Corneal morphometry prior to and five years after corneal stromal photoablation: the possible role of topical anesthesia on postablative corneal morphometry

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SUMMARY

The aim of this study was to investigate central corneal thickness values prior to and five years after ablation of the central cornea using 193 nm UV radiation. Thirty eight eyes of 38 subjects were analysed in a prospective study. Central corneal thickness measurements were carried out prior to and 60 months after corneal stromal photoablation under a 160 µm flap with the Summit Excimed SVS plus excimer laser (Summit Technology, Inc. Walthan, MA). Mean intended ablation depth was 55±20 µm. Central corneal thickness measurements were carried out with the DGH 2000 AP ultrasonic pachymeter (DGH Technology, Inc., San Diego, USA). Consecutive central corneal thickness readings were made until three consecutive measurements were within 5 mm of each other. The mean of these three consecutive readings was used as the value of central corneal thickness in this study.

Preoperative mean central corneal thickness was 556±55 µm; five years later it was 513.41 µm ($p<0.001$). The difference between the "*theoretical*" postablative corneal thickness values and the "real" corneal thickness values observed 60 months after stromal photoablation was also significant ($p<0.001$).

Five years after central corneal stromal photoablation using 193 nm UV radiation there was a disparity between the programmed postoperative residual corneal thickness and the corneal thickness obtained by ultrasound pachymetry. Further research is neccesary in order to identify possible unexpected values of corneal thickness after a paracentral corneal stromal photoablation has been carried out.

Key words: Central corneal thickness – Ultrasound pachymetry – Excimer laser

INTRODUCTION

It is essential to carry out a preoperative central corneal thickness measurement before myopic excimer laser surgery (Price et al., 1999) in order to avoid the risk of postsurgical keratectasia (Wang et al., 1999; Schmitt-Bernard et al., 2000).

Moreover, assessment of corneal thickness is very important because the excimer laser ablation nomogram depends on corneal thickness

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values (Probst and Machat, 1996). It has been reported that it is essential to measure this thickness before scheduling LASIK surgery in order to ensure that central thickness will be sufficient to prevent leaving the corneal bed too thin after treatment, because the residual bed depth is dependent on the depth of laser ablation (Price et al., 1999).

There is a growing body of literature on the corneal thickness values of non-photoablated corneas after the introduction of excimer laser surgery (Rapuano et al., 1993; Higgis et al., 1993; Terry et al., 1996; Longanesi et al., 1996; Lam and Douthwaite, 1998; Marsich and Bullimore, 2000; Sanchis Gimeno et al., 2001; Sanhermelando et al., 2002).

Nonetheless, the long-term effect that 193 nm UV excimer laser corneal stromal photoablation has on central corneal thickness remains unclear because there is no information about the long-term changes that this radiation can induce in central corneal thickness values.

The objective of the present work was to ascertain the long-term changes that corneal stromal photoablation using 193 nm UV radiation can induce in central corneal thickness by measuring central corneal thickness values before and five years after stromal photoablation.

Materials and methods

We carried out a study involving 38 patients (38 eyes). The tests were run at our refractive surgery unit. All procedures were conducted in accordance with the principles of the Helsinki Declaration. Detailed consent forms were obtained from each of the patients.

All patients were over 18 years old and had stable refraction at least 18 months before surgery. The characteristics of the subjects are shown in Table 1. There were 19 women (50.00%) and 19 men (50.00%).

All patients underwent an examination in accordance with the established protocol (Sanchis Gimeno et al., 2000; Lleó et al., 2001; Alonso et al., 2002; Sanchis Gimeno et al., 2003). This included: best corrected visual acuity, manifest and cycloplegic refraction (KR 7000-P Topcon Corp, Tokyo, Japan), slit-lamp examination (Haag Streit Biomicroscope 900, Bern, Switzerland), ultrasonic pachymetry (DGH 2000 AP ultrasonic, DGH Technology Inc, Exton, PA), Goldmann applanation tonometry (Goldmann Applanation Tonometer, Haag Streit, Bern, Switzerland), corneal topography (EyeSys Corneal Analysis System, Houston, TX), and dilated fundus examination.

Patients with corneal topographic alteration (e.g., keratoconus, corneal dystrophies, etc.) were not included in this study. Patients with an organic pathology that could affect the regenerative process of the cornea (e.g., diabetes mellitus, diseases of the immune system, collagen-related diseases, etc.) were excluded. Finally, patients who had previously been treated for ocular hypertension or glaucoma were not included.

All corneal stromal photoablations were performed by the same surgical team. A 160 µm corneal flap was created by means of the Ruiz microkeratome (Chiron ALK). A suction pressure greater than 65 mmHg was ensured by measuring IOP with a Barraquer tonometer. Subsequent central corneal stromal bed photoablation under the flap was carried out with the Summit Excimed SVS plus excimer laser (Summit Technology, Inc. Walthan, MA), using 180 mJ/cm^2 and 10 Hz repetition rate. A multizone ablation was used in all eyes within a maximum diameter of 6.0 mm.

The surgical protocol was standardized for all patients. The postoperative pharmacological protocol included 0.35% neomycin, B 6000 UI polymyxin, and 0.1% dexamethasone at a dose of one drop every 8 hours for the first week; this was progressively withdrawn during the second week, and the treatment was halted in the third week.

Central corneal thickness evaluation was performed by a physician with the ultrasonic DGH 2000 AP ultrasonic pachymeter (DGH Technology, Inc., San Diego, CA, USA) prior to and five years after corneal photoablation. Only patients with manifest postoperative refraction ranging from - 0.50 to + 0.50 diopters five years after photoablation were evaluated.

Central corneal thickness measurements were obtained under corneal anesthesia with the eye in primary gaze position. After anesthetising the cornea with 0.4% oxybuprocaine clorhydrate tear drops each patient was asked to blink before central corneal thickness measurement to avoid any bias due to corneal drying. The patient was required to look straight ahead while the pachymeter probe was placed on the centre of the cornea. Consecutive readings were made

Table 1.- Characteristics of the subjects.

	AGE	MSE*	BCVA**	GAT†
n	38	38	38	38
Mean	28.88	-2.78	0.77	14.75
SD	5.12	0.11	0.13	1.74
Minimum	19	-2.00	0.4	12
Maximum	46	-4.00	1.00	18

* Manifest spherical equivalent refraction (diopters); ** Best corrected visual acuity; † Goldmann applanation tonometry (mmHg).

until three consecutive measurements were within 5 µm of each other. The mean of these three readings was used as the value of the central corneal thickness (Sanchis Gimeno et al., 2001). Examination times ranged from 09:00 a.m. to 13:00 p.m. The probe was sterilized with alcohol after contact with each patient.

After obtaining data for each patient, a statistical study was conducted using the Kolgomorov-Smirnov test. Differences between data sample means were determined by Student's t-test and *P* values of less than 0.05 were considered statistically significant.

Results

Table 2 shows the preoperative corneal thickness values, the "*theoretical*" postablative corneal thickness values, and the corneal thickness values obtained after photoablation. The difference between the mean preoperative central corneal thickness values and the real mean central corneal thickness values observed 60 months later was significant ($p<0.001$).

The difference between the mean "*theoretical*" postablative corneal thickness values and the "real" mean corneal thickness values obtained 60 months after stromal photoablation was also significant ($p<0.001$).

Figure 1 shows the analysis of the central corneal thickness values of each subject.

Discussion

Refractive surgery by means of corneal photoablation using a 193 nm excimer laser is carried out worldwide in order to correct refractive errors. Corneal thickness must be measured prior to this surgery (Price et al., 1999) and ultrasound pachymetry is used to obtain corneal thickness values because it is recognized as an accurate method for the study of corneal thickness (Doughty and Zaman, 2000).

Refractive techniques with the excimer laser are based on stromal photoablation, with the consequent changes in the biophysical properties of the cornea, including a thinning out of corneal thickness at the expense of the ablated stroma. Intended ablation depth is programmed before scheduling the corneal refractive procedure and, theoretically, postablative corneal thickness values are known before photoablation is carried out.

Nevertheless, the results obtained from the patients analyzed in our study indicate that five years after corneal photoablation the central corneal thickness values obtained differ respect to the expected theoretical values.

In our study we used the same pachymeter for each exploration and corneal thickness measurements were carried out by the same individual in an unmasked fashion. This physician was aware of the patients' pre- and post-operative status and this could bias the corneal thickness measurements made in the post-operative period. Nevertheless, we attempted to avoid differences in corneal indentation among different observers by using only one observer. All readings were carried out according to a set timetable (between 09:00 and 13:00 p.m.), hence ensuring reliable and reproducible results.

Regarding the corneal thickness values obtained, some aspects merit comment: It has been demonstrated that the corneal epithelium and stroma do not regain biomechanical stability until almost a year after ablation with the excimer laser (Bohm et al., 1997). During the first few months after surgery, the cornea undergoes in a continuous regenerative process involving epithelial and stromal edematization. We believe that using central corneal thickness values five years after photoablation and once the post-surgical reparation process has finalized (Amm et al., 1996) ensures that the readings will not be influenced by corneal irregularities typical of the wound healing process.

We performed corneal stromal ablation by means of LASIK. The corneal stroma is not a uniform morphological unit. Upon studying the fibrous populations, a decrease in their density is seen, spreading from Bowman's layer to Descemet's membrane (Saraux et al., 1985).

Table 2.- Presurgical central corneal thickness values, intended ablation depth, theoretical postoperative corneal thickness values and corneal thickness values obtained five years after photoablation

	CCT prior to photoablation (mm)	**Intended ablation depth (mm)**	**Theoretical CCT 5 years later (mm)**	**CCT obtained 5 years later (mm)**
Mean	556	55	501	516
SD	31	20	40	41
Minimum	485	22	413	420
Maximum	602	103	571	581

CCT = Central corneal thickness

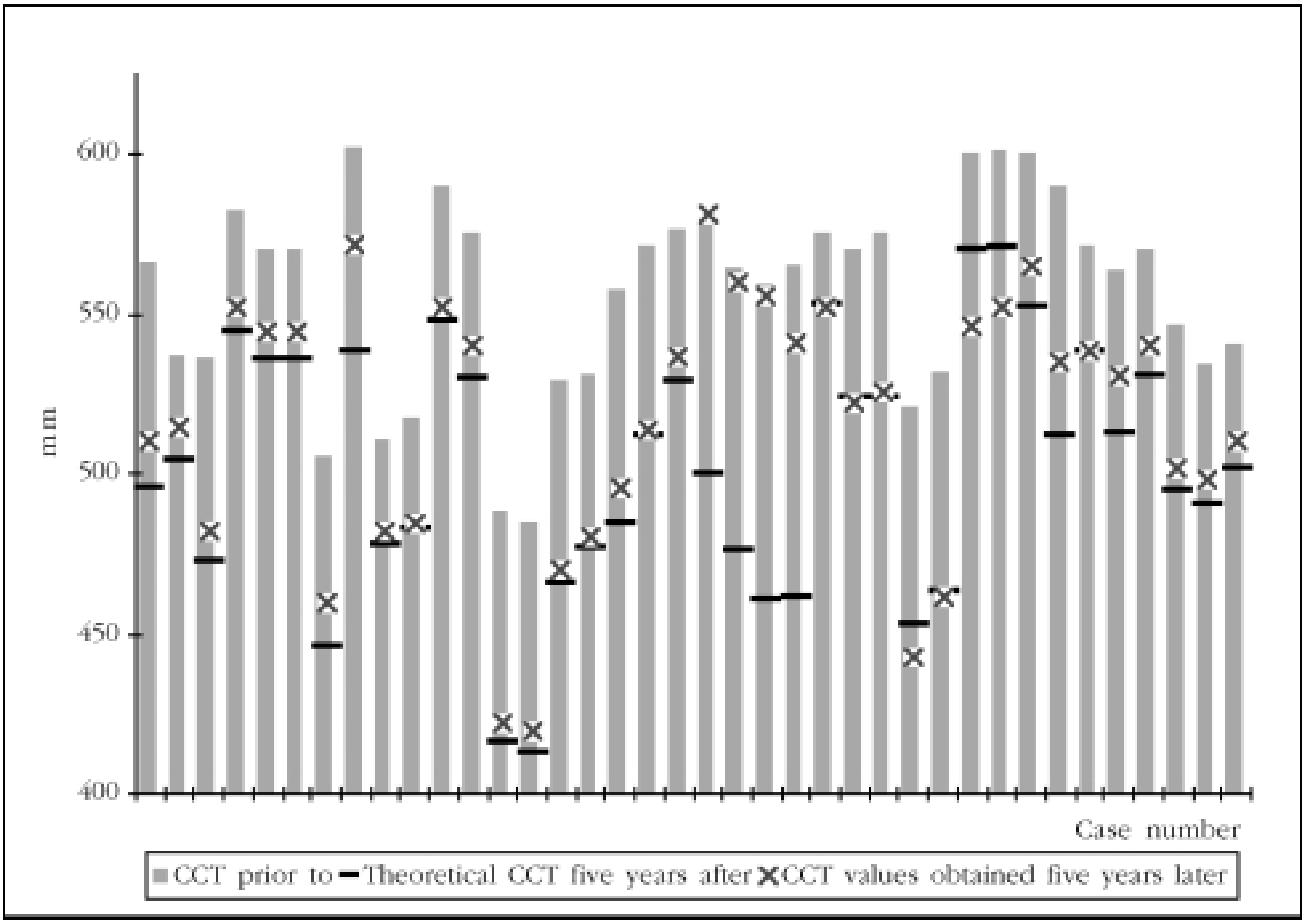

Figure 1.- Central corneal thickness (CCT) values prior to and five years after corneal photoablation (μm).

Corneal morphology shows more rigid corneal layers which then give way to slackened, more elastic layers (Seiler et al., 1992). It is therefore reasonable to assume that middle and posterior stromal ablation (under LASIK technique) alter the cornea's biomechanical properties. This could be one of the main causes for the disparities between the theroretical corneal thickness values and the values obtained by ultrasound pachymetry 60 months after photoablation.

Following LASIK, the ensuing regenerative process may lead to morphological variations in the cornea. The presence of irregularities and morphological changes in apparently healthy corneas treated by excimer laser surgery –whose clinical repercussions remain uncertain (Bohnke et al., 1998)– lead us to wonder whether the disparities between the theoretical postoperative corneal thickness values and the ultrasound pachymetric values obtained 60 months after photoablation might be due to changes in the biomechanical properties of the cornea. Moreover, applanation ultrasound corneal thickness values must be affected by changes in corneal rigidity after photoablation. Furthermore, it has been confirmed (Mardelli et al., 1997) that the physical properties of the new collagen deposited during the healing process can alter the cornea's resistance to applanation. It is also known that laser photoablation appears to stimulate wound healing by enhancing collagen accumulation in the wound, and that not only the absolute concentration but also the structure and type of collagen present may be decisive factors in establishing the integrity of the tissue (Asencio-Arana and Martínez Soriano, 1988; Asencio-Arana et al., 1992).

It has furthermore been postulated that changes occur in degree of hydration (Patel and Aslanides, 1996) and rigidity of the corneal stroma during the healing process following photoablation (Schipper et al., 1995) and this could influence post-surgical applanation ultrasound corneal thickness values.

The increase in the quantity of proteoglycans and hyaluronic acid in the context of the corneal repair process after laser photoablation elicits an accumulation of water in the stroma, hence altering stromal hydration and making the corneal stroma more flexible (Patel and Aslanides, 1996); this increased flexibility facilitates corneal applanation when using the ultrasound pachymeter.

In the light of the above, the corneal thickness values obtained after photoablation with applanation ultrasound must be lower than the expected theoretical values. Nevertheless, in the present study the results were higher than expected.

A possible explanation for the increased values of the corneal thickness obtained five years after photoablation with respect to the theoretical values could be the corneal anesthesia used during ultrasound pachymetry.

In one study, the use of corneal anesthetic eye drops induced a significant increase in central corneal thickness (Herse and Siu, 1992). In their work, those authors attributed the increase in corneal thickness, which appeared between 1 and 2 minutes after instilling two drops of corneal anesthetics, to the appearance of a transitory edema of the corneal stroma.

They explained this on the basis of the corneal edema recovery function, since it is possible to calculate the percentage recovery per hour from the exponential deswelling model described by other authors (Mandell et al., 1989; Polse et al., 1989; Herse, 1990).

Moreover, when the anesthetic diffuses deep into the corneal stroma it may inhibit the cellular metabolism of the keratocytes and the posterior layers of the cornea. Inhibition of endothelial cell metabolism may lead to corneal edema (Penna and Tabbara, 1986). Brewitt et al. (1980) described corneal epithelial cell reactions as a consequence of topical anesthetics after a single application of 0.2% benoxinate ointment. Some of the reactions they reported included a marked decrease in the microvilli and microplicae, disruption of the intercellular spaces, and a prominence of the cell nucleus which, under normal conditions, is not visible.

Wilson et al. (1988) observed that the corneal epithelium sloughs off cells directly into the precorneal tears. By irrigating tears from the surface of the cornea under different circumstances it is possible to compare the rates at which cells are sloughed off. In that experiment the rate of appearance of cells following one drop of topical anesthetic was compared with the same eye without the drop of anesthetic. Initially, the anesthetized cornea sloughed off fewer cells but later more were sloughed off. This effect lasted for at least 6 hours and showed that the return to normal sensation is only the initial part of a recovery process that takes much longer. The anesthesia, in the strict sense, wore off in 30 minutes but there was a longer lasting effect which the authors referred to as a little-known aspect of corneal physiology; namely, the rate at which cells slough off from the corneal surface. Possibly, a change in the rate at which cells slough off from the corneal surface after corneal photoablation could explain the differences between the theoretical and the real corneal thickness found by us five years later.

To sum up, several factors can affect long term corneal thickness values after stromal photoablation using 193 nm UV radiation, and further research is necessary to confirm our results and to study the specific effect that corneal photoablation using 193 nm excimer lasers has on the different corneal layers.

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