Patient Selection, Surgical Tips, and Clinical Results in ReLex SMILE

Volkan Hürmeriç[1]

ABSTRACT

Over the past decade, the most critical advancement in corneal refractive surgery has been the development of ReLex SMILE (RS). RS has been a reliable alternative in treating myopic and astigmatic patients without using an excimer laser. By using a single laser system, RS has managed to decrease surgery time, postoperative discomfort, and dryness in laser vision correction. Our evolving understanding of the procedure improved refractive results. Today RS is accepted to have similar efficacy, predictability, and safety as femtosecond laser-assisted LASIK. In this review, I would like to discuss the most critical factors, surgical tips and tricks that affect success in RS surgery.

Keywords: Refractive surgery, Cornea, ReLex SMILE.

INTRODUCTON

In refractive surgery, small-incision lenticule extraction (SMILE) is the most recent development in femtosecond laser-based techniques. Femtosecond lasers have been used for LASIK flap creation, intracorneal ring segment tunnel preparation, pocket creation for intrastromal inlays, penetrating, and lamellar keratoplasty, and astigmatic keratotomy.[1] ReLex SMILE (RS) is a revolutionary corneal refractive laser technique that can correct refractive errors in a single-step procedure that eliminates the creation of corneal flaps. RS is performed in a single laser platform and decreases surgical time, laser energy, intraoperative patient discomfort, and surgical costs. The first RS surgery was performed in 2007 and has been commercially available since 2012. Sekunda has published the first clinical results of RS in 2011.[2,3] Since then, it has been accepted favorably by patients and refractive surgeons. The number of patients having ReLex SMILE treatment increases every year, and an estimated more than 4 million patients had the procedure until now.

ReLex SMILE eliminates flap-related complications of the traditional LASIK surgery and has minimal effect on the ocular surface. RS preserves higher biomechanical stability and decreases the risk of dry eye.[4] Seven to 8 minutes will take to perform bilateral ReLex SMILE in experienced hands. Femtosecond lenticule extraction involves intrastromal dissection of a refractive lenticule and eliminates the need to use an excimer laser for refractive correction. Avoidance of flap creation represents a preferable option in patients who want minimally invasive treatments and refractive candidates at risk for traumatic flap dislocation, such as athletes.

Today femtosecond laser-assisted LASIK (FS-LASIK) is the gold standard in refractive surgery; however, ReLex SMILE can change this in the next decade. Long-term results of ReLex SMILE are stable and effective.[4,5] The efficacy, predictability, and safety of RS are comparable to FS-LASIK. Because of this reason, small incision lenticule extraction can be considered as the next generation of laser vision correction.[6,7]

VisuMax femtosecond laser system (Carl Zeiss Meditec AG, Jena, Germany) is the only commercially available laser system that can perform ReLex SMILE. Other laser platforms will also be commercially available to perform ReLex SMILE in the near future.[8] Some of the subjects discussed in this paper will not apply to ReLex SMILE performed in laser systems other than Visumax. In this paper, I wanted to review the current status of RS treatment

1- Associate Prof. Dunyagoz Hospital, Ophthalmology Department, Ankara Turkey

Received: 02.05.2021
Accepted: 15.07.2021

Glo-Kat 2021; 16: 63-73

DOİ: 10.37844/glauc.cat.2021.16.12

Correspondence Adress:
Volkan Hürmeriç
Dunyagoz Hospital, Ophthalmology Department, Ankara, Turkey
Phone: +90 532 365 9475
E-mail: hurmeric@me.com

and highlight the most essential clinical and surgical factors that affect the outcome. This paper will be a guide to help surgeons who want to start performing RS.

PATIENT SELECTION AND SURGICAL PLANNING

Preoperative evaluation of ReLex SMILE is similar to all refractive surgery procedures. The surgeon must evaluate ocular and systemic conditions that could affect the treatment and foresee patient-related specific risk factors. Systemic and ocular contraindications for RS are not different from that of LASIK and PRK.

In FS-LASIK, we prepare a corneal flap with a diameter of 8.4-9.1 mm and a thickness of 90-130 microns. Refractive correction is made after lifting the flap with an excimer laser in the second part of the treatment. In FS-LASIK, the residual corneal bed is planned higher than 300 microns. In RS we use a femtosecond laser to prepare refraction correcting lenticule under unaffected anterior corneal stroma and epithelium which is called a cap. Optical zone diameter in RS can be selected up to 7.5 mm in RS. Residual stromal bed in RS can be selected as low as 250 microns. Vertical side cuts incisions are used for lenticule removal in RS. I strongly recommend using two small incisions: a 2-mm incision superonasal and a 2-mm incision superotemporal. These vertical incisions do not induce any detectable irregular astigmatism in an astigmatic keratotomy-like fashion.[2]

SURGICAL PROCEDURE

Topical anesthesia must not be performed before the patient has entered the surgery room. The patient is positioned under an illuminated curved suction cone and asked to fixate on the internal blinking green target light. The lid speculum must not be inserted until the laser is ready and the patient correctly positioned and coaxially aligned with the suction cone. The lid speculum is inserted after the laser controls are ready. I strongly do not recommend using BSS to clean the ocular surface because BSS causes more dry spots and irritates the patient in our clinical experience. We recommend using a wet sponge to swap the cornea gently to remove residual secretions from the cornea.

The patient is then raised to contact the interface, and a meniscus tear film appears. The ring of the watermark will guide the surgeon as the contact zone. At this point, the patient will see the fixation target more clearly. The centration must be attempted on the coaxial sighted corneal light reflex, and the suction ports are activated to fixate the eye at this position. If the surgeon is not satisfied with the centralization, the suction can be released, and the docking procedure can be repeated. If the laser shows a tendency to apply the suction at the same decentered position, the treatment should be postponed for half an hour and repeated. Delaying the treatment will keep the cornea under topical anesthesia and increase dryness on the ocular surface resulting in increasing the risk of developing dark spots during the laser treatment. If dark spots are higher than usual in the first stage of the treatment, the surgery must be postponed to another day to achieve optimum refractive results (Figure 1).

Laser parameters

Conventional laser settings in RS will be repetition rate 500 kHz, pulse energy 120 to 140 nJ, spot distance 2 to 5 mm,

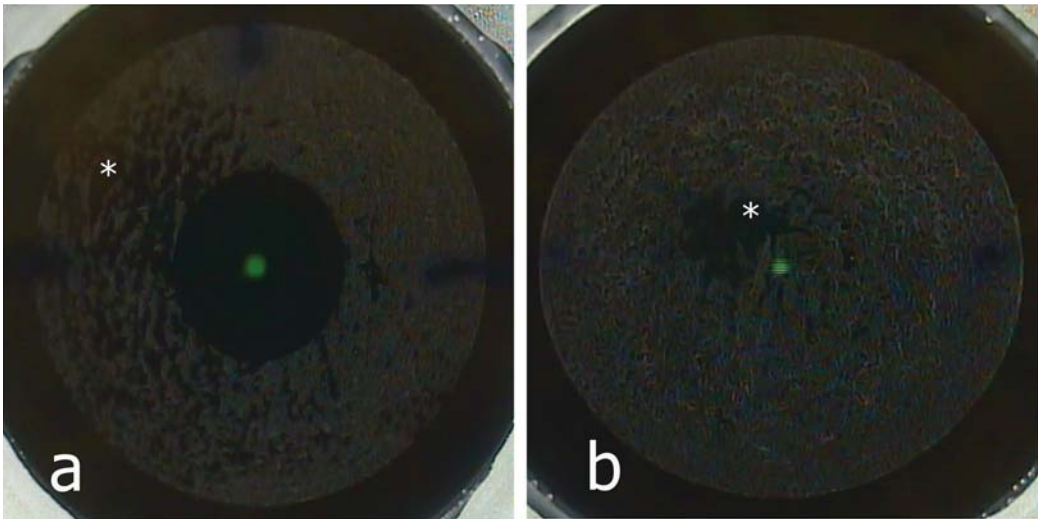

Figure 1: *Surgical view of dark spots developed in lenticular cut. Surgery must be postponed in Figure 1a. Treatment can be completed in Figure 1b; however, there is a risk of developing postoperative astigmatism.*

lenticule side-cut angle 70-90 degrees, lenticule diameter 6.2 to 7.00 mm, cap diameter 7.2 to 7.9 mm (0.5 to 1.0 mm greater than the lenticule diameter), cap thickness 100 to 140 mm, side-cut circumferential length 2to 3.5 mm, and minimum lenticule side-cut thickness 15 (10-20) mm.

Docking:

The standard surgical technique of ReLex SMILE involves docking, femtosecond laser application, lenticule dissection, and the extraction of the lenticule. Almost every ophthalmologist who is planning to learn ReLex SMILE surgery concentrates on removing the lenticule from the cornea. Removing the lenticule requires skill and takes some time to master the technique. However, the most crucial part of ReLex SMILE is the docking stage, and every step in docking seriously affects the refractive outcome of our patients. Most of the difficulties we experience during lenticule removal and less-than-perfect refractive outcomes are caused by mistakes made in the docking procedure.

The surgeon must show the utmost concentration on three critical issues during the docking procedure. The surgeon should control the patient's behavior and cooperation, check the ocular surface, and has to centralize the laser to the visual axis at the same time. The ideal refractive technique should be easy to perform, and it must not be depended on the surgeon's surgical skills. The requirement for surgeon control is an important difference between ReLex SMILE and excimer lasers. The laser system centralizes the ablation according to the pupil center or visual axis during excimer laser ablation, corrects cyclotorsion, and the eye-tracker system compensates for the patient's eye movements. Cooperation of the patients rarely becomes an issue for the surgeon in excimer laser treatments. If the patient is very anxious, it may be challenging to control these three issues simultaneously in ReLex SMILE. The surgeon's reaction in an uncooperative patient will be to finish the treatment as quickly as possible. To finish the treatment quickly, the surgeon may overlook the debris and dry spots on the ocular surface, resulting in dark spots.[7] The centralization and cyclotorsion may not be ideal, resulting in coma and residual astigmatism.

During docking, proper head-positioning is essential. The patient must lay down in the center of the surgical bed. The height of the headrest must be leveled according to the patient's comfort. Medially tilting will help avoid nasal contact with the cone of the glass interface. Multiple docking attempts will increase epithelial irregularities and the risk of developing dark spots. Before redocking attempts, wiping the undersurface of the interface with a wet sponge is recommended.

Centralization:

Eye tracker-based centralization has been used in excimer lasers to optimize functional outcomes and improve visual, refractive, and wavefront results. New generation excimer laser systems have been reported to have improved centralization than the previous excimer lasers.[9] In RS treatment, centralization entirely relies on the patient's fixation, and subjective alignment of the treatment is both an advantage and a disadvantage. In RS, significant decentralization may result in severe coma and astigmatism (Figure 2). On the other hand, treating the patient directly on the visual axis with targeting coaxial corneal light reflex can achieve good refractive results.[10] The patient must fixate on a blinking green light before the suction process. In this way, the patient's visual axis and corneal vertex are centered on the contact glass's vertex, which is centered on the laser system and the center of the lenticule. The surgeon can verify centralization with the first Purkinje reflex or the pupil's center. When the suction is applied, contact glass can also shift coaxially to best-fit corneal shape and result in slight decentralization.

RS can achieve similar centration to the eyes treated with MEL 80 and 90 excimer laser systems (Carl Zeiss Meditec, Jena, Germany).[11] Subjective alignment is a risk in uncooperative and anxious patients. Mild decentralization has been reported not to have a severe effect on the refractive correction but causes an increase in postoperative coma and spherical aberration.[12,13] However, these studies use different techniques to analyze centralization, making it harder to compare the results interchangeably.

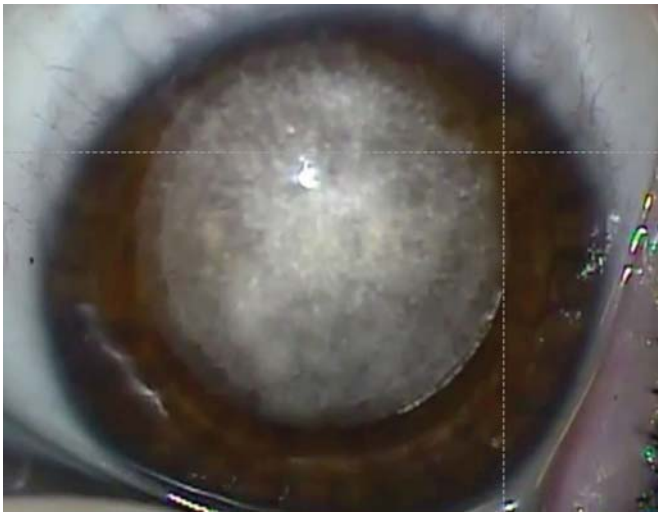

Figure 2: *Surgical view of a patient with severely decentered treatment. The surgery is cancelled in the patient.*

Cyclotorsion:

One of the potential limitations of ReLex SMILE is the lack of control centralization and cyclotorsion. RS does not have an active eye-tracking system used during the scanning procedure. Misalignment of astigmatism treatment decreases the flattening effect and causes an under-correction of the magnitude of astigmatism. Theoretically, 8 degrees of misalignment will cause a 25% under-correction in astigmatism magnitude.[14] According to Alpin's study, 10 degrees misalignment causes a 6% decrease in the correction. Twenty-degree misalignment causes a 24% decrease at the intended correction.[15] The surgeon should centralize the laser according to the visual axis and check cyclotorsion. Corneal reference marks should be placed when the patient was seated upright at the slit lamp at 3 and 9 o'clock position with a sterile skin marker. A third mark perpendicular to the horizontal marks at 6 o'clock will help manual alignment of the patient interface during suction (Figure 3).

Cyclotorsion compensation significantly improves visual and refractive results in RS.[16] In a series of 622 patients, 71.5% of the patients required manual axis compensation.[17] Surgeons must compensate for axis alignment and locate the visual axis according to the visual axis in patients with high astigmatism (astigmatism higher than 1.50 D). Misalignment of the visual axis causes loss of visual acuity postoperatively in these patients.

Femtosecond laser application:

After the femtosecond laser application starts tracking systems are not required in RS. The application of suction will eliminate the need for a tracking system, and the eye will maintain its desired position throughout the treatment. During the RS application, femtosecond laser will make four sequential photo-disruptive incisions that create an intrastromal lenticule. The total time for all laser incisions is between 20-35 seconds.

The first lenticule cut (underside-posterior surface of the lenticule) is the most important incision of the treatment, making the refractive correction. The lenticule cut is prepared from the periphery to the center (spiral in pattern).

The second cut will be the vertical lenticule side cut. Side-cut thickness does not have any refractive effect; however, to balance tissue preservation and ease of lenticule dissection, the side-cut thickness must not be selected lower than 10 microns and higher than 20 microns. In patients lower than 2 D spherical error, I do not recommend using side cut thickness lower than 20 microns. In patients higher than 4 D of spherical error, 10 microns side cut thickness will be optimum for lenticule extraction.

The third cut will be the cap interface (upper side-anterior surface of the lenticule). Anterior lenticule surface cut is prepared from the center to the periphery (spiral out pattern). After the lenticule is removed, the remaining anterior section of the disconnected residual stromal tissue and the overlapping epithelium is referred to as "cap." The cap cut interface is prepared parallel to the cornea surface, and it does not have any refractive effect.

The fourth cut will extend to the ocular surface from the anterior surface of the intrastromal lenticule for surgical maneuvers. Mono-incisional or bi-incisional approach can be selected. A 2-mm incision superonasal and a 2-mm

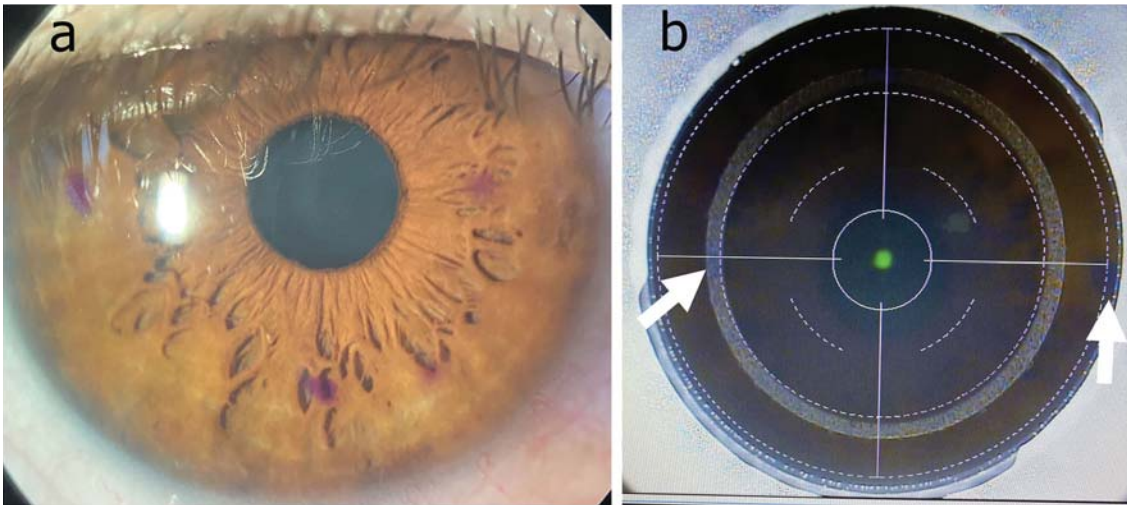

Figure 3: *Three-point marking of the cornea in a patient with high astigmatism. Corneal markings are prepared at the slip lamp while the patient was in a sitting position. (a) Slit-lamp view (b) Surgical view.*

incision superotemporal incision can be prepared. The second incision is used as a separate entrance in cases with difficulty in lenticule dissection.

Lenticule dissection and extraction:

In the first step small incision is opened with a small, pointed spatula or a Sinskey tip to guide the anterior plane, delineating the anterior edge of the lenticule. The incision guiding the posterior plane is opened on the far side of the small incision separating the openings to the anterior and posterior planes. In the second step, the anterior edge (cap cut) is separated with a spoon-shaped dissector. The interface can be dissected with a single sweep starting from the temporal border to the nasal side. The surgeon can also dissect the cap cut similar to separating a femtosecond laser LASIK flap. It is essential to use the least possible number of maneuvers to complete the dissection in RS. In the third step, the lenticular edge is separated. While dissecting the lenticular cut, the anterior edge will be loose, and there will not be adhesive stability against the separation force of the blunt instrument. A single separating sweep similar to the cap cut separation will loosen the lenticule entirely, and it may become challenging to separate the lenticule from the periphery due to a lack of counter-reaction. It is also more challenging to separate the lenticular cut than the cap cut. The surgical instrument must always apply a counterforce to the dissecting tissue. A small undissected peripheral sector with a shape of a triangle will help while rotating the bulb of the dissector at the edge of the lenticule (Figure 4).[18]

Once both planes had been separated, the lenticule can be extracted with a 23-gauge forceps from the main incision. Chung's swing technique, lenticulerhexis, lenticuloschisis, hydroexpression, and optical coherence tomography assisted lenticule extraction have been suggested for successful lenticule extraction in RS (Figure 5).

Unintended posterior plane dissection and tearing of the lenticule are the significant risks involved in lenticule dissection (Figure 6). It is essential to find the first dissection plane over the roof of the lenticule first.[1] If the blunt spatula undermines the base of the lenticule first, it can be harder to find the second dissection plane. Lenticule will stick to the superior corneal layers, and it may become invisible. If the second dissection plane cannot be found after the first several attempts, inadvertent dissection of the lenticule base must be suspected. At the edge of the lenticule anterior dissection, the plane extends 1 mm more than the refractive plane. If the surgical instrument is in

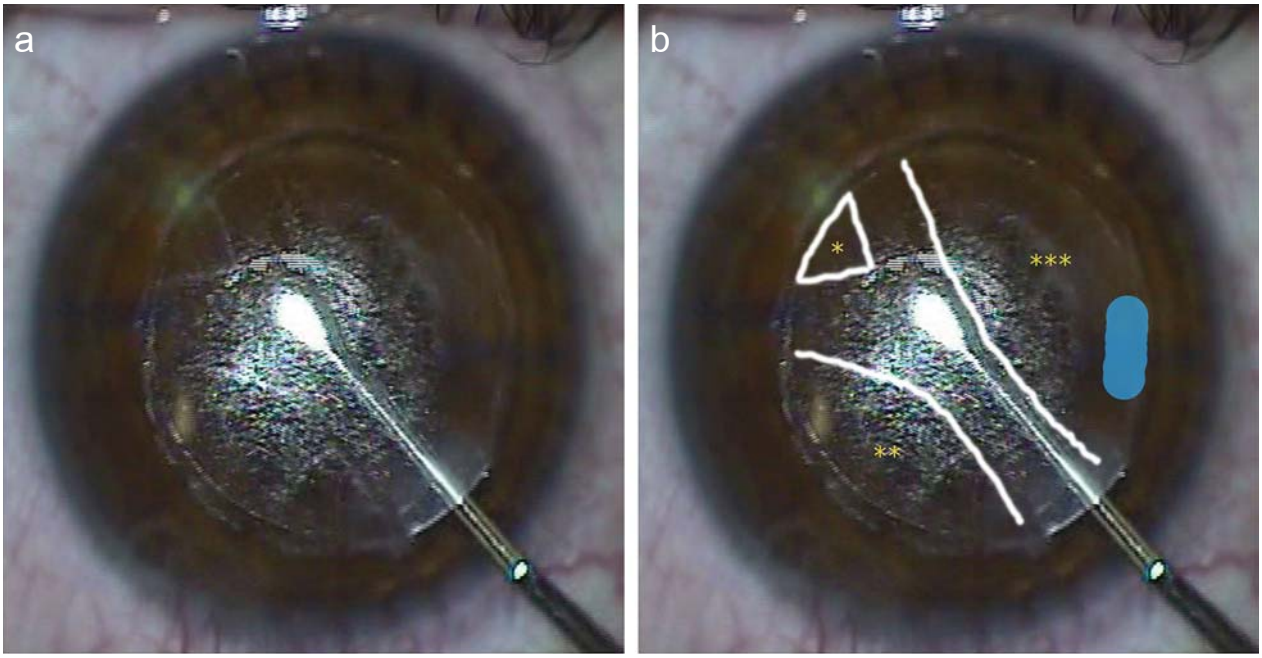

Figure 4: *Surgical steps to separate lenticular interface. Surgical view (a), "Inverted piece sign" formation (b). The lenticule (posterior) cut can be divided into two halves with a single push of the separator. Then the separator is moved back and then moved towards the left-hand side to prepare a triangle-shaped unseparated part (*). The separation of the lenticule resembles a "inverted piece sign" at this point. The left half (**) of the interface is separated first. The right half is separated (***) with a circular sweep leaving the superior edge intact (blue market area). The last place to separate in the interface is the triangle-shaped white marked area (*) . At this point the lenticule is attached only at the blue marked edge and can be easily extracted with a forceps.*

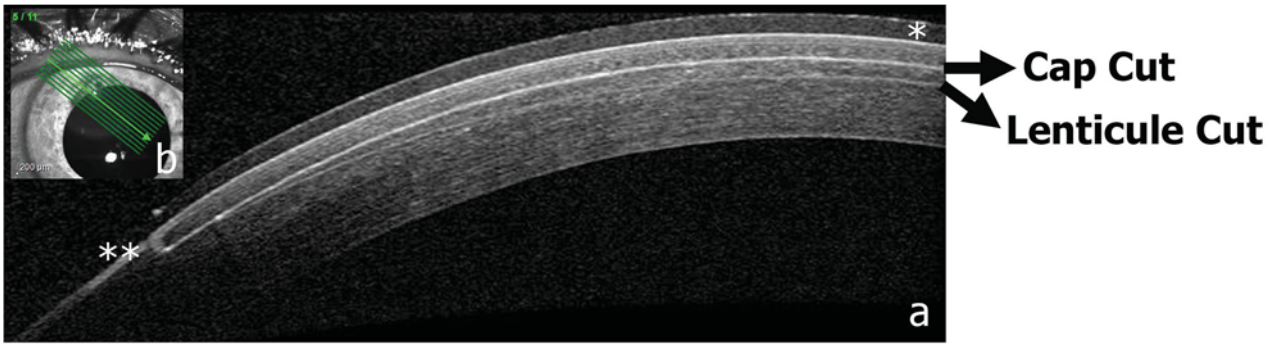

Figure 5: *Anterior segment optical coherence tomography (AS-OCT) images in a patient with difficulty in finding the second interface. During the surgery, cap (anterior) cut is separated easily, and white-ring sign is not observed. Multiple attempts failed to separate the lenticular cut due to excessive opaque bubble layer formation. The surgery is postponed, and AS-OCT images are taken to confirm the integrity of the femtosecond incisions. a) AS-OCT images of femtosecond incisions b) Position of the displayed AS-OCT section on the cornea. A bandage contact lens is on the cornea (*). Corneal incisions (**) and the dissected cap cut have a brighter reflectivity in AS-OCT images. Unseparated lenticular cut demonstrates a darker reflectivity. AS-OCT demonstrates that femtosecond laser cuts are intact. A second attempt to find the lenticular interface has been successful, and the surgery was completed without any complication.*

Figure 6: *Surgical view of a lenticular tear. Yellow asterisk in all images shows the position of the lenticular tear (*) a) Opaque bubble layers cause difficulty in cap (anterior) cut dissection. Horizontal tear is noticed at the paracentral area of the lenticule. b) Second corneal incision is used to dissect remaining lenticule tissue without complete fragmentation of the lenticule. c) The lenticule is inspected after extraction. The lenticule is complete without any residual fragments left in the interface.*

the base of the lenticule and the anterior plane was not dissected, the side-cut of the lenticule can be noticed as a light reflection on top of the dissecting instrument (white ring sign) (Figure 7).[19] In the standard dissection of the cap cut, the tip of the dissector would cover the lenticule base. If the difficulty in finding the second plane of the lenticule persists for a long time, it is recommended to perform an anterior OCT to understand the anatomy of the lenticule and act accordingly (Figure 5). After the lenticule extraction, it can be hydrated with balanced salt solution and inspected for completeness and edge smoothness (Figure 6).

Topical antibiotics and steroid drops are administered after the surgery. Plastic shields are not necessarily needed postoperatively. Bandage contact lenses can be used in patients with epithelial disruption at the incision area. Patients are recommended to use a topical steroid (dexamethasone, loteprednol, bethametasone) and antibiotic (moxifloxacin, ofloxacin, levofloxacin, besifloxacin) drop for 1 to 2 weeks postoperatively. Artificial tear drops can be used for one month.

Applicability and Nomogram

Today RS can be used in patients with mild to moderate myopia (-0.50 to -10.00 D) and astigmatism (-0.25 to -5.00 D). The range of spherical error that can be corrected with Visumax is between -0.50 to -12.50 D. Although it is not commercially available, hyperopic correction is possible

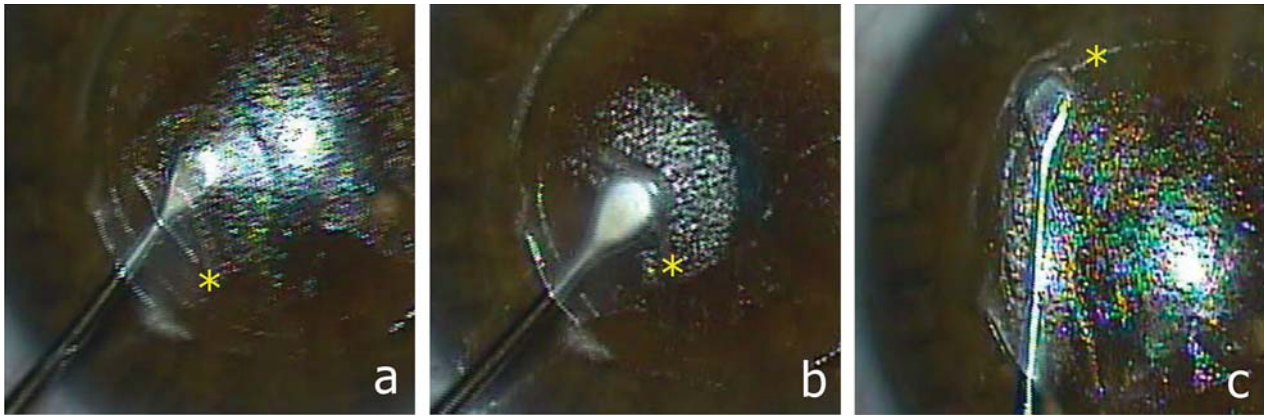

Figure 7: *White ring sign in ReLex SMILE lenticule separation a) The bulb of the surgical instrument is in the lenticular (posterior) cut. The edge of the lenticule can be noticed as a light reflection on top of the dissecting instrument (*) b) When the separator is in the cap (anterior) cut, the edge of the lenticule is blocked by the instrument (*) c) The bulb of the separator in the lenticular cut. The side-cut of the lenticule can be noticed as a light reflection on top of the dissecting instrument (white ring sign)(*)*

with RS with promising results.[20,21] The minimum corneal thickness requirement is 475 to 490 microns, and minimum residual stromal thickness is recommended between 250 to 275 microns according to traditional LASIK parameters. These parameters may be modified in the future as RS lacks flap creation and provides a higher degree of corneal stability.

Over and under-correction has been reported in ReLex SMILE studies. Several studies have reported postoperative spherical equivalent between ±0.50 D in 67 to 84% of the patients (22-24). In our series of 84 patients, we have achieved ±0.50 D in 82% of our patients at postoperative 12 months. Like all refractive procedures, a nomogram is still needed in RS.[25] However, the nomogram in RS is more straightforward than the nomogram used in excimer lasers. Excimer lasers are affected by the humidity of the environment, and the nomograms must be adjusted according to the patient's age. Theoretically, ReLex SMILE does not need a nomogram, and it does not require adjustments according to the age of the patients. In a recent study, patients older than 40 years demonstrated under-correction compared with patients younger than 35 years of age in RS.[26]

The nomogram in ReLex SMILE depends on personal experience, and a basic nomogram can be applied. In patients higher than four diopters 10% increase in attempted correction is suggested. In patients having with the rule astigmatism 0.50 D, in oblique astigmatism 0.25 D, higher refractive correction should be applied. In patients with against the rule astigmatism, no correction is necessary.[27] Machine learning models achieve significantly more efficient results in RS.[28]

COMPLICATIONS

The majority of RS-related complications can be avoided with experience. It is important to emphasize that most of the complications do not affect the visual outcome in RS. Suction loss, black spots, and opaque bubble layers may result in difficulties in lenticule extraction, cap perforation, lenticule tears.[7]

The most common intraoperative complication in RS is minor epithelial abrasions at the incision.[29] A bandage contact lens must be used for easier recovery in these cases. Lenticule extraction difficulties, minor tears at the incision, suction loss, central abrasions, cap perforations can be seen during RS. The most severe intraoperative complication of RS is incomplete removal of the lenticule. RS has a steep learning curve, and the risk of lenticule tears will be higher in the first cases.

Suction loss is more commonly observed in RS because it has lower suction pressure than traditional femtosecond lasers. It is most likely caused by patient eye contraction or sudden patient eye movement. Narrow eyelid fissure, lid squeezing, smaller corneas, conjunctival chemosis, and uncooperative patients increase suction loss risk. If the suction is lost in the first (posterior) cut of the treatment, it is recommended not to continue with RS and convert to LASIK. Immediate retreatment can be performed with the same laser parameters unless the suction loss occurs during the posterior lenticular cut more than 10% of the first cut is created. If cap thickness can be decreased by 30 microns, RS retreatment can be performed even in cases with posterior cut suction loss after 10% completion. However, there is a risk of developing unintentional dissection of

two different planes causing lenticule tear and irregular astigmatism. In a series of 8490 eyes, the suction loss has been reported in 0.4% of cases. %51 of the cases occurred during cap cut, and 75% of the cases occurred in the right eye.[30]

Late postoperative complications in RS include minor haze, dry eye, epithelial islands at the incision, epithelial ingrowth, fibers in the interface, diffuse lamellar keratitis, infections, and ectasia.[7,31]

CLINICAL RESULTS AND DISCUSSION

Every step of ReLex SMILE has a different effect on the outcome. The surgeon should be aware of the continuation of the treatment at every stage. If an adverse event happens, the surgeon should make the correct decision in a matter of seconds. To make a correct decision, we must know every factor affecting the laser performance. The safest decision will always be to continue the treatment as LASIK. The patient's compliance is an essential factor in ReLex SMILE. Because of this reason, the surgeon must calm the patients and help them undergo the laser in an ideal way.

The energy level of the laser suite is also an essential factor in ReLex SMILE. Every Visumax system has a specific energy level and an ideal spot separation. Energy setting is not interchangeable within different Visumax systems. Because of this reason, every surgeon must find the ideal energy level in their system. Higher energy levels will result in opaque bubble layers (OBL), and lower energy levels will result in dark spots. Both of these will cause difficulty in lenticule separation.

Clinical studies demonstrated similar or better refractive and visual outcomes of RS when compared with LASIK.[4,32,33] Several studies have reported long-term results of RS. In 2008-2009, 91 eyes were treated with RS for the first time.[2] Fifty-six patients of this cohort volunteered for reexamination 5 and 10 years postoperatively. In the fifth postoperative year, 48.2% of eyes were within ±0.5 D, and 78.6% were within ±1.0 D (34). The regression was 0.48 D, and the efficacy index was 0.9 in 5 years. In the tenth postoperative year, 64.3% of eyes were within ±0.50 D, and 82.1% were within ±1.00 D of target refraction (4). The regression was 0.30 D in 10 years, and the results were stable and showed no late side-effects. However, these studies were performed with a 200 Khz Visumax, a prototype laser. Recently published studies with the new Visumax laser platform delivers superior refractive outcomes to the first RS results and comparable with LASIK outcomes.[35,36] Advancements in RS technology, energy settings, and scan patterns also improve current RS results.

Ağca et al.[37] reported five years postoperative RS results in patients higher than 6 D myopia. At 1-year, 70% and 97% of the eyes were within ±0.50D and ±1.00 D of the intended correction. At 5-years, 59% and 92% percent of the eyes were within ±0.50D and ±1.00 D of the intended correction. These results demonstrate regression of the refractive correction in the long term and adjusting target correction accordingly to increase long-term success. In LASIK, a mean regression of 0.63-0.97 D is also reported after six years.[35,36] RS has comparable clinical results when compared with other corneal refractive techniques. RS performed better than LASEK in correcting high astigmatism.[37] RS has also shown to have lower high order aberrations when compared with FS-LASIK in several studies.[38,39]

RS preserves the anterior lamella, the strongest part of the cornea.[40] Because of this reason, RS is accepted to have a less biomechanical effect on the cornea. It is proposed that RS causes 70% less disruption of the anterior lamella of the cornea when compared to LASIK. Mathematical remodeling and finite element analysis support the theory that RS maintains a stronger cornea.[41] CorVis ST (CST) (Oculus Optikgeräte, Wetzlar, Germany) is a novel noncontact tonometer that uses a high-speed Scheimpflug camera which can demonstrate corneal biomechanical changes after crosslinking and refractive surgery better than an ocular response analyzer (Reichert Ophthalmic Instruments, Depew, NY). Shen[42] demonstrated the highest corneal deformation after FS-LASIK compared with LASEK and RS.Khamar et al.[43] reported less biomechanical effect with RS cap when compared with LASIK flap.

Postoperative ectasia is still a feared complication of corneal refractive surgery.[44] RS is not immune to this problem, and utmost care must be used to exclude cases with suspected corneal abnormalities. There is no safe limit of tissue alteration in at-risk corneas.[44] Because of this reason, it is recommended to use the same tomographic and topographic screening criteria that have been developed for LASIK and PRK in patient selection for RS.[40,45] There are several case reports of corneal ectasia developed after RS. Most of these patients have significant preoperative topographic irregularities, which are traditionally accepted as a contraindication for LASIK.[46-48] There are also reported cases that developed post-ReLex SMILE ectasia with preoperative normal topographies.[50] Shetty has reported an observational retrospective study in which lenticules of 178 patients were preserved three years postoperatively.[50] One of these patients from this cohort developed corneal ectasia with normal preoperative tomographic and biomechanical indexes. Validation of lysyl oxidase (LOX) expression in

this lenticule by reverse transcription-polymerase chain reaction demonstrated lover LOX levels in the cornea compared with lenticules collected from healthy eyes. LOX is a natural collagen crosslinking enzyme produced in the extracellular matrix and known to be reduced in ectatic eye diseases.[51] Lower LOX levels may explain corneas that develop ectasia with normal preoperative corneal indices undergoing RS surgery. Combining RS with intraoperative accelerated crosslinking has been reported to prevent the risk of future ectasia in borderline corneas.[52] Further studies and long-term results are needed to confirm the effect of this novel technique.

Another advantage of RS is better protection of superficial corneal nerves, which decreases the risk of dry eye. In their first reported RS study, Sekundo has reported less superficial punctate corneal staining and subjective dry eye symptoms in RS when compared with femtosecond lens extraction (FLEX).[2] Demirok et al.[5] has compared the effects of FS-LASIK and RS on corneal sensation and dry eye. In this bilateral study, FS-LASIK was performed on one eye, and RS was performed on the fellow eye of the same patients. Corneal sensitivity was decreased in both groups; however, it was significantly better in RS eyes at postoperative one week, one month, and three months. There was no significant difference in corneal sensitivity between FS-LASIK and RS at postoperative six months. Tear break-up time (TBUT), tear film osmolarity (TFO), and Schirmer score was not different between both techniques. Li[53] has compared corneal sensitivity between FS-LASIK and RS with Cochet- Bonnet esthesiometer (Luneau, Paris, France).RS treated eyes showed better central corneal sensation and better recovery than in the Femto-LASIK-treated eyes at all postoperative follow-up visits. Wei et al.[54] reported that corneal sensation had recovered to preoperative levels three months after SMILE surgery but did not recover by six months after Femto-LASIK. Denoyer et al.[55] has reported better OSDI, TBUT, tear osmolarity, and dry eye severity score in RS compared to LASIK.At postoperative six months, none of the RS group were using frequent tear substitutes versus 20% of the LASIK group needed. A recent meta-analysis demonstrated that RS had an overall lower impact on the ocular surface and corneal innervation than the FS-LASIK did during the 1- and 6-month observation periods.[56] Surgically induced breakdown of the sub-basal corneal nerves during flap creation was accepted as the reason for worse postoperative ocular surface parameters in FS-LASIK than RS. As a result, we can accept that RS has a fewer negative impact on the ocular surface and shows superiority over FS-LASIK by exhibiting a lower risk of postoperative dry eye.

Several alternative laser systems can also perform small incision lenticule extraction. FemtoLDV Z8 (Ziemer Ophthalmic Systems AG, Port, Switzerland) is the second laser system to perform RS, and its new lenticule application is called CLEAR (Corneal lenticule extraction for advanced refractive correction). CLEAR has a new guided lenticule extraction technique using two small incisions that delineates the anterior and posterior planes of the lenticule separately. Using two different incisions to separate anterior and posterior edges separately eliminates one of the most critical and challenging surgical steps of the standard RS technique. Another advantage of FEMTO LDV is the ability to recenter the treatment area without releasing the suction.[57] The system can detect corneal markings, and the software can correct cyclotorsion and centration accordingly.

ATOS (SCHWIND Kleinostheim · Germany) is a recently introduced femtosecond laser system that can perform RS surgery with pupil recognition, centralization, and cyclotorsion compensation. Similar to Visumax, ATOS also uses a curved interface. Atos received CE mark in 2020. There is no peer-reviewed data about the clinical results of ATOS today.

In conclusion, ReLex SMILE has been a revolution in corneal refractive surgery and has become a successful alternative to FS-LASIK. Ever-increasing RS numbers is also an indication of the success of this novel technique. The worldwide success of small incision lenticule extraction encouraged other companies to develop alternatives to RS. Further availability of different laser platforms will expand small incision lenticule extraction usage and success. In our clinical practice, RS has been our preferred surgical technique in treating myopia and astigmatism. Our results demonstrated a significant decline in the percentage of FS-LASIK treatments in favor of RS every year. I encourage my colleagues to prefer RS in their refractive practice.

REFERENCES

1. Farid M, Steinert RF. Femtosecond laser-assisted corneal surgery. Curr Opin Ophthalmol 2010; 21:288-92.
2. Sekundo W, Kunert K, Russmann C, et al. First efficacy and safety study of femtosecond lenticule extraction for the correction of myopia: six-month results. JCRS 2008, 34:1513-20.
3. Sekundo W, Kunert KS, Blum M. Small incision corneal refractive surgery using the small incision lenticule extraction (SMILE) procedure for the correction of myopia and myopic astigmatism: results of a 6 month prospective study. Br J Ophthalmol 2011;95:335-9.
4. Blum M, Lauer AS, Kunert KS, et al. 10-Year Results of Small Incision Lenticule Extraction. J Refract Surg 2019;35:618-23.

5. Demirok A, Ozgurhan EB, Agca A, et al. Corneal sensation after corneal refractive surgery with small incision lenticule extraction. Optom Vis Sci 2013;90:1040-7.
6. Moshirfar M, McCaughey MV, Reinstein DZ, et al. Small-incision lenticule extraction. J Cataract Refract Surg 2015;41:652-65.
7. Krueger RR, Meister CS. A review of small incision lenticule extraction complications. Current opinion in ophthalmology 2018;29:292-8.
8. Wang M, Zhang F, Copruz CC, Han L. First Experience in Small Incision Lenticule Extraction with the Femto LDV Z8 and Lenticule Evaluation Using Scanning Electron Microscopy. Journal of Ophthalmology 2020;2020:6751826.
9. Kanellopoulos AJ, Asimellis G. LASIK Ablation Centration: An Objective Digitized Assessment and Comparison Between Two Generations of an Excimer Laser. J Refract Surg 2015;31:164-9.
10. Lazaridis A, Droutsas K, Sekundo W. Topographic Analysis of the Centration of the Treatment Zone After SMILE for Myopia and Comparison to FS-LASIK: Subjective Versus Objective Alignment. J Refract Surg 2014;30:680-6.
11. Reinstein DZ, Gobbe M, Gobbe L, et al. Optical Zone Centration Accuracy Using Corneal Fixation-based SMILE Compared to Eye Tracker-based Femtosecond Laser-assisted LASIK for Myopia. J Refract Surg 2015;31:586-92.
12. Huang J, Zhou X, Qian Y. Decentration following femtosecond laser small incision lenticule extraction (SMILE) in eyes with high astigmatism and its impact on visual quality. 2019:1-9.
13. Jun I, Kang DSY, Reinstein DZ, et al. Clinical Outcomes of SMILE With a Triple Centration Technique and Corneal Wavefront-Guided Transepithelial PRK in High Astigmatism. J Refract Surg 2018;34:156-63.
14. Stevens JD. Astigmatic Excimer Laser Treatment: Theoretical Effects of Axis Misalignment. European Journal of Implant and Refractive Surgery 1994;6:310-8.
15. Alpins NA. Vector analysis of astigmatism changes by flattening, steepening, and torque. Journal of Cataract& Refractive Surgery 1997;23:1503-14.
16. Chen P, Ye Y, Yu N, et al. Comparison of Small Incision Lenticule Extraction Surgery With and Without Cyclotorsion Error Correction for Patients With Astigmatism. Cornea 2019;38:723-9.
17. Chen P, Ye Y, Yu N, et al. Correction of Astigmatism With SMILE With Axis Alignment: 6-Month Results From 622 Eyes. J Refract Surg 2019;35:138-45.
18. Reinstein DZ, Archer TJ, Carp GI. The surgeons guide to Small incision lenticule extraction. Slack Incorporated 2018; 221-3.
19. Jacob S, Nariani A, Figus M, et al. White ring sign for uneventful lenticule separation in small-incision lenticule extraction. J Cataract Refract Surg 2016;42:1251-4.
20. Reinstein DZ, Pradhan KR, Carp GI, et al. Small Incision Lenticule Extraction (SMILE) for Hyperopia: Optical Zone Centration. J Refract Surg 2017;33:150-6.
21. Pradhan KR, Reinstein DZ, Carp GI, et al. Small Incision Lenticule Extraction (SMILE) for Hyperopia: 12-Month Refractive and Visual Outcomes. J Refract Surg 2019;35:442-50.
22. Yao P, Zhao J, Li M, et al. Microdistortions in Bowman's Layer Following Femtosecond Laser Small Incision Lenticule Extraction Observed by Fourier-Domain OCT. J Refract Surg. 2013. 29:668-74
23. Kanellopoulos AJ. Topography-Guided LASIK Versus Small Incision Lenticule Extraction (SMILE) for Myopia and Myopic Astigmatism: A Randomized, Prospective, Contralateral Eye Study. J Refract Surg 2017;33:306-12.
24. Reinstein DZ, Carp GI, Archer TJ, et al. Outcomes of Small Incision Lenticule Extraction (SMILE) in Low Myopia. J Refract Surg 2014;30:812-8.
25. Qian Y, Huang J, Zhou X, et al. Comparison of femtosecond laser small-incision lenticule extraction and laser-assisted subepithelial keratectomy to correct myopic astigmatism. J Cataract Refract Surg 2015;41:2476-86.
26. Primavera L, Canto-Cerdan M, Alió JL, et al. Influence of age on small incision lenticule extraction outcomes. Br J Ophthalmol 2020.(Basım aşamasında)
27. Ganesh S, Brar S, Pawar A. Results of Intraoperative Manual Cyclotorsion Compensation for Myopic Astigmatism in Patients Undergoing Small Incision Lenticule Extraction (SMILE). J Refract Surg 2017;33:506-12.
28. Cui T, Wang Y, Ji S, et al. Applying Machine Learning Techniques in Nomogram Prediction and Analysis for SMILE Treatment. Am J Ophthalmol 2020;210:71-7.
29. Ivarsen A, Asp S, Hjortdal J. Safety and complications of more than 1500 small-incision lenticule extraction procedures. Ophthalmology 2014;121:822-8.
30. Liu M, Wang J, Zhong W, et al. Impact of Suction Loss During Small Incision Lenticule Extraction (SMILE). J Refract Surg 2016;32:686-92.
31. Zhao J, He L, Yao P, et al. Diffuse lamellar keratitis after small-incision lenticule extraction. J Cataract Refract Surg 2015;41:400-7.
32. Lin F, Xu Y, Yang Y. Comparison of the Visual Results After SMILE and Femtosecond Laser-Assisted LASIK for Myopia. J Refract Surg 2014;30:248-4.
33. Breyer DRH, Beckers L, Hagen P, et al. [Comparison of Long-term Results with Small Incision Refractive Lenticule Extraction (ReLEX SMILE) vs. Femto-LASIK]. Klin Monbl Augenheilkd 2019;236:1201-7.
34. Blum M, Täubig K, Gruhn C, et al. Five-year results of Small Incision Lenticule Extraction (ReLEx SMILE). Br J Ophthalmol 2016;100:1192-5.
35. Alió JL, Soria F, Abbouda A, et al. Laser in situ keratomileusis for -6.00 to -18.00 diopters of myopia and up to -5.00 diopters of astigmatism: 15-year follow-up. J Cataract Refract Surg 2015;41:33-40.
36. Shalchi Z, O'Brart DPS, McDonald RJ, et al. Eighteen-year follow-up of excimer laser photorefractive keratectomy. J Cataract Refract Surg 2015;41:23-32.
37. Agca A, Çakır İ, Tülü Aygün B, et al. Visual and Refractive Outcomes of Small-Incision Lenticule Extraction in High Myopia: 5-Year Results. Journal of Ophthalmology 2018;2018:5893126.

38. Lee H, Yong Kang DS, Reinstein DZ, et al. Comparing corneal higher-order aberrations in corneal wavefront-guided transepithelial photorefractive keratectomy versus small-incision lenticule extraction. J Cataract Refract Surg 2018;44:725-33.

39. Fu Y, Yin Y, Wu X, et al. Clinical outcomes after small-incision lenticule extraction versus femtosecond laser-assisted LASIK for high myopia: A meta-analysis. PLoS ONE 2021;16:e0242059.

40. Dawson D, Grossniklaus HE, McCarey BE, et al. Biomechanical and wound healing characteristics of corneas after excimer laser keratorefractive surgery: is there a difference between advanced surface ablation and sub-Bowman's keratomileusis? JRS. 2008 24, 90-6.

41. Moshirfar M, Albarracin JC, Desautels JD, et al. Ectasia following small-incision lenticule extraction (SMILE): a review of the literature. Clin Ophthalmol 2017;11:1683-8.

42. Shen Y, Chen Z, Knorz MC, et al. Comparison of Corneal Deformation Parameters After SMILE, LASEK, and Femtosecond Laser-Assisted LASIK. J Refract Surg 2014;30:310-8.

43. Khamar P, Shetty R, Vaishnav R, et al. Biomechanics of LASIK Flap and SMILE Cap: A Prospective, Clinical Study. J Refract Surg 2019;35:324-32.

44. Randleman JB. Ectasia After Corneal Refractive Surgery: Nothing to SMILE About. J Refract Surg 2016;32:434-5.

45. Muftuoglu O, Ayar O, Hurmeric V, et al. Comparison of multimetric D index with keratometric, pachymetric, and posterior elevation parameters in diagnosing subclinical keratoconus in fellow eyes of asymmetric keratoconus patients. J Cataract Refract Surg 2015;41:557-65.

46. El-Naggar MT. Bilateral ectasia after femtosecond laser-assisted small-incision lenticule extraction. J Cataract Refract Surg 2015;41:884-8.

47. Wang Y, Cui C, Li Z, et al. Corneal ectasia 6.5 months after small-incision lenticule extraction. J Cataract Refract Surg 2015;41:1100-6.

48. Mattila JS, Holopainen JM. Bilateral Ectasia After Femtosecond Laser-Assisted Small Incision Lenticule Extraction (SMILE). J Refract Surg 2016;32:497-500.

49. Sachdev G et al. Unilateral corneal ectasia following small-incision lenticule extraction. JCRS. 2015;41:2014-2018.

50. Shetty R, Kumar NR, Khamar P, et al. Bilaterally Asymmetric Corneal Ectasia Following SMILE With Asymmetrically Reduced Stromal Molecular Markers. J Refract Surg 2019;35:6-14.

51. Pahuja N, Kumar NR, Francis M, et al. Correlation of clinical and biomechanical outcomes of accelerated crosslinking (9 mW/cm2 in 10 minutes) in keratoconus with molecular expression of ectasia-related genes. Curr Eye Res. 2016;41:1419-23.

52. Ganesh S, Brar S. Clinical Outcomes of Small Incision Lenticule Extraction with Accelerated Crosslinking (ReLEx SMILE Xtra) in Patients with Thin Corneas and Borderline Topography. Journal of Ophthalmology 2015;2015:263412.

53. Li M, Zhou Z, Shen Y, et al. Comparison of Corneal Sensation Between Small Incision Lenticule Extraction (SMILE) and Femtosecond Laser-Assisted LASIK for Myopia. J Refract Surg 2014;30:94-100.

54. Wei S, Wang Y. Comparison of corneal sensitivity between FS-LASIK and femtosecond lenticule extraction (ReLEx flex) or small-incision lenticule extraction (ReLEx smile) for myopic eyes. Graefes Arch Clin Exp Ophthalmol 2013;251:1645-54.

55. Denoyer A, Landman E, Trinh L, et al. Dry eye disease after refractive surgery: comparative outcomes of small incision lenticule extraction versus LASIK. Ophthalmology 2015;122:669-76.

56. Kobashi H, Kamiya K, Shimizu K. Dry Eye After Small Incision Lenticule Extraction and Femtosecond Laser-Assisted LASIK: Meta-Analysis. Cornea 2017;36:85-91.

57. Izquierdo L, Sossa D, Ben-Shaul O, et al. Corneal lenticule extraction assisted by a low-energy femtosecond laser. J Cataract Refract Surg 2020;46:1217-21.