The Role of Iris Color in Femtosecond Laser-Induced Miosis in Patients Undergoing Cataract Surgery

Tarek Ibrahim, MD, PhD1,2, Phillip Goernert, PhD3 and Guillermo Rocha, MD, FRCSC, FACS1,4,5

1Ocular Microsurgery & Laser Centre, Brandon, Manitoba, Canada
2Eye Consultant Centre, Visiting Consultant, Dubai, UAE
3Department of Psychology, Brandon University, Manitoba, Canada
4Department of Ophthalmology, University of Manitoba, Canada
5Brandon Regional Health Centre, Prairie Mountain Health, Manitoba, Canada

Abstract

Purpose
To measure Femtosecond laser (FSL)-induced miosis and to determine if correlation with iris color exists in patients undergoing Femtosecond Laser Assisted Cataract Surgery (FLACS)

Methods
Patients were divided into 3 groups based on iris color: blue (Group 1; N=62), hazel (Group 2; N=48) and brown (Group 3; N=27). Intra operative miosis was graded into 4 categories (from 0 to +3) following FSL use. FSL-induced miosis was observed preoperatively, immediately after FSL use, and immediately before phacoemulsification "shifting time". FSL suction time and shifting time were also collected.

Results
Of the 137 eyes, 82% of Group 1, 40% of Group 2, and 22% of Group 3 showed miosis. Kruskal-Wallis test showed significance of eye color on FSL-induced miosis (H (2) = 35.67, p < .01); Dunn Q tests of the groups’ mean rankings showed that the degree of FSL-induced miosis was significantly higher in the blue eye color group than in either other eye color group (both p-values < .05). The difference in the degree of FSL-induced miosis between the hazel and brown eye color groups was not significant (p > .05).

Conclusion
Light-colored irides may be more susceptible to FSL energy than darker irides. There is a significant relationship between blue color irides and pupillary constriction during post-FSL pre-treatment in cataract surgery. Clinical measures might be taken in light colored irides undergoing FLACS to avoid intra operative complications.
Introduction

When femtosecond laser (FSL) technology was introduced in the early 2000s, it provided surgeons with new means to perform corneal procedures that ranged from corneal flap creation in laser in situ keratomileusis (LASIK) to penetrating keratoplasty, among others [1-6]. However, as pupil dilation is not necessary in LASIK so intraoperative miosis was neither debated nor analyzed.

Advances in FSL technology have allowed surgeons to use these devices for portions of cataract surgery [7,8]. The literature supports the use of FSL to improve the consistency of capsulotomy in terms of size, shape, and centration, and to decrease ultrasound (U/S) power and time used during phacoemulsification [7,9-11].

Femtosecond laser-assisted cataract surgery (FLACS) can be used for capsulotomy creation and crystalline lens fragmentation, but requires an adequate pupillary diameter to minimize complications. Nagy et al. [12], noted, for example, that the FSL shockwaves created during use may affect the surrounding tissue and recommended a 6.5 mm pupil for a 5 mm diameter capsulotomy, and a 6.0 mm pupil diameter for a 4.5 mm diameter capsulotomy. Adequate pupil dilation is an essential aspect of FSL pre-treatment to ensure safe and efficient phacoemulsification. Studies have shown that the prevalence of significant intraoperative miosis ranges between 10% and 32% [12-14]. To date, factors including patient age, FSL application time and energy dissipation, increased intraocular pressure during docking, the patient interface, and overall cataract density may be causal [12,14-17], but no single factor has been well correlated to FSL-induced miosis. In fact, the importance of an adequate pupil size is twofold: initially, to determine whether a suitably sized laser capsulotomy can be created (relevant to FLACS), and intraoperatively, to diminish the impact on complication rates during phacoemulsification, irrigation/aspiration and intraocular lens implantation (relevant to both manual surgery and FLACS).

We postulated that light-colored irides may be more affected by the FSL beam than darker irides. To the best of our knowledge, this is the first evaluation of iris color as a factor for FSL-induced miosis.

Patients and Methods

This study comprised eyes that underwent FLACS with the Victus femtosecond laser platform (Bausch & Lomb, Bridgewater, NJ, USA) and phacoemulsification with the Stellaris PC (Bausch&Lomb) at Brandon Regional Health Centre, Manitoba, Canada, between October 2015 and March 2016. The study was approval by the Research Ethics Board (REB) of Manitoba University and was performed in accordance with the tenets of the Declaration of Helsinki.

Pupil dilation was recorded immediately before and immediately after FSL and once the phacoemulsification began. To compare the differences between light, medium, and dark irides, we included patients with blue, brown, or hazel irides (Figures 1-3). Two investigators (T.I. and G.R.) qualified iris color; if the two investigators disagreed or color was not apparent, those eyes were excluded from analysis. Other eye colors (e.g., green, gray, violet) were not evaluated for study inclusion.

Miosis was graded into 0, +1, +2, and +3 depending on the degree of pupillary constriction and anatomic factors, such as the

Figure 1: Blue Color Iris

Figure 2: Hazel Color Iris
Iris color, pupil size (degree of miosis) before the procedure, pupil size (degree of miosis) immediately after FSL, and pupil size (degree of miosis) prior to phacoemulsification initiation were recorded. FSL suction time and shifting time (time between end of FSL and initiation of phacoemulsification) also were collected.

Subjects were enrolled in this study if they had an unremarkable ocular history, could achieve adequate pupillary dilation as determined by the surgeon (typically ≥ 6mm), and met the iris color mandates. Exclusion criteria included patients with history of intraocular surgery or trauma, pseudoexfoliation syndrome, glaucoma medication use, inflammatory eye disease, preoperative zonular weakness, systemic use of alpha-blockers for benign prostatic insufficiency (i.e., tamsulosin), or poor pupil dilation.

FSL settings are shown in Table 1. In all cases the primary incision was performed manually based on surgeon preference. All surgeries were performed in the same operating room where the FSL resides.

Surgical technique

Patient preparation for surgery was done through a standing order for all cases. At arrival (one hour before surgery), patients were administered one tablet of lorazepam 0.5 mg sublingual (Pfizer Inc., New York, NY, USA); one drop of tetracaine hydrochloride 0.5% eye drops (Bausch + Lomb) was instilled bilaterally. The same protocol for preoperative medical mydriasis was used for all patients: A pre-prepared wick soaked with a mixture of tropicamide 1% (Alcon Laboratories, Ft. Worth, Texas, USA), phenylephrine 2.5% (Alcon Laboratories), homatropine 2% (Alcon Laboratories), ketorolac 0.45% (Allergan, Dublin, Ireland) and moxifloxacin HCl ophthalmic solution 0.5%
(Alcon Laboratories) was inserted into the inferior conjunctival fornix of the operative eye for 15 minutes. The eye was checked; if adequate mydriasis was not achieved, another wick was inserted for another 15 minutes. All procedures were performed under topical anesthesia.

FSL pre-treatment included capsulotomy (0.5 mm safety distance to pupil margin), crystalline lens fragmentation (four radial and three circular cuts were used in all cases), and two clear cornea 0.9mm side-ports in all eyes. The main incision (1.8 mm) was done manually using a keratome in all cases followed by phacoemulsification. All eyes were injected intracameral with preservative-free anesthetics (lidocaine HCL 1%, Alveda Pharmaceuticals, Toronto, Canada) at the beginning of the phacoemulsification procedure. Single use povidone iodine 5% (Bausch + Lomb) was instilled in all cases at the start and at the end of the procedure. No intra operative complications were noted. All patients received the same postoperative medical treatment regimen: a combination of an antibiotic, steroid, and non steroidal anti-inflammatory agent.

**Statistical analysis**

A Kruskal-Wallis test was used to show the effect of eye color on FSL-induced miosis. Follow-up Dunn Q tests of the groups’ mean rankings was used to show the significance of the degree of miosis in relation to each eye color group. A p-value lower than 0.05 was considered statistically significant.

**Results**

A total of 137 eyes were enrolled in the study out of 422 eyes. Eyes excluded had different eye color than the established criteria, previous ocular morbidity or lack of adequate mydriasis. All cases included in the study met the pre-operative dilation requirements of at least 6mm pupillary diameter. Select demographic data are provided in Table 2.

Group 1 showed an overall rate of miosis of 82.26% (51/62 eyes); 51 eyes at the end of FSL application and four additional eyes after shift (6.45% after shift). Group 2 showed a rate of miosis of 39.58% (19/48 eyes) 19 eyes at the end of FSL application and added no eyes after shift. Group 3 showed a rate of miosis of 22.22% (6/27 eyes); six eyes at the end of FSL and one additional eye (3.71%) after shift. A Kruskal-Wallis test shows that there was a significant effect of eye color on FSL-induced miosis (H (2) = 35.67, p < .01). Follow-up Dunn Q tests of the groups’ mean rankings shows that the degree of FSL-induced miosis was significantly higher in Group 1 than in either Group 2 or Group 3 (both p-values < .05). The difference in the degree of FSL-induced miosis between Group 2 and Group 3 was not significant (p > .05). There was no significant difference in age, suction time, or shifting time across the three iris color groups (all p-values > .05), (Tables 3& 4).

**Table 1: Femtosecond laser parameters**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Value</th>
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<tbody>
<tr>
<td>Capsulotomy</td>
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<td>Diameter (mm)</td>
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<td>Line spacing (μm)</td>
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</tr>
<tr>
<td>Spot spacing (μm)</td>
<td>5</td>
</tr>
<tr>
<td>Energy (μJ)</td>
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<tr>
<td>Lens Fragmentation</td>
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<tr>
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<tr>
<td>Spot spacing (μm)</td>
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</tr>
<tr>
<td>Energy (μJ)</td>
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<tr>
<td>Radial cuts</td>
<td></td>
</tr>
<tr>
<td>Number</td>
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</tr>
<tr>
<td>Outer diameter (mm)</td>
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<tr>
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<td>Energy (μJ)</td>
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</tr>
</tbody>
</table>
Discussion

Pupillary mydriasis is considered essential for safe and efficient cataract surgery [11]. Intraoperative miosis limits the surgeon's ability to visualize the cataract and makes capsulorrhexis creation more challenging. Difficulties with small pupils intraoperatively can result in surgical complications such as posterior capsular tears, iris trauma, vitreous loss, retained lens material, cystoid macular edema, and retinal detachment [9,18].

There are several situations and conditions that may contribute to the inability to achieve or maintain adequate pupillary dilation during phacoemulsification, including pseudoexfoliation syndrome, posterior synechiae, elderly patients with atrophic iris changes, and patients on chronic glaucoma medications [18]. Despite the fact that these conditions are documented at the time of patient preparation for surgery, at least 2% of all cataract cases demonstrate surgically significant miosis (pupil diameter of < 5 mm) [18]. Although phacoemulsification and FSL systems have improved capsulorrhexis and corneal wound reproducibility, there remains continued debate on the advantages of these FSL systems in terms of procedural safety and outcomes [19-23].

A high incidence of intraoperative miosis has been the most frequently reported complication by FLACS surgeons [7,8,16,24,25]. One theory on the phenomenon is that laser emissions applied to intraocular tissues might release cytokines [26,27]. As a result of the cytokine release, prostaglandin is released from the ciliary body into the anterior chamber [16,17,24,26]. Although the use of FSL - specifically the capsulotomy part of the procedure - may trigger prostaglandin release, some authors believe the release is caused by mechanical forces (suction or applanation) [18,28], while others suggest laser application time or shifting time between FSL pre-treatment and the start of phacoemulsification may contribute to the development of miosis [7,8].

Our study assessed the diameter of the pupil before and after FSL and at the start of phacoemulsification to account for the shifting time. We found a significant decrease in the pupil area after FSL pre-treatment, adding to the published literature on the topic of FLACS-related complications [7,18,28-30].

However, our study also found a significant correlation between FSL-induced miosis and iris color, which has not been investigated previously. When intraocular tissues undergo trauma (e.g., cataract surgery), Numerous inflammatory factors may be released from the lens, iris, and trabecular meshwork [11,31]. Inflammatory cytokines interleukin (IL)-1β, IL-6, and PGE2 have been found to increase significantly after FLACS in the aqueous humor [11,31], which may be the cause of intraoperative miosis seen in these patients. In cases of +2 and +3 miosis, mostly blue irides, surgical measures such as intraocular injection of mydriatics and/or the use of iris devices to properly dilate the pupil at the time of phacoemulsification may have to be undertaken. If the inflammatory factors are, indeed, the cause of intraoperative miosis, our results show people with blue irides are more susceptible to the femtosecond laser beam than people with brown or hazel irides. These factors would, therefore, activate more inflammatory cytokines and prostaglandins in people with blue irides. To the best of the authors' knowledge, this marks the first report that suggests blue eyes may be more susceptible to FSL energy.

In our study, we did not find statistical significant differences in patient age (72.10 ± 11.09), suction time (2.79 ± 0.59 minutes) or shifting time (6.96 ± 0.83 minutes) and the FSL-induced miosis. These findings disagree with findings in some studies that correlates exposure time of the tissue to the laser emissions and the increased prostaglandin release from intraocular tissues [7,8]. Our shifting time is shorter than reported in those studies, however, as our FSL machine resides in the same OR. It is worth mentioning that some studies had the same as ours although the shifting time was up to 40 minutes [30,32].

The maximum mydriatic effect should be taken into consideration. One study reported that the maximum mydriatic effect of several combinations of tropicamide and phenylephrine lasted between 60 minutes and 75 minutes [32], long enough to cover the 40 minutes needed to shift between laser pre-treatment and phacoemulsification. This may explain why the shifting time and changes in the pupil area were not correlated in other studies.

We recommend special preparatory measures to be in place in case a blue iris eye is undergoing FLACS. Proper preoperative mydriasis, the preparation of intraocular pupillary dilators and having access to iris devices are some of the measures that might be necessary in these cases.

Diakonis et al., compared FSL-induced miosis with different
machines, with the Victus machine incurring the least FSL-induced miosis [27]. The Victus uses high pressure during corneal applanation with its intelligent pressure sensors; these may potentially induce transient anterior segment ischemia that decreases circulation within the iris sphincter, which in turn does not allow the muscles to contract to induce post-FLACS miosis [16,33,34].

We are aware of some limitations of this study, including the lack of an objective assessment of pupil size. Accurate and objective pupil measurement in a surgical setting is limited due to sterility concerns. In our study, we based our measurement on anatomic factors the distance between capsulotomy and pupillary margins. We compensated for this disparity by assessing the pupil under the surgical microscope with the lowest possible illumination. We also limited our observations to only blue-, hazel-, or brown-colored eyes, as determined by two of the investigators. We cannot be certain our results would be duplicated in people with other-colored eyes, or that other researchers would categorize patients’ eye color in a similar manner. We attempted to overcome this potential limitation by having two of the investigators categorize eye color separately. In cases where the investigators disagreed on eye color, the patient was not included in the analysis.

In conclusion, this study found a significant correlation between blue irides and papillary constriction post FSL pre-treatment during cataract surgery. These results are clinically significant in that measures could be taken preoperatively in individuals with blue irides, or considerations may be needed if the FSL is not located in the same operating room as where the phacoemulsification will take place.

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Ethics Approval

Research Ethics Board (REB), University of Manitoba, Canada

Financial Disclosures

Dr. Rocha has received speaker fees from Bausch + Lomb, Dr. Ibrahim is a consultant for Bausch + Lomb, and Dr. Goernert has no financial interest or proprietary interest in any material or method mentioned.

References


