

Transepithelial corneal cross-linking using an enhanced riboflavin solution



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Transepithelial CXL

- ▶ **intact epithelium** = barrier for riboflavin
- pharmacological cleavage of tight-junctions with
 - BAC, chlorobutanol, EDTA, gentamicin, tetracaine
- intrastromal application of riboflavin (pockets)
- injection of riboflavin into the stroma (needles)
- iontophoresis



Transepithelial CXL

- „...Safety would be enhanced with a transepithelial procedure that keeps the epithelial barrier function intact and avoids wound-response reactions in the stroma....“:
- persistent epithelial defects
- melting processes
- infections
- developing of permanent stromal scars



Transepithelial CXL

- „...designed to **avoid** the early postoperative **pain** and temporary **worsening of vision**...“



Transepithelial CXL

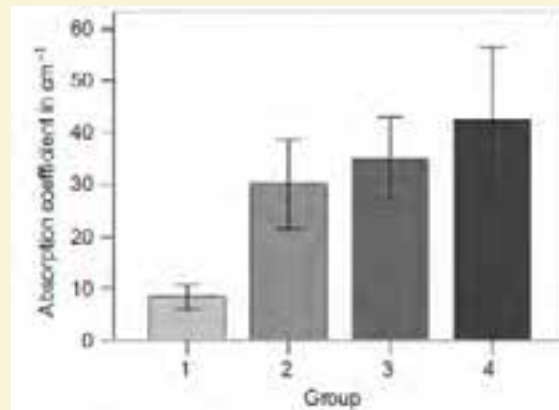


FIGURE 2. The absorption coefficients of group 2 (BAC 0.02%) as well as of groups 3 (BAC 0.04%) and 4 (epithelial debridement) significantly increased as compared to group 1 (intact epithelium). Statistical analysis found no difference among groups 2, 3, and 4 with regard to the absorption coefficient.

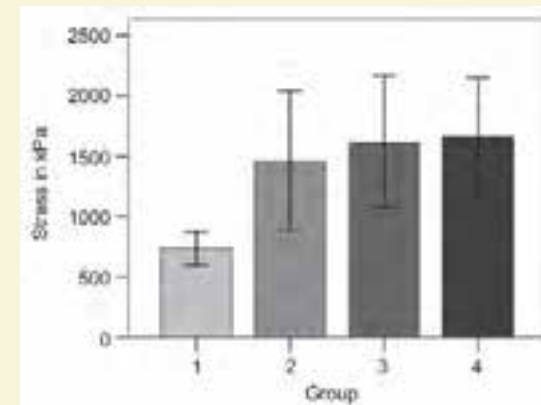
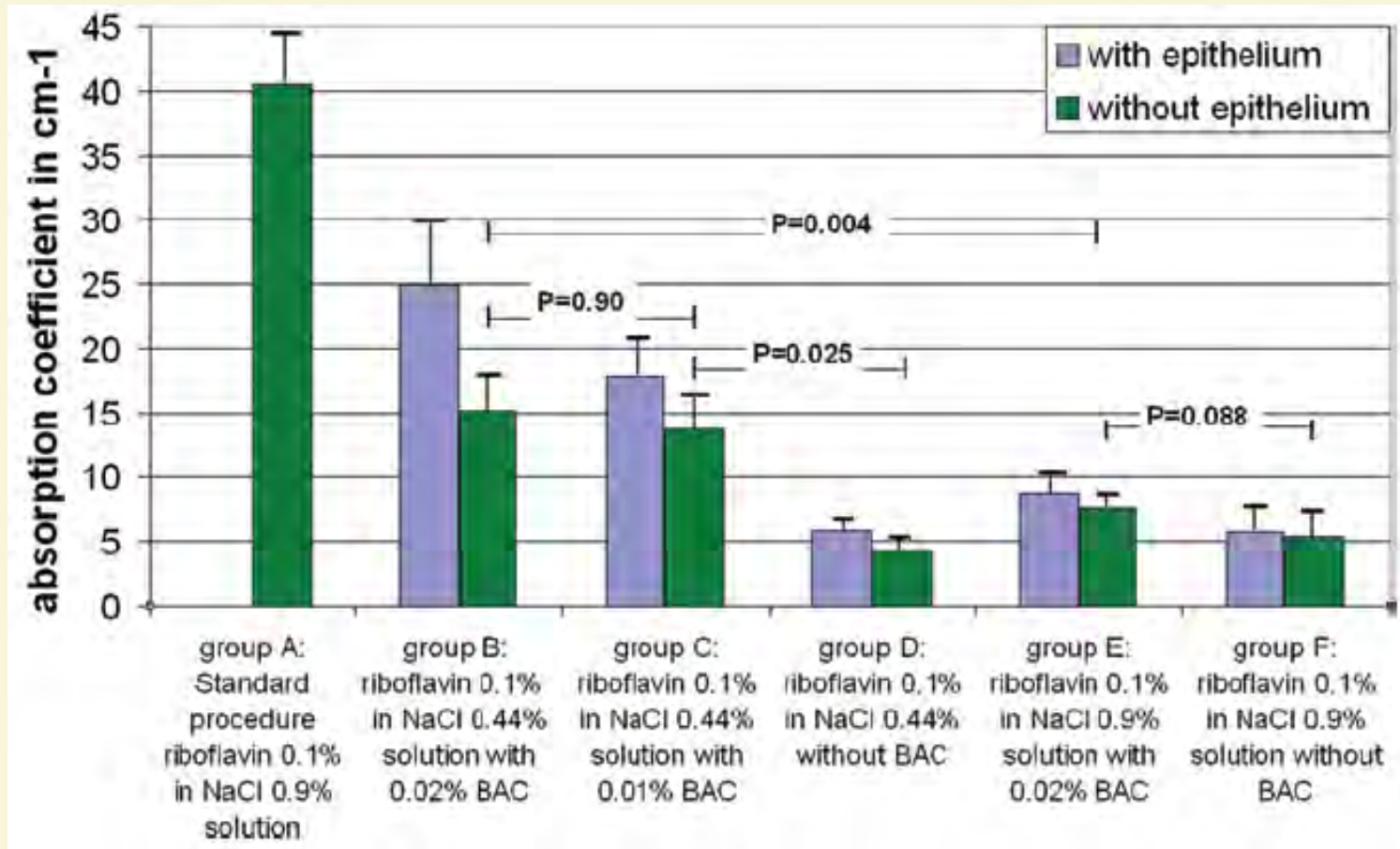


FIGURE 3. Stress values for 10% strain in kPa. Significant stiffening effects were found in group 2 (BAC 0.02%), group 3 (BAC 0.04%), and group 4 (standard protocol) as compared to group 1 (intact epithelium). There were no statistically significant differences among groups 2, 3, and 4.



Transepithelial CXL





Transepithelial Corneal Cross-linking Using an Enhanced Riboflavin Solution

Zisis Gatzoufas, MD, PhD; Frederik Raiskup, MD, PhD, FEBO; David O'Brart, FRCS, FRCOphth, MD; Eberhard Spoerl, PhD; Georgios D. Panos, MD(Res); Farhad Hafezi, MD, PhD

- prospective, interventional multicenter cohort study
- 26 eyes of 26 patients
- 16 ♂, 10 ♀
- Age: 27,6±6,4y.
- F/U: 12m.



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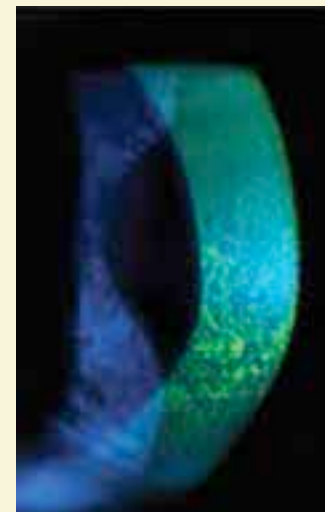
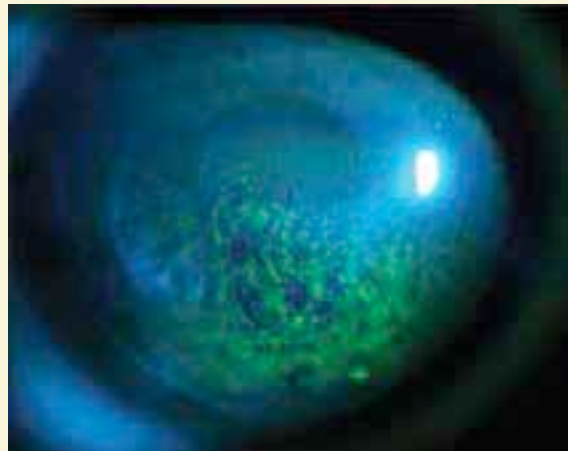
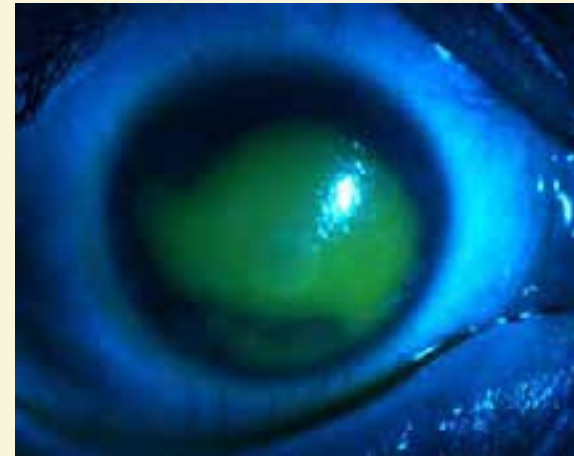
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- proparacaine 0,5% drops instilled 5 min. before the procedure
- modified riboflavin solution instilled every minute for 30 min.
- pachymetry
- CXL: 9mW/cm² for 10 min.



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TABLE 1
Clinical Outcomes After Transepithelial Corneal Cross-linking at 6 and 12 Months Postoperatively

Parameter	Baseline	6 Months	12 Months	P
Kmax (D)	59.5 ± 9.0 (35.6 to 75.2)	59.4 ± 8.9 (35.6 to 75.2)	59.2 ± 8.8 (35.3 to 74.4)	.86
UCVA (logMAR)	0.97 ± 0.97 (0.52 to 1.30)	1.02 ± 0.24 (0.70 to 1.30)	1.00 ± 0.28 (0.40 to 1.30)	.52
CDVA (logMAR)	0.53 ± 0.54 (0.22 to 1.00)	0.59 ± 0.28 (0.22 to 1.30)	0.57 ± 0.22 (0.22 to 1.00)	.14
CTP (μm)	417 ± 14 (301 to 456)	414 ± 14 (290 to 445)	412 ± 15 (285 to 446)	< .01

Kmax = maximum keratometry; D = diopters; UCVA = uncorrected visual acuity; CDVA = corrected distance visual acuity; CTP = corneal thinnest point

- postop. epithelial defects in 46%
- marked SPK's or loose epithelium 23%
- failure in 46% (increase > 1,0 D in Kmax at 12 m. after TE-CXL)
- no infection, sterile infiltrates, haze



Transepithelial CXL: Literature

- Filippello M, Stagni E, O'Brart D. JCRS 2012: „...**appeared to halt keratoconus progression, with a statistically significant improvement in visual acuity and topographic parameters**“ **cohort study**
 - Lesniak SP, Hersh PS. JCRS 2016: „...**statistically significant improvement in maximum K values and CDVA at the 6-month follow-up.**“ **prospective clinical trial**
-
- Leccisotti A, Islam T. JRS 2010: „ **A limited but favorable effect ... The effect appears to be less pronounced than ...CXL with de-epithelialization.**“ **prospective, consecutive study**
 - Koppen C, Wouters K, Mathysen D et al. JCRS 2012: „**Transepithelial CXL ...less effective than standard CXL...**“ **cohort study**



Transepithelial CXL: Literature

- Caporossi A, Mazzotta C, Paradiso AL et al. JCRS 2013: „**Functional results after TE-CXL showed keratoconus instability, in particular in pediatric patients...**“ **prospective case series**
- Kocak I, Aydin A, Kaya F et al. JFO 2014: „**...TE-CXL does not effectively halt the progression of keratoconus...**“ **prospective case series**



Transepithelial CXL: Literature

- Touboul D, Efron N, Smadja D et al. JRS 2012: „**In vivo corneal confocal microscopy ...TE-CXL did not appear to alter corneal morphology.**“
- Caporossi A, Mazzotta C, Baiocchi S et al. EJO 2012: „**...TE-CXL showed a limited apoptotic effect..., about one-third of classic epi-off...**“
- Mastropasqua L, Nubile M, Lanzini M et al. Cornea 2013: „**...marked corneal modification, which were poorly evident in the TE-CXL...**“



Transepithelial CXL (???)

- „Methods: **Gentamicin, BAC, EDTA** were instilled for **3 hours**, then **oxybuprocaine** for **30 min**. Riboflavin 0.1% in 20% dextran T500 and **oxybuprocaine** were instilled for **30 min**. Finally, UVA irradiation to the central 7.5mm of the cornea was applied for **30 min**, while **riboflavin** was instilled every 5 min.“



Transepithelial CXL: Future?

- Bottos KM, Oliveira AG, Bersanetti PA et al. PLoS ONE 2013 8(6):
„**Riboflavin nanoemulsion was able to penetrate the corneal epithelium...**“
- Torricelli AAM, Ford MR, Singh V et al. Exp Eye Res 2014:
BAC-EDTA transepithelial riboflavin-UVA crosslinking has greater biomechanical stiffening effect than standard epithelium-off in rabbit corneas.



29-y. ♂ CDVA (CL)=0,8

- 12/2008: LE CXL standard protocol:
 K_{apex} : 72,58D \rightarrow 62,38D
- K_{apex} : 60,2D \rightarrow 61,5D
01/2014: LE TE-CXL (CT 380 μ m)
 K_{apex} : 60,5D
- K_{apex} : 64,3D 11/2016: LE CXL (CT 377 μ m, \emptyset epithelium 338 μ m, after hypoosmolar solution 493 μ m)

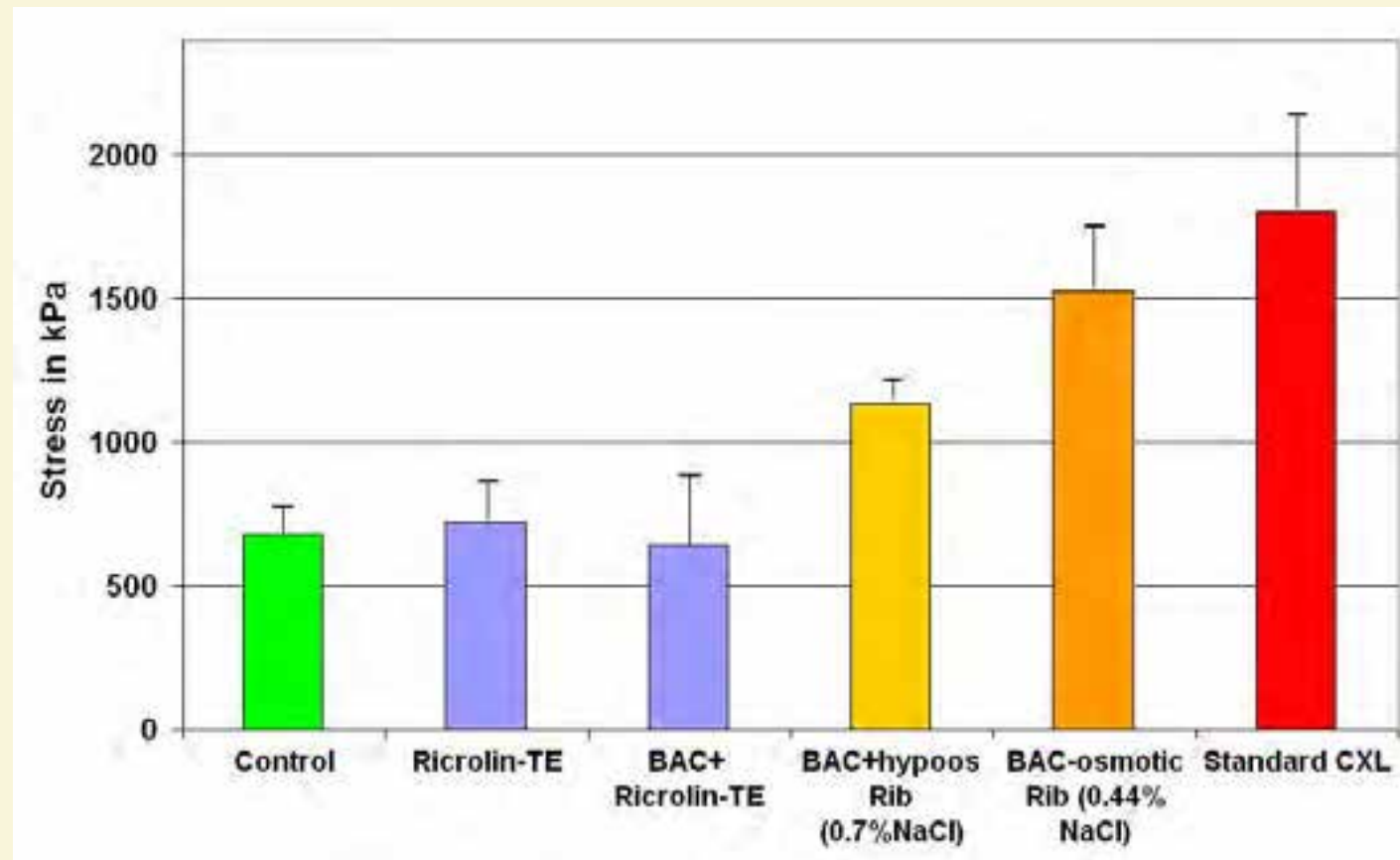


3 weeks after TE-CXL: AS OCT





Transepithelial CXL



no dextran, hypoosomolar solution, 0.01 %BAC