

In vivo confocal microscopy findings after SMILE refractive surgery technique

Hallazgos in vivo mediante microscopía confocal en cirugía refractiva SMILE

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Abstract

Objective: To evaluate confocal microscopy finding after SMILE surgery by in vivo confocal microscopy and stromal lenticule and stromal interface accuracy planed vs measured. **Method:** Thirty eyes of 15 patients were evaluated before and 1 month after SMILE surgery by using confocal microscopy. Cellular morphology was studied. Planed stromal lenticule thickness was compared vs measured stromal lenticule thickness after surgery by comparing the total stromal corneal thickness before vs after surgery. Stromal corneal interface was evaluated and depth of this planed interface was compared vs measured post-surgery interface depth. **Results:** Sub-epithelial nerve plexus was absent at 1 month after surgery. Activated keratocytes were found before and after stromal corneal interface depth. There was not statistical significant difference between mean planed stromal lenticule vs. post-surgery measured (102.3 ± 25.7 vs. $104.2 \pm 29.9 \mu\text{m}$; $p = 0.73$). There was not statistical significant difference between mean planed stromal interface depth vs. post-surgical measured (113.7 ± 8.2 vs. $120.5 \pm 17.3 \mu\text{m}$; $p = 0.058$). **Conclusions:** Confocal microscopy is useful to evaluate changes after SMILE surgery; lenticule thickness and stromal interface depth are exact.

Keywords: SMILE. Cornea. Refractive surgery. Confocal microscopy.

Resumen

Objetivo: Evaluar los hallazgos mediante microscopía confocal in vivo de pacientes operados de cirugía SMILE, la exactitud del lenticulo estromal y la profundidad de la interfaz estromal planeados versus medidos. **Método:** Treinta ojos de 15 pacientes operados de SMILE se estudiaron mediante microscopía confocal antes y al mes de la cirugía. Se evaluaron la morfología celular, el espesor del lenticulo estromal planeado versus el medido en el posoperatorio mediante la diferencia entre el espesor estromal preoperatorio y el postoperatorio, así como la interfaz estromal, y se comparó la profundidad de esta interfaz estromal planeada con la medida en el posoperatorio. **Resultados:** Se observó la ausencia del plexo nervioso subepitelial al mes del posoperatorio y una activación de queratocitos anterior y posterior a la profundidad de la interfaz estromal. No hubo diferencia en el lenticulo estromal planeado versus el medido en el posoperatorio (102.3 ± 25.7 vs. $104.2 \pm 29.9 \mu\text{m}$; $p = 0.73$). No hubo diferencia entre la profundidad de la interfaz estromal planeada y medida (113.7 ± 8.2 vs. $120.5 \pm 17.3 \mu\text{m}$; $p = 0.058$). **Conclusiones:** Tras la cirugía SMILE se pueden evaluar los cambios mediante microscopía confocal; el espesor del lenticulo y la profundidad de la interfaz son exactos.

Palabras clave: SMILE. Córnea. Cirugía refractiva. Microscopía confocal.

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Introduction

Refractive surgery has seen a continuous evolution in the last few years with the purpose of obtaining better results and decrease the possibility of complications, such as dry eye^{1,2} or postoperative corneal ectasias³⁻⁵.

One of the most novel techniques in refractive ectasia is SMILE (*Small Incision Lenticule Extraction*), which offers the advantage of decreasing the risk of complications mentioned above^{6,7}.

The purpose of this study is to evaluate the findings through confocal microscopy in patients that undergo SMILE, and determining the accuracy of the stromal lenticule thickness and the depth of the stromal interface in comparison with the media.

Method

Thirty eyes of 15 patients (8 women and 7 men) were subject, with informed consent, to refractive surgery using the SMILE technique. The study included all patients who were candidates for refractive surgery with SMILE technique⁶, and excluded those who were not candidates for the technique and those with previous eye surgery. The average age was 29.1 ± 5.1 years (range: 21-37), and the average for the equivalent preoperative spherical was -7.16 ± 2.58 diopters. The procedure was performed with the femtosecond laser system (VisuMax®, Zeiss, Oberkochen, Germany) and the usual SMILE⁷ technique. Postoperative treatment involved tobramycin plus topical dexametasone (Tobradex®, Alcon, Texas, USA), one drop four times a day for 2 weeks, and lubricant (Systane®, Alcon, Texas, USA) every 2 hours for 1 month.

The expected average for the creation of the stromal lenticule thickness was $102.3 \pm 25.7 \mu\text{m}$ and the average depth of the corneal interface for the creation of the lenticule using the femtosecond laser system was $113.7 \pm 8.2 \mu\text{m}$.

An *in vivo* confocal microscopy exam was performed to all corneas of all patients before the SMILE surgery and one month after surgery with a slit confocal microscope (Confoscan 4, Fortune Technologies, Vigonza, Italy). In each confocal microscopy exam a sequence of digital images (JPEG) was obtained through four consecutive tracings of the total corneal thickness, where one tracing is equivalent to obtaining images from endothelium to epithelium, that is, posterior to anterior. The Z ring device (Confoscan, Fortune Technologies, Italy) was used to maintain

contact with the cornea and obtain reliable thickness measurements, avoiding the anteroposterior movement of the eye ball.

The images were automatically captured in the hard disk of a computer for their analysis.

Postoperative morphological findings of the corneal structures were evaluated and compared with the preoperative findings.

The difference between the expected lenticule thickness and the lenticule thickness was measured after surgery through the subtraction of the total preoperative and postoperative corneal thickness with the Navis v program. 3.5.0. (NIDEK, Multi-Instrument Diagnostic System, Japan).

The planned corneal interface depth for the creation of the lenticule was compared to the obtained depth by locating said stromal interface, identified by the presence of hyperreflective particles in the corneal stroma using Navis v. 3.5.0.

Results

In all patients it was possible to perform the confocal microscopy before and after surgery. The corneal epithelium and endothelium had normal morphological characteristics in the postoperative period in all assessed corneas (Fig. 1).

The subepithelial nervous plexus was absent in all operated corneas (Fig. 2).

In all cases, it was possible to locate and evaluate the stromal lenticule interface by finding hyperreflective particles in that portion of the corneal stroma. Such particles were appreciated in abundance and in multiple sized (Fig. 3).

Activated keratocytes were found both in the portion immediately before the stromal interface and the portion just after in the depth of the corneal stroma depth (Fig. 4).

The planned lenticule was $102.3 \pm 25.7 \mu\text{m}$ and the postoperative lenticule measured was $104.2 \pm 29.9 \mu\text{m}$ on average; the difference between both was not statistically significant ($p = 0.73$, Student t-test).

The planned depth in the cornea of the interface for the creation of the lenticule with the use of femtosecond laser system was $113.7 \pm 8.2 \mu\text{m}$, and the depth measured after surgery was $120.5 \pm 17.3 \mu\text{m}$ on average; the difference between both was not statistically relevant either ($p = 0.058$, Student t-test).

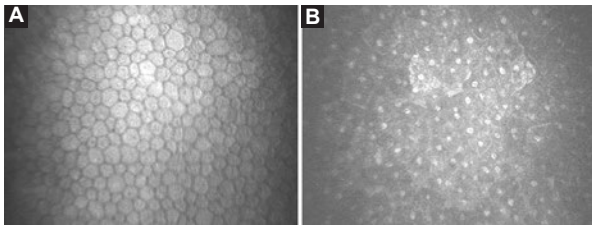


Figure 1. **A:** photo of confocal microscopy of the corneal endothelium one month after SMILE surgery, where normal morphological characteristics were observed ($340 \times 255 \mu\text{m}$). **B:** photo of confocal microscopy of the superficial epithelium one month after SMILE surgery, where normal morphological characteristics were observed ($340 \times 255 \mu\text{m}$).

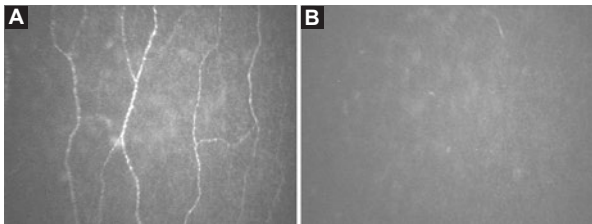


Figure 2. **A:** photo of confocal microscopy of the subepithelial nervous plexus of the cornea prior to SMILE surgery, where normal morphological characteristics were observed ($340 \times 255 \mu\text{m}$). **B:** photo of confocal microscopy of the subepithelial nervous plexus of the cornea one month after SMILE surgery, where its absence is evidenced ($340 \times 255 \mu\text{m}$).

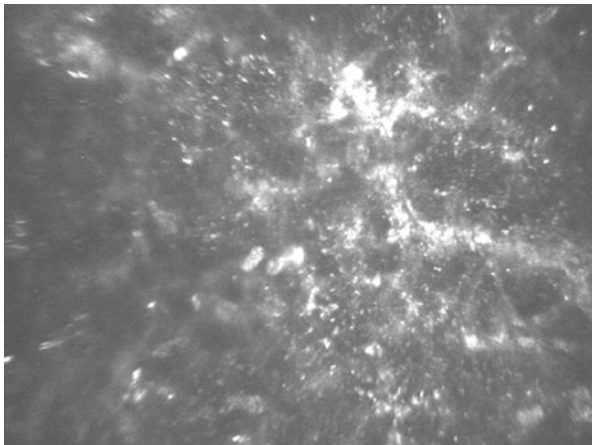


Figure 3. Fotografía de microscopía confocal de la interfaz estromal de la córnea al mes del posoperatorio de SMILE, en la cual se observan abundantes partículas hiperreflécticas de diferentes dimensiones ($340 \times 255 \mu\text{m}$).

Discussion

This study found that the corneal epithelium and endothelium have normal morphological characteristics

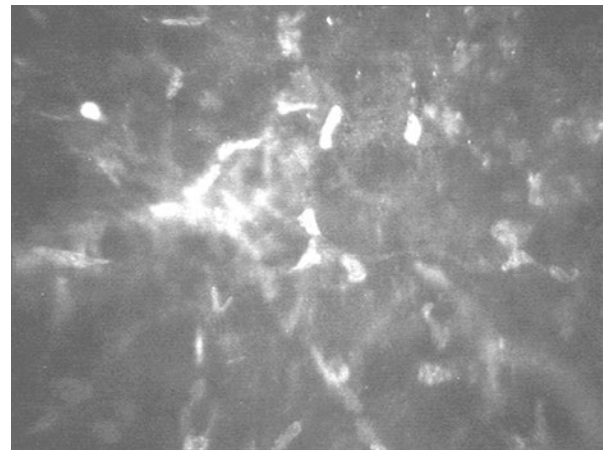


Figure 4. Fotografía de microscopía confocal de la porción justo posterior a la interfaz estromal en la profundidad del estroma de la córnea, en la que se observan múltiples queratocitos activados ($340 \times 255 \mu\text{m}$).

after the SMILE procedure, which coincides with other refractive surgery techniques, such as LASIK (*Laser in Situ Keratomileusis*)⁸.

The subepithelial nervous plexus was absent in all operated corneas (Fig. 2). The subepithelial nervous plexus was absent in all operated corneas (Fig. 2). On the other hand, the SMILE refractive surgery technique offers the expectation of producing less dry eye complications, due to a lower transitional decrease of the subepithelial nervous plexus compared to the one reported for previous techniques, such as PRK (*Photorefractive Keratectomy*) and LASIK⁸⁻¹⁰. In contrast, the SMILE technique states that, as the corneal stroma interface is deeper, compared to LASIK, such transitional decrease of the subepithelial nervous plexus is lower^{11,12}. In reference to the above, previous studies using confocal microscopy have reported that there is better recovery in the density of the subepithelial nervous plexus in patients operated with SMILE than in those operated with LASIK, in follow ups of up to 3 months^{13,14}. In the present study we found the absence of subepithelial nervous plexus in the postoperative period of SMILE, in a very similar way to what had been reported for PRK and LASIK^{8-10,15}; however, this can be due to the fact that only one evaluation was conducted using confocal microscopy one month after SMILE surgery.

The presence of keratocyte activation is a constant finding in refractive surgery with PRK, LASIK, Epi-LASIK, and SMILE, due to the scarring of the corneal stroma, whether that is due to the cut effect of the corneal interface or the response to stroma ablation using the

excimer laser^{8,9,15-18}; for this reason, keratocyte activation finding in the anterior and posterior portions of the corneal interface with the SMILE technique is expected.

Regarding the risk of appearance of secondary ectasias, such as complications in refractive surgery in all its variants, it is widely known that it depends, in large part, on the corneal depth lost by corneal ablation (as with PRK and LASIK) and the corneal interface depth created (as with LASIK)^{4,19,20}. In case of SMILE technique, there are two factors: an interface is created at a certain depth, and the stroma thickness is lost by the extraction of the stromal lenticle^{6,7}. Therefore, it is essential to know the corneal stroma depth where the interface is created and the thickness of the stromal lenticle extracted. In this study no statistically significant difference was found in the planned depth of the corneal interface compared to the depth found through postoperative confocal microscopy, or the planned stromal lenticle thickness compared to the measured thickness. The SMILE technique was precise and the preoperative values established by the femtosecond system were reliable.

Conclusions

This study provides evidence of the similarity of confocal microscopy findings between the SMILE, LASIK, and PRK techniques, in regard to the transitional denervation of the subepithelial nervous plexus and the keratocyte activation, as well as in regard to the corneal stroma interface. The accuracy of stromal lenticle thickness measurements and stromal interface depth in SMILE was also proven.

Ethical disclosures

Protection of People and Animals. The authors state that the procedures followed are in compliance with the ethical standards of the responsible human experimenting and the World Medical Association and the Declaration of Helsinki.

Data Confidentiality. The authors state that the protocols of their work center regarding the publication of patient data have been followed.

Right to privacy and informed consent. The authors have obtained informed consent from the

patients and/or subjects mentioned in the article. This document is owned by the corresponding author.

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Conflicts of interest

There is no conflicts of interest for any of the authors.

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