

Keratoconus new stuff!



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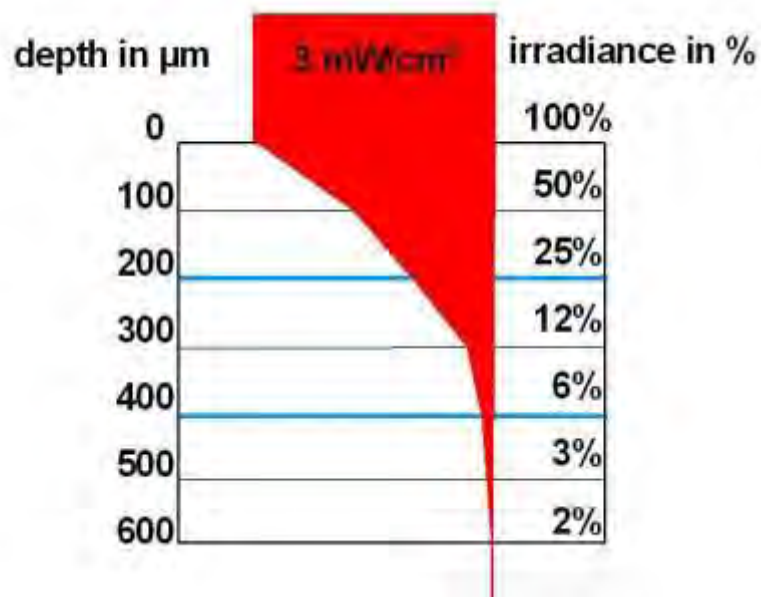
Financial Disclosures:

- Alcon/Wavelight (MAB)
- Bausch & Lomb (Crystalens)
- Ocular Therapeutix
- Seros Medical(MAB)
- Avedro (MAB)



Decrease of UV-intensity

courtesy E. Spoel MD



3.00 mW/cm^2

1.49 mW/cm^2

0.74 mW/cm^2

0.36 mW/cm^2

0.18 mW/cm^2

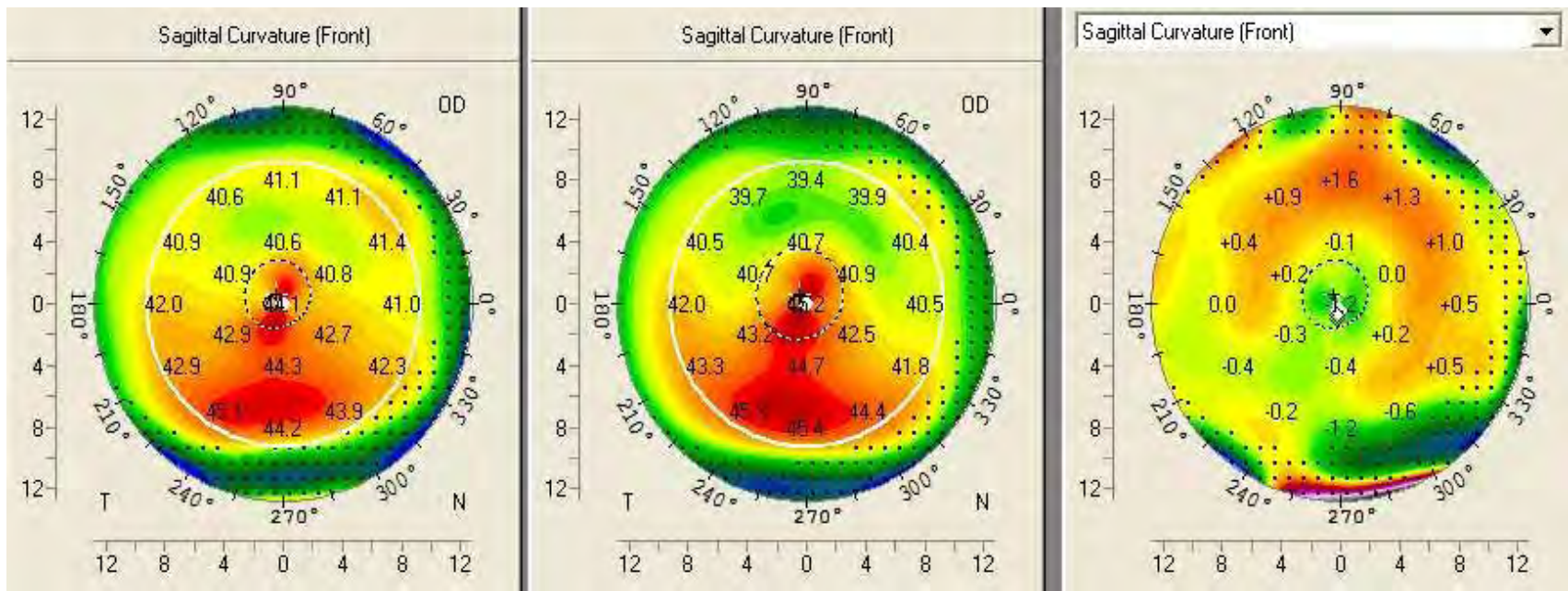
0.09 mW/cm^2



Dresden protocol 3mw/cm²

Post-LASIK ectasia: -1 -1.75@ 75. Pach 445, Treated with epi-on CXL (C3R in California (!) in 2006) 3mW/cm² for 30'.



Same case seen 3 years later with ectasia progression



We introduced: Higher fluence CXL: 6 mW/cm²

AAO 2008:
CXL for 15
minutes
utilizing
7mW/cm²
fluence




Shorter duration, higher ultraviolet A irradiation (UVA) fluence collagen cross-linking (CCL) for keratoconus (KCN)

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Background:
We have presented our experience over the last 6 years in using this entity in its standard form in past AAO meetings. With goal to shorten the duration and potentially increase efficacy we opted to study a model of CCL of higher UVA light intensity (from 3mW to 7 mW/cm²) and the same adjunct 0.1% topical riboflavin sodium phosphate solution.

Objective: To evaluate the safety and efficacy of higher UVA fluence and shorter duration for collagen cross-linking in KCN.

Design: Prospective, randomised comparative case series.

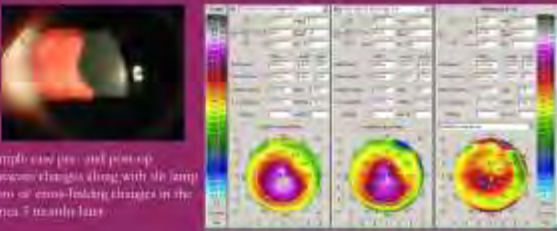
Methods: 15 patients with bilateral keratoconus were studied. All cases were evaluated for UCVA, BSCVA, refraction, keratometry changes (K), topography changes, endothelium cell changes and cornea clarity. All eyes received CCL with topical 0.1% riboflavin solution drops and in regard to UVA they were randomized for each patient; 15 eyes were CCL with 7mW/cm² for 15 minutes and the 15 contra lateral eyes with 3mW/cm² for 30 minutes. Mean follow up was 1.5 years.

| | UCVA | BSCVA | Sph. DQ change | Cylinder (D)pre | KCC change | Topo change | Comp. contacts |
|-----|------|-------|----------------|-----------------|------------|-------------|----------------|
| 7mW | 0.2 | 0.3 | 1.5D | 2.2D | 100 | 2.3 | 0 |
| 3mW | 0.2 | 0.3 | 1.4D | 2D | 200 | 2.1 | 0 |

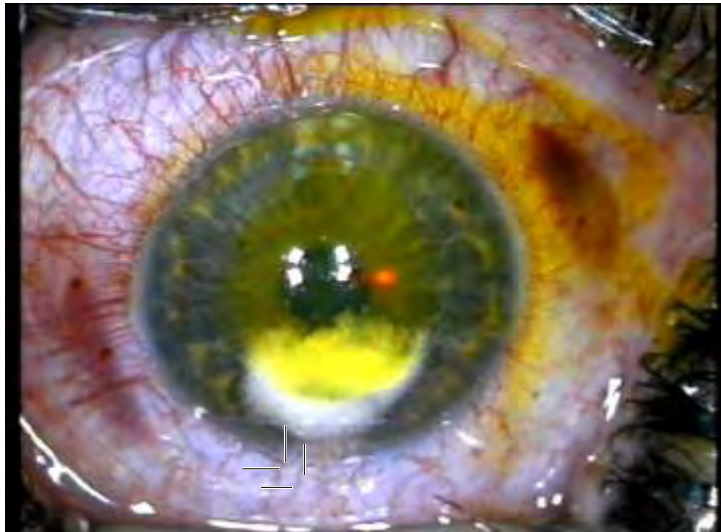
Results:
The mean improvement of UCVA was 0.2 to 0.4, BSCVA improved from 0.4 to 0.7, The average change of spherical equivalent was 1.5D reduction in myopia, the average change in cylinder was 2.1D reduction, The average highest keratometry was 51.2D pre-op and changed to 48.5D post-op. **There was no statistical difference in the means in the 2 groups.**

Conclusions:
Shorter duration, higher UVA fluence CCL appears to be as safe and as effective in stabilization of ectasia in KCN. It may cause less cell toxicity due to lesser cornea dehydration (less time) and shorter exposure of keratocytes and endothelial cells to UV light along with riboflavin. Further studies are needed to validate this data.

Example case pre- and post-op:
Binocular changes along with the lamp photo of cross-linking changes in the cornea 7 months later.




Introduction of riboflavin in a femto-pocket CXL with 10mW/cm² for 10 minutes



NEW TECHNIQUE

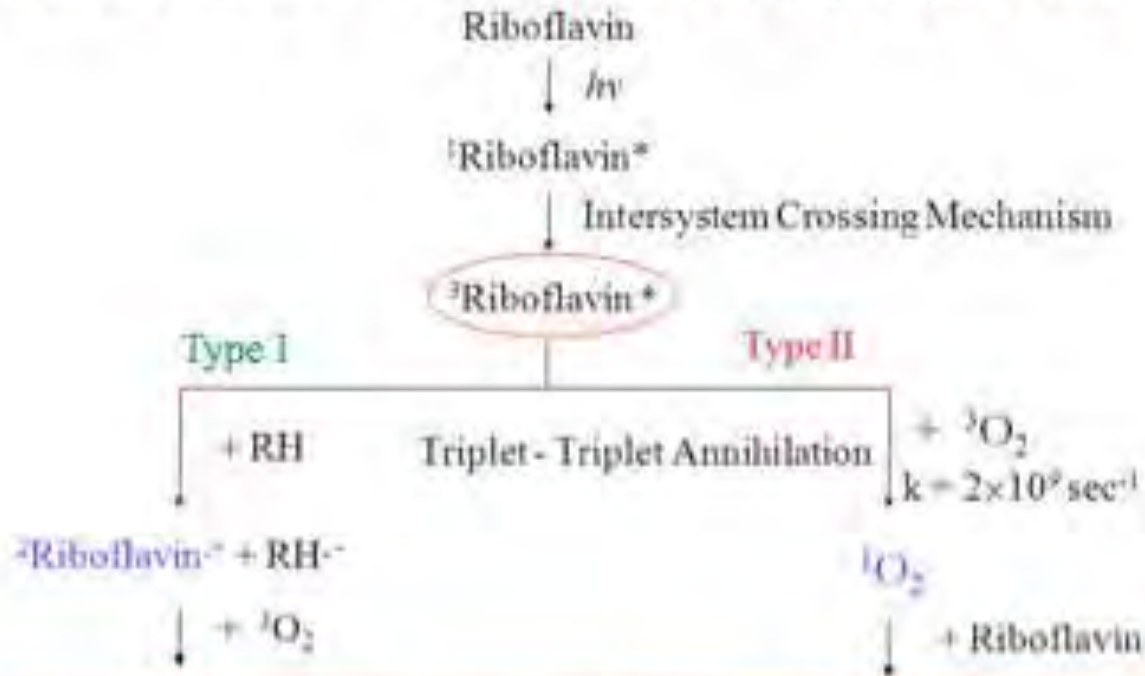


Collagen Cross-linking in Early Keratoconus With Riboflavin in a Femtosecond Laser-created Pocket: Initial Clinical Results

Anastasios John Kanellopoulos, MD

Theoretical Model for Cross-linking

2 General Paths For Riboflavin And Oxygen Reactions



90% Crosslinking 10%

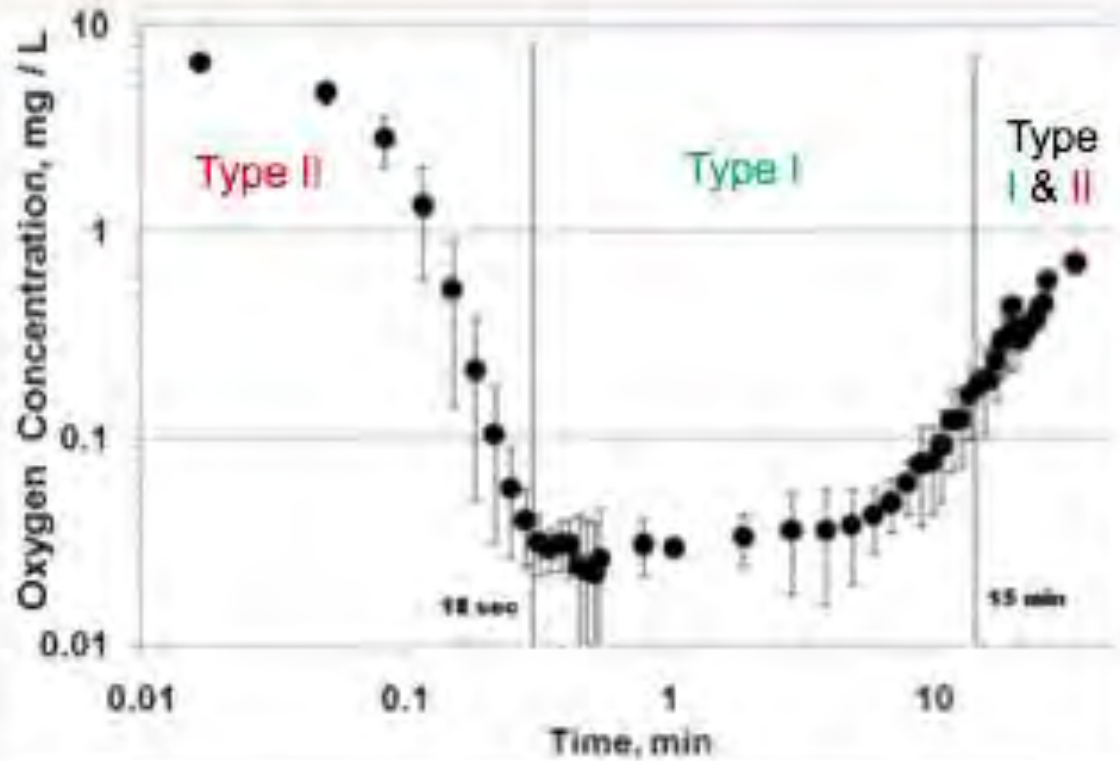
avedra

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Oxygen Depletion Over 30 Minutes

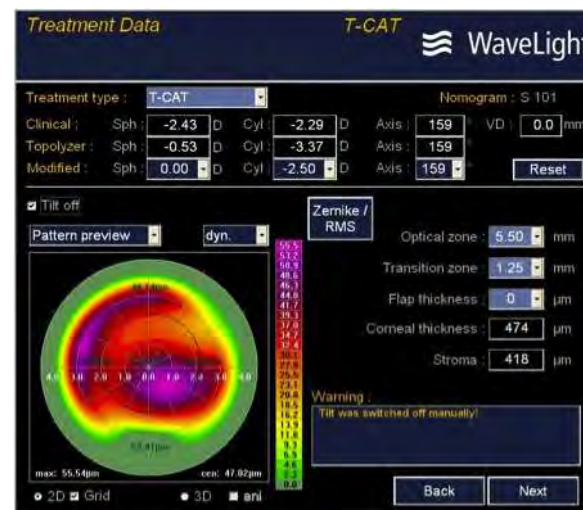
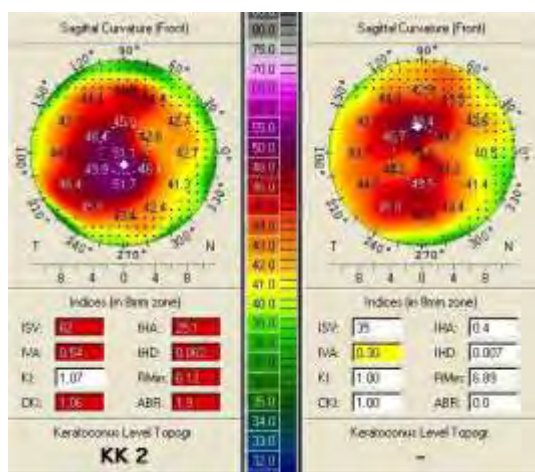


Depletion and gradual replenishment of dissolved oxygen below a 100 μm thick corneal flap, saturated with 0.1% RF during 3 mW/cm^2 UVA irradiation at 25 $^{\circ}\text{C}$.

avedra



The Athens Protocol: Simultaneous surface ablation and CXL for correction of Refractive error in eyes with early keratoconus



ISRS/AAO keynote



The Athens Protocol: topo-guided PRK+6mW/cm² CXL x15'

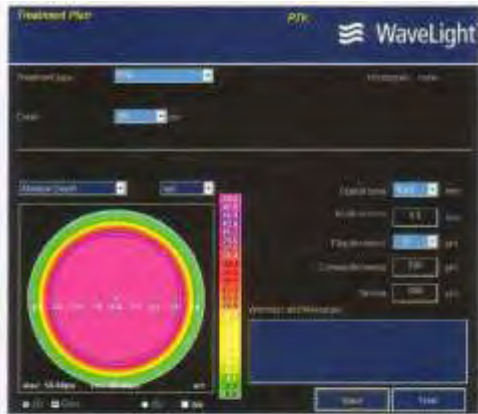


Figure 4.1: Epithelium removed with 50 micron PTK

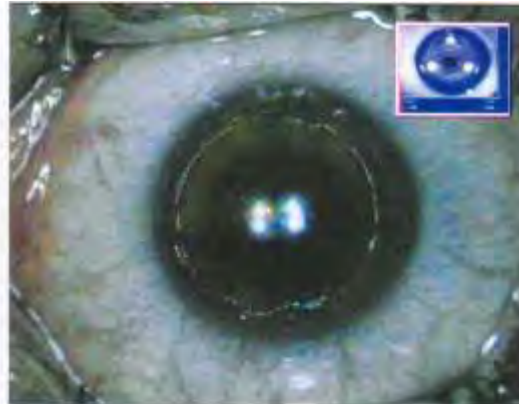


Figure 4.3: Topography-guided PRK to correct part of the refractive error (TCAT treatment plan) maximal thickness removal 50 microns

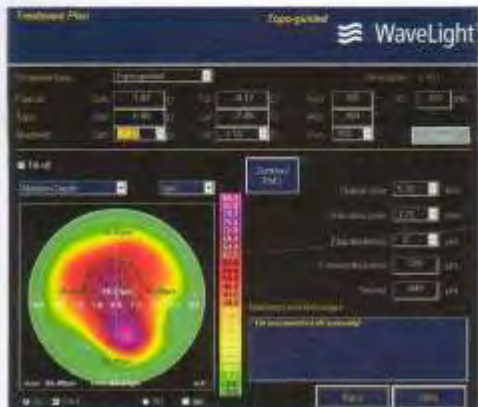


Figure 4.2: TC at treatment plan

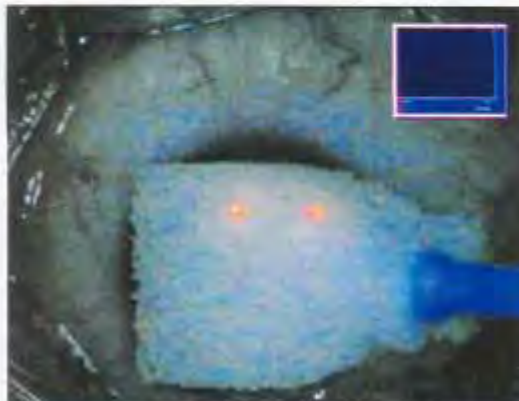
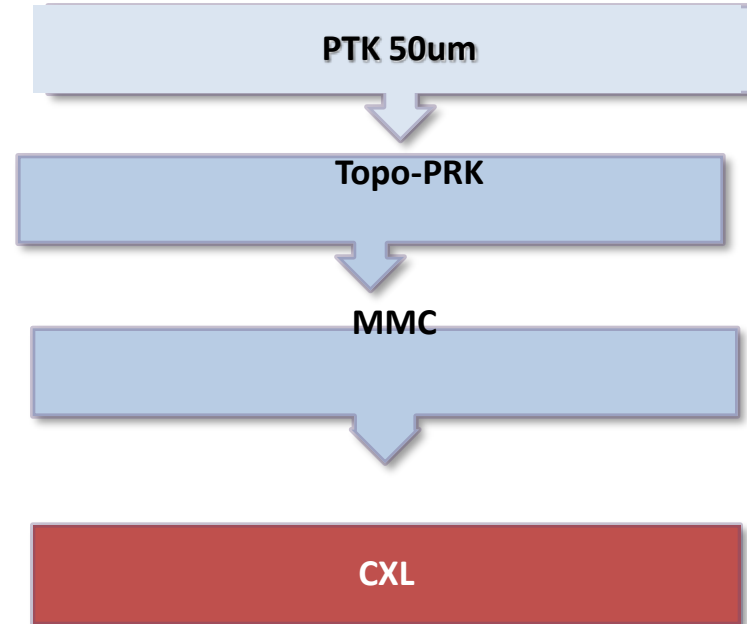
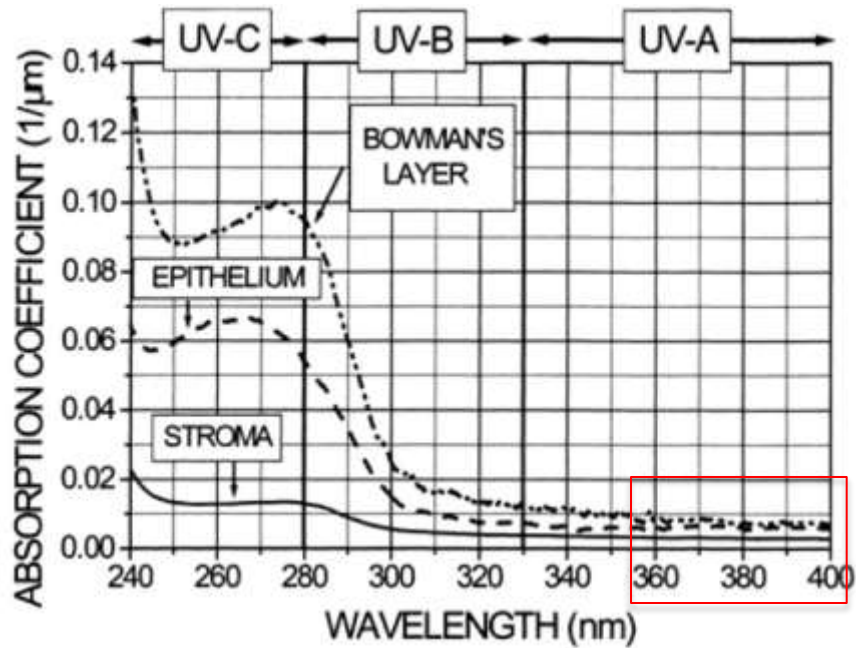


Figure 4.4: MMC solution 0.02% for 20 seconds



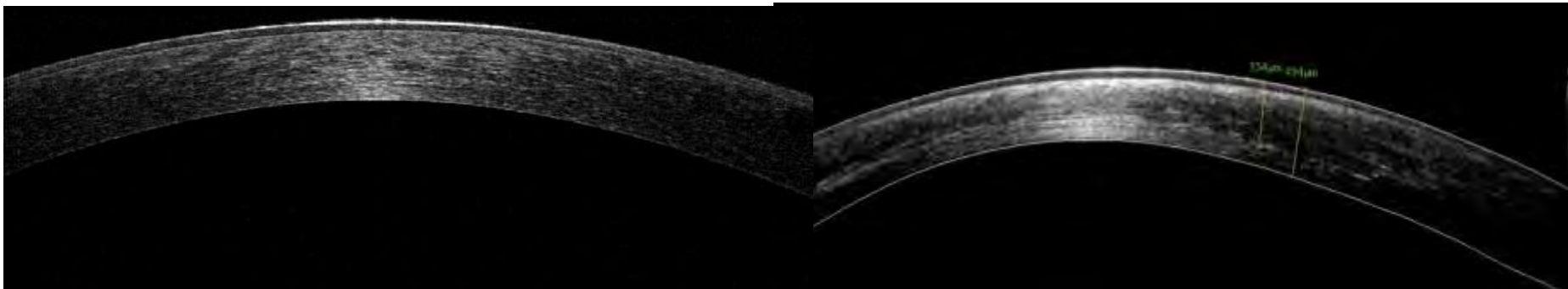


Comparison of Sequential vs Same-day Simultaneous Collagen Cross-linking and Topography-guided PRK for Treatment of Keratoconus

Anastasios John Kanellopoulos, MD

JRS Sept 2009

Kolozsvári et al
IOVS 2002;43:2165-2168



New York University
School of Medicine

Kanellopoulos, MD

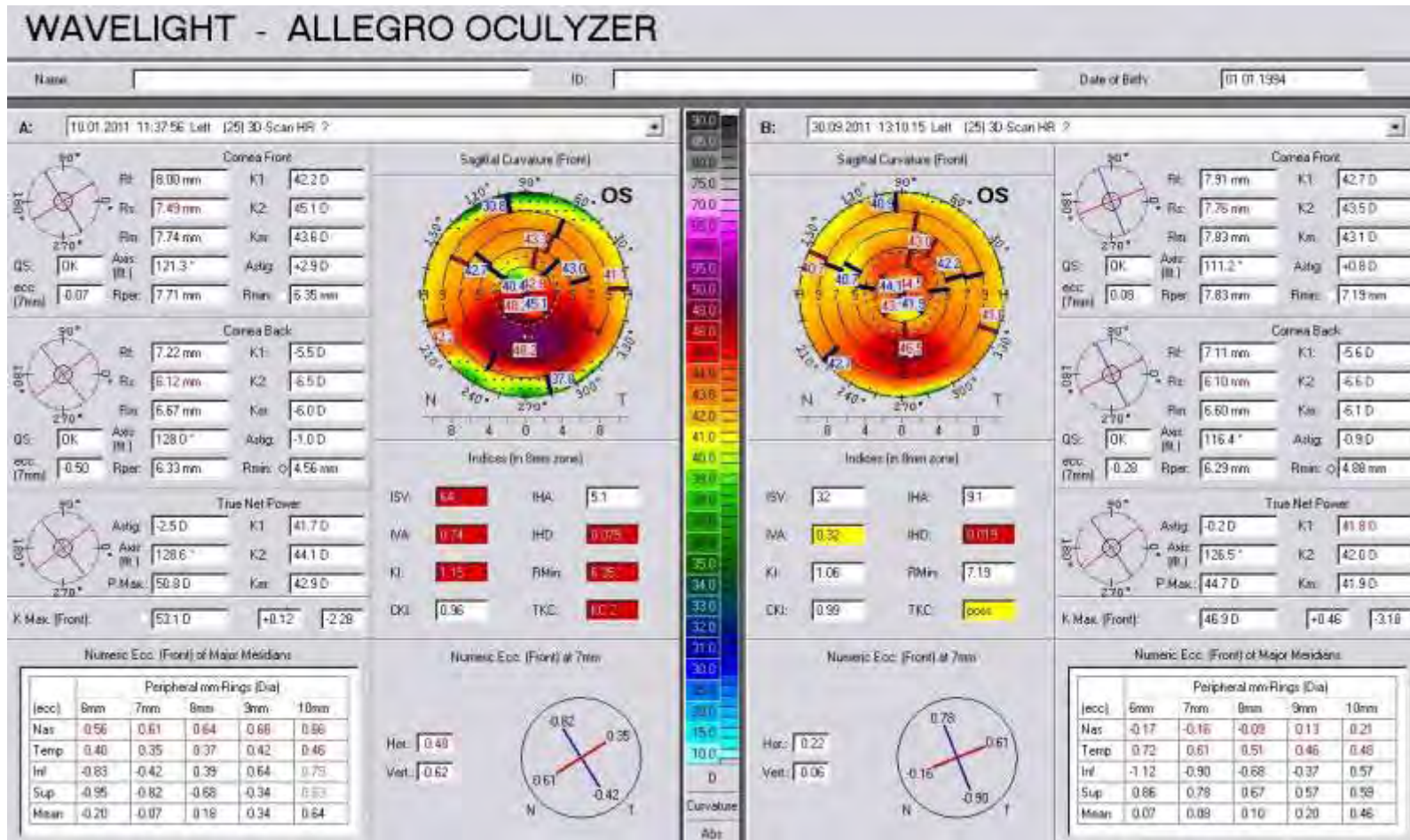
LaserVision.gr
Institute for laser



Topometric improvement: Significant reduction in IHD

Myopia induction!

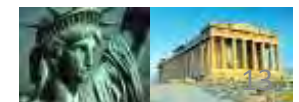
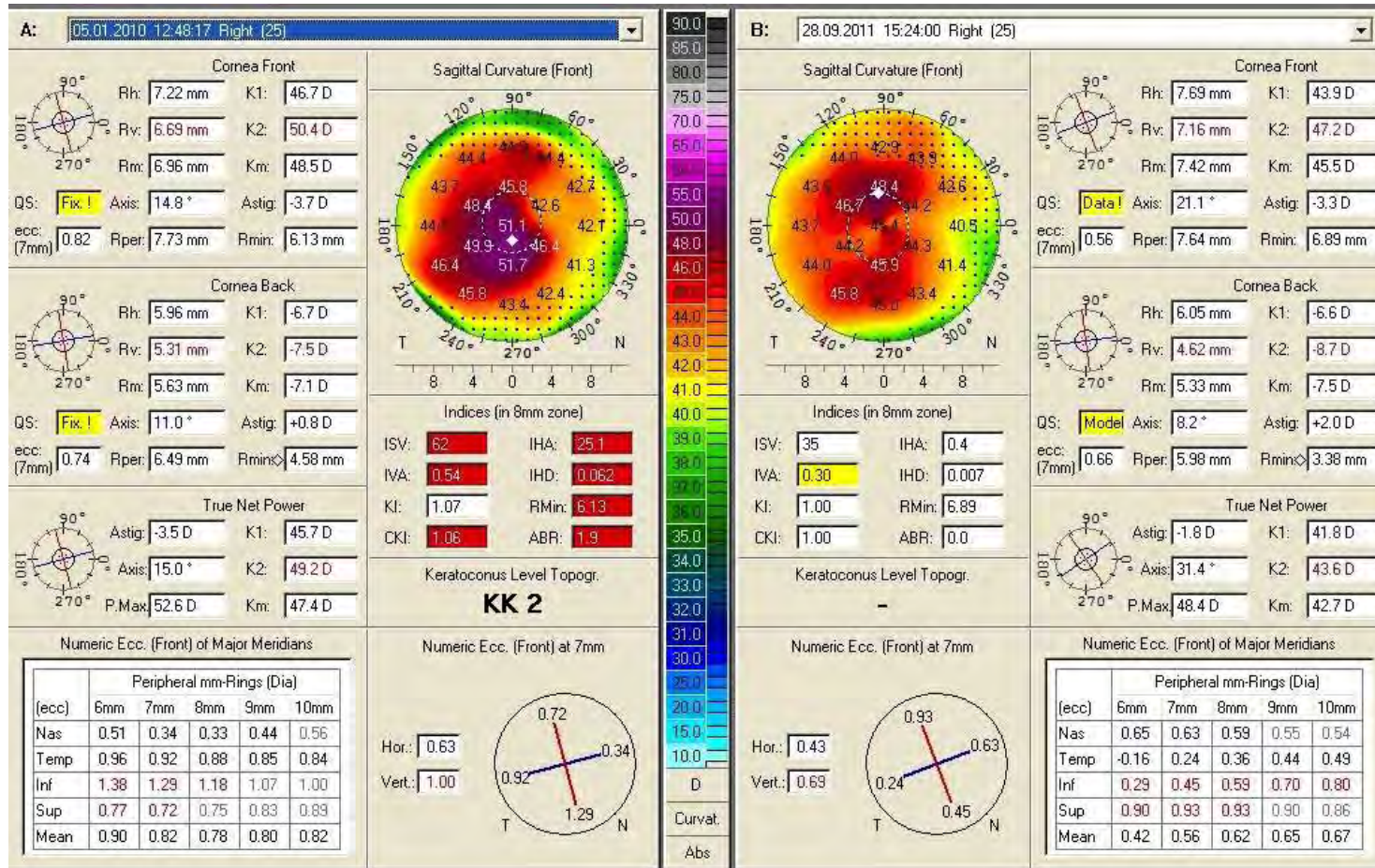
Refraction from +0.75-3.50@10 (20/60) to -0.75-0.75@170 (20/20) due to improvement of the topometric parameters



2 year follow up in a 15 y/o

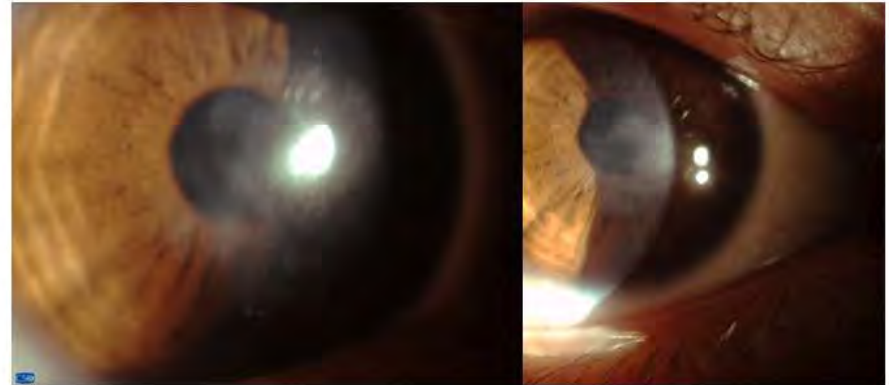
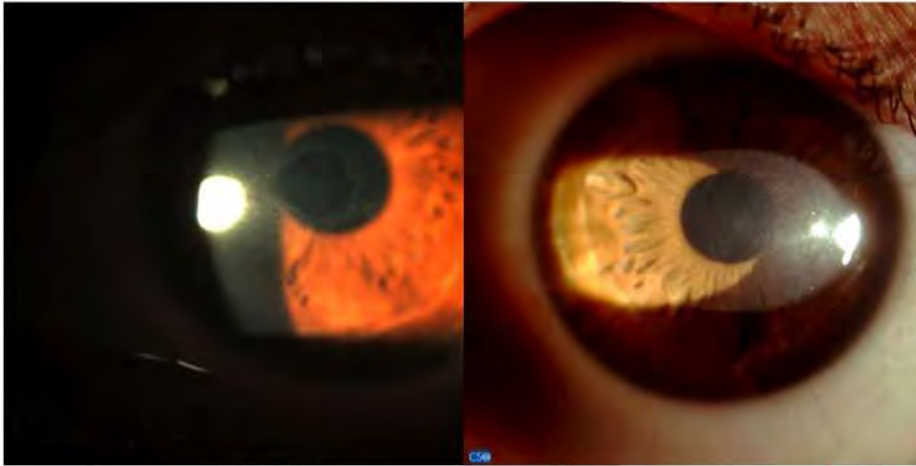
Topometric improvement:

Significant reduction in IHD (Index of Height Decentration)

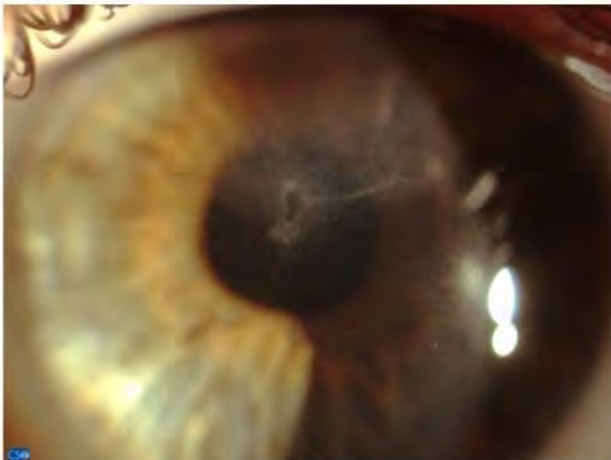


Healing delay-day4-ok on 1 month

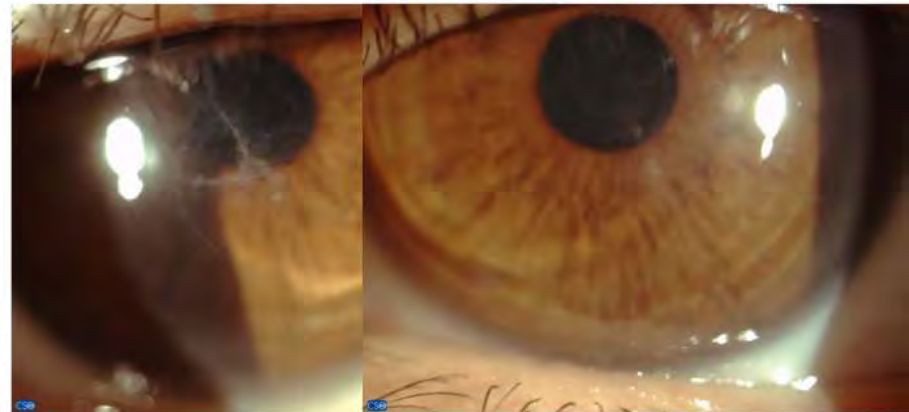
PRK-like haze 1 year after, in heavy sunbathing improved with steroids



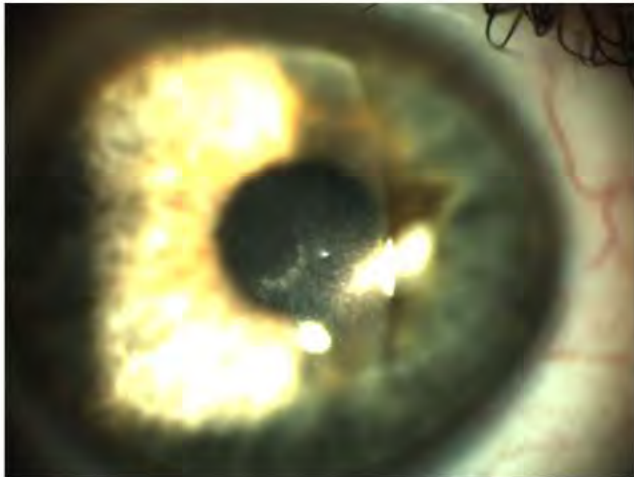
Week 2



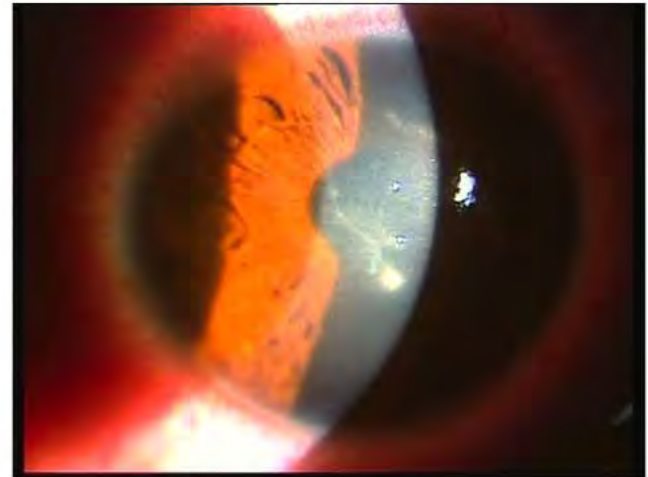
Week 2



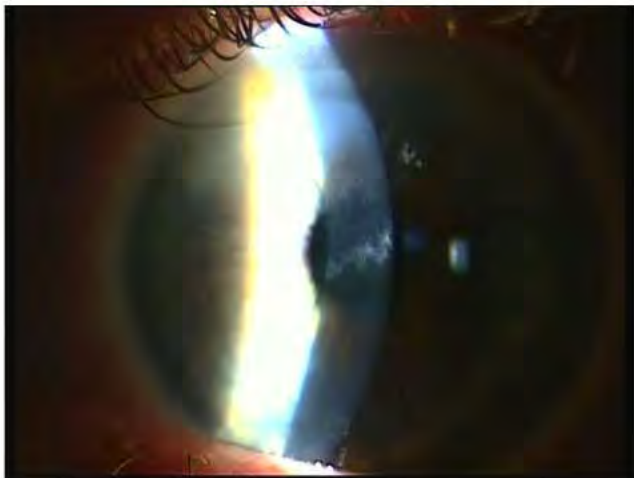
Salzman's-like nodule(s) can persist to 3 months postop



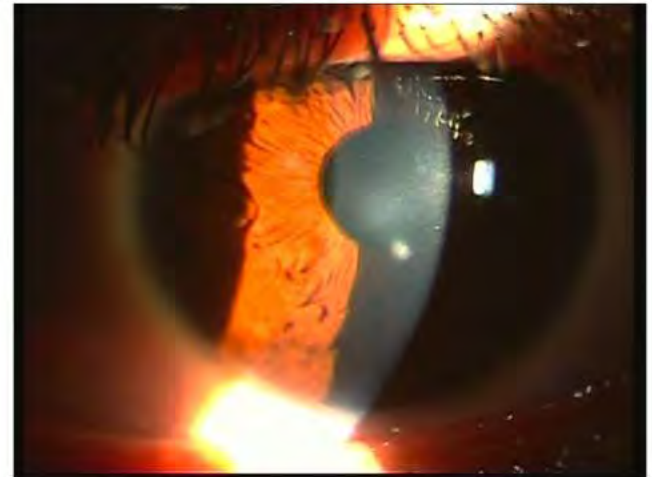
Delayed epithelial healing with
white spots



Haze

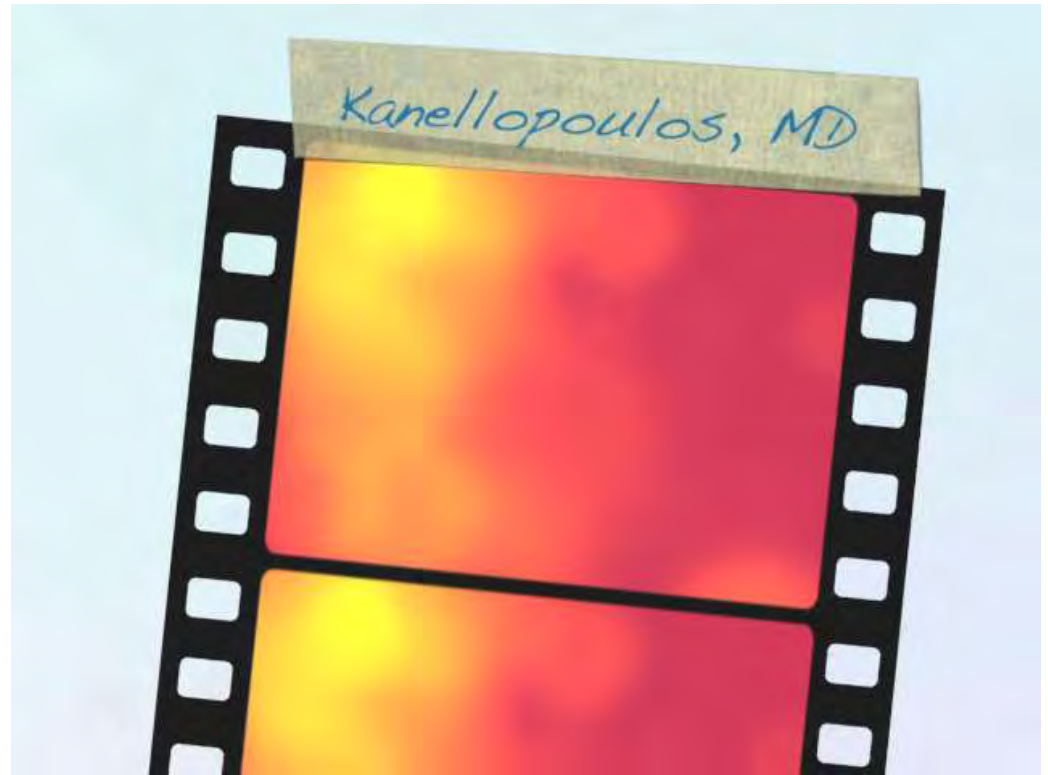


Faint Scar and white spot



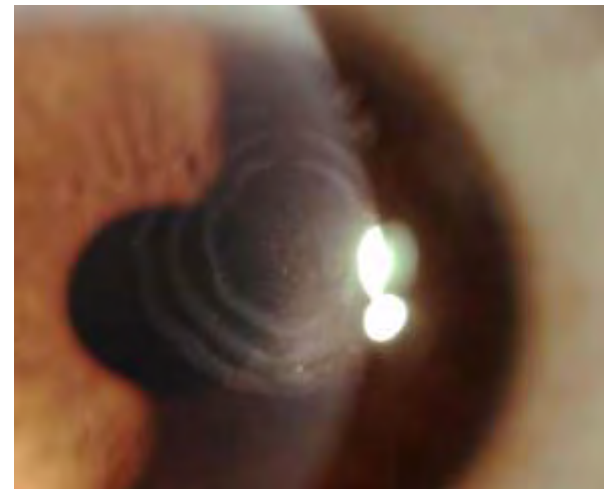
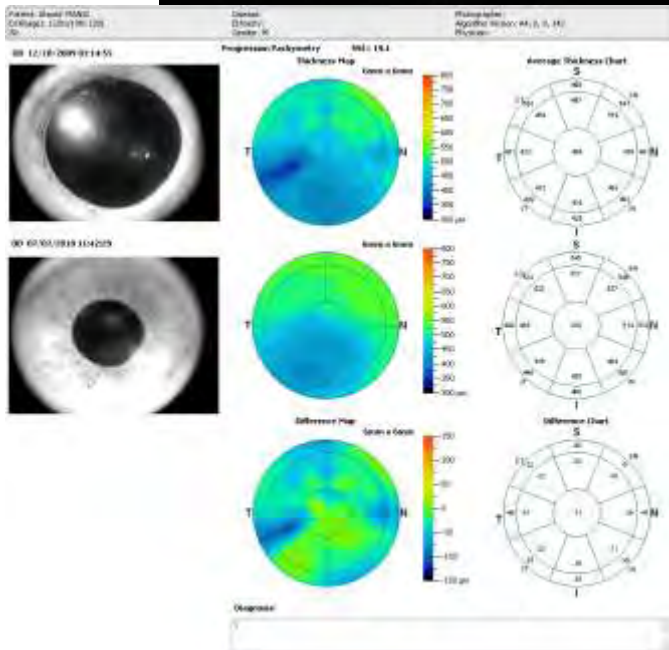
Cornea remodeling without tissue removal shrinkage + CXL (10mW/cm² x 10')

- Avedro,
Keraflex first
reports
- Kanellopoulos,
Herakar:TRXL



10 minute postop-Cornea OCT -8 months follow-up

No regression of the flattening effect!



Reactive epithelial hyperplasia

- Maybe the earliest sign of keratoconus
- Our data reproducibly support that ectatic corneas have in average THICKER epithelium than normal, in contract to previous understanding and despite the fact that it maybe thinner over the cone
- A simple index of “reactive cornea thickness” generated by HR Schemflug or OCT may becoma the hallmark of ectasia dagnosis

- **CXL and long term Hyperopic LASIK stability. Initial clinical findings in a contralateral eye study**

Purpose: The evaluation of the safety and efficacy of the application of intrastromal CXL in a contralateral eye study in routine hyperopic LASIK

Methods: 27 consecutive hyperopic and hyperopic astigmatic bilateral topography-guided LASIK patients were randomized to receive 5 minutes of 10mW/cm² CXL after in-the-flap administration of a single drop of 0.1% sodium phosphate riboflavin solution. All cases were treated with the Allegretto 400Hz Eye-Q excimer laser and femtosecond laser flap creation. Peri-operative refractive error, keratometric, topographic and topometric measurements were evaluated with a mean follow-up of 23 months (22-35).

Results: Mean sphere was +3.25D, Cyl: -1.75D. The CXL cases demonstrated a mean regression from treatment of +0.22D (diopters), the non-CXL cases: + 0.72 D, showing a very strong statistically significant difference even in the first 6 patients despite the expected flattening effect of CXL.

Conclusions: These preliminary data suggest that the combination of CXL in hyperopic LASIK may offer a very significant synergy in efficacy, suggesting that hyperopic LASIK long term regression may be more related to cornea biomechanical changes, than just residual accommodation.

Conclusions higher fluence CXL

Our current protocols

1-**Athens Protocol: topoPRK +10'x 10mw/cm²**

2-**LASIK Xtra: 1' (60") 30mW/cm²**

2-**PRK Xtra: 1' (60") 30mW/cm²**

3-**Transepithelial CXL: 0.25% riboflavin +
30mW/cm² X 3' (180")**

3-**Infection: 0.25% riboflavin + 45mW/cm² x 5
minutes**



Conclusions higher fluence CXL

Appears to be more effective if **Type I** model of CXL holds true

Customised fluence and riboflavin concentration may personalize CXL as a biomechanical stromal modulator for many applications:

May prevent regression in hyperopia

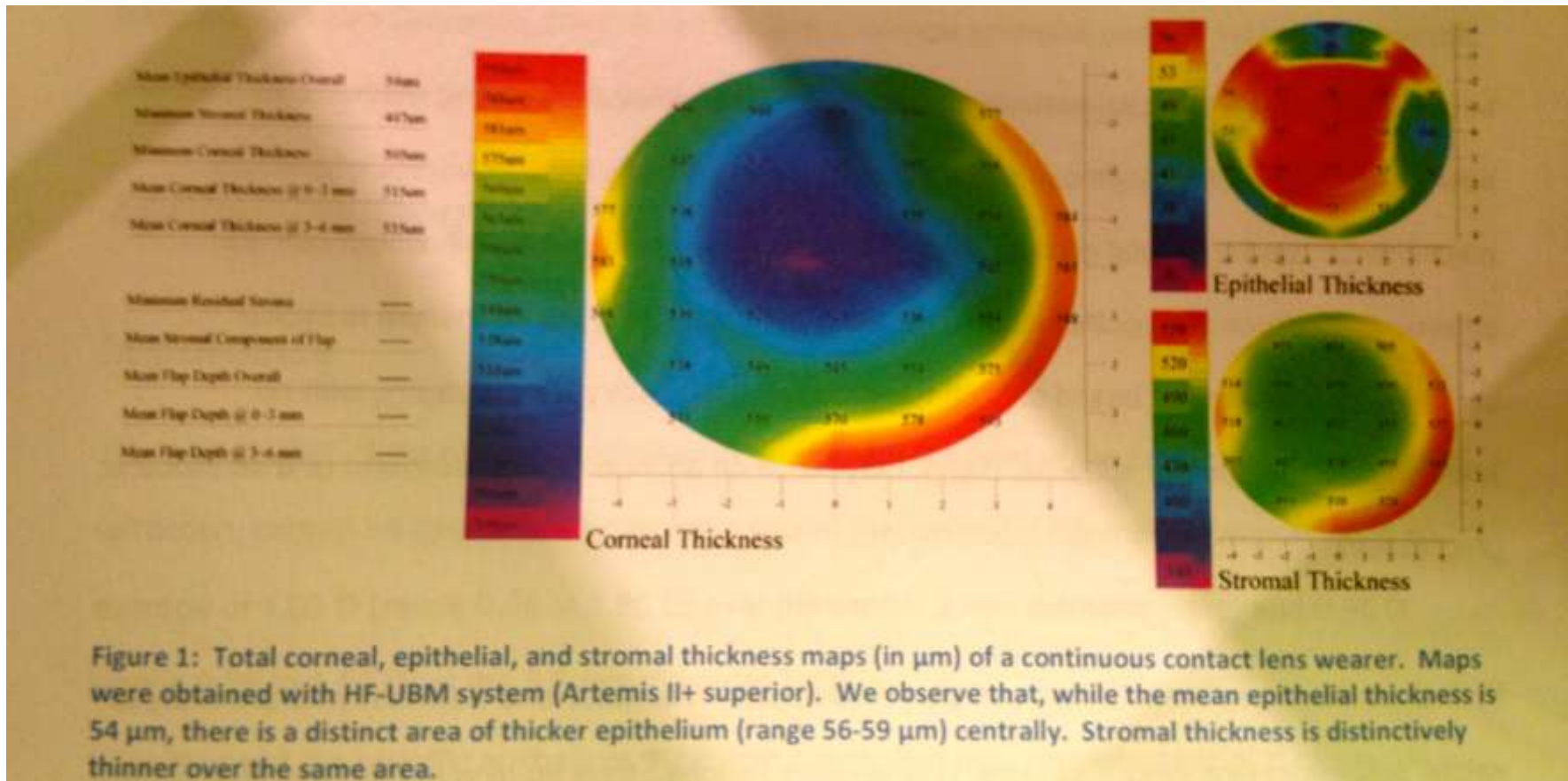
LASIK Xtra appears to have only potential advantages

May become the standard of care for PRK (reduce scarring, epithelial hyperplasia)



HFU UBM

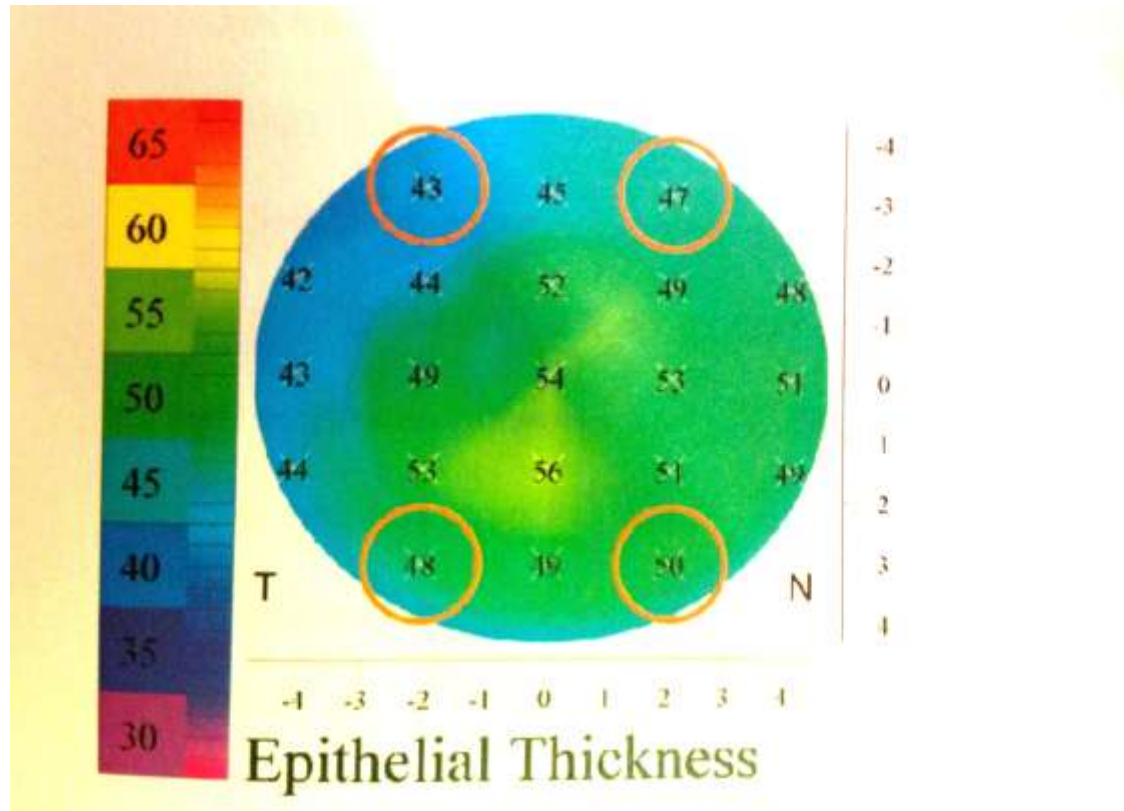
Collaboratorss: G. Asimelis, I. Aslanides



Keratoconus = thin
epithelium?

WRONG!

Epithelial maps in KCN



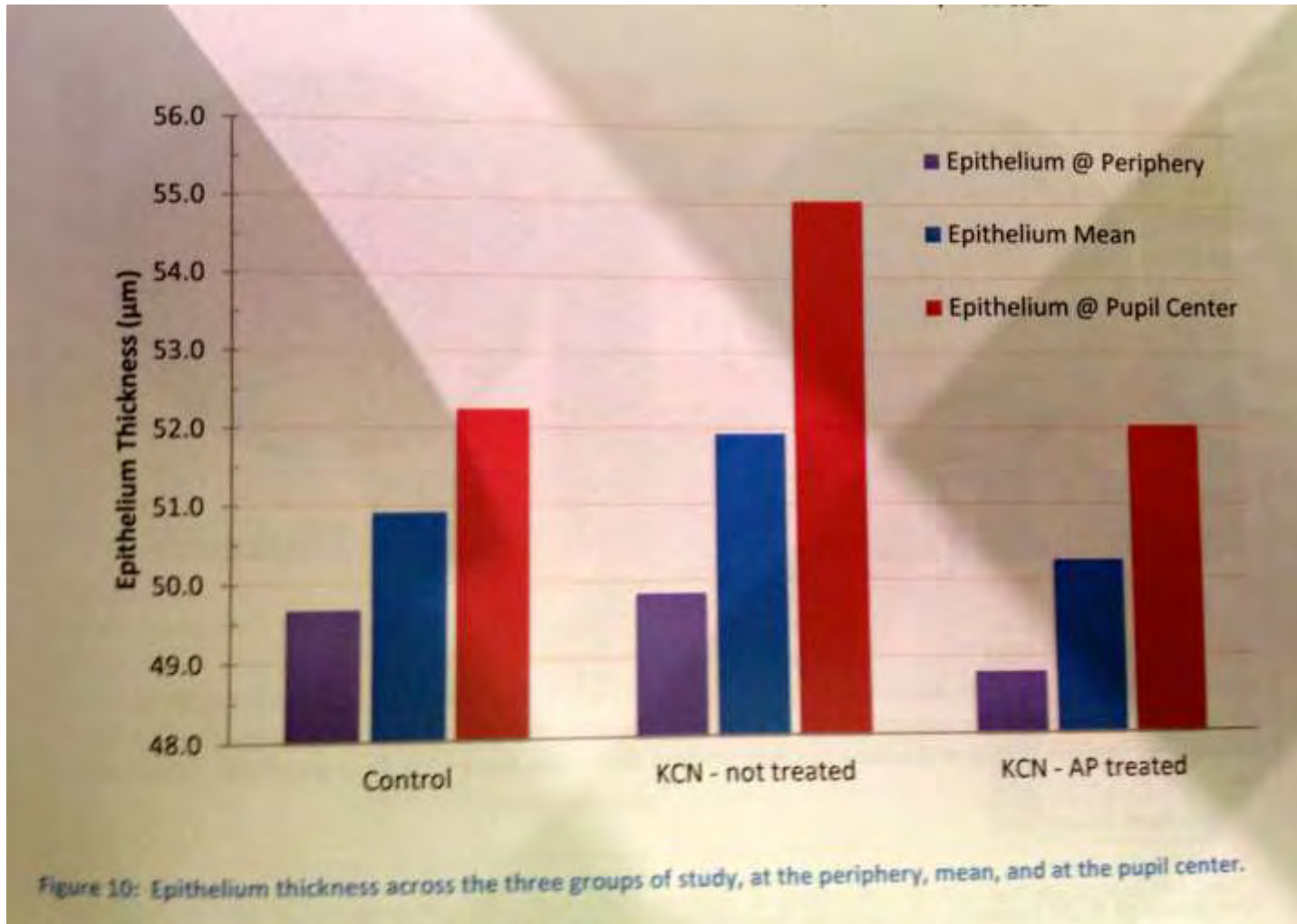
Epithelial maps in KCN

| Group | Age | | | | N of people | N of eyes |
|-------------------|---------|-------|-----|-----|-------------|-----------|
| | average | StDev | Min | Max | | |
| Control | 32.4 | 12.7 | 16 | 68 | 32 | 50 |
| KCN - not treated | 28.4 | 6.8 | 16 | 45 | 25 | 39 |
| KCN - AP treated | 29.2 | 9.4 | 16 | 72 | 42 | 70 |

Table 1: Age statistics of the three groups of study.

| Group | Epithelium Mean | | | | Epithelium @ Pupil Center | | | | Epithelium @ Periphery | | |
|-------------------|-----------------|-------|-----|-----|---------------------------|-------|-----|-----|------------------------|-------|-----|
| | Average | StDev | Min | Max | Average | StDev | Min | Max | Average | StDev | Min |
| Control | 50.9 | 3.8 | 43 | 58 | 52.3 | 4.9 | 42 | 60 | 49.7 | 3.1 | 43 |
| KCN - not treated | 51.9 | 3.3 | 45 | 57 | 55.1 | 3.7 | 46 | 60 | 49.8 | 3.7 | 43 |
| KCN - AP treated | 50.2 | 3.8 | 39 | 57 | 52.0 | 5.6 | 37 | 60 | 48.8 | 3.7 | 41 |

Ectatic corneas are thicker!



Conclusions higher fluence CXL

CXL can sterilize the stroma higher fluence and higher riboflavin % may be useful

The apoptosis of keratocytes may have unknown benefit to epithelial hyperplasia and risks

Potential endothelial toxicity

Potential limbal cell cell and/or goblet cell toxicity from collateral Rib⁺ interaction

CXL may prove to be the standard collagen stabilizer and adjunct disinfectant in LASIK, PRK and even cataract surgery



Thank you

