Optical side-effects of fs-laser treatment in refractive surgery investigated by means of a model eye

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Abstract: Optical side-effects of fs-laser treatment in refractive surgery are investigated by means of a model eye. We show that rainbow glare is the predominant perturbation, which can be avoided by randomly distributing laser spots within the lens. For corneal applications such as fs-LASIK, even a regular grid with spot-to-spot distances of ~3 µm is sufficient to minimize rainbow glare perception. Contrast sensitivity is affected, when the lens is treated with large 3D-patterns.

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References and links

1. S. Nolte, “Micromachining,” in Ultrafast Lasers: Technology and Applications, M. E. Fermann, A. Galvanauskas, and G. Sucha, eds. (Marcel Dekker, New York, 2002).
2. K. Stonecipher, T. S. Ignacio, and M. Stonecipher, “Advances in refractive surgery: microkeratome and femtosecond laser flap creation in relation to safety, efficacy, predictability, and biomechanical stability,” Curr. Opin. Ophthalmol. 17(4), 368–372 (2006).
3. T. Ripken, U. Oberheide, C. Ziltz, W. Ertmer, G. Gerten, and H. Lubatschowski, “Fs-laser induced elasticity changes to improve presbyopic lens accommodation,” Proc. SPIE 5688, 278–287 (2005).
4. Z. Nagy, A. Takacs, T. Filkorn, and M. Sarayba, “Initial clinical evaluation of an intraocular femtosecond laser in cataract surgery,” J. Refract. Surg. 25(12), 1053–1060 (2009).
5. S. Toropygin, M. Krause, I. Riemann, M. Hild, P. Mestres, B. Seitz, E. Khurieva, K. W. Ruprecht, U. Löw, Z. Gatzioufas, and K. König, “In vitro noncontact intravascular femtosecond laser surgery in models of branch retinal vein occlusion,” Curr. Eye Res. 33(3), 277–283 (2008).
6. L. Ding, W. H. Knox, J. Bühren, L. J. Nagy, and K. R. Huxlin, “Intratissue refractive index shaping (IRIS) of the cornea and lens using a low-pulse-energy femtosecond laser oscillator,” Invest. Ophthalmol. Vis. Sci. 49(12), 5332–5339 (2008).
7. L. J. Nagy, L. Ding, L. Xu, W. H. Knox, and K. R. Huxlin, “Potention of femtosecond laser intratissue refractive index shaping (IRIS) in the living cornea with sodium fluorescein,” Invest. Ophthalmol. Vis. Sci. 51(2), 850–856 (2010).
8. L. Xu, W. H. Knox, M. DeMagistris, N. Wang, and K. R. Huxlin, “Noninvasive intratissue refractive index shaping (IRIS) of the cornea with blue femtosecond laser light,” Invest. Ophthalmol. Vis. Sci. 52(11), 8148–8155 (2011).
9. A. Vogel, J. Noack, G. Hüttman, and G. Paltauf, "Mechanisms of femtosecond laser nanosurgery of cells and tissues," Appl. Phys. B 81(8), 1015–1047 (2005).
10. T. Juhasz, G. A. Kastis, C. Suárez, Z. Bor, and W. E. Bron, "Time-resolved observations of shock waves and cavitation bubbles generated by femtosecond laser pulses in corneal tissue and water," Lasers Surg. Med. 19(1), 23–31 (1996).
11. R. R. Krueger, J. L. Thornton, M. Xu, Z. Bor, and T. J. van den Berg, "Rainbow glare as an optical side effect of IntraLASIK," Ophthalmology 115(7), 1187–1195.e1 (2008).
12. S. Bamba, K. M. Rocha, J. C. Ramos-Esteban, and R. R. Krueger, "Incidence of rainbow glare after laser in situ keratomileusis flap creation with a 60 kHz femtosecond laser," J. Cataract Refract. Surg. 35(6), 1082–1086 (2009).
13. M. Peter, R. Kammel, R. Ackermann, S. Schramm, B. U. Seifert, K. Frey, M. Blum, S. Nolte, and K. S. Kunert, "Analysis of optical side-effects of fs-laser therapy in human presbyopic lens simulated with modified contact lenses," Graefes Arch. Clin. Exp. Ophthalmol. 250(12), 1813–1825 (2012).
14. S. Norby, P. Piers, C. Campbell, and M. van der Moor, “Model eyes for evaluation of intraocular lenses,” Appl. Opt. 46(26), 6595–6605 (2007).
15. W. J. Benjamin and Q. A. Cappelli, “Oxygen permeability (Dk) of thirty-seven rigid contact lens materials,” Optom. Vis. Sci. 79(2), 103–111 (2002).
16. M. Sachsenweger, Augenheilkunde, Duale Reihe (Georg Thieme Verlag, 2002), Vol. 2.
17. E. A. Hermans, M. Dubbelman, R. Van der Heijde, and R. M. Heethaar, “Equivalent refractive index of the human lens upon accommodative response,” Optom. Vis. Sci. 85(12), 1179–1184 (2008).
18. R. C. Bakaraju, K. Ehrmann, D. Falk, A. Ho, and E. Papas, “Physical human model eye and methods of its use to analyse optical performance of soft contact lenses,” Opt. Express 18(16), 16868–16882 (2010).
19. H. Wässle and B. B. Boycott, “Functional architecture of the mammalian retina,” Physiol. Rev. 71(2), 447–480 (1991).
20. S. L. Polyak, The Retina (University of Chicago Press, Chicago, 1941).
21. A. Gullstrand, “Zusätze von A. Gullstrand,” in Handbuch der physiologischen Optik von H. von Helmholtz, A. Gugelmann, J. von Kövesdy, and W. Nagel, eds. (Verlag von Leopold Voss, Hamburg und Leipzig, 1909).
22. J. Németh, O. Fekete, and N. Peszenlehner, “Optical and ultrasound measurement of axial length and anterior chamber depth for intraocular lens power calculation,” J. Cataract Refract. Surg. 29(1), 85–88 (2003).
23. L. Wang, M. Shirayama, X. J. Ma, T. Kohnen, and D. D. Koch, “Optimizing intraocular lens power calculations in eyes with axial lengths above 25.0 mm,” J. Cataract Refract. Surg. 37(11), 2018–2027 (2011).
24. T. Grosvenor and R. Scott, “Role of the axial length/corneal radius ratio in determining the refractive state of the eye,” Optom. Vis. Sci. 71(9), 573–579 (1994).
25. C. Hönninger, M. Pützner, B. Ortg, R. Ackermann, R. Kammel, J. Limpert, S. Nolte, and A. Tünnermann, “Femtosecond fiber laser system for medical applications,” Proc. SPIE 7203, 72030W, 72030W-6 (2009).
26. H. Uozato and D. L. Guyton, “Centering corneal surgical procedures,” Am. J. Ophthalmol. 103(3 Pt 1), 264–275 (1987).
27. M. Hammer, D. Schweitzer, W. Ziegler, M. Wiechmann, and J. Strobel, “Intrastromale refraktive Chirurgie mit ultrakurzen Laserpulsen Ergebnisse erster In-vitro-Experimente [Intrastromal refractive surgery with ultra-short laser pulses. Results from initial in vitro experiments],” Ophthalmologe 99(10), 756–760 (2002).
28. J. Y. Kim, M. J. Kim, T. I. Kim, H. J. Choi, J. H. Pak, and H. Tchah, “A femtosecond laser creates a stronger flap than a mechanical microkeratome,” Invest. Ophthalmol. Vis. Sci. 47(2), 599–604 (2006).
29. A. Vестерграа, A. Ivarsen, S. Asp, and J. O. Hjortdal, “Femtosecond (FS) laser vision correction procedure for moderate to high myopia: a prospective study of ReLEx® flex and comparison with a retrospective study of FS-laser in situ keratomileusis,” Acta Ophthalmol. (Copenh.) (2012), http://onlinelibrary.wiley.com/doi/10.1111/j.1755-3768.2012.02406.x/abstract;jsessionid=709547A0B32B5AF6026818404FFA2F39.d03t01.
30. H. Lubatschowski, S. Schumacher, M. Fromm, A. Wegener, H. Hoffmann, U. Oberheide, and G. Gerten, “Femtosecond lentotomy: generating gliding planes inside the crystalline lens to regain accommodation ability,” J. Biophotonics 3(5-6), 265–268 (2010).
31. A. J. Augustin, Augenheilkunde (Springer-Verlag, Heidelberg, 2007).
32. S. Schumacher, M. Fromm, U. Oberheide, P. Bock, I. Imbschweiler, H. Hoffmann, A. Beineke, G. Gerten, A. Wegener, and H. Lubatschowski, “Femtosecond-lentotomy treatment: six-month follow-up of in vivo treated rabbit lenses,” Proc. SPIE 7373, 73730H, 73730H-8 (2009).
33. R. Ackermann, K. S. Kunert, R. Kammel, S. Bischoff, S. C. Bühren, H. Schubert, M. Blum, and S. Nolte, “Femtosecond laser treatment of the crystalline lens: a 1-year study of possible cataракtogenesis in minipigs,” Graefes Arch. Clin. Exp. Ophthalmol. 249(10), 1567–1573 (2011).
34. M. P. Poudel, “Study of self-focusing effect induced by femtosecond photodisruption on model substances,” Opt. Lett. 34(3), 337–339 (2009).
35. D. Giguére, G. Olivié, F. Vidal, S. Toetsch, G. Girard, T. Ozaik, J. C. Kieffer, O. Nada, and I. Brunette, “Laser ablation threshold dependence on pulse duration for fused silica and corneal tissues: experiments and modeling,” J. Opt. Soc. Am. A 24(6), 1562–1568 (2007).
36. M. Miclea, U. Skrzyczek, S. Faust, F. Fankhauser, H. Graener, and G. Seifert, “Nonlinear refractive index of porcine cornea studied by z-scan and self-focusing during femtosecond laser processing,” Opt. Express 18(4), 3700–3707 (2010).
37. B. Vasudevan, T. L. Simpson, and J. G. Sivak, “Regional variation in the refractive-index of the bovine and human cornea,” Optom. Vis. Sci. 85(10), 977–981 (2008).
38. V. Nuzzo, M. Savoldelli, J. M. Legeais, and K. Plamann, “Self-focusing and spherical aberrations in corneal tissue during photodisruption by femtosecond laser,” J. Biomed. Opt. 15(3), 038003 (2010).
39. A. K. Riau, R. I. Angunawela, S. S. Chaurasia, D. T. Tan, and J. S. Mehta, “Effect of different femtosecond laser-firing patterns on collagen disruption during refractive lenticule extraction,” J. Cataract Refract. Surg. 38(8), 1467–1475 (2012).
40. A. K. Dexl, O. Seyeddain, W. Riha, M. Hohensinn, T. Rückl, V. Reischl, and G. Grabner, “One-year visual outcomes and patient satisfaction after surgical correction of presbyopia with an intraocular inlay of a new design,” J. Cataract Refract. Surg. 38(2), 262–269 (2012).
41. S. Schumacher, U. Oberheide, M. Fromm, T. Ripken, W. Ertmer, G. Gerten, A. Wegener, and H. Lubatschowski, “Femtosecond laser induced flexibility change of human donor lenses,” Vision Res. 49(14), 1853–1859 (2009).
1. Introduction

A key benefit of femtosecond (fs-)laser technology is to provide micromachining at moderate pulse energies, resulting in minimal damage to the surrounding material [1]. This makes it a suitable tool also for medical applications. In clinical ophthalmology, the main focus is currently on corneal applications such as fs-LASIK [2], but fs-lasers provide additional advantages for applications in deeper eye segments. Due to the nonlinear tissue interaction, the laser focus may, in principle, be set at any position within the eyeball. Therefore, fs-laser techniques are considered as a treatment for presbyopia [3], for capsulorhexis and lens fragmentation [4], or even vitreoretinal surgery [5].

Although there are new approaches which use low pulse energies for local refractive index modifications [6–8], current techniques rely on tightly focusing the fs-laser beam, resulting in photodisruptions with extensions of a few micrometers [9,10]. To treat an extended area, a multitude of these disruptions has to be applied, usually performed by fast laser scanners. In ophthalmology, however, this could be a major drawback of fs-laser techniques, as the resulting laser pattern may act as an optical grating. Previous studies indeed report on perceptions of rainbow glare as a mild side-effect of fs-LASIK [11,12]. Furthermore, a recent clinical trial investigated fs-modified contact lenses (CLs) to simulate the effect of a laser treated cornea or crystalline lens [13]. It was shown that the perception of rainbow glare increased significantly when CLs were treated with a regular grid. A simple implementation of randomly varying scan velocities, however, led to a significant decrease of rainbow glare perception.

Clinical trials are extensive research projects, limiting the amount of laser patterns that may be investigated. Moreover, numerical simulations are also not straightforward, as optical design software usually deals with either diffractive or refractive phenomena. Modeling the induction of rainbow glare by a grid within the cornea or lens, however, has to take into account both effects. Therefore, a model eye was developed to easily investigate different fs-laser patterns within the cornea or lens. According to the above mentioned clinical trial, rainbow glare is the predominant optical side effect of fs-laser treatment. Furthermore, a decrease in contrast sensitivity was observed, which was below statistical significance, but might become more important when the crystalline lens is treated with multiple layers. Therefore, the focus of this study is on the investigation of these two effects. In particular, we do not address high order aberrations such as coma or spherical aberration, for which model eyes are usually designed in IOL research [14].

2. Methods

2.1 Model eye

A sketch of the model eye is shown in Fig. 1, and the specifications of the optical components are summarized in Table 1. The artificial cornea is located within an indentation, which can be closed by a cover glass to serve as a humidity chamber. For the cornea, we chose an anterior radius of curvature (aROC) of 8.6 mm, as it allows the optional use of standard daily wear CLs, as used in the clinical trial [13]. In this study, however, customized rigid CLs (Boston ES®, Bausch & Lomb, USA) were used to simulate fs-laser treatment of the cornea. Despite of the humidity chamber, they provided more reliable results than the use of soft CLs in preliminary tests. The rigid CLs have ROCs of 8.6 mm on both surfaces (~0.0 D) and a thickness of 400 µm. This thickness is comparably large, but actually used to correct high hyperopia [15]. Moreover, it facilitates the axial alignment of the laser focus within the CL.

The pupil is centered on the optical axis and has a diameter of 3 mm, which is typical under daylight conditions [16]. The crystalline lens is made of Boston ES®. It has a refractive index of 1.443, which is close to the equivalent refractive index of the human lens (n = 1.435) [17]. The ROCs of the anterior and posterior lens surface are comparable to the study of Bakaraju et al., which used similar rigid CL material [18]. Asphericity of the optical components was neglected, as higher order aberrations were not investigated in this study. The artificial vitreous chamber is moved by means of a motorized translation stage.
Table 1. Parameters of the model eye

| Surface             | ROC (mm) | Distance to next (mm) | Material         | Refractive index | Diameter/side length (mm) |
|---------------------|----------|-----------------------|------------------|------------------|--------------------------|
| CL front (optional) | 8.60     | 0.40                  | Boston ES® clear | 1.443            | 11.5                     |
| CL back (optional)  | 8.60     |                       | Boston ES® clear | 1.443            | 11.5                     |
| cornea front        | 8.60     | 0.45                  | Boston ES® clear | 1.443            | 11.5                     |
| cornea back         | 6.40     | 3.20                  | distilled water  | 1.334            | 11.5                     |
| pupil               | —        | 0.45                  | (distilled water)| —                | —                        |
| crystalline lens front | 11.85  | 3.60                  | Boston ES® clear | 1.443            | 9.0                      |
| crystalline lens back | −6.35 | 15.88*               | distilled water  | 1.334            | 9.0                      |
| glass window        | infinity | 1.0                  | glass            | 1.517            | 20.2                     |
| air gap             | infinity | 0.125                | air              | 1.0              | —                        |
|                     | 0.55     |                       | glass            | 1.50             | —                        |
|                     | 0.55     |                       | air              | 1.0              | —                        |
| CMOS sensor         | —        | —                    | —                | —                | 4.61 × 3.69              |

*The distance between the crystalline lens and glass window is adjusted by means of the motorized translation stage.

(M126.PD1, Physik Instrumente (PI) GmbH & Co KG, Germany), providing an accuracy of 2.5 µm. A color CMOS-camera (DCC1645C, Thorlabs Inc., USA) beneath a glass window on the bottom of model eye serves as artificial retina. Its resolution is 1280 × 1024 pixels at a pixel size of 3.6 µm × 3.6 µm, which is comparable to the cone distance in primate retina (2–3 µm) [19]. For symmetry reasons, only the central 1024 × 1024 pixels (3.7 mm × 3.7 mm) were analyzed, which corresponds to the size of the macula lutea (3–5 mm) [20].

At far fixation, ray tracing simulations (ZEMAX-EE Version 10, ZEMAX Development Corporation, USA) yield an axial length (AL) of 25.4 mm with rigid CL and 25.7 mm without CL, respectively. Due to the high corneal aROC, this is slightly longer than the AL of Gullstrand’s [21] and similar eye models, but still typical for ‘long eyes’ [22,23]. Moreover, it matches an AL/aROC-ratio of ~3.0, which was found for emmetropic eyes [24]. All chambers of the model eye are filled with distilled water. To avoid air bubbles, the eye is assembled upside down, while the vitreous chamber is closely attached to the anterior eye segment. After water filling is finished, the model eye is attached to the translation stage in correct orientation, and the vitreous chamber is separated from the anterior segment. The resulting gap between both components requires upright operation. Therefore, a 5 cm-mirror was mounted directly above the eye at 45 degree angle for eye chart imaging.
2.2 Laser treatment

For laser treatment of artificial lenses or CLs, a fiber laser system was used, operating at a wavelength of 1030 nm. A detailed description of the laser can be found elsewhere [25]. For this study, it was operated at a repetition rate of 200 kHz and a pulse duration of 320 fs (sech^2). An external acousto-optic modulator (AOM) (MCQ40, AA sa, France) was used to step down the repetition rate to 25–100 Hz for periodic laser patterns. This was necessary to match the maximum velocity of the air bearing stage (ABL 1500, Aerotech Inc., USA), onto which the artificial lenses or CLs were attached for laser treatment. For this feasibility study, the air bearing stage provides better control and feedback than a 3D-scanner system, which would be required in clinical use. The initial beam had a diameter of 2.9 mm (1/e^2) and was focused by a 10× microscope objective (NA = 0.25). For this setup, threshold pulse energies for reliable photodisruptions in Boston ES® were $E_{\text{pulse}} \approx 600$ nJ, verified under the optical microscope. All experiments were performed ~30% above threshold ($E_{\text{pulse}} = 800$ nJ), yielding a spot size of ~5 µm (Fig. 2a). For all samples, the pattern had a circular shape with a diameter of 4 mm. The investigation of different centering references was beyond the scope of this basic study [26]. Thus, all laser patterns were centered on the optical axis. Horizontal and vertical centering of the sample was monitored by means of a CMOS-camera, imaging the focal plane of the laser focusing objective. The resulting centering precision of the laser pattern was a few tens of µm.

The investigated laser patterns are summarized in Table 2. We chose spot-to-spot distances of 3 µm and 10 µm, which are also used in fs-LASIK [27–29]. However, at high repetition rates (~1 MHz), which are desirable to reduce time for treatments, current scanner technology is at its limit [25]. In this case, a line by line scan is the simplest strategy, as it avoids additional accelerations of the scanner mirrors along the scan line. Therefore, a line by line pattern within a rigid CL (CL10 µm) and crystalline lens (1L10 µm, 3L10 µm) were tested. Furthermore, we investigated the amount of rainbow glare when the optical axis (d spared = 2 mm) remains untreated (1 sparedL10 µm), as proposed by Lubatschowski et al. (d spared = 1 mm) [30]. For lower laser repetition rates ($\leq$500 kHz), more complex laser patterns may be

| Location pattern | CL10 µm | 1L10 µm | 1S10 µm | 1R10 μm | 1R full 10 μm |
|------------------|---------|---------|---------|---------|--------------|
| CL line by line | lens line by line | lens line by line | lens spiral | lens spiral | lens line by line |
| Remark           | —       | —       | central 2 mm spared | —       | random velocities /line distances 10 μm (mean) |
| Spot distance    | 10 µm   | 10 µm   | 10 µm   | 10 µm   | 10 µm (mean) |
| Layers           | 1, 3    | 1       | 1, 3, 5 | 1       | 1; 10 (mean) |

Table 2. Parameters of investigated laser patterns
applied, among which the most common is a spiral pattern [29]. Therefore, we tested spiral patterns with 1, 3 and 5 layers within the crystalline lens (1S10µm, 3S10µm, 5S10µm).

In addition, two random patterns were applied. The first pattern (1Rline10µm) was the same as in the clinical trial of Peter et al. in order to verify the subjects’ visual impression [13]. Furthermore, a random pattern (1Rfull10µm) was applied (Fig. 2b), having the same amount of spots as the regular grids (~125,000). Under the condition of a minimum next neighbor distance of 5 µm and a resolution of 1 µm, the air bearing stage was subsequently moved to each random position, by operating the external AOM in single pulse mode.

2.3 Optometry

As the model eye does not feature autofocus, images were acquired by moving the vitreous chamber in steps of 25 µm around the visual best focus. Then, the best focus position was determined from this image set by means of a customized LabVIEW-program (LabVIEW & NIVision 8.5, National Instruments Corp., USA), using the inbuilt Prewitt-filter. Further image evaluation was performed on this best focus image.

Rainbow glare was investigated by means of a high power LED (DRAGON-X® DX1-W3-865, Osram AG, Germany), which was placed on the optical axis at a distance of 3 m without ambient light. The illuminance level at the model eye due to the LED was set to 3.5 lux (lux-meter: Voltcraft MS-1300, Conrad Electronic SE, Germany), simulating high beams of an oncoming vehicle at night [31]. The best focus image of the LED was determined by a separate image set, acquired under ambient light conditions. Furthermore, white balance of all images showing glare was adapted to the LED (6500 K); brightness and contrast were similarly optimized for all images. To provide also an objective measure for rainbow glare, the pixel values of the raw images were numerically analyzed as follows. A pixel was marked as “rainbow glare” when the intensity of the RGB-channel to be analyzed was 25% higher than the other two channels. To determine the area which is irradiated by glare on the artificial retina, all “rainbow glare”-pixels were summed up. In addition, their mean value should provide a measure for its strength.

Visual acuity was investigated by means of Landolt rings (0.4, 0.3, 0.2, 0.15, 0.0, −0.1 logMAR), which were placed at a distance of 4 m. A 400W halogen floodlight was used as light source, providing a homogeneous illumination of the Landolt ring chart (~680 lux). Contrast sensitivity was evaluated by Landolt rings (1.2, 1.3 logMAR), which were placed at a distance of 0.5 m. At this distance, the intensity on the Landolt ring (black) and within (white) the ring reaches constant maximum and minimum values so that the actual contrast is measured. The test charts were numerically analyzed by measuring the highest and lowest pixel value along a line between two diametric points on the Landolt ring (dashed line in Fig. 8).

3. Results

Figure 3 shows the numerical evaluation of rainbow glare for all investigated lenses and CLs. Except for the random patterns, the mean value of the red, green and blue channels is relatively constant at ~30. However, the number of pixels—i.e. the area irradiated by rainbow glare—varies by 4 orders of magnitude.

Comparing lens CL10µm to 1L10µm, the number of pixels is ~10 times higher, when the lens is laser treated instead of the CL. As shown in Figs. 4a and 4b, the diffraction orders are closer together, but the overall structure of the rainbow patterns looks similar. Therefore, the main reason for the larger number of pixels is the shorter distance to the retina, when the lens is treated.

Leaving the optical axis untreated (1spareL10µm) reduces the number of pixels by a factor of ~10. Even better performance is obtained when using a spiral pattern. Figure 4c shows rainbow glare induced in lens 1S10µm, where the strong colored line does not appear due to the rotational symmetry of the pattern. Overall, spiral patterns induce less rainbow glare than line by line patterns. However, strong rainbow colors still appear, when the lens is treated.
Fig. 3. Number of pixels, for which the intensity of the RGB-channel to be analyzed is 25% higher than the other two channels; the ordinate shows their mean intensity value. Colors indicate the corresponding RGB-channel. For the lens with laser spots at random positions, the number of pixels is exactly zero.

Fig. 4. Rainbow glare induced in lens CL10µm (a), 1L10µm (b) and 1S10µm (c). For the green RGB-channel, the inset indicates the pixels which were identified as “rainbow glare”.

Fig. 5. Rainbow glare induced in lens 5S10µm (a) and 1S3µm (b). Note that the full camera frame is shown to visualize rainbow glare at the edges. The dashed square indicates the area which was numerically analyzed.

with multiple layers. This is exemplified in Fig. 5a, showing rainbow glare induced by 5 spiral layers within the lens.

Figure 5b shows the induced rainbow glare, when the lens is treated with a single spiral pattern with 3 µm spot-to-spot distance (1S3µm). Due to the smaller grating constant, most of
the dominant diffraction order lies beyond the artificial retina. The smaller grating constant also increases the grating efficiency. Thus, the number of blue pixels (Fig. 3) is ~3 times higher than for lens 1S10 µm, although only a small part of the diffraction order lies within the analyzed square (Fig. 5, dashed line).

Although spiral patterns perform better than line by line patterns, even a single spiral (1S10 µm) induces ~10,000 blue pixels. Thus, further reduction of rainbow glare is necessary, in particular, when considering multiple layers. For this purpose, Figs. 6a and 6b compare an untreated lens with a lens with random pattern (1Rline10 µm).

Although rainbow colors are nearly entirely suppressed, there remains a strong white line, leading to even higher RGB-values than for all other patterns (Fig. 3). A higher degree of randomness is provided by lens 1Rfull10 µm. The visual impression does not show rainbow glare at all (Fig. 6c), and the numerical analysis indeed yields zero red and blue pixels. Only 43 green pixels are found, which is ~20 times less than the next best pattern (1S10 µm).

Figure 7 shows the numerical evaluation of contrast for different visual acuity levels. All single layer patterns with spot-to-spot distances of 10 µm show similar contrast for all acuity levels, whereas contrast decreases for 3 and 5 layer patterns and lens 1S3 µm. Figure 8 shows the visual impression for an untreated lens and lenses 3S10 µm, 1S3 µm. While 3 spirals with 10 µm spot separation do not change visual performance, it clearly degrades for lens 1S3 µm. The only lens which showed a similarly bad performance was lens 5L10 µm.

![Fig. 6. Rainbow glare induced in an untreated lens (a), lens 1Rline10 µm (b) and 1Rfull10 µm (c).](image)

![Fig. 7. Maximum contrast for different visual acuity levels. Level “1.3 logMAR” was investigated only for untreated, spiral and random position lenses.](image)
4. Discussion

Our investigations have shown that rainbow glare may be a serious issue for fs-laser treatment in refractive surgery. However, corneal applications have to be clearly distinguished from applications in deeper eye segments.

Concerning corneal fs-laser treatment, the situation is more relaxed. Recent fs-LASIK techniques use spot-to-spot distances of ~3 µm at pulse energies of a few hundred nJ [29], while older techniques relied on ~10 µm patterns at a few µJ [11]. Previous studies report that rainbow glare perception was significantly reduced when ~10 µm-patterns were applied at low pulse energy [11,12]. Moreover, glare was less pronounced in myopic than in hyperopic eyes, which usually have shorter ALs. Figure 5 confirms these results. Due to the small diffraction angle, the 10 µm-pattern (1S10µm) induces rainbow glare on the retina. In case of the 3 µm-pattern (1S3µm), however, most of the strong diffraction order lies beyond the artificial retina, although the pattern is located within the crystalline lens. Adding ~2.5 mm for the anterior chamber depth and ~1.5 mm for the semi-thickness of the crystalline lens means that all of the first diffraction order would lie outside of the retina. Moreover, the flap is opened after laser treatment, breaking up the stringent periodicity of the original laser pattern. Therefore, rainbow glare is a minor side-effect in fs-LASIK with spot-to-spot distances of ~3 µm.

The situation is different when considering lenticular applications. In contrast to fs-LASIK, laser spots within the crystalline lens are persistent. An animal study with rabbits reports that the laser pattern was still visible six months after treatment, though steadily fading [32]. In a 1-year follow-up with minipigs, the laser pattern turned out to be stable throughout the study [33]. Therefore, the 3 µm-pattern cannot be used due to bad contrast sensitivity (Fig. 8). Moreover, due to the large corneal aROC, our model eye simulates ‘long eyes’. For shorter ALs, an even larger amount of the strong diffraction order would fall on the artificial retina.

In clinical practice, additional side-effects have to be considered which are not simulated by the homogenous CL material used in our eye model. Although it has been shown that solid model systems such as gelatin or fused silica [34,35] are better suited than water [36], for example, they do not account for inhomogeneities of the corneal tissue and inter-subject variations [36,37]. Especially, nonlinear phenomena such as self-focusing depend critically on actual tissue properties and focusing conditions [36,38]. Furthermore, a recent study has shown that there is a difference in visual outcome between laser patterns which are centrifugally or centripetally applied [39]. This difference is explained by the deformation of
the corneal tissue during laser treatment, which is also not described by the solid CL material of our eye model.

Furthermore, we would like to point out that our study does not make a statement on refractive index contrast between the laser spots and the surrounding tissue. For example, it is not yet clear, if the laser spots within the crystalline lens are refilled by aqueous humor or remain hollow. However, microscope images of laser treated in vitro lenses (Fig. 9) look similar to laser treated CL material (Fig. 2). Therefore, the likely difference in grating efficiency between laser treated crystalline lenses and CL material may only gradually influence rainbow glare and contrast sensitivity, respectively.

![Microscope image (5x) of a spiral fs-laser pattern within a porcine lens. The spot/line distance is 5 µm/20 µm.](image)

Thus, random laser patterns seem to be the only solution to avoid rainbow glare of fs-laser treatment within the eyeball. This is also confirmed by the results of a one-year follow-up after implantation of an intracorneal inlay, which has a pattern of 8400 randomly distributed holes [40]. None of the patients reported perception of rainbow glare. The random pattern of lens 1R_{rand}10_{um}, providing a resolution of 1 µm, may be regarded as an optimum, as in clinical practice the positioning accuracy will be governed by lens movement or aberrations induced by beam propagation through anterior eye segments. Furthermore, Schumacher et al. indicate that even a real-time adaption of laser pulse energy might be necessary to account for inhomogeneities of the human lens tissue [41].

Therefore, further studies, aiming at fs-laser treatment in deeper eye segments, will have to find a compromise between time for treatments and the degree of randomness to be applied.

5. Conclusion

As a conclusion, we have shown that rainbow glare is the dominant optical side effect in fs-refractive surgery. For corneal treatments, it can be avoided by spot-to-spot distances of ~3 µm. For fs-laser treatment of the crystalline lens, rainbow glare may nearly entirely be suppressed by a random distribution of the laser spots within the lens. Contrast sensitivity is affected when the lens is treated with more than 3 layers.

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