LABORATORY SCIENCE

Biocompatibility of intraocular lens power adjustment using a femtosecond laser in a rabbit model

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Purpose: To evaluate the biocompatibility (uveal and capsular) of intraocular lens (IOL) power adjustment by a femtosecond laser obtained through increased hydrophilicity of targeted areas within the optic, creating the ability to build a refractive-index shaping lens within an existing IOL.

Setting: John A. Moran Eye Center, University of Utah, Salt Lake City, Utah, USA.

Design: Experimental study.

Methods: Six rabbits had phacoemulsification with bilateral implantation of a commercially available hydrophobic acrylic IOL. The postoperative power adjustment was performed 2 weeks after implantation in 1 eye of each rabbit. The animals were followed clinically for an additional 2 weeks and then killed humanely. Their globes were enucleated and bisected coronally just anterior to the equator for gross examination from the Miyake-Apple view to assess capsular bag opacification. After IOL explantation for power measurements, the globes were sectioned and processed for standard histopathology.

Results: Slitlamp examinations performed after the laser treatments showed the formation of small gas bubbles behind the lenses that disappeared within a few hours. No postoperative inflammation or toxicity was observed in the treated eyes, and postoperative outcomes and histopathological examination results were similar to those in untreated eyes. The power measurements showed that the change in power obtained was consistent and within ±0.1 diopter of the target.

Conclusions: Consistent and precise power changes can be induced in the optic of commercially available IOLs in vivo by using a femtosecond laser to create a refractive-index shaping lens. The laser treatment of the IOLs was biocompatible.

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Studies have shown that despite the many advances in cataract surgery, incorrect intraocular lens (IOL) power remains 1 of the most frequent causes of IOL exchange.[1–3,A] We recently published an overview of the adjustable IOL technologies that are available or under development, which could be used to mitigate the problem of incorrect IOL power.[4] These include IOL technologies that can be adjusted using secondary surgical procedures and IOLs that can be adjusted noninvasively in the postoperative setting. Calhoun Vision's light-adjustable IOL is the noninvasive adjustable IOL closest to commercial availability in the United States because it is undergoing the third and final phase of U.S. Food and Drug Administration clinical trials.[5,6] Among other noninvasive adjustable IOL technologies under development discussed in our review paper is refractive-index shaping using the femtosecond laser.[4]

Perfect Lens LLC has developed a femtosecond laser system for IOL power adjustment based on the concept of refractive-index shaping. The system uses green light (520 nm) and operates with energy levels that are below the threshold for ablation or cuts. Intraocular lens power changes are obtained through a laser-induced chemical reaction in a targeted area of the IOL optic substance, with a

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localized increase in hydrophilicity and decrease in the refractive index. Simultaneous with these changes, the laser builds a refractive-index shaping lens within the targeted area. Studies using hydrophobic and hydrophilic acrylic IOLs have shown the consistency and precision of the power changes that can be induced in the optic of commercially available IOLs in vitro.[7,8,B] To our knowledge, the current study is the first to evaluate the biocompatibility and efficacy of this technology in vivo, using the rabbit model.

MATERIALS AND METHODS

Six New Zealand white female rabbits weighing 2.8 to 3.2 kg were acquired from approved vendors in accordance with the requirements of the Animal Welfare Act for use in this study. All rabbits were treated in accordance with guidelines set forth by the Association for Research in Vision and Ophthalmology and the Animal Welfare Act regulations as well as the *Guide for the Care and Use of Laboratory Animals*.

Each animal was prepared for surgery by pupil dilation with cyclopentolate hydrochloride 1.0% and phenylephrine 2.5% drops, as described in previous studies.[9–11] Anesthesia was obtained with an intramuscular injection of ketamine hydrochloride (50 mg/kg) and xylazine (7 mg/Kg) in a mixture of 7:1, respectively. All surgeries were performed by the same surgeon (N.M.). Using aseptic technique and a surgical microscope, a fornix-based conjunctival flap was fashioned. A 3.0 mm limbal incision was made using a 3.0 mm keratome, and sodium hyaluronate 1.6% (Amvisc Plus) was injected intracamerally. A capsulorhexis forceps was used to create a well-centered continuous curvilinear capsulotomy with a diameter aimed at 5.5 mm. After hydrodissection, the phaco handpiece (Infiniti System, Alcon Laboratories, Inc.) was inserted into the posterior chamber for removal of the lens nucleus and cortical material. One milliliter of epinephrine 1:1000 and 0.5 mL of heparin (10 000 USP units/mL) were added to each 500 mL of irrigation solution to facilitate pupil dilation and control inflammation. The endocapsular technique was used with the phacoemulsification to take place entirely within the capsular bag. The residual cortex was then removed by irrigation/aspiration. The same ophthalmic viscosurgical device was used to inflate the capsular bag, and a single-piece hydrophobic acrylic preloaded yellow IOL (CT Lucia 601PY, Carl Zeiss Meditec AG) was then injected in the capsular bag. All IOLs used in the study had the same labeled power. Wound closure was achieved with a 10-0 monofilament nylon suture after removal of OVD.

An ointment combination (neomycin/polymyxin-B sulfates and dexamethasone) was applied to the eyes after the surgery was performed, and the ointment was used 4 times a day for the first postoperative week. In the second postoperative week, each animal received topical prednisolone acetate drops 4 times per day.

The eyes of the rabbits were evaluated by slitlamp examination and scored for ocular inflammatory response weekly after pupil dilation. A standard scoring method in 11 categories was used at each examination, including assessment of corneal edema and the presence of cell and flare within the anterior chamber. Retroillumination images with the dilated pupil were obtained for photographic documentation regarding inflammatory reactions, anterior capsule opacification (ACO), posterior capsule opacification (PCO), and observed capsule fibrosis. The ACO at the area of the anterior capsule contacting the anterior optic surface was scored from 0 to 4. The PCO behind the IOL optic was scored from 0 to 4.

Intraocular Lens Power Adjustment by Laser

Postoperative IOL power adjustment was performed 2 weeks after IOL implantation in only 1 of the eyes, and the rabbits were followed clinically for an additional 2 weeks. The eye to receive the power adjustment was selected as a function of the clarity of the capsular bag in front of the lens (no or minimum proliferation or pearl formation in front of the lens, no or minimum ACO or capsulorhexis phimosis). For the laser adjustment, each animal was prepared by pupil dilation and anesthesia as done for the surgical implantation procedure. The rabbit was placed horizontally on a support/bed constructed with a 3-dimension printer (allowing rotation/tilt of the animal in different directions), with the designated eye facing up to allow the connection to the patient interface (Figure 1, *A*). The interface was purpose-designed for the rabbit eye based on measurements described in a previous study[12] (Figure 1, *B*). Alignment of the rabbit eye and docking to the laser system through the interface were then performed under the control of the video and optical coherence tomography (OCT) systems of the laser device, with subsequent laser treatment targeted at a +3.6 diopter (D) power change. A forceps was used to displace the nictating membrane of the rabbit eye immediately before docking. Slitlamp examination of the eyes was performed immediately after laser treatment and at different timepoints after treatment.

Pathology

After the final clinical examination 4 weeks postoperatively, the animals were anesthetized and humanely killed with a 1 mL

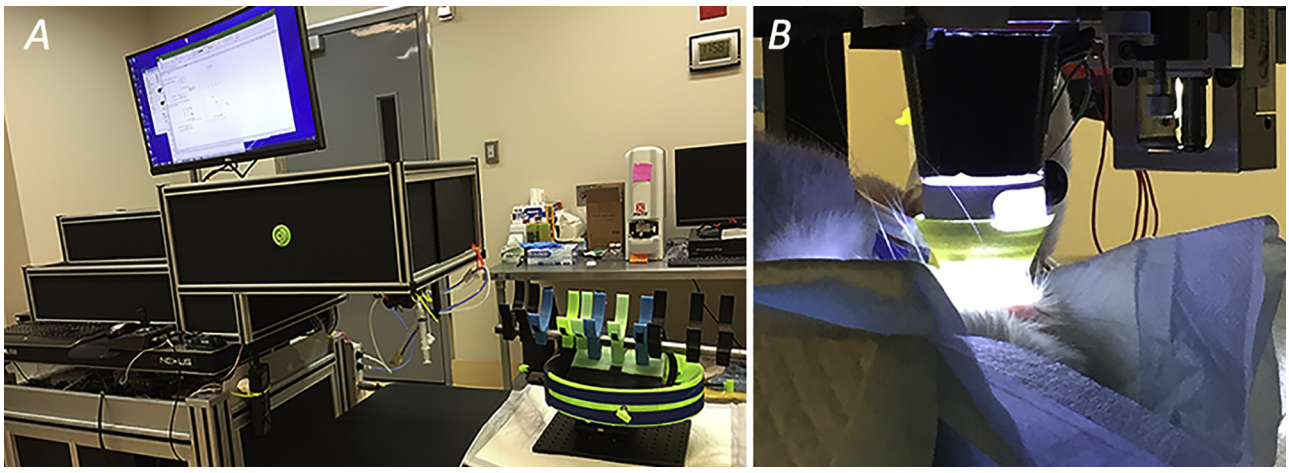

Figure 1. *A*: Setup for the in vivo rabbit study with the laser system and the support/bed for the animal, constructed with a 3-dimension printer. *B*: Rabbit eye docked to a cup filled with a balanced salt solution (liquid interface) before laser treatment of the IOL.