Article

Further Enhancement of Intraocular Open-Capsule Devices for Prevention of Posterior Capsule Opacification

Lee Slutzky[1] and Guy Kleinmann[1,2]

[1] The School of Medicine of the Hebrew University and Hadassah, Jerusalem, Israel
[2] Department of Ophthalmology, Kaplan Medical Center, Rehovot, Israel

Correspondence: Guy Kleinmann, Department of Ophthalmology, Kaplan Medical Center, PO Box 1, Rehovot 76100, Israel. e-mail: guy.kleinmann@hsc.utah.edu

Purpose: We improve the intraocular open-capsule devices (IOCD) for the prevention of posterior capsule opacification (PCO).

Methods: A total of 45 New Zealand rabbit eyes were divided into six similar groups after crystalline lens evacuation. Each group was implanted with a hydrophilic intraocular lens (IOL) and a hydrophilic IOCD of different designs. In the first experiment (Part A), a square design ring with and without large apertures was compared to a round design ring without apertures. In the second experiment (Part B), a square design ring with large apertures was compared to square design IOCDs with small apertures of high and low density. PCO and Soemmering's ring were evaluated clinically, by the Miyake Apple view, and histologically. The results were compared to a control group of eyes implanted with a hydrophilic IOL only.

Results: All devices showed significant prevention of PCO and Soemmering's ring compared to the control group. Part A: the square design with apertures had the lowest level of peripheral lens epithelial cells proliferation (protrusions). Part B: modifying the size and density of the apertures had no influence on those protrusions.

Conclusions: The IOCD significantly reduced the rate of PCO and its precursor, Soemmering's ring. The rings with the square edges and apertures produced the best results. The study was underpowered to determine the influence of the apertures design.

Translational Relevance: The IOCD has the potential to prevent up to 80% of the PCO cases; the most common complication after cataract surgery. The design of the ring is important for its success.

Introduction

Posterior capsular opacification (PCO) is the most common complication following cataract surgery.[1–5] PCO is caused by lens epithelial cells (LECs) that remain at the capsular bag periphery after the surgery. The LECs first proliferate at the bag periphery where they produce Soemmering's ring, after which they migrate into the visual axis, leading to opacification of the center of the posterior capsule resulting in reduced visual acuity.[6,7] Progression in surgical techniques and intraocular lens (IOL) design has reduced PCO but did not eliminate prevalence, and 20% to 40% of the patients currently report a decline in visual acuity related to PCO from 2 to 5 years postoperatively.[7] The most common and effective treatment for PCO is laser capsulotomy, which, itself, is not a complication-free procedure, with the reported complications including cystoid macular edema, retinal detachment, and damage to the lens itself.[8–11] Various approaches have been investigated to reduce the prevalence of PCO, among them mechanical and pharmaceutical techniques as well as different lens shapes and materials.[12–14] Although the situation has improved, prevention of this complication remains elusive.

It recently has been hypothesized that maintaining an open capsular bag postoperatively can reduce the PCO rate. This theory was supported by reports on the Synchrony IOL (Abbott Medical Optics, Santa Ana, CA) which demonstrated surprisingly low PCO rates.[15–17] That success was attributed to its design,

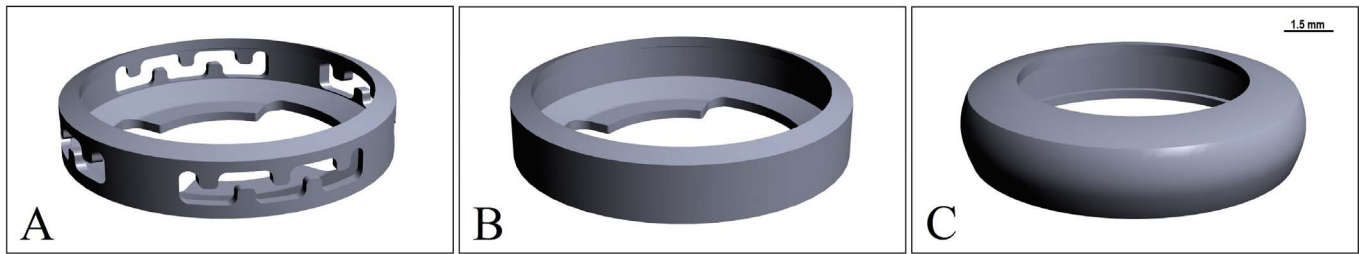*translational* vision science & technology

Figure 1. Schematic illustration of the different ring designs used in Part A. (A) Design R1. (B) Design R2. (C) Design R3.

which opens the capsular bag and creates a separation between the anterior and posterior capsules.[18,19] The concept also was supported by a rabbit study of another bulky IOL, which maintains an open capsule, the FluidVision IOL (PowerVision),[20] and by studies investigating a new modified Zephyr IOL (Anew Optics, Inc., Newton, MA).[18] Several theories were put forth for the mechanism of PCO prevention in these cases. It was proposed that by allowing the aqueous humor to reach the remaining LECs and supplying nutrition (including transforming growth factor [TGF]-β2, which minimizes epithelial-to-mesenchymal transition), the cells' ischemia can be prevented, and the release of interleukin-1, which stimulates processes, such as mitosis and collagen synthesis by the LECs, can be diminished.[7,21,22]

Several intracapsular rings also had been considered for PCO prevention. Hara et al.[23] was the first group to develop an intracapsular ring design. They tested it in rabbits, monkeys, and later even in a young human eye, and showed significant reduction of PCO and the capsulotomy rate.[23–26] A similar concept for PCO prevention was described by Nishi et al.[12,27,28] These rings were intended to create mechanical blockage for preventing the LECs that remain at the equator of the capsular bag from migrating into the center of the posterior capsule. In a previous article, we had developed and investigated the open capsule hypothesis by testing a special design of an intracapsular ring that opens the capsular bag.[29] Our findings showed a significant reduction in Soemmer-

ing's ring and PCO formation (80% and 69%, respectively) in rabbit eyes implanted by the experimental ring compared to eyes implanted with hydrophilic acrylic IOLs and no device.[29] There had, however, been several cases of LECs breakthrough and growth through the apertures in the side wall of the ring. The aim of the current follow-up study was to further improve the intraocular open-capsule device (IOCD). We compared the round to the square edge designs of the ring, and investigated the importance of the apertures in the side wall of the device. We also investigated the influence of the size and density of the apertures in the side wall of the device on LEC protrusion.

Materials and Methods

Animals

We obtained from approved vendors 45 eyes of 23 New Zealand White (NZW) rabbits of the same age and sex and weighing 2.4 to 3.2 kg. The rabbits were housed and cared for at Harlan Biotech, Rehovot, Israel (ISO 9001:2008 Certificate No.: GB06/68708). The care of the rabbits was in accordance with the guidelines set forth by the Association for Research in Vision and Ophthalmology (ARVO) Animal Statement for the Use of Animals in Ophthalmic and Vision Research and the Guide for the Care and Use of Laboratory Animals. The animals were quarantined for a minimum of seven days before the

Figure 2. Schematic illustration of the different ring designs used in Part B. (A) Design RC. (B) Design RH. (C) Design RL.
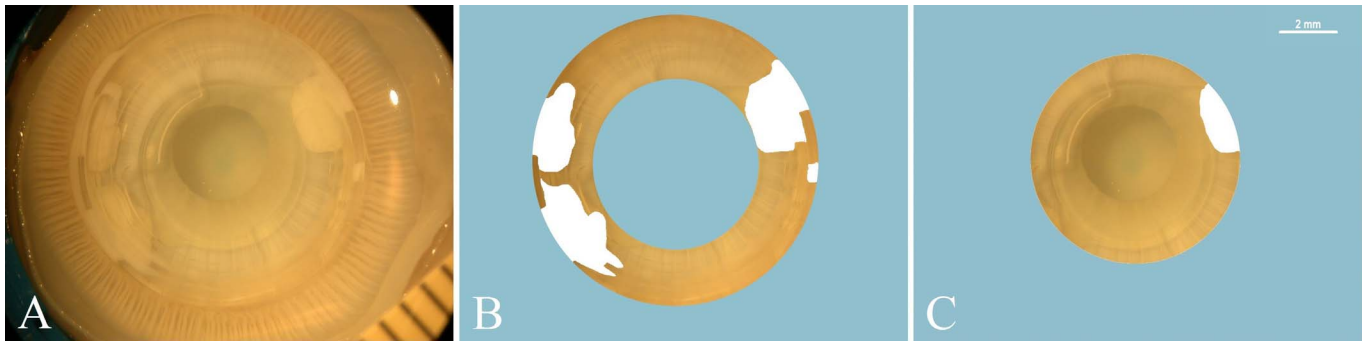
Figure 3. Example of manual marking of Soemmering's ring area using the Matlab program (the central 6 mm are excluded). (A) Miyake-Apple posterior view. (B) schematic illustration of manual marking of Soemmering's ring corresponding to the Miyake-Apple posterior view. (C) Schematic illustration of manual marking of the Soemmering's ring protrusions through the device.

beginning of the study. The study was approved by the Israel National Council for Animal Experimentation.

Each rabbit was examined before the beginning of the study for their general health and for any ophthalmologic disease or abnormal variance in eye shape or size. All animals weighed at least 2.5 kg upon arrival and were kept in the same housing environment. They were given the same diet and subjected to precisely the same treatment aside from the different device implanted during the procedure. At the termination of the study, or if otherwise deemed necessary, the rabbits were euthanized by an intravenous (IV) overdose of Na-pentobarbitone.

Methods

Each animal was prepared for surgery by pupil dilation with 1% cyclopentolate hydrochloride (Cyclogyl, Bausch & Lomb, Rochester, NY) and 2.5% phenylephrine drops (AK-Dilate; Akorn, Lake Forest, IL). Anesthesia was provided by an intramuscular (IM) injection of ketamine hydrochloride 35 mg/kg (Ketalar; Pfizer, New York, NY), and xylazine hydrochloride 7 mg/kg (Rompun; Bayer, Leverkusen, Germany) in a mixture of 7:1, respectively. One drop of topical benoxinate hydrochloride anesthetic (Localin; Dr. Fischer Dermapharm, Bnei-Brak, Israel) was applied to each eye before surgery. Eye movement and respiration were monitored intraoperatively, and supplemental anesthetics were given IM as needed.

Part A

A total of 21 eyes of 11 NZW rabbits were divided randomly into three groups after removal of the crystalline lens. One of three variations of our IOCD

was implanted into the empty capsular bag followed by implantation of a hydrophilic acrylic IOL (SeeLens AF, Hanita Lenses, Israel). Group R1 ($n = 7$) was implanted with a square-edged vertical wall device for enhancement of the capsular bend, with extensions for IOL positioning and large apertures for fluid flow (4.3 mm^2 × 4). Group R2 ($n = 8$) was implanted with the same square-edge design device but without apertures on its side wall. Group R3 ($n = 7$) was implanted with a round wall device to fit the capsule angle, preserving the capsular bag shape (this design also had no apertures in its side wall). Schematic drawings of the devices are presented in Figure 1. Protrusions of Soemmering's ring via the apertures of the devices were scored as being mild, moderate, or severe by a slit-lamp evaluation, the Miyake-Apple view, and histology.

Part B

In the second experiment, three additional devices were developed based on the results of Part A of the study, all containing an improved square edge design but differing in aperture size and density. Group RC

Table 1. Histologic Grading System for PCO Severity

Grade	Finding
0	No LECs on the posterior capsule
1	Minimal LEC proliferation in at least one location
2	Mild LEC proliferation in at least one location
3	Moderate LEC proliferation in at least one location
4	10 or more layers of LEC in at least one location

Table 2. Clinical PCO Score Six Weeks Following Surgery of the Groups in Part A

Group	n	Mean	SD	Median	Range	P Value, Test vs. Control	P Value, Between Groups	PCO Decrease
R1	6[a]	0.7	0.8	0.5	0–2	0.007	[R1,R2]: 0.154 (1.7[b])	75%
R2	7[a]	1.4	1	1	0–3	0.051	[R2,R3]: 1.000 (1.3[b])	51%
R3	7	1.4	0.5	1	1–2	0.04	[R3,R1]: 0.085 (1.2[b])	51%
Control	6	2.83	1.25	3.25	0.5–4	NA	NA	NA

[a] Measurement was not possible in one eye.
[b] Post hoc calculation of minimum detectable difference with $\alpha = 0.05$, $1 - \beta = 0.8$.

($n = 8$) was implanted with the original aperture structure of the intracapsular device (0.8 mm$^2 \times 8$), occupying 53 percentage of the side wall. Group RH ($n = 7$) was implanted with small apertures (0.13 mm$^2 \times 40$), occupying 49% of the side wall (high density). Group RL ($n = 9$) was implanted with small apertures (0.13 mm$^2 \times 20$), occupying 26% of the side wall (low density). Schematic drawings of the devices are presented in Figure 2.

A combination of dexamethasone, neomycin sulfate, and polymyxin B sulfate eye drops (Maxitrol; Alcon, Fort Worth, TX) was applied four times daily for the first three postoperative weeks. Postoperative follow-up included a weekly slit-lamp examination for the 6-week study duration, including evaluation of general inflammation markers, the IOL, device, and clinical scoring of the PCO (the evolution based on the combination of the area and severity of the opacity of the PCO in the central 3 mm between 0 and 4, where 0 = no PCO and 4 = severe PCO). A slit-lamp photograph also was obtained at each follow-up.

At the end of the study, the rabbits were given a 1.2 mL IM injection of a 7:1 mixture of ketamine and xylazine, and euthanized with a 1 mL IV injection of pentobarbital sodium and phenytoin sodium (Euthasol Euthanasia solution; Virbac Animal Health, Inc., Ottawa, ON, Canada). The eyes then were enucleated, fixed in formalin 10%, and bisected at the equator plane, after which they were assessed and photo-

graphed macroscopically using the Miyake-Apple view.

Matlab Evaluation

Soemmering's ring was evaluated in the same way as in our previous report.[29] Briefly, the area of Soemmering's ring was marked manually on the Miyake-Apple view images (excluding the 6 mm central zone) and calculated in mm^2 and as a percentage from the entire capsular bag area. In Part B of the study, the areas of the Soemmering's ring that penetrated inward to the device's internal ring (defined as protrusions) were marked and quantified in a similar way as the Soemmering's ring (Fig. 3). Protrusions were defined as penetrations inward to the device's internal ring.

Histology

The bisected eyes were dehydrated, immersed in paraffin, sliced into three sections via the pupil, and stained with hematoxylin & eosin (H&E), after which a histopathologic evaluation of PCO was performed by an experience pathologist (Avraham Niska) according to the grading system detailed in Table 1. All groups in both experiments were compared to the control group from our previous study[29] that had undergone the same procedures, including implanta-

Table 3. Histology PCO Score of the Groups in Part A

Group	n	Mean	SD	Median	Range	P Value, Test vs. Control	P Value, Between Groups	Decrease in LEC Proliferation
R1	6[a]	0.5	1.2	0	0–3	0.019	[R1,R2]: 0.519 (1.7[b])	77%
R2	7[a]	0.1	0.4	0	0–1	0.000	[R2,R3]: 0.356 (0.53[b])	95%
R3	6[a]	0	0	0	0–0	0.000	[R3,R1]: 0.363 (1.7[b])	100%
Control	6	2.17	0.41	2.0	2–3	NA	NA	NA

[a] Measurement was not possible in one eye.
[b] Post hoc calculation of minimum detectable difference with $\alpha = 0.05$, $1 - \beta = 0.8$.
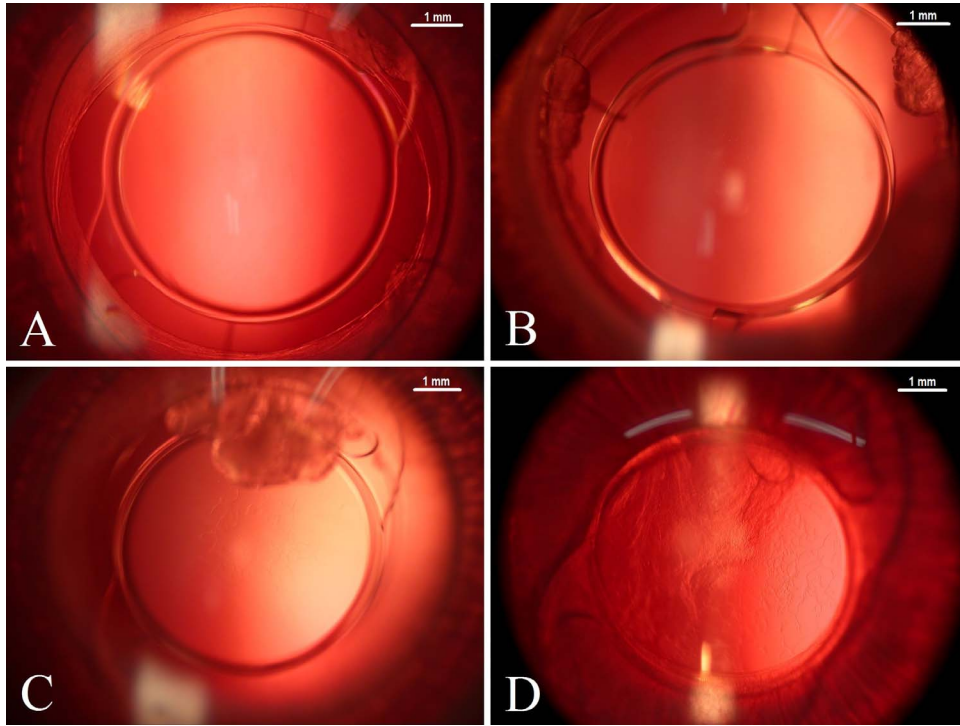
Figure 4. Representative clinical slit-lamp photographs of eyes from each group of Part A at the 6-week follow-up examination demonstrating the difference between the posterior capsule opacification compared to the control group. (A) Group R1. (B) Group R2. (C) Group R3. (D) Control group.
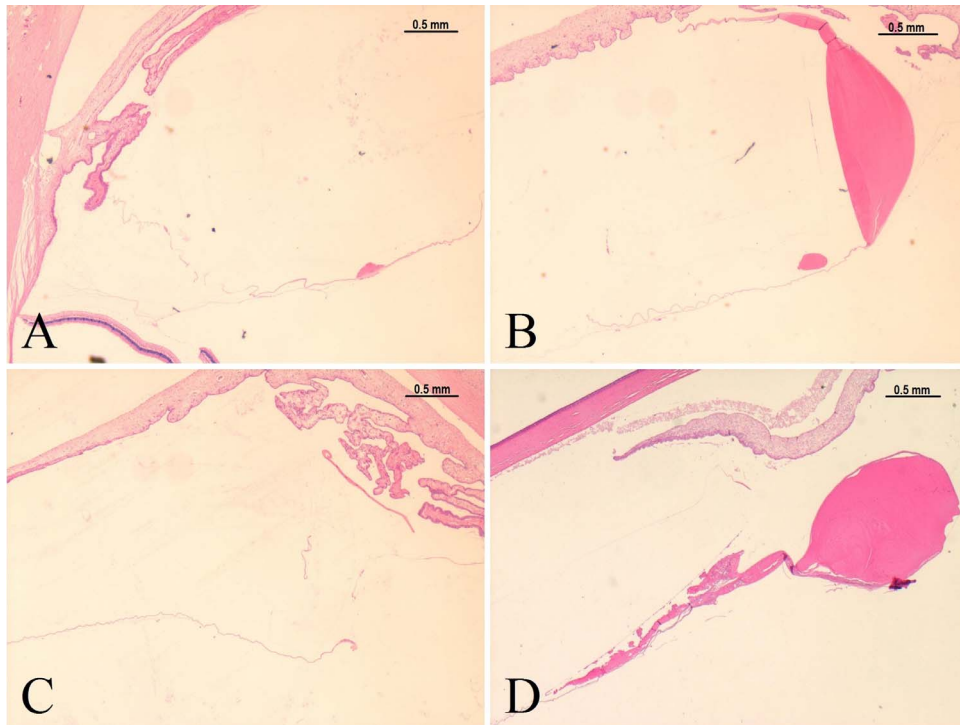

Figure 5. Representative light microscopy photographs of histological sections of eyes from each group of Part A demonstrating the difference of the lens epithelial cell proliferation compared to the control group. (A) Group R1. (B) Group R2. (C) Group R3. (D) Control group (hematoxylin & eosin staining, original magnification ×40).

Table 4. Severity of Protrusion of the Groups in Part A

Group	n	Mild	Moderate	Severe
R1	6	2	2	–
R2	5	1	3	–
R3	6	–	–	4

tion of SeeLens AF IOLs but without any added device.

The Test Device

The test device (Hanita Lenses, Hanita, Israel) was composed of a closed circular ring made from hydrophilic acrylic material and had a total diameter of 11 mm and a height of 1.5 mm. The different designs that were tested in the current study differed in the edge design (round versus square) and in the apertures of the sidewall of the ring (none, large, 4.3 mm^2 × 4; original, 0.8 mm^2 × 8; small with high density, 0.13 mm^2 × 40; and small with low density, 0.13 mm^2 × 20). The unique square edge design of the ring (included in all but one design) evolved in the second part of this study to include two more triangle protrusions at its lower part that aim to further block the migration of the lens epithelial cells into the visual axis (can be noticed later in Fig. 8A, 8C). Also in the second part of the study, the platforms were extended to a diameter of 4.75 mm to ease implantation of the IOL into the ring. The ring internal profile was narrowed and made into a trapeze shape to better fixate the haptics of the IOL in the ring and to ensure better prediction of the IOL position.

Statistical Analysis

The data were expressed as mean, standard deviation (SD), and median. The significance of the differences was estimated using Student's *t*-test, with a 2-tailed distribution. Differences were considered statistically significant when the *P* value was less than 0.05. All analyses were done with Excel software (Excel 2010; Microsoft Corporation, Redmond, WA). Post hoc power calculation to detect minimal detectable difference was performed using a sample size/power calculator on the website of Biomathematics/Biostatistics Division, Department of Pediatrics at Columbia University Medical Center (http://www.biomath.info).

Results

Part A

All surgeries were uneventful. The following complications were observed during the postoperative follow-up: the data on the right eye of animal #4 (implanted with test device R2) were removed from further evaluation as of study day 5 due to severe inflammation, and the data of the right eye of animal #8 (implanted with test device R1) were removed from further slit-lamp evaluations at 4 weeks postoperatively due to mild and moderate corneal and conjunctival edema observed at two and three weeks after implantation, precluding the evaluation of almost all parameters.

All devices maintained an open capsule and reduced the PCO rate compared to the control group. The slit-lamp mean PCO severity grades at the end of the study were 0.7, 1.4, and 1.4 for groups R1, R2, and R3, respectively. These results were significantly lower than the severity in the control group (2.83), with a 75% (*P* = 0.007), 51% (*P* = 0.051), and 51% (*P* = 0.04) reduction, respectively. On histology, the mean PCO severity grades were

Figure 6. Representative light microscopy of histological sections of eyes from each study group demonstrating the histological appearance of the Soemmering's ring protrusions in each tested group. (A) Group R1. (B) Group R2. (C) Group R3 (hematoxylin & eosin staining, original magnification ×40).

Table 5. Clinical PCO Score Six Weeks Following Surgery of the Groups in Part B

Group	n	Mean	SD	Median	Range	P Value, Test vs. Control	P Value, Between Groups	PCO Decrease
RC	8	0.4	0.7	0	0–2	0.000	[C,H]: 0.837 (1.1[a])	86%
RH	7	0.4	0.7	0	0–2	0.000	[H,L]: 0.297 (1.1[a])	86%
RL	9	0.8	0.8	0.5	0–2	0.000	[L,C]: 0.372 (1.1[a])	72%
Control	6	2.83	1.25	3.25	0.5–4.0	NA	NA	NA

[a] Post hoc calculation of minimum detectable difference with $\alpha = 0.05$, $1 - \beta = 0.8$.

0.5, 0.1, and 0 for groups R1, R2, and R3, respectively, compared to 2.17 in the control group, representing a 77% ($P = 0.019$), 95% ($P < 0.001$), and 100% ($P < 0.001$) reduction, respectively (Tables 2, 3; Figs. 4, 5).

Protrusions of Soemmering's ring were observed in all groups, the highest severity being observed in group R3 (implanted with a rounded design) and the least severity in group R1 (implanted with a square design containing apertures; Table 4; Fig. 6). The locations of the protrusions were different between groups: it was through the apertures in group R1, posterior to the device in group R2, and anterior to the device in group R3.

Part B

All the surgeries were uneventful. There were no postoperative complications, and all eyes completed the follow-up period. The grades for PCO and Soemmering's ring were low in all three study groups at the end of the study, with mean slit-lamp PCO scores of 0.4, 0.4, and 0.8, which were significantly lower than the result of the control group (2.83), with an 86% ($P < 0.001$), 86% ($P < 0.001$), and 72% ($P < 0.001$) reduction for RC, RH, and RL, respectively (Table 5, Fig. 7). The mean histology PCO scores were 0, 0.4, and 0.7 (RC, RH, and RL, respectively), which also were statistically significant lower than the
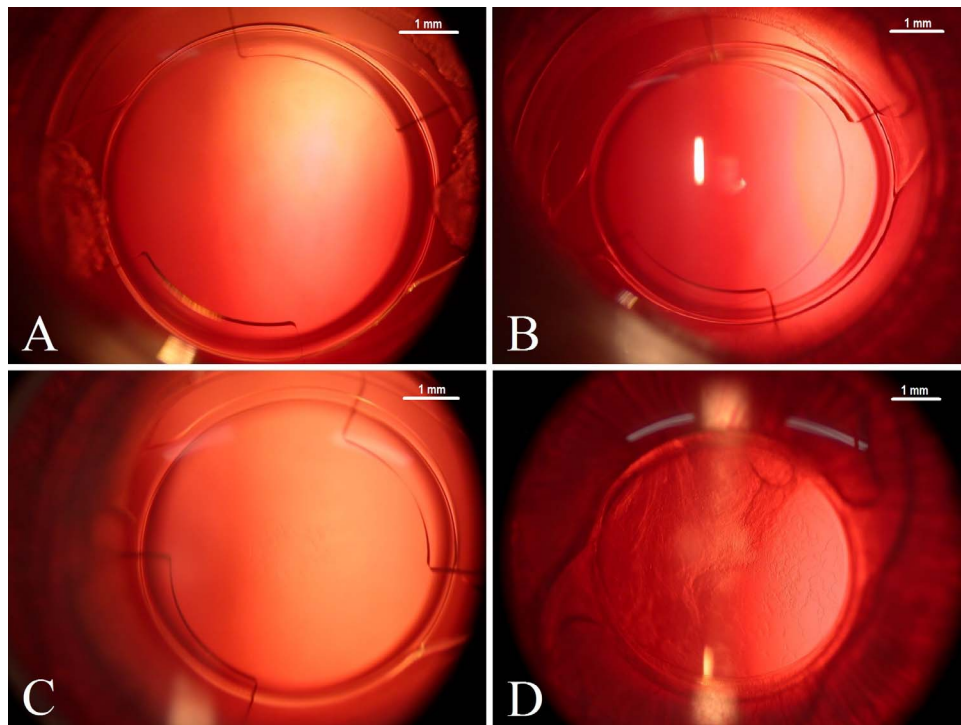

Figure 7. Representative clinical slit-lamp photographs of eyes from each group of Part B at the 6-week follow-up examination demonstrating the difference between the study groups and the control group. (A) Group RC. (B) Group RH. (C) Group RL. (D) Control group.

Table 6. Histology PCO Score of the Groups of Part B

Group	n	Mean	SD	Median	Range	P Value, Test vs. Control	P Value, Between Groups	Decrease of LEC Proliferation
RC	7[a]	0	0	0	0–0	0.000	[C,H]: 0.356 (1.3[b])	100%
RH	7	0.4	1.1	0	0–3	0.000	[H,L]: 0.682 (1.7[b])	82%
RL	9	0.7	1.1	0	0–3	0.000	[L,C]: 0.111 (1.2[b])	68%
Control	6	2.17	0.41	2	2–3	NA	NA	NA

[a] Measurement was not possible in one eye.
[b] Post hoc calculation of minimum detectable difference with $\alpha = 0.05$, $1 - \beta = 0.8$.

control group (2.17), representing a 100% ($P <$ 0.001), 82% ($P < 0.001$), and 68% ($P < 0.001$) reduction for RC, RH, and RL, respectively (Table 6, Fig. 8). The Soemmering's ring area was 33% in group RC, 29% in group RH and 34% in group RL compared to 92% in the control group, a 64% ($P < 0.001$), 69% ($P < 0.001$), and 63% ($P < 0.001$) reduction in Soemmering's ring coverage, respectively (Table 7). Areas of Soemmering's ring protrusions through the device were similar for all three study groups (Table 8).

Post hoc power calculation to detect minimal detectable difference between the study groups in Parts A and B, demonstrated that the study was underpowered to detect small differences between the groups so it was not possible to conclude that the tested groups were similar.

Discussion

Even with the improved skills and new technologies, PCO still is the most common complication following an uneventful cataract surgery. Great efforts have been expended to reduce the rate of PCO, including pharmacologic measures,[21,22] surgical techniques,[31] devices,[23–28] preventive laser treatment,[32,33] IOL materials,[13,18,31,34,35] and IOL de-
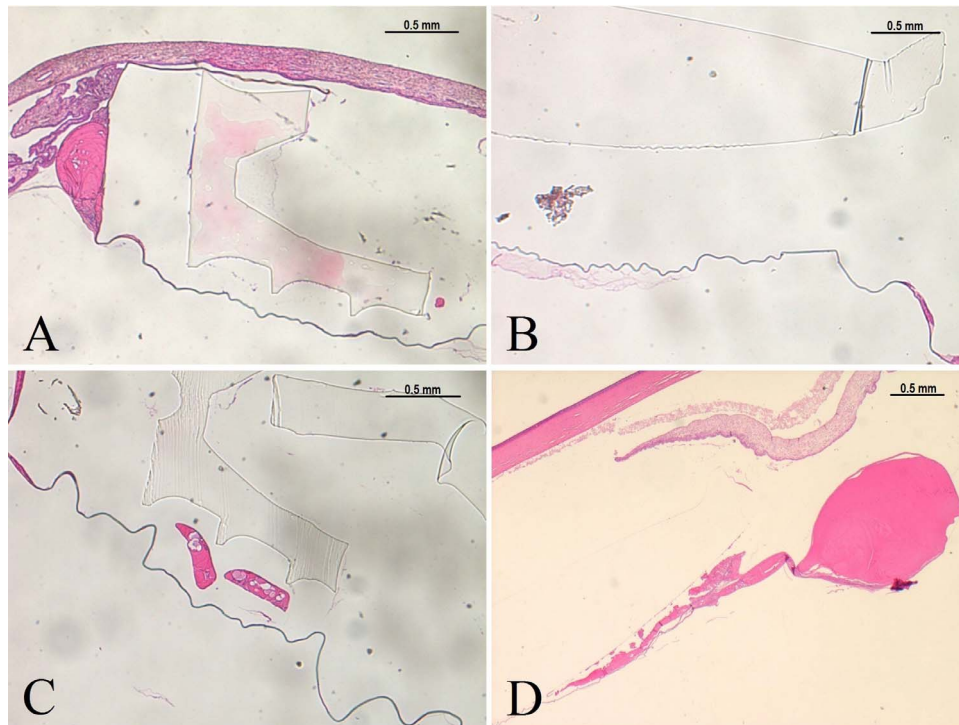

Figure 8. Representative light microscopy photographs of histological sections of eyes from each group of Part B demonstrating the differences of the lens epithelial cell proliferation between the study groups and the control group. (A) Group RC. (B) Group RH. (C) Group RL. (D) Control group (hematoxylin & eosin staining, original magnification ×40).

Table 7. Evaluation of Soemmering's Ring of the Groups in Part B[a]

Group	n	Analysis	Mean	SD	Median	Range	P Value, Test vs. Control	P Value, Between Groups	Decrease of Soemmering's Ring
RC	8	mm^2	19.3	9.3	18.1	7.2–32.8	0.000	[C,H]: 0.632 (16[b])	64%
		%	33.1	15.9	31.1	12.4–56.3			
RH	7	mm^2	16.7	10.9	20.5	0.7–28.8	0.000	[H,L]: 0.554 (16[b])	69%
		%	28.7	18.6	35.1	1.2–49.4			
RL	9	mm^2	19.9	9.7	17.8	8.4–37.5	0.000	[L,C]: 0.899 (14[b])	63%
		%	34.1	16.7	30.5	14.4–64.3			
Control	6	mm^2	52	9.8	52	39.9–67.9	NA	NA	NA
		%	91.8	6.2	91.5	84.4–100			

[a] Matlab analysis.
[b] Post hoc calculation of minimum detectable difference with $\alpha = 0.05$, $1 - \beta = 0.8$.

signs.[12–19,36] Adding a sharp posterior edge to IOLs has reduced significantly the PCO rates and the subsequent need for Nd:YAG laser capsulotomy. However, Menapace et al.[28] showed that the barrier effect of sharp-edged IOLs wears off over time.[28] Cheng et al.[4] also showed that the overall impact of the sharp-edged IOLs resulted in delay of PCO formation rather than prevention,[37] and with decreasing implantation age and increasing life expectancy, it is affecting ever-increasing numbers of patients and a greater burden in terms of healthcare costs.

We had earlier described the beneficial effect of an IOCD in the prevention of PCO and its precursor, Soemmering's ring (primary PCO prevention).[29] The purpose of the current study was to optimize the design of the open-capsule device for more enhanced prevention of PCO. In the first part of the study (Part A), we evaluated the influence of the apertures in the device sidewall and the shape of the wall design (round vs. square) on device efficacy. The results demonstrated that all devices significantly reduced the PCO rate and Soemmering's ring formation in comparison with the control group from our previous

study. The device with the round edge design, however, produced a much greater protrusion of the LECs anterior to the device. Fewer protrusions were found in the eyes that were implanted with the square edge design without the apertures, and the protrusions in those eyes were located posterior to the rings. The fewest numbers of cell protrusions were in the design with the square edge and the apertures in the ring side wall (similar to the first design from our previous study). The cells grew through the apertures in that design. Based on the findings of Part A, we decided to continue with the square edge design for the second part of this study.

In Part B, we investigated the influence of the size and density of the sidewall apertures on LEC protrusions through the apertures. We speculated that there would be less cell protrusion through smaller apertures, and tested two densities of apertures to ensure that sufficient aqueous humor would reach the equatorial LECs. Unlike the significant reduction in the PCO rate and Soemmering's ring formation demonstrated by all the tested designs compared to the control group, there was no

Table 8. Evaluation of Soemmering's Ring Protrusions of the Groups of Part B[a]

Group	n	Analysis	Mean	SD	Median	Range	P Value Between Groups
RC	8	mm^2	5.1	4.5	4.3	0.3–13.8	[RC,RH]: 0.644 (6.5[b])
		%	11.6	10.2	9.8	0.6–31.2	
RH	7	mm^2	4.1	3.8	3.8	0–8.2	[RH,RL]: 0.947 (6.2[b])
		%	9.3	8.6	8.7	0–18.5	
RL	9	mm^2	4.2	4	2.8	0–9.8	[RL,RC]: 0.677 (5.9[b])
		%	9.6	9	6.4	0.1–22.2	

[a] Matlab analysis.
[b] Post hoc calculation of minimum detectable difference with $\alpha = 0.05$, $1 - \beta = 0.8$.

difference in the amount of cell protrusion through the large and small apertures. The density of the small apertures also had no influence on the PCO rate and Soemmering's ring intensity or the amount of cell protrusion. The cell protrusion, was not completely eliminated in any of the ring models.

Limitation of our study include: (1) Difference between different device groups was found not to be statistically significant. However, this does not indicate that there was no difference in the performance between the devices. Post hoc calculation of minimum detectable difference demonstrated that the study was underpowered to detect small differences between the different study groups. Statistical power of the study could have been increased using larger sample size, allowing to conclude regarding the difference between different approaches. (2) Since we used only three sections from each eye for the histology analysis it did not cover the whole area of the central capsule. This may underestimate the PCO rate so the slit-lamp clinical evaluation may be more accurate in the evaluation of the PCO prevention.

Rabbit eyes serve as an excellent PCO model since a few weeks for the rabbit eye equals a few years for the human eye. The accepted follow-up time of this model is 4 weeks,[15] and we chose to extend the follow-up to 6 weeks to allow for enough time to adequately study the effectiveness of the devices, Although the results of preventing PCO were excellent, we believe that the cell protrusions that were found in all the groups might have been at least partially related to the rabbit model and may not have occurred in the human eye.

In conclusion, PCO continues to account for the most important complication after an uneventful cataract surgery, and even though progress has been made in the understanding of the mechanism[38] and in various prevention methods,[39] the only method that has shown some form of safe preventive abilities to date has been the introduction of sharp-edged IOLs.[39] Our current study has yielded significant results in achieving PCO prevention, and we recommend further studies in humans to validate the efficacy of our improved device in the prevention of PCO and its consequences.

Acknowledgments

References

1. Nishi O. Posterior capsule opacification, part 1: experimental investigations. *J Cataract Refract Surg*. 1999;25:106–117.
2. Karahan E, Er D, Kaynak S. An overview of Nd: YAG laser capsulotomy. *Med Hypothesis Discov Innov Ophthalmol*. 2014;3:45–50.
3. Tiwari A, Ram J, Luthra-Guptasarma M. Targeting the fibronectin type III repeats in tenascin-C inhibits epithelial-mesenchymal transition in the context of posterior capsular opacification. *Invest Ophthalmol Vis Sci*. 2015;56:272–283.
4. Chang A, Behndig A, Rnbeck M, Kugelberg M. Comparison of posterior capsule opacification and glistenings with 2 hydrophobic acrylic intraocular lenses: 5- to 7-year follow-up. *J Cataract Refract Surg*. 2013;39:694–698.
5. Iwase T, Oveson BC, Nishi Y. Posterior capsule opacification following 20- and 23-gauge phaco-vitrectomy (posterior capsule opacification following phacovitrectomy). *Eye (Lond)*. 2012;26:1459–1464.
6. Wormstone IM, Wang L, Liu CS. Posterior capsule opacification. *Exp Eye Res*. 2009;88:257–269.
7. Awasthi N, Guo S, Wagner BJ. Posterior capsular opacification: a problem reduced but not yet eradicated. *Arch Ophthalmol*. 2009;127:555–562.
8. Javitt JC, Tielsch JM, Canner JK, et al. National outcomes of cataract extraction. Increased risk of retinal complications associated with Nd:YAG laser capsulotomy. The Cataract Patient Outcomes Research Team. *Ophthalmology*. 1992;99:1487–1498.
9. McLeod SD. Risk factors for posterior capsule opacification. *Br J Ophthalmol*. 2005;89:1389–1390.
10. Senne FM, Temporini ER, Arieta CE, Pacheco KD. Perception of difficulties with vision-related activities of daily living among patients undergoing unilateral posterior capsulotomy. *Clinics (Sao Paulo)*. 2010;65:459–468.

11. Michelson J, Werner L, Ollerton A, et al. Light scattering and light transmittance in intraocular lenses explanted because of optic opacification. *J Cataract Refract Surg*. 2012;38:1476–1485.

12. Nishi O, Nishi K, Wickström K. Preventing lens epithelial cell migration using intraocular lenses with sharp rectangular edges. *J Cataract Refract Surg*. 2000;26:1543–1549.

13. Cheng JW, Wei RL, Cai JP, et al. Efficacy of different intraocular lens materials and optic edge designs in preventing posterior capsular opacification: a meta-analysis. *Am J Ophthalmol*. 2007; 143:428–436.

14. Kohnen T, Fabian E, Gerl R, et al. Optic edge design as long-term factor for posterior capsular opacification rates. *Ophthalmology*. 2008;115: 1308–1314, 1314.e1–3.

15. Werner L, Pandey SK, Izak AM, et al. Capsular bag opacification after experimental implantation of a new accommodating intraocular lens in rabbit eyes. *J Cataract Refract Surg*. 2004;30: 1114–1123.

16. McLeod SD, Vargas LG, Portney V, Ting A. Synchrony dual-optic accommodating intraocular lens. Part 1: optical and biomechanical principles and design considerations. *J Cataract Refract Surg*. 2007;33:37–46.

17. Ossma IL, Galvis A, Vargas LG, Trager MJ, Vagefi MR, McLeod SD. Synchrony dual-optic accommodating intraocular lens. Part 2: pilot clinical evaluation. *J Cataract Refract Surg*. 2007; 33:47–52.

18. Kavoussi SC, Werner L, Fuller SR, et al. Prevention of capsular bag opacification with a new hydrophilic acrylic disc-shaped intraocular lens. *J Cataract Refract Surg*. 2011;37:2194–2200.

19. Leishman L, Werner L, Bodnar Z, et al. Prevention of capsular bag opacification with a modified hydrophilic acrylic disk shaped intraocular lens. *J Cataract Refract Surg*. 2012;38:1664–1670.

20. Floyd AM, Werner L, Liu E, et al. Capsular bag opacification with a new accommodating intraocular lens. *J Cataract Refract Surg*. 2013;39: 1415–1420.

21. Saika S, Okada Y, Miyamoto T, Ohnishi Y, Ooshima A, McAvoy JW. Smad translocation and growth suppression in lens epithelial cells by endogenous TGF beta2 during wound repair. *Exp Eye Res*. 2001;72:679–686.

22. Kurosaka D, Nagamoto T. Inhibitory effect of TGF-beta 2 in human aqueous humor on bovine lens epithelial cell proliferation. *Invest Ophthalmol Vis Sci*. 1994;35:3408–3412.

23. Hara T, Hara T, Sakanishi K, Yamada Y. Efficacy of equator rings in an experimental rabbit study. *Arch Ophthalmol*. 1995;113:1060–1065.

24. Hashizoe M, Hara T, Ogura Y, Sakanishi K, Honda T, Hara T. Equator ring efficacy in maintaining capsular bag integrity and transparency after cataract removal in monkey eyes. *Graefes Arch Clin Exp Ophthalmol*. 1998;236: 375–379.

25. Hara T, Hara T, Hara T. Preventing posterior capsular opacification with an endocapsular equator ring in a young human eye: 2-year follow-up. *Arch Ophthalmol*. 2007;125:483–486.

26. Hara T, Hara T, Narita M, Hashimoto T, Motoyama Y, Hara T. Long-term study of posterior capsular opacification prevention with endocapsular equator rings in humans. *Arch Ophthalmol*. 2011;129:855–863.

27. Nishi O, Nishi K, Menapace R, Akura J. Capsular bending ring to prevent posterior capsule opacification: 2 year follow-up. *J Cataract Refract Surg*. 2001;27:1359–1365.

28. Menapace R, Sacu S, Georgopoulos M, Findl O, Rainer G, Nishi O. Efficacy and safety of capsular bending ring implantation to prevent posterior capsule opacification: three-year results of a randomized clinical trial. *J Cataract Refract Surg*. 2008;34:1318–1328.

29. Alon R, Assia EI, Kleinmann G. Prevention of posterior capsule opacification by an intracapsular open capsule device. *Invest Ophthalmol Vis Sci*. 2014;55:4005–4013.

30. Palanker DV, Blumenkranz MS, Andersen D, et al. Femtosecond laser-assisted cataract surgery with integrated optical coherence tomography. *Sci Transl Med*. 2010;2:58ra85.

31. Schriefl SM, Menapace R, Stifter E, Zaruba D, Leydolt C. Posterior capsule opacification and neodymium:YAG laser capsulotomy rates with 2 microincision intraocular lenses: four-year results. *J Cataract Refract Surg*. 2015;41:956–963.

32. Zhang Z, Huang W, Lei M, et al. Laser-triggered intraocular implant to induce photodynamic therapy for posterior capsule opacification prevention. *Int J Pharm*. 2016;498:1–11.

33. Luft N, Kreutzer TC, Dirisamer M, et al. Evaluation of laser capsule polishing for prevention of posterior capsule opacification in a human ex vivo model. *J Cataract Refract Surg*. 2015;41: 2739–2745.

34. Leydolt C, Kriechbaum K, Schriefl S, Pachala M, Menapace R. Posterior capsule opacification and neodymium:YAG rates with 2 single-piece hy-

translational vision science & technology

drophobic acrylic intraocular lenses: three-year results. *J Cataract Refract Surg*. 2013;39:1886–1892.

35. Hollick EJ, Spalton DJ, Ursell PG, et al. The effect of polymethylmethacrylate, silicone, and polyacrylic intraocular lenses on posterior capsular opacification 3 years after cataract surgery. *Ophthalmology*. 1999:106:49–55.

36. Schriefl SM, Leydolt C, Stifter E, Menapace R. Posterior capsular opacification and Nd:YAG capsulotomy rates with the iMics Y-60H and Micro AY intra-ocular lenses: 3-year results of a randomized clinical trial. *Acta Ophthalmol*. 2015; 93:342–347.

37. Vock L, Menapace R, Stifter E, Georgopoulos M, Sacu S, Bühl W. Posterior capsule opacification and neodymium:YAG laser capsulotomy rates with a round-edged silicone and a sharp-edged hydrophobic acrylic intraocular lens 10 years after surgery. *J Cataract Refract Surg*. 2009; 35:459–465.

38. Wormstone IM, Eldred JA, Experimental models for posterior capsular opacification research. *Exp Eye Res*. 2016;142:2–12.

39. Nibourg LM, Gelens E, Kuijer R, Hooymans JMM, van Kooten TG, Koopmans SA. Prevention of posterior capsular opacification. *Exp Eye Res*. 2015;136:100–105.