

Intraoperative flap-related complications in FemtoLASIK surgeries performed with VisuMax[®] femtosecond laser: A ten-year Romanian experience

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Abstract. Incidence and clinical results of intraoperative flap and interface-related complications were investigated after Femtosecond-LASIK surgery, where flap creation was performed with VisuMax[®] femtosecond laser. A retrospective 10-year cohort study was conducted including all eyes treated for all refractive errors by Femtosecond-LASIK technique. All the flaps were made by the same refractive surgeon with the VisuMax[®] (Carl Zeiss Meditec) femtosecond laser. We report the intraoperative flap and interface-related complications in these eyes, also describing their management. The study included 4,032 eyes. Flap and interface-related complications were: opaque bubble layer (OBL) 21.18%, suction loss 1.29%, difficult docking 0.69%, difficult dissection of the flap 0.59%, bleeding from limbal blood vessels 0.35%, de-epithelialization of the flap 0.12%, and interface debris 0.025%. These situations were appropriately addressed, with favorable outcomes. Flap creation is an important step in LASIK surgery. The predictability and safety have improved since the flap incision is assisted by a femtosecond laser, but complications of the flap and interface can still occur during the flap creation. Refractive surgeons should be aware and properly manage any unusual situation.

Introduction

Laser-assisted *in situ* keratomileusis (LASIK) is the default choice of refractive surgery procedures as it can be addressed to a wide spectrum of ametropias and can treat high order wavefront aberrations or topographic irregularities (1,2). Since

some complications of the mechanical microkeratome (free caps, incomplete, irregular or displaced flaps) can be avoided using the femtosecond laser technology, many surgeons prefer using this new technology to perform the LASIK flaps (1,2). Comparing to mechanical microkeratome, femtosecond laser can create customized flaps - centration, diameter, thickness of the flap, position and length of the hinge and also the side cut angle can be set by the surgeon according to the characteristics of each patient (1-4).

However, the Femtosecond-LASIK (FemtoLASIK) technique is not risk-free (1,2). Performing the flap assisted by the femtosecond laser can produce specific cavitation bubble related complications: opaque bubble layer (OBL), button-hole formation and presence of an air bubble in the anterior chamber (1,5). Complications of the classic LASIK technique can also be encountered (1).

Ten years after having started the Femtosecond-LASIK surgeries in Romania, we are reviewing our results, in order to assess the incidence of intraoperative flap and interface-related complications and their management.

Patients and methods

Data collection. A retrospective, non-comparative consecutive case series study was performed on eyes with different refractive errors that underwent FemtoLASIK surgeries. Patients were operated by the same refractive surgeon (H.T.S.) in two refractive centers: Europe Eye - Metropolitan Hospital in Bucharest and Timisoara Clinical Emergency Hospital, between June 2011 and April 2020. For the flap creation step all surgeries were performed using VisuMax[®] (Carl Zeiss Meditec) femtosecond laser.

A descriptive case series is reported of the intraoperative flap and interface-related complications encountered to the eyes included in the study.

Inclusion and exclusion criteria. Inclusion criteria for the surgery were as follows: patients ≥ 22 years of age with no refractive change for at least 2 years before surgery, central endothelial cell count $\geq 2,000$ cells/mm², stable peripheral retina (normal or already treated by laser photocoagulation

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if at-risk peripheral lesions were present) and good compliance (1,6).

Eye-related exclusion criteria for the surgery were: evidence or suspected ectasia, thinnest point on pachymetry $\leq 500 \mu\text{m}$, insufficient corneal thickness for laser ablation (estimated residual thickness of the stromal bed after treatment $\leq 300 \mu\text{m}$), severe dry eye syndrome, any sign of ocular inflammation or infection (1,6), any ocular disease that might interfere with visual acuity (e.g., cataract, congenital or acquired macular pathology, optic nerve pathology) (1,7-13), any previous ocular trauma, any previous ocular procedures (e.g., vitreo-retinal surgery, glaucoma laser procedures or glaucoma surgery) (14-21), and patients taking medications with high risk of ocular side effects (e.g., amiodarone, isotretinoin) (1,22).

Orbital anatomy was assessed in order to permit the proper suction cup positioning. There were excluded patients with very deep-set eyes, patients with narrow palpebral fissures or periocular tumors (23-25).

Pregnancy or lactation were exclusion criteria for the surgery (1,6). Also excluded were patients with systemic diseases that could interfere with the wound-healing process (e.g., diabetes mellitus, autoimmune disorders) (1,6,26,27) or with risk of postoperative low visual acuity due to possible vascular complications including ischemic optic neuropathy or vascular occlusion (e.g., severe systemic hypertension, severe dyslipidemia and cardiovascular diseases) (7,9,28-30).

The psychological profile was also considered and patients with unreasonable expectations or unable to understand the perioperative conditions were excluded.

Preoperative assessment. Patients underwent preoperative ocular examination that included: uncorrected and corrected distance visual acuity, manifest and cycloplegic refractions, fogging refraction (in hyperopic and mixed astigmatic patients), non-contact tonometry, keratometry, ultrasound corneal pachymetry, white-to-white corneal diameter, corneal topography and tomography (Scheimpflug), pupillometry, corneal endothelial cell count, anterior segment slit-lamp examination and mydriatic fundus examination.

Soft contact lens wearing should have been discontinued 2 weeks prior to preoperative investigations and then 2 weeks prior to surgery.

The study was approved by the Ethics Committee of 'Carol Davila' University of Medicine and Pharmacy (Bucharest, Romania). After being fully informed about the benefits and risks of the procedure, all patients signed an informed consent in accordance with the Declaration of Helsinki.

Surgical technique. All surgeries were performed using the same protocol and technique, by a single refractive surgeon (HTS) with the same femtosecond laser (VisuMax[®], Carl Zeiss Meditec).

Topical anesthesia with oxybuprocaine 0.4% was used before surgery. The eyelids were sterilized with 10% povidone-iodine solution, then a sterile surgical drape was applied and a lid speculum was inserted. The eye to be treated was positioned under the femtosecond laser integrated surgical microscope. The patient was asked to fix the target flashing light. The size of the docking cup was chosen according to

the white-to-white corneal diameter. While the patient was asked not to move the head, after an appropriate centration, the surgeon initiated the automatic suction. When the suction was complete, the surgeon initiated the femtosecond laser procedure, settled at 1,043 nm wavelength and 500 kHz pulse frequency. For the corneal flap cutting, the parameters were 7.9-8.9 mm diameter, 100-130 μm depth, 3.45-3.84 mm hinge width (50° angle) in superior position and 90° side cut angle. In patients operated in both eyes, the procedure started with the right eye, and then the fellow eye was treated identically.

The dissection of the flap was performed using a double-ended flap lifter. After drying the corneal bed with special sponges, the underlying stroma was treated for refractive correction using an excimer laser. According to situation, when both eyes needed to be treated, the right eye was treated first. At the end of the surgery, a disposable bandage contact lens was applied and antibiotic (moxifloxacin 0.5%) and artificial tear drops were instilled in the treated eye/eyes.

Patients were examined at the slit lamp thirty minutes after the surgery, in order to assess the flap position, the flap regularity and the interface clarity.

Postoperative care. Postoperative treatment started after the surgery and consisted in topical eye drops: antibiotic q.d.s. for one week (moxifloxacin 0.5%), non-steroid anti-inflammatory t.d.s. for 2 weeks (pranoprofen 0.1% or indomethacin 0.1%), artificial tears q.d.s. for 12 months and steroids (fluorometolone 0.2%), recommended to be applied q.d.s. for 2 weeks, then gradually tapered (t.d.s., b.d.s. and q.d. 2 weeks each).

The bandage contact lens was removed at the first day postoperative visit when the evaluation consisted in measurement of the manifest refraction, uncorrected distance visual acuity and slit-lamp examination of the cornea.

The following postoperative visits were carried out at one, three, six and twelve months. At every of these examinations a slit-lamp examination of the anterior segment and several investigations were performed: manifest refraction, uncorrected distance visual acuity, non-contact tonometry, corneal topography and tomography (Scheimpflug). For the eyes where a residual refraction was determined or the visual acuity was uncorrelated with the manifest refraction, we also tested the corrected distance visual acuity and the cycloplegic refraction.

Results

Patient demographics and operative data. Four thousand and thirty-two eyes (2,086 right eyes and 1,946 left eyes) from 2,310 patients (1,344 females and 966 males) were reviewed in our retrospective interventional consecutive case series study. Mean patient age at the time of surgery was 31.28 ± 6.724 years (range, 22-49 years). One thousand seven hundred and twenty-two patients had FemtoLASIK performed bilaterally on the same day (3,444 eyes) and 588 patients had unilateral FemtoLASIK, being anisometropic cases (588 eyes). Eight hundred and ninety-six eyes (22.22%) had myopic FemtoLASIK surgery, 1,498 eyes (37.15%) were operated for myopic astigmatism, 1,036 eyes (25.69%) were mixed astigmatic eyes before surgery, 406 eyes (10.07%) were operated for hyperopic astigmatism and 196 eyes (4.87%) underwent FemtoLASIK surgery for hyperopia.

Table I. Intraoperative flap and interface-related complications.

Intraoperative complications	No of cases (%)
Difficult docking	28 (0.69)
Suction loss	52 (1.29)
Cavitation gas bubble related complications	854 (21.18)
Opaque bubble layer (OBL)	854 (21.18)
Vertical gas breakthrough with buttonhole formation	0 (0)
Air bubbles in the anterior chamber	0 (0)
Bleeding from limbal blood vessels	14 (0.35)
Difficult dissection of the flap	24 (0.59)
Free flap	0 (0)
De-epithelialization of the flap	5 (0.12)
Interface debris	1 (0.025)

Table II. Intraoperative suction loss.

Time of suction loss	No of cases (%)
During building-up the vacuum	31 (1.02)
During the flap creation	1 (0.025)
After the flap was created but before the side cutting began	4 (0.1)
During the side cutting	16 (0.15)

Intraoperative flap and interface-related complications.

Intraoperative flap and interface complications included difficult docking (n=28; 0.69%), suction loss (n=52; 1.29%), cavitation gas bubble related complications (n=854; 21.18%), bleeding from limbal blood vessels (n=14; 0.35%), difficult dissection of the flap (n=24; 0.59%), de-epithelialization of the flap (n=5; 0.12%) and interface debris (n=1; 0.025%) (Table I).

Difficult docking was encountered in 28 cases (0.69%) due either to unfavourable orbital anatomy or to inappropriate patient cooperation. All cases required multiple repeated maneuvers of repositioning of the docking cup.

Suction loss occurred in 52 eyes (1.29%). The causes for suction loss were: excessive eyelid squeezing (19 eyes, 0.47%), inappropriate docking (16 eyes, 0.39%), patient head movement (12 eyes, 0.29%), conjunctiva penetrating under the suction cup (2 eyes, 0.05%), flat corneas (keratometric power - 38.50D, respectively, 38.75D for the same patient, 0.05%) and interruption of the power supply of the femtosecond laser machine (1 eye, 0.025%). There were different situations of losing suction (Table II). In most cases (31 eyes, 1.02%) suction break occurred during building up the vacuum, requiring another placement of the suction cup. The challenging situations were losing suction after the femtosecond laser treatment began. If the suction loss occurs after flap creation has started, managing the case may be quite complicated. In one patient, in the left eye, the second to be treated, the suction loss occurred during

Treatment data

Treatment pack size: **S**
Suction time (hh:mm:ss): **00:00:23**

Flap data

Diameter (mm): **7.90**
Thickness (μm): **110**
Side cut angle ($^\circ$): **90**
Hinge position ($^\circ$): **90**
Hinge angle ($^\circ$): **50**
Hinge width (mm): **3.45**

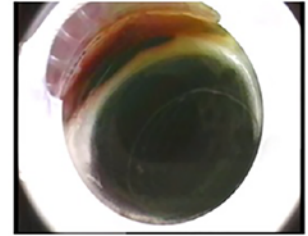
Treatment result

Treatment interrupted.

Progress indicator:

Flap cut 3.60 mm (diameter)
Flap side cut not started

Residual stromal thickness (μm): **438**



Treatment data

Treatment pack size: **S**
Suction time (hh:mm:ss): **00:00:21**
Restart at: **Flap cut**

Flap data

Diameter (mm): **7.90**
Thickness (μm): **110**
Side cut angle ($^\circ$): **90**
Hinge position ($^\circ$): **90**
Hinge angle ($^\circ$): **50**
Hinge width (mm): **3.45**

Predicted result

Flap side cut and flap cut prepared.

Residual stromal thickness (μm): **438**

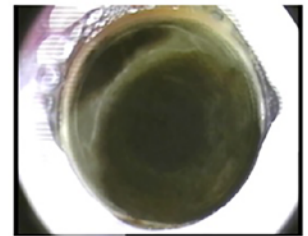


Figure 1. Upper, suction loss and femtosecond laser treatment interrupted after the flap cut but before starting the side cut. Lower, after re-docking, the procedure was successfully completed. Adapted from 'Femtosecond Laser - Excimer Laser Platform for ametropias surgery (Doctoral dissertation)', by Tăbăcaru B (2019), 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania.

the flap creation. In this one case (0.025%), we dissected the flap in the right eye where the femtosecond laser treatment was already performed, but without excimer laser treatment, then the procedure was aborted and rescheduled after three months for both eyes. At retreatment time, the femtosecond laser treatment for the left eye was set and performed 20 μm deeper, followed by excimer laser treatment and for the right eye, the already cut flap was only lifted and the excimer laser was applied. In all the other cases, the suction loss occurred either after the flap cut was done but before side cut creation (4 eyes, 0.1%) (Fig. 1) or during the side cut time (16 eyes, 0.15%) (Fig. 2). In all these cases the surgeon could recenter the suction cup, the eyes could be re-docked and the femtosecond procedure could be continued from the moment when the suction was lost.

In order to assess the impact of the OBL on the laser procedure we divided the OBL according to its extension and position, as follows: minimal (OBL located at the periphery of the flap and/or width <2 mm), moderate (OBL located near the pupillary area and/or width between 2-4 mm) and severe (OBL located centrally and/or width >4 mm). Mild OBL was encountered (Fig. 3) in 742 cases (18.40%), moderate OBL (Fig. 4) in 112 cases (2.77%) and not severe OBL (Table III). In none of the OBL cases was difficulties or incidents encountered in

Treatment data

Treatment pack size: **S**
 Suction time (hh:mm:ss): **00:00:24**

Flap data

Diameter (mm): **8.00**
 Thickness (µm): **115**
 Side cut angle (°): **90**
 Hinge position (°): **90**
 Hinge angle (°): **50**
 Hinge width (mm): **3.49**

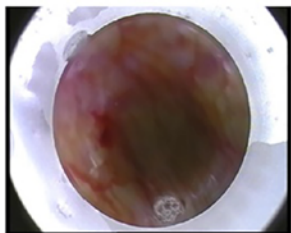
Treatment result

Treatment interrupted.

Progress indicator:

Flap cut completed
 Flap side cut **18.8%**

Residual stromal thickness (µm): **445**



Treatment data

Treatment pack size: **S**
 Suction time (hh:mm:ss): **00:00:26**
 Restart at: **Flap cut**

Flap data

Diameter (mm): **8.00**
 Thickness (µm): **115**
 Side cut angle (°): **90**
 Hinge position (°): **90**
 Hinge angle (°): **50**
 Hinge width (mm): **3.49**

Predicted result

Flap side cut and flap cut prepared.

Residual stromal thickness (µm): **445**

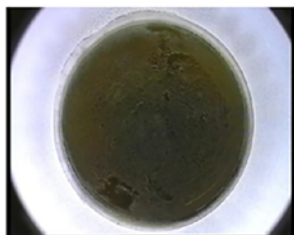


Figure 2. Upper, suction lost and femtosecond laser treatment interrupted during side cut creation. Lower, after re-docking, the procedure was successfully completed. Adapted from 'Femtosecond Laser - Excimer Laser Platform for ametropias surgery (Doctoral dissertation)', by Tăbăcaru B (2019), 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania.

dissecting or lifting the flap or in the subsequent excimer laser treatment. No other cavitation bubble complication such as buttonhole formation or presence of air bubbles in the anterior chamber were encountered.

Bleeding from limbal blood vessels immediately after the flap creation occurred in 14 cases (0.35%), all those patients being chronic contact lens wearers before the surgery. In all the cases, the haemorrhage was stopped before the excimer laser ablation and there were no visual consequences.

In 24 eyes (0.59%) the dissection of the flap was difficult to perform, due to the impossibility of opening of the side cut on its entire circumference. All cases were preceded by suction loss, leading to the presence of some adhesions at the side cut or incomplete side cut. Dissection of the areas of adhesion and flap lifting were possible using a spatula, a LASIK flap forceps and a crescent blade (Fig. 5).

Epithelial defects of the flap (Fig. 6) were encountered in 5 eyes (0.12%) and this situation was due to multiple surgical maneuvers in the context of inappropriate patient cooperation (3 eyes, 0.07%) or anterior basement membrane dystrophy (both eyes of the same patient, 0.05%). Surgical approach included de-epithelialization of the entire corneal surface, permanent removal of the epithelial debris avoiding contact with flap margins and continuous wear of the bandage contact lens until complete re-epithelialization occurred.



Figure 3. Mild OBL. Reprinted from 'Femtosecond Laser - Excimer Laser Platform for ametropias surgery (Doctoral dissertation)', by Tăbăcaru B (2019), 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania. OBL, opaque bubble layer.



Figure 4. Moderate OBL. Reprinted from 'Femtosecond Laser - Excimer Laser Platform for ametropias surgery (Doctoral dissertation)', by Tăbăcaru B (2019), 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania. OBL, opaque bubble layer.

Table III. Intraoperative OBL.

Type of OBL	No of cases (%)
Mild OBL (OBL located at the periphery of the flap and/or width <2 mm)	742 (18.40)
Moderate OBL (OBL located near the pupillary area and/or width 2-4 mm)	112 (2.77)
Severe OBL (OBL located centrally and/or width >4 mm)	0 (0)

OBL, opaque bubble layer.

Immediately after the surgical procedure, when assessing the flap position and interface clarity at the slit-lamp, we found in one eye (0.025%) a textile debris at the flap interface (Fig. 7). Surgical solution was lifting the flap, removal of the textile debris by irrigating the interface with saline solution and proper repositioning of the flap.

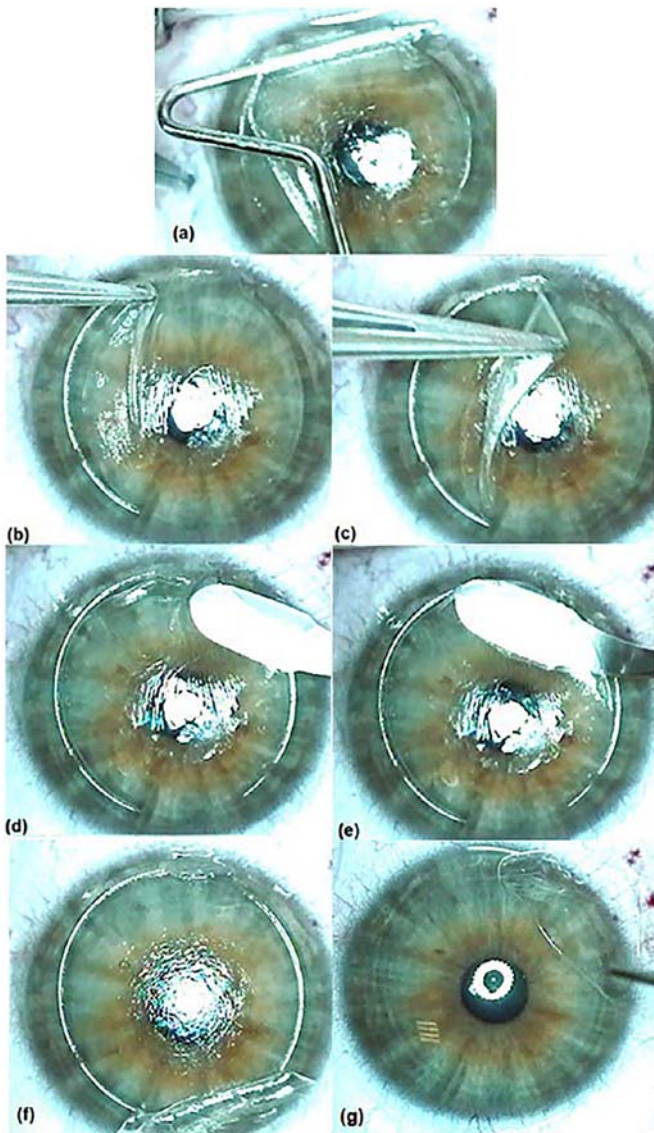


Figure 5. Intraoperative steps of difficult side cut dissection: (a) impossibility of standard dissection; (b and c) side cut dissection using flap forceps; (d and e) side cut dissection using crescent blade; (f) flap lift succeeded; (g) final aspect after bandage contact lens was applied. Adapted from 'Femtosecond Laser - Excimer Laser Platform for ametropias surgery (Doctoral dissertation)', by Tăbăcaru, B (2019), 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania.

Discussion

Laser refractive surgery techniques and technology have undergone continuous advancements in the last decades, being increasingly precise and highly predictable (1,2,31,32). Although small incision lenticule extraction (SMILE) is the newest and promising refractive technique with controversial advantages (31), LASIK is still currently the most popular refractive procedure worldwide, as it can be used to correct all types of ametropias, between large diopters limits (1,2,33-35). The essential step of LASIK is the corneal flap creation which is performed nowadays in the most modern way, assisted by a femtosecond laser (1,33). Compared with the mechanical microkeratome, the femtosecond laser-assisted flaps are more precise, more accurate, can be customized and have a high reproducibility (1,2,36). However, this step is not risk-free

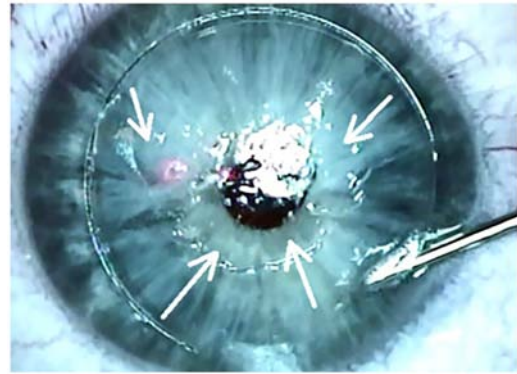


Figure 6. Epithelial defects (white arrows) of the flap. Reprinted from 'Femtosecond Laser - Excimer Laser Platform for ametropias surgery (Doctoral dissertation)', by Tăbăcaru, B. (2019), 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania.

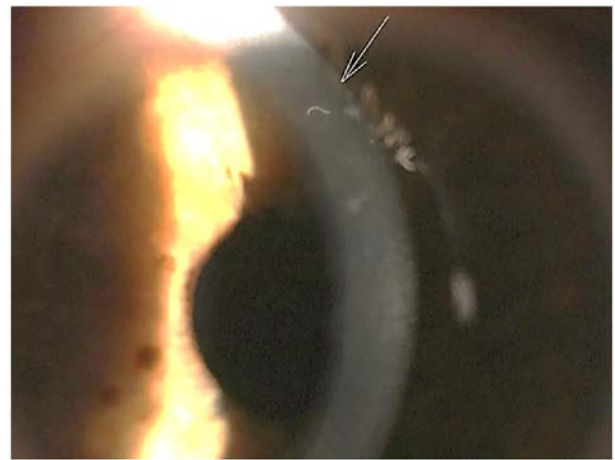


Figure 7. Textile debris at the interface (white arrow). Reprinted from 'Femtosecond Laser - Excimer Laser Platform for ametropias surgery (Doctoral dissertation)', by Tăbăcaru B (2019), 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania.

but fortunately, flap-related complications are quite rare in FemtoLASIK technique (1,33).

Docking is the step that connects the eye to the femtosecond laser system. The time required for proper docking reduces with the learning curve (37). Docking can be difficult in case of deep set orbits or tight palpebral aperture (38).

Suction loss is a femtosecond laser specific complication. The suction loss occurs more likely when the suction cup is not perfectly applied on the eye, allowing the fluid to pass between the eye and the suction cup (39). Other predisposing factors for suction loss are: flat corneas, excessive tearing reflex, narrow palpebral aperture, bad positioning of the patient, poor compliance of the patient due to anxiety or inability to follow instructions (40-42). Suction loss can occur in any step of flap creation. Managing the result of a suction break varies according with the moment of occurrence. If the suction loss occurs during the flap creation, the procedure should be aborted and rescheduled for up to 2 months (1,42). If the suction loss occurs either after the flap was fully created or during the creation of the side cut, the procedure can be resumed from the moment of interruption after proper re-docking (1,42).

Cavitation gas bubbles produced by the femtosecond laser can lead to specific complications (1,42). OBL occurs when these bubbles expand and become trapped in the anterior stroma, at the interface plane (1,42). The incidence of OBL ranges up to 48% (42,43), its formation being influenced by flap diameter under 8 mm (44), thick corneas (43,45), high hysteresis (43,45) and laser settings such as: spot spacing, pocket size and energy level (42). Severe OBL presence can interfere with interface dissection (42) and can disturb eye tracking of the excimer laser (46). In addition to the OBL, the cavitation gas bubbles can produce other complications: vertical gas breakthrough with buttonhole formation or presence of the bubbles in the anterior chamber (42).

Bleeding from limbal blood vessels in chronic contact lens wearers can be avoided using, if possible, smaller suction cups. If perilimbal haemorrhage lead to interface haze, according to severity it is possible either to medically treat with steroid drops or to lift the flap and to irrigate the interface with saline solution (47,48).

Compared with microkeratome-created flaps, dissecting and lifting the femtosecond laser-assisted flaps can be more difficult, the risk of flap tears being increased (42). If a small peripheral flap tear is present and the dissection is complete, the excimer ablation can be performed (42). In case of large or central flap tear, the procedure is recommended to be aborted, considering further a surface ablation (42).

Epithelial defects are uncommon in FemtoLASIK technique (42). Predisposing factors include: use of excessive topical anaesthetic, recurrent erosion syndrome and anterior basement membrane dystrophy (42). Manipulation of the spatula along the side cut edge can produce epithelial defects (42).

Interface debris can result due to Meibomian gland secretions, eyelashes, textile material from compresses or sponges, or talc from gloves (42). Despite prevention methods, debris is still reported to be noted at the postoperative visit (42). If it is not visually significant or it does not cause infection or inflammation, interface debris can be just observed. Otherwise, flap lifting and thoroughly irrigation of the interface is necessary (42).

FemtoLASIK technique has revolutionized refractive surgery since its introduction. Although the procedure is highly safe, complications can occur (49). Refractive surgeons should be aware of all the intraoperative flap-related complication in FemtoLASIK procedure. Fortunately, these complications are rare and with proper management, studies have shown no alteration of the visual function (33).

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author (HTS) upon reasonable request.

Authors' contributions

BT, HTS, SS, MZ and VM contributed to the conception and design of the study, the acquisition, analysis and interpretation of the data. BT, HTS, SS, MZ and VM also contributed to the drafting of the manuscript and its critical revision for important intellectual content. MM contributed to the analysis and interpretation of the data, the drafting of the manuscript and its critical revision for important intellectual content. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the study in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of 'Carol Davila' University of Medicine and Pharmacy (Bucharest, Romania). All participants signed an informed consent.

Patient consent for publication

This manuscript does not contain case details, personal information or images that may enable an individual to be identified.

Competing interests

The authors have no financial or proprietary interest to declare in any device presented in this article.

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