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Patient and methods: A patient with bilateral keratoconus underwent bilateral CXL with a stabilization of corneal topography after treatment. Customized PRK (topography-guided) was performed in the left eye at 2 years after CXL.

Results: Immediately after PRK the eye showed progression of the keratoconus, whereas the right eye treated by CXL only remained stable.

Conclusion: PRK after CXL might be a treatment option in particular cases, however, with the risk of re-progression. More information is needed about indications and contraindications of this approach.
Keratoconus exacerbation after cross-linking and surface ablation – a case report

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Abstract

**Purpose:** Topography-guided photorefractive keratectomy (PRK) in cases of forme fruste keratoconus is considered a treatment option for optical rehabilitation. Recently this approach was proposed for keratoconus corneas after corneal cross-linking (CXL). We report a case where the photoablation reinitiated progression of keratoconus.

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**Conclusion:** PRK after CXL might be a treatment option in particular cases, however, with the risk of re-progression. More information is needed about indications and contraindications of this approach.
Biomechanical [1] and biochemical [2] properties of the cornea can be modified by means of cross-linking using ultraviolet (UV) light in combination with riboflavin (CXL). This treatment stiffens the cornea and as a consequence may inhibit progression of keratoconus [3] or iatrogenic keratectasia [4]. Other promising applications of corneal cross-linking (CXL) are currently under investigation such as arrest of corneal melting [5], reduction of corneal stroma edema in Fuchs dystrophy [6], and CXL in combination with intrastromal rings [7].

Once the progression of keratoconus is stopped after CXL there is still the question of optical rehabilitation. Although most of the patients can go back to contact lenses in some cases of contact lens-intolerance alternatives of optical rehabilitation are necessary such as intrastromal rings and shallow surface ablation. Kanellopoulos [8] recently reported a case of successful PRK treatment in a keratoconus eye that had previously been cross-linked.

In this case report, we present a keratoconus patient with successful stabilization of the cornea after CXL for more than two years and with immediate re-progression of keratoconus after a subsequent PRK.
Patient and Methods

A 21 year old male patient suffering from keratoconus underwent CXL in both eyes in 2004 at the University Eye Clinic, Dresden, Germany. Keratoconus progression was documented in the years before CXL by Scheimpflug topography (Pentacam, Oculus, Wetzlar, Germany). Postoperative topography documented a halt in progression of keratoconus during 2 years after CXL. Uncorrected visual acuity (UCVA) was 20/100 in the right eye and 20/200 in the left eye and best spectacle-corrected visual acuity (BSCVA) was 20/40 OD (manifest refraction -1.75 cyl -1.0 X 20) and 20/40 OS (manifest refraction -0.5 cyl -3.0 X 180). By means of a pin hole, BSCVA was 20/30 in both eyes. Slit lamp examination revealed discrete anterior stromal scarring in both eyes and Vogt-striae in the left eye, but no demarcation line. Corneal ultrasound pachymetry (SP-2000, Tomey, Nagoya, Japan) yielded a central thickness of 460µm in the right and 405µm in left eye with a thinnest reading of 385µm at the cone peak. Corneal topography (Pentacam, true net power, Fig. 1a) demonstrated a typical keratoconus with steepest K-readings of approximately 56 D in both eyes. The patient could neither tolerate rigid nor soft contact lenses and was not satisfied with the visual acuity obtained with glasses. Treatment alternatives such as intrastromal rings and deep lamellar keratoplasty were discussed but the patient preferred a shallow surface ablation for his non-dominant left eye with the perspective that a deep lamellar keratoplasty was still an option even if keratoconus progression would be reinitiated by the ablation.
CXL

CXL was performed at the Department of Ophthalmology of the University Hospital Dresden, Dresden, Germany using an early version of the treatment parameters [3] differing from the currently used technique in a shorter application of riboflavin of only 10 minutes. All other parameters such as irradiation time, UV fluence, wavelength, riboflavin concentration and medical postoperative management were similar to the current standard procedure [9].

PRK

After a manual abrasion of the epithelium ultrasound pachymetry yielded a stromal thickness of 355 microns at the thinnest point. A customized surface ablation (T-CAT, WaveLight, Erlangen, Germany) based on Scheimpflug imaging was performed with an optical zone of 5.0 mm in diameter and an attempted hyperopic correction of +5.0 cyl -3.0 X 179 aiming on a target refraction of approximately -4.0D. The strong hyperopic treatment was used to save tissue in the central cornea and at the cone peak [10]. The photoablation was achieved with the Concerto excimer laser (WaveLight, Erlangen, Germany) working at a repetition rate of 500 Hz. At the end of the treatment, mitomycin 0.02% was applied for 30 seconds followed by irrigation with chilled balanced salt solution. After the treatment, a bandage lens soaked with 0.3 % preservative-free ofloxacin (Floxal UD, Chauvin Novopharma AG, Steinhausen, Switzerland) was applied and Floxal drops were applied until the epithelium was healed.
Results

The right eye with CXL only continued to demonstrate stable corneal topographies.

Prior to the photoablation performed at 2.5 years after CXL, the left eye showed similar findings.

Already 3 days after PRK at the slit lamp a protrusion of the central cornea was visible and at one month post PRL keratoconus had clearly progressed (Fig. 2b) with a BSCVA of 20/200 (manifest refraction -4.0 cyl -5.0 X 170). This progression continued until 6 months after PRK as documented by corneal topography (Fig. 2c) and refraction (BSCVA of 20/200 with a manifest refraction of -12.0 cyl -6.0 X 05). At this point we proposed a deep lamellar keratoplasty.
Discussion

Cases of forme fruste keratoconus (achieved naturally or by means of CXL) and contact lens intolerance have not many options to achieve a sufficient visual acuity. Spherocylindrical spectacle correction cannot compensate for the irregular component of the astigmatism and keratoplasty is not yet appropriate regarding the relatively good BSCVA of 20/40 [10]. The remaining alternatives include intrastromal rings and surface ablation.

The main problem of surface ablation after CXL is an unknown requirement regarding the residual thickness of the stromal bed to prevent progression of the keratoconus cornea. Only few cases are reported with surface ablation in formes frustes of keratoconus [11] and only one case was so far presented with customized PRK after CXL[8]. Corneal cross-linking is a treatment option for progressive keratectasia with small complication and failure rates [12] because stiffening of the extracellular matrix a biomechanical stabilization of the cornea is obtained. In other words, the progressive form of a keratoconus is turned into its abortive form, the forme fruste. The cross-linking effect is limited to the anterior corneal stroma up to a depth of 270 to 330 µm [13]. Since also in the normal human cornea, the anterior stroma has a higher biomechanical strength compared to the posterior part [14] CXL reestablishes the natural stiffness-gradient across the keratoconus cornea. Experimental data demonstrated that the biomechanics of the keratoconus cornea is probably a factor of 2 weaker compared to the normal cornea [15]. On the other hand, corneal rigidity is increased after CXL by a factor 4 [14]. Therefore, CXL may compensate for the biomechanical weakness of the keratoconic cornea.
In regular corneas gross estimations led to a minimal residual stromal thickness after LASIK of 250µm [16]. Later on, cases of iatrogenic keratectasia in corneas thicker than 250 µm were reported [17] and today we recommend a residual stromal thickness of 300 microns.

In analogy, in keratoconic eyes after CXL a minimal residual stromal thickness of at least 300 µm could be assumed to maintain corneal stability and to prevent keratoconus progression.

In the case presented the corneal thickness at the thinnest point was 355 µm after epithelium removal. Fig. 2a demonstrates the ablation pattern for the target emmetropia with an ablation depth of approximately 48µm at the point of thinnest stroma. Adding some hyperopia correction aiming on a target myopia of -4.0D the ablation depth at the thinnest point is only 16µm (Fig 2b).

The residual stromal thickness in this case is still 340µm and, therefore, we speculated the thickness to be sufficient even after PRK treatment to maintain corneal stability. However, the re-progression of keratoconus suggest an insufficient residual stromal thickness or an inadequate biomechanical strength of the cornea although CXL was performed.

Forme fruste keratoconus (FFKC) may serve as a model for the keratoconus cornea post CXL. In FFKC the cornea has regained its biomechanical stability without surgical intervention most probably due to an age-related increase in collagen cross-links [19]. In such cases, surface ablation can help to improve the optical homogeneity of the corneal surface [11, 19, 20].

However, strict inclusion criteria were accepted in the small pilot series of patients presented: among others residual central corneal thickness (ultrasound) was higher than 450 microns and the ablation depth was less than 50 microns [11]. Comparing these inclusion criteria of our study on surface ablation in FFKC with the case presented here, we fell short regarding age (21 years instead of >25years), corneal thickness (385µm instead of >500µm), residual stromal thickness (325µm instead of >450 µm) and K-readings (56D instead of <49D). The outcome of this case
indicates that the lower limit of 450 μm for residual corneal thickness applied in FFCK-cases (450μm) should also be maintained after CXL rather than that of normal corneas (300μm).

Another reason for the failure in this patient may be insufficient corneal stiffening due to the inappropriate CXL technique. The current protocol of riboflavin/UVA cross-linking includes riboflavin application for 30 minutes prior to UV-irradiation [9]. An application time of only 10 minutes (as performed in this case) significantly reduces the intrastromal riboflavin concentration and, therefore, radical formation rate and number of cross-links [9].

In summary, we present a case of successful CXL in a cornea with progressive keratoconus. After surface ablation with only minimal ablation depth over the thinnest area of the cornea the keratoconus decompensated and significant progression occurred. Before using surface ablation as a standard option after CXL, better recommendations for inclusion criteria especially the residual stromal thickness have to be established.
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Legends

Fig. 1
(1a) Corneal topography at 2 ½ years after CXL (arrow indicates thinnest point of the cornea) prior to PRK. (1b) Corneal topography of the same eye at 1 month and (1.c) at 6 months after PRK.

Fig. 2
Topography-guided ablation pattern with target refraction emmetropia (2a) and myopia of -4.0 D (2b). The ablation depths shown in the lower right corner (act) indicate the ablation at the thinnest point.
Figure
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Figure