Corneal stroma demarcation line after standard and high-intensity collagen crosslinking determined with anterior segment optical coherence tomography

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PURPOSE: To use anterior segment optical coherence tomography (AS-OCT) to compare corneal stroma demarcation line depth after corneal collagen crosslinking (CXL) with 2 treatment protocols.

SETTING: Vardinoyiannion Eye Institute of Crete, Faculty of Medicine, University of Crete, Heraklion, Crete, Greece.

DESIGN: Prospective comparative interventional case series.

METHODS: Corneal collagen crosslinking was performed in all eyes using the same ultraviolet-A (UVA) irradiation device (CCL-365). Eyes were treated for 30 minutes with 3 mW/cm^2 according to the standard Dresden protocol (Group 1) or for 10 minutes with 9 mW/cm^2 of UVA irradiation intensity (Group 2). One month postoperatively, 2 independent observers measured the corneal stroma demarcation line using AS-OCT.

RESULTS: Sixteen patients (21 eyes) were enrolled. Group 1 comprised 7 patients (9 eyes) and Group 2, 9 patients (12 eyes). The mean corneal stroma demarcation line depth was 350.78 μm ± 49.34 (SD) (range 256.5 to 410 μm) in Group 1 and 288.46 ± 42.37 μm (range 238.5 to 353.5 μm) in Group 2; the corneal stroma demarcation line was statistically significantly deeper in Group 1 than in Group 2 (P=.0058, t test for unpaired data).

CONCLUSION: The corneal stroma demarcation line was significantly deeper after a 30-minute CXL treatment than after a 10-minute CXL procedure with high-intensity UVA irradiation.

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Keratoconus is a noninflammatory corneal disorder characterized by progressive thinning, irregular steepening of the cornea, and apical scarring causing gradual loss of visual acuity.[1] Corneal collagen crosslinking (CXL) is a minimally invasive surgical treatment used to strengthen the tissue of the ectatic cornea and arrest keratoconus progression.[2,3] The CXL procedure involves 30 minutes of ultraviolet-A (UVA) irradiation at an intended irradiance of 3.0 mW/cm^2 with a total surface dose of 5.4 J/cm^2 (Dresden protocol[2]).

According to the photochemical law of reciprocity (Bunsen-Roscoe law), the same photochemical effect is achieved with reduced illumination time and correspondingly increased irradiation intensity, meaning that a 10-minute illumination at 9.0 mW/cm^2 should provide the same effect as a 30-minute illumination at 3.0 mW/cm^2. Several new commercially available CXL devices offer high UVA irradiation intensity with relevant time settings.

After CXL, a corneal stroma demarcation line is detectable on slitlamp examination at a depth of

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approximately 300 μm as early as 2 weeks after treatment.[4] A corneal stroma demarcation line after CXL can also be detected using confocal microscopy and anterior segment optical coherence tomography (AS-OCT), possibly representing the effectiveness of the CXL treatment.[5–8]

The purpose of this study was to evaluate and compare the depth of the corneal stroma demarcation line using AS-OCT after CXL for 2 treatment protocols using a new high-intensity UVA irradiation device.

PATIENTS AND METHODS

This prospective comparative interventional case series comprised patients with progressive keratoconus. Institutional review board approval was obtained. All patients were appropriately informed before their participation in the study and gave written informed consent in accordance with institutional guidelines according to the Declaration of Helsinki.

The clinical diagnosis of keratoconus was based mainly on corneal topography data (iTrace, Tracey Technologies) and clinical signs, such as Fleischer rings, Vogt striae, stromal thinning, and conical protrusion. Inclusion criteria were progressive keratoconus, age older than 18 years, corneal thickness greater than 400 mm, no other corneal or anterior segment pathologic signs, and no pregnancy or lactation. Keratoconus was graded with the Amsler-Krumeich classification[9]; only patients with grades I and II were included in the study.

In all cases, the CXL treatment was performed with a new high-intensity UVA illuminator (CCL-365, Peschke Meditrade GmbH). The selection of the CXL illumination treatment protocol was random. Patients were treated for 30 minutes at an intended irradiance of 3.0 mW/cm^2 according to the Dresden protocol[2] (Group 1) or for 10 minutes in an intended irradiance of 9.0 mW/cm^2 (Group 2).

Data obtained from the patient records included age, sex, preoperative ultrasound corneal pachymetry (Corneo-Gage Plus, Sonogage, Inc.), preoperative keratometry (K) readings, and AS-OCT scans (Visante OCT 3.0, Carl Zeiss Meditec AG) 1 month postoperatively.

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Surgical Technique

The same surgeon (G.D.K.) performed all procedures under sterile conditions. After topical anesthesia of proxymetacaine hydrochloride 0.5% eyedrops (Alcaine) was administered, the corneal epithelium within an 8.0 to 9.0 mm diameter was mechanically removed with a rotating brush. After epithelial removal, riboflavin (0.1% solution of 10 mg riboflavin-5-phosphate in 10 mL dextran-T-500 20% solution, Medio-Cross, Peschke Meditrade GmbH) was instilled on the center of the cornea every 3 minutes for approximately 30 minutes. Ultraviolet-A irradiation was applied using the high-intensity UVA illuminator. Before treatment, the intended irradiance was calibrated using a UVA light meter (YK-35UV, Lutron Electronic Enterprise Co. Ltd.), which is supplied with the UVA device. Irradiance was performed for 30 minutes at an intended irradiance of 3.0 mW/cm^2 and for 10 minutes at an intended irradiance of 9.0 mW/cm^2, corresponding to a total surface dose of 5.4 J/cm^2 in all cases. During UVA irradiation, riboflavin solution was applied every 3 minutes to maintain corneal saturation with riboflavin. At the end of the procedure, a silicone–hydrogel bandage contact lens with a 14.0 mm diameter, 8.6 base curvature, and oxygen permeability of 140 barrers (lotrafilcon B [Air Optix], Alcon Laboratories Inc.) was applied until full reepithelialization.

Postoperative medication included nepafenac suspension 0.1% (Nevanac) 3 times a day for the first 2 postoperative days and chloramphenicol–dexamethasone drops (Dispersadron) 4 times daily until the removal of the bandage contact lens. After removal of the contact lens, patients received fluorometholone 0.1% drops (FML), which were tapered over 2 weeks. Patients were encouraged to use artificial tears at least 6 times a day for 3 months.

Anterior Segment Optical Coherence Tomography

All scans were performed under the same light conditions 1 month postoperatively. Patients were asked to fixate on the optical target in the system. The image was captured when the corneal reflex, a vertical white line along the center of the cornea, was visible. The high-resolution corneal scan was used to produce an enhanced image of the cornea on the horizontal meridian (0 to 180 degrees). The stromal demarcation line was identified in the enhanced corneal image, and the demarcation line depth was measured using the flap tool provided by the manufacturer. The demarcation line depth was measured centrally by 2 independent observers (K.I.T., M.A.G.). The visibility of the demarcation line was scored to obtain accuracy of the measurements (0 = line not visible; 1 = line visible, but measurement not very accurate; 2 = line clearly visible). Only measurements with a score of 2 were included in the study.

Statistical Analysis

All data were collected in an Excel spreadsheet (Microsoft Corp.). Statistical analysis of the results was performed using Stata software (version 12.0, Statacorp LP). Normality of the distribution of all measurements was confirmed using the Shapiro-Wilk test, which is more appropriate for small sample sizes (<50 participants) than the Kolmogorov-Smirnov test. The *t* test for unpaired