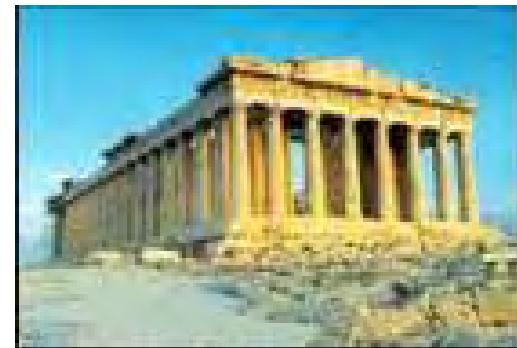


DSEAK course

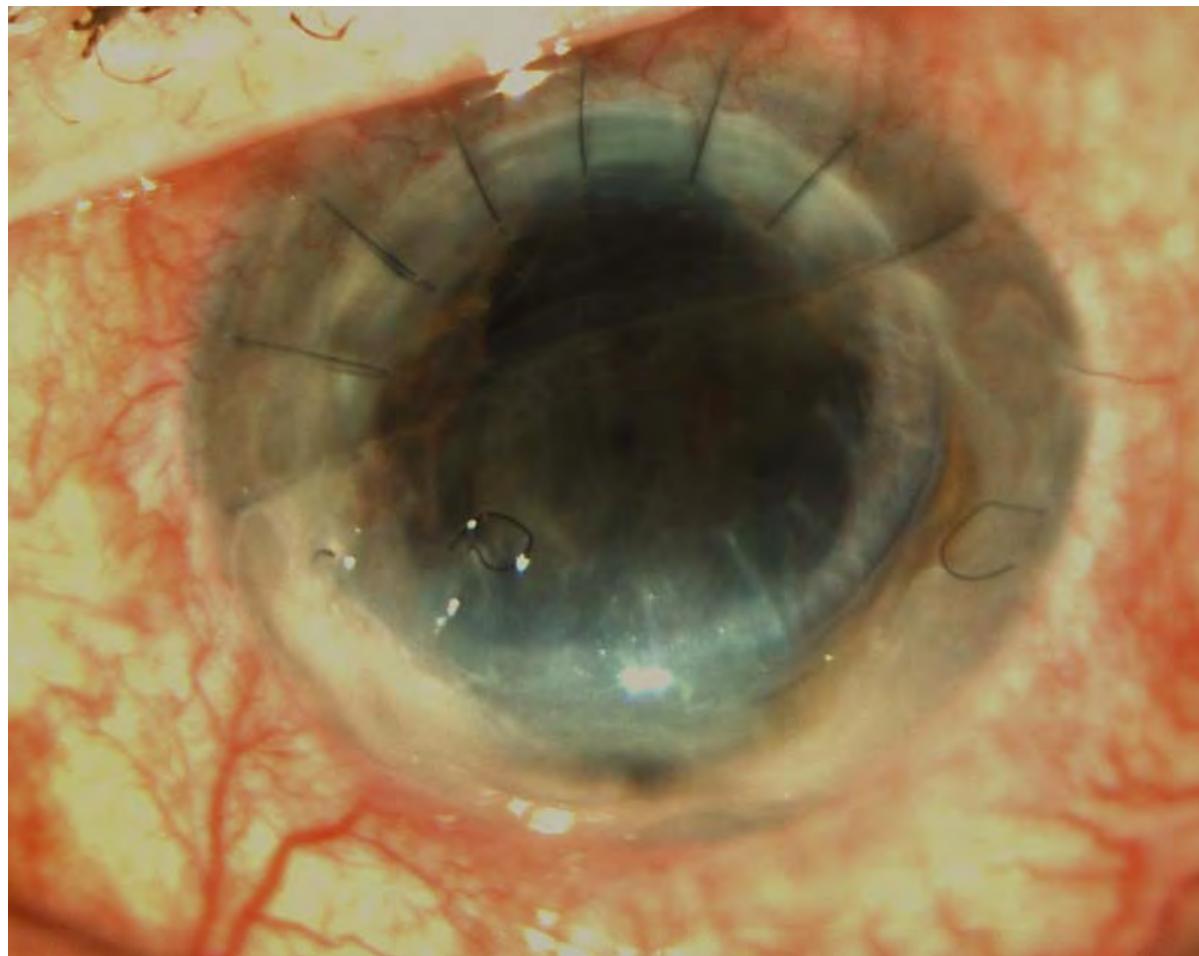


A. John Kanellopoulos, MD
Clinical Associate Professor NYU Medical School, NY
Director, Laservision.gr Institute, Athens, Greece

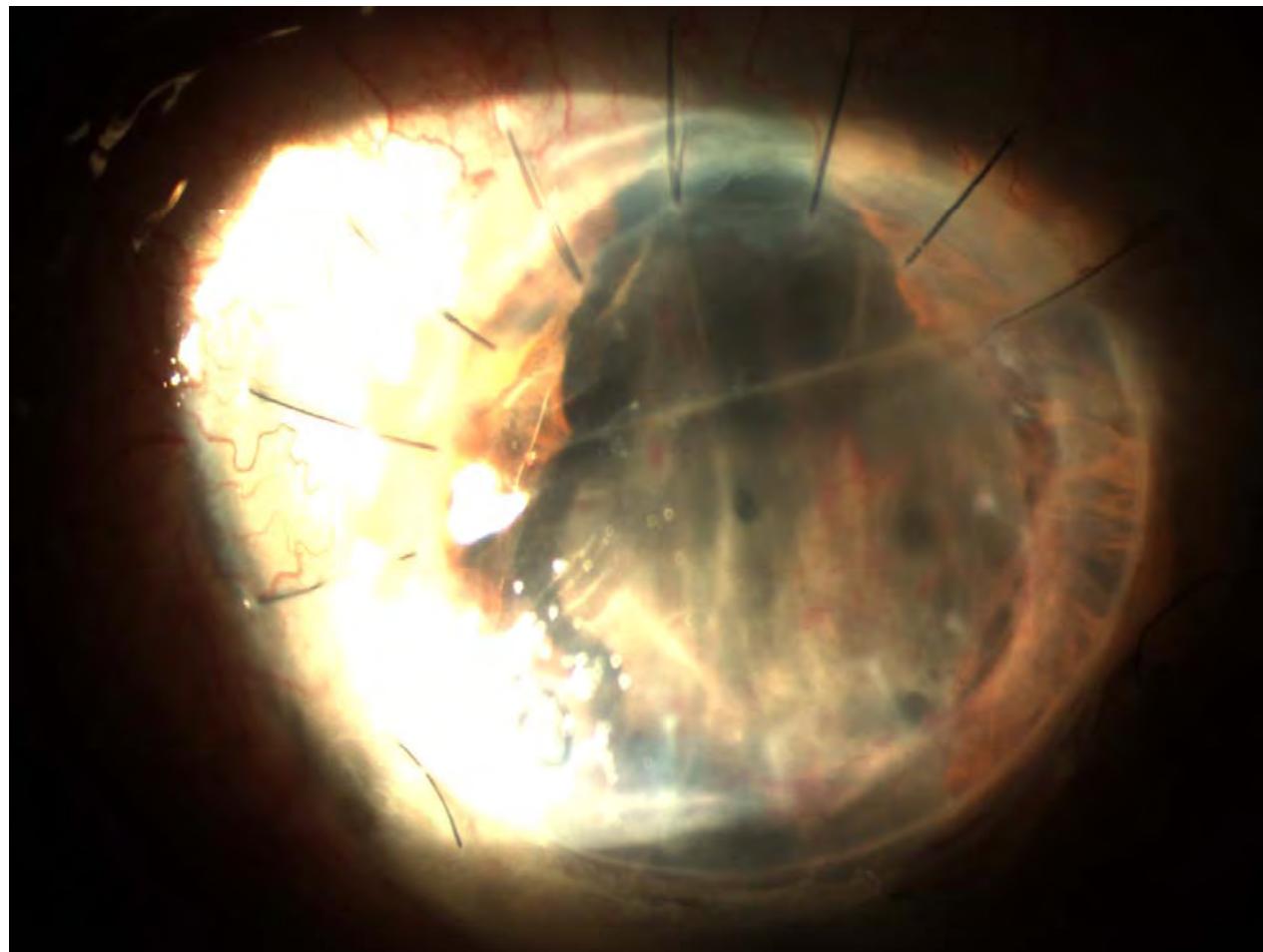
financial disclosures

Wavelight, (Alcon)
B&L
Priavision

Mistake:
I did PK on a psych pt



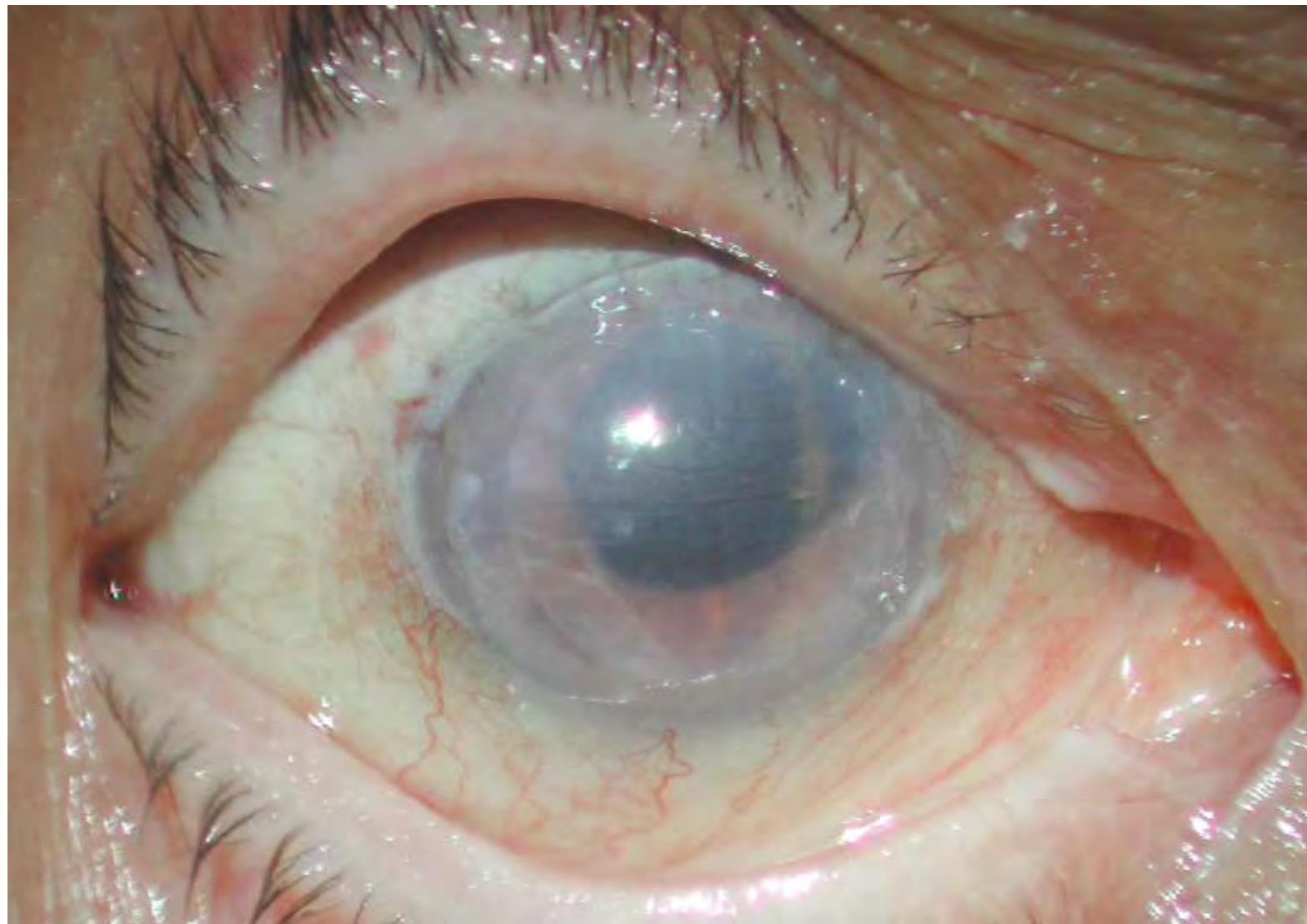
Ruptured 6 hours sutures explanted IOL



Perfect case 20/40 UCVA



3 months later...



Edema Ta 18

Patient: Elli LARKOU
DOB (age): 01/01/1940 (69)
ID:

Disease: DSEAK
Algorithm Version: A3, 5, 2, 5
Gender: F

Photographer:
Exam Date: 02/20/2009
Physician: KONTIS, Lise

OS CL - Line SSI = 46.3 6.00mm Scan Length

250 µm

of Averages:11

Average

No Average

Diagnosis:

Report Date: Friday February 20 01:33:25 2009

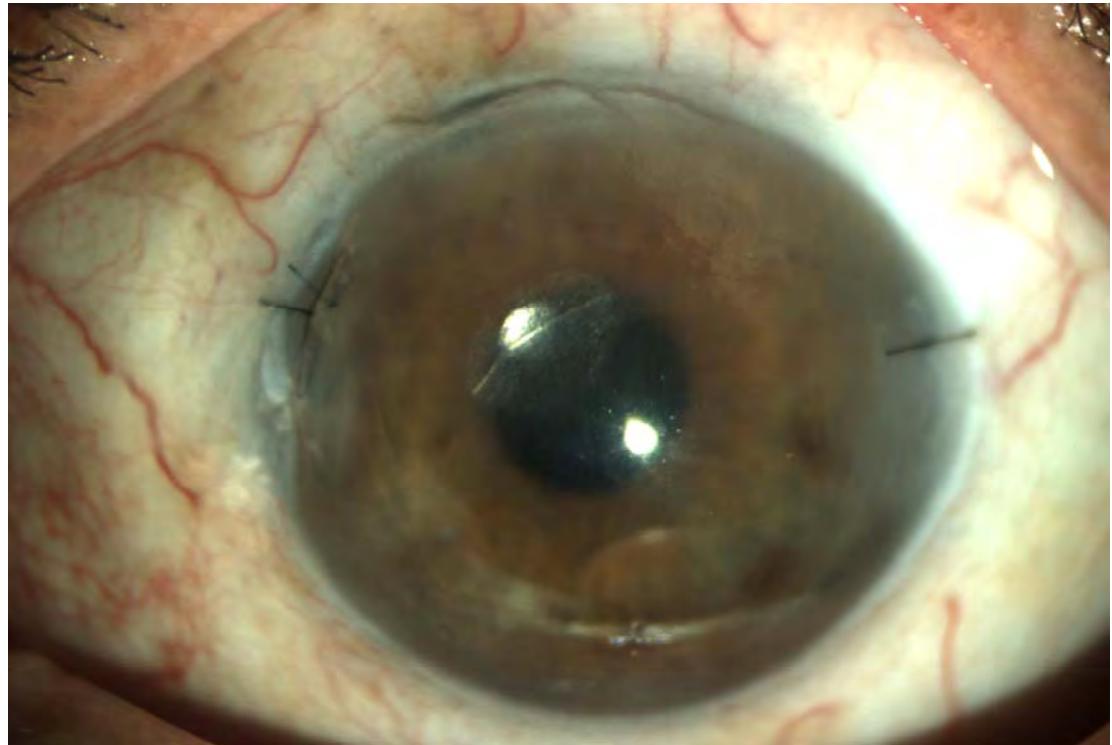
Following pressure control (pneumotonometry was 40)





Dislocated graft in an Aphakic
case pt refused 4th Sx

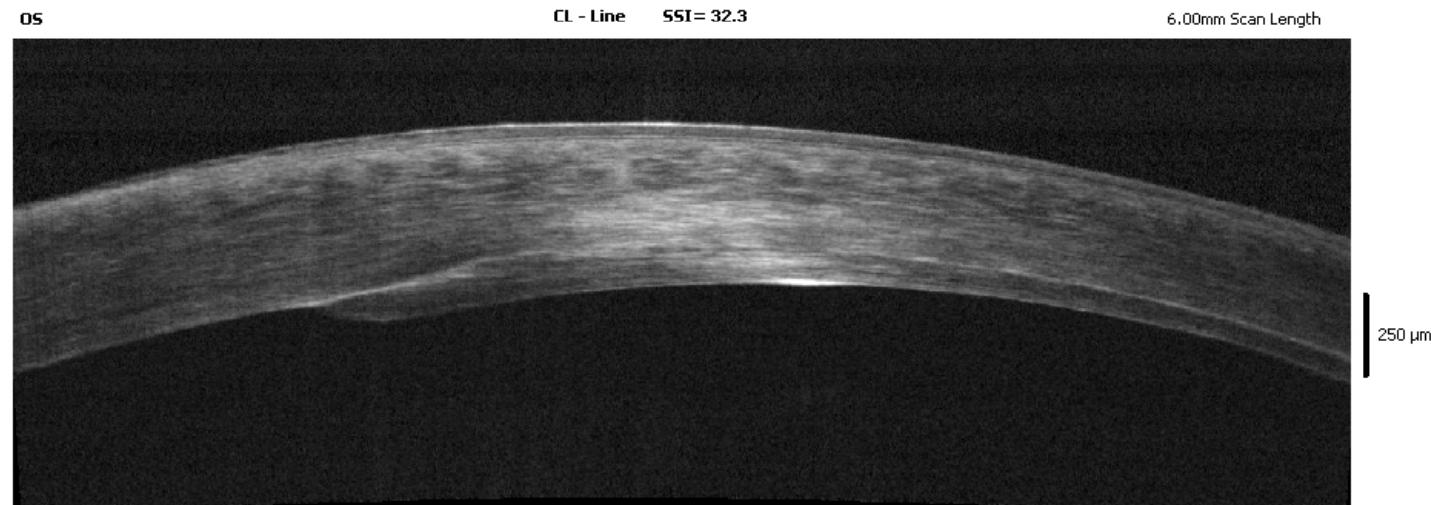
Inferiorly displaced graft Va 20/60



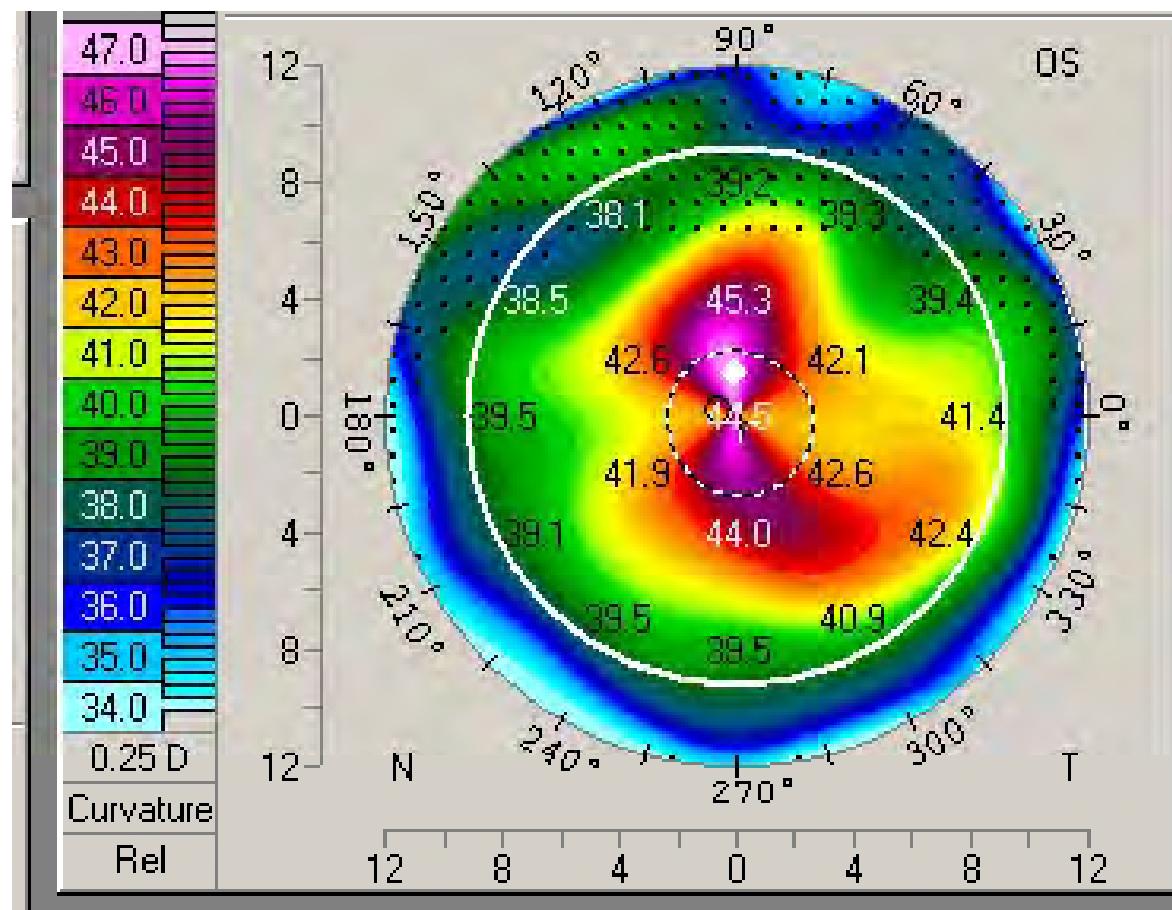
Patient: Eleni ANASTASIADOU
DOB (age): 01/01/1927 (82)
ID:

Disease: SCREENING
Algorithm Version: A4, 0, 0, 143
Gender: F

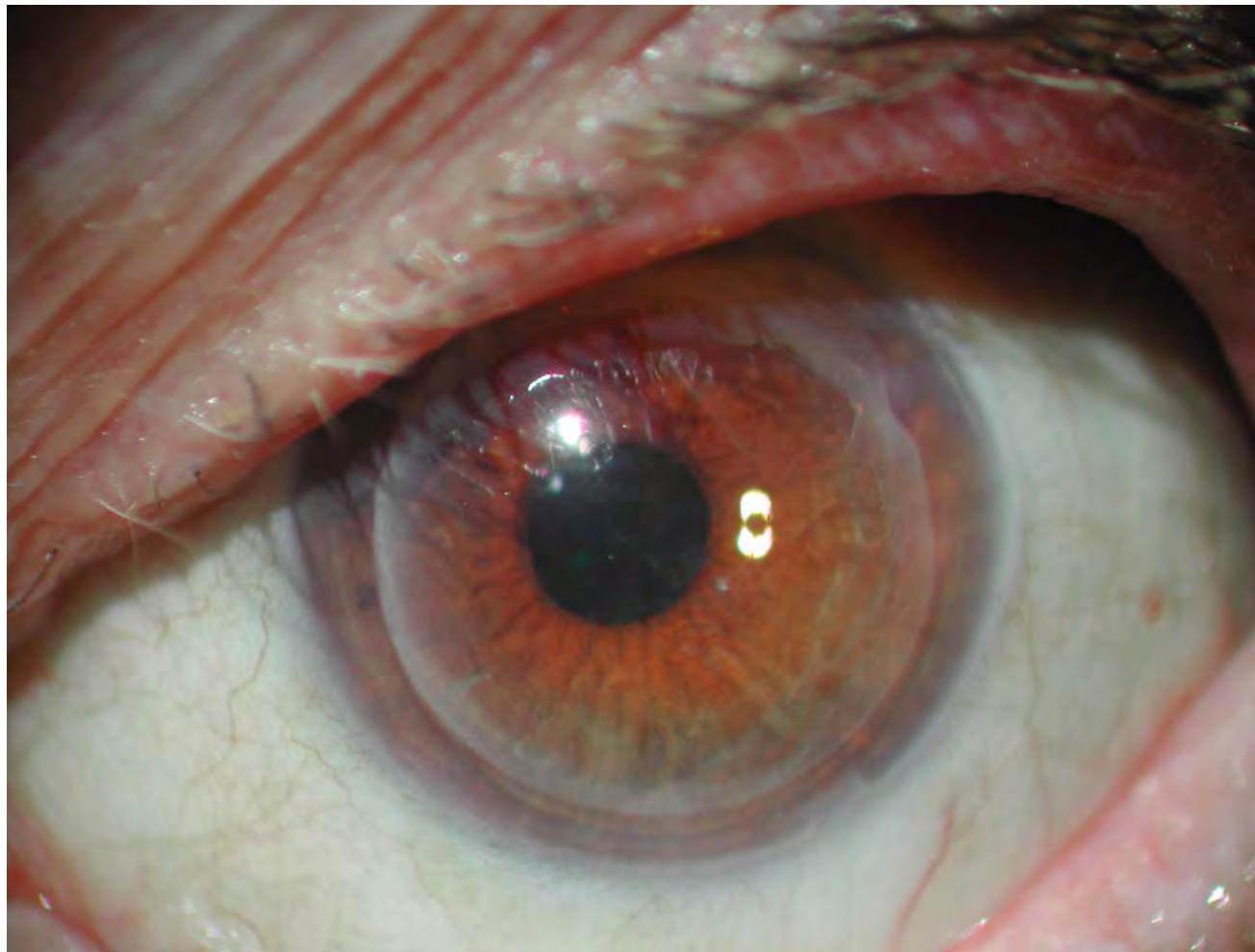
Photographer:
Exam Date: 05/13/2009
Physician: CHIRIDOU, Marianthi



Check pre-op Cylinder



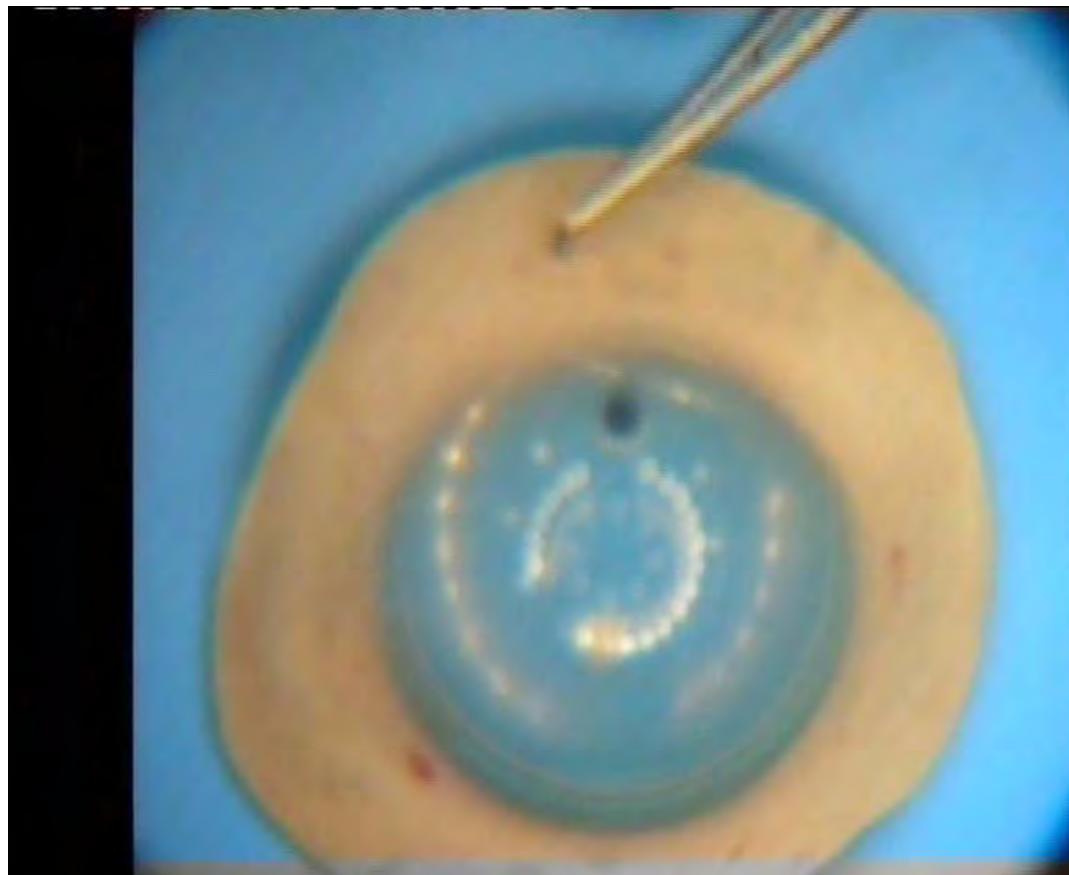
Perfect DSEAK?



BSCVA 20/400!



Femto-assisted graft harvesting



Intralase-assisted Descemet's membrane stripping endothelial keratoplasty(I-DSEK)

AAO meeting 2007, Poster 034



Henry D. Perry, MD¹, A. John Kanellopoulos, M.D. ^{2,3} Gregory Pamel, MD²,

LaserVision.gr
Institute for Laser
Athens, GREECE
www.laservision.gr

1- 3-Ophthalmic Consultants of Long Island, NY.

2-Department of Ophthalmology, New York University / Manhattan Eye, Ear, and Throat Hospital, New York, NY¹

3-Laser Vision.gr Eye Institute, Athens Greece².

INTRODUCTION:

The goal of this small clinical study was to simplify and enhance the donor endothelial preparation of DSEAK (Descemet's membrane stripping endothelial automated keratoplasty) with the use of a mechanical microkeratome) surgery with the use of the keratoplasty options of the Intralase. The femtosecond laser was used to prepare the endothelial donor graft in an artificial donor anterior chamber



OD (left): Penetrating Keratoplasty 4 years 20/25 with -4 -3.5 X 85 S(right): DSEK 6 months 20/40 uncorrected

METHODS

6 cases of I-DSEK were evaluated for UCVA, BCVA, refraction, topographic, pachymetric, endothelial cell count (ECC) with 12 month follow-up

SURGICAL TECHNIQUE:

Using the artificial anterior chamber by (Moria) the donor cornea was fixated. Then a 400 micron depth, 1.5 mm diameter and 0 degree hinge flap was generated with the FS 60, Intralase femtosecond laser. The total flap was removed and a 8.5mm central disc was then trephined from the donor tissue placed on a tanna trephine (Moria) endo-side up. The endothelial graft created was implanted using a standard DSEAK technique under peribulbar anesthesia and with instrumentation by Moria.

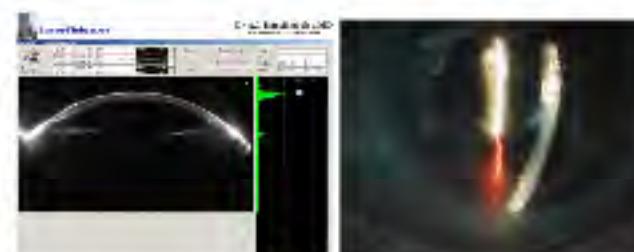
RESULTS:

An 8.5mm graft of 100 micron thickness was placed through a 4.5mm incision. Mean values at day 1, week 1, month 1 and 6 months were respectively:

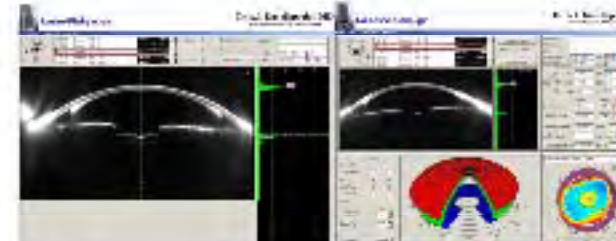
UCVA: 20/100, 20/60, 20/50 and 20/50. BCVA: 30/100, 20/50, 20/40, 20/38. Topographic cylinder: 1.5D, 3D, 0.5D, 0.5D. ECC: unavailable, 2550, 2550, 1500. Pachymetry in microns: 750, 650, 620, 615.



85 y/o ABK pt 6 months postop 20/60 with s=9D -1 X90



67y/o 7months post I-DSEK for PK. UCVA 20/50, BCVA 20/40. The Pentacam image demonstrates the thin centrally and peripherally endothelial graft. The clinical picture on the right shows the same point.



A microkeratome DSEAK case on the Left and an Intralase assisted DSEK case on the Right studied with the pentacam (thicker edges in the left case)

Mean Values

| | UCVA | BCVA | CYL | TOPOG CYL | PACT |
|-----------|--------|--------|------|-----------|------|
| 1st Day | 20/100 | 20/100 | 2.5D | | 750 |
| 1st Week | 20/60 | 20/50 | 1.5D | 2550 | 650 |
| 1st Month | 20/50 | 20/40 | 0.5D | 2550 | 620 |
| 6th Month | 20/50 | 20/38 | 0.5D | 2500 | 615 |

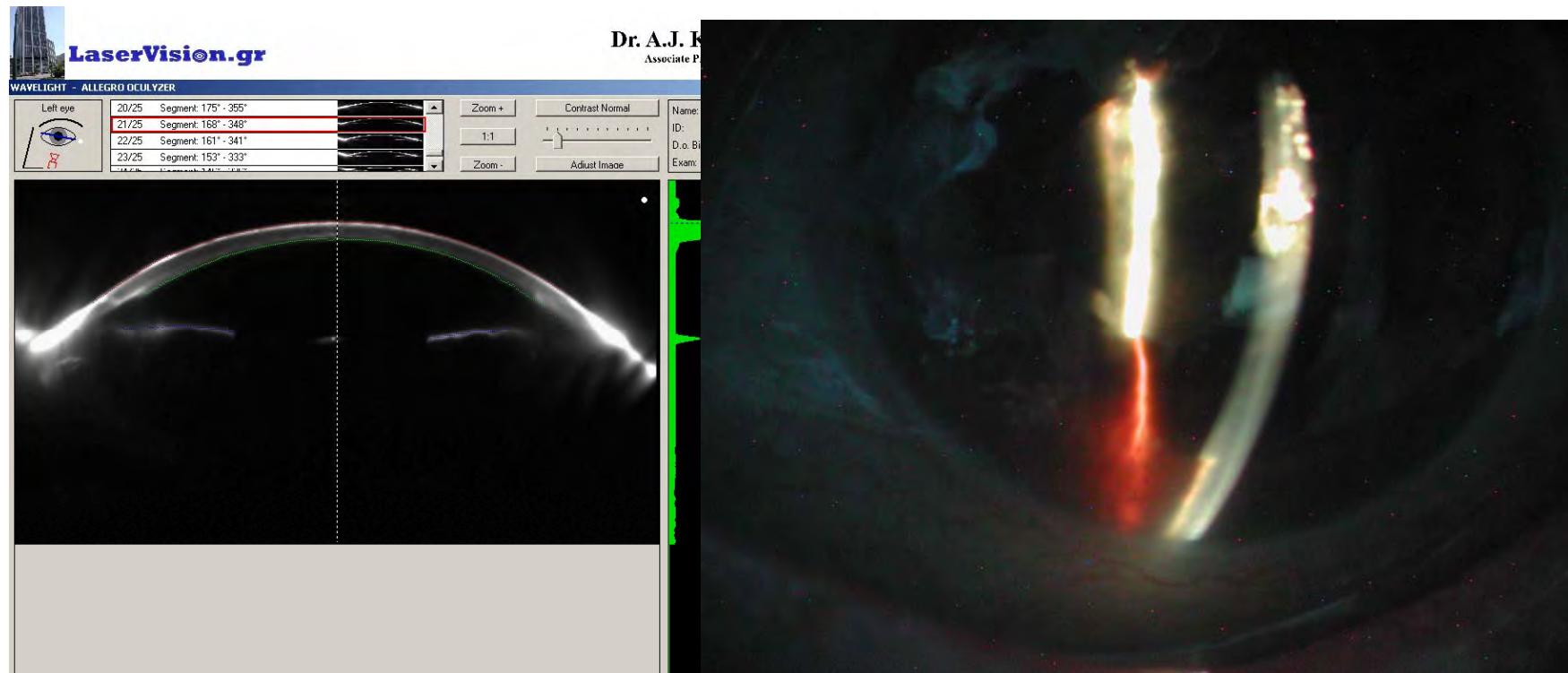
CONCLUSIONS:

I-DSEK appears to be a safe and effective alternative to Penetrating Keratoplasty and DSEAK(assisted by a mechanical microkeratome). The use of the femtosecond laser in order to help prepare the donor endothelial graft offers great precision in thickness parameters allowing for rapid visual rehabilitation. With a thin graft in the periphery, adhesion may be facilitated minimizing peripheral graft dehiscence and possible dislocation. The donor tissue appears to clear and stabilize as early as 1 week.

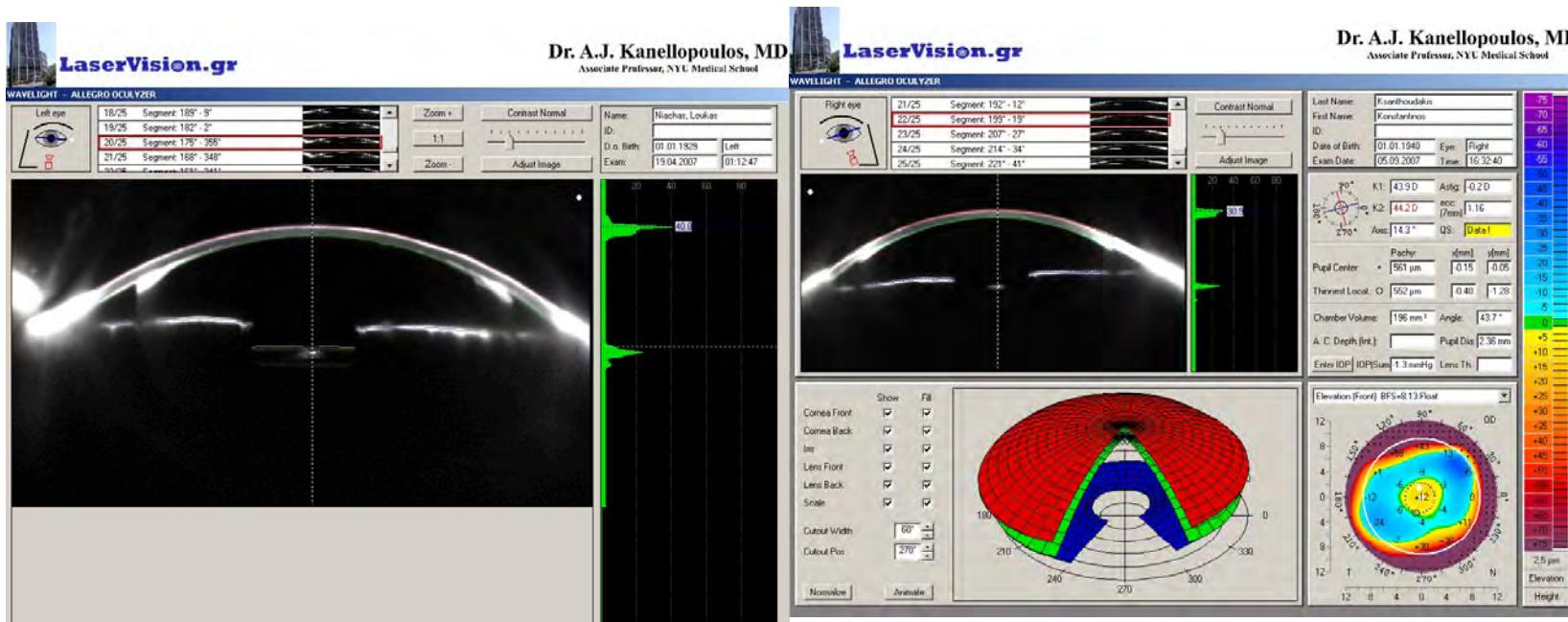
The "deep" flap creation with the Intralase may result in concentric striae in the tissue separation . This can be avoided by a double pass for total flap initially at 200 microns and then an addition 200 microns with the Intralase.

A video presentation of this technique is available in our website:

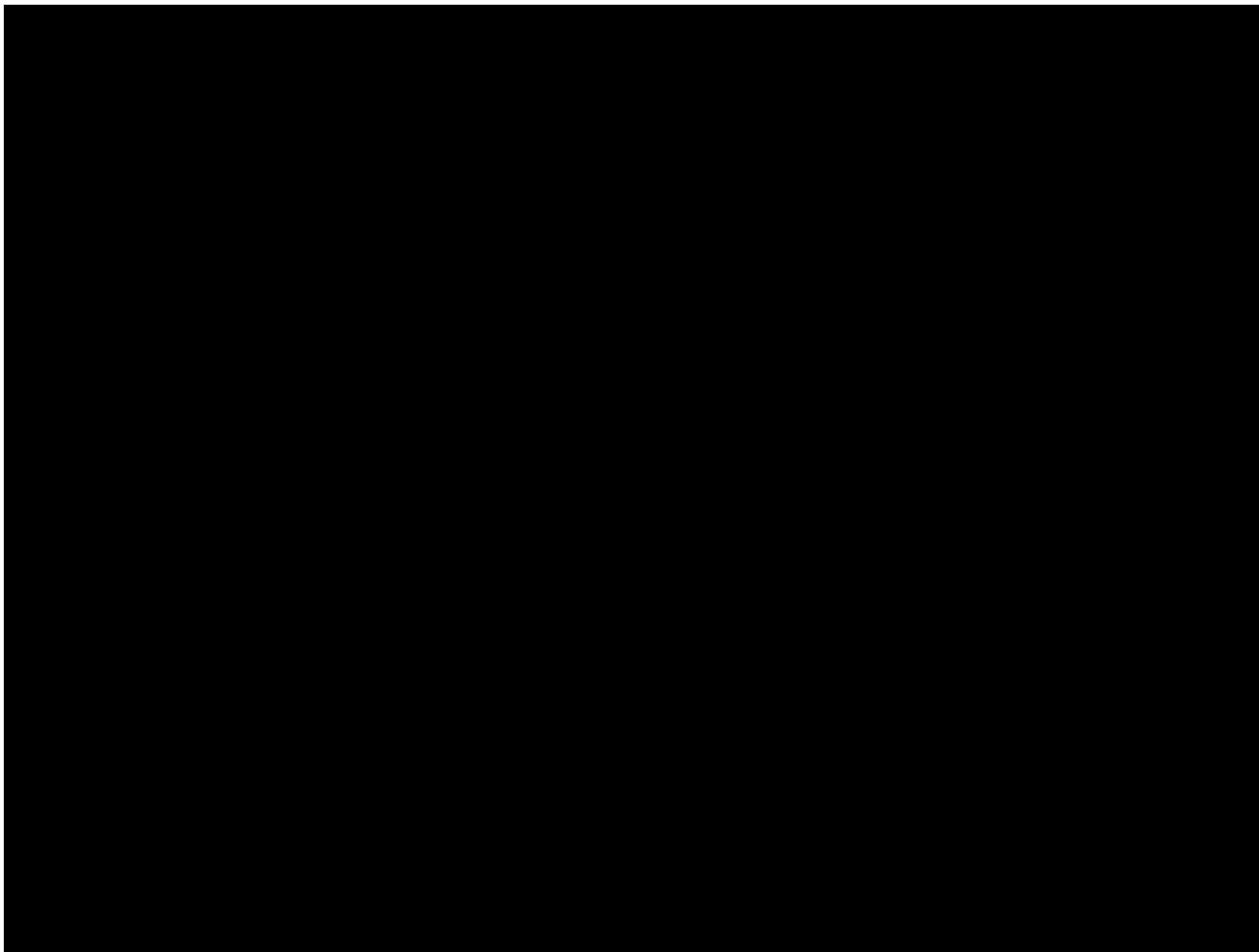
67 y/o 7 months post I-DSEK for PBK UCVA 20/50, BSCA 20/40



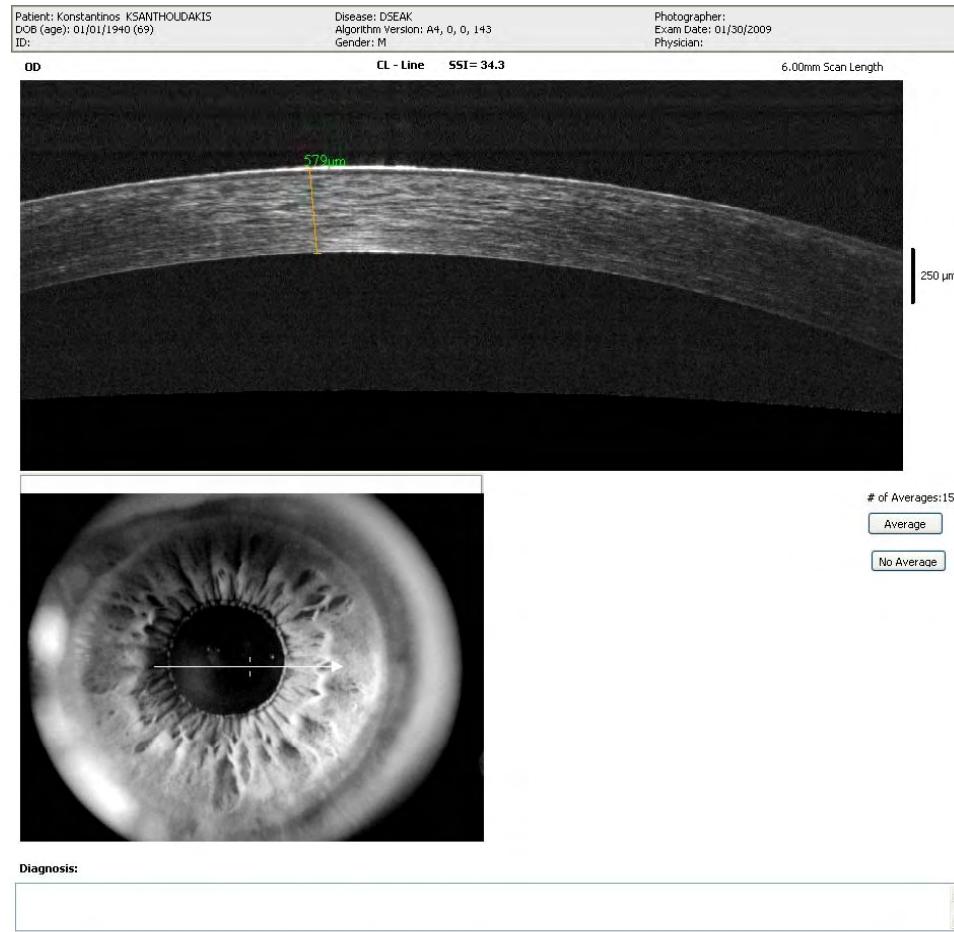
A microkeratome DSEAK case on the Left and an Intralase assisted DSEK case on the Right studied with the pentacam (thicker edges in the left case)



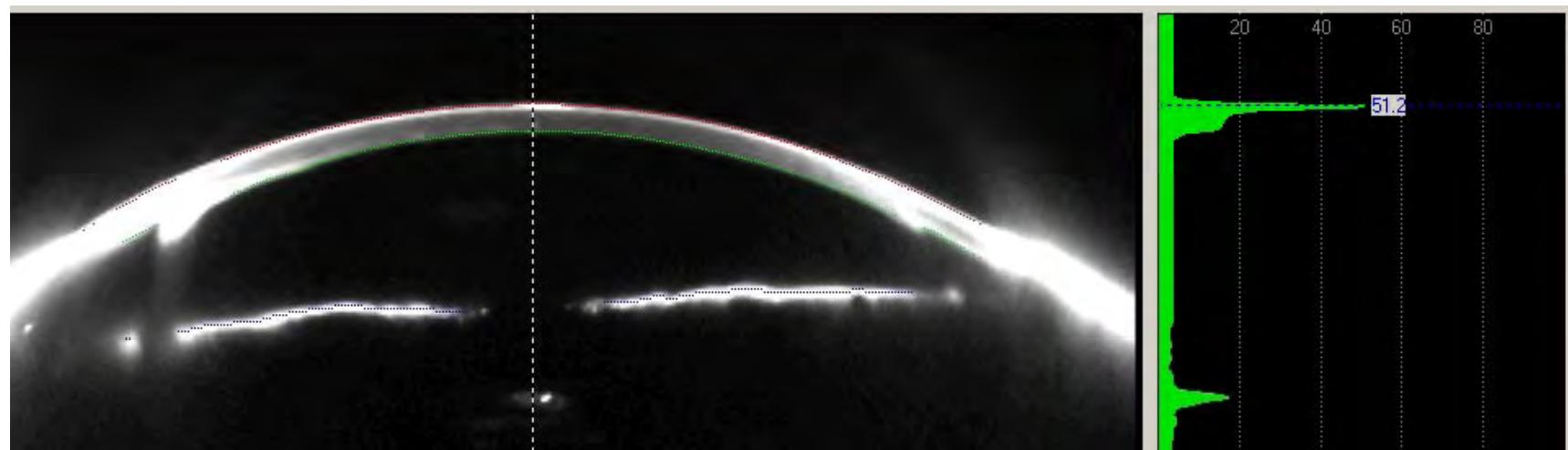
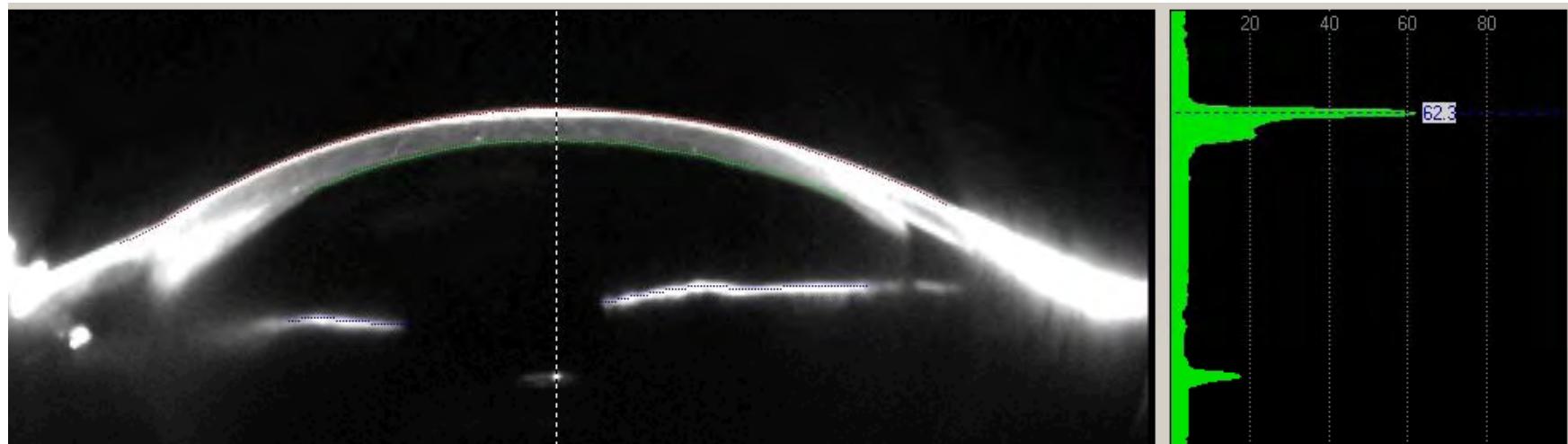
DSEAK with anterior scarring treated with PTK/PRK



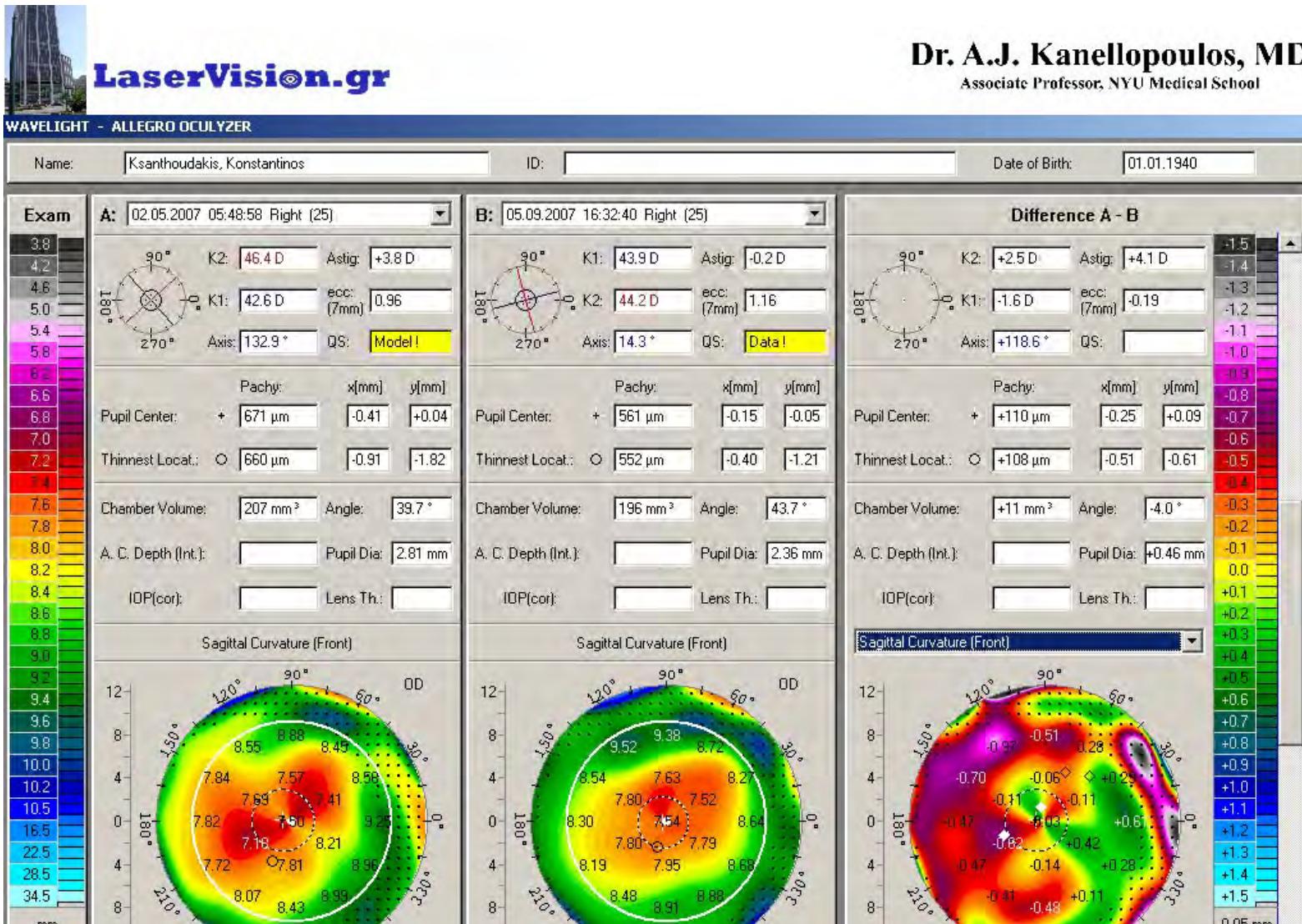
Post PTK/PRK



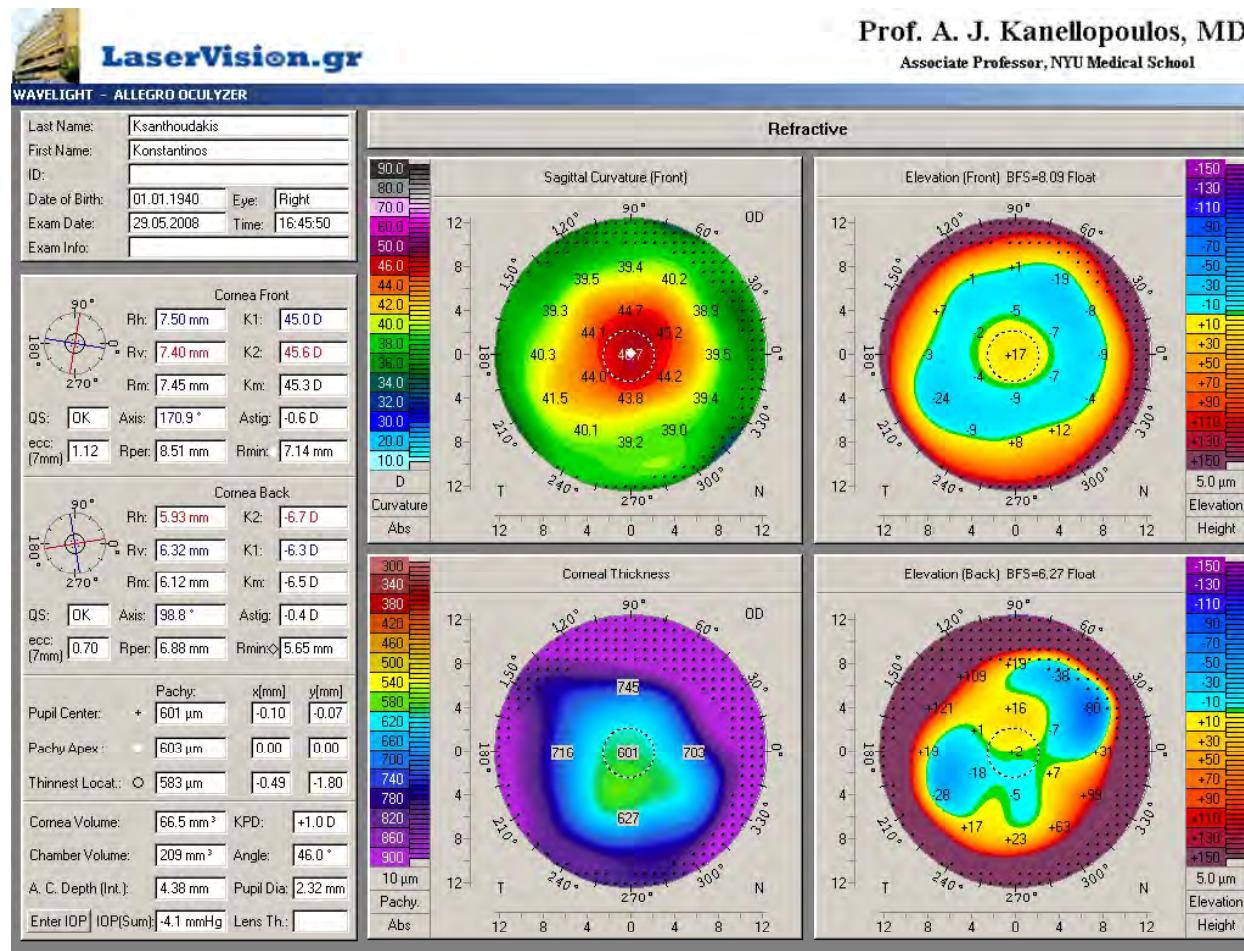
Anterior K clarity before and after



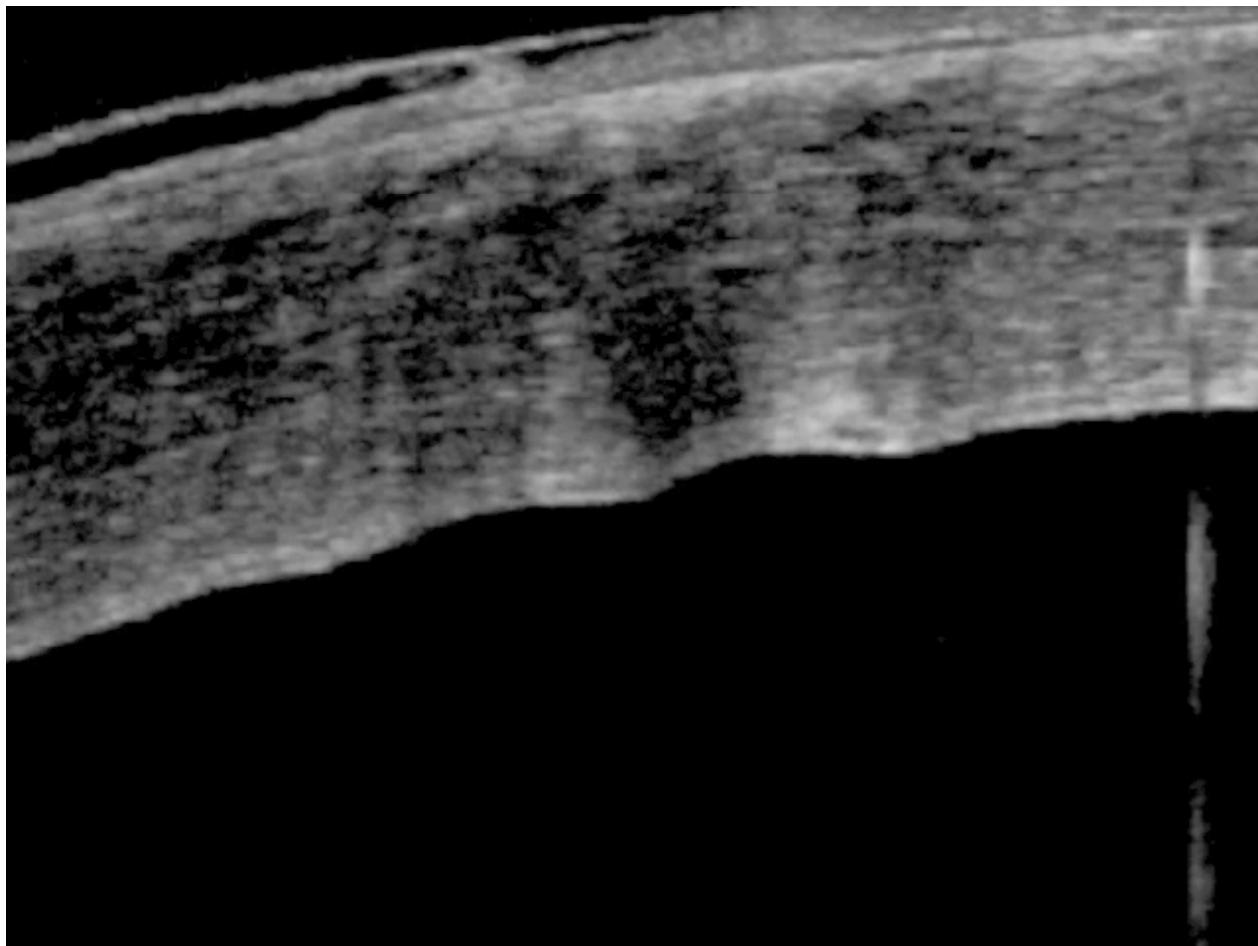
Topo-guided PRK



Post PTK/PRK



Femtosecond laser-assisted CXL for bullous keratopathy



ORIGINAL ARTICLE

Staged, Intrastromal Delivery of Riboflavin With UVA Cross-linking in Advanced Bullous Keratopathy: Laboratory Investigation and First Clinical Case

Ronald R. Krueger, MD, MSE; Jerome C. Ramos-Esteban, MD; A. John Kanellopoulos, MD

ABSTRACT

PURPOSE: To evaluate the safety and efficacy of staged ultraviolet A (UVA) cross-linking following intrastromal 0.1% riboflavin administration in eyes with advanced corneal edema.

METHODS: Ten eye bank corneas divided in two groups ($n=5$) were placed on a pressurized artificial anterior chamber following Descemet's membrane stripping. Two consecutive corneal pockets (350- and 150- μm depth) were sequentially created using a femtosecond laser. Sequential intrastromal injections of 0.1% riboflavin (0.2 mL) followed by either UVA irradiation (15 mW/cm²) for 7 minutes or exposure to air were performed for each pocket. Corneal clarity and central thickness were measured before and after the two UVA cross-linking steps. The same steps were clinically applied in an 84-year-old woman with bullous keratopathy prior to corneal transplantation and followed for 6 months.

RESULTS: The corneal clarity improved in the treated but not the control eyes. The mean central corneal thickness was significantly reduced by 256 μm (ultrasound, $P=.0002$) and 273 μm (Scheimpflug, $P=.0004$) in treated eyes, but only 100 μm (ultrasound, $P=.048$) and 107 μm (Scheimpflug, $P=.075$) in the control eyes. The clinical treatment of corneal edema showed improved clarity and reduced central corneal thickness from 675 to 550 μm (ultrasound) and 696 to 571 μm (Scheimpflug) at 1 month. Best spectacle-corrected visual acuity improved from finger counting to 20/80 at 1 week and beyond, postponing corneal transplantation for >6 months.

CONCLUSIONS: Staged UVA cross-linking (15 mW) with femtosecond laser facilitated intrastromal 0.1% riboflavin administration may be a safe (no corneal scarring) and effective (marked reduction of edema) temporizing alternative method for managing bullous keratopathy. *J Refract Surg* 2008;24:xxx-xxx.

Aphakic/pseudophakic bullous keratopathy is a visually disabling corneal disorder due to endothelial cell dysfunction and decompensation.¹ Without sufficient endothelial pump function, the cornea swells and fluid accumulates in the extracellular spaces between collagen fibers and lamellae. The altered corneal fiber spacing affects corneal transparency and leads to light scatter with a reduction of visual function. The condition worsens as the epithelium becomes edematous with the formation of bullae, leading to profound visual loss and disabling pain.

Although corneal decompensation can be partially relieved with exposure to hypertonic saline and chemical agents, such as dextrose, permanent and complete compaction of fibers with restoration of corneal transparency cannot be achieved in these edematous corneas, except by the surgical replacement of endothelial cells after penetrating or posterior lamellar keratoplasty.^{2,3}

Riboflavin 0.1% ultraviolet A (UVA) collagen cross-linking is a photochemical reactive process that has been clinically used for stabilizing progressive keratoconus⁴⁻⁷ and postoperative LASIK astigmatism^{8,9} over the past 5 years. The technique typically requires the removal of the corneal epithelium and saturation of the corneal stroma with riboflavin, a low molecular weight compound, which easily diffuses through the cornea into the anterior chamber. The riboflavin molecule collects alongside the collagen to be cross-

From Cole Eye Institute, Cleveland Clinic Foundation, Cleveland, Ohio (Krueger, Ramos-Esteban); NYU Medical School, New York, NY (Kanellopoulos); and LumenVite, Inc, Atlanta, Georgia (Kanellopoulos).

This study was supported by a Cleveland Clinic Institutional Grant from Research to Prevent Blindness Inc, New York, NY, and with corneal tissue from the Eye Bank for Sight Restoration, New York, NY.

The authors have no financial interest in the materials presented herein.

Presented in part at the International Congress of Corneal Cross Linking, December 7-9, 2007, Zurich, Switzerland; American Society of Cataract and Refractive Surgeons annual meeting, April 1-4, 2008, Chicago, IL; and World Ophthalmology Congress, June 28-July 1, 2008, Hong Kong.

Correspondence: A. John Kanellopoulos, MD, LumenVite, 2 Marquette Ave, Atlanta, Georgia 31232. Tel: 404 260 7472/777; Fax: 404 260 7472/780; E-mail: jkanel@lumenvite.com

UVA Cross-linking in Advanced Bullous Keratopathy/Krueger et al

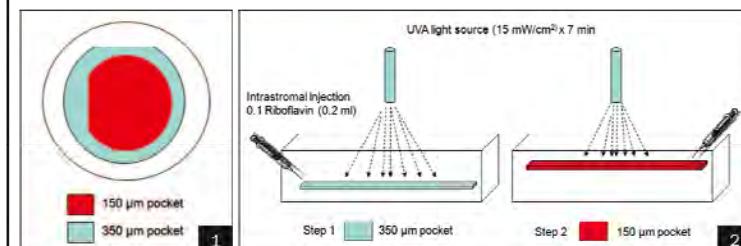


Figure 1. Schematic representation of the pockets created during staged intrastromal injection of 0.1% riboflavin and UVA cross-linking. **Figure 2.** Staged intrastromal injection of 0.1% riboflavin and UVA cross-linking.

linked and is photosensitized by the exposed UVA light in the presence of oxygen to create a reactive singlet oxygen species that induces collagen cross-linking. Although stromal absorption of riboflavin is best achieved with repeated topical application after epithelial cell removal due to evaporative losses and bleaching effects, some investigators choose to keep the epithelium in place and attempt to loosen the epithelial tight junctions to facilitate riboflavin diffusion with prolonged use of topical anesthetics.

One author in our group (A.J.K.) recently conceptualized a new method of riboflavin application in keratoconic eyes through a femtosecond laser-created central stromal pocket. In this technique, a superficial (300 μm) lamellar pocket was generated; together with a 5° to 10° externalizing side cut with the assistance of a femtosecond laser (IntraLase FS80; Advanced Medical Optics [AMO], Irvine, Calif). The pocket allowed for superficial intrastromal administration of riboflavin (0.1% solution without removal of the epithelium, and after cross-linking with 365 nm UVA light [6 mW/cm² for 15 minutes]), produced similar results compared to published studies⁴⁻⁶ as well as our own traditional epithelial removal technique.

Because of our success with this method and greater thickness present in an edematous cornea, we decided to apply this concept in two stages and at two deeper stromal locations to achieve deeper penetration of collagen cross-linking in corneas with experimental bullous keratopathy.

In this study, we propose that riboflavin UVA collagen cross-linking of edematous corneas in the posterior and mid corneal stroma can strengthen interfiber attachments and reduce the potential space for fluid accumulation, which is characteristic in bullous

keratopathy. We believe this may lead to improved stromal compaction and optical function in edematous corneas.

MATERIALS AND METHODS

SURGICAL TECHNIQUE

Ten human cadaver corneas were prepared by stripping Descemet's membrane from their posterior surface and placing them in an artificial anterior chamber constantly pressurized (20 mmHg [27.2 cm H₂O]) (Kanematsu Products Inc, Desville, NJ). Each cornea was then positioned and appressed beneath an IntraLase FS80 femtosecond laser, where two nonconsecutive corneal puncta were created using a raster pattern with a pulse energy of 1.15 μJ and a spot size separation of 8 μm . The first pocket was set at 360- μm depth and 7.5-mm diameter with a superior side cut of 10° (350° hinge angle) and a side cut angle of 70°. The next pocket was set at 150- μm depth and 7-mm diameter, also with a 10° side cut (350° hinge angle), but 90° away from the initial side cut (Fig 1). Following blunt dissection of the first pocket with a Jumissen muscle hook (Remex International, St Petersburg, Fla) at 350 μm , a single dose (0.2 mL) of 0.1% riboflavin phosphate sodium solution was instilled. Within 5 minutes, yellow "scaling" of the middle and posterior stroma was visualized, and the first stage of UVA exposure was begun (Fig 2). Injection of riboflavin 0.1% solution was determined to be the best method to ensure the delivery of an adequate concentration of the medication to the target tissue. High intensity UVA exposure (15 mW/cm²) was selected to quickly achieve intrastromal cross-linking prior to clearance of the single dose of riboflavin from the stroma. Intrastromal injection maintains evaporative losses that can occur on the surface of the cornea. In addition, this

TABLE 1

Mean Corneal Clarity Score and Central Corneal Thickness Measurements With Ultrasound and Scheimpflug Pachymetry Before and After Staged UVA Cross-linking and Sham Treatment

| Group | Clarity Score | | Ultrasound CCT (μm) | | Scheimpflug CCT (μm) | |
|--------------|---------------|---------|---------------------|----------|----------------------|----------|
| | Before | After | Before | After | Before | After |
| UVA | 2.0 | 3.2±0.4 | 844±56.8 | 888±19.4 | 852±57.8 | 879±29.2 |
| Air exposure | 2.0 | 2.2±0.4 | 814±92.4 | 714±28.8 | 822±92.4 | 715±23.5 |

CCT, central corneal thickness.

Note: Statistically differences ($P < .05$) in relation with mean preoperative baseline and after staged intrastromally delivered riboflavin. UVA, collagen cross-linking treatment was represented in parentheses.

delivery method also reduces bleeding, estimates at the deeper pocket (300 μm) is irradiated first and the most superficial pocket (150 μm) is irradiated last.

The 10 corneas were then divided into two groups. In the first group (UVA group), 5 corneas were exposed to 365-nm UVA light at an irradiance of 30mW/cm² for 7 minutes (PikaVision Inc, Minnetonka Park, Calif) to achieve deep collagen cross-linking. In the second group (air exposure group), 5 corneas were exposed to air as a sham control. Following the first session of cross-linking, the second pocket at 150 μm was irradiated with a blunt Jannsen nozzle hook and an additional single dose (0.5 mL) of 0.1% riboflavin solution instilled and allowed to "soak" into the middle and superficial stroma. Corneas in the UVA group then received the second session of UVA exposure at 30mW/cm² for 7 minutes, whereas the corneas in the air exposure group were again exposed to air as a sham control.

Postoperative ultrasound central corneal thickness was 676 μm and Scheimpflug central corneal thickness was 886 μm. After signing an informed consent and receiving topical anesthetic in the left eye, the patient had two lamellar pockets created in a similar manner to the experimental model, and a single dose (0.5 mL) of 0.1% riboflavin was instilled into the deepest (300 μm) pocket first followed by cross-linking using a KeraCare UVA light delivery system (PikaVision Inc) at 18 mW/cm² for 7 minutes. Afterwards, the second cross-linking procedure was performed in the same manner, following instillation of 0.1% riboflavin into the 150-μm pocket. The eye was then postoperatively examined at 1 day, 1 week, 1 month, and 6 months. Corneal clarity scores were determined by slit-lamp examination, and central corneal thickness was prospectively followed using ultrasound and Scheimpflug pachymetry.

Clinical Case

After obtaining appropriate informed consent, an 84-year-old female patient with pseudophakic bullous keratopathy underwent the staged cross-linking procedure in her left eye (Figure, A, B). The risks, benefits, and alternatives to this procedure were explained to the patient. The patient was advised for an elective penetrating keratoplasty in her left eye to relieve symptoms of painful epithelial bullae and decreased visual acuity. The patient decided to undergo this procedure to relieve pain symptoms and prevent intraoperative complications associated with a penetrating keratoplasty such as a suprachoroidal hemorrhage or endophthalmitis. The patient understood that this procedure is still in its experimental stage and that if it failed she would have to undergo the scheduled penetrating keratoplasty.

Preoperative ultrasound central corneal thickness was 676 μm and Scheimpflug central corneal thickness was 886 μm. After signing an informed consent and receiving topical anesthetic in the left eye, the patient had two lamellar pockets created in a similar manner to the experimental model, and a single dose (0.5 mL) of 0.1% riboflavin was instilled into the deepest (300 μm) pocket first followed by cross-linking using a KeraCare UVA light delivery system (PikaVision Inc) at 18 mW/cm² for 7 minutes. Afterwards, the second cross-linking procedure was performed in the same manner, following instillation of 0.1% riboflavin into the 150-μm pocket. The eye was then prospectively examined at 1 day, 1 week, 1 month, and 6 months. Corneal clarity scores were determined by slit-lamp examination, and central corneal thickness was prospectively followed using ultrasound and Scheimpflug pachymetry.

UVA Cross-Linking in Advanced Bullous Keratopathy/Kraeger et al

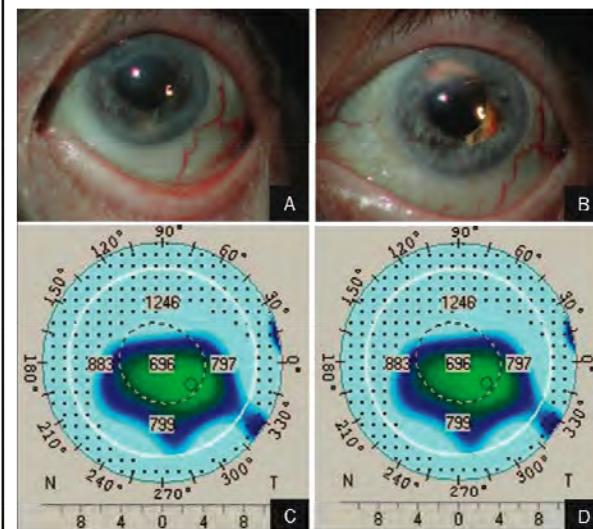


Figure 3. Clinical photographs and Scheimpflug corneal thickness maps of an 84-year-old woman with pseudophakic bullous keratopathy **A, C**) before and **B, D**) 1 month after staged intrastromally delivered riboflavin-UVA collagen cross-linking.

RESULTS

Corneal Clarity

The mean corneal clarity score and mean central corneal thickness for the UVA and air exposure groups are recorded before and after staged intrastromal cross-linking in Table 1. Before pocket creation, mean clarity score for both experimental groups was 2.0, and mean ultrasound and Scheimpflug central corneal thicknesses were 844±56.8 μm and 852±57.8 μm for the UVA group and 814±92.4 μm and 822±84.9 μm for the air exposure group, respectively. After UVA versus sham (air) exposure, mean clarity score was 3.2±0.4 for the UVA group and 2.2±0.4 for the air exposure group, whereas mean ultrasound and Scheimpflug central corneal thicknesses were 888±19.4 μm and 879±29.2 μm for the UVA group and 714±28.8 μm and 715±23.5 μm for the air exposure group, respectively.

MEAN CORNEAL CLARITY SCORE

A statistically significant increase in mean clarity score of 1.2 ($P < .001$) occurred after UVA riboflavin cross-linking in the UVA group, whereas a modest but not statistically significant increase of 0.2 in mean clarity score was also observed in the air exposure

group after sham treatment, which was mainly due to a change in clarity in one of the corneas.

MEAN ULTRASOUND CENTRAL CORNEAL THICKNESS

A statistically significant decrease in mean ultrasound central corneal thickness of 28 μm ($P = .0002$) occurred after UVA riboflavin cross-linking in the UVA group, and in the air exposure group, ultrasound central corneal thickness was also statistically reduced by 100 μm ($P = .048$) after sham treatment.

MEAN SCHAIMPFLUG CENTRAL CORNEAL THICKNESS

A statistically significant decrease in the mean Scheimpflug central corneal thickness of 273 μm ($P = .0004$) occurred after UVA riboflavin cross-linking in the UVA group, whereas in the air exposure group, Scheimpflug central corneal thickness was reduced by 107 μm after sham treatment, which was not statistically significant ($P = .075$).

CLINICAL CASE

Prior to staged intrastromal cross-linking, the patient's left cornea was thickened and swollen with mild epithelial edema, resulting in persistent pain and diminished visual acuity of finger counting. Baseline corneal clarity score was recorded as 2, and ultrasound

Patient: Evangelos OIKONOMOU
DOB (age): 01/01/1931 (77)
ID:

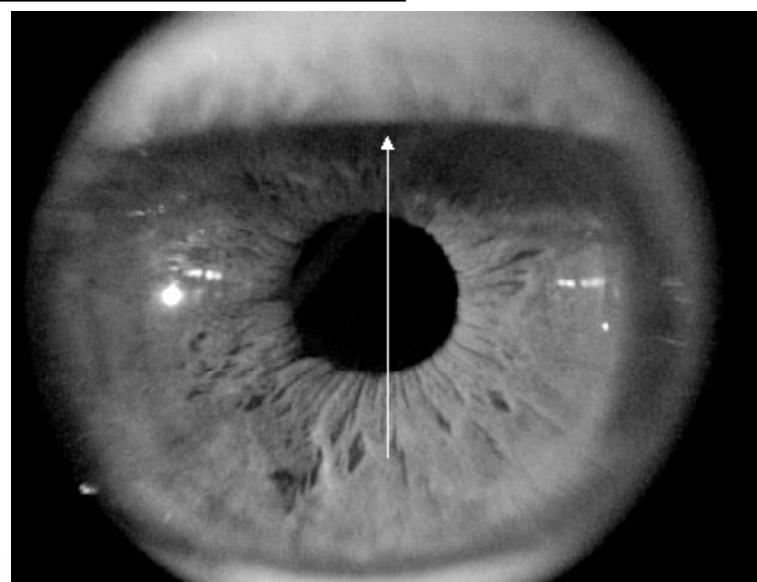
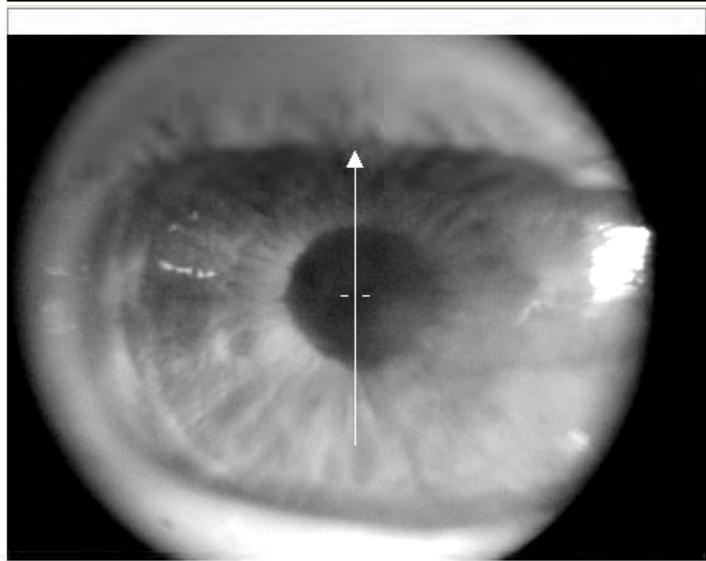
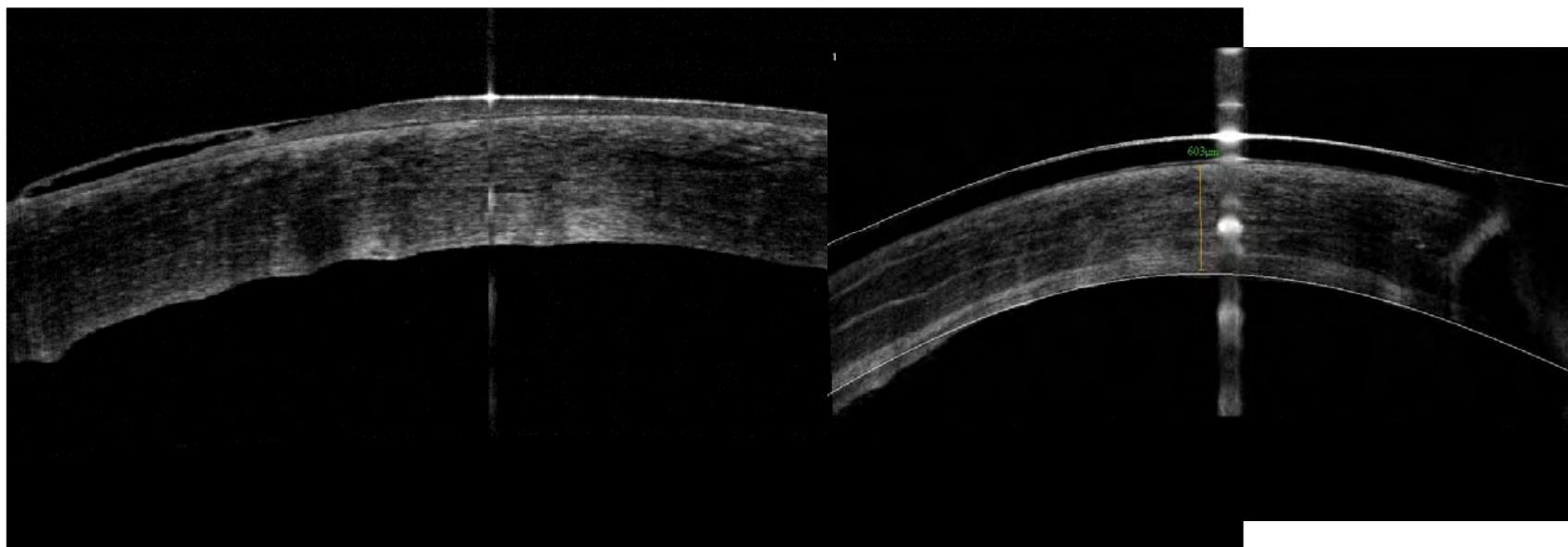
Disease:
Algorithm Version: A3, 5, 2, 5
Gender: M

Photographer:
Exam Date: 12/03/2008
Physician:

OS

CL - Line SSI = 29.9

6.00mm Scan Length



Diagnosis:

Kanellopoulos MD www.brilliantvision.com

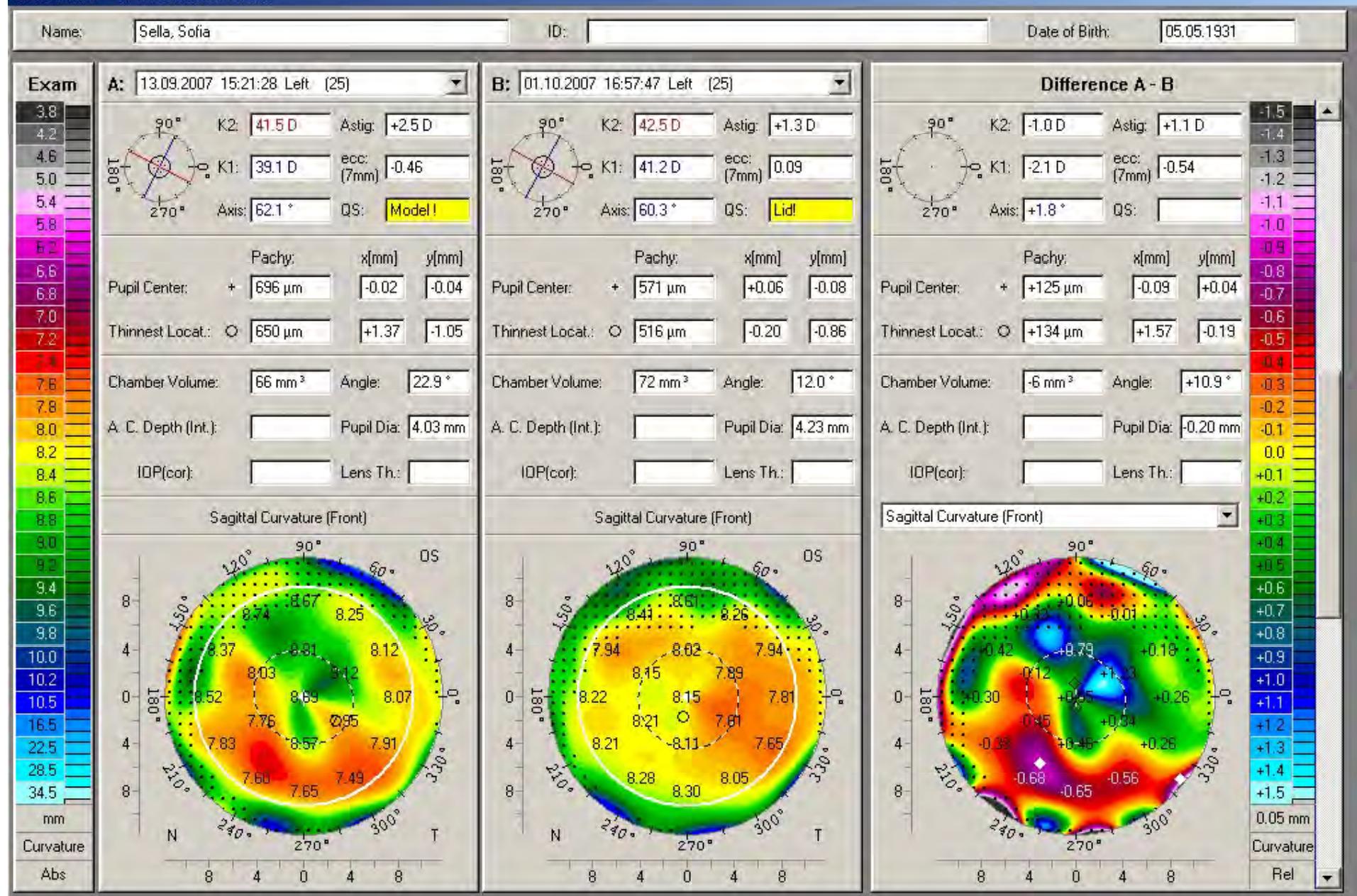
Report Date: Thursday December 04 09:20:08 2008



LaserVision.gr

Dr. A.J. Kanellopoulos, MD
Associate Professor, NYU Medical School

WAVELIGHT - ALLEGRO OCULYZER



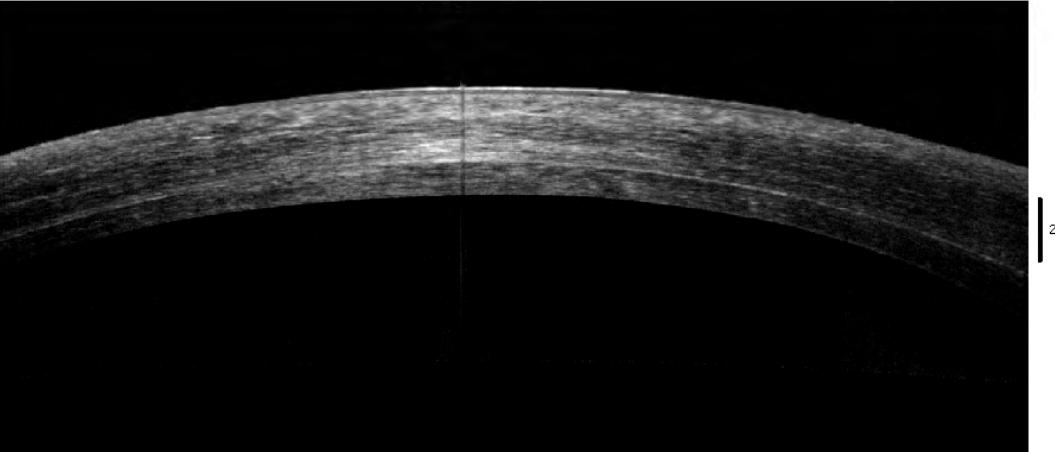
DSEAK in a CXL'ed cornea

Patient: Elisavet PARASKEVA
DOB (age): 10/27/1932 (76)
ID:

Disease:
Algorithm Version: A3, 5, 2, 5
Gender: F

Photographer:
Exam Date: 12/06/2008
Physician:

OD CL - Line SSI = 44.6 6.00mm Scan Length

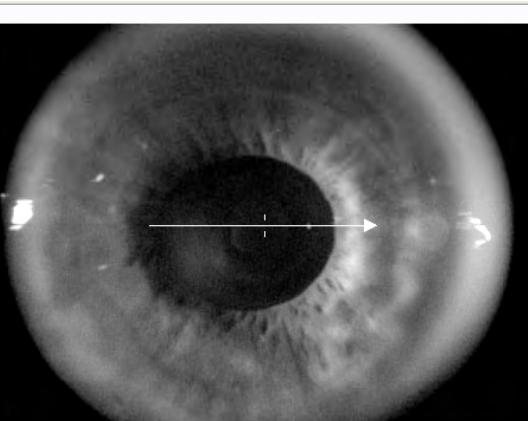


250 µm

of Averages: 16

Average

No Average



Diagnosis:

Report Date: Monday December 08 04:31:48 2008

A photograph of a sunset over a coastal landscape. In the foreground, a small white boat with a red motor is docked at a dark, rocky shore. The water is calm with some ripples. In the background, there are more rocks and a distant shoreline under a sky transitioning from orange to dark blue.

Thank you