular pathology other than cataract, no other previous surgery, no epithelial defects, and no current irritation or dry eye disorder. All patients underwent a complete ophthalmologic evaluation. In all cases, clear corneal incision, phacoemulsification, and implantation of an intracapsular intraocular lens was performed by the same surgeon (AJK). The Constellation microsurgical system (Alcon Laboratories, Inc., Ft. Worth, TX) was employed for phacoemulsification and cataract removal. Ultrasound energy employed for phacoemulsification was on average 5 J (range: 1.8 to 7.2 J). No postoperative complications were observed in any case enrolled in the study.

Instrumentation

The RTVue-100 spectral-domain AS-OCT system (Optovue Inc.), running on analysis and report software version A6 (9.0.27), was employed in the study. Data output included total corneal and epithelial thickness maps corresponding to a 6-mm diameter area. In all cases, to avoid potential artifacts (eg, due to possible drop instillation), OCT imaging preceded the ocular clinical examination during each visit. All OCT imaging was conducted by the same trained investigator. The settings were: L-Cam lens, 8 meridional B-scans per acquisition, consisting of 1,024 A-scans each with 5-µm axial resolution, acquired in approximately less than a second. Images with quality as determined by the signal strength index parameter (a measure of the average signal strength across the scan) of more than 30 were considered for the study. These eight radial meridional scans were employed by the system software to produce, by interpolation, the three-dimensional thickness maps.

Data Collection and Analysis

The preoperative imaging was performed the day preceding the surgery, and the postoperative measurements were performed 1 day, 1 week, 1 month, and 3 months after surgery. Two consecutive individual acquisitions were obtained in each case to ensure data validity.

The main analysis report produced by the AS-OCT system displayed total corneal (reported as pachymetry) and epithelial three-dimensional thickness maps covering the 6-mm diameter area. As shown in **Figure 1**, each pachymetry map is divided in 17 sectors. Specifically, these are the 2-mm diameter pupil center disk of 12.56 mm^2 area, 8 sectors within the annulus between the 2- to 5-mm zones, each of 8.24 mm^2 area, and 8 sectors within the annulus of 5- to 6-mm

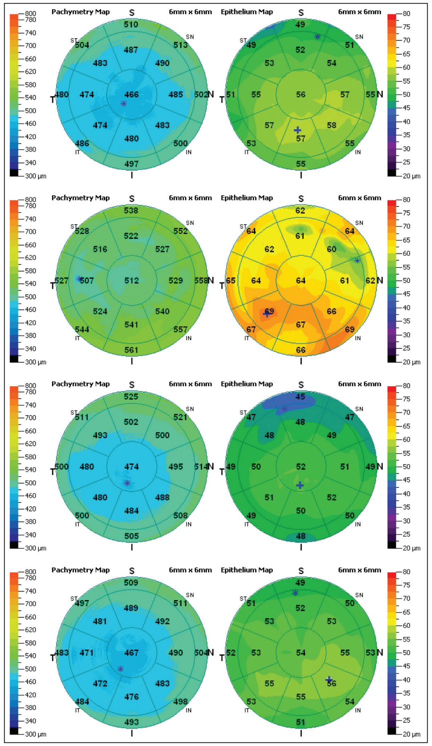

Figure 1. Longitudinal display of total corneal (left) and epithelial thickness (right) progression with three-dimensional pachymetry maps. From top to bottom: preoperative, 1 day, 1 week, and 4 weeks postoperatively. This image series belongs to the right eye of a 56-year-old male patient. * = thickness minimum (both corneal and epithelial maps); + = thickness maximum (epithelial map only).

zones, each of 4.32-mm^2 area. For each of these sectors, average thickness was displayed numerically in integer form with a minimum difference of 1 µm over the corresponding area.

In this study, the reported central corneal thickness (CCT) was provided by the integer indication over the center disk, and minimum corneal thickness was provided by the data output in the form of a table. The 'epithelium center' thickness was provided by the integer indication over the center disk. Mean epithelial thickness was computed by the average of all segments, and peripheral

ORIGINAL ARTICLE

Longitudinal Postoperative LASIK Epithelial Thickness Profile Changes in Correlation With Degree of Myopia Correction

Anastasios John Kanellopoulos, MD; George Asimellis, PhD

ABSTRACT

PURPOSE: To evaluate epithelial thickness profile changes following myopic femtosecond laser-assisted LASIK in relation to the degree of myopia corrected, evaluated with a spectral-domain anterior-segment optical coherence tomography system.

METHODS: Sixty-one consecutive cases were observed for corneal epithelial thickness distribution preoperatively and at 1 day, 1 week, 1 month, and 1 year postoperatively. Epithelial thickness mapping was obtained with a spectral-domain optical coherence tomography system (Optovue Inc., Fremont, CA). Descriptive statistics investigated epithelial thickness at the central 2-mm area, the mean over the central 6-mm area, and mid-peripherally at the 5-mm ring area.

RESULTS: Preoperatively, the pupil center epithelial thickness was 51.67 ± 2.57 µm (range: 45 to 56 µm), mean was 51.76 ± 2.66 µm (range: 45 to 57 µm), and mid-periphery was 51.78 ± 2.71 µm (range: 46 to 57 µm). Compared to the preoperative values, the epithelial thickness for the center, mean, and mid-periphery was -0.30, +1.07, and +1.35 µm at 1 week, +1.58, +2.88, and +3.31 µm at 1 month (P = .0036, < .001, and < .001), and +1.42, +2.90, and +3.19 µm at 1 year postoperatively (P = 0.146, < .001, and < .001), respectively. The correlation analysis between the epithelial thickness increase and the spherical equivalent of myopic correction showed a trend toward epithelial thickness increase with the amount of myopic ablation, particularly at the mid-peripheral 5-mm area.

CONCLUSIONS: In this comprehensive study of postoperative corneal epithelial thickness remodeling following femtosecond laser-assisted myopic LASIK correction, an increase at the 1-month and up to 1-year postoperative interval suggested postoperative epithelial activity in connection to the extent of ablation.

[*J Refract Surg.* 2014;30(3):166-171.]

Epithelial thickness changes have been reported in studies of microkeratome-assisted myopic excimer laser refractive correction[1,2]; in many of these studies, the noted central epithelial thickness increase has been associated with refractive regression.[3-5] Extending beyond central thickness evaluation, three-dimensional full-cornea evaluation by scanning ultrasound has demonstrated that the change in epithelial thickness following myopic ablation was lenticular in shape.[6]

This study employs clinical spectral-domain anterior-segment optical coherence tomography (AS-OCT) imaging in the evaluation of quantitative and qualitative three-dimensional corneal epithelial layer thickness changes in a large number of myopic LASIK cases, in which a femtosecond laser was employed for the flap creation and a high-pulse rate excimer laser provided the myopic ablation. This study aims to investigate longitudinal postoperative changes in epithelial thickness distribution, centrally, on average, and mid-peripherally, and to investigate the possible association of epithelial thickness changes with the extent of attempted myopic correction.

PATIENTS AND METHODS

This observational, longitudinal study received approval from the ethics committee of our institution, and adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained from all patients at the time of the first clinical visit.

Inclusion-Exclusion Criteria

The study group consisted of patients with unoperated, normal eyes with no current or past ocular pathology other

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doi:10.3928/1081597X-20140217-03

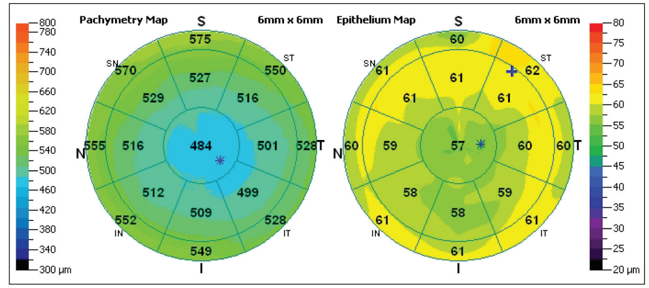

Figure 1. Detail from the analysis and report software main report, showing corneal and epithelial three-dimensional pachymetry maps over the 6-mm corneal diameter in a postoperative LASIK examination. The patient (left eye) received treatment for -4.75 diopters of sphere and -0.75 diopters of astigmatism,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

Epithelial Thickness Profile Changes/Kanellopoulos & Asimellis

TABLE 2

Descriptive Statistics for the Postoperative Epithelium Thickness Changes (µm)

	1 Day			1 Week			1 Month			12 Months		
Parameter	Center	Mean	Mid	Center	Mean	Mid	Center	Mean	Mid	Center	Mean	Mid
Average	-0.08	-0.34	-0.39	-0.30	1.07	1.35	1.58	2.88	3.31	1.42	2.90	3.19
SD	±3.12	±3.40	±3.49	±2.52	±2.28	±2.38	±2.73	±3.15	±3.25	±2.62	±2.73	±2.82
Maximum	7	7.33	7.4	5	6.75	7.7	10	11.25	12	7	9.23	11.21
Minimum	-6	-8.33	-8.8	-6	-3.25	-3.2	-4	-2.33	-2.2	-5	-2.79	-2.10
P^a	.897	.587	.534	.522	.037	.0125	.0036	< .001	< .001	.0146	< .001	< .001

Mid = mid-periphery; SD = standard deviation
[a]Paired Student's t test.

in **Figure 2**, there is a correlation between the degree of myopic ablation and increase of epithelial thickness. Specifically for the mid-peripheral epithelial thickness increase, the linear fit trend line describing this correlation had a Pearson product-moment correlation coefficient r = 0.831, and was described by the equation derived from our results: increase in epithelial thickness (y, in µm) = -1.39 × myopic ablation (x in D) + 9.77 µm.

For each degree of myopic ablation, the corresponding increase of epithelial thickness on the mid-periphery was on the scale of 1 µm. Similar results, but with a lesser degree of correlation, were obtained for the center and the mean epithelial thickness increase (r = 0.631 and 0.519, respectively).

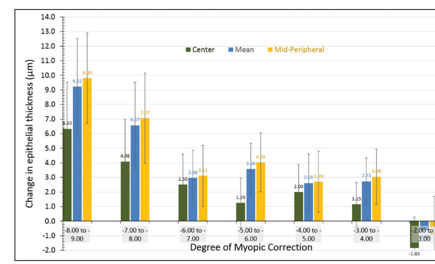

Figure 2. The correlation of increase in epithelial thickness at the center (green dots), on the mean over the 6-mm diameter (blue), and on the 5-mm mid-peripheral zone (yellow) 1 month following myopic LASIK correction. There were 4 cases between -8 and -9 diopters (D), 7 cases between -7 and -8 D, 10 cases between -6 and -7 D, 8 cases between -5 and -6 D, 15 cases between -4 and -5 D, 13 cases between -3 and -4 D, and 6 cases between -2 and -3 D. Error bars indicate standard deviation.

DISCUSSION

Accurate and repeatable quantitative assessment of corneal epithelial thickness distribution has been

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AU2

Epithelial Remodeling After Femtosecond Laser–Assisted High Myopic LASIK: Comparison of Stand-alone With LASIK Combined With Prophylactic High-fluence Cross-linking

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

Purpose: The aim of this study was to evaluate the possible topographic epithelial profile thickness changes (remodeling) after high myopic femtosecond laser in situ keratomileusis (LASIK) with concurrent prophylactic high-fluence cross-linking (CXL) in comparison with standard femtosecond LASIK.

Methods: Preoperative and 6-month postoperative 3-dimensional epithelial thickness distribution maps were investigated through a clinical spectral domain anterior-segment optical coherence tomography in 2 groups of femtosecond laser–assisted myopic LASIK cases. Group A represented 67 eyes treated additionally with concurrent prophylactic CXL (LASIK-Xtra); group B represented 72 eyes subjected to stand-alone femtosecond LASIK. Optical coherence tomography measurements of the epithelial thickness over the center 2-mm-diameter disk, mid-peripheral 5-mm rim, and overall (the entire 6-mm-diameter disc area) were investigated.

Results: The comparison of matched myopic correction subgroups indicated statistically significant differences in the epithelial thickness increase specifically between high myopia subgroups. For example, in group A (LASIK-Xtra), the mid-peripheral epithelial thickness increase was +3.79 and +3.95 μm for the "−8.00 to −9.00 diopter" and "−7.00 to −8.00 diopter" subgroups, which compare with increased thickness in group B (stand-alone LASIK), of +9.75 μm (P = 0.032) and +7.14 μm (P = 0.041), respectively, for the same subgroups.

Conclusions: Application of prophylactic CXL concurrently with high myopic LASIK operation results in a statistically significant reduced epithelial increase in comparison with the stand-alone LASIK. This comparison is observed between matched high myopic correction subgroups. This difference may correlate with higher regression rates and/or may depict increased biomechanical instability in the stand-alone LASIK.

Key Words: anterior segment optical coherence tomography, epithelial imaging, epithelial thickness distribution, epithelial layer topography, myopic LASIK, femtosecond LASIK, LASIK-Xtra, high-fluence cross-linking, prophylactic cross-linking

(*Cornea* 2014;0:1–7)

The concept of a proactive intervention involving in situ cross-linking (CXL) application concurrent with laser in situ keratomileusis (LASIK) surgery has been introduced by the term "LASIK-Xtra."[1,2] The concept has been based on successful treatments and femtosecond laser–created intrastromal pocket CXL implementation[3,4] in a patient population who seems to have a high rate of keratoconus. The rationale for such a prophylactic action in routine LASIK is to strengthen the cornea, particularly in high myopic cases with thin residual stroma and younger patients who may have not yet exhibited ectasia risk factors.[5,6] Our experience with high myopic corrections without any such preventive application is suggestive of a long-term corneal steepening trend (refractive regression toward a myopic shift).[7] Because of this troublesome finding, and the high incidence of keratoconus in our patient populace, in situ CXL may be justified in high myopic LASIK cases.

Refractive regression has been associated with substantial postoperative epithelial thickness changes[8,9] after LASIK myopic correction.[10–12] Specifically, postoperative epithelial evaluation after myopic LASIK has demonstrated a topographically nonuniform increase in the epithelial thickness,[13] dependent on the extent of myopia corrected.

We have recently investigated epithelial remodeling after femtosecond laser–assisted LASIK.[14] The study, conducted with Fourier-domain anterior-segment optical coherence tomography (AS-OCT), in large myopic corrections [eg −8.00 diopter (D)] indicated 1-year postoperative central epithelial thickness increase of up to +6 μm and localized increase at the 5-mm mid-peripheral rim of up to +9 μm.

This study aimed to comparatively investigate the potential differences in epithelial remodeling between 2 groups, a LASIK-Xtra and a stand-alone LASIK group, in which no concurrent CXL is applied. The epithelial study was facilitated by 3-dimensional epithelial thickness maps produced by a clinically available spectral domain AS-OCT system.

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A. J. Kanellopoulos is a consultant and holds advisory positions with Alcon/WaveLight, Allegran, Avedro, and i-Optics. G. Asimellis has no funding or conflicts of interest to disclose.

Design and conduct of the study (A.J.K.); collection (A.J.K. and G.A.), management (A.J.K.), analysis (G.A.), and interpretation of the data (A.J.K. and G.A.); manuscript preparation (G.A.), review (A.J.K. and G.A.), and approval (A.J.K.).

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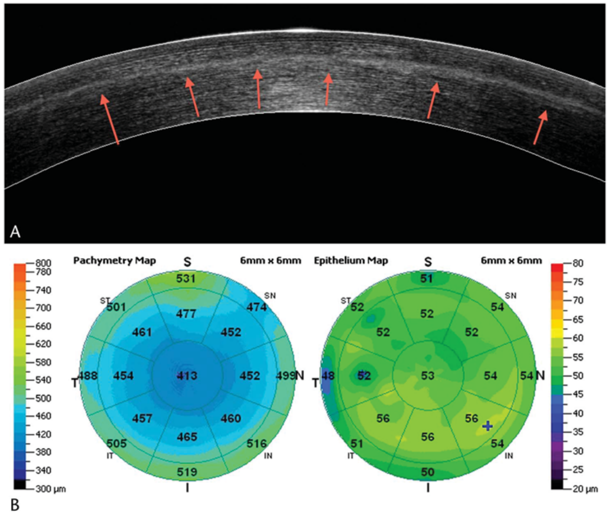
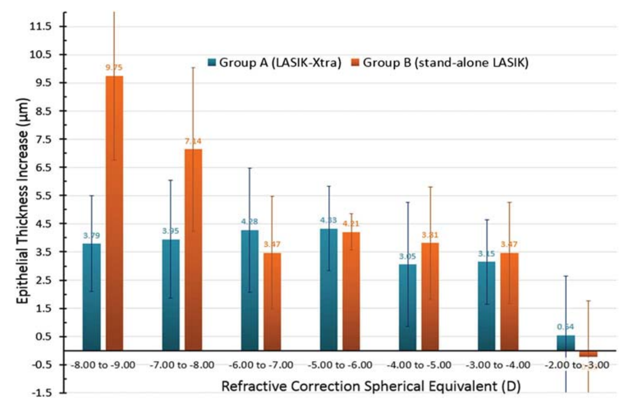


AU14

FIGURE 1. A, AS-OCT high-resolution cross-sectional meridional image of a right eye treated with LASIK-Xtra for −8.00 D of sphere and −0.25 D of astigmatism, and was it imaged 6 months postoperatively. There is a clear depiction of the central corneal epithelial layer, Bowman membrane, anterior stroma, Descemet membrane, and anterior chamber. Deep stromal hyperreflective lines may correlate with the depth of the CXL-effect achieved with the LASIK-Xtra procedure according to our previous reported findings. B, Detail from of the analysis and report software main report, showing corneal and epithelial 3-dimensional pachymetry maps over the 6-mm corneal diameter. The symbol * indicates thickness minimum (both corneal and epithelial maps), and the symbol + thickness maximum (epithelial map only).

Cornea • Volume 0, Number 0, Month 2014 *Topographic Epithelial Profile Thickness Changes*

FIGURE 2. Correlation of increase in epithelial thickness at the 5-mm mid-peripheral zone, 6 months postoperatively, in comparison for the 2 groups, with refractive correction spherical equivalent.



Recent FDA topography-guided LASIK data-2013

4.8. Efficacy Outcomes

Changes In Manifest Refraction, Refractive Stability, Vector Analyses, Changes In UCVA, Patient-Reported Outcomes

A summary of key efficacy variables at each of the postoperative visits is provided below in Table 16 for the myopia cohort treated with Topo-guided (T-CAT) LASIK.

		Month 1	Month 3	Month 6	Month 9	Month 12
EFFICACY VARIABLES						
MRSE ± 0.50 D	n/N	220/248	227/247	227/244	221/237	218/230
	(%)	(88.71%)	(91.90%)	(93.03%)	(93.25%)	(94.78%)
	(CI)	(84.1, 92.4)	(87.8, 95.0)	89.1, 95.9)	(89.3, 96.1)	(91.1, 97.3)
MRSE ± 1.00 D	n/N	244/248	244/247	241/244	235/237	229/230
	(%)	(98.39%)	(98.79%)	(98.77%)	(99.16%)	(99.57%)
	(CI)	(95.9, 99.6)	(96.5, 99.7)	(96.4, 99.7)	(97.0, 99.9)	(97.6,100.0)
MRSE ± 2.00 D	n/N	248/248	247/247	243/244	237/237	230/230
	(%)	(100.0%)	(100.0%)	(99.59%)	(100.0%)	(100.0%)
	(CI)	(98.5,100.0)	(98.5,100.0)	(97.7,100.0)	(98.5,100.0)	(98.4,100.0)
UCVA 20/20 or better	n/N	217/248	229/247	217/244	212/237	213/230
	(%)	(87.50%)	(92.71%)	(88.93%)	(89.45%)	(92.61%)
	(CI)	(82.7, 91.3)	(88.7, 95.6)	(84.3, 92.6)	(84.8, 93.1)	(88.4, 95.6)
UCVA 20/40 or better if BCVA 20/20 or better preop	n/N	239/242	239/241	235/238	231/232	224/225
	(%)	(98.76%)	(99.17%)	(98.74%)	(99.57%)	(99.56%)
	(CI)	(96.4, 99.7)	(97.0, 99.9)	(96.4, 99.7)	(97.6,100.0)	(97.5,100.0)

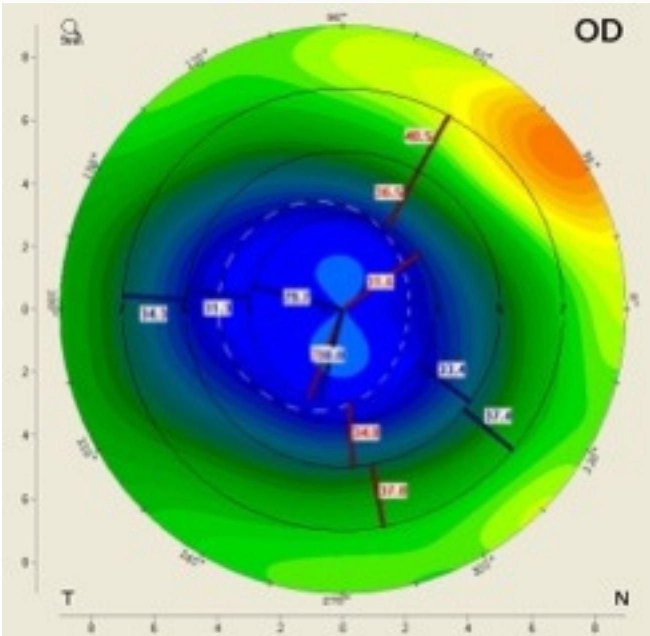
Table 16: Summary Of Key Efficacy Parameters After Topo-guided (T-CAT) LASIK

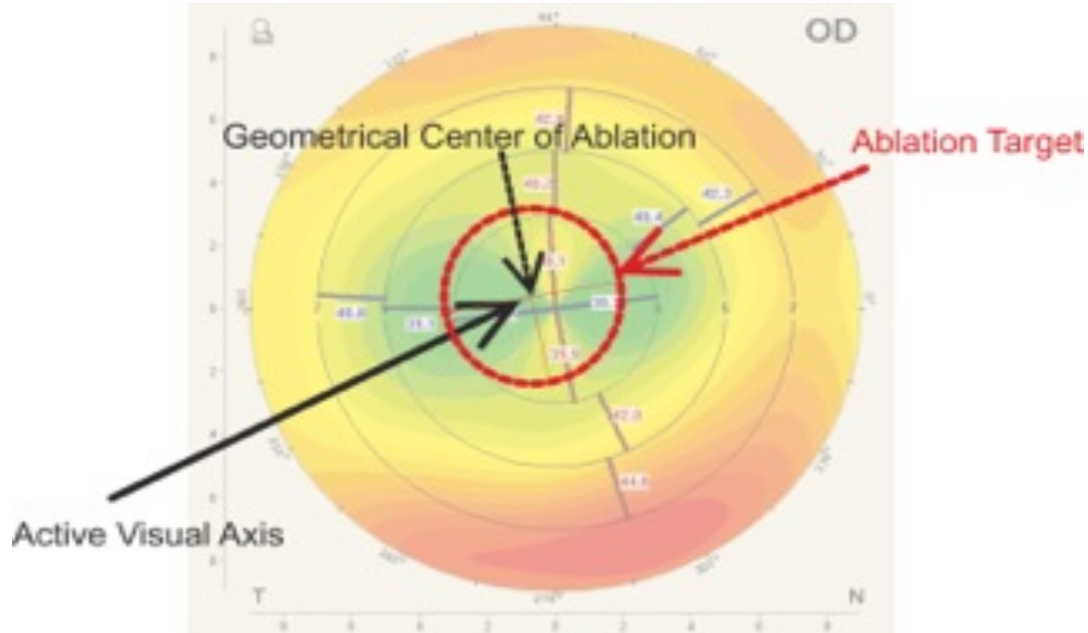
WaveLight ALLEGRETTO WAVE® Eye-Q Excimer Laser - P020050/S012
, Summary of Safety and Effectiveness Data (SSED)
http://www.accessdata.fda.gov/cdrh_docs/pdf2/P020050S012b.pdf
Accessed August 27, 2014

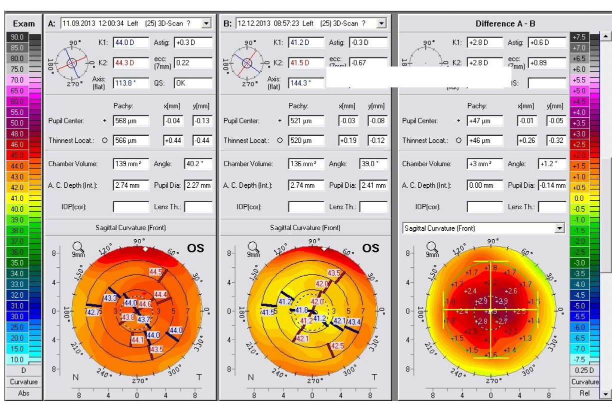
UCVA 20/20 or better	n/N	217/248	229/247	217/244	212/237	213/230
	(%)	(87.50%)	(92.71%)	(88.93%)	(89.45%)	(92.61%)
	(CI)	(82.7, 91.3)	(88.7, 95.6)	(84.3, 92.6)	(84.8, 93.1)	(88.4, 95.6)
UCVA 20/40 or better if BCVA 20/20 or better preop	n/N	239/242	239/241	235/238	231/232	224/225
	(%)	(98.76%)	(99.17%)	(98.74%)	(99.57%)	(99.56%)
	(CI)	(96.4, 99.7)	(97.0, 99.9)	(96.4, 99.7)	(97.6,100.0)	(97.5,100.0)

Table 16: Summary Of Key Efficacy Parameters After Topo-guided (T-CAT) LASIK

New Study from Athens:
How to objectively assess excimer laser centration delivery?







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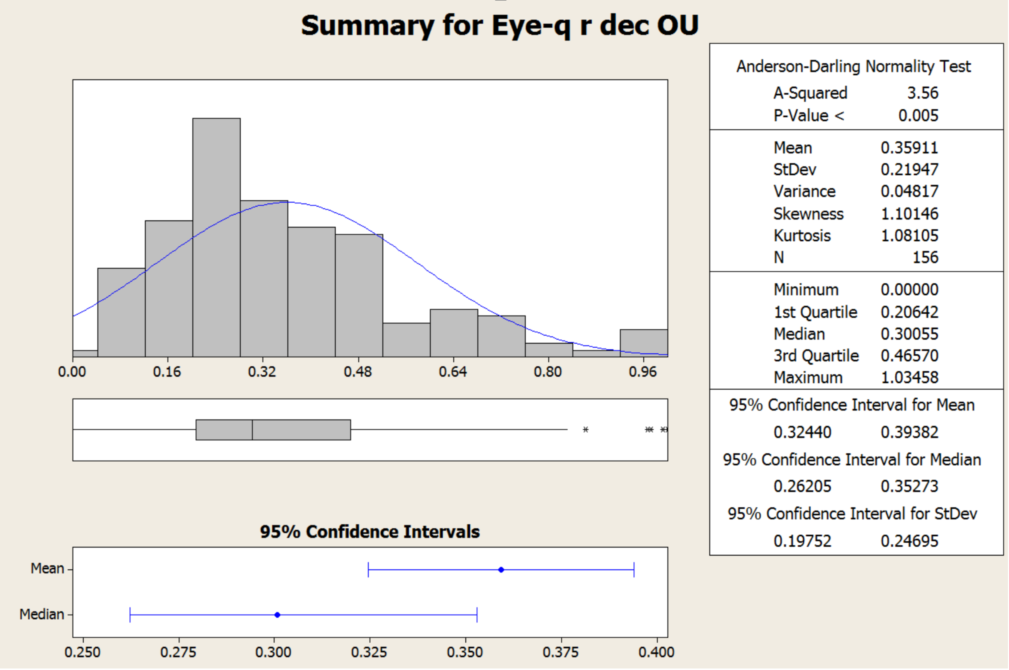
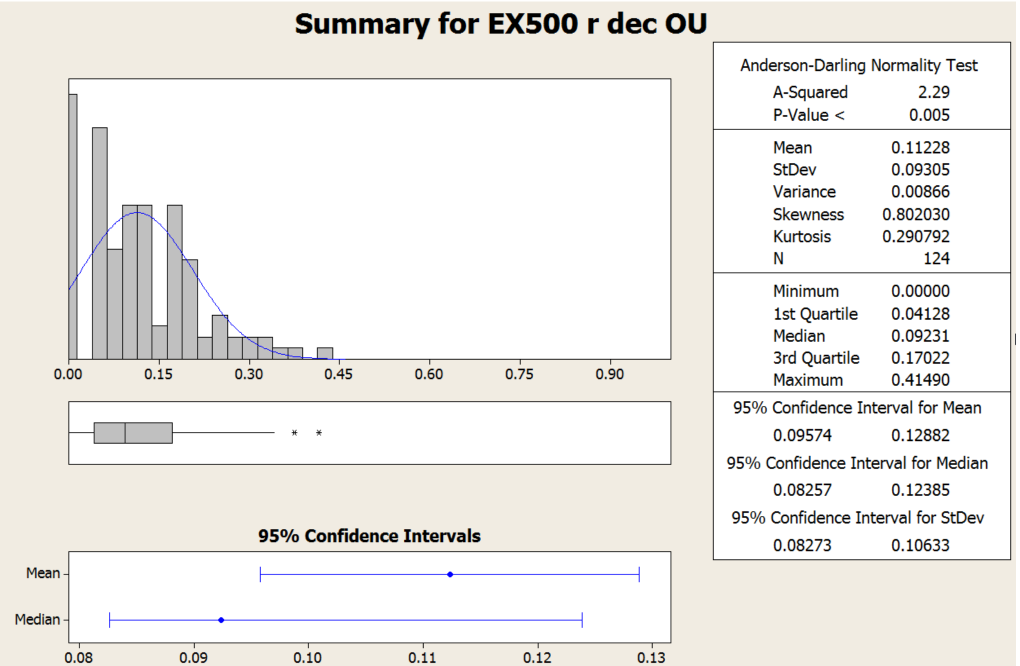
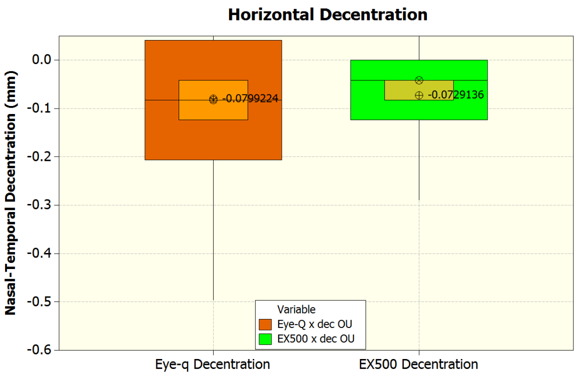
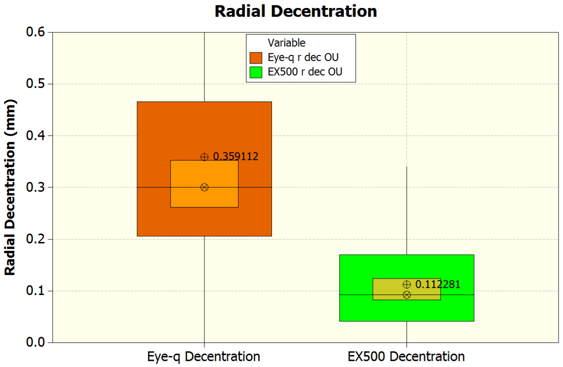
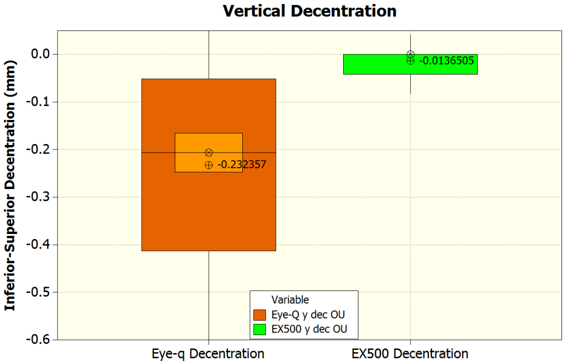
Wavelight 400Hz Vs EX500 centration IIT study











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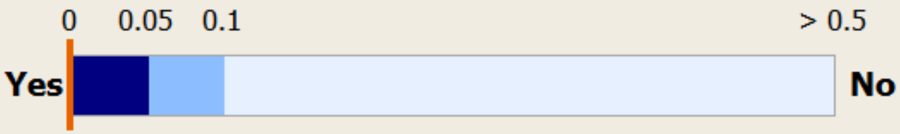
2-Sample t Test for the Mean of Eye-q r dec and EX500 r dec
Summary Report

Do the means differ?



P = 0.000
The mean of Eye-q r dec is significantly different from the mean of EX500 r dec ($p < 0.05$).

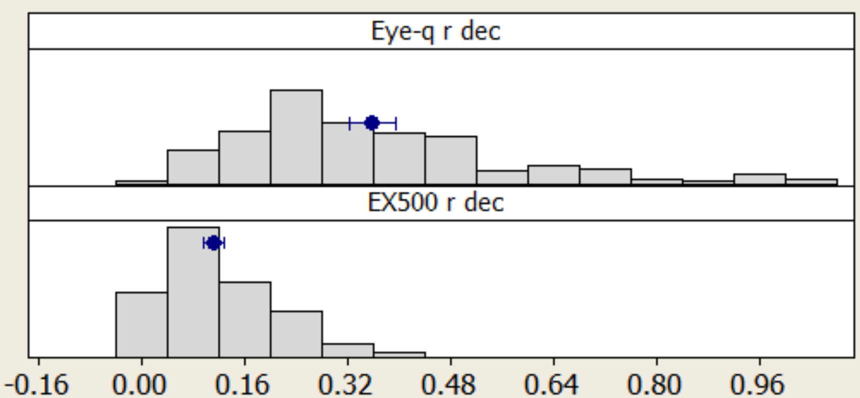
Statistics	Eye-q r dec	EX500 r dec
Sample size	156	124
Mean	0.35911	0.11228
95% CI	(0.3244, 0.3938)	(0.09574, 0.12882)
Standard deviation	0.21947	0.093047

Difference between means*	0.24683
95% CI	(0.20848, 0.28518)

* The difference is defined as Eye-q r dec - EX500 r dec .

95% CI for the Difference
Does the interval include zero?

Distribution of Data
Compare the data and means of the samples.



Comments

-- Test: You can conclude that the means differ at the 0.05 level of significance.
-- CI: Quantifies the uncertainty associated with estimating the difference from sample data. You can be 95% confident that the true difference is between 0.20848 and 0.28518.
-- Distribution of Data: Compare the location and means of samples. Look for unusual data before interpreting the results of the test.

Conclusions

- Today's highly customized ablation tools offer visual rehabilitation in a broad range of corneas: regular to highly irregular.
- Imaging, refraction, epithelial profiles and centration delivery appear pivotal elements
- The Alcon/Wavelight topography guided platform (Placido disc and Scheimpflug) offers effective options to predictably achieve excellent laser refractive surgery outcomes and additionally in more complicated cases: cornea normalization and enhanced visual function