LASER-INDUCED REFRACTIVE INDEX MODIFICATION OF INTRAOCULAR LENSES

C. Bacharis[1], G. Tsilikas[1], I. Sianoudis[2], M. Makropoulou[1], G. Zoulinakis[1] and A.A. Serafetinides[1]

1. National Technical University of Athens (NTUA), School of Applied Mathematical and Physical Sciences, Department of Physics, "Optoelectronics, Lasers and Applications" laboratory, Zografou Campus, Gr-157780, Athens, Greece.
2. Technological Educational Institute (TEI) of Athens, Department of Optics & Optometry, Egaleo Gr-12210, Athens, Greece.

Abstract

The purpose of this work is to modify non-invasively the refractive power of an already implanted intraocular lens (IOL) in situ, with the appropriate laser parameters. Preliminary experimental results on the effect of short and ultra-short laser radiation on IOL polymer refractive capacity will be presented. We applied pulsed laser radiation with different parameters, in sub-ablation threshold energy fluence values, on commercially available hydrophobic and hydrophilic acrylic IOLs. The laser sources were a Ti:Sapphire laser (λ= 800nm, pulse width t_p=48 fs, frequency=85 MHz) and an Er:YAGlaser (λ= 2940nm, pulse width t_p=6 ns). The morphology of the IOL surface and quantitative measurements of the refractive index were examined at various settings of laser parameters. Quantitative measurements of the refractive index were performed by measuring the IOLs' power with laboratory lensmeter and Abbe refractometer. The experimental results of refractive power value measurements and the fs laser photo-induced modification of refractivity mechanism are discussed. Before translating this research in clinical applications, more research is further needed, in order to modify accordingly the optical properties of the bulk polymer material without any alteration in IOL light transmittance behaviour. In conclusion, we hypothesize that using a femtosecond laser at energy levels that are well within existing safety limits (according to both the polymer biocompatibility and cornea and retina protection) the laser should be able to adjust a lens for almost any refractive characteristic.

Keywords: intraocular lenses, refractive index modification, fs laser – polymers interaction

1. Introduction

The human eye is a complex visual system, consisting of the cornea, the crystalline lens, the vitreous and the retina. Over time, the crystalline lens becomes less transparent and forms a clouding, blurry structure called cataract. This blurry structure prevents the lens from clear focusing light on the retina and accounts for about half of all cases of severe loss of vision worldwide[1]. There is no pharmaceutical or lens-based approach to treat cataract apart from surgery. Ophthalmologists treat cataract by removing the blurred crystalline lens and inserting a relatively flexible, artificial lens implant (intraocular lens, IOL) in the capsular bag. Today, cataract extraction with intraocular lens implantation is the most widely performed surgery worldwide. However, there are some postoperative complications such as diffractive aberrations, capsular opacification or discoloration. Imperfections in wound healing and lens positioningcan generate refractive errors, as farsightedness, nearsightedness and astigmatism. For example, a common postoperative problem in cataract surgery is the loss of accommodation, due to crystalline lens dislocation. Usually, the refractive power of the implanted IOL is not sufficient for optimal far and near vision (monofocal IOL), requiring the patient to use prescription eye wear. To resolve this problem, several types of intraocular lenses have been developed aiming to provide good far and near vision. For example, for the ability to see at different distances again, multifocal IOLs have been developed.[2]Several materials and patterns are still studied for the formation and etching of IOLs in order to improve the quality of vision postoperatively. Materials that are most commonly used in IOL production are polymethylmethacrylate (PMMA), hydrophilic and hydrophobic combination of highly purified monomers, copolymer of hydroxyethyl methacrylate and methacrylate. Among the different types of IOLs, there are polymer implants that have the possibility of refractive power-modification after the lens insertion in the eye, the so-called light-adjustable IOLs.[3] According to that, the intraocular implant is made of a unique silicone matrix with embedded photosensitive silicone macromers. The lens power can be adjusted to the patient's specific visual needs by directing a low-intensity beam of ultraviolet light onto the lens. The beam induces polymerization of the silicone macromers within the lens material, a couple of days after the eye has healed. Recently, in their comprehensive overview of IOLs technologies, Ford *et al*[3] came in the conclusion that light-adjustable IOL technologies will change the practice of cataract surgery for the next generation of ophthalmic surgeons once these, or similar technologies permitting postoperative power adjustment, become readily available.

2. Laser-induced microstructuring of intraocular lenses

Apart from the efforts for light-adjustable IOLs, the modification of an IOL's surface with laser radiation is a subject of great interest for both physicists' and ophthalmologists' communities. Recently, the use of ultra-short near-infrared pulsed lasers was proposed, based on the interrelation of the laser beam parameters and mechanisms of interaction together with the IOL material's optical properties.[4] However, it is important to notice that in ultra-short pulsed laser processing, absorption has no significant role and, therefore, the relevant laser-polymer interaction mechanisms are more complicated. Unlike ultraviolet excimer lasers already used in polymer microstructuring, which are linearly absorbed in polymers through electronic transitions, ultrashort femtosecond laser pulses are delivered to the sample *via* nonlinear multiphoton absorption[5].

In previous works, researchers from NTUA' "Optoelectronics, Lasers and Applications" laboratory tried to perform all the preliminary experiments for a non-invasive modification of an implanted IOL, by using the appropriate laser light to modify the intraocular implant optical parameters, without diminishing the optical quality. For that purpose and for assessing the ablative and the sub-ablation laser parameters (e.g. laser emission wavelengths, energy fluence and pulse duration), multiple solid-state laser sources were used, emitting between UV and mid-IR wavelengths. These were tested also as alternatives to ArF excimer laser (λ=193 nm), already used worldwide for myopia correction [6-10].The ablation behaviour of up-to-date IOL materials was investigated regarding the ablation rates, surface quality and efficiency. More specifically, one purpose of the above cited research was the *in situ* IOL polymer resurfacing by laser ablation. The idea was fascinating as it allows the possibility to direct and focus a suitable laser radiation for the *in situ* modification in an already implanted IOL polymer with varied diopters. However, indifferent of any good laser ablated polymer surface quality obtained, undesirable side effects provoked by ablation debris were possibly raised. Obviously, any alteration or material debris deposition, induced by the incident laser radiation on polymer surface, is a discarded effect, as a potential source of visible light scattering and/or a cause for cell attachment and clouding of implanted IOLs.

Another important parameter under consideration is the IOL polymer material aging and its relevance to lens physical (optical, thermal, mechanical) and chemical properties. Indeed, our studies demonstrated that artificial aging of PMMA following pre-exposure to UV light, radically changes its mechanical properties from a ductile material to a relatively brittle one, while it influences the ablation behaviour with UV-IR laser irradiation. An example can be seen in figure 1a, where the morphology of the mid-IR laser irradiated IOL surface, examined with scanning electron microscopy (SEM), shows no perforation and relatively smooth non-ablated area. These experiments were performed on PMMAIOLs (Artisan, model AC-60B), irradiated by a Q-switched Er:YAG laser (λ=2.94 μm, pulse duration t_p=180 ns, laser fluence 2.63 – 4.60 J/cm^2). Comparatively, the possible IOLs polymer surface modification was also investigated, when laser ablation was conducted after pre-ablation exposure of IOLs to UV lamp light for artificial aging of the IOL polymer (λ=370nm, irradiance 2.70 mW/cm^2, exposure time 15 - 30 min). Figure 1b shows the magnification of the arrow indicated irradiated area of fig. 1a, which reveals the formation of small polymer spherules on the IOL due to the surface melting and the following free solidification of the intraocular lens material.

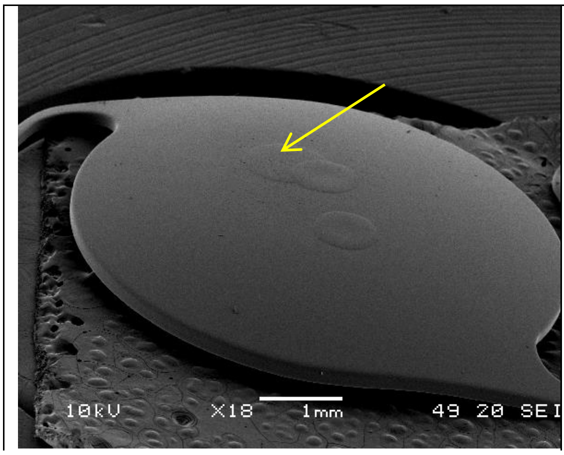

Figure 1a. SEM image of a PMMA IOL (model AC-60B), irradiated by a Q-switched Er:YAG laser (λ=2.94 μm).

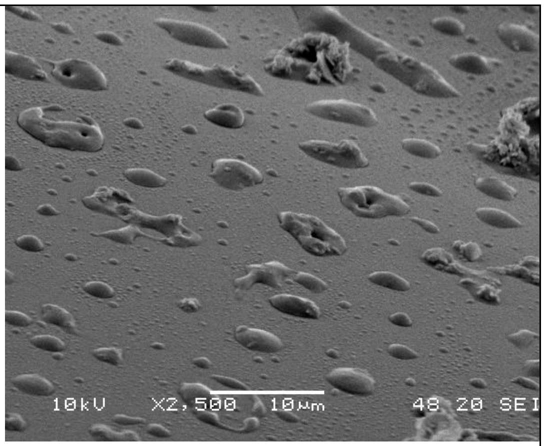

Figure 1b. Detail from the Er:YAG laser spot area, indicated by arrow in the previous SEM image of the PMMA IOL.

Definitely, as we already mentioned, pre-exposure to UV light influences the physico-chemical polymer properties The IOLs exposed in ultraviolet light before laser ablation

appeared transparent in mid-IR laser irradiation and no perforation was observed. On the contrary, non UV pre-irradiated IOLs were penetrated by Er:YAG laser, for the same laser fluences (unpublished results).One possible explanation may be the following: the IOLs polymeric chains, when irradiated by ultraviolet radiation, create cross-links making the material stiffer. The loss of the material elasticity, due to crosslinking, changes its predisposition to ablative laser radiation effect.
Regarding the problem of post-surgery IOL failure, either due to dislocation or to aging, the collaborating researchers – authors of this work envisage that a non-invasive modification of an implanted IOL could be possible, but without undesirable side effects.
The approach taken in our research group to correct intraocular lens power after the lens has been put inside the eye and to avoid any IOL explantation shall be mainly an alteration of the refractive index of the polymer. Certainly, since the IOL is to be altered non-invasively once implanted the change in refractive power must be induced by guiding light to the implant. It is helpful to stress here that the above mentioned experimental findings clearly demonstrate that it is possible to change intentionally the IOL optical properties using light.

3. Laser-induced refractive index alteration of intraocular lenses

The refractive index is a fundamental physical quantity that characterizes optical materials in various experiments. Knowledge of accurate dispersion of optical media is essential in understanding various linear and nonlinear optical phenomena[11]. For example, Sahler *et al* in their current research [4] reported that the refractive properties of an IOL can be customized after implantation, using a femtosecond laser that alters the hydrophilicity of defined zones within an IOL and thus build a refractive index shaping lens within that zone. The change in hydrophilicity drives a large, repeatable, and homogeneous change in refractive characteristics. Apart of this hypothesis, different approaches were also reported regarding the mechanism(s) of femtosecond laser – IOLs material interactions resulting in their refractive index change. The Wayne H. Knoxgroup in the Institute of Optics, University of Rochester, suggested that the laser-induced crosslinking within a hydrophilic material creates an increase in the refractive index [12].
Consequently, as laser physics and technology develops, it seems inevitable in modern ophthalmology that *in situ* refractive modification on implanted intraocular lenses will open the door to new altitudes of other vision defect's correction. In this point, it is well-intentioned to summarize the transmission characteristics of light in the optical part of the electromagnetic spectrum (from UV to IR), through the ocular media of the human eye (schematically illustrated in Figure 2). This is directly related to the wavelength of the laser radiation that could be considered for *in situ* interventions. For laser radiation entering the eye:

- Radiation in the near ultraviolet wavelengths (UVA, λ= 315 - 400 nm) is mostly absorbed in the lens of the eye, while radiation in the far ultraviolet (UVB, λ= 280 - 315 nm and UVC, λ= 100 - 280 nm) is mostly absorbed in the cornea.
- Radiation in the visible (λ= 400 -760 nm) and near infrared (λ= 760 - 1400 nm) is transmitted to the retina, while in the far infrared (λ= 1400 nm - 1 mm) is absorbed to the cornea.

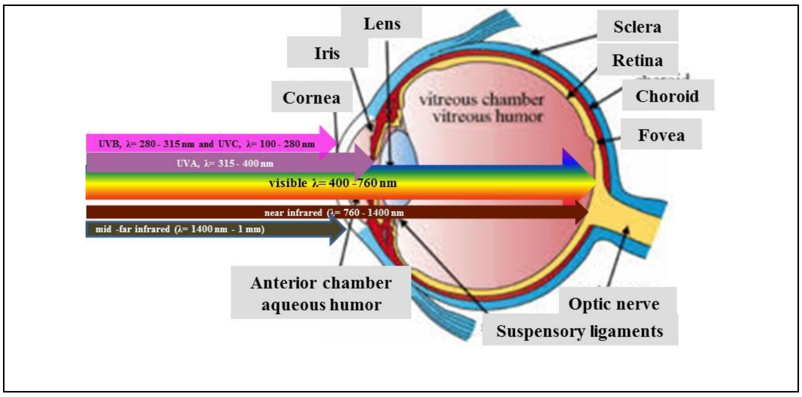

Figure 2. Light transmittance through human eye

The appropriate laser radiation can be used to modify the intraocular implant optical parameters, by modifying the refractive power of the IOLs polymeric material with the relevant laser system. Therefore, the accurate laser parameters for exclusively refractive index shaping must be further studied, especially when radiation passes through ocular media to target the already implanted IOLs. Categorically, due to the absorption properties of the cornea and the transmissivity of ocular media to retina, (fig. 2) there are restrictions to the wavelength that can be used. Moreover, the exact refractivity modification mechanism must also be elucidated, to avoid any photo-chemically induced non-biocompatible polymer alteration.
From the illustrated data of light transmittance through human eye, shown in fig. 2, it is evident that for any intervention on IOL only, avoiding possible harmful effects in the surrounding ocular media, one must use either lasers emitting in UVA (absorbed in the level of eye lens) or a properly focused beam in the visible to near infrared range.

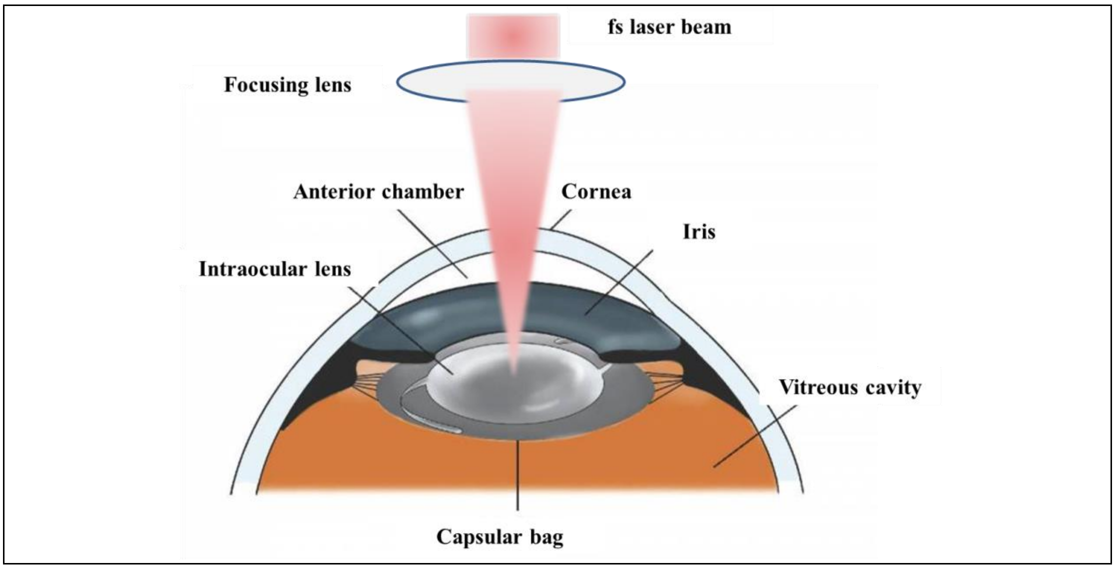

Figure 3. Modification of the refractive index of an implanted intraocular lens by a femtosecond laser. (image modified after https://retinavitreous.com/treatments/dislocated_iol.php)

The two most important ocular structures that could be damaged during the photo-induced refractive index change of the IOL are the cornea and the retina. As it is shown schematically in figure 3, the laser intervention could be localized on the IOL level that coincides with the prescribed beam focus, while the defocused laser beam continue the travel to retina in energy fluences lower than the safety levels, if all the experimental parameters are properly chosen.

In this work, we present our experimental effort of applying ultra-short laser radiation on IOL, aiming to modify the polymer refractive capacity. A Ti:Sapphire laser source (FemtoLaser) emitting within the near-infrared spectrum (λ= 800 nm), with pulse width t_p= 48 fs, frequency= 85 MHz and mean power P= 360 mW was applied on commercially available hydrophobic and hydrophilic acrylic IOLs at room temperature (~25°C) in air, in sub-ablation regime. After exposure to fs laser radiation, the morphology of the ablated IOLs' surface was examined at various settings of laser pulses, with scanning electron microscopy (SEM) imaging. Our previous quantitative measurements of the refractive index and the IOLs power laser-induced modification were taken also in consideration [13]. Moreover, the relevant physico-chemical background of IOL focal length alteration through refractive index tuning are considered, according to Ding *et al* [14]. Recently, it was reported that exposure to the laser can alter the hydrophilicity and the optical behaviour of the acrylic material [15]. The change in hydrophilicity drives a large, repeatable, and homogeneous change in refractive characteristics.
The experimental results of the initial (indicated by the manufacturer) refractive power values of intraocular lenses and the calculated final power values after fs laser irradiation show a linear relationship between them [13], which means that the laser processing ended in the same degree of change in refractive power in all intraocular lenses measured.

4. Concluding remarks and perspectives

The pulsed lasers in infrared have several effects on acrylic lens material, the most recognized of which is that the heat produced by the laser results in changes in the physico-chemical properties of the material. Additionally, if the proper wavelength and pulse width is used, exposure to the laser can alter the hydrophilicity and the optical behaviour of the acrylic material [15]. Because this process does not require the accumulation of heat, it can be used with a fast speed, allowing *in vivo* application [15].The last indicates that an ultra-short pulsed laser, e.g. a femtosecond laser, is preferable for non-invasive interventions.
Our first preliminary results [13] indicate that a small modification (~ 0.25 D) of the refractive power was achieved, with the non-ablative laser parameters used also in this work. However, as it seems that the change in refractive index shall be large enough (e.g. a change in focal length of at least 1D of a typical IOL is favorable), more research is further needed, in order to modify accordingly the optical properties of the bulk polymer material without any alteration in IOL light transmittance behaviour. According to a reported hypothesis, the underlying mechanism for refractivity modification is a cross-linking procedure, which involves a photo-induced photochemical process[12].
Definitely, reliable and pre-defined power changes can be induced in the optical properties of commercially available hydrophobic and/or hydrophylic acrylic lenses *in vivo* by using a femtosecond laser. Using a femtosecond laser at energy levels that are

well within existing safety limits, (according to the polymer biocompatibility, as well as to cornea and retina protection), the laser should be able to adjust a lens for almost any refractive characteristic. In this way, the creation of customized- multifocal intraocular lens for each eye according to patient specific needs is possible, innovative and very interesting. It will provide very satisfactory far, middle and near vision restoration after a cataract surgery as well as a high level of spectacle independence for most patients. So, the goal that has to be achieved is to find an easy and relatively cheap method to change the refractive power of an IOL, using a fs laser with appropriate intensity and wavelength. Thus, both problems of presbyopia and cataract could be also solved.

Financial Disclosure: The presenting author or any co-author has no financial interest in the subject matter or has not received money from any mentioned company.

References

1. Khairallah, M., et al., Number of People Blind or Visually Impaired by Cataract Worldwide and in World Regions, 1990 to 2010. Investigative Ophthalmology & Visual Science, 2015. 56(11): p. 6762-6769.
2. Davison, J.A. and M.J. Simpson, History and development of the apodized diffractive intraocular lens. Journal of Cataract & Refractive Surgery. 32(5): p. 849-858.
3. Ford, J., L. Werner, and N. Mamalis, Adjustable intraocular lens power technology. Journal of Cataract & Refractive Surgery. 40(7): p. 1205-1223.
4. Sahler, R., et al., Creation of a refractive lens within an existing intraocular lens using a femtosecond laser. Journal of Cataract & Refractive Surgery. 42(8): p. 1207-1215.
5. Eaton, S.M., et al., Femtosecond laser microstructuring for polymeric lab-on-chips. Journal of Biophotonics, 2012. 5(8-9): p. 687-702.
6. Spyratou, E., et al., Conical Structures on Acrylic Intraocular Lens (IOLs) Materials after 193-nm Excimer Laser Ablation. Mater. Sc. Appl, 2012. 3: p. 414-424.
7. Lagiou, D.P., et al. UV laser ablation patterns in intraocular lenses. in Seventeenth International School on Quantum Electronics: Laser Physics and Applications. 2013. SPIE.
8. Apostolopoulos, A., et al. UV solid state laser ablation of intraocular lenses. in Medical Laser Applications and Laser-Tissue Interactions VI. 2013. Munich: Optical Society of America.
9. Serafetinides, A.A., et al. Alternatives to excimer laser refractive surgery: UV and mid-infrared laser ablation of intraocular lenses and porcine cornea. in 14th International School on Quantum Electronics: Laser Physics and Applications. 2007. SPIE.

10. Serafetinides, A.A., et al., Ultrashort laser ablation of PMMA and intraocular lenses. Applied Physics A, 2008. 93(1): p. 111-116.
11. Nishiyama H, H.Y., Femtosecond Laser Nonlinear Lithography. InTech, 2010.
12. L, D., Micro-processing of Polymers and Biological Materials Using High Repetition Rate Femtosecond Laser Pulses. 2009, University of Rochester: New York, United States
13. Bacharis K, T.I., Konstantinou A, Ntoumou E, Sianoudis I, Makropoulou M, Serafetinidis A., Refractive index modification of intraocular lenses with femtosecond laser action, in ESCRS. 2017: Lisbon.
14. Ding, L., et al., Intratissue Refractive Index Shaping (IRIS) of the Cornea and Lens Using a Low-Pulse-Energy Femtosecond Laser Oscillator. Investigative Ophthalmology & Visual Science, 2008. 49(12): p. 5332-5339.
15. Bille, J.F., et al., Chemical basis for alteration of an intraocular lens using a femtosecond laser. Biomedical Optics Express, 2017. 8(3): p. 1390-1404.