Int Ophthalmol
DOI 10.1007/s10792-016-0323-3

ORIGINAL PAPER

Opaque bubble layer incidence in Femtosecond laser-assisted LASIK: comparison among different flap design parameters

Leonardo Mastropasqua · Roberta Calienno · Manuela Lanzini · Niccolò Salgari · Sergio De Vecchi · Rodolfo Mastropasqua · Mario Nubile

Received: 28 June 2016 / Accepted: 8 August 2016

Abstract The purpose of this study was to evaluate the incidence of opaque bubble layer (OBL) in femtosecond laser-assisted in situ keratomileusis (LASIK) flaps created with the support of Visumax Carl Zeiss femtosecond laser, planned with different flap diameters (7.90, 8.0, and 8.20 mm) and the same laser energy and power settings. Incidence of intraoperative OBL in flaps of consecutive 108 patients (216 eyes) subjected to bilateral femtosecond-assisted LASIK was considered. Flap creation was performed with the same laser design parameters (spot distance and energy offset) and different presetting diameters of 7.90 mm (72 eyes, group 1), 8 mm (72 eyes, group 2), and 8.20 mm (72 eyes, group 3). The incidence of OBL was considered and its extension was reported measuring involvement of different four corneal flap quadrants in which was theoretically divided the entire flap area; based on these data, OBL presence was classified as none (no evidence of OBL), minimal (minimal presence in not more that one quadrants corneal flap), mild (OBL presence in almost two or three quadrants without tendency to invade central cornea), and moderate (OBL presence in almost three quadrants with tendency to invade central cornea). In group 1, the incidence of OBL was of 23.6 % (17 eyes) with a mild/moderate presence; in group 2, incidence was 20.8 % (15 eyes) with mild presence. Group 3 presented a reduced OBL incidence (4.1 %, 3 eye) with a minimal presence. No statistically significant difference was found between group 1 and 2 ($p = 0.8414$).We found statistically significant differences between group 1 and group 3 ($p = 0.0012$) and between groups 2 and 3 ($p = 0.0044$). A significant reduction and extension of OBL incidence were evident when LASIK flap settings diameter was increased, and flap edge was closer to the contact glass border; this is probably consequent to a more effective gas dispersion outside of corneal flap.

Keywords Refractive surgery · Opaque bubble layer · LASIK · Femtosecond laser

L. Mastropasqua · R. Calienno (✉) · M. Lanzini · N. Salgari · M. Nubile
Department of Medicine and Ageing Sciences, Ophthalmology Clinic. University "G. d'Annunzio" of Chieti-Pescara, Via dei Vestini, 66100 Chieti, Italy
e-mail: mastropa@unich.it

R. Calienno
e-mail: roberta.calienno@gmail.com

M. Lanzini
e-mail: m.lanzini@unich.it

N. Salgari
e-mail: n.salgari@gmail.com

M. Nubile
e-mail: m.nubile@unich.it

S. De Vecchi
Carl Zeiss S.p.A., Refractive Service, Milan, Italy
e-mail: sergio.devecchi@zeiss.com

R. Mastropasqua
Ophthalmic Clinic of Verona, Verona, Italy
e-mail: rodolfo.mastropasqua@gmail.com

Published online: 12 August 2016

Introduction

Femtosecond laser (FSL) technology was first developed in 1990s [1] and was rapidly adopted in the surgical field of ophthalmology. Femtosecond lasers emit light pulses of short duration (10–15 s) at 1053 nm wavelength that cause photodisruption of the tissue with minimum collateral damage [1–3]. This enables bladeless incisions to be performed within the tissue at various patterns and depth with high precision.

In fact, FSL is capable of causing disruption in corneal stromal tissue through the principle of photoionization, resulting in the rapid formation of a cloud of free electrons and ionized molecules. Small volumes of tissue are vaporized, with the formation of cavitation bubbles made up of carbon dioxide and water. This gas is dissipated in the tissue, forming a cleavage plane [4].

Improvements in the technology occurred quickly, with the increase in pulse frequency and reduction in the amount of energy released, so that only the desired tissue was affected while adjacent areas remained intact, thereby ensuring fewer harmful effects [5, 6].

The femtosecond laser has revolutionized corneal and refractive surgery increasing its safety, precision, and predictability over traditional microkeratomes [7]. Advantages of femtosecond laser-assisted in situ keratomileusis (FSL-LASIK) over conventional microkeratome-assisted procedure, consist of reduced incidence of flap complications (button hole or free cap formation) and ability to cut thinner flaps [8].

Furthermore, FSL flap creation also allows to obtain greater surgeon choice of flap diameter, thickness, side-cut angle, hinge position, and length; application of femtosecond laser in refractive surgery, and specifically in LASIK flap creation, has made this surgery safer and more predictable and accurate [9, 10].

On the other side, also this advanced procedure presents specific kind of complications; opaque bubble layer (OBL) is produced by gas bubbles that accumulate in the superficial layers of the stromal bed after laser action in LASIK flap creation, creating a diffuse tissue opacity [11, 12].

In literature, two distinct types of OBL were already reported: the hard OBLs that look denser and occur when the laser applies additional pulses and the soft ones that are more transparent [13].

It was demonstrated that excessive OBL may interfere with flap creation and separation and with excimer laser tracking system, and this can delay the surgical procedure, so OBL could affect FSL-LASIK procedure [11].

The aim of this study was to evaluate OBL incidence in FSL-LASIK flaps creation planned with different flap diameters (7.90, 8.0, and 8.20 mm) and the same laser energy and power settings.

Materials and methods

This study is consistent with the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject at the time of the LASIK intervention during the preoperative screening visit.

The study group consisted of 108 consecutive patients (216 eyes) treated with bilateral primary hyperopic femtosecond-assisted LASIK between January 2015 and October 2015; procedures were performed by the same surgeon (L.M.) at the National Centre of High Technology (CNAT) in Ophthalmology of University "G d'Annunzio" (Chieti-Pescara, Italy).

The patients were aged 35–66 (average 50 $\pm$ 21 SD) years; inclusion criteria were mild to moderate hyeropia (SE from +1.50 to +4.00 D) with adequate corneal keratometric parameters (from 41.00 to 43.00 D) and adequate pachimetry, with no other known ocular pathologies. Patients with anterior segment disease, abnormal corneal topography, and other known ocular disease were excluded.

All surgeries were performed using the MEL 80 excimer laser system (Carl Zeiss Meditec AG, Jena, Germany) after a flap was created with the use of VISUMAX platform (500 kHz) (Carl Zeiss Meditec AG, Jena, Germany).

The flaps were all created with a predefined thickness of 110 µm, a 70-degree side-cut angle, and different diameters from 7.90 to 8.20 mm. Patients were equally divided before surgery in three groups (group 1 7.90 mm, group 2 8.00 mm, and group 3 8.20 mm) with different flap diameters based on white-to-white and keratometric values.

The setting values for flap creation are reported in detail in Table 1.

The Visumax contact glass is available in 3 diameters: small (S), medium (M), and large (L), with the size chosen also depending on the white-to-white diameter.

Table 1 Femtosecond laser setting values for flap creation

	Flap	Flap side
Spot distance (μm)	4.20	1.70
Track distance(μm)	4.20	1.70
Energy offset	44	44
Scan direction	Spiral in	N/A
Scan mode	Single	N/A

Surgeon used the S contact glass in all three groups.

Visumax platform doesn't allow by now to set flap diameter of 8.20 mm with a S contact glass but only with a M or L sizes.

In view of these considerations, surgeon planned treatment on femtosecond laser such as having to use a M size glass, despite using a S size contact glass.

Docking technique was regular with no complications in all patients.

The eventual formation and development of OBL were detected by the operating microscope after flap creation and were confirmed by slit lamp examination.

When OBL presence was detected, stromal ablation was not performed immediately after flap creation but postponed (about 20 min) in order to favor bubbles dispersion.

Then, stromal ablation was performed in all patients using the MEL 80 excimer laser platform (Carl Zeiss Meditec AG, Jena, Germany).

The postoperative regimen included antibiotic eye drops (Nettacin, Netilmicyn 0.3 %, SIFI, Catania, Italy) four times daily for 1 week and steroid eyedrops (Etacortilen, Dexamethasone 0.15 %, SIFI, Catania, Italy) four times daily tapered over a 3 weeks period.

We have considered OBL incidence in different groups, and in order to quantify OBL extension, corneal flaps were theoretically divided into four quadrants for analysis, discerning OBL presence as none (not evidence of OBL), minimal (minimal presence in not more that one quadrants corneal flap), mild (OBL presence in almost two or three quadrants without tendency to invade central cornea), and moderate (OBL presence in almost three quadrants with tendency to invade central cornea).

Fisher's test for statistical analysis was performed using GraphPad Software (San Diego, CA, USA) to consider statistical differences among groups in corneal flap quadrants OBL involvement (Fig. 1).

Results

OBLs in all groups present *soft* characteristics and didn't invade central cornea, expanding mainly in the peripheral side-cut area.

The maximum OBL percentage was evident in group 1 with 23.6 % (17 eyes) of medium incidence in 3 quadrants (mild/medium presence; Fig. 2); in group 2, the percentage was 20.8 % (15 eyes) with medium involvement of not more than 2 corneal flap quadrants (mild presence; Fig. 3).

Group 3 showed OBL presence only in 3 eyes (4.1 %) with not more than one involved corneal flap quadrant (minimal presence; Fig. 4).

Comparison between group 1 and 2 obtained by means of Fisher's test is considered to be not statistically significant (two-tailed p value equals 0.8414). We found statistically significant differences between group 1 and group 3 (two-tailed $p = 0.0012$) and between groups 2 and 3 (two-tailed $p = 0.0044$) (Graph 1).

Discussion

Creation of a LASIK flap with a femtosecond laser is considered advantageous to microkeratome for a more centered, higher controlled geometry, both in depth as well as diameter [15].

The incidence of complications such as button hole, epithelial abrasion, incomplete flap, free cap, Bowman

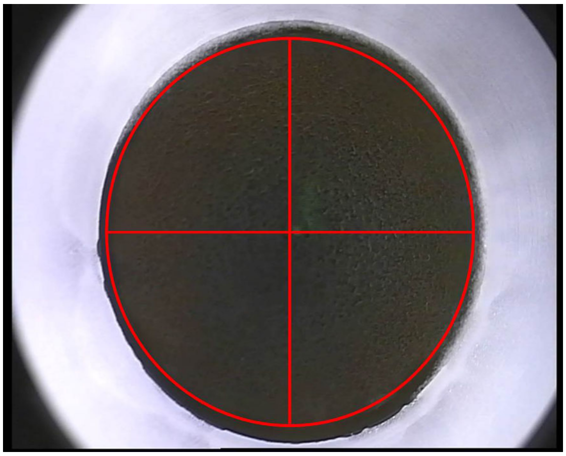


Fig. 1 Corneal flap quadrants in which was theoretically divided FSL-LASIK corneal flap

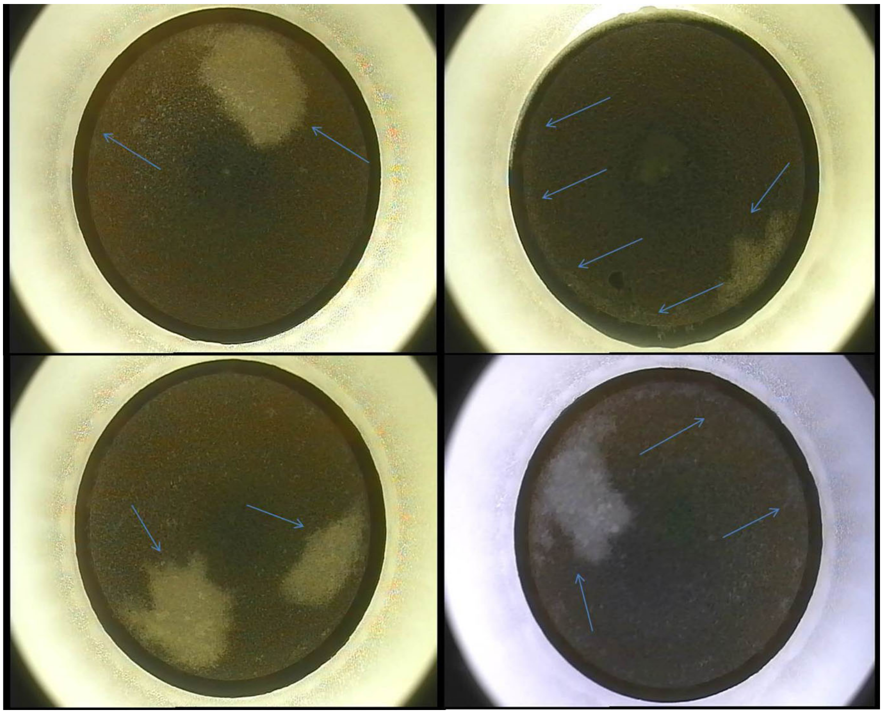


Fig. 2 OBL incidence was evident in group 1 with 23.6 % (17 eyes) of medium incidence in 2−3 quadrants (mild/medium presence); we consider OBL presence and also OBL fine opacity at the flap margin (*blue arrows*)

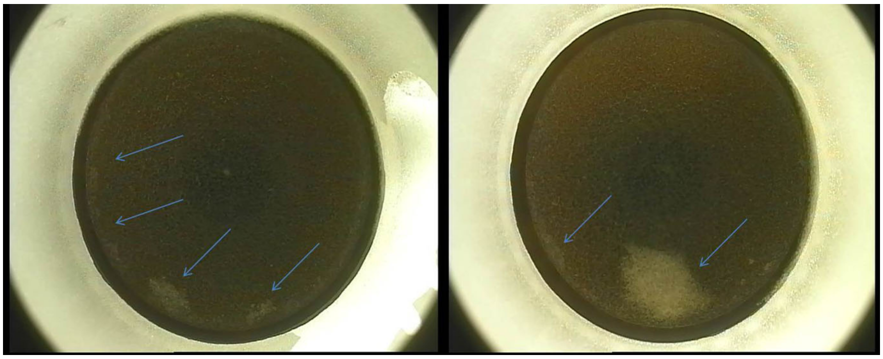


Fig. 3 In group 2, OBL presence was 20.8 % (15 eyes) with medium involvement of not more than 2 corneal flap quadrants (mild presence)

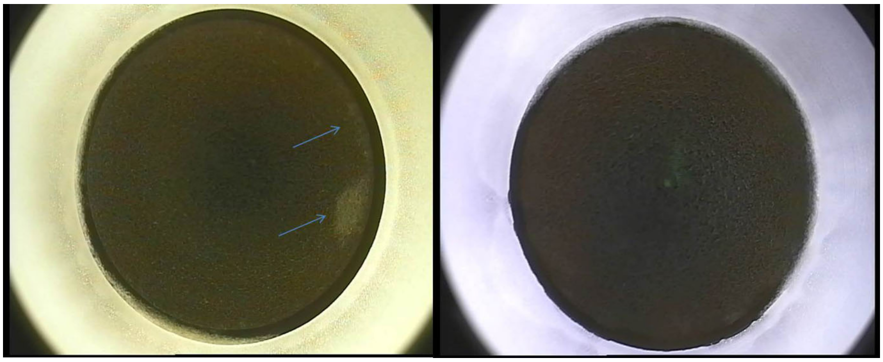
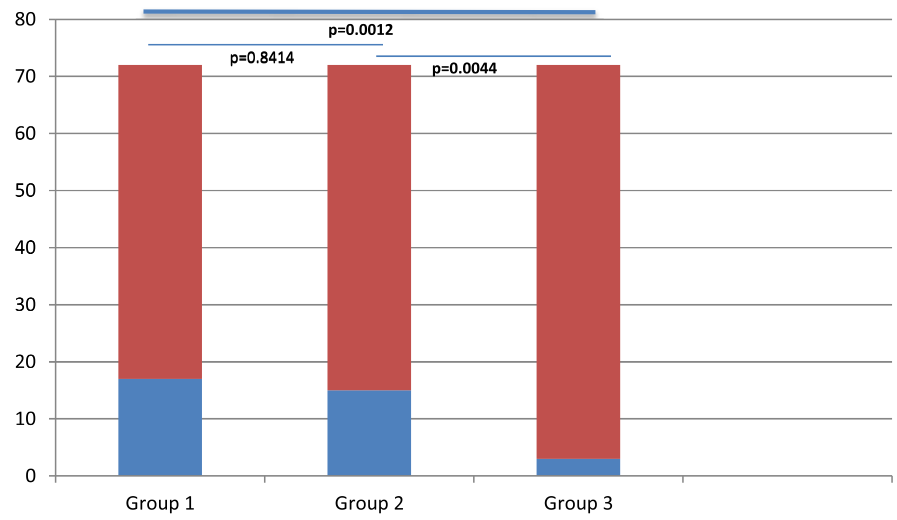


Fig. 4 Group 3 showed OBL presence only in 3 eyes (4.1 %) with not more than one involved corneal flap quadrant



Graph 1 OBL incidence in the three different groups

stripe, and irregular cuts are substantially reduced with femtosecond lasers.

However, there are some complications specifically related to femtosecond lasers such as cavitation gas bubbles, known as OBL; although OBL tends to disappear within minutes, their presence hinders surgeon using excimer laser's eye tracker to visualize and locate the pupil respectively [1].

The exact origin of these bubbles is unknown but the most credible theory suggests that they originate from stray laser pulses into the aqueous humor or migration of the corneal stromal gas bubbles retrograde through Schlemm's canal. Alterations in pulse duration that enable reduction in collateral tissue damage could help to reduce the formation of cavitation bubbles [16].

Chun-Hsiu Liu and collegues hypothesized that the occurrence of OBL may be affected by the biomechanical properties of the cornea. In fact, gas bubbles produced by a femtosecond laser have been shown to travel the pathway of least resistance, and under high pressure due to high vacuum and corneal compression, corneal rigidity can reactively produce a counterbalance force to oppose the applanation pressure. Thicker corneas can provide greater rigidity and produce more resistance, thereby restricting the clearance of the cavitation bubbles and increasing the occurrence of OBLs [11].

Similarly, also, steeper cornea and a hard-docking technique could be risk factors for an OBL as already reported in literature [13].

Also, laser energy and pulse rate are determinants in flap creation by a femtosecond laser and in OBL incidence. In fact a higher pulse repetition rate reduces the required laser pulse energy, resulting in less tissue inflammation, and closer spot separation, as a result of higher pulse rates, improves the quality of the cleavage plane.

Therefore higher pulse rates, resulting in a better quality of laser interface, can also reduce cavitation bubbles, facilitating flap lifting [4].

In this study, we consider to evaluate OBL incidence in LASIK flaps planned with different flap diameters (7.90, 8.0, and 8.20 mm) and the same laser energy and power settings; compared with previous studies already present in literature using a 15/60 kHz femtosecond laser [11, 13], the current study, using a higher pulse rate laser (500 kHz), showed a reduced incidence of OBLs in all groups (33.3 % overall compared with 52.5 and 56.4 %) with presence of only soft type; this may be certainly explained by the fact that higher pulse rate and reduced spot distance (4.20 μm instead of 6 μm) produce a more complete and regular interface plane, facilitating OBL incidence reduction.

Furthermore, innovative Visumax interface system allows to reduce docking phase complications, and this could positively influence OBL presence; in fact, it has been suggested that the harder one applanates the cornea (the so-called hard-docking technique), the greater the risk for opaque bubble layer formation [13].

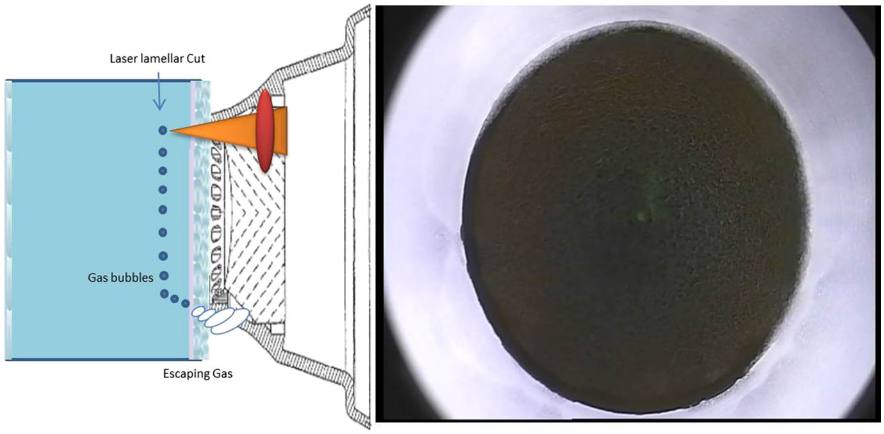


Fig. 5 When a larger flap diameter is planned (8.2 mm), the distance between the flap edge and the contact glass margin is reduced, ensuring a smoother emission of the compressed air generated by the intracorneal femtosecond laser action as a relief valve

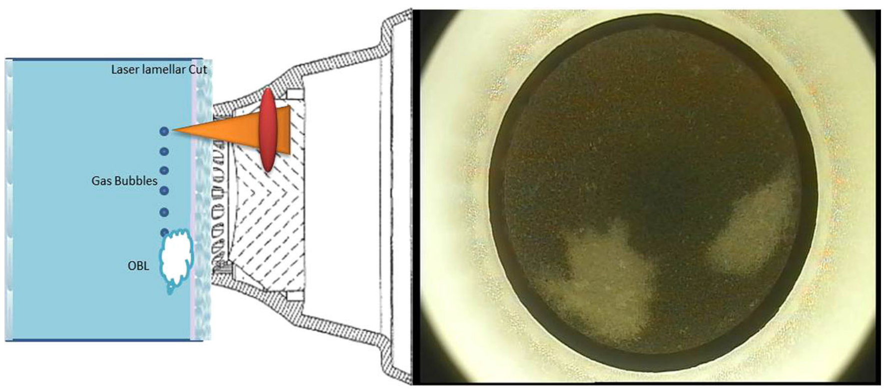


Fig. 6 A smaller flap does not allow a "safety valve" phenomenon, and would facilitate the gas entrapment into stromal lamellae and the formation of OBL

Kaiserman and collegues [14], in a previous paper, already concluded that smaller flaps were associated with a more opaque bubble layer (range from 8.2 to 9 mm); our results confirm and support these considerations, further reducing flap diameter from 7.90 to 8.2 mm in hyperopic LASIK.

This is probably related to the fact that flap diameter increase, being the S contact glass fixed diameter 8.5 mm, allows to reduce the distance between the flap edge and the contact glass margin, ensuring a smoother emission of the compressed air generated by the intracorneal femtosecond laser action as a relief valve (Fig. 5); differently, a smaller flap does not allow a "safety valve" phenomenon, and would facilitate the gas entrapment into stromal lamellae and the formation of OBL (Fig. 6).

In particular, our results show significant difference in OBL incidence and extension when flap diameter was increased to 8.20 mm; our hypothesis must be certainly confirmed by support of other studies that would consider the impact of OBL on visual acuity and quality of vision, considering that an excessive opaque bubble layer could interfere with flap separation and with excimer laser ablation, particularly in hyperopic LASIK when excimer laser treatment was then performed in corneal periphery (whereas OBL often occurs), because of frequent eye tracking loss or difficulty to obtain with consequences on postsurgical refractive outcome.

In conclusion, new generation femtosecond laser advent, characterized by high rate pulse and reduced spot separation, has already allowed to considerably diminish OBL incidence and extension; in order to further reduce this complication rate, flap diameter increase, when it is possible compatibly with corneal parameters, seems to represent a valid support.

Compliance with ethical standards

Conflict of interest The article has not been presented in a meeting. The authors did not receive any financial support from any public or private source. The authors have no financial or proprietary interest in a product, method, or material described herein. No conflict of interest is present for all authors in this paper.

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