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Research Article

The Incidence and Natural History of Subjectively and Objectively Determined Metrics of Light Scattering in Femtosecond Laser-Assisted *In Situ* Keratomileusis

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Abstract

Purpose: To assess the incidence and long-term persistence of both subjective (rainbow glare phenomenon) and objective metrics of light scattering (stray light measurement) in femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK).

Settings: Cleveland Clinic Foundation, Cole Eye Institute

Design: Prospective, contralateral eye study in which 54 myopic eyes of 27 patients underwent LASIK using the ALLEGRETTO® Eye-Q excimer laser. Flap creation was created by IntraLASE FS60 (IL) in one eye and Wave Light FS200 (FS) in the contralateral eye. Rainbow glare and stray light measurements (C-Quant, Oculus Inc, Lynnwood, WA) were obtained preoperatively, and at 1 week, 1, 3, and 9 months postoperatively. Manifest and wavefront refractions were performed at each postoperative visit.

Results: Stray light measurements in both IL and FS groups peaked at 1 week postoperatively (log 1.28 ± 0.16, p = 0.02 and log 1.26 ± 0.12, p = 0.039, respectively) with statistically significant improvement at 3 months (log 1.12 ± 0.35, p = 0.007 and log 1.20 ± 0.15, p = 0.04) and 9 months (log 1.11 ± 0.17, p = 0.008 and log 1.15 ± 0.14, p = 0.011). No statistically significant differences were found between IL and FS eyes at all time points. 11 patients reported postoperative rainbow glare at 1 week (42%), which decreased to 6 patients at 9 months (33%) in the IL treated eye. 14 patients reported postoperative rainbow glare at 1 week (54%), which decreased to 7 patients at 9 months (39%) in the FS treated eye.

Conclusion: Both rainbow glare and objective light scatter were greatest at 1 week and were significantly reduced by 1 to 3 months postoperatively. Rainbow glare is a mild optical side effect of femtosecond laser LASIK that improves with time.

Keywords: *Femtosecond; LASIK; Rainbow Glare; C-Quant*

Abbreviations

RG: Rainbow Glare; LASIK: Laser-Assisted *In Situ* Keratomileusis; FS-LASIK - Femtosecond Laser-Assisted *In Situ* Keratomileusis; kHz: Kilohertz; IL: IntraLase FS60; FS: WaveLight FS200; UDVA: Uncorrected Distance Visual Acuity; CDVA: Corrected Distance Visual Acuity; SD-OCT: Spectral Domain Optical Coherence Tomography; Cpwr: Cornea Power; ANOVA: Analysis of Variance; WRSE: Wavefront Refraction Spherical Equivalent; MRSE: Manifest Refraction Spherical Equivalent

Introduction

Rainbow glare (RG) is a post femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK) phenomenon first reported by Krueger., *et al.* in 2008 [1]. The glare is defined as a pattern of evenly spaced, spectral bands of light perceived around a single point light source in a dark environment, with the shorter blue wavelengths closer to the light source and longer red wavelengths of light further away from the light source [2]. Krueger., *et al.* demonstrated that the microscopic basis for RG is due to the constructive diffractive effect on the uniform grating pattern of evenly spaced femtosecond laser raster spots as polychromatic light passes through the flap interface [1]. An increased incidence of RG has been associated with several factors including: increased depth of myopic ablation, hyperopic ablation, postoperative

coma, halos, glare, and starbursts, and increased time between maintenance evaluations of the laser platform [1,3]. Studies have been performed using several different laser platforms (15 kHz and 60 kHz IntraLase, and Wavelight FS-200), but all three have shown cases of RG [4,5].

It has been noted that the symptoms of RG are most evident when a pinpoint light is provided against a dark background, which explains why the majority of patients have symptoms while driving at night [1,3]. Although there are many means to reduce the incidence of RG (such as tighter spacing and lower energy), the potential for RG in post FS-LASIK patients will remain until a randomized beam pattern can be used for creation of FS-LASIK flaps. The purpose of this study is to report the evolution and prevalence of RG in post FS-LASIK for myopia.

Materials and Methods

Design

This study was a prospective, contralateral eye study performed at the Cleveland Clinic Foundation, Cole Eye Institute between December 6, 2011 to January 15, 2013. The Institutional Review Board at the Cleveland Clinic approved the protocol (IRB number: 11-744), which adhered to tenets of the Declaration of Helsinki of 1975.

Participants

Initially 54 myopic eyes of 27 patients were enrolled in this study, but 7 of the 27 patients were lost to follow up by the conclusion of the study. Thirty-six myopic eyes of 18 patients (age range 21 to 36) completed the study and attended the 9 month postoperative appointment.

Examples of disqualifying pathologies and exclusion criteria included active herpetic keratitis or other herpetic ocular involvement, prior refractive surgery, keratoconjunctivitis sicca, significant untreated dry eye syndrome, corneal ectatic disorders (pellucid marginal degeneration, keratoconus, and keratoglobus), corneal degenerations and disorders, history of excessive keloid formation, pregnancy, breastfeeding mothers, age less than 18 years old, irregular astigmatism, and acute eye diseases (active diabetes mellitus, glaucoma, uveitis, etc.).

Informed consent was obtained from each patient before participating in the research study.

Surgical technique

All patients underwent FS-LASIK using the ALLEGRETTO® Eye-Q excimer laser (Alcon Laboratories, Fort Worth, Texas) by a single experienced surgeon (RRK). Flap creation was constructed by using the IntraLASE FS60 (IL) (Johnson and Johnson Vision, Irvine, California, USA) in one eye and WaveLight FS200 (FS) (Alcon Laboratories, Fort Worth, Texas) in the contralateral eye. Femtosecond laser use was determined by alternating right and left eyes by the day of the week in which the surgery was scheduled (Tuesday: FS OD, IL OS, Thursday: IL OD, FS OS). All flaps were created with a superior hinge, an intended flap thickness of 110 μm, diameter of 8.7 mm, side cut angle of 55 degrees, bed energy of 0.8 mJ, and spot and line separation of 7.0 μm. Both eyes were treated with the Allegretto Wave Eye-Q Excimer Laser System (Alcon Laboratories). All eyes were treated with the wavefront-optimized ablation profile, optical zone of 6.5 mm, and transition zone of 1.5 mm centered on the patient's pupil: Postoperatively, patients were instructed to use one drop of prednisolone acetate 1% ophthalmic solution and one drop of moxifloxacin 0.5% ophthalmic solution 4 times daily for 1 week, along with artificial tears as needed.

Measurements

Stray light measurements (C-Quant, Oculus Inc, Lynnwood, WA) were obtained preoperatively and at 1 week, 1, 3 and 9 months postoperatively. Manifest and wavefront refractions were performed at each postoperative visit. RG phenomenon (radiating colors around a white ophthalmic light source under mesopic and scotopic conditions) was tested by asking the same standardized questions about its presence while shining a point light source at the patient in a dark exam room at 1 week, 1, 3 and 9 months postoperatively.

Additionally, uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), manifest refraction, cycloplegic refraction, corneal topography (Atlas 9000; Carl Zeiss Meditec Inc, Dublin, California, USA), corneal power changes by SD-OCT (6 mm Pachymetry + Corneal power software [Cpwr] scans; RTVue-100; Optovue, Fremont, California, USA), and wavefront analysis (LADARWave aberrometer; Alcon Laboratories, Inc, Fort Worth, Texas, USA) were performed preoperatively, and at 1 week, 1, 3, and 9 months postoperatively.

Statistical analysis

Statistical analysis was performed using the JMP 10.0 software (SAS Institute Inc, Cary, North Carolina, USA). Student t-test was used to evaluate differences between groups, and one-way repeated measures analysis of variance (ANOVA) was used to compare stray light measurements across the different postoperative time points.

Results

Fifty-four eyes of 27 myopic patients were initially enrolled in this study. The preoperative refractive error ranged from -1.125 to -7.250 D (mean -3.25 ± 1.90D) and the mean age of participants at the time of the study was 27 years. The number of patients present at 1 week, 1, 3, and 9 months follow up appointments were n = 26, 26, 21, and 18, respectively. Eighteen patients (36 eyes) attended the 9 month postoperative visit, which amounted to two-thirds of the total initial enrolment. The mean preoperative and postoperative results for wavefront refraction spherical equivalent (WRSE), manifest refraction spherical equivalent (MRSE), corneal power (Cpwr) measured by SD-OCT (6 mm Pachymetry +Cpwr scans), spherical aberration, and coma are listed in table 1a and 1b.

1a	**FS**					
	Number of Eyes (n)	**MRSE (D)**	**WRSE (D)**	**Cpwr (D)**	**Spherical Aberration (µm)**	**Coma (µm)**
Pre-operative	27	-3.25 ± 1.93 (range -1.125 to -7.250)	-3.25 ± 1.97 (range -0.915 to -7.75)	43.19 ± 1.52 (range 40.2 to 46.3)	0.19 ± 0.12 (range 0 to 0.49)	0.20 ± 0.10 (range 0.01 to 0.43)
1 wk post-op	26	0.14 ± 0.28 (range 1.0 to 0.0)	-0.08 ± 0.53 (range 0.89 to -0.45)	39.92 ± 2.91 (range 33.3 to 43.7)	0.14 ± 0,12 (range 0.05 to 0.40)	0.19 ± 0.13 (range 0.02 to 0.54)
1 month post-op	26	0.08 ± 0.19 (range 0.0 to -0.37)	-0.03 ± 0.43 (range 0.47 to -0.645)	39.84 ± 2.95 (range 33.1 to 43.4)	0.18 ± 0.21 (range 0.01 to 0.53)	0.19 ± 0.10 (range 0.02 to 0.46)
3 months post-op	21	0.06 ± 0.16 (range 0 to -0.25)	-0.25 ± 0.49 (range 0.52 to -0.90)	40.15 ± 2.90 (range 33.8 to 43.4)	0.11 ± 0.11 (range 0.00 to 0.34)	0.20 ± 0.11 (range 0.00 to 0.46)
9 months post-op	18	0.02 ± 0.08 (range 0 to -0.25)	-0.26 ± 0.5(range 0.46 to -0.90)	40.21 ± 2.03 (range 33.9 to 43.9)	0.15 ± 0.09 (range 0.01 to 0.34)	0.21 ± 0.13 (range 0.08 to 0.53)
1b	**IL**					
	Number of Eyes (n)	**MRSE**	**WRSE**	**Cpwr (D)**	**Spherical Aberration (µm)**	**Coma (µm)**
Pre-operative	27	-3.24 ± 1.95 (range -1.0 to -7.125)	-3.20 ± 1.99 (range -0.955 to -7.11)	43.32 ± 1.38 (range 40.5 to 45.8)	0.18 ± 0.12 (range 0.00 to 0.47)	0.21 ± 0.09 (range 0.00 to 0.47)
1 wk post-op	26	-0.03 ± 0.17 (range 0.0 to -0.5)	-0.28 ± 0.42 (range 1.03 to -1.04)	40.11 ± 2.28 (range 35.1 to 43.2)	0.11 ± 0.10 (range 0.01 to 0.39)	0.19 ± 0.14 (range 0.02 to 0.52)
1 month post-op	26	0.05 ± 0.25 (range 0.375 to -0.375)	-0.24 ± 0.52 (range 0.63 to -1.45)	40.07 ± 2.32 (range 33.9 to 43.1)	0.12 ± 0.12 (range 0.00 to 0.42)	0.18 ± 0.12 (range 0.01 to 0.52)
3 months post-op	21	-0.05 ± 0.16 (range 0.0 to -0.25)	-0.38 ± 0.51 (range 0.42 to -1.23)	40.37 ± 2.36 (range 34.1 to 43.7)	0.11 ± 0.10 (range 0.00 to 0.33)	0.18 ± 0.12 (range 0.00 to 0.48)
9 months post-op	18	-0.04 ± 0.16 (range 0.0 to -0.5)	-0.36 ± 0.38 (range 0.21 to -1.025)	40.39 ± 1.70 (range 38.24 to 43.70)	0.13 ± 0.09 (range 0.01 to 0.32)	0.21 ± 0.09 (range 0.01 to 0.48)

Table 1a and 1b. *Manifest Refraction, Wavefront Refraction, and Corneal Power post-Femto LASIK in FS and IL Groups, respectivelyWRSE: Wavefront Refraction Spherical Equivalent; MRSE: Manifest Refraction Spherical Equivalent; Cpwr: Corneal Power Measured by SD OCT (6 mm Pachymetry +Cpwr scans).*

Objective stray light measurements in both IL and FS eyes peaked at 1 week postoperatively (log 1.28 ± 0.16, p = 0.02 and log 1.26 ± 0.12, p = 0.039, respectively) with statistically significant improvement at 3 months (log 1.12 ± 0.35, p = 0.007 and log 1.20 ± 0.15, p = 0.04) and 9 months (log 1.11 ± 0.17, p = 0.008 and log 1.15 ± 0.14, p = 0.011) (Table 2 and Figure 1). There were no statistically significant differences between IL and FS groups at each timepoint.

C-Quant					
	pre-op	**1 week post-op**	**1 month post-op**	**3 months post-op**	**9 months post-op**
FS	Log 1.25 ± 0.18	Log 1.26 ± 0.12 (p = 0.039)	Log 1.23 ± 0.12 (p = 0.082; compared to 1 wk post-op)	Log 1.20 ± 0.15 (p = 0.04; compared to 1 wk post-op)	Log 1.15 ± 0.14 (p = 0.011; compared to 1 wk post-op)
IL	Log 1.22 ± 0.18	Log 1.28 ± 0.16 (p = 0.02)	Log 1.24 ± 0.13 (p = 0.069; compared to 1 wk post-op)	Log 1.12 ± 0.35 (p = 0.007; compared to 1 wk post-op)	Log 1.11 ± 0.17 (p = 0.008; compared to 1 wk post-op)

Table 2: *Stray light measurements pre and post-Femtosecond laser LASIK.*

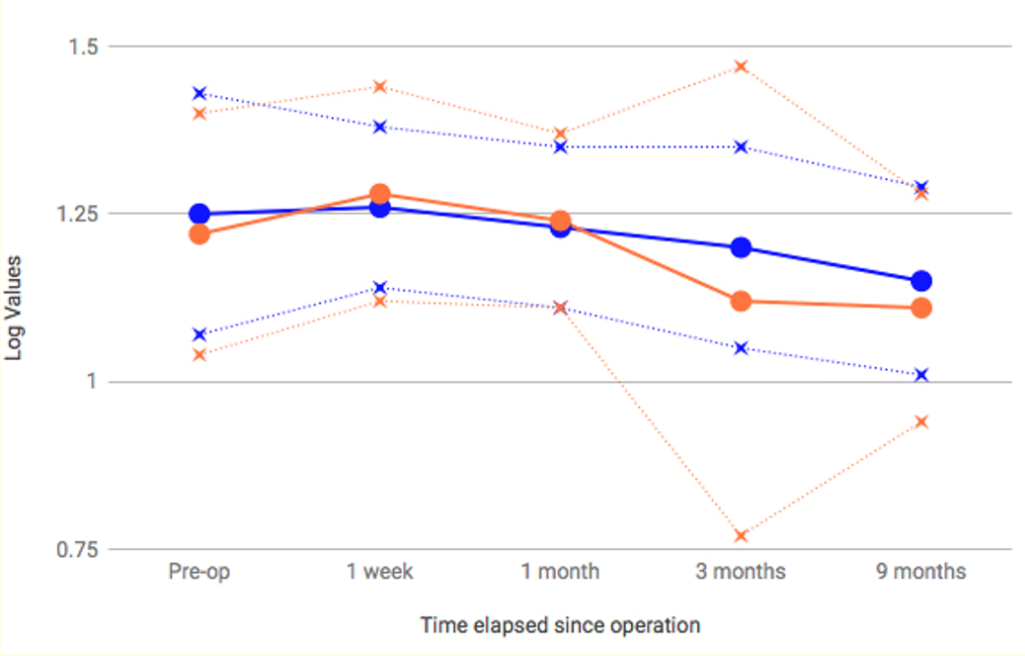

Figure 1: *Stray light measurements (C-Quant) pre and post FS-LASIK.*
Royal blue data points with bold interconnecting line segments represent FS C-Quant logarithmic values at each time point. Orange data points with bold interconnecting line segments represent IL C-Quant logarithmic values at each time point. Blue stars represent the variation from the logarithmic values for FS. Orange stars represent the variation from the logarithmic values for the IL.

In IL treated eyes, 11 patients (42%) reported RG at 1 week postoperatively, 9 (35%) at 1 month, 5 (24%) at 3 months, and 6 (33%) at 9 months (Table 3). In the FS treated eyes, 14 patients (54%) reported RG at 1 week postoperatively, 11 (42%) at 1 month, 5 (24%) at 3 months, and 7 (39%) at 9 months (Table 3). Overall, there was statistically significant improvement in postoperative RG in both groups at the 3 month and 9 month postoperative visits ($p < 0.001$). RG and light scattering measurements did not correlate with refractive error, age, or sex.

Rainbow Glare				
	1 week post-op (n = 26)	**1 month post-op (n = 26)**	**3 months post-op (n = 21)**	**9 months post-op (n = 18)**
FS	14 (54%)	11 (42%)	5 (24%); ($p < 0.001$)	7 (39%); ($p < 0.001$)
IL	11 (42%)	9 (35%)	5 (24%); ($p < 0.001$)	6 (33%); ($p < 0.001$)

Table 3: *Postoperative rainbow glare phenomena in FS and IL groups.*

Discussion

Prior studies have established the credibility and importance of assessing stray light in the evaluation of optical side effects of femtosecond lasers [6,7]. In this prospective, contralateral eye study, each study eye was subjected to a one-minute C-Quant (C-Quant, Oculus Inc, Lynnwood, WA) test at each visit, which resulted in a logarithmic value. The average log-value for each platform at each time point pre- and post-femtosecond LASIK is demonstrated in table 2. C-Quant values in both groups peaked at 1 week, but there was a statistically significant reduction in C-Quant values at 3 months and 9 months postoperatively (Table 2 and Figure 1). Notably, there were no statistically significant differences in stray light measurements between the IL and FS groups at each time point, which indicates that the femtosecond laser platforms were equivalent with respect to postoperative light scatter.

In a study that used contact lenses treated with femtosecond laser, Peter., *et al.* demonstrated that subjective RG was higher in patients receiving femtosecond altered contact lenses with a regular grid pattern as compared to those who received a lens with a random laser pattern [6]. This supported the hypothesis that a regular and repeatable pattern of laser grid applications (i.e. grating pattern) through use of a femtosecond laser is responsible for the regular diffraction of light and the subjective complaint of RG [1]. Our study used two different laser platforms that both employ regular grid patterns while producing a femtosecond laser flap. We found that there was a peak incidence of RG at 1 week postoperatively with subsequent decrease in incidence (Table 3). The incidence of RG (subjective symptom) correlated well with chronological timing of the rise and fall of stray light measurements (objective measurement). Interestingly, other studies have shown that 1 week after FS-LASIK, corneas treated with the IntraLase system for flap creation demonstrated hyperreflective areas in the stromal flap interface as measured by *in vivo* corneal confocal microscopy [8]. These spots matched the theoretical dimensions and separation pattern of the microscopic laser spot applications [9-11]. Taking together the results of our study and the findings of Sonigo., *et al.* the evolution of these hyperreflective areas correlate well with the timing and incidence of RG and stray light measurements.

By two months postoperatively, Sonigo., *et al.* found that the hyperreflective spots had disappeared in all eyes treated with IntraLase, which also correlates with the statistically significant reduction in RG in our study at 3 and 9 months postoperatively. However, there was a case report of a patient treated with the FS platform who had RG at 3 months postoperatively with evidence of hyperreflective spot-like zones corresponding to the programmed spot separation detected on *in vivo* confocal microscopy [5]. This may suggest that different laser platforms and different laser settings may cause patients to retain these hyperreflective spots for different amounts of time. There also may be interpatient differences that are more difficult to quantify and observe, such as a patient's propensity to heal.

Given that RG and stray light measurements did not correlate with postoperative clinical outcomes (Table 1a and 1b), and that there was decreasing incidence of RG with time, patients undergoing FS-LASIK can be encouraged that these optical side effects are mostly mild and typically resolve with time.

Nevertheless, our findings were statistically significant in regards to C-Quant values and RG incidence peaking at 1 week post FS-LASIK. We would presume that there would be a statistical difference in the reduction in RG after two months postoperatively seeing as the hyperreflective areas in the cornea stroma tend to disappear at this point in time, but due to our study design, patients were not followed up at this time point. Instead, patients were followed up at 1 month and 3 months postoperatively. Additionally, it must be noted that each variable that was controlled in this study (spot separation, spot size, bed energy, flap thickness, etc.) could be varied in clinical practice, and thus, affect the incidence and natural progression of light scatter and RG after FS-LASIK. In fact, a model eye study has shown that 3 μm spot separation significantly reduces the incidence and severity of RG as compared to 10 μm spot separation [12]. A different study using corneal inlays with a random distribution of holes did not have any reported cases of RG [13].

The results of this study should be interpreted correctly. Our results indicate that the peak logarithmic values measured by C-Quant were highest at one week post-operatively and subsequently decreased until the 9 month post-op appointment. We presume that this is due in part to dissipating light-scattering effects of the raster spot pattern that occurs with time, however, another post-femtosecond LASIK corneal change, such as the presence of interface haze or epithelial remodeling, could also contribute to post-operative light scattering effects observed in our study. Thus, the authors conclude that a major contribution of this study was to demonstrate the steady regression of light scattering effects observed post-operatively in IL and FS laser platforms used for FS-LASIK regardless of the underlying cause of these light scattering effects.

A review of literature suggests that the incidence of patient reported symptoms of RG in IntraLase platforms varies from 2.5% to 19.1% depending on the model and variations in treatment used [2]. Given the frequent occurrence and occasional persistence of RG, it is important to counsel the patient on potential treatment options. At times, observing and reassuring the patient that there is no further detrimental effect of RG to the patients' visual outcomes may suffice. In other instances, patients may desire full resolution of RG, and it is important to know treatment options, such as attempting to lift the initial flap and then apply excimer ablation to the posterior flap surface [14]. Most importantly, regular laser system maintenance, modification of spot size, and variation in raster spot pattern (random or spiral) should be employed by the refractive surgeon to prevent a high incidence of RG in clinical practice [1,3].

Conclusion

In conclusion, our study investigated the optical side effect of RG and its evolution in post FS-LASIK patients. The results of our study will enable us to better educate patients on RG and its tendency to gradually improve with time. In addition, given the correlation between C-Quant values and RG at each time point, light scattering measurements could be useful for monitoring subjective symptoms postoperatively.

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No additional contributors meet the acknowledgement criteria.

Disclosures

Dr. Rocha and Dr. Mercer declare no financial interest related to this manuscript. Dr. Krueger and Dr. Dupps are consultants for Alcon.

Biblioghraphy

1. Krueger RR., *et al*. "Rainbow glare as an optical side effect of IntraLASIK". *Ophthalmology* 115.7 (2008): 1187-1195.

2. Moshirfar M., *et al*. "Rainbow glare after laser-assisted in situ keratomileusis: a review of literature". *Clinical Ophthalmology* 10 (2016): 2245-2249.

3. Bamba S., *et al*. "Incidence of rainbow glare after laser in situ keratomileusis flap creation with a 60 kHz femtosecond laser". *Journal of Cataract and Refractive Surgery* 35.6 (2009): 1082-1086.

4. Salz JJ. "Difficult and Complicated Cases in Refractive Surgery: Suction Loss After Complete Raster Pattern and No Side Cut, No Flap Lift, and Rainbow Glare". Berlin Heidelberg: Springer (2014).

5. Gatinel D., *et al*. "Unilateral rainbow glare after uncomplicated femto-LASIK using the FS-200 femtosecond laser". *Journal of Refractive Surgery* 29.7 (2013): 498-501.

6. Peter M., *et al*. "Analysis of optical side-effects of fs-laser therapy in human presbyopic lens simulated with modified contact lenses". *Graefe's Archive for Clinical and Experimental Ophthalmology* 250.12 (2012): 1813-1825.

7. Barreto J Jr., *et al*. "Intraocular straylight and contrast sensitivity after contralateral wavefront-guided LASIK and wavefront-guided PRK for myopia". *Journal of Refractive Surgery* 26.8 (2010): 588-593.

8. Sonigo B., *et al*. "In vivo corneal confocal microscopy comparison of intralase femtosecond laser and mechanical microkeratome for laser in situ keratomileusis". *Investigative Ophthalmology and Visual Science* 47.7 (2006): 2803-2811.

9. Sugar A. "Ultrafast (femtosecond) laser refractive surgery". *Current Opinion in Ophthalmology* 13.4 (2002): 246-249.

10. Sletten KR., *et al*. "An in vivo model of femtosecond laser intrastromal refractive surgery". *Ophthalmic Surg Lasers.* 30.9 (1999): 742-749.

11. Binder PS. "Flap dimensions created with the IntraLase FS laser". *Journal of Cataract and Refractive Surgery* 30.1 (2004): 26-32.

12. Ackermann R., *et al*. "Optical side-effects of fs-laser treatment in refractive surgery investigated by means of a model eye". *Biomedical Optics Express* 14.2 (2013): 220-229.

13. Dexl AK., *et al*. "One-year visual outcomes and patient satisfaction after surgical correction of presbyopia with an intracorneal inlay of a new design". *Journal of Cataract and Refractive Surgery* 38.2 (2012): 262-269.

14. Gatinel D., *et al*. "Simultaneous Correction of Unilateral Rainbow Glare and Residual Astigmatism by Undersurface Flap Photoablation After Femtosecond Laser-Assisted LASIK". *Journal of Refractive Surgery* 31.6 (2015): 406-410.

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