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Comparative study of results of standard corneal collagen cross linking vs. corneal crosslinking by iontophoresis of riboflavin

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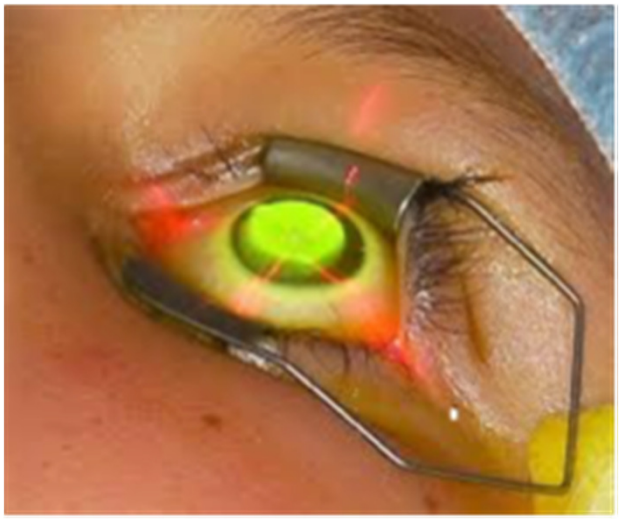
Valencia 2015

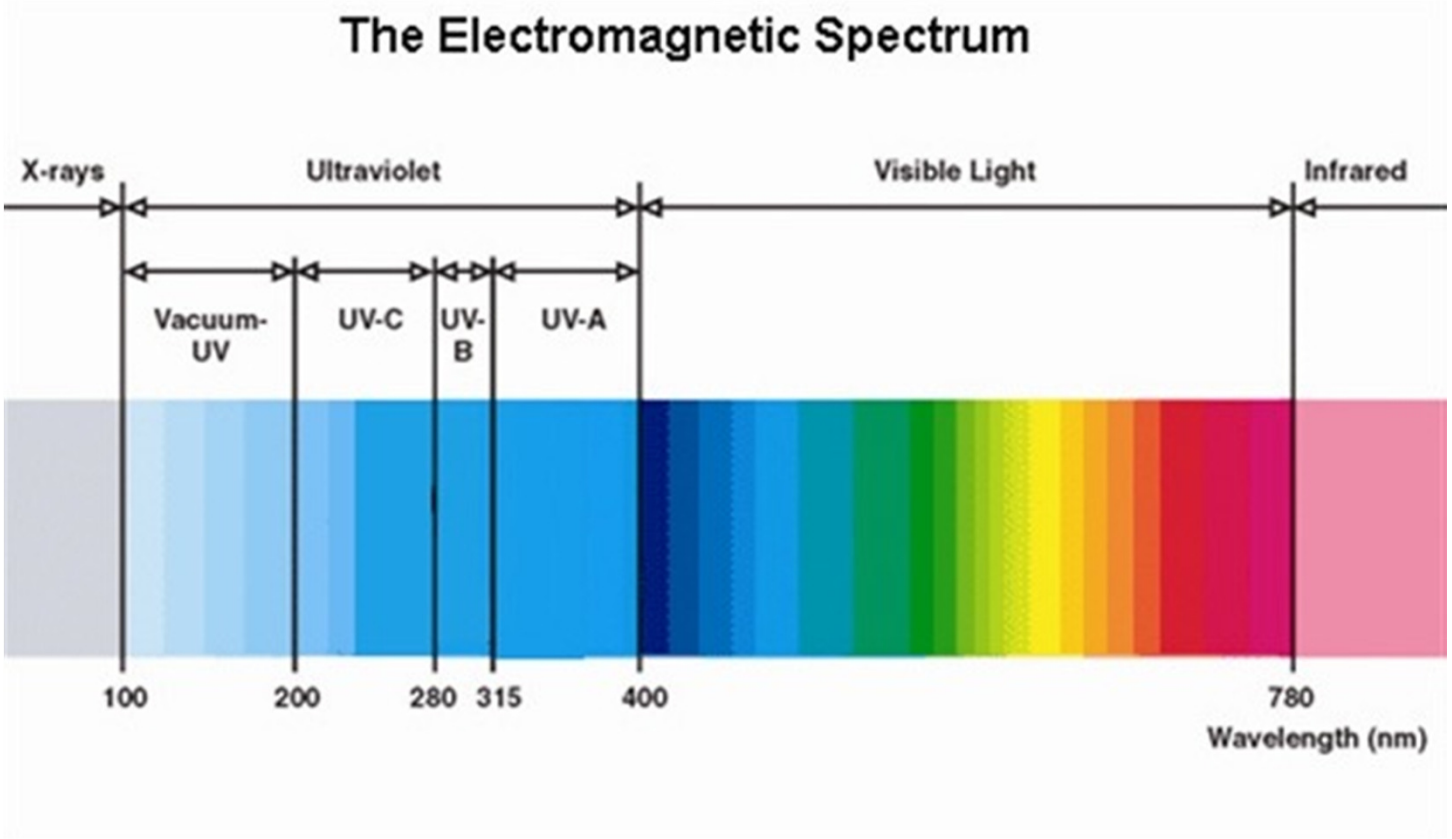
INTRODUCTION

Corneal collagen crosslinking was successfully introduced by Wollensak et al. in 2003 and became a standard, minimally invasive, and safe treatment for progressive keratoconus and secondary ectasia.



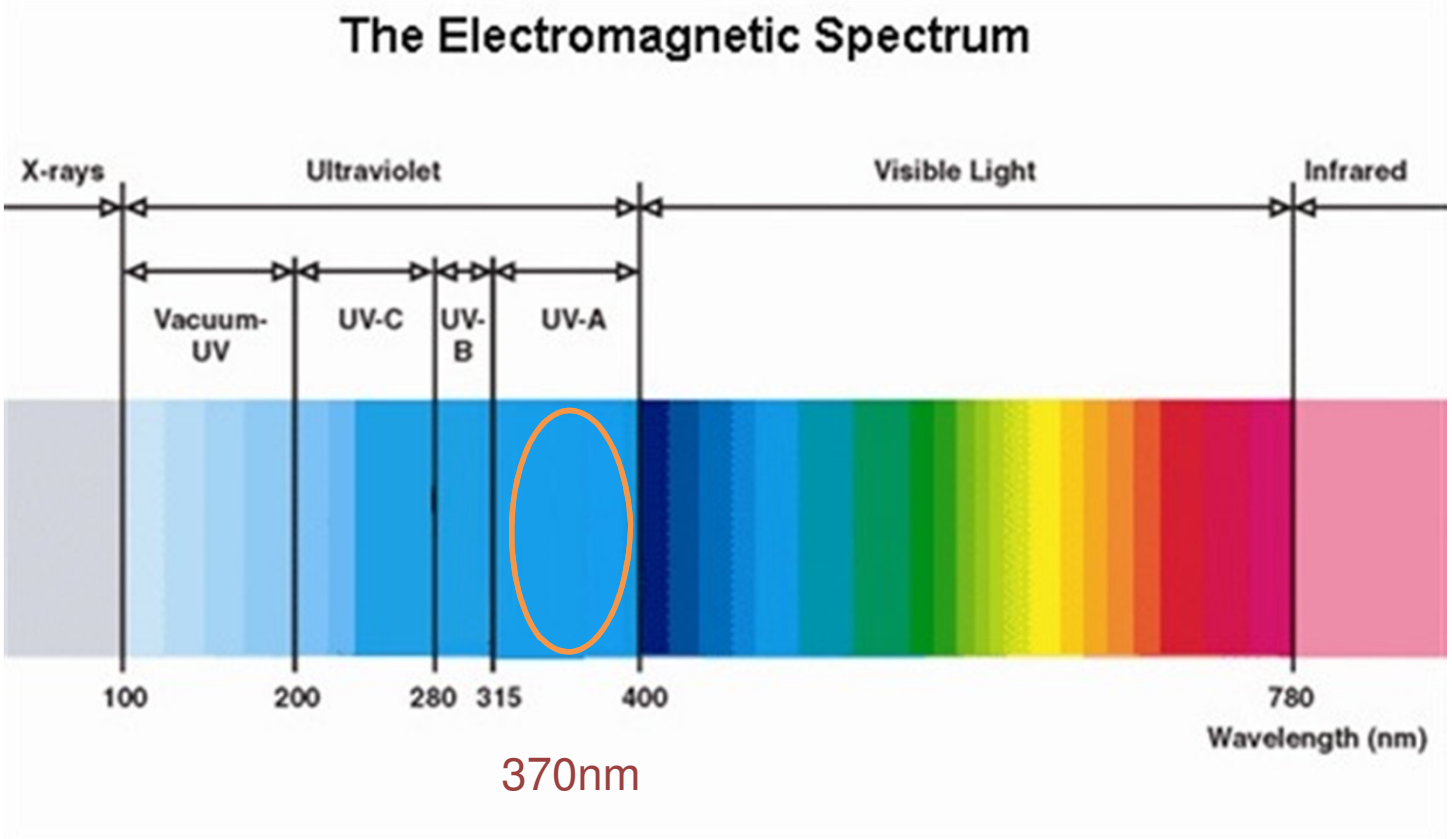
In Ufa Eye Research Institute CXL was introduced in 2007.

INTRODUCTION

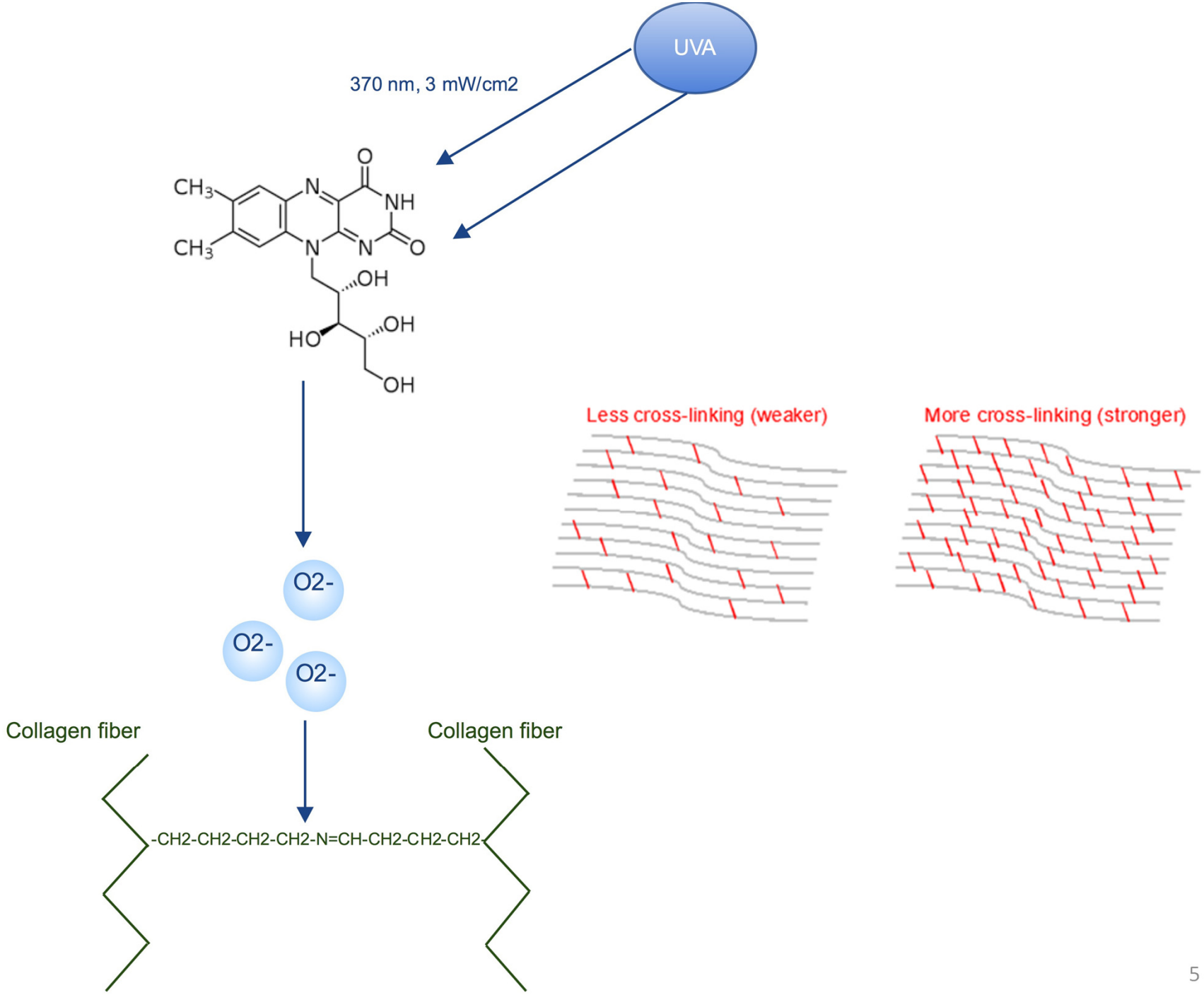


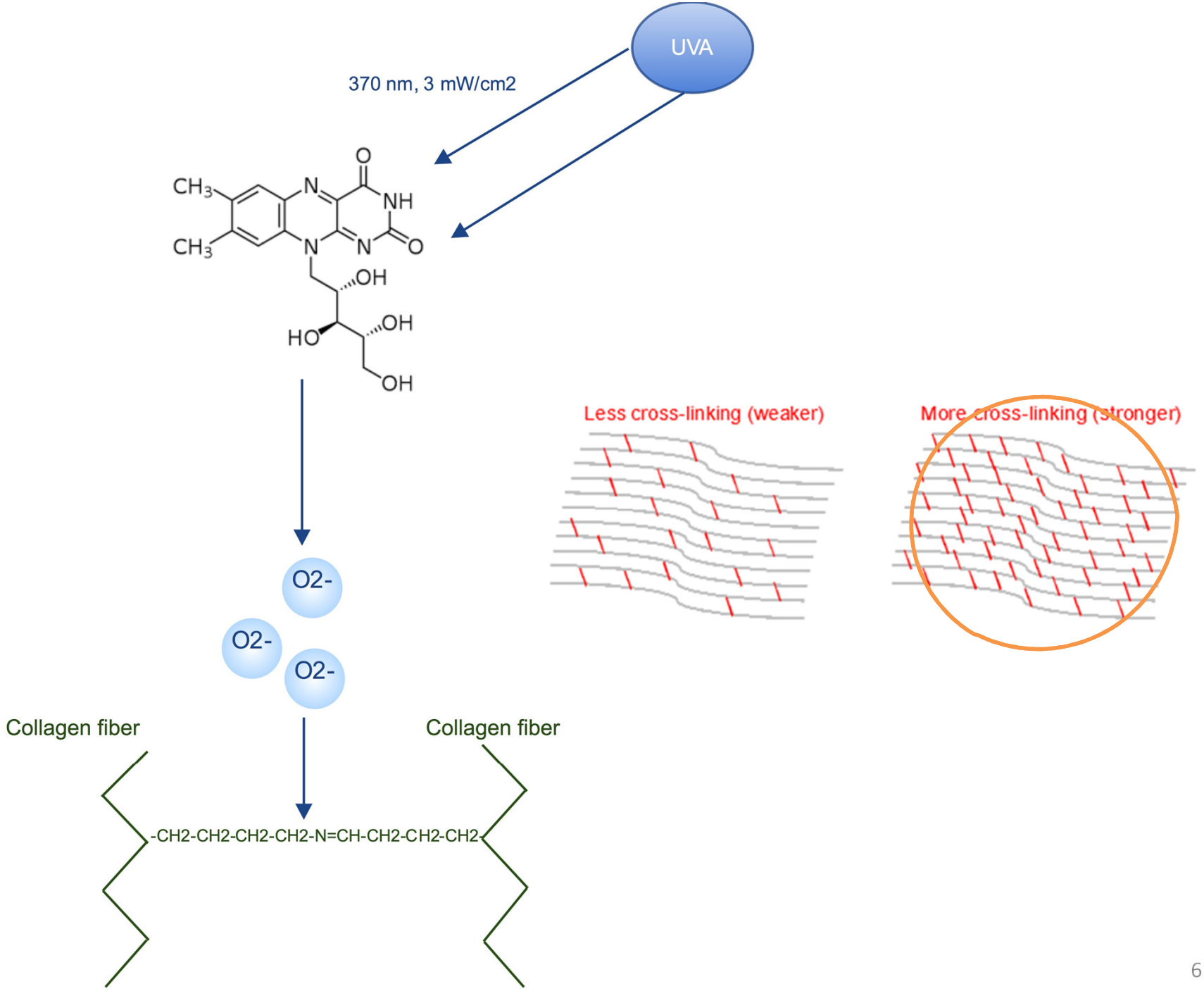
electromagnetic radiation with a wavelength from 400 nm to 100 nm, shorter than that of visible

INTRODUCTION



370nm


UVA
370 nm, 3 mW/cm2
O2-
O2-
O2-
Collagen fiber
Collagen fiber
-CH2-CH2-CH2-CH2-N=CH-CH2-CH2-CH2-
Less cross-linking (weaker)
More cross-linking (stronger)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PURPOSE

-In the present study we compared transepithelial CXL using iontophoresis with riboflavin to standard CXL in patients with progressive keratoconus to identify if the epi-on CXL by iontophoresis is equally effective.

MATERIAL AND METHODS

156 eyes of 126 patients patients with progressive keratoconus who underwent CXL procedure at Ufa Eye Research Institute from January 2010 to December 2014 with follow-up for 2 years.

The study was approved by the ethics committee of Ufa Eye Research Institute (Ref number 467.34.8469) following the tenets of the Declaration of Helsinki and local laws regarding research on human subjects and registered at ClinicalTrials.gov (NCT02456961)

MATERIAL AND METHODS

This study included 156 eyes from 126 patients:
- 87 men (64.4%) and 39 women (35.6%),
- aged 16–48 (average, 28.4 ± 2.5) years old.

- 149 eyes - progressive keratoconus I–III (Amsler classification (without stromal scarring)),
- 7 eyes had post-LASIK keratoectasia (2–4 years after LASIK).

Depending on the method of CXL, patients were divided into two groups:
- (1) 66 patients (77 eyes) - standard CXL,
- (2) 60 patients (79 eyes) - transepithelial CXL via iontophoresis.

MATERIAL AND METHODS

- INCLUSION CRITERIA

- <18 years old
- documented progression of disease: an increase in the steepest keratometry value by 1.0 diopter (D) or more in manifest cylinder, or an increase of 0.5 D or more in manifest spherical equivalent refraction by repeated keratotopography within 1 year.

- EXCLUSION CRITERIA

- pachymetry less than 400 µm,
- history of previous ocular infection (e.g. herpes),
- pregnancy or breastfeeding,
- corneal scarring.

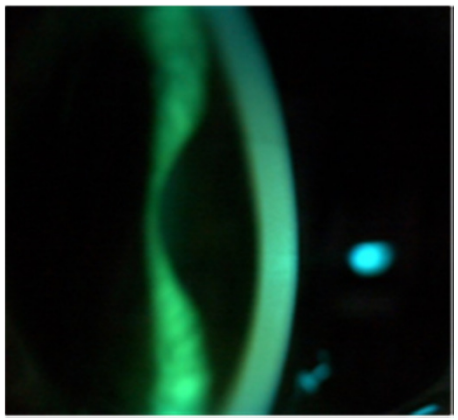
MATERIAL AND METHODS

Standard examination was done to assess :
- uncorrected distance visual acuity (UDVA),
- corrected distance visual acuity (CDVA),
- refractometry,
- keratometry,
- corneal topography (ODP-scan ARK-1000),
- pachymetry, and postoperative demarcation line depth (Visante OCT, Carl Zeiss, Germany).

Examination: at baseline, 1 week, and 1, 6 ,12, 24 months post CXL.

CXL

Standard CXL	*Transepithelial CXL*
The epi-off technique was performed following the Dresden protocol with - Epithelial removal (9 mm); - Application of riboflavin 0.1% with dextran (T-500); - Surface UVA irradiation at a 5-cm distance for 30 minutes. - During UVA exposure, riboflavin + dextran drops were continued every 2 minutes.	Impregnation of the cornea with a riboflavin 0.1% hypotonic solution was performed by using an iontophoresis device (galvanizator; Potok-1, Russian Federation) - Application of riboflavin 0.1% with dextran (T-500); - Surface UVA irradiation at a 5-cm distance for 30 minutes. - During UVA exposure, riboflavin + dextran drops were continued every 2 minutes.

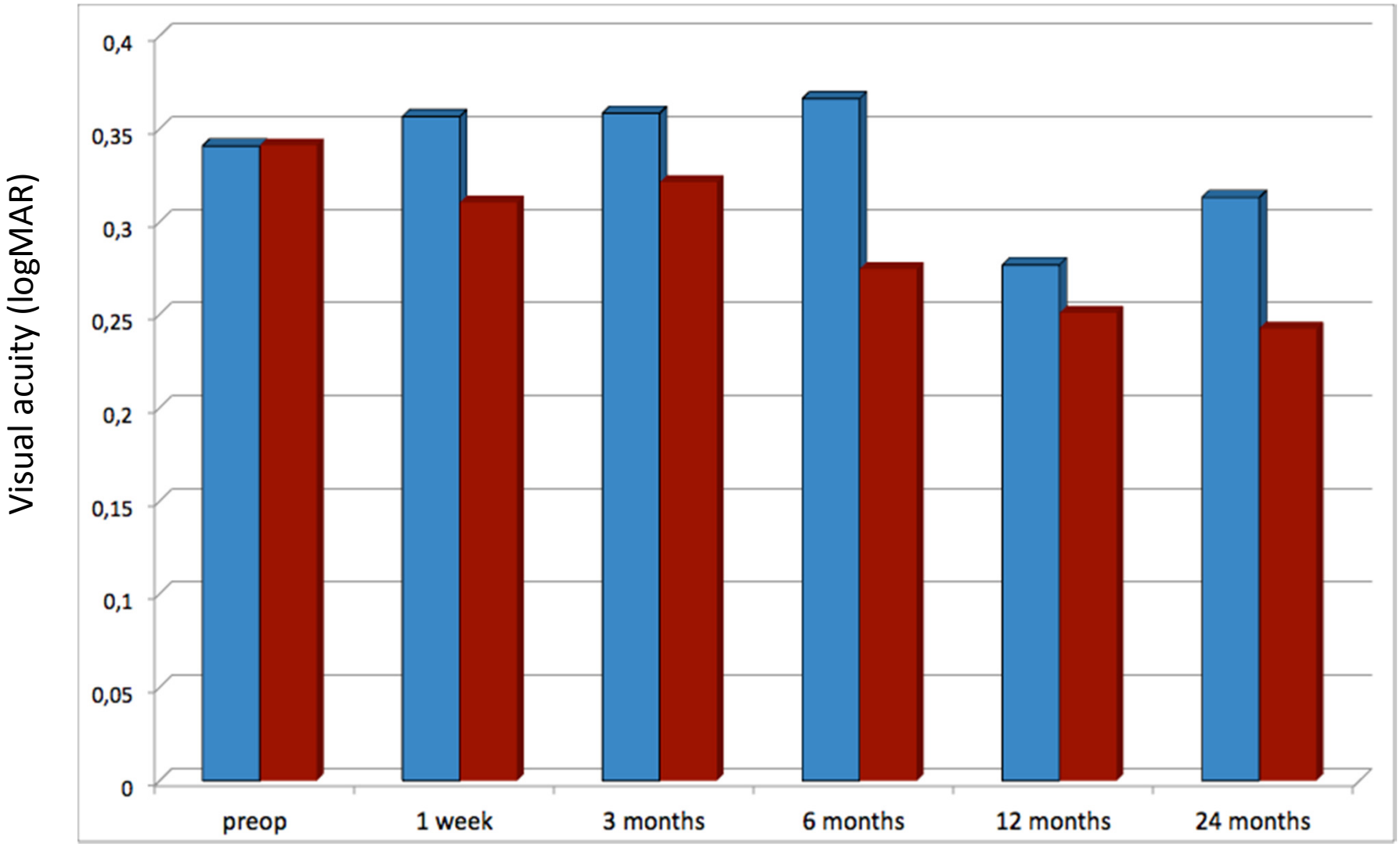


Bikbova, G. and Bikbov, M. (2014), Transepithelial corneal collagen cross-linking by iontophoresis of riboflavin. Acta Ophthalmologica, 92: e30–e34

Transepithelial via iontophoresis versus epi-off CXL for keratoconus, baseline characteristics (n = 156)

Parameter	Standard CXL (77 eyes)	Transepithelial CXL (79 eyes)
Age, y (range)	29 (18–42)	28 (18–44)
Keratometry, D (mean ± SD)	47.56 ± 3.45	46.90 ± 3.29
Uncorrected distance visual acuity, LogMAR (mean ± SD)	0.80 ± 0.46	0.82 ± 0.38
Spherical equivalent (D)	5.39 ± 3.84	3.95 ± 4.03
Corrected distance visual acuity, LogMAR (mean ± SD)	0.34 ± 0.32	0.34 ± 0.30
Pachymetry thinnest point, µm (mean ± SD)	486.52 ± 38.25	478.36 ± 46.68
Endothelium, cells/mm^2	2734 ± 296	2741 ± 315

CORRECTED DISTANCE VISUAL ACUITY



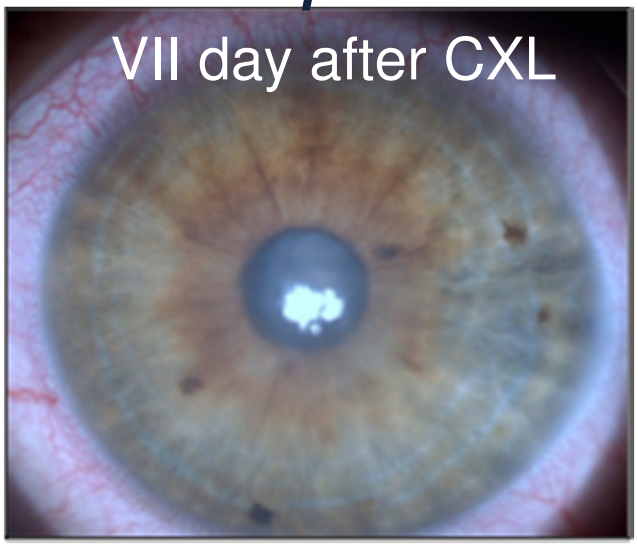
Difference in CDVA (LogMar) in standard vs transepithelial corneal crosslinking for keratoconus.

There was statistically significant difference in CDVA between two groups with better outcome in transepithelial CXL group (P= .042).

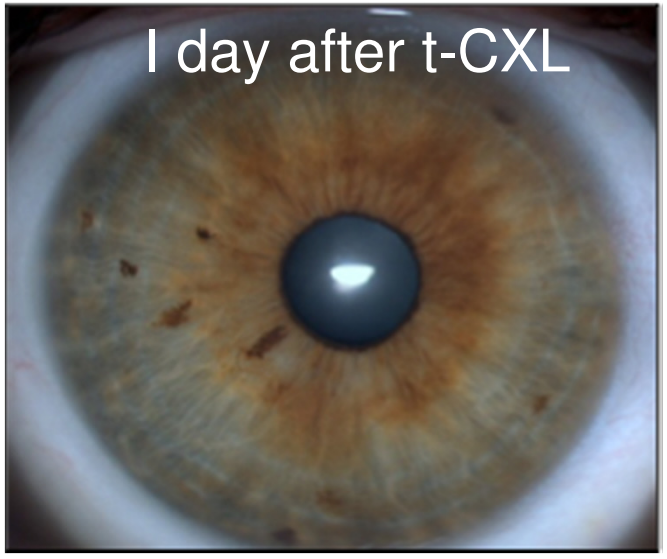
After 6 months there were the largest difference observed between two groups (P=.039), however no significant difference were found in 24 months after treatment (P=.851)

This difference in the CDVA over time between groups can be explained by the formation of haze in the first group and/or by epithelium remodeling postoperatively

Standard vs transepitelial CXL-?

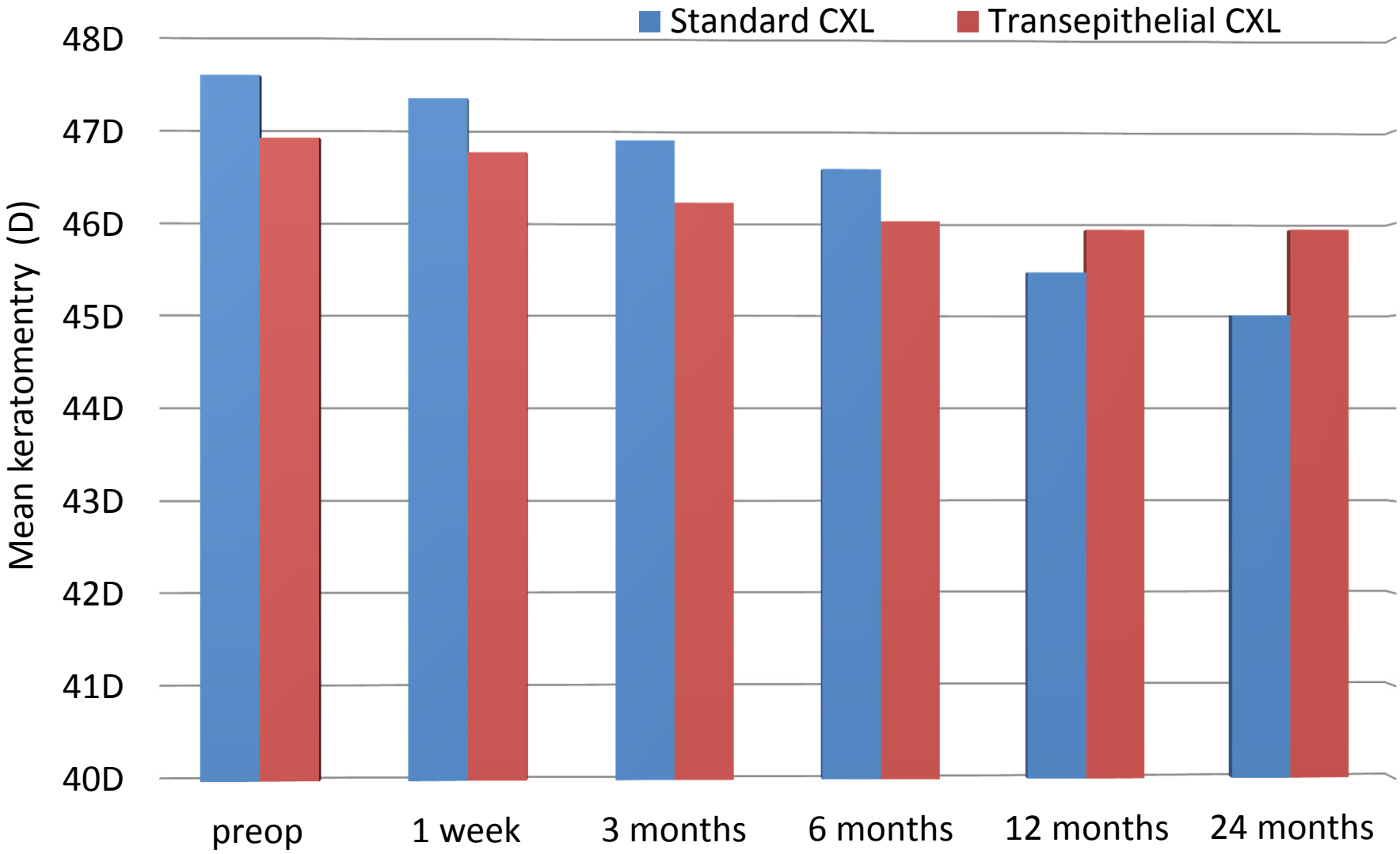


Standard CXL



transepithelial CXL

KERATOMETRY

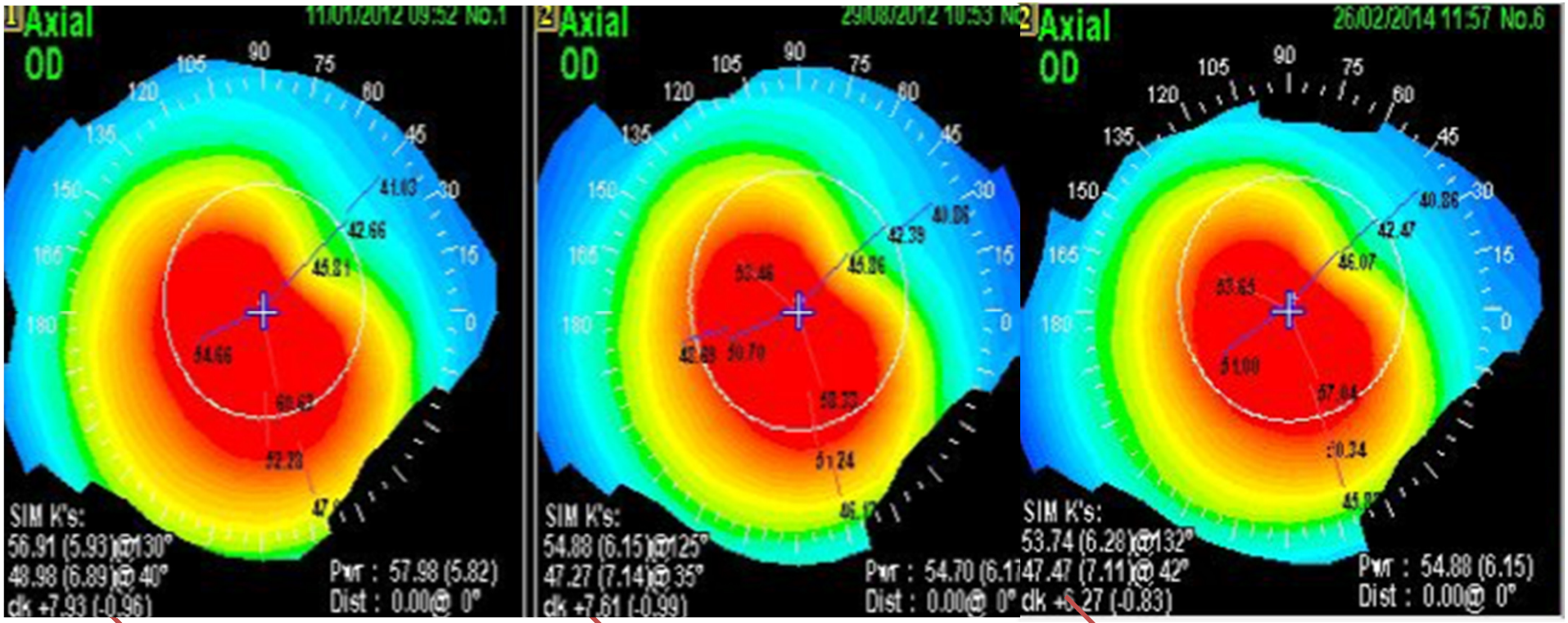


Difference in keratometry values in standard vs transepithelial corneal crosslinking for keratoconus.

KERATOMETRY

Patient K,23 y.o-preop

- 6 months after t-CXL
- 2 years after t-CXL



- 56,91
- 48,98

54,88

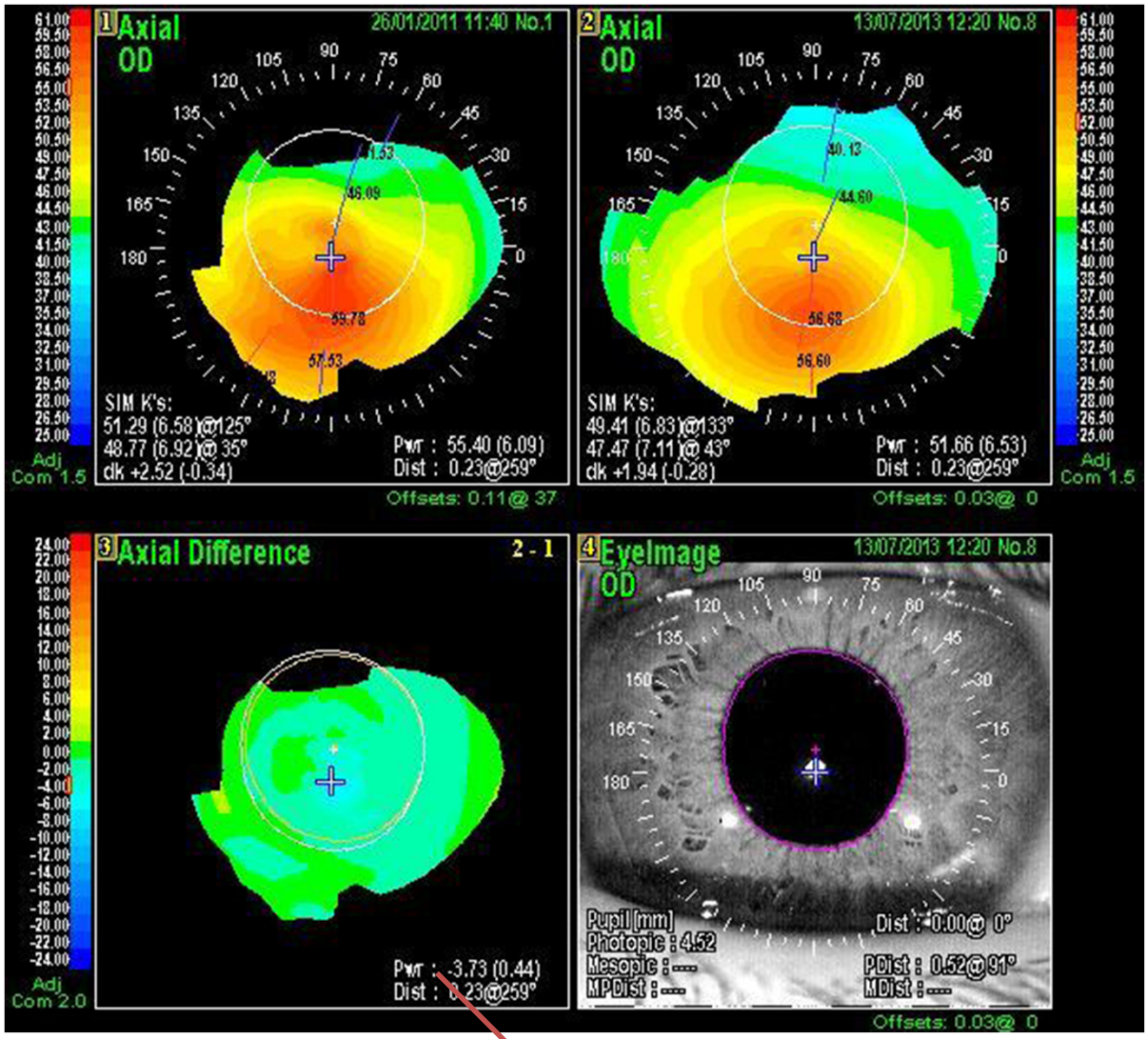
47,27

53,74

47,47

Patient SH, 28 y.o

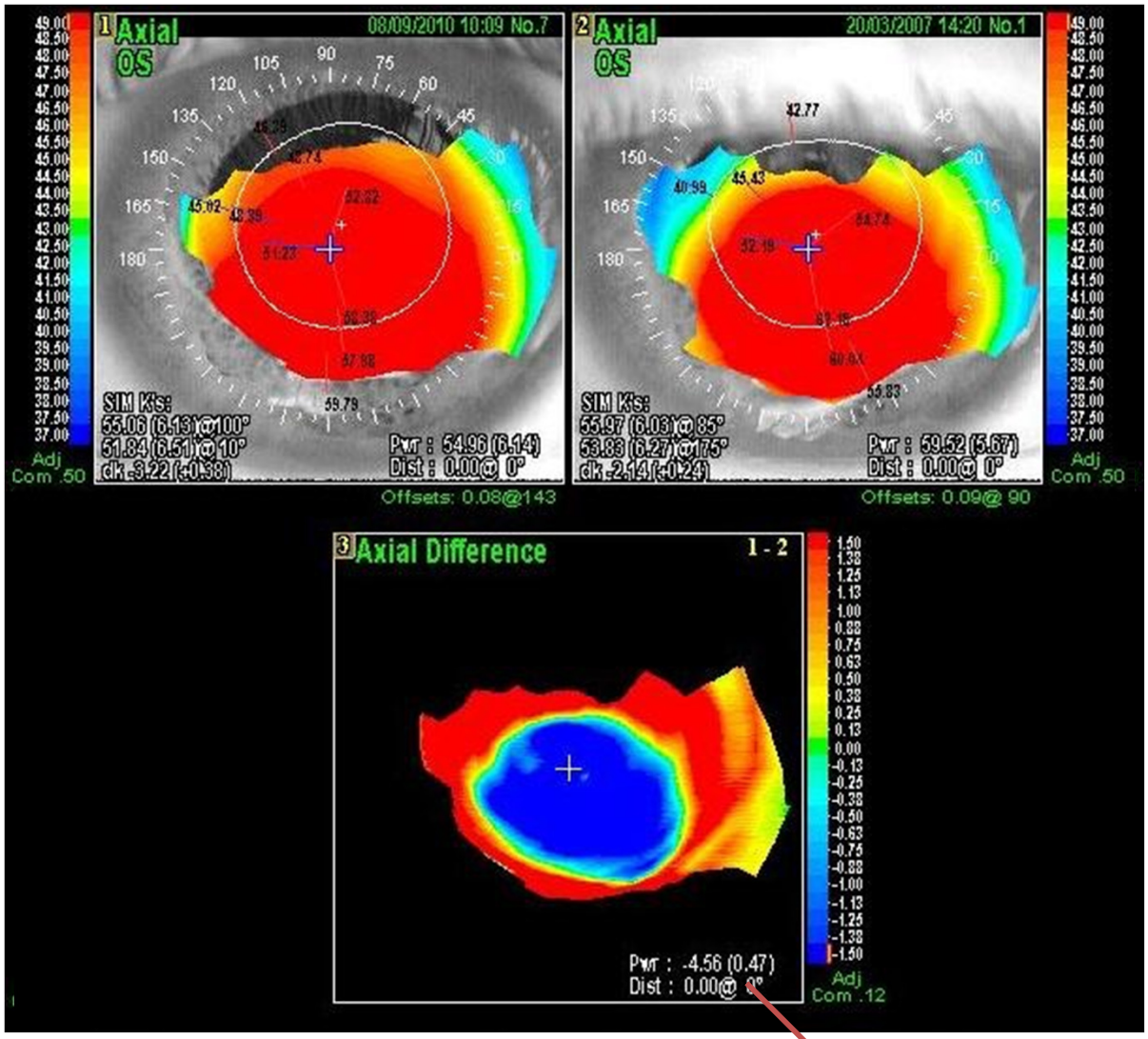
- preop
- 2 years after t-CXL



- -3,73D

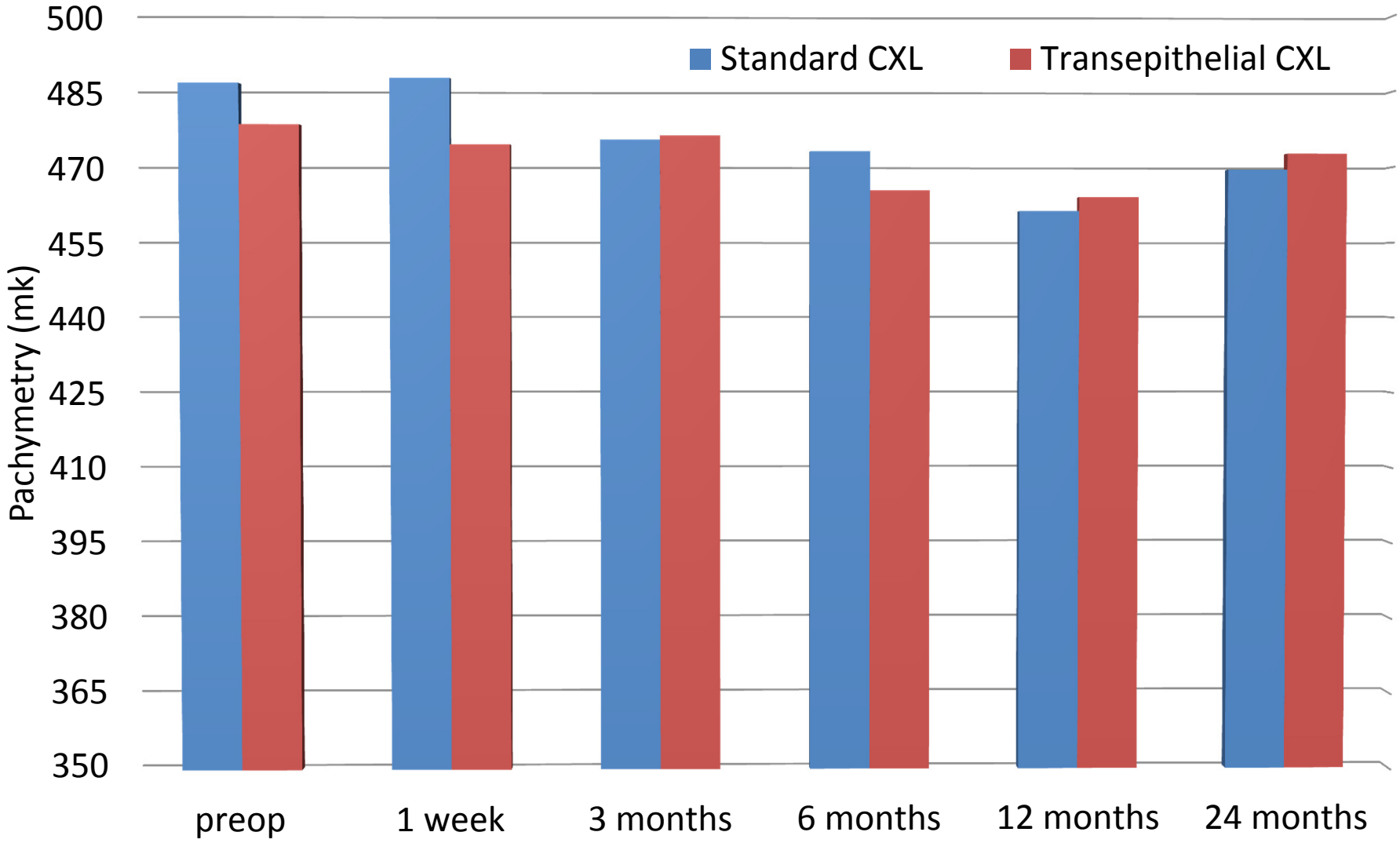
Patient T, 32 y.o

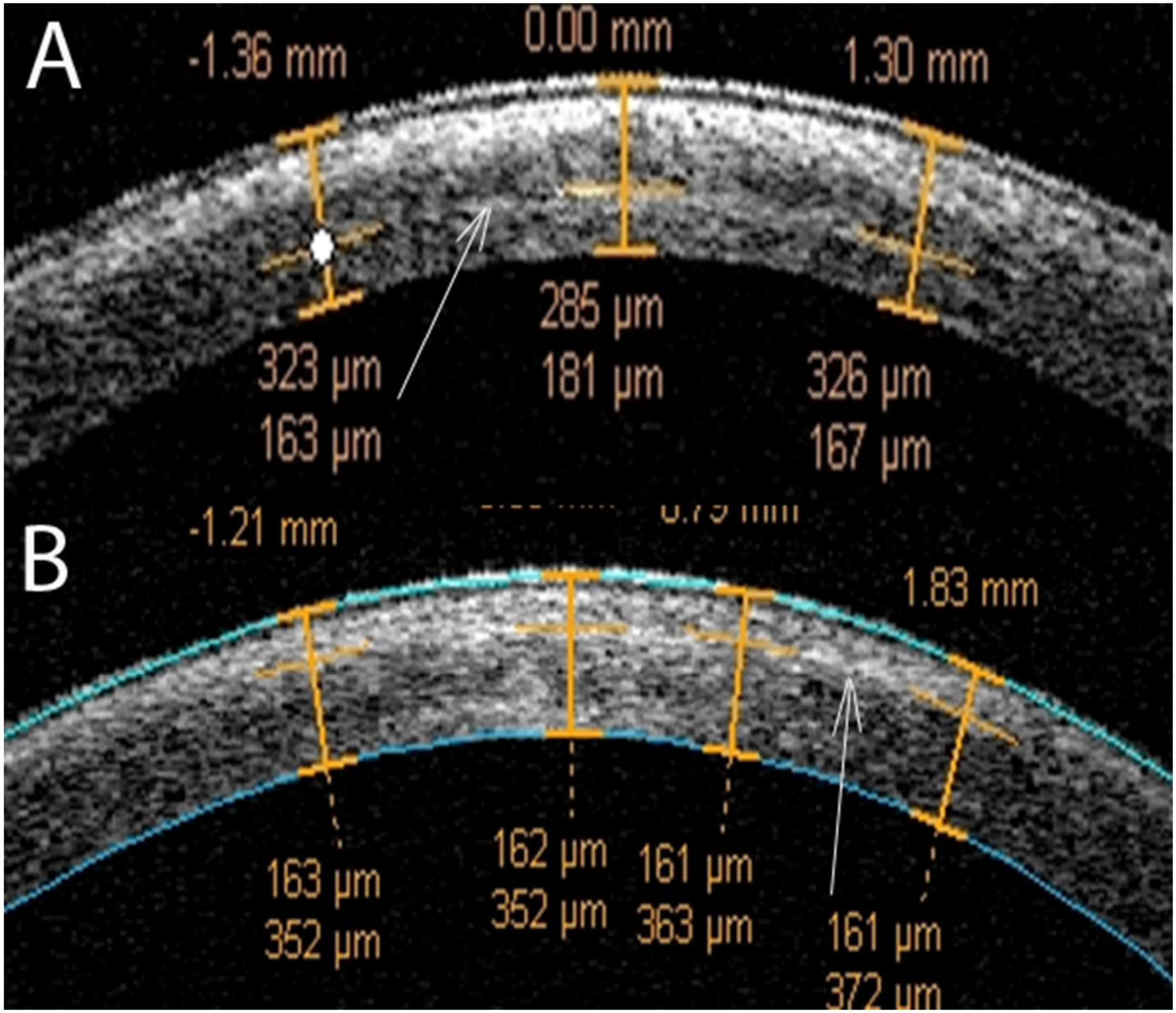
- 2 years after standard CXL
- preop



- -4,56D

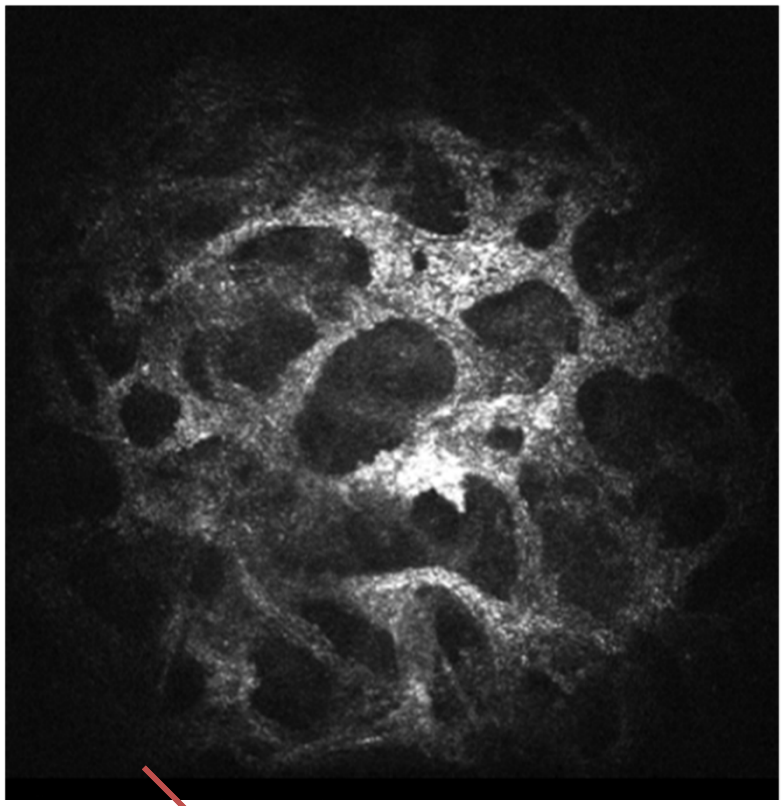
PACHYMETRY


500
485
470
455
440
425
410
395
380
365
350
Pachymetry (mk)
Standard CXL
Transepithelial CXL
preop
1 week
3 months
6 months
12 months
24 months



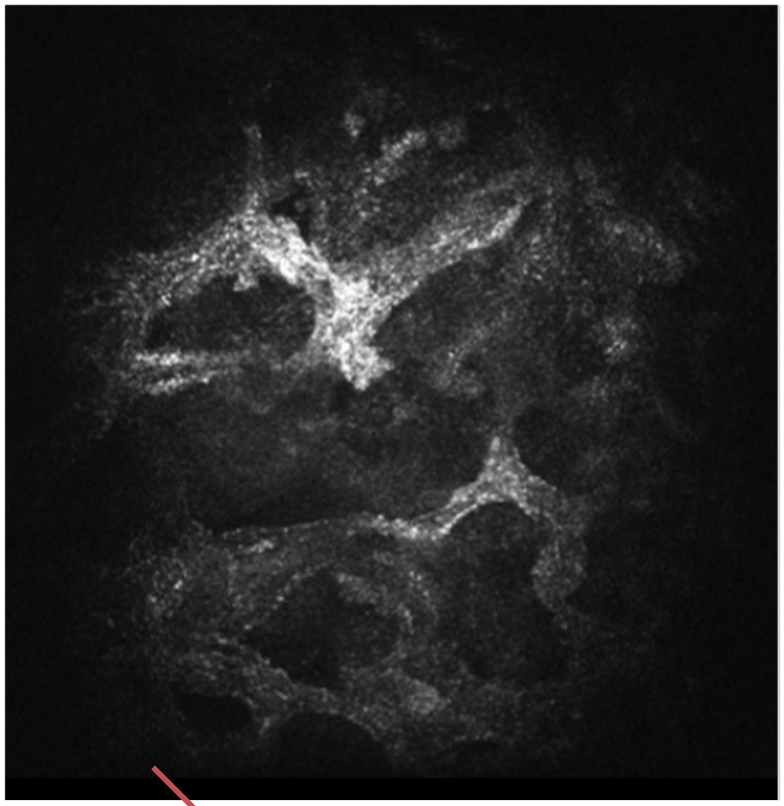
Demarcation line on OCT images of cornea; (top) after standard CXL, (bottom) after transepithelial CXL via iontophoresis. Arrows show the demarcation line.

Standard CXL



240-309 µm

t-CXL (ionto)



150-210 µm

DISCUSSION

Transepithelial CXL via iontophoresis of riboflavin was effective to stop keratoconus progression after 2 years, with a statistically significant improvement in the visual and topographic parameters.

Demarcation line was more superficial and pachymetry reduction was less compared to patients with standard CXL treatment.

Demarcation line was observed in only 48% patients 1 month after transepithelial CXL and was completely absent in all these patients at 3 months post-CXL.

The average keratometry decrease in 2 years in the standard CXL group was more significant (-2,06 D) comparing with the transepithelial group (-0,97 D).

The transepithelial CXL group also had a significant CDVA increase. This difference in the CDVA over time between groups may be explained by the formation of haze in the first group and/or by epithelial remodelling postoperatively

CONCLUSION

Transepithelial collagen crosslinking by iontophoresis is an effective method for riboflavin impregnation of the corneal stroma and prevention of the progression of keratoconus.

It also significantly reduces the duration of the procedure and makes it more comfortable for the patients. However, the effectiveness of procedure is reduced, probably because of an insufficient supply of riboflavin during UVA irradiation.

Nevertheless, even with a smaller effect, stabilization of disease was achieved for 24 months, and this procedure can be recommended for use with thin corneas, in pain-intolerant patients, and in older patients with slowly progressing keratoconus

Thank you.