Refractive Changes Following CXL

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Keratoconus is characterized by two structural changes: progressive increase in corneal curvature (ie, ectasia) and corneal thinning. Generally manifested between the ages of 20 and 30 years, this refractive error causes a progressive deterioration of vision in the affected cornea. In more advanced cases of keratoconus, poor corneal optical quality also results.

Penetrating keratoplasty (PKP) is one option for the treatment of keratoconus, but many authors[1,2] consider it as the last resort because of the risks of graft rejection, unpredictable visual outcomes, and development of high astigmatism. The advantages of postponing PKP are many; even following a successful procedure, the mean survival rate of the corneal graft is 16.88 years.[3] As a consequence, young patients undergoing PKP may have to repeat the procedure.

ORIGINAL SURGICAL TECHNIQUES

Recently, alternative and novel surgical and medical treatments for keratoconus have allowed us to further avoid, or at least delay, PKP. Conservative surgical techniques include asymmetric radial keratotomy (ARK)[4], mini asymmetric radial keratotomy (MARK)[5], circular keratotomy, and intrastromal corneal ring segments (ICRS).[6,7] These techniques address the refractive problems of keratoconus by reducing corneal curvature and effectively improving visual performance.

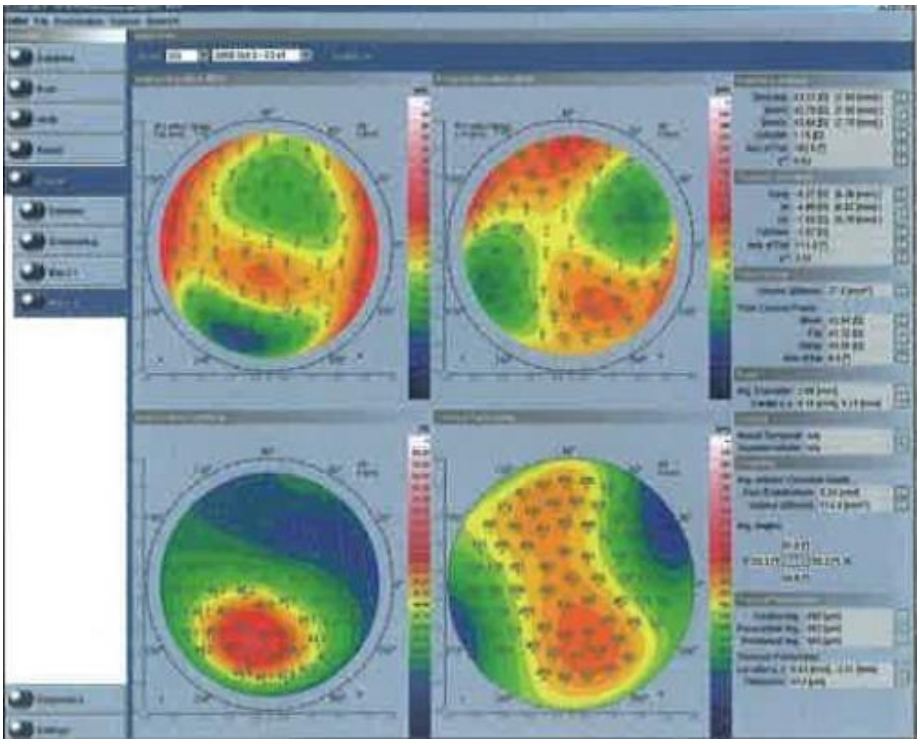

Figure 1. Scheimpflug measurement of corneal optical density.

Another original technique recently developed is corneal collagen crosslinking (CXL).[1,8-10] This treatment directly addresses the intrinsic structural weakness responsible for the progressive deformation of the cornea in keratoconus patients. CXL combines local application of riboflavin solution with UV-A light, a technique initially described by surgeons at the Dresden Clinic.[1] Keratoconus progression was stopped in all treated eyes, with a slight reversal and flattening of keratoconus observed in 42% of eyes.

Laboratory tests in the Dresden study revealed that the maximum effect of the treatment occurs in the anterior 300 µm of the cornea. The level of energy that is cytotoxic for the corneal endothelium is reached only in human corneas with a stromal thickness of less than 400 µm. It was concluded that treatment is safe and effective in corneas with thickness measurements above that value.

VISUAL IMPROVEMENTS NOTED

The primary intention behind CXL is to reinforce corneal structural properties and halt keratoconus progression; however, this treatment also conveys a significant visual improvement. The enhancement of vision was quantified, for example, in the Dresden

study[1] as 1.4 Snellen lines. UCVA and BCVA frequently improve following CXL, although the quantity of improvement is not entirely predictable. Patients often report sharper, less distorted, and clearer vision.

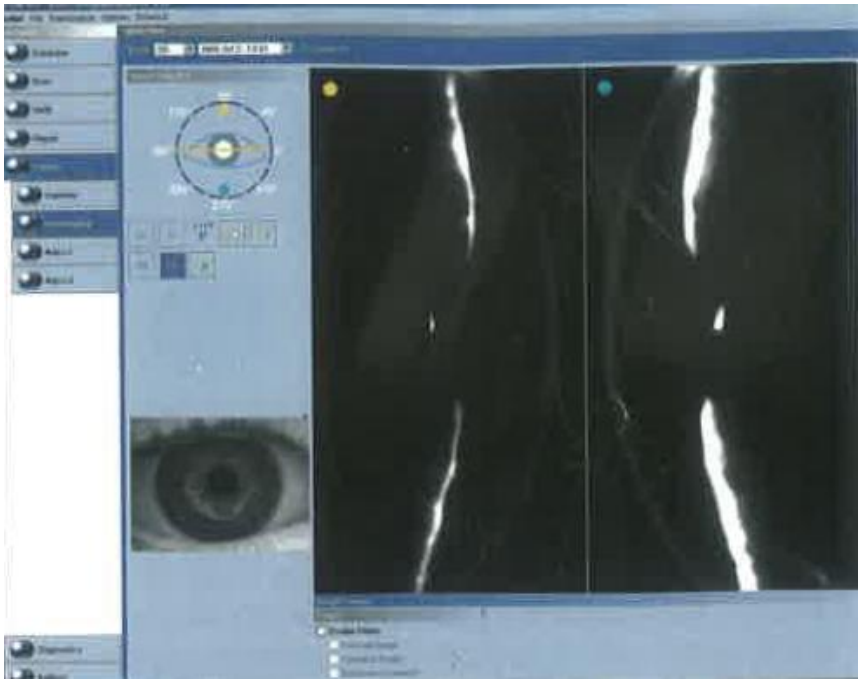

Figure 2. Pre- and postoperative data from the corneal density measurement were used to evaluate changes induced by CXL.

In keratoconus patients, diminished visual performance, including BCVA, is partly caused by abnormal higher-order aberrations associated with other optical defects. These aberrations (eg, coma, trefoil, astigmatism) are significantly higher in patients with keratoconus compared with normal eyes.[11] Reduction of corneal curvature and topography changes following CXL may reduce these aberrations. We can measure corneal wavefront aberrations using Zernike polynomial analysis, based on computerized corneal topography. These measurements allow us to study the refractive profile of eyes with corneal abnormalities.

We recently conducted a study to investigate refractive changes following CXL by analyzing higher-order corneal wavefront aberrations and corneal curvature indices. We also asked patients to complete a questionnaire to assess the subjective characteristics of improvement. Subjective and quantitative measurements were then compared, along with corneal curvature readings.

MATERIALS AND METHODS

We recruited 40 eyes (40 patients) for CXL treatment. UCVA and BCVA, computerized corneal topography, axial biometry, pachymetry, endothelial cell count, keratometry, and slit-lamp examination were performed on all patients. We used computerized corneal topography equipment and specific software (EyeTop Software; Costruzione Strumenti Oftalmici, Scandicci, Italy) to measure refractive aberrations preoperatively and at 1, 3, and 6 months following treatment. This software also allows elaborate analysis of higher-order aberrations at three pupil diameters (3, 5, and 7 mm). We chose 5 mm as the value for our study.

We used the Galilei Double Scheimpflug Analyzer (Ziemer Group, Port, Switzerland) to measure corneal optical density (Figures 1 and 2).

Data from the corneal densitometry measurement, based on the logarithmic relationship between incident and emergent light, is acquired and instantly elaborated by the Galilei analyzer. We performed corneal densitometry pre- and postoperatively to evaluate changes induced by CXL.

PROCEDURE

After applying topical anesthesia (benoxinate chloride 0.4%), we removed the corneal epithelium with an ophthalmic scalpel (MicroFeather; Feather Safety Razor Co., Ltd., Osaka, Japan) under a surgical microscope. For the UV-A source, we used the UV-X illumination system (Version 1000; IROC AG, Switzerland). Riboflavin solution was applied starting 30 minutes before treatment at 10-minute intervals until UV-A application. Riboflavin was then applied six times at 5-minute intervals during UV-A application, with a total UV-A exposure time of 30 minutes.

After treatment, a bandage contact lens was placed, and topical antibiotics and nonsteroidal antiinflammatory drugs were prescribed. Clinical examination was performed 1 and 3 days following treatment, when the contact lens was removed. Corneal epithelial healing was checked with slit-lamp examination. Follow-up also occurred at 1, 3, and 6 months and included all exams performed in the pretreatment work-up, such as measurement of higher-order refractive aberrations. The following

parameters were chosen as indicators: astigmatism, trefoil, coma, and average corneal curvature values.

At the end of follow-up, patients were asked to answer a visual performance questionnaire (Figure 3).

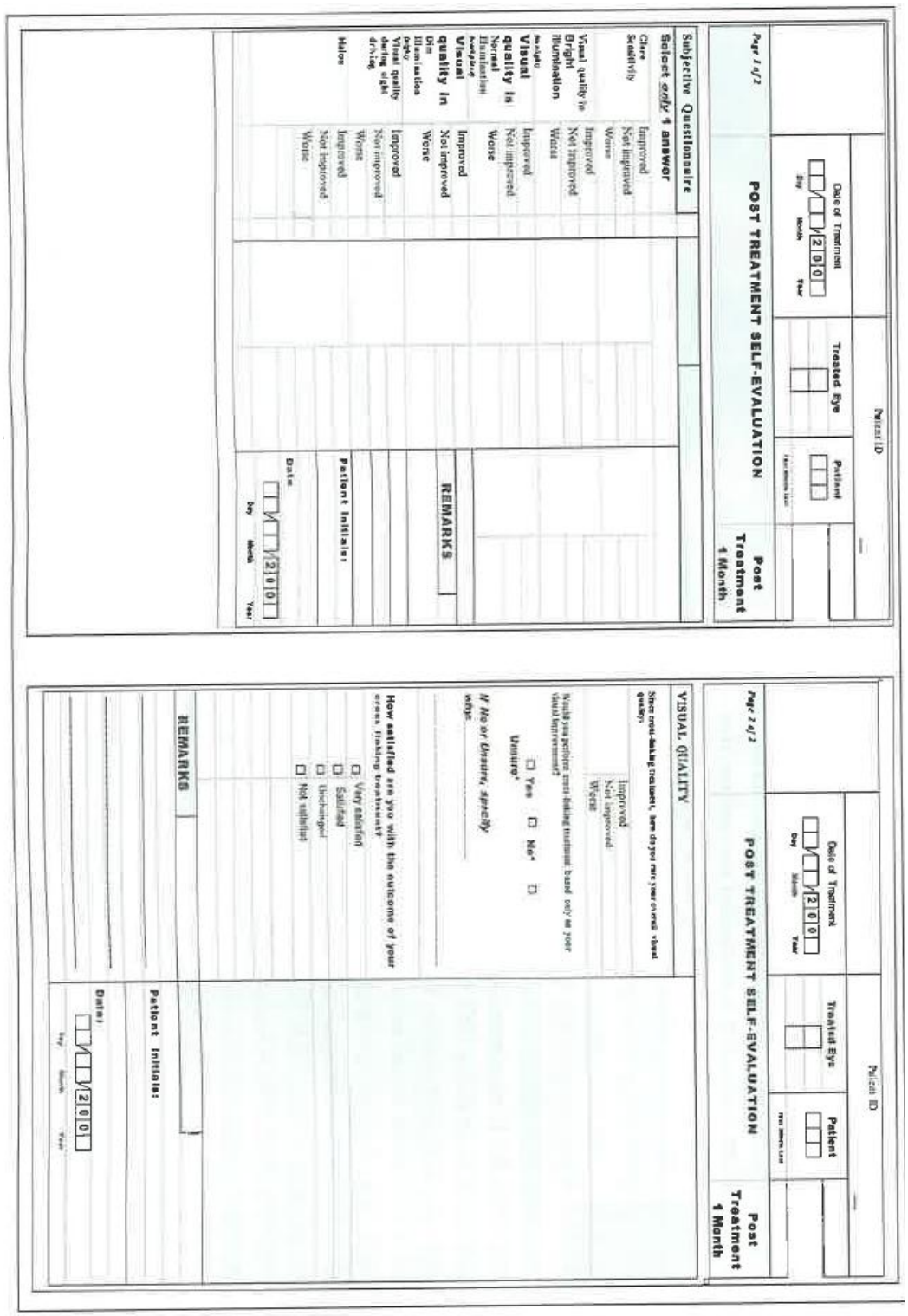

Figure 3. Visual performance questionnaire

The self-evaluation questionnaire referred to general visual quality in different light conditions (ie, bright, dim, and night driving); presence or absence of halos or glare; and general considerations, such as degree of satisfaction with the treatment.

RESULTS

The average reduction in corneal curvature was 1.20 D (49.50 D preoperative vs 48.30 D postoperative). Patients' average UCVA and BCVA before treatment were 3/20 and 11/20, respectively, improving to an average of 6/20 and 14/20, respectively, following CXL.

Coma, trefoil, and astigmatic aberration values did not improve at 1- and 3-month follow-up visits. Surprisingly, these values increased slightly at this stage in a large proportion of patients (58%). The values finally decreased at 6 months. Astigmatic aberrations decreased from an average of 4.7 μm preoperatively to 3.8 μm postoperatively, an average reduction of 0.9 μm. Trefoil decreased from an average of 1.25 μm to 0.80 μm pre- versus postoperatively, showing an average reduction of 0.45 μm. Coma decreased from an average of 4.9 μm to 4.2 μm, an average reduction of 0.7 μm.

Densitometry revealed an increase in corneal density in treated eyes (Figure 4). Additionally, the subjective patient questionnaires showed that 39% percent reported considerable improvement in visual performance, 43% reported slight or appreciable improvement, and 18% reported no or uncertain improvement.

DISCUSSION

It must be emphasized that the main aim of CXL is to increase corneal structural strength. Its direct biomechanical consequences cause stabilization or reduction of corneal ectasia and curvature. The increase in corneal optical density, measured using the Galilei Dual Scheimpflug Analyzer, was significant in all cases and correlates with the structural changes of the cornea. This may be considered as an early indicator of the treatment's efficacy.

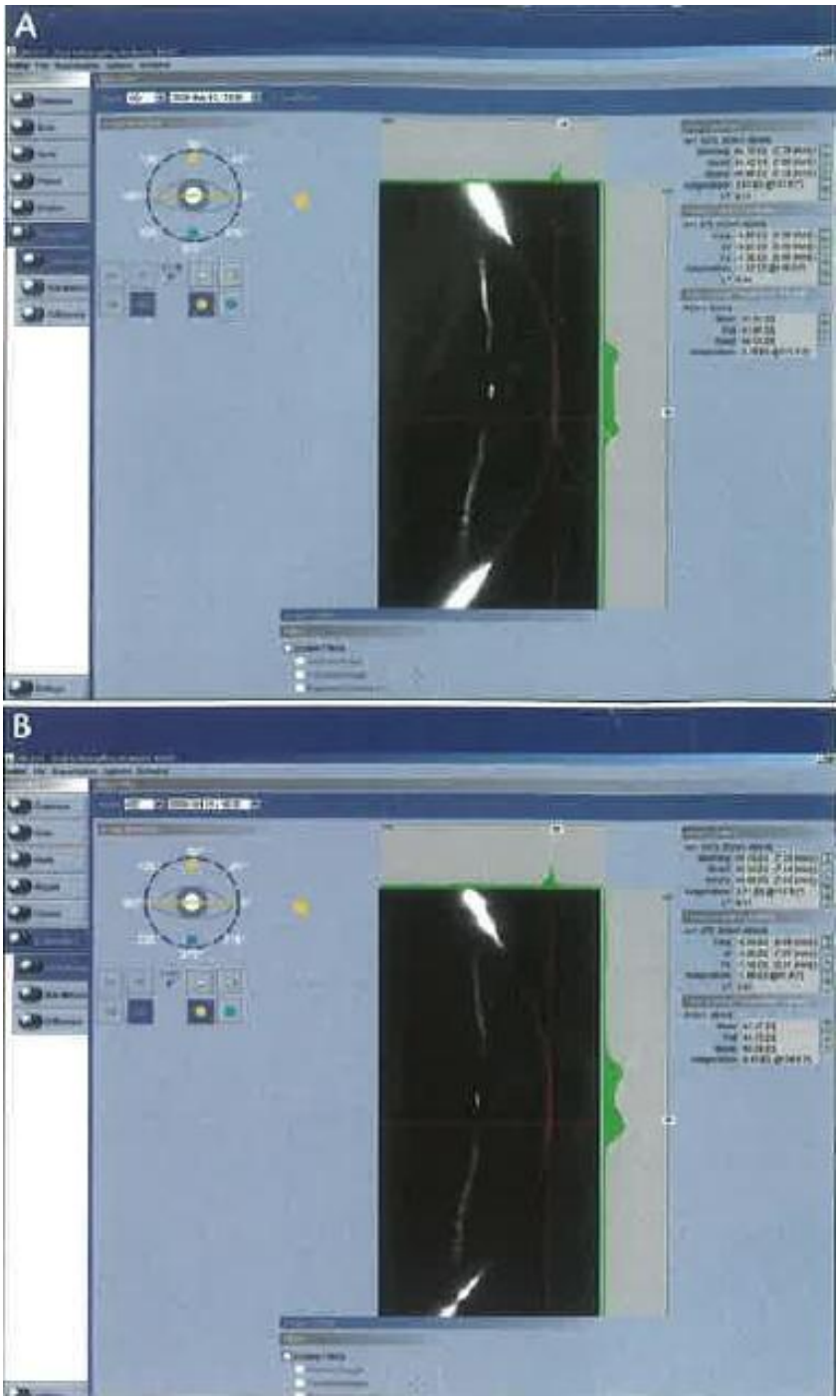

Figure 4. (A, B) There was increased corneal density in treated eyes.

Our results confirm that the most consistent improvements after CXL concerned the considerable decrease in corneal curvature values in a large number of eyes. Reduction of higher-order aberrations were also investigated; however, these changes were less consistent and appeared later in the follow-up. In fact, in early stages of follow-up, higher-order aberrations increased. This clinical behavior was attributed to superficial

corneal irregularity and superficial corneal edema and haze, which caused the cornea to thicken.

With the gradual clearing of corneal haze, a decrease in coma, trefoil, and astigmatic corneal aberrations occurred at the 6-month follow-up. The degree of visual improvement was gradual and included considerable improvement in UCVA, BCVA, and visual quality.

Since the amount of visual improvement following CXL can be unforeseeable, a number of authors[6,7] have combined the insertion of intrastromal corneal rings and CXL, reporting improved refractive result versus CXL alone. We have successfully associated MARK surgery and CXL to obtain a significant reduction of corneal curvature and improved BCVA and UCVA, complimenting the increase of corneal resistance secondary to CXL.

The improvement of vision and refractive aberrations is a complex phenomena, one that is not always proportional to the structural modifications of the cornea. In fact, the degree of visual improvement following CXL is unpredictable and may be due to a combination of factors, including corneal flattening and a slight reduction of higher-order refractive aberrations.

REFERENCES

1. Wollensak G. - *Crosslinking treatment of progressive keratoconus: new hope*. Curr Opin Ophthalmol. 2006; 17: 356-360.
2. Krumeich JH, Keziran GH. - *Circular keratotomy to reduce astigmatism and improve vision in stage I and II keratoconus*. J Refract Surg. 2009; 25: 357-365.
3. Williams KA, Lowe MT, Bartlett CM, Kelly L, Coster DJ. - *The Australian Corneal Graft Registry*, 2007 Report. Adelaide, Australia; Flinders University Press; 2007.
4. Abbondanza M. - *Asymmetric Radial Keratotomy for the Correction of Keratoconus*. J Refract Surgery. 1997; 13 (3): 302-307.
5. Abbondanza M. - *Mini Cheratotomia Radiale Asimmetrica (Mini ARK) per la correzione chirurgica del cheratocono in fase iniziale, nell'ipermetropia e nelle miopie lievi*. Esperienze. 1997; 12 (1): 21-24

6. Chan CK, Sharma M, Boxer Wachler BS. - *The effect of Inferior segment Intacs with and without corneal collagen crosslinking with Riboflavin (C3-R)*. J Cataract Refract Surg. 2007; 33: 75-80.
7. Sharma M, Boxer Wachler BS. - *Comparison of single segment and double segment Intacs for keratoconus and post LASIK ectasia*. Am J Ophthal. 2006; 141: 891-895.
8. Wollensak G, et al. - *Stress-strain measurements of human and porcine corneas after riboflavin-ultraviolet-A-induced cross-linking*. J Cataract Refract Surg. 2003; 29 (9): 1780-1785.
9. Wollensak G, et al. - *Collagen Fiber Diameter in the Rabbit Cornea After Collagen Crosslinking by Riboflavin/UVA*. Cornea. 2004; 23 (5): 503-507.
10. Wollensak G, et al. - *Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus*. Am J Ophthalmol. 2003; 135 (5): 620-627.
11. Caporossi A, Mazzotta C, Baiocchi S. - *Technological innovations in corneal cross-linking*. Ophthalmology Times Europe. 2007; 3 (7): 34-37.