

# A Technique to Reduce Incidence of Opaque Bubble Layer Formation During LASIK Flap Creation Using the VisuMax Femtosecond Laser

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## ABSTRACT

**PURPOSE:** To identify risk factors for opaque bubble layer (OBL) formation and compare the incidence of OBL using a cone modification technique versus the original technique for LASIK flap creation using the VisuMax laser (Carl Zeiss Meditec, Jena, Germany).

**METHODS:** This retrospective study examined videos of flap creation using the VisuMax laser to identify OBL occurrence. Eyes were divided into three groups: eyes where OBL occurred using the original technique (OBL group), eyes where OBL did not occur using the original technique (no OBL group), and eyes in which the cone modification technique was used for LASIK flap creation (larger flap diameter) (cone modification technique group). Preoperative measurements including simulated keratometry (flat and steep) values, white-to-white distance (WTW), pachymetry, patient age and gender, amount of correction, flap parameters, energy setting, corneal hysteresis, and corneal resistance factor were analyzed to identify parameters with statistical difference between the OBL and no OBL groups. Incidence of OBL was compared between the original and cone modification techniques.

**RESULTS:** OBL incidence was significantly lower with the cone modification technique (7.6%; 7 of 92 eyes) than with the original technique (28.8%; 34 of 118 eyes) (Fisher's exact test,  $P = .0009$ ). Factors identified with a significant difference between eyes with and without OBL using the original technique were: corneal thickness (OBL:  $561.2 \mu\text{m}$ , no OBL:  $549.6 \mu\text{m}$ ,  $P = .0132$ ), WTW diameter (OBL: 11.6 mm, no OBL: 11.9 mm,  $P = .0048$ ), corneal resistance factor (OBL: 10.4 mm Hg, no OBL: 9.6 mm Hg,  $P = 0.0329$ ), and corneal astigmatism (OBL: 0.80 diopter, no OBL: 1.00 diopter,  $P = .0472$ ).

**CONCLUSIONS:** Less astigmatic, thicker, denser, and smaller corneas increased the risk of OBL using the original technique for flap creation. The cone modification technique was associated with lower risk of OBL formation, even in eyes with significant risk factors for OBL using the original technique.

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Femtosecond laser flap creation is the most commonly used method for LASIK flap creation.<sup>1</sup> Both surgeons and patients recognize the increased accuracy and safety of these instruments over mechanical microkeratomes. Flap thickness is more accurate using the femtosecond laser compared to mechanical microkeratomes.<sup>2</sup> Unwanted side effects can occur with the use of the femtosecond laser, which include transient light sensitivity syndrome,<sup>3</sup> increased corneal forward light scatter and backscatter,<sup>4,5</sup> and opaque bubble layer (OBL).<sup>6</sup> OBL is a temporary whitening of the cornea resulting from femtosecond laser-generated intracorneal gas that cannot escape during flap creation. Hurmeric et al. demonstrated by ultra-high-resolution optical coherence tomography that the OBL layer usually extends anterior to the flap interface up to Bowman's layer when using the VisuMax laser (Carl Zeiss Meditec, Jena, Germany).<sup>7</sup> In a study by Kaiserman et al.,<sup>6</sup> the incidence of OBL with a femtosecond laser was 56.4%.

Two types of OBL exist. Hard (or early) OBL appears rapidly and occurs when there is corneal whitening, advancing ahead of the laser cut. This opacity can interfere with subsequent laser photodisruption and thus render flap lift in the area of OBL challenging. The VisuMax laser operates at 500 kHz and uses low energies. This creates a smooth flap interface. Because the laser pulses firing into the OBL are of low energy, they can be ineffective in photodisruption because of the opacification. This can lead to a challenging flap lift. In addition, hard OBL can lead to erroneous residual bed measurements and can interfere with

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excimer laser tracking systems. Soft (or late) OBL appears slowly behind the advancing raster pattern in areas where the flap cut has already occurred. Soft OBL does not have clinical significance<sup>6,8</sup> and therefore eyes in which soft OBL occurred during flap creation were not included in this study. Throughout the rest of this article, the term OBL will refer to hard OBL. **Figure A** and **Videos 1-3** (available in the online version of this article) demonstrate the appearance of hard OBL, soft OBL, and no OBL, respectively.

Mastropasqua et al.<sup>9</sup> described a new technique for reducing the incidence of OBL when using the VisuMax laser by increasing the flap diameter to be closer to the edge of the contact glass. This is achieved by programming the treatment for a larger contact glass than is actually used for the treatment. Using the VisuMax laser with the small contact glass, they reported that the incidence of OBL was 23.6% with a 7.9-mm flap diameter, 20.8% with mild presence for an 8-mm flap diameter, and 4.1% with minimal presence for an 8.2-mm flap diameter.<sup>9</sup>

The purpose of this study was to identify risk factors for OBL formation and compare the incidence of OBL using a cone modification technique versus the original technique for LASIK flap creation using the VisuMax laser.

**PATIENTS AND METHODS**

This was a single-center retrospective study that adhered to the tenets of the Declaration of Helsinki. Approval was obtained from the University of California Los Angeles Institutional Review Board. All eyes that were videotaped undergoing LASIK flap creation using the VisuMax laser by a single surgeon (DRH) between December 2014 and February 2016 were obtained from the surgery log. Videos of flap creation were examined to identify flaps in which OBL occurred.

**SURGICAL TECHNIQUE**

All LASIK flaps were created using the VisuMax 500-kHz femtosecond laser system. The settings for

TABLE 1  
**Laser Settings for Flap Creation With the VisuMax 500-kHz Femtosecond Laser**

Setting	Flap	Flap Side-cut
Programmed flap thickness (μm)	100 to 110	NA
Spot distance (μm)	4.0 to 4.5	1.8
Track distance (μm)	4.5	1.8
Energy offset (nJ)	135 to 170	170
Scan direction	Spiral in	NA
Scan mode	Single	NA

NA = not applicable  
The VisuMax femtosecond laser is manufactured by Carl Zeiss Meditec, Jena, Germany.

flap creation are described in detail in **Table 1**. The flaps were created using two different techniques.

In the original technique, the small cone (S cone) was programmed into the computer and used for the procedure. **Table 2** specifies the flap diameter selected based on the keratometry readings.

In the cone modification technique, the medium cone (M cone) was programmed into the computer but the S cone was used for the procedure. By programming an M cone, a larger flap diameter is allowed by the software. The S cone is recommended for most eyes that have moderate to small white-to-white (WTW) measurements because it affords the most reliable suction. Using a medium cone on moderate to small WTW corneas can lead to suction loss. The maximum flap diameter programmed using the cone modification technique and an S cone should never exceed 8.1 mm. If the keratometry readings exceed 48.00 diopters (D), the maximum flap diameter programmed should not exceed 8 mm. In this study, the flap diameters ranged from 7.9 to 8 mm for the original technique and from 8 to 8.1 mm with the cone modification technique. Flap diameter was specified as listed in

TABLE 2  
**Flap Diameter Settings for Different K Readings Using the Original and Cone Modification Techniques**

Average K Radius (mm)	Average K (D)	Flap Diameter (mm) Original	Flap Diameter (mm) Cone Modification
6.8	49.63	7.9	8.0
7.1	47.54	7.9	8.0
7.4	45.60	8.0	8.1
7.7	43.83	8.0	8.1
7.9	42.72	8.0	8.1
8.2	41.16	8.0	8.1

K = keratometry; D = diopters

**Table 2.** Hinge position was either superior or temporal and always with a hinge angle of 50°.

Eyes were divided into three groups: eyes in which OBL occurred using the original technique for flap creation (OBL group), eyes in which OBL did not occur using the original technique (no OBL group), and eyes in which the cone modification technique was used for flap creation (cone modification group).

Preoperative parameters analyzed were simulated keratometry values, WTW diameter, corneal thickness, patient age and gender, amount of correction, corneal astigmatism, corneal hysteresis, and corneal resistance factor. Intraoperative parameters analyzed were flap diameter, programmed flap thickness, measured flap thickness, energy setting, and room temperature/humidity. The Galilei G4 Dual Scheimpflug and Placido System (Zeimer Ophthalmic Systems AG, Port, Switzerland) and Ocular Response Analyzer (Reichert Instruments, Depew, New York) were used to measure the preoperative parameters.

In the original technique, if the patient underwent bilateral LASIK, only a single eye per patient enrolled was included for further statistical analysis. For example, if one eye developed OBL and the other eye did not, then only the eye that developed OBL was included in the study. If bilateral OBL occurred, the eye with the larger area of OBL was included. If OBL did not develop in either eye, a coin flip was used to choose which eye to include in the study. One calculated parameter, the difference between the white-to-white distance and the flap diameter (WW-FD), was calculated for each eye and analyzed.

The incidence of OBL using each of the techniques was calculated by considering all eyes operated on from days when videos of all eyes were available across the entire study period. Incidence of OBL was the total number of eyes with OBL (including both eyes from the same patient if bilateral OBL occurred) divided by the total number of eyes operated on.

### STATISTICAL ANALYSIS

All statistical analyses were performed with SAS software (version 9.3, SAS Institute, Inc., Cary, NC). The Kruskal–Wallis test was used for the comparisons of continuous preoperative and intraoperative parameters between eyes with and without OBL. The Fisher exact test was used for the comparisons of categorical preoperative and intraoperative parameters between eyes with and without OBL. Statistically significant parameters in the univariate analysis were considered as potential risk factors for OBL. A multivariate logistic regression model with stepwise variable selection was used to identify final, independent risk factors for OBL after adjusting for the effects of all other factors. A *P* value of less than .05 was considered statistically significant.

### RESULTS

This study enrolled 210 eyes to calculate the incidence of OBL using the original and cone modification techniques. One hundred eighteen eyes were treated with the original technique and 92 eyes were treated with the cone modification technique. Thirty-four eyes developed OBL using the original technique and 7 eyes developed OBL using the cone modification technique. The incidence of OBL was significantly lower with the cone modification technique 7.6% (7 of 92 eyes) than with the original technique 28.8% (34 of 118 eyes) (Fisher exact, *P* = .0009) (**Figure 1**).

As shown in **Table A** (available in the online version of this article), there were no statistical differences in the preoperative parameters between the OBL and no OBL groups (original technique) and the cone modification group except for older age in the original technique group versus the cone modification group ( $37.7 \pm 13.2$  vs  $32.6 \pm 9.1$  years) (*P* = .016).

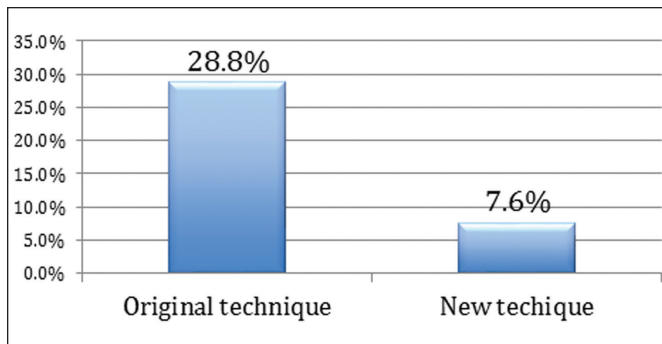
In this study, a range of spot distances, track distances, and energy settings were used with the original technique because the laser was being optimized in the early part of the study period. However, the mean energy in patients treated with the original technique who developed OBL ( $157.5 \pm 9.8$  nJ) was not statistically significantly different than in eyes that did not develop OBL ( $156 \pm 8.5$  nJ) (**Table B**, available in the online version of this article).

In the OBL group, 26 eyes that developed OBL were included in the analysis. In the no OBL group, 36 eyes in which no OBL occurred were included in the analysis. **Table B** compares the preoperative and intraoperative parameters of eyes with and without OBL using the original technique.

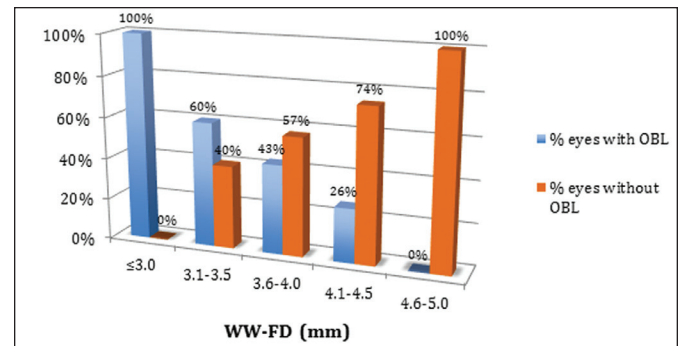
Using the original technique, eyes that developed OBL had the following characteristics that were statistically significantly different from those that did not develop OBL: smaller WTW diameter (*P* = .0048), thicker mean preoperative corneal thickness (*P* = .0132), higher corneal resistance factor (*P* = .0329), and smaller amount of astigmatism (*P* = .0472).

Additionally, the WW-FD was smaller in eyes that developed OBL (*P* = .0045) compared to those that did not develop OBL. **Figure 2** shows the dramatic decrease in the incidence of OBL with increasing WW-FD.

Stepwise variable selection in a multivariable logistic regression model was applied using the following parameters: corneal thickness, WTW diameter, corneal resistance factor, corneal astigmatism, and average, flat, and steep keratometry values. Multivariate logistic regression showed that a smaller WTW diameter was the only independent risk factor affecting the chance of OBL occurring (odds ratio = 0.17, 95% confidence



**Figure 1.** Opaque bubble layer (OBL) incidence: original technique versus cone modification (new) technique.



**Figure 2.** Percentage of eyes with and without opaque bubble layer (OBL) versus difference between the white-to-white and the flap diameter (WW-FD) using the original technique.

interval = 0.04 to 0.7;  $P = .0135$ ). No other parameter contributed significantly to the model.

## DISCUSSION

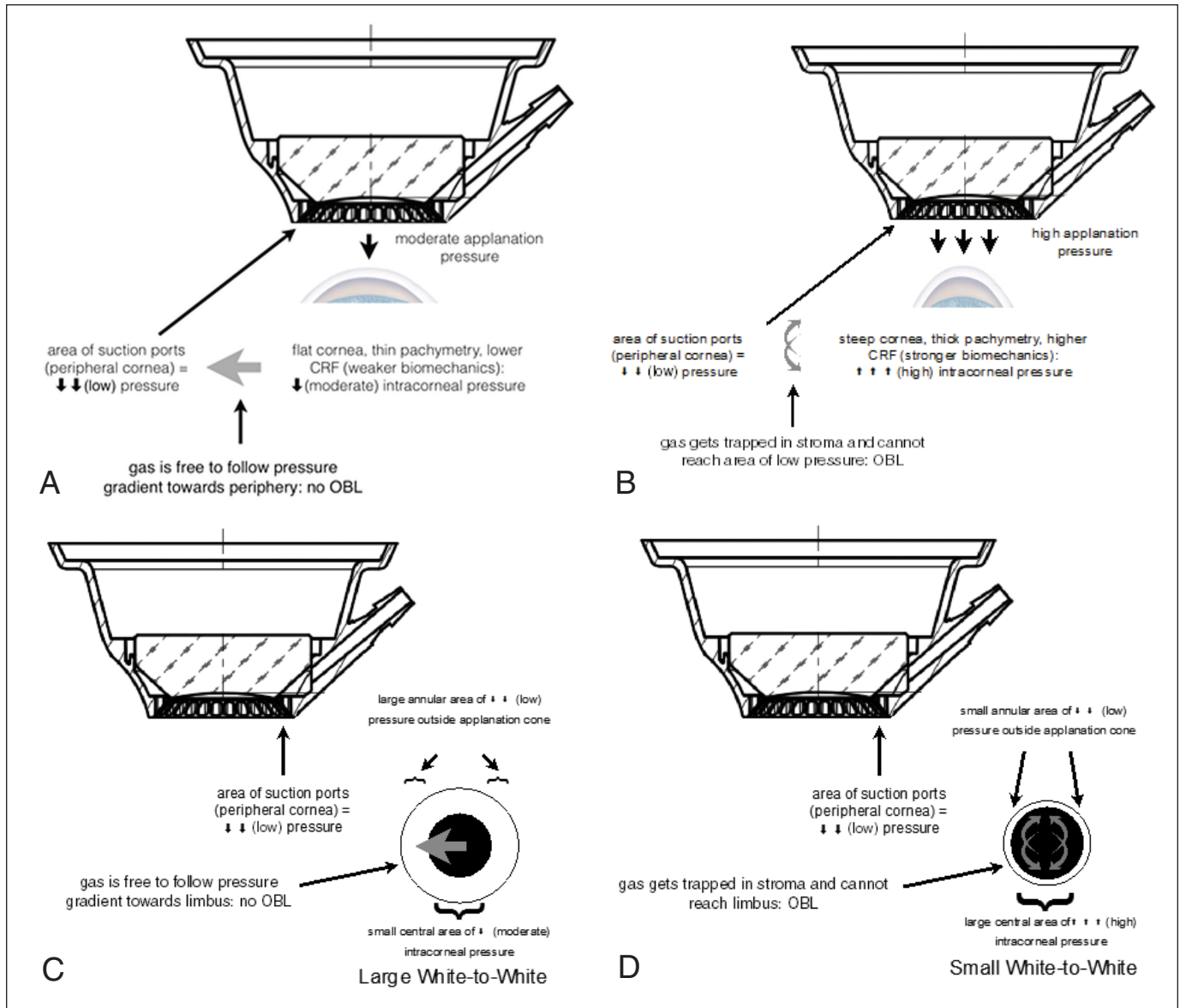
Overall, this study demonstrates that a cone modification technique for VisuMax femtosecond laser LASIK flap creation using a larger flap diameter reduces the incidence of OBL formation during flap creation. In addition, characteristics of the cornea that contribute to the formation of OBL during femtosecond laser flap creation were identified. The presence of OBL can present challenges for the refractive surgeon, including challenging flap lifts and interruption of the eye tracker during excimer laser ablation.

OBL forms as a result of the photodisruptive mechanism of the femtosecond laser. The gas bubbles are initially under high pressure as they expand before cooling. These high-pressure gas bubbles travel along the path of least resistance, which can include the interlamellar spaces of the cornea, the subepithelial space,<sup>10</sup> a deep stromal pocket, or extraocular space. This may even include retrograde movement through the episcleral veins into the anterior chamber.<sup>11</sup> Both the Intralase iFS (Abbott Medical Optics, Santa Ana, CA) and FS 200 (Alcon Laboratories, Fort Worth, TX) systems make use of a raster pattern photodisruption, beginning near the limbus at the hinge. This pattern lends itself to the placement of an evacuation path for the gas to escape into a deep stromal pocket or extraocular space.<sup>12</sup> The VisuMax laser uses a spiral pattern for photodisruption, a scheme that does not allow for a clinically useful evacuation path for the gas. The incidence of OBL when using a femtosecond laser for flap creation varies in the literature, from 5% up to 48%.<sup>12,13</sup> Liu et al.<sup>8</sup> reported an incidence of 52.5% in a series of 40 eyes using the Intralase 60-kHz laser: 40% with a hard pattern and 12.5% with a soft pattern.

In our study, we found that when using the original technique for flap creation, smaller flap diameter,

smaller WTW diameter, thicker cornea, higher corneal resistance factor, and lower corneal astigmatism were all significantly associated with an increased incidence of OBL. Kaiserman et al.<sup>6</sup> found that a smaller flap and thicker cornea were associated with a higher incidence of OBL; however, an underlying mechanism was not elucidated. Courtin et al.<sup>13</sup> demonstrated that a thicker cornea and higher corneal hysteresis were associated with an increased risk of OBL. The authors found that higher corneal hysteresis independently correlated with higher incidence of OBL in linear regression analysis, although the correlation was weak ( $r = 0.353$ ). Courtin et al. used the FS 200 femtosecond laser instead of the VisuMax laser, so the flap diameter, flap thickness, spot separations, raster pattern, and energy offset all differed from our study. Interestingly, although we did not find a statistical difference in mean corneal hysteresis between eyes that developed OBL and those that did not, we did find another biomechanical parameter (corneal resistance factor) to have a statistically significant difference between the two groups. We have demonstrated in previous studies that corneal resistance factor is the most significant biomechanical marker in distinguishing normal from abnormal corneas (eg, keratoconus), with higher corneal resistance factor readings occurring in the normal, stiffer cornea and lower corneal resistance factor readings in the keratoconic, softer cornea.<sup>14</sup> Accordingly, the fact that the mean corneal resistance factor was higher in corneas that developed OBL supports the hypothesis that a stiffer cornea is a risk factor for OBL. Overall, it may be that a more rigid, less elastic cornea might increase OBL occurrence due to the lower capacity for reversible deformation of the cornea with a greater gas bubble infiltration between stromal lamellae.

Son et al.<sup>15</sup> found that OBL occurring after the posterior lenticular cut tends to develop in thicker corneas, thinner lenticules, and a more anteriorly located posterior lenticular cut in small incision lenticule extraction (SMILE) surgery. In our study, we found that



**Figure 3.** Schematic diagrams describing a proposed mechanism of increased or decreased risk of opaque bubble layer (OBL). (A) Corneal parameters hypothesized to lead to decreased risk of OBL. (B) Corneal parameters hypothesized to lead to increased risk of OBL. (C) Role of large white-to-white diameter in process of OBL formation. (D) Role of small white-to-white diameter in process of OBL formation. CRF = corneal resistance factor

eyes developing OBL using the original technique had thicker mean preoperative corneal thickness, smaller WTW diameter, higher corneal resistance factor, and lower corneal astigmatism. **Figure 3** demonstrates our hypothesis as to why these parameters are associated with a higher incidence of OBL. With the lower applanation pressure associated with a flatter keratometry value, less compressibility with a thinner cornea, and softer biomechanics associated with a lower corneal resistance factor, the gas is able to follow the pressure gradient from the center (moderate pressure) to the periphery (lower pressure) and, consequently, does not get trapped in the intralamellar spaces of the cornea.

Higher resistance to gas outflow (thicker, denser cornea) presumably leads to migration of gas inward toward the central cornea rather than out through the subconjunctival space, resulting in sequestration of gas in the area of the flap. Thicker corneas are more compressible and may produce more resistance, thereby restricting the clearance of gas bubbles.<sup>16</sup> Under high pressure during applanation, a more rigid cornea (higher corneal resistance factor) may produce larger counterbalance force to resist the applanation pressure, which may restrict the departure of bubbles.<sup>16,17</sup> Lower astigmatism leads to applanation pressure that is more radially uniform so there is no meridian that allows for easier outflow of the gas

bubbles to the conjunctival space versus higher astigmatism where there is a meridian in which the applanation pressure is relatively lower. All of these features lead to a higher chance of OBL occurring, as shown in **Figure 3**.

We also found that in using the old technique, a smaller WW-FD was significantly associated with OBL. Kaiserman et al.<sup>6</sup> and Liu et al.<sup>8</sup> both concluded that a smaller flap diameter was associated with increased OBL formation, but neither study examined the WTW diameter and its relation to flap diameter. Mastropasqua et al.<sup>9</sup> concluded that OBL incidence decreases when the distance between the flap edge and the contact glass margin is reduced. Our results confirm and support these considerations. The literature on the relationship between WW-FD and OBL development during femtosecond laser flap creation is sparse. The mechanism behind why a smaller WW-FD is significantly associated with OBL has not been previously described. Our hypothesis is displayed in **Figure 3**. With a larger WTW diameter, a relatively large area of low pressure is present outside the suction cone which facilitates outflow of gas from the higher pressure region inside the cone (**Figure 3C**). Conversely, with a smaller WTW diameter, a relatively small area of low pressure outside the suction cone does not allow adequate gas flow outward from the larger area of high pressure inside the cone, leading to sequestration of gas in the area of the flap. Additional research is needed to further elucidate the mechanism behind this significant relationship between WTW diameter and OBL risk (**Figure 2**).

To minimize the possibility of OBL, surgeons can adjust the flap diameter. We used a modest increase in flap diameter, adding only 0.1 mm with the cone modification technique, and found a markedly reduced incidence of OBL. By initiating bubble formation as close as possible to the edge of the suction cone (low pressure region), an outward pathway for gas migration is more reliably established. Although this larger flap diameter may decrease the WW-FD difference, it does not increase the incidence of OBL because the effect of initiating gas bubble formation as close as possible to the low-pressure region is a much stronger effect than the decrease in WW-FD difference. Increasing the flap diameter too much will risk an incomplete side cut because the position of this cut can fall outside of the applanation area. For corneas with maximum keratometry readings less than 48.00 D, an 8.1-mm diameter should be used. For keratometry readings greater than 48.00 D, an 8-mm diameter should be used.

As mentioned earlier, a range of energy settings were used during flap creation (135 to 170 nJ). In eyes using the original technique, we did not find a significant difference in energy settings used during flap creation be-

TABLE 3  
**Multiple Risk Factors for OBL Formation in Both Eyes of a Sample Patient With a Thick Cornea, No Astigmatism, and Small WTW Distance**

Parameter	Right Eye	Left Eye
Refraction (sphere)	-2.25	-1.75
Corneal thickness ( $\mu\text{m}$ )	584	584
Average K (D)	47.8	47.6
WTW distance (mm)	10.7	10.7
Flap diameter (mm)	7.8 (old)	8 (new)
Presence of OBL	Yes	No

OBL = opaque bubble layer; WTW = white-to-white; K = keratometry; D = diopters

tween eyes that developed OBL versus eyes that did not. In the current study, a slightly higher energy was used for flap creation using the cone modification technique (170 nJ) versus the original technique (156 nJ). If the energy level were to affect the incidence of OBL, one would expect a higher incidence of OBL using the cone modification technique, given the higher energy settings. The opposite effect was seen in our study: a significantly lower incidence of OBL using the cone modification technique suggests that energy level has a less important effect on OBL incidence than flap diameter, at least when using the VisuMax laser. This may not be generalizable to other femtosecond lasers due to the relatively lower energy that the VisuMax laser employs.

**Table 3** and **Videos 1** and **3** (available in the online version of this article), show the development of OBL in the right eye (**Video 1**) but not in the left eye (**Video 3**) of a patient with significant risk factors for OBL formation. The original technique for flap creation was used in the right eye and the cone modification technique was used in the left eye. This is not to suggest that the cone modification technique eliminates the formation of OBL in all eyes that are high risk.

We have presented a cone modification technique for flap creation using the VisuMax laser with a larger flap diameter and identifying risk factors for OBL formation. This cone modification technique is associated with significantly lower risk of OBL formation, even in eyes with significant risk factors for OBL using the original technique. Although our study only looked at using the small cone size with a medium cone software setting, the investigators have experimented with the same principle of enlarging the flap diameter of 0.1 mm greater using a medium cone size with a large cone software setting. This strategy works well to minimize OBL formation in situations where the use of a medium cone is

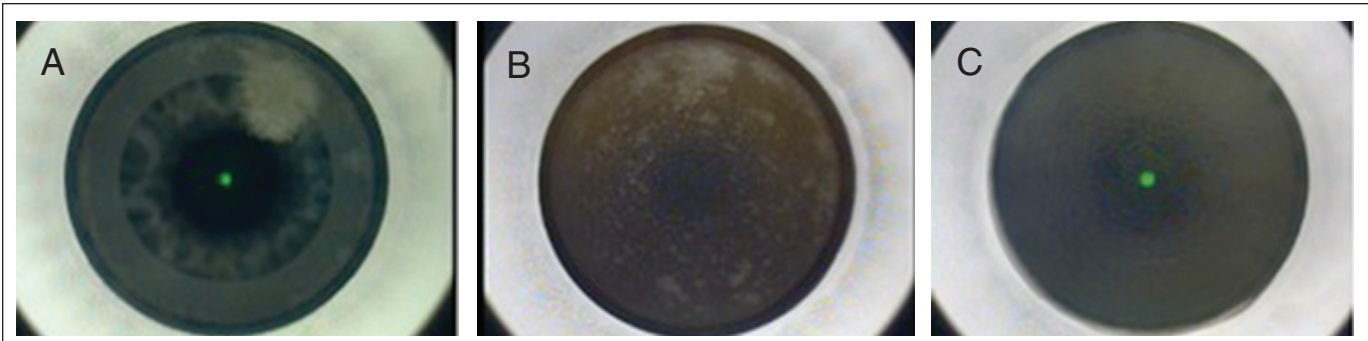
desirable (eg, large WTW diameter and hyperopic and/or high astigmatic ablations). Further investigations may include the development of a formula based on WTW diameter, keratometry thickness, and keratometry readings to recommend cone size and flap diameter to minimize OBL risk for each individual cornea. In addition, the identification of risk factors for OBL formation may be beneficial in customizing surgical parameters for the SMILE procedure to minimize risk of OBL formation, thus facilitating dissection of the two tissue planes required during this alternative laser refractive procedure.

#### AUTHOR CONTRIBUTIONS

*Study concept and design (NW, JGD, TKB, DD, DRH); data collection (NW, TKB, DD, LZ); analysis and interpretation of data (NW, JGC, JGD, TKB, DD, DRH); writing the manuscript (NW, JGC, DD, DRH); critical revision of the manuscript (NW, JGC, JGD, TKB, DD, LZ, DRH); administrative, technical, or material support (DD, DRH); supervision (DRH)*

#### REFERENCES

- Duffey RJ, Leaming D. U.S. Trends in Refractive Surgery: 2015 ISRS Survey. Presented at the International Society of Refractive Surgery meeting; November 13, 2015; Las Vegas, NV.
- Sugar A. Ultrafast (femtosecond) laser refractive surgery. *Curr Opin Ophthalmol*. 2002;13:246-249.
- Stonecipher KG, Dishler JG, Ignacio TS, Binder PS. Transient light sensitivity after femtosecond laser flap creation: clinical findings and management. *J Cataract Refract Surg*. 2006;32:91-94.
- Patel SV, Maguire LJ, McLaren JW, Hodge DO, Bourne WM. Femtosecond laser versus mechanical microkeratome for LASIK: a randomized controlled study. *Ophthalmology*. 2007;114:1482-1490.
- Krueger RR, Thornton IL, Xu M, Bor Z, Van den Berg TJTP. Rainbow glare as an optical side effect of IntraLASIK. *Ophthalmology*. 2008;115:1187-1195.
- Kaiserman I, Maresky HS, Bahar I, Rootman DS. Incidence, possible risk factors, and potential effects of an opaque bubble layer created by a femtosecond laser. *J Cataract Refract Surg*. 2008;34:417-423.
- Hurmeric V, Yoo SH, Fisher J, Chang VS, Wang J, Culbertson WW. In vivo structural characteristics of the femtosecond LASIK-induced opaque bubble layers with ultrahigh-resolution SD-OCT. *Ophthalmic Surg Lasers Imaging*. 2010;41(suppl):S109-S113.
- Liu CH, Sun CC, Hui-Kang Ma D, et al. Opaque bubble layer: incidence, risk factors, and clinical relevance. *J Cataract Refract Surg*. 2014;40:435-440.
- Mastropasqua L, Calienno R, Lanzini M, et al. Opaque bubble layer incidence in femtosecond laser-assisted LASIK: comparison among different flap design parameters. *Int Ophthalmol*. 2017;37:635-641.
- Srinivasan S, Herzig S. Sub-epithelial gas breakthrough during femtosecond laser flap creation for LASIK. *Br J Ophthalmol*. 2007;91:1373.
- Lifshitz T, Levy J, Klemperer I, Levinger S. Anterior chamber gas bubbles after corneal flap creation with a femtosecond laser. *J Cataract Refract Surg*. 2005;31:2227-2229.
- Kanellopoulos AJ, Asimellis G. Three-dimensional LASIK flap thickness variability: topographic central, paracentral and peripheral assessment, in flaps created by a mechanical microkeratome (M2) and two different femtosecond lasers (FS60 and FS200). *Clin Ophthalmol*. 2013;7:675-683.
- Courtin R, Saad A, Guilbert E, Grise-Dulac A, Gatinel D. Opaque bubble layer risk factors in femtosecond laser-assisted LASIK. *J Refract Surg*. 2015;31:608-612.
- Zhang L, Danesh J, Tannan A, Phan V, Yu F, Hamilton DR. Second-generation corneal deformation signal waveform analysis in normal, forme fruste keratoconic, and manifest keratoconic corneas after statistical correction for potentially confounding factors. *J Cataract Refract Surg*. 2015;41:2196-2204.
- Son G, Lee J, Jang C, Choi KY, Cho BJ, Lim TH. Possible risk factors and clinical effects of opaque bubble layer in small incision lenticule extraction (SMILE). *J Refract Surg*. 2017;33:24-29.
- Shah S, Laiquzzaman M, Cunliffe I, Mantry S. The use of the Reichert ocular response analyser to establish the relationship between ocular hysteresis, corneal resistance factor and central corneal thickness in normal eyes. *Cont Lens Anterior Eye*. 2006;29:257-262.
- Kotecha A. What biomechanical properties of the cornea are relevant for the clinician? *Surv Ophthalmol*. 2007;52(suppl 2):S109-S114.



**Figure A.** Representative photographs of (A) hard opaque bubble layer (OBL), (B) soft OBL, and (C) no OBL.

TABLE A  
**Preoperative Parameters of Eyes With the Original Technique  
 (With and Without OBL) and Cone Modification Technique<sup>a</sup>**

Parameter	Old Technique	Cone Modification Technique	P
Age (y)	37.7 ± 13.2	32.6 ± 9.1	.016 <sup>b</sup>
Manifest sphere (D)	-3.80 ± 1.70	-4.00 ± 1.90	.33
Manifest cylinder (D)	0.50 ± 0.60	0.50 ± 0.50	.95
Pachymetry (μm)	556.0 ± 33.7	553.7 ± 25.9	.65
K1 (D)	43.50 ± 1.50	43.30 ± 1.40	.46
K2 (D)	44.40 ± 1.40	44.20 ± 1.40	.54
K-Avg (D)	43.90 ± 1.40	43.80 ± 1.40	.57
Corneal astigmatism (D)	0.9 ± 0.5	0.9 ± 0.6	.89
Corneal steep axis (°)	85.1 ± 73.9	84.7 ± 70.3	.77
White-to-white distance (mm)	11.8 ± 0.4	11.8 ± 0.4	.83
Corneal resistance factor (mm Hg)	9.9 ± 1.6	9.9 ± 1.5	.72

OBL = opaque bubble layer; D = diopters; K1 = flat keratometry; K2 = steep keratometry; K-Avg = average keratometry

<sup>a</sup>Values are mean ± standard deviation.

<sup>b</sup>P ≤ .05.



TABLE B  
**Preoperative and Intraoperative Parameters of Eyes  
 With and Without OBL Using the Original Technique<sup>a</sup>**

Parameter	With OBL	Without OBL	P
Preoperative			
Age (y)	35.6 ± 11.3	39.2 ± 14.4	.3645
Manifest sphere (D)	-4.00 ± 1.70	-3.70 ± 0.40	.6734
Manifest cylinder (D)	0.40 ± 0.40	0.60 ± 0.70	.2357
Pachymetry (μm)	565.8 ± 31.5	548.8 ± 33.8	.0132 <sup>b</sup>
K1 (D)	44.00 ± 1.50	43.10 ± 1.30	.0306 <sup>b</sup>
K2 (D)	44.80 ± 1.40	44.10 ± 1.30	.0771
K-Avg (D)	44.40 ± 1.40	43.60 ± 1.30	.0550
Corneal astigmatism (D)	0.80 ± 0.50	1.00 ± 0.50	.0472 <sup>b</sup>
Corneal axis (°)	102 ± 71.6	72.9 ± 74	.0667
White-to-white distance (mm)	11.6 ± 0.5	11.9 ± 0.4	.0048 <sup>b</sup>
Corneal hysteresis (mm Hg)	6.7 ± 1.4	6.6 ± 1.3	.5451
Corneal resistance factor (mm Hg)	10.4 ± 1.7	9.6 ± 1.5	.0329 <sup>b</sup>
Intraoperative			
Flap diameter (mm)			.1929
7.8	2 (100%)	0 (0%)	
7.9	18 (43%)	24 (57%)	
8	6 (33%)	12 (67%)	
WW-FD	3.7 ± 0.4	4.0 ± 0.4	.0045 <sup>b</sup>
Programmed flap thickness (μm)	101 ± 18.6	105.3 ± 2.4	.1140
Measured flap thickness (μm)	124.1 ± 10.1	120.9 ± 14.3	.3476
Energy (nJ)	157.5 ± 9.8	156 ± 8.5	.2010
Temperature (°F)	69.5 ± 0.9	69.5 ± 1.0	.7591
Relative humidity (%)	53.3 ± 4.9	55.0 ± 4.1	.2328

OBL = opaque bubble layer; D = diopters; K1 = flat keratometry; K2 = steep keratometry; K-Avg = average keratometry; WW-FD = difference between white-to-white and flap diameter

<sup>a</sup>Values are mean ± standard deviation.

<sup>b</sup>P ≤ .05.