

Central Corneal Regularization – Optimization of Uncorrected Visual Acuity in Keratoconus Patients

Central Corneal Regularization – Optimierung des unkorrigierten Visus bei Keratokonuspatienten

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Schlüsselwörter

- Central Corneal Regularization
- Oberflächenlaser
- Cross-linking
- Keratokonus

Key words

- central corneal regularization
- surface ablation
- cross-linking
- keratoconus

Abstract

Background: Combined excimer laser correction and corneal cross-linking is a promising concept in treating keratoconus patients. Central corneal regularization represents advanced topography-guided custom ablation for ectatic corneas, aiming at correcting irregular astigmatism and at increasing the optical regularity of the corneal surface.

Patients and Methods: In a prospective single centre study, 10 keratoconus patients underwent combined treatment with corneal cross-linking and central corneal regularization by an iRES-Laser. Uncorrected visual acuity at 1 and 3 months postoperatively represented the primary endpoint.

Results: Mean preoperative uncorrected decimal visual acuity was 0.15 (\pm 0.28 standard deviation). Mean postoperative visual acuity was 0.28 (\pm 0.47) at one month and 0.24 (\pm 0.25) at three months, respectively.

Conclusions: Combined corneal cross-linking and central corneal regularization treatment has the potential to achieve a clinically significant improvement of uncorrected visual acuity.

Zusammenfassung

Hintergrund: Die Kombination von Excimerlaser-Behandlung und kornealem Cross-linking ist ein vielversprechendes Konzept für die Behandlung von Keratokonuspatienten. Central Corneal Regularization stellt eine neuartige, topografiegeführte Laserabtragung für ektatische Hornhäute dar, die auf eine optimal reguläre Oberfläche abzielt.

Patienten und Methoden: In einer prospektiven monozentrischen Studie wurden 10 Keratokonuspatienten einer kombinierten Behandlung aus kornealem Cross-linking und Central Corneal Regularization mit dem iRES-Laser unterzogen. Primärer Endpunkt war die Entwicklung des unkorrigierten Visus 1 und 3 Monate nach Behandlung.

Ergebnisse: Der mittlere unkorrigierte Dezimalvisus betrug präoperativ 0,15 (\pm 0,28 Standardabweichung). Postoperativ betrug der Visus 0,28 (\pm 0,47) nach einem bzw. 0,24 (\pm 0,25) nach 3 Monaten.

Schlussfolgerungen: Die Kombination aus kornealem Cross-linking und Central Corneal Regularization hat das Potenzial, den unkorrigierten Visus von Keratokonuspatienten klinisch signifikant zu verbessern.

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Background

Keratoconus represents a chronic progressive disease in which ectasia and distortion of the cornea lead to deteriorating visual acuity due to induced myopia and irregular astigmatism (● Fig. 1 a, b). With corneal cross-linking (CXL), a semi-surgical treatment is available that stops keratoconus progression and hence preserves visual acuity. In order to improve visual acuity rather than just preserving it, CXL can be combined with precedent same-day excimer laser surface ablation. The original concept used transepithelial topography-

guided photorefractive keratectomy and was first described by Kanellopoulos et al [1]. With the development of the iVIS™ suite (Ligi Technologie Medicali s.r.l., Taranto, Italy), a surgical platform was introduced with the potential to optimize surface ablation outcomes due to customized optical zones and individually calculated transition zones, a concept that has been shown to be efficient in combined excimer laser and CXL treatments in keratoconus patients [2]. Central Corneal Regularization (CCR) is a new therapeutic treatment modality within the iVIS™ suite specifically designed to partially reverse corneal ectasia



by reducing the elevation of the cone and smoothening the overall contour (● Fig. 1 c). The purpose of the present pilot study is to report preliminary results in non-comparative consecutive case series of keratoconus patients undergoing a combined CCR and CXL treatment.

Patients and Methods

The inclusion criteria comprised a documented keratoconus progression and a visual acuity (regardless whether uncorrected, spectacle-corrected, or contact lens-corrected) the patient considered to be still useful in daily life. The definition of progression was based on the criteria by Wittig-Silva et al. (i.e. either a decrease in sphere by ≥ 0.5 dpt, or an increase in cylinder magnitude by ≥ 1.0 dpt, or an increase in the steepest keratometry value by ≥ 0.5 dpt within the last 12 months) [3]. Exclusion criteria included prior corneal surgery and a predicted minimal corneal thickness of less than 400 μm after CCR. Informed consent was obtained from each patient, taking specifically into account the limited database for excimer laser surgery immediately followed by CXL. Preoperatively, clinical assessments of uncorrected and best spectacle-corrected visual acuity, intraocular pressure, and anterior and posterior segment evaluation were performed. Follow-up appointments were scheduled 1 day, 4 days, 1 week, 1 month, and 3 months after surgery.

Three modules of the iVIS™ platform were used for data acquisition, treatment planning and surgical delivery of CCR: high definition corneal elevation maps with a statistically validated repeatability of ≤ 3 μm were acquired with a PrecisoHD™ tomographer [4]. Treatments were planned using the CCR mode in the CIPTAmax™ software [5] with calculated optical zones between 1.0 and 1.5 mm (● Fig. 2). A 1000 Hz iRes™ excimer laser with a spot size of 0.65 mm was used for a two-step transepithelial surface ablation: first, the elevation of the cone was reduced and a continuous refractive transition zone was created. Then, the remaining epithelium within a 9.0 mm zone was removed to facilitate subsequent CXL.

Before CXL, instrument wipes (Visiwipe™, Beaver-Visitec International, Waltham, USA) were tailored to mask the limbus. Ultrasonic pachymetry (Corneo-Gage™, Sonogage, Cleveland, OH) was used to monitor stromal thickness during CXL. As long as a minimal thickness of 400 μm was confirmed, an isotonic riboflavin solution (Medio-Cross D®, Medio-Haus Medizinprodukte GmbH, Neudorf, Germany) was applied topically every 2 to 3 minutes. A hypotonic riboflavin solution (Vitamin B2 Streuli®, Streuli Pharma, Uznach, Switzerland) was used to increase stromal thickness in the event minimal pachymetry readings were below 400 μm . After 30 minutes, riboflavin penetration into the anterior chamber was confirmed at a slit lamp. For UV-A irradiation, a CCL-365 vario™ cross-linking system (MLase AG, Germering, Germany) was used according to the manufacturer's guidelines. Irradiation parameters were 9.0 mW/cm² for 10 minutes within a 9.0 mm treatment diameter. Throughout the irradiation phase, riboflavin solution was applied every 2–3 minutes, ensuring that the stromal surface was kept moist and that the stromal thickness remained above 400 μm .

Until postoperative epithelial closure was confirmed, the eyes were dressed with a soft therapeutic contact lens and the patients were treated with topical ofloxacin 0.3% (Floxal UD®, Bausch & Lomb Swiss AG, Zug, Switzerland) and topical dexamethasone 0.1% (Dexafree UD®, Excelvision, Annonay, France)

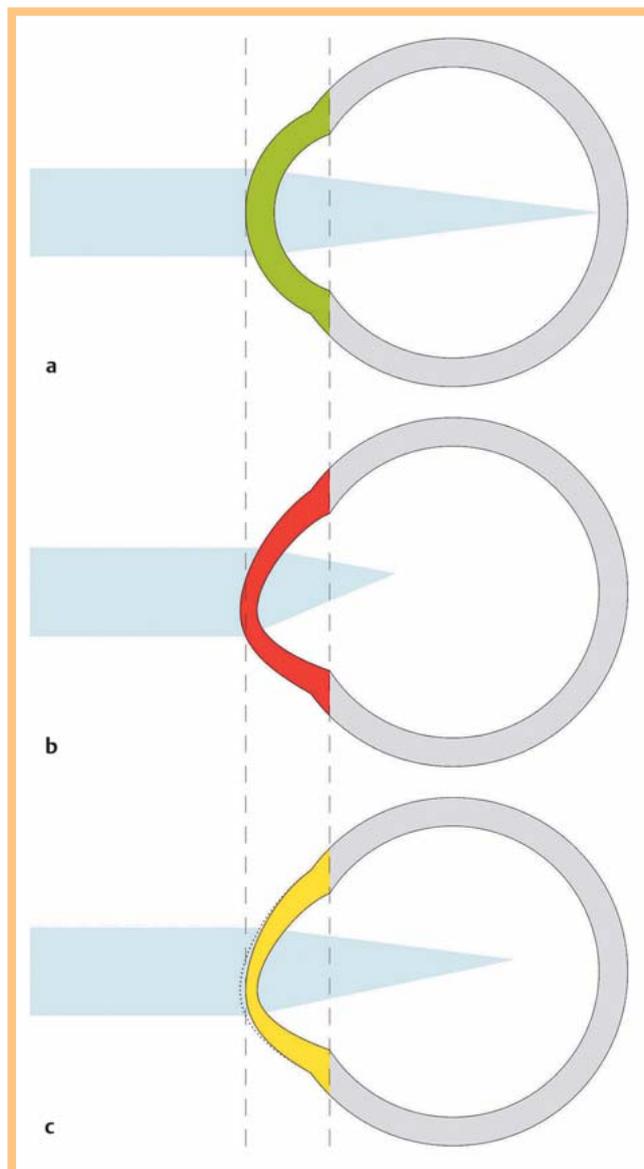


Fig. 1 Cross section of corneal contour and of optical path in keratoconus and after CCR. **a** Healthy cornea in an emmetropic eye. **b** Corneal ectasia in keratoconus, inducing axial myopia, curvature myopia, and irregular astigmatism. **c** Ectatic cornea after CCR with ablated cone and continuous refractive surface, leading to a reduction in both myopia and astigmatism. CCR = Central Corneal Regularization.

both four times a day. After epithelial closure, treatment consisted of topical fluorometholone 0.1% (FML® Liquifilm, Allergan, Freienbach, Switzerland), gradually reduced from five times to three times a day. Visual acuity values were transferred into log-MAR units for calculating mean values.

Results

At present, 10 eyes of 10 patients (1 female, 9 male) completed the 3-month-follow up and were included into the present pilot study. Mean age was 22 years, ranging from 14 to 34 years. Mean preoperative cylinder magnitude was 4.05 dpt (± 2.34 dpt standard deviation), mean preoperative maximum curvature was 54.18 (± 6.53) dpt.

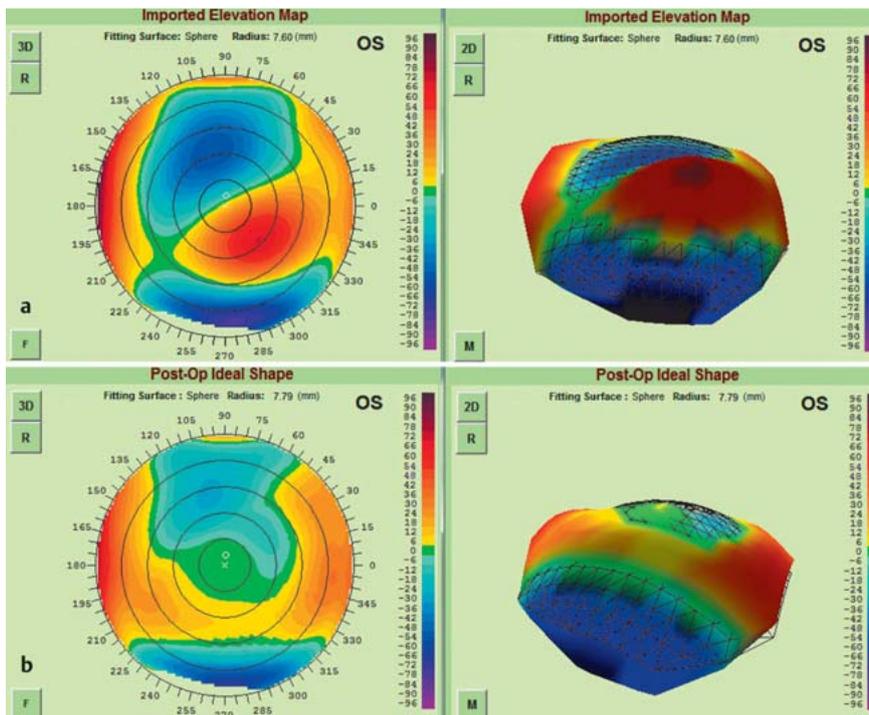


Fig. 2 Preoperative (a) and postoperative (b) elevation map. Two-dimensional (left) and three-dimensional (right) elevation map before (a) and after (b) CCR. Note the preoperative island pattern typical of ectasia and the small but centered optical zone after surface ablation. CCR = Central Corneal Regularization.

Changes in uncorrected visual acuity in terms of line numbers are summarized in **Table 1**. One month after combined CCR and CXL treatment, 9 out of 10 patients gained lines of uncorrected visual acuity. Three months postoperatively, 7 patients gained between 2 and 8 lines of uncorrected visual acuity, whereas 3 patients lost between 1 and 6 lines. In two cases, the loss of lines was due to delayed healing of the epithelium, in one case there was increasing haze after untimely cessation of topical steroids. Mean changes in uncorrected visual acuity, in best spectacle-corrected visual acuity and in spherical equivalent are shown in **Table 2**, indicating an improvement for all the parameters observed.

Table 1 Gain and loss in uncorrected visual acuity after combined CCR and CXL treatment. Changes of uncorrected visual acuity in 10 patients 1 and 3 months postoperatively. Data are provided as number of patients gaining or losing a specific number of lines at both time points. CCR = Central Corneal Regularization; CXL = Corneal Cross-linking

Changes in lines	1 month postop.	3 months postop.
+ 8		1
+ 7	1	1
+ 6	1	
+ 5		1
+ 4	2	
+ 3		1
+ 2	2	3
+ 1	3	
0		
- 1		1
- 2	1	
- 3		1
- 4		
- 5		
- 6		1

Discussion

The spherocylindrical change that can be observed after sole CXL for keratoconus is in the range of 2 diopters of flattening after 12 months with a high inter-individual variance [6]. Advanced topography-guided surface ablation prior to CXL has therefore the potential to further increase refractive outcomes in keratoconus patients. CCR represents the newest approach in this field, a therapeutic treatment modality that partially inverts corneal ectasia by creating a 1.0–1.5 mm optical zone surrounded by a continuous refractive surface aiming at an optimal optical smoothness. From the patient’s perspective, an increase in uncorrected visual acuity can be expected that possibly is more pronounced and might be reached earlier than with sole CXL. Accordingly, the present pilot study concentrated on the change in uncorrected visual outcome which indeed showed a promising improvement in the majority of the 10 patients as early as 1 month postoperatively. The reason for the loss of lines observed in some patients are consistent with complications usually found after sole CXL and do not seem to represent new problems induced by the preceding CCR. In summary, the study is a valid proof of concept but

Table 2 Mean changes in visual acuity and spherical equivalent after combined CCR and CXL treatment. Data are provided as mean plus standard deviation. CCR = Central Corneal Regularization; CXL = Corneal Cross-linking

	preop.	1 month postop.	3 months postop.
Uncorrected visual acuity (decimal acuity)	0.15 ± 0.28	0.28 ± 0.47	0.24 ± 0.25
Best spectacle-corrected visual acuity (decimal acuity)	0.44 ± 0.59	0.50 ± 0.62	0.62 ± 0.71
Spherical equivalent (dpt)	- 3.11 ± 3.41	-2.00 ± 3.08	-1.33 ± 2.01

no further conclusions can be drawn at this stage due to its limited number of patients and the short follow-up. Based on the results from recent reports with longer follow-ups and larger patient numbers it can be expected that simultaneous topography-guided excimer ablation and CXL treatment leads to a stable improvement in both uncorrected and best-corrected visual acuity [2, 7, 8] which is associated with a high level of patient satisfaction [8] and an improvement in the self-reported quality of life [9].

On a broader scale, the combined CCR and CXL procedure described here expands the number of treatment options that are currently available for keratoconus patients [10]. Originally introduced to defer the need for corneal transplantation, procedures such as toric intraocular lenses and intracorneal ring segments can also be combined with CXL in order to stop disease progression and to permanently correct for some amount of astigmatism at the same time. The combined CCR and CXL provides an even less invasive approach to the same goal as no intracorneal tunnels, lens incisions, and implants are required. However, eligible patients need to be recruited rather early in the course of the disease because the minimal corneal thickness after the excimer ablation must still be above the safety threshold of 400 µm for CXL.

Conflict of Interest

▼
No financial interests (CK, FB, PB, MAT).

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