Capsular bag opacification after experimental implantation of a new accommodating intraocular lens in rabbit eyes

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Purpose: To evaluate the development of capsular bag opacification in rabbit eyes after implantation of an intraocular lens (IOL) designed to minimize contact between the anterior capsule and the IOL and ensure expansion of the capsular bag.

Setting: David J. Apple, MD Laboratories for Ophthalmic Devices Research, John A. Moran Eye Center, University of Utah, Salt Lake City, Utah, USA.

Methods: Ten New Zealand white rabbits had a study IOL (new accommodating silicone IOL [Synchrony, Visiogen, Inc.]) implanted in 1 eye and a control IOL (1-piece plate silicone IOL with large fixation holes) implanted in the other eye. Intraocular lens position, anterior capsule opacification (ACO), and posterior capsule opacification (PCO) were qualitatively assessed using slitlamp retroillumination photographs of the dilated eyes. Anterior capsule opacification and PCO were graded on a 0 to 4 scale after the eyes were enucleated (Miyake-Apple posterior and anterior views after excision of the cornea and iris). The eyes were also evaluated histopathologically.

Results: The rate of ACO and PCO was significantly higher in the control group. Fibrosis and ACO were almost absent in the study group; the control group exhibited extensive capsulorhexis contraction, including capsulorhexis occlusion. Postoperative IOL dislocation into the anterior chamber and pupillary block syndrome were observed in some eyes in the study group.

Conclusions: The special design features associated with the study IOL appeared to help prevent PCO. Complications in the study group were probably caused by the increased posterior vitreous pressure in rabbit eyes compared to human eyes and the relatively large size of the study IOL relative to the anterior segment of rabbit eyes.

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In the past decade, we have witnessed increasing efforts from manufacturers, research scientists, and surgeons to develop new intraocular lenses (IOLs) for cataract surgery. This has been done in conjunction with, sometimes as a consequence of, the development of better surgical techniques. Energy and funding are being spent on complex IOLs that not only restore the refractive power of the eye but also provide special features such as multifocality, toric correction, and pseudoaccommodation. The latter feature has been of special interest, with recent development of IOLs designed to restore the amplitude of accommodation of the human eye.[1–4]

Experimental techniques such as endocapsular phacoemulsification through a barbell-like or buttonhole capsulotomy and capsular refilling with an inflatable endocapsular balloon or with precured silicone polymeric gels have been used in animal models to preserve accommodation. However, capsule fibrosis/

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opacification appear to gradually reduce the accommodation amplitude obtained with these techniques.[5–9]

Intraocular lenses that propose to restore accommodation have generally been designed to enable forward movement of the optic during accommodation.[1–4] This mechanism is observed with the lenses of some animals such as snakes.[10–12] However, it is not known whether the ability of new IOL designs to move the optic forward will be impaired by long-term postoperative fibrosis/opacification of the capsular bag. This involves not only posterior capsule opacification (PCO)[13–15] but also anterior capsule opacification (ACO), which has been considered a significant complication only in cases such as capsulorhexis phimosis.[16,17]

Visiogen, Inc. recently designed an accommodating silicone IOL that has special features to minimize contact between the anterior capsule and the IOL and ensure expansion of the capsular bag.[18] This study analyzed the outcome of fibrosis/opacification in the capsular bag of rabbit eyes implanted with this new IOL.

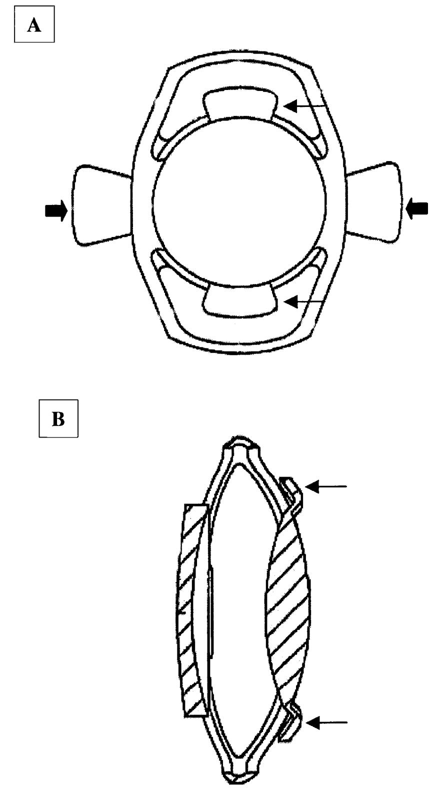

Figure 1. (Werner) Anterior (*A*) and lateral (*B*) views of the Synchrony IOL. The large expansions on the posterior surface (large arrows, *A*) provide IOL stability and prevent posterior excursion of the posterior optic. The small expansions on the anterior surface (small arrows) prevent complete contact between the anterior capsule and the anterior IOL surface.

Materials and Methods

The Synchrony (Visiogen, Inc.) is a single-piece IOL manufactured from silicone (Figure 1). The IOL has 2 main components (anterior and posterior); each has the general design of a plate-haptic silicone IOL and the 2 are connected by a bridge through the haptics with a spring function. The posterior aspect is designed with a significantly larger surface area than the anterior aspect to maintain stability in the capsular bag during the accommodation/unaccommodation process. The anterior optic has 2 expansions oriented parallel to the haptic component that lift the capsulorhexis edge up, preventing complete contact between the anterior capsule and the anterior surface of the IOL. In this dual-optic IOL system, the anterior IOL has a high plus power beyond that required to produce emmetropia, while the posterior IOL has a minus power to return the eye to emmetropia.

The IOL is designed to work in concert with the capsular bag, according to the traditional Helmholtz theory of accommodation. The distance between the 2 optics is stated to be minimum in the unaccommodated state and maximum in the accommodated state, with anterior displacement of the anterior optic.[1,18] Unpublished studies performed in our laboratory using human and rabbit cadaver eyes demonstrated that this IOL could be implanted without distortion/ovalization of the capsulorhexis opening and the capsular bag.

Ten New Zealand white rabbits weighing 3.0 to 3.5 kg were acquired from approved vendors in accordance with the requirements of the Animal Welfare Act. The rabbits were operated on by the same surgeon (L.G.V.). Ten IOLs of each type were implanted; the study IOL was implanted in 1 eye of each rabbit and the control IOL in the fellow eye. Control IOLs were single-piece plate silicone IOLs with large fixation holes (Staar Elastic Lens®, model AA4207VF, Staar Surgical), as their design is similar to the design of each major component of the Synchrony.

Each animal was prepared for surgery by pupil dilation, and anesthesia was administered by an intramuscular injection of ketamine hydrochloride (35 to 44 mg/kg) and xylazine (5 to 8 mg/kg) in a 7:1 mixture. Using an aseptic technique and a surgical microscope, a 3.2 mm clear corneal incision was made. Heparin 1.0 mL (10 000 USP units/mL) was injected into the anterior chamber, followed by injection of an ophthalmic viscosurgical device (OVD) (sodium hyaluronate 1.0% [Healon®]). A capsulorhexis forceps was used to create a continuous curvilinear capsulorhexis, which was targeted to be slightly smaller than the optic diameter of the IOL. The phaco handpiece was inserted into the posterior chamber for aspiration of the lens substance and cortical material. Epinephrine 1:1000, 0.5 mL, and 0.5 mL of heparin (10 000 USP units/mL) were added to each 500 mL of irrigation solution. After the IOL was removed, OVD was used to inflate the capsular bag. The wound was extended to 4.5 mm in both eyes. The IOL was then inserted in the capsular bag, and the OVD was removed. The study IOL was folded according to instructions provided by the manufacturer and inserted with a forceps. The control IOL was inserted with a forceps without folding. Wound closure was achieved with 10-0 nylon sutures.

Correct in-the-bag placement of the IOL and centration were verified at the end of the procedure. The axis of IOL fixation was noted for each eye at the end of the surgery (for comparison with the axis observed postoperatively) and after the rabbits were killed and the eyes enucleated. Postoperative topical therapy included combination antibiotic–steroid eye ointment and tropicamide drops for 1 week.

All eyes were evaluated by slitlamp examination and scored for ocular inflammatory response at 1 day and 1, 2, and 3 weeks. This was assessed on a scale of 0 to 3 (0 = no response; 1 = mild response; 2 = moderate response; 3 = severe response) for flare and cells. Photographs were taken with a camera fitted to the slitlamp. Retroillumination images with the pupil fully dilated were obtained for the purpose of photographic documentation of IOL fixation, centration, rotation, tilt, PCO, and ACO.

After 5 to 6 weeks, the animals were anesthetized and killed. The globes were enucleated and placed in 10% neutral buffered formalin for 24 hours. They were then bisected coronally just anterior to the equator. Gross examination and photographs from the posterior aspect (Miyake-Apple view) and the anterior aspect (after removal of the cornea and iris) were obtained. Intraocular lens fixation, haptic position, IOL decentration, and presence or absence of IOL tilt were evaluated from the posterior and anterior views. The extent and severity of PCO and ACO were also evaluated from these views. The intensity of ACO, central PCO, and Soemmering's ring formation was qualitatively scored from 0 to IV (according to standard photographs), and the area of Soemmering's ring formation was noted from 0 to IV (according to the number of quadrants involved). Because of the special design of the study IOL, interlenticular opacification (ILO) between the 2 optic components was also evaluated.

After gross examination and photographs, all globes were sectioned and the capsular bags (together with the IOLs) were processed for standard light microscopy and stained with hematoxylin-eosin, periodic acid-Schiff (PAS), and Masson's trichrome.

Results

Appropriate folding of both optic components of the study IOL and appropriate positioning of the folded IOL within the insertion forceps were necessary to avoid unfolding the posterior optic component during implantation. The study IOLs were easily inserted through

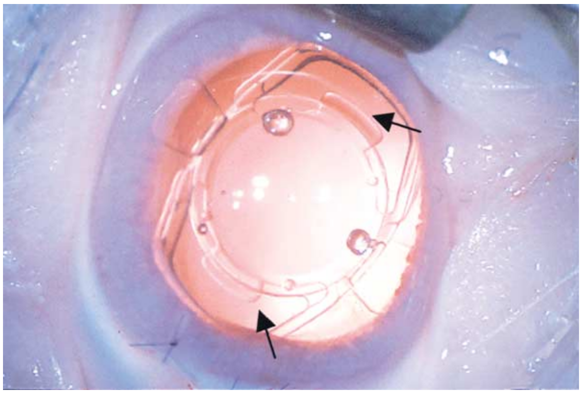

Figure 2. (Werner) Gross photograph through the operating microscope shows a study IOL implanted in the bag. The arrows show the expansions on the anterior optic, which were designed to lift the capsulorhexis edge anteriorly.

the 4.5 mm incision in all cases and placed in the capsular bag (Figure 2). If part of the IOL was found outside the bag, in-the-bag placement was achieved by manipulation with a forceps or spatula. The rabbits were numbered consecutively from 1 to 10.

On day 1, 3 study IOLs in eyes with a capsulorhexis larger than the IOL optic were partially or totally dislocated into the anterior chamber (rabbits 1, 8, and 10). Study IOLs in eyes with a capsulorhexis that was smaller than the optics of the IOLs and covered the optic edge for almost 360 degrees were well fixated in the capsular bag. However, the capsular bag–IOL complex pushed the iris forward (rabbits 3 to 6). This was observed to a smaller degree when the capsulorhexis did not cover the optic edge for almost 360 degrees (rabbits 2, 7, and 9).

At 1 week, 3 of 4 eyes in which the study IOL was implanted through a capsulorhexis that was smaller than the IOL optics and covered the optic edge for almost 360 degrees presented with various degrees of synechias between the pupillary margin and the anterior surface of the IOL or capsulorhexis margin, inadequate pupil dilation, and iris bombe (rabbits 3, 4, and 6). The clinical aspect of these eyes improved immediately after surgical synechiolysis and peripheral iridectomy.

A mild inflammatory reaction was observed the first week, sometimes with small amounts of fibrin formation in the anterior chamber. This was comparable in study and control eyes with the exception of the study eyes presenting posterior synechias, inadequate pupil dilation, and iris bombe that had moderate inflamma-

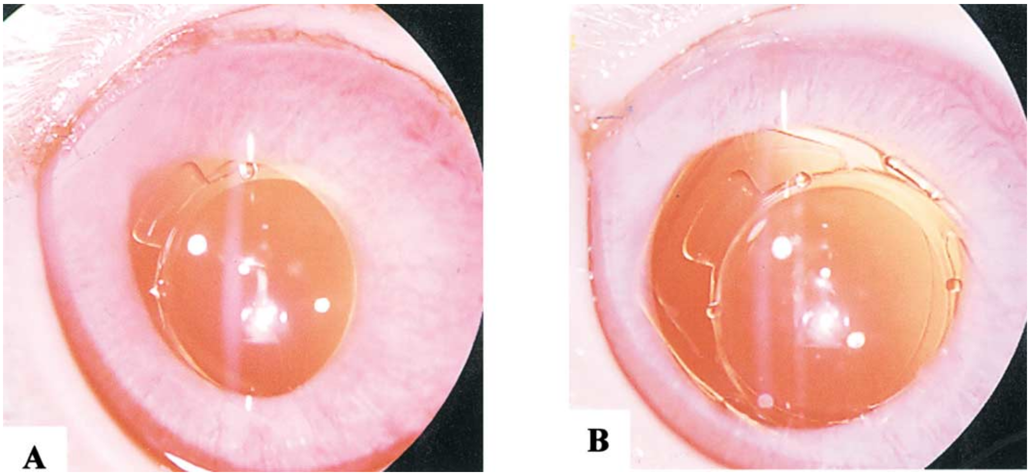

Figure 3. (Werner) Slitlamp photographs taken the first (*A*) and third (*B*) weeks show no variation in the axis of fixation of the study IOL (rabbit 7, right eye).

tory reactions in the anterior chamber that improved after surgical synechiolysis/iridectomy and treatment with combination antibiotic–steroid drops (rabbits 3, 4, and 6). Corneal edema, when present, was limited to the incision site in both groups, with the exception of the 3 eyes in which the study IOL partially or completely dislocated into the anterior chamber. Because of significant corneal edema and probable pain, these 3 rabbits (1, 8, and 10) were killed in the second week.

After in-the-bag implantation, the position of the study IOL did not significantly change postoperatively and only slight variations of the fixation axis were observed in some cases (less than 1 clock hour; Figure 3). The control IOL was apparently relatively small for the rabbit eyes, and decentration of the IOL was observed in some cases, although significant variations of the fixation axis were not noted postoperatively. Control IOLs fixated approximately or at the 3 o'clock to 9 o'clock meridian presented significant inferior decentration early in the postoperative period (Figure 4).

Minimal or no contraction of the capsulorhexis opening over the IOL optic was observed in the study group. The anterior capsule remained clear or fibrosis/opacification was observed at the level of the capsulorhexis edge (Figure 5). Significant degrees of fibrosis/opacification of the capsulorhexis edge were observed in the control group, with progressive contraction of the capsulorhexis edge during the postoperative period in all cases and complete occlusion of the capsulorhexis opening in some cases (Figures 4, 6, and 7, *B*). Posterior capsule opacification was generally more significant in the control group (Figure 7), and this observation was confirmed during gross examination of the enucleated eyes (Figure 8).

The 7 remaining rabbits were killed between the fifth and sixth weeks. Table 1 presents the results of evaluation of the enucleated rabbit eyes from the posterior view. The PCO observed at the level of the IOL optic (defined as central PCO) was greater in the control group (Figure 8). Soemmering's ring formation (intensity and area) also appeared to be greater in the control group. In some cases, a tendency of Soemmering's ring to protrude between the optic components of the study IOL was observed at the level of the periphery of the optics; it did not reach the central space between the components (Figure 9).

Evaluation of sequential histologic sections obtained from the enucleated eyes confirmed the gross findings of central PCO and Soemmering's ring formation (Figure 10).

Discussion

Prevention of opacification in the capsular bag after cataract extraction and IOL implantation, especially the fibrotic types, appears to be even more important now with the increased interest in the development of accommodating IOLs. There are concerns that late postoperative capsular bag fibrosis might prevent long-term functioning of these lenses. This may be associated with not only PCO but also ACO.[1–9]

Most clinical cases of PCO are caused by the proliferation of remnant or regenerated equatorial lens epithe-

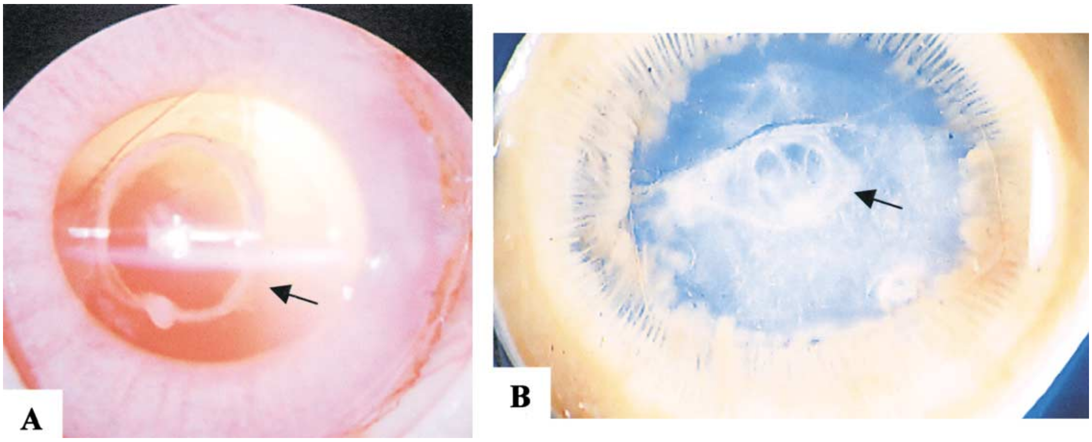

Figure 4. (Werner) Slitlamp photograph (*A*) taken the first postoperative week shows IOL decentration (rabbit 6, left eye). Gross photograph after enucleation of the same eye (*B*, posterior or Miyake-Apple view) confirms the significant inferior IOL decentration. Note the progressive fibrosis/opacification and contraction of the capsulorhexis (arrows).

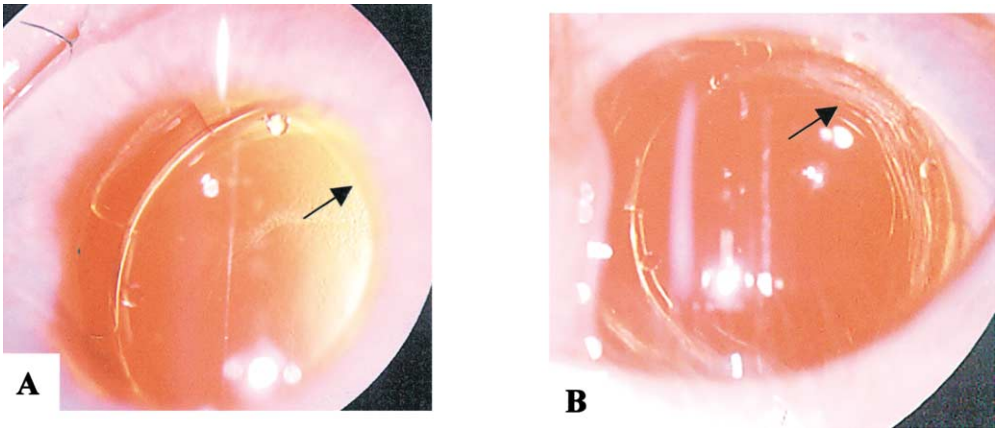

Figure 5. (Werner) Slitlamp photographs at the third week show the capsulorhexis margin (arrows). *A*: Rabbit 2, right eye; clear anterior capsule. *B*: Rabbit 5, left eye; minimal fibrosis/opacification of the capsulorhexis edge.

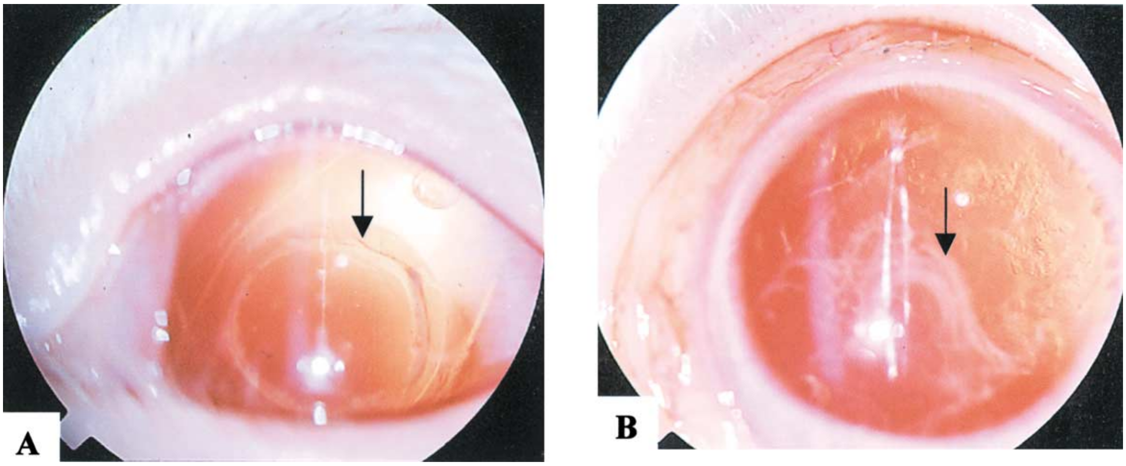

Figure 6. (Werner) Slitlamp photographs at the first (*A*) and third (*B*) weeks show progressive fibrosis/opacification and contraction of the capsulorhexis (arrows). Note the significant PCO present the third week (rabbit 4, left eye).

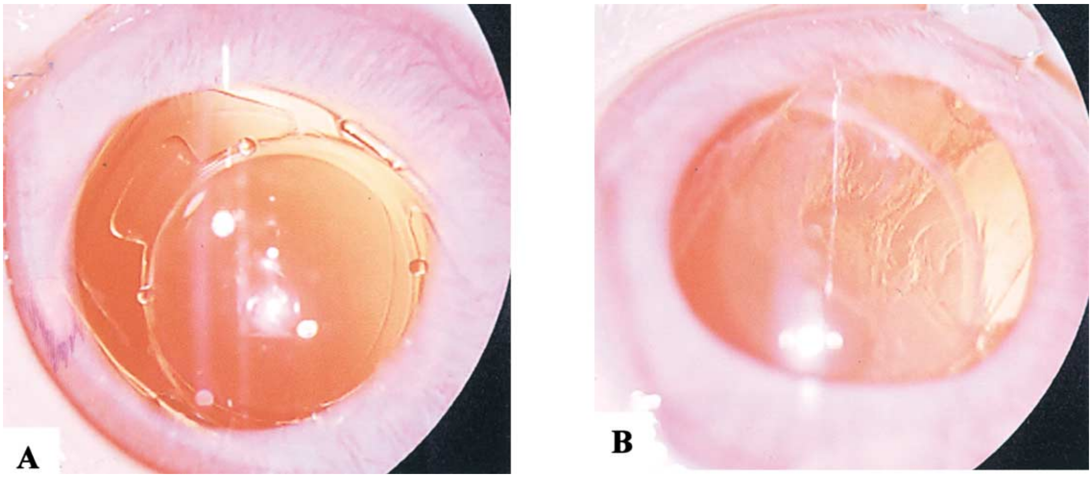

Figure 7. (Werner) Slitlamp photographs of both eyes of rabbit 7 at the third week. *A*: Right eye; clear anterior and posterior capsules. *B*: Left eye; fibrosis/opacification of the capsulorhexis edge and significant PCO.

lial "E" cells (LECs) left in the capsular bag after cataract surgery.[19] Anterior capsule opacification is probably based entirely on the fibrous metaplasia of residual "A" cells attached to the inner surface of the anterior capsule, where it maintains in contact with the IOL material. Studies performed in our laboratory using pseudophakic human eyes obtained postmortem that were implanted with different IOLs demonstrated that the rate of ACO is higher with silicone IOLs, especially the plate designs.[16,17] This is probably because of the relatively large

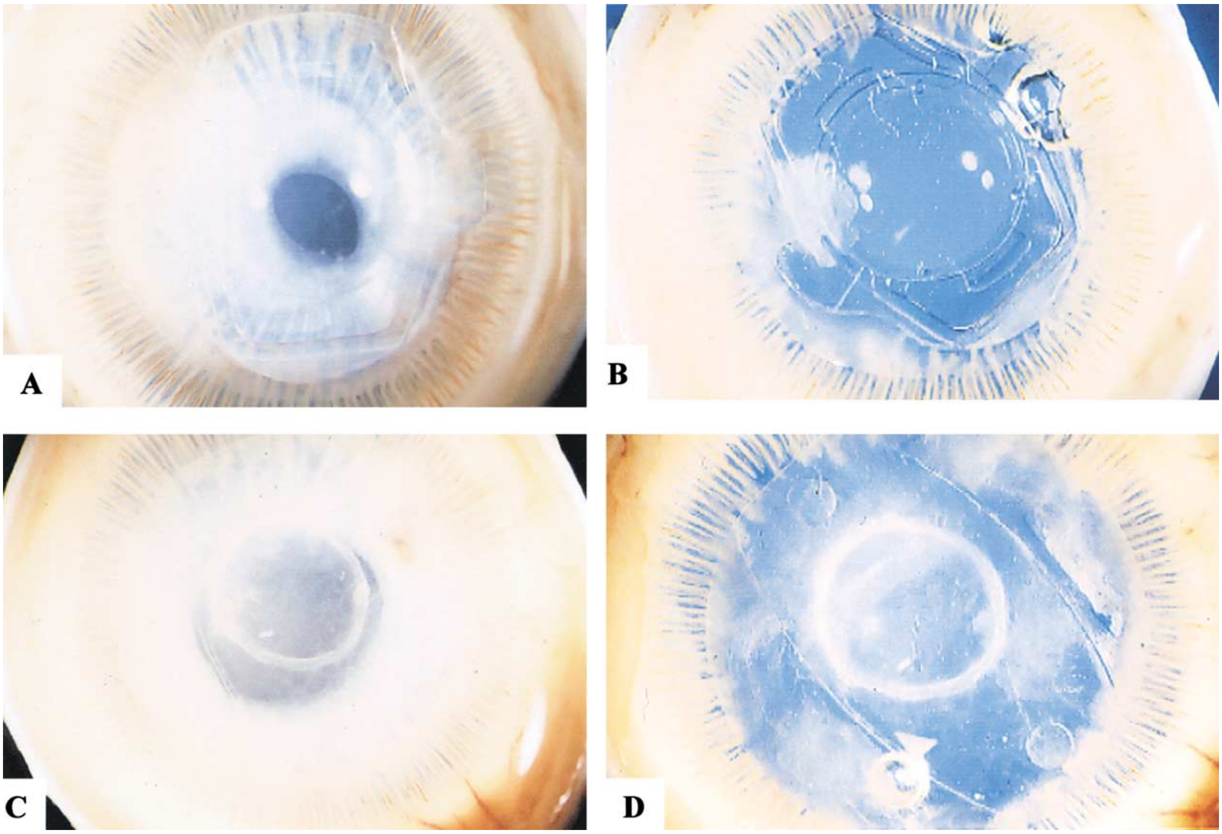

Figure 8. (Werner) Gross photographs of both eyes of rabbit 5 from a posterior view before (*A* and *C*) and after (*B* and *D*) removal of the cornea and iris. Capsulorhexis fibrosis/opacification and contraction and PCO are more significant in the eye with the control IOL (*C* and *D*).

Table 1. Grading of PCO in enucleated rabbit eyes from the posterior or Miyake-Apple view.

Rabbit Eye	IOL (Study/Control)	PCO Central (Intensity)*	Soemmering's Ring (Intensity/Area)†
2/OD	Study	I	I/I
3/OD	Study	I	III/I
4/OD	Study	I	II/I
5/OS	Study	0	III/II
6/OD	Study	II	II/II
7/OD	Study	0	III/II
9/OD	Study	0	I/IV
Mean ± SD		0.714 ± 0.7559	3.714 ± 1.889
2/OS	Control	II	II/II
3/OS	Control	III	IV/I
4/OS	Control	IV	IV/II
5/OD	Control	II	II/III
6/OS	Control	III	III/IV
7/OS	Control	IV	IV/II
9/OS	Control	IV	IV/III
Mean ± SD		3.142 ± 0.899	7.714 ± 3.352

*PCO central (intensity): $P<.05$

†Soemmering's ring (intensity × area): $P<.05$

Rabbits 1, 8, and 10 were excluded from analysis because of partial or total dislocation of the study lens into the anterior chamber; they were killed earlier.

area of contact between the plate-haptic silicone material and the anterior capsule, in sharp contrast to 3-piece IOLs in which contact is limited to the surface of the optic.[16,17] Anterior capsule opacification is essentially a fibrotic entity, and as some of the recently developed accommodating IOLs are manufactured from silicone with basically a plate design,[1,3,4] studies of the prevention of this postoperative complication are important.

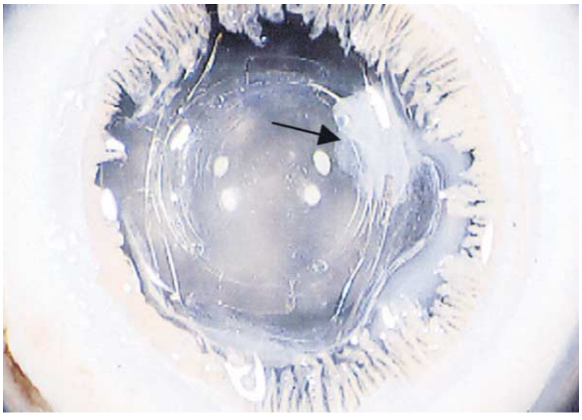

Figure 9. (Werner) Gross photograph of the left eye of rabbit 5 from an anterior view after removal of the cornea and iris. Note the protrusion of the material within Soemmering's ring into the peripheral space between the optic components of the study IOL (arrow).

Hara et al.[20–23] performed studies of anterior capsule transparency after cataract extraction with IOL implantation. They observed that the anterior capsule remains transparent where it maintains tight contact with the posterior capsule. They also evaluated a spring-loaded IOL with some design features similar to the study IOL analyzed by us.[21] The Hara IOL had 2 6.0 mm poly(methyl methacrylate) (PMMA) optics connected with obliquely arranged polyvinylidene fluoride loops with a horizontal length of 10.0 mm. Intraocular lenses with anteroposterior lengths of 4.0 and 8.0 mm were implanted in rabbit eyes. The surgical technique involved endocapsular phacoemulsification through a small upper central anterior capsulotomy. After the capsular bag was completed evacuated, cryopexy was applied to the entire anterior capsule in an attempt to remove the LECs. The anterior capsule opening was extended to 6.0 mm on both horizontal sides for IOL implantation; thus, almost complete capsular bags were retained. In rabbit eyes with thin (4.0 mm) spring-

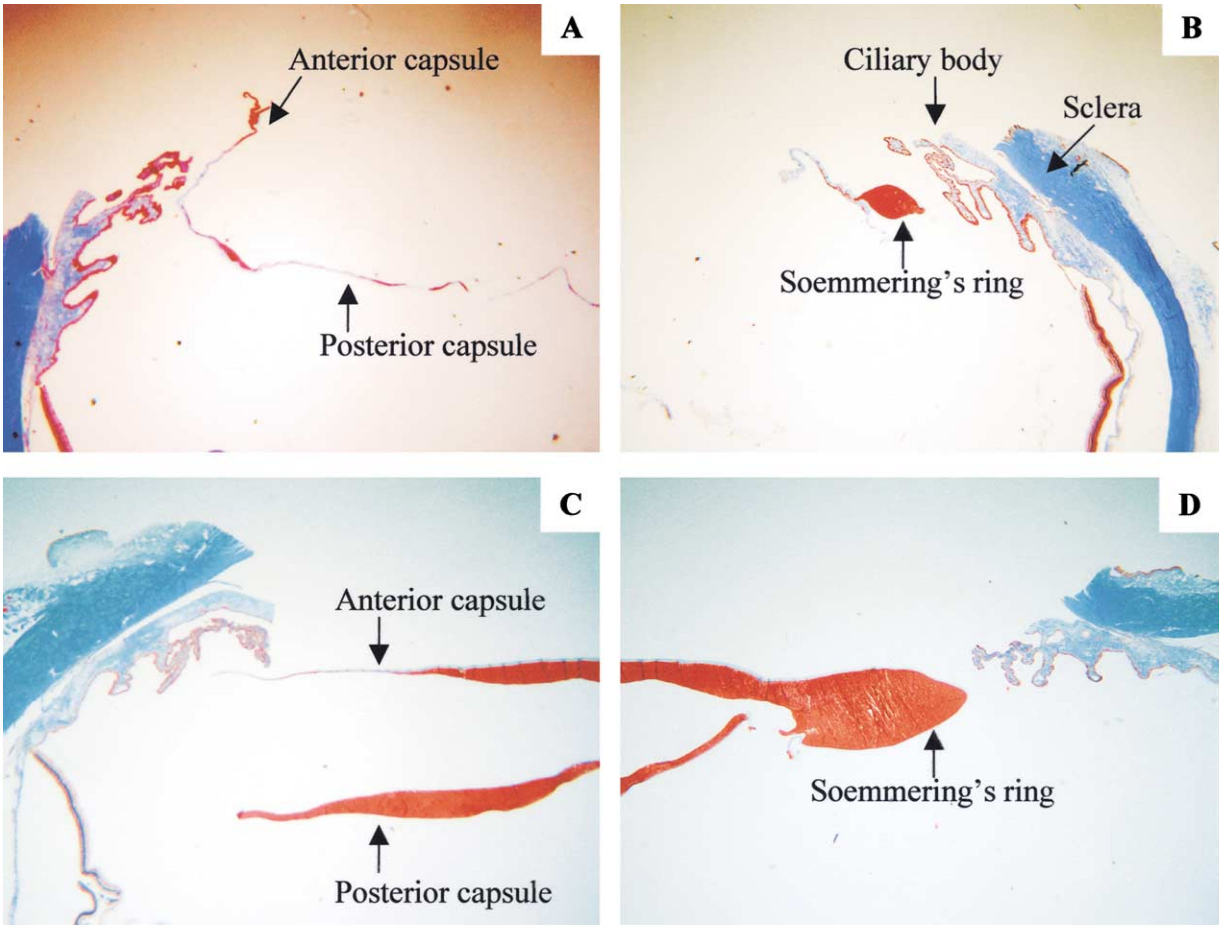

Figure 10. (Werner) Photomicrographs of rabbit 2. Minimal regenerative/proliferative IOL material is attached to the posterior capsule in the eye with the study IOL (*A* and *B*). The amount of material in the eye with the control IOL is more significant (*C* and *D*). Soemmering's ring formation is seen in both eyes (*B* and *D*) (Masson's trichrome stain; original magnification ×10 [*A* and *B*] and ×40 [*C* and *D*]).

loaded IOLs, the entire anterior capsule was opacified; in rabbit eyes with thick (8.0 mm) spring-loaded IOLs, the anterior capsule remained transparent. Hara et al. postulated that the anterior capsules retained their transparency in the eyes implanted with thick spring-loaded IOLs because of mechanical compression against the LECs.

In the current study, the anteroposterior length of the accommodating IOL was smaller than that in Hara's studies. Also, no attempts were made to remove LECs from the inner surface of the anterior capsule. The capsulorhexis was targeted to be smaller than the IOL optic, with the edge covering the optic for 360 degrees. However, the elastic nature of the rabbit capsule, similar to that in pediatric eyes, makes a capsulorhexis in this animal more difficult to control.[24] Analyses of the eyes implanted with the study IOL revealed that the anterior capsule remained clear where it was not in contact with the IOL optic material. This was because the edge of the capsulorhexis was outside the optic area or was lifted by the expansion of the anterior optic. In this model, we did not find direct mechanical compression of the LECs on the inner surface of the anterior capsule, as in the study by Hara and coauthors.[21] However, the degree of capsular bag expansion provided by the study IOL may have played a role in the maintenance of anterior capsule transparency and the prevention of capsular bag contraction and capsulorhexis phimosis. Expansion of the capsular bag is probably responsible for the less significant PCO observed in the study group.

The possibility of ILO with this IOL was addressed in this study because of the 2 optic components. Analyses of ILO cases in our laboratory led us to conclude that the opacification within the interlenticular space is derived from retained/regenerative cortex and pearls in a process similar to the pathogenesis of the pearl form of PCO.[25–27] It has to be considered that the rabbit is an accelerated model for PCO. Progressive regrowth of the crystalline lens material is observed in the postoperative period, thus Soemmering's formation is generally abundant with this animal.

Contrary to what is observed in human eyes, complete filling of the capsular bag by the regenerating/proliferating lens material can occur in the rabbit eye if the follow-up is long enough.[28] Because of this, it would not be surprising to see protrusion of the progressively larger Soemmering's ring between the optic components of the study IOL. This tendency was observed in some cases at the level of the periphery of the optic components but did not reach the central space (Figure 9). The same phenomenon is not expected to occur in human eyes after implantation of the study IOL associated with careful cortical cleanup and eventual polishing of the lens capsule. Human eyes do not have the same lens regenerative/proliferative capacity as rabbit eyes. Also, to our knowledge, ILO has not been reported in association with silicone IOLs. It is generally associated with implantation of 2 piggyback, hydrophobic acrylic IOLs having adhesive surface properties. For 2 years, Joel Shugar, MD, has placed a pair of plate-haptic silicone IOLs in the capsular bag with the haptics 90 degrees apart and has seen no opacification in this series (L.J. Rongé, "Preventing Problems with Piggyback IOLs," EyeNet, June 2002, pages 21–22).

In summary, the study IOL was easy to implant through a 4.5 mm incision. Postoperative dislocation of some study IOLs into the anterior chamber and pupillary block syndrome in some eyes were probably because rabbit eyes have greater posterior vitreous pressure than human eyes and the study IOL was relatively large for the anterior segment of the rabbit eye. These complications might have been prevented by intraoperative iridectomy. The study group performed better in relation to capsular bag opacification, with minimal fibrosis/opacification of the capsulorhexis edge, no case of capsulorhexis contraction, and significantly less PCO. However, the amplitude of accommodation eventually provided by the new IOL design has to be addressed in another model (eg, primates) and in clinical trials.

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