VISIOENG

FONDAZIONE G.B. BIETTI
PER LO STUDIO E LA RICERCA IN OFTALMOLOGIA - ONLUS
IRCCS - Istituto di Ricovero e Cura a Carattere Scientifico
Rome (ITALY) - www.fondazionebietti.it

Consiglio Nazionale delle Ricerche

Efficacy of transepithelial corneal cross-linking using iontophoresis

Experimental studies on eye-bank donor eyes

and

Preliminary results on the clinical trial NCT02117999

Marco Lombardo, MD, PhD

Senior Researcher IRCCS Fondazione G.B. Bietti

CEO Vision Engineering Italy srl

OUTLINE

1 – In vitro studies on CXL using iontophoresis

1.1 Corneal diffusion

1.2 UV-A corneal absorbance

1.3 Corneal biomechanics

2 – Randomized Clinical Trial: preliminary results at 3 months follow-up

3 – Conclusions

Background - 1

Controversial data have been reported on the **effect of transepithelial corneal CXL** to slow down progressive keratoconus in patients.

The studies on riboflavin diffusion through the corneal epithelium and on the effect of TE-CXL have been carried out **using conventional dextran-enriched solutions**.

Dextran-enriched solutions are not adequate to claim that riboflavin cannot diffuse through the intact corneal epithelium.

Background - 2

Transepithelial corneal CXL

PROS

1) No complications related to epithelial removal (pain, haze, infection)

2) Fast visual rehabilitation (socially important)

CONS

1) Controversial data on former TE-CXL techniques:

- inadequate permeation of riboflavin in the stroma

- low or limited cross-linking effect

Background - 3

In laboratory studies*, **iontophoresis** has been shown to deliver riboflavin (dextran-free, hypotonic solution) efficiently through the intact epithelium and to improve the mechanical stiffness of the stroma after rapid UV irradiation.

*

1) Arboleda A et al. Evaluating in vivo delivery of riboflavin with coulomb-controlled iontophoresis for corneal collagen cross-linking: a pilot study. Invest Ophthalmol Vis Sci 2014; 55(4): 2731-2738.
2) Mastropasqua L et al. Structural modifications and tissue response after standard epi-off and iontophoretic corneal crosslinking with different irradiation procedures. Invest Ophthalmol Vis Sci 2014; 55(4): 2526-2533.
3) Cassagne M et al. Iontophoresis transcorneal delivery technique for transepithelial corneal collagen crosslinking with riboflavin in a rabbit model. Invest Ophthalmol Vis Sci 2014; E-published.
4) Lombardo M et al. Biomechanical changes of the human cornea following transepithelial corneal cross-linking using iontophoresis. J Cataract Refract Surg 2014; in press.
5) Lombardo M et al. Corneal light backscattering following transepithelial corneal cross-linking using iontophoresis in donor human corneal tissues. J Cataract Refract Surg 2014, in press.

Iontophoresis

Iontophoresis for corneal CXL is a noninvasive technique

in which a weak electric current (1 mA for 5 minutes)

is used to enhance the penetration of riboflavin-5-phosphate into the stroma.

Current
hav
f rabbits
re.

Curren
ionto
op
scleral
the
y.

Purpose

We aimed to evaluate both the **diffusion of riboflavin in the stroma** and the **corneal stiffening effect in human eye globes** in response to rapid* UV-A transepithelial corneal cross-linking using iontophoresis (**T-ionto CXL**) in comparison with **standard CXL**.

***T-ionto CXL** was performed using 10 mW/cm^2 UV-A lamp

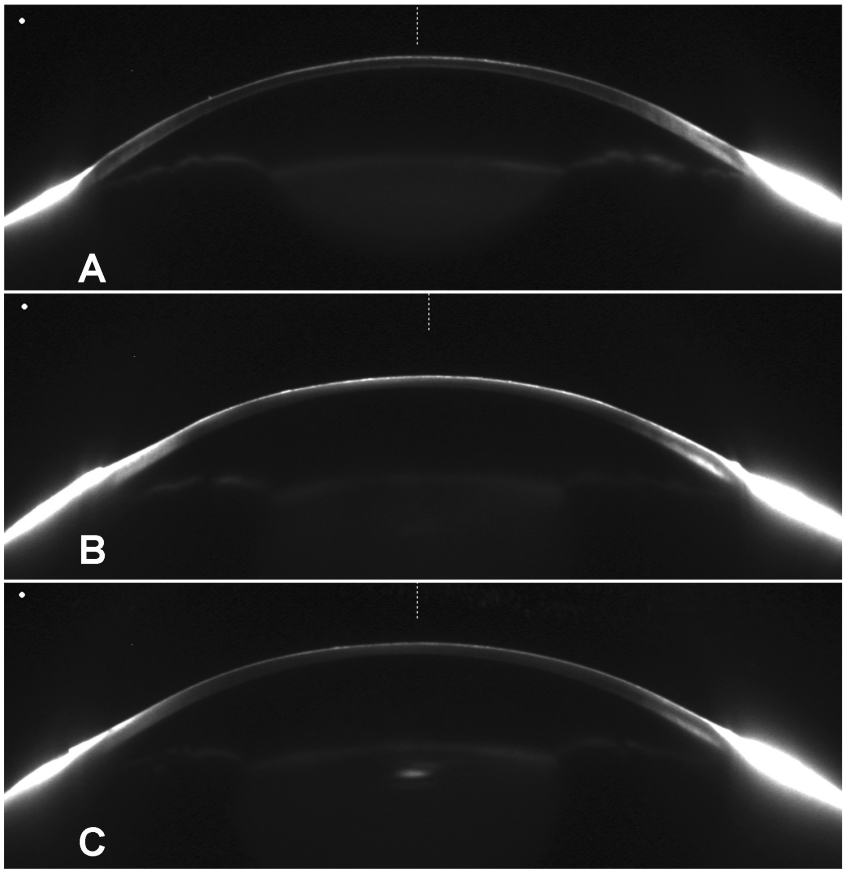
Methods

N=4 eye globes were treated with T-ionto CXL and N=4 eyes with standard CXL.

A purpose-designed instrument, ie, the Ocular Biomechanics Modulator (OBM), combined to a Scheimpflug camera, was used to perform the experiments.

Densitometry 1

Scheimpflug images

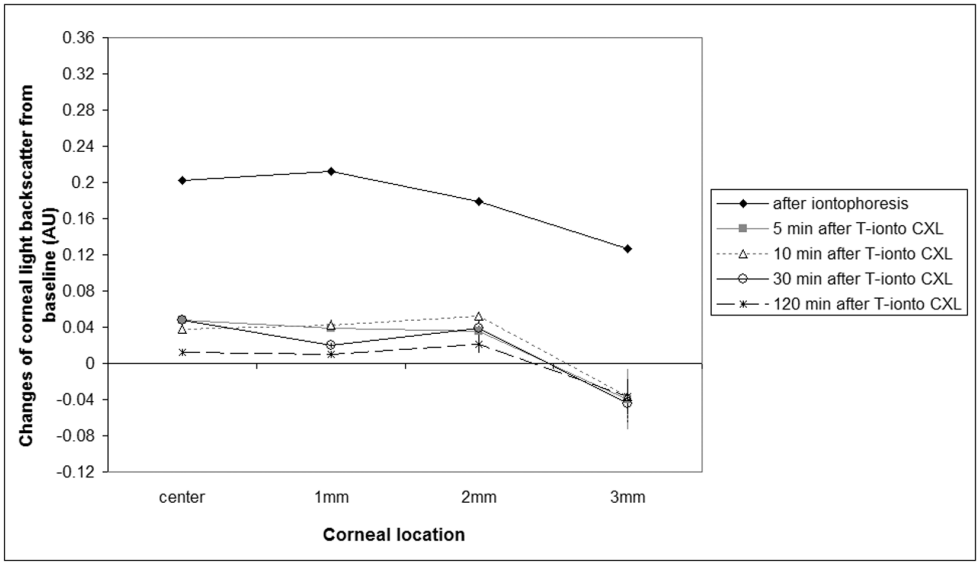


A) Baseline

B) After iontophoresis

C) 5 min after **T-ionto CXL**

Results

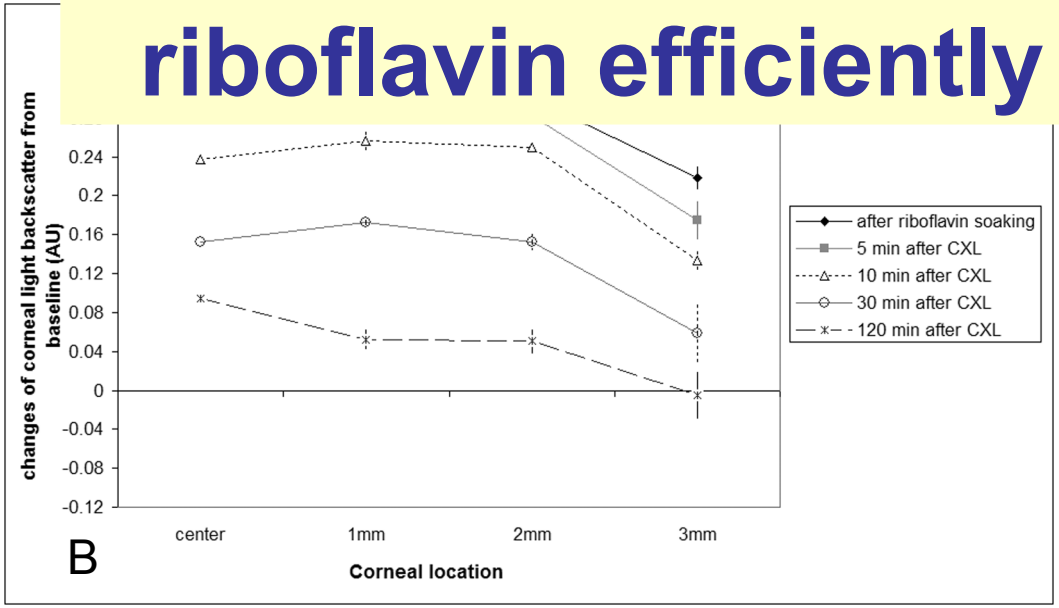


Average changes of corneal light backscattering, with respect to baseline measurements, in specimens that underwent **T-ionto CXL**.

Densitometry 2

A) Average changes (±SD; vertical bars) of corneal light backscattering, with respect to baseline measurements, in specimens that underwent **T-ionto CXL**.

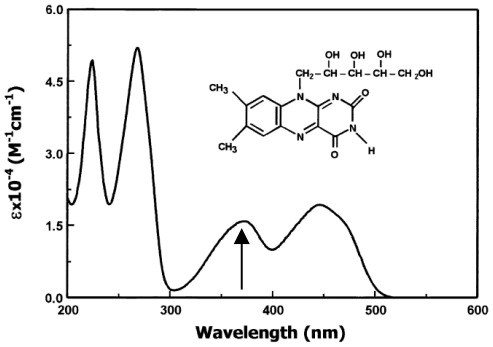
Iontophoresis is effective to deliver riboflavin efficiently in the stroma



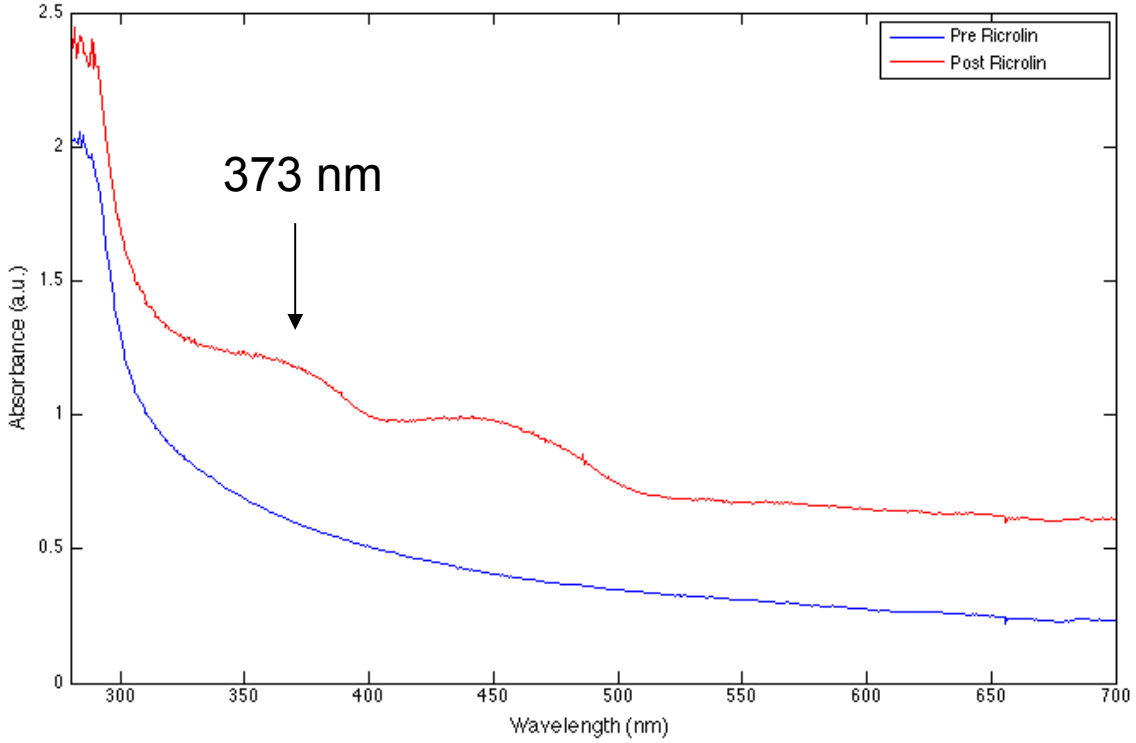
B) Average changes (±SD) of corneal light backscattering, with respect to baseline measurements, in specimens that underwent **Standard CXL**.

UV-A corneal absorbance - 1

Riboflavin absorbance



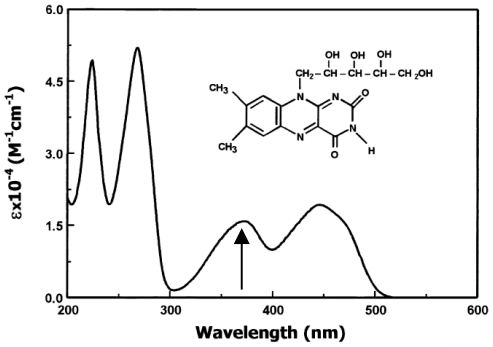
Conventional stromal soaking



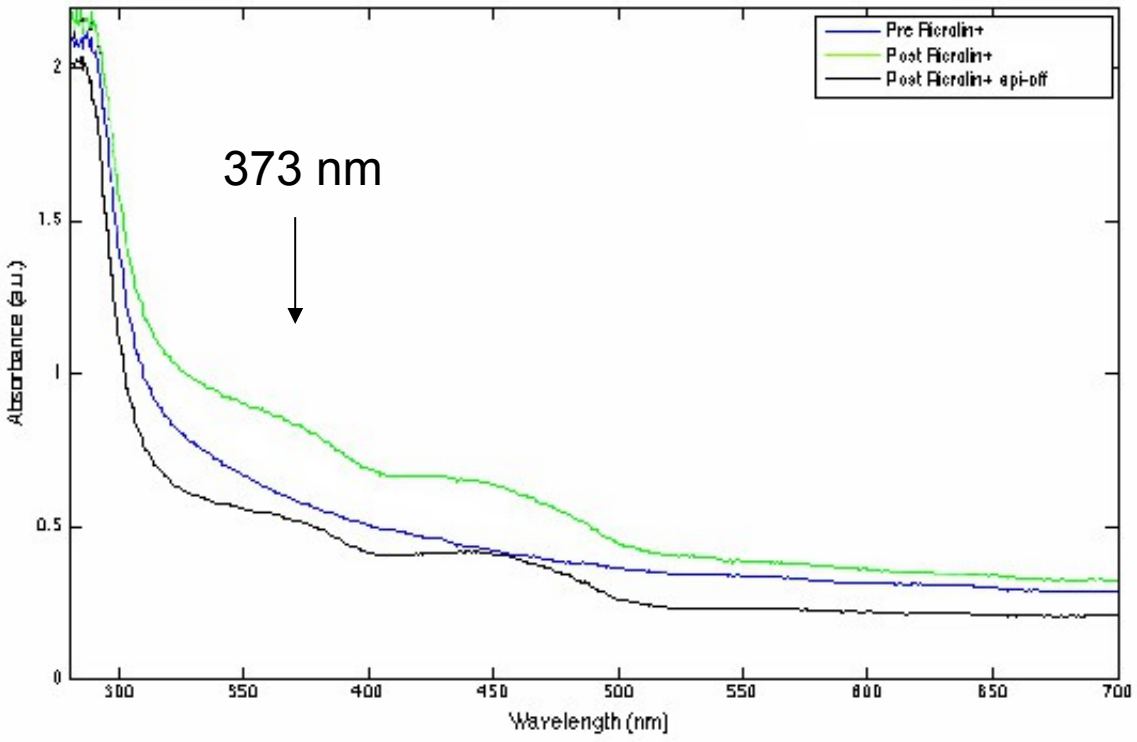
Corneal absorbance (280-700 nm) before (blue) and after (red) stromal soaking with 20% dextran-0.1% riboflavin

UV-A corneal absorbance - 2

Riboflavin absorbance



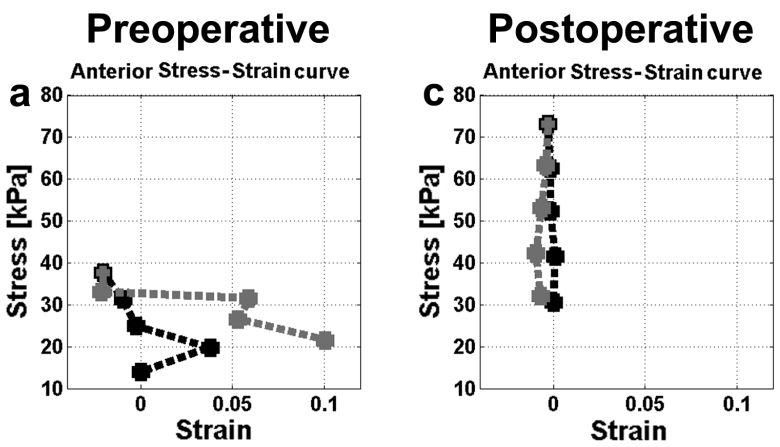
Iontophoresis



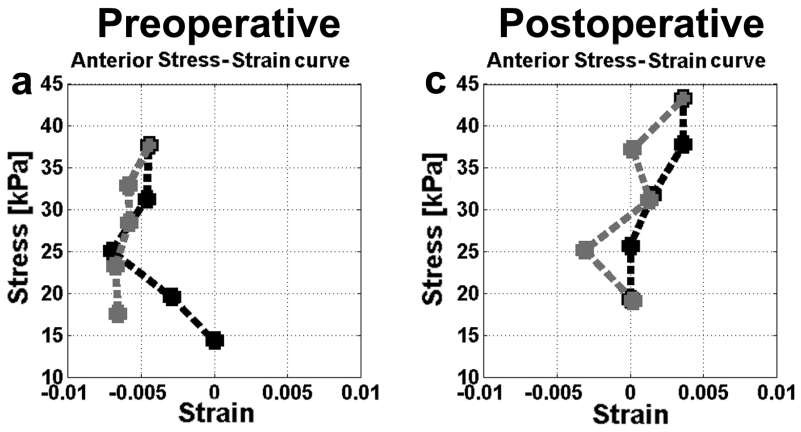
Corneal absorbance (280-700 nm) before (blue), after (green) corneal soaking with dextran free 0.1% riboflavin and after de-epithelialization (black).

Biomechanics - 1

*Stress-Strain curves for the anterior cornea before and after **T-ionto CXL***



*Stress-Strain curves for the anterior cornea before and after **Standard CXL***



After T-ionto CXL

The Young's modulus on average increased 1.8 times (from 1.6 ± 1.0 to 2.9 ± 1.6 MPa).

After standard CXL

The Young's modulus on average increased 1.9 times (from 1.3 ± 0.9 to 2.5 ± 1.4 MPa).

After both CXL procedures, stress-strain loading curves of the anterior cornea were steeper than preoperatively.

The area inside the loading and unloading curves (hysteresis) was found to be smaller than preoperatively.

Biomechanics - 2

TE-CXL with IONTOPHORESIS vs Standard CXL

Same effectiveness as the standard procedure but…
NO RISK OF HAZE
NO RISK OF INFECTION
FASTER VISUAL REHABILITATION

Randomized Clinical Trial

A RCT is ongoing at the IRCCS Fondazione G.B. Bietti, Rome, Italy

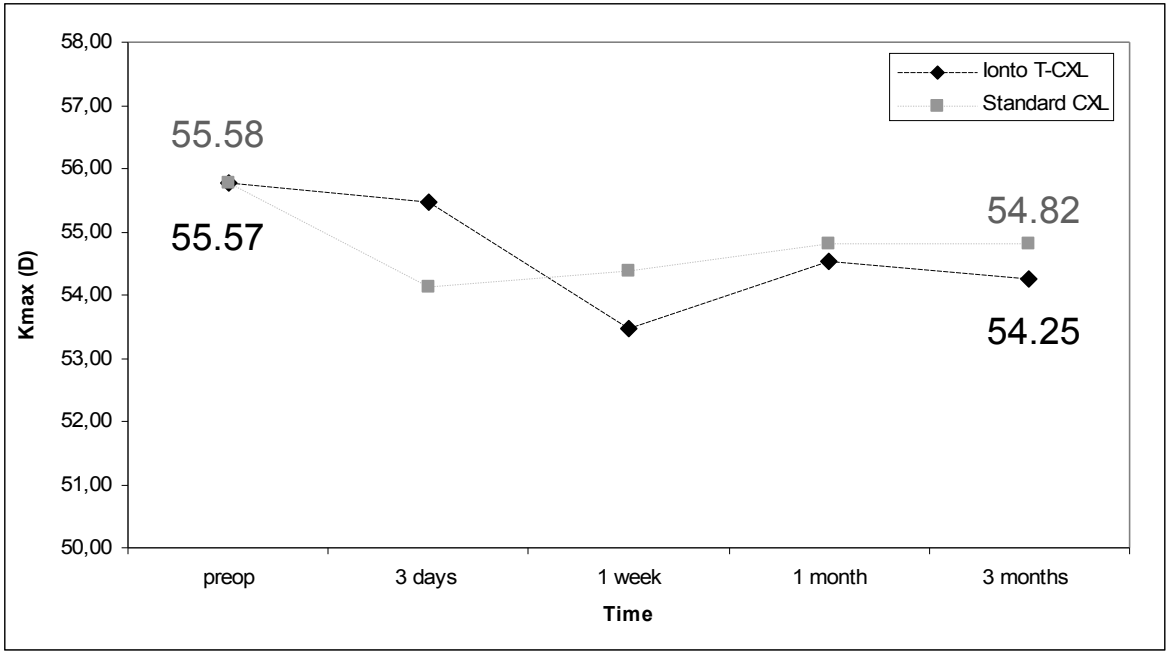
Clinical Trial NCT02117999

Randomized clinical trial comparing transepithelial corneal cross-linking using iontophoresis and standard corneal cross-linking for the treatment of keratoconus

PI: Dr. Marco Lombardo

Randomized Clinical Trial - Corneal topography

At 3-months follow-up, both CXL procedures halted keratoconus progression



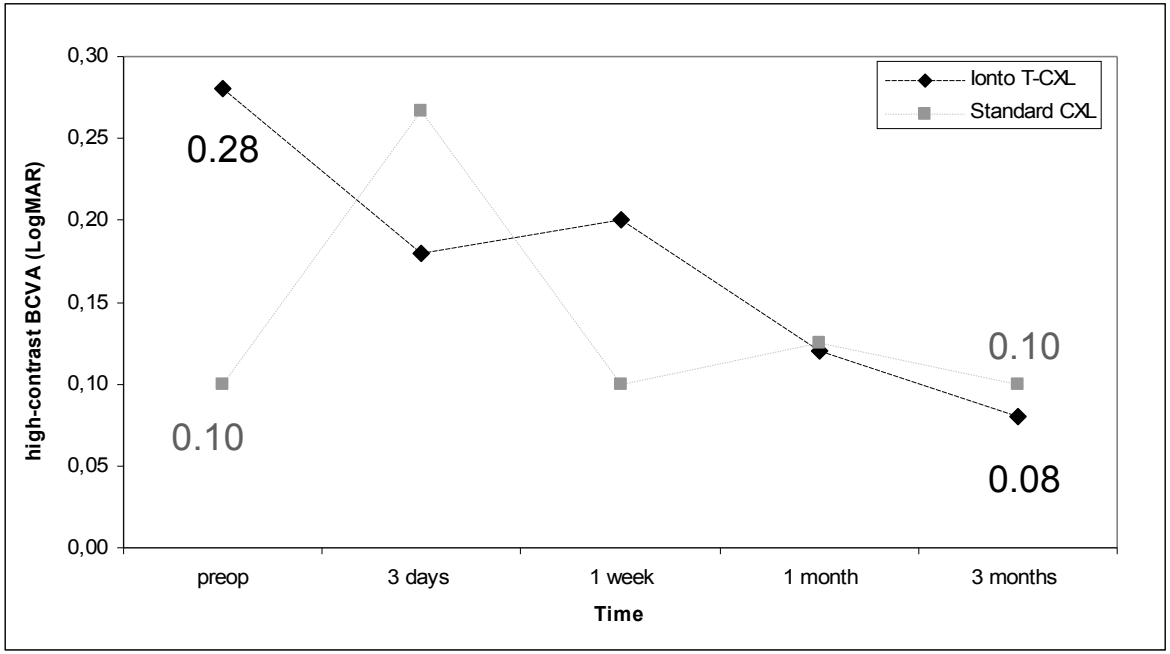
5 and 4 cases underwent T-ionto CXL and Standard CXL respectively

Average age 28.0 and 28.8 years respectively

Progressive keratoconus showing Kapex >1 D over 1 year follow-up

Randomized Clinical Trial - Visual performance

BCVA improved after T-ionto CXL in all cases



n. of letters (ETDRS)

<u>T-ionto CXL</u>: from 41 preop (20/40) to 52 at 3-months (20/25)

<u>Standard CXL</u>: from 54 preop to 53 at 3-months

Conclusions

IN LABORATORY:

1) Iontophoresis was shown to deliver efficiently riboflavin through the epithelium.

2) After T-Ionto CXL, the corneal tissue became stiffer than preoperatively.

The results of T-ionto CXL were mostly comparable to those obtained with standard CXL

IN CLINIC:

3) The preliminary results on patients treated by T-ionto CXL are demonstrating that the procedure is effective to halt keratoconus progression, while improving the corneal optical performance and vision function.

Marco Lombardo can be reached at mlombardo@visioeng.it