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

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- None

Introduction

- The key concept is the oxygen, which is the third and, so far, most underestimated component of cross-linking. Oxygen is necessary to cause the photochemical reaction that, in the riboflavin-soaked cornea irradiated with UV light, leads to structural changes of the collagen fibers.
- This new approach raises the irradiancy level of the UVA laser from 3 mW/m^2 to 7 mW/m^2 and fractions the doses of the energy delivery with a “pulse” irradiation using cycles of 30 seconds on and 30 seconds off. The method should provide more oxygen into the collagen matrix than the standard procedure, leading to optimization of the collagen oxidative delamination reaction

Can we safely shorten current CXL time?

Published reports on PDT and anti-bacterial studies with UVA/PS show

- High oxygen depletion (~0%) in the presence of proteins, bacteria, collagen, and UVA + photo-sensitizers (especially with high quantum efficiencies such as riboflavin -RF), reducing singlet oxygen formation
- ROS generation is very fast(~ ns) and linear with UVA fluence, while re-oxygenation is often the rate limiting step in the entire sequence.

We are investigating an alternative CCL approach: Equi-dosed, time fractionated, UVA fluence maximized, pulsed exposure cycling (UVA OFF till stromal re-oxygenation steady state, then UVA ON to generate ROS rapidly until full oxygen depletion).

- Measured ROS lifetimes (~ 10 us) in RF + collagen may help determine a UVA pulsing rate when ON (at 2x the ROS lifetime frequency~100KHz), further reducing UVA damage/apoptosis.

- Equi-dosing the new UVA exposure with current standard/efficiency (3x30= 5.4J/cm2, @50%) may set the maximum number of ON/OFF cycles required for higher fluence(~15mW/cm2) x ON time(~3 mins).

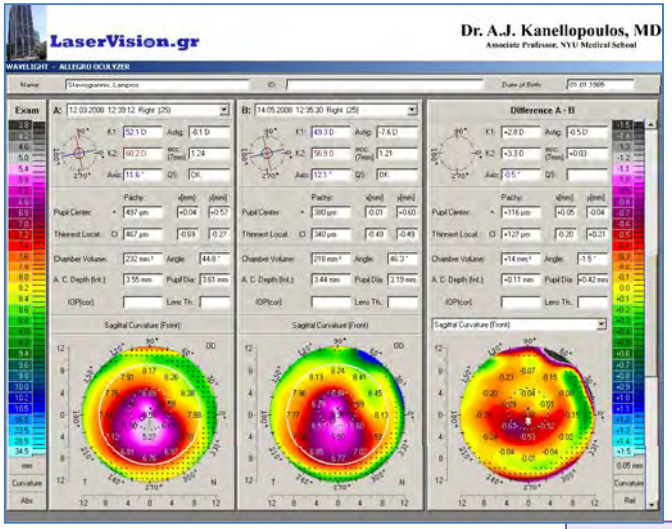
Methods:

- 30 KCN cases were evaluated for UCVA, BSCVA, refraction, keratometry (K), topography, endothelium and clarity.
- 15 eyes were CCL with 7mW/cm2 for 15 minutes and 15 eyes with 3mW/ cm2 for 30 minutes.
- Both groups received 0.1% riboflavin solution every 2 minutes. Mean follow up was 1.5 years

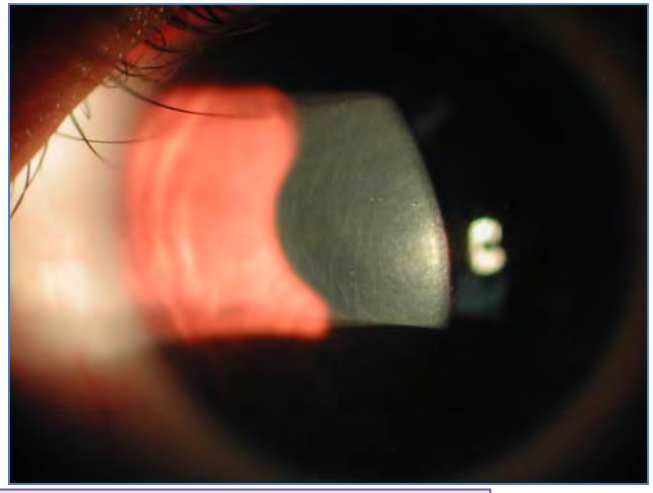
Results:

- The mean improvement of UCVA was 0.2 to 0.4, BSCVA 0.4 to 0.7, 1.5D reduction in myopia, 2.1D reduction in cylinder, K: 51.2 to 48.5 There was no statistical difference in the means in the 2 groups.

Clinical improvement at 3 months



Clinical signs of CCL



Conclusions:

- Shorter duration, higher UVA fluence CCL appears to be safe and as effective in stabilization of ectasia in KCN.
- It may result in less keratocyte loss as most human cells are more resistant to shorter exposure time, even at higher fluence UV light
- This work suggests that perhaps higher fluence pulsed UV exposure may be as effective and even safer.

Discussion

The amount of UV light to which an eye is exposed in the early afternoon in Athens is, on average, 10 mW/cm^2. So the amount of UV light is not something we should be worried about.

It is the interaction with riboflavin that can make it potentially dangerous, but the better penetration of the photosensitizing agent and the shorter laser time with pulse delivery effectively compensates for the increased fluence.

We have evaluated and presented previously the effects of applying the riboflavin solution intra-corneally by utilizing a femtosecond laser pocket as well as a prophylactic measure in refractive surgery patients who may be at risk of developing ectasia.