Interlenticular opacification: Dual-optic versus piggyback intraocular lenses

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PURPOSE: To evaluate and compare the incidence of capsular bag opacification, particularly interlenticular opacification (ILO), in rabbit eyes implanted with a dual-optic silicone intraocular lens (IOL) or piggyback lenses.

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

METHODS: Ten dual-optic study IOLs (Synchrony), 10 control pairs of piggyback silicone-plate lenses, and 10 control pairs of piggyback single-piece hydrophobic acrylic lenses were implanted in the capsular bag of 30 rabbit eyes following phacoemulsification. After a 6-week follow-up, the rabbits were killed and their eyes enucleated. Anterior capsule opacification and posterior capsule opacification were graded on a 0 to 4 scale from a posterior or Miyake-Apple view. Interlenticular opacification was noted in relation to the center of the interlenticular space (periphery, paracentral, and central area) and to the number of quadrants involved. The eyes were then evaluated histopathologically.

RESULTS: Postoperative inflammatory reaction was similar in all groups. Interlenticular opacification formation was statistically different among the 3 groups of lenses (ILO extension, $P = .0013$, and ILO extension $\times$ ILO quadrants, $P = .0023$; Kruskal-Wallis test). Pairwise post comparisons of ILO formation showed that the differences between the study IOL group and the silicone-plate lens group were not significant. Interlenticular opacification post comparisons between the hydrophobic acrylic lenses and the study lens or the silicone-plate lenses were significant ($P = .002$ and $P = .001$, respectively). Histopathologic examination showed extension of the proliferating cortical material from the peripheral Soemmering's ring into the interlenticular space, causing ILO, especially with the pairs of hydrophobic acrylic lenses.

CONCLUSIONS: In this rabbit model, ILO was significantly associated with pairs of hydrophobic acrylic lenses implanted in the bag. This study appears to confirm clinical observations that implantation of 2 silicone-plate lenses in the bag is not associated with ILO. There was also a relative lack of ILO with the dual-optic silicone lens.

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Theoretical studies using model eyes demonstrate that dual-optic intraocular lens (IOL) systems may represent an advantage over mono-optic systems in terms of amplitude of accommodation obtained with optic movement during efforts for accommodation. This appears to be particularly valid if there is anterior translation of the anterior optic with no change in the position of the posterior optic.[1,2] Therefore, dual-optic IOLs have been developed, including the Synchrony lens (Visiogen, Inc.). This is a 1-piece silicone lens with an anterior high plus-power optic and a posterior minus-power optic connected by bridges through the haptics with spring function. The development of the Synchrony, as well as preliminary results from experimental implantation in cadaver and rabbit eyes, have been described.[3,4]

The presence of 2 IOL optics in the capsular bag raises concerns about the possibility of ingrowth of regenerative/proliferative crystalline lens material between them, with formation of interlenticular opacification (ILO).[5–10] The aim of this study was to evaluate the outcome of opacification within the capsular bag, including anterior capsule opacification (ACO) and posterior capsule opacification (PCO), but focusing on ILO associated with 2 types of piggyback IOLs compared with the Synchrony.

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MATERIALS AND METHODS

Fifteen New Zealand white rabbits weighing 3.2 to 3.5 kg were acquired from approved vendors in accordance with the requirements of the Animal Welfare Act for use in this study. Ten study IOLs (Synchrony; group 1), 10 control pairs of silicone-plate lenses (AA4207VF, Staar Surgical; group 2), and 10 control pairs of single-piece hydrophobic acrylic lenses (AcrySof SA30AT, Alcon Laboratories; group 3) were used in this study. The lenses were implanted in a randomized manner by the same surgeon (N.M.) in a way to ensure 3 bilateral combinations of the different IOL groups, with 5 rabbits in each combination. All the lenses had the same dioptric power (+20.0 diopters [D]).

Each animal was prepared for surgery by pupil dilation; anesthesia was obtained with an intramuscular injection of ketamine hydrochloride (35 to 44 mg/kg) and xylazine (5 to 8 mg/kg) in a mixture of 7:1. A 3.2 mm partial-thickness limbal incision was then made, and the anterior chamber was entered, followed by injection of an ophthalmic viscosurgical device (OVD) (sodium hyaluronate 1.6% [Amvisc Plus]). A capsulorhexis forceps was used to create a continuous curvilinear capsulotomy with a diameter of approximately 4.5 to 5.0 mm. After hydrodissection, the phaco handpiece (Alcon Coopervision Series 10,000) was inserted into the posterior chamber for removal of lens nucleus and cortical material. One half 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 same OVD was then used to inflate the capsular bag.

The AcrySof lenses were injected into the capsular bag using the manufacturer's recommended injector system. For the pair of silicone-plate lenses and the study lens, the incision size was increased to 4.0 to 4.5 mm. The silicone lenses were inserted with forceps, without previous folding, and the Synchrony lens was folded before insertion with forceps. Both lenses in the pairs of control piggyback IOLs were implanted in the capsular bag and oriented perpendicular to each other. Wound closure was achieved with 10-0 monofilament nylon suture after the OVD was removed.

Of the 10 eyes implanted with the study lens, 5 had a peripheral iridectomy. This was done because, in a previous study,[4] some eyes implanted with the Synchrony lens presented with pupillary block syndrome postoperatively, which was relieved by the performance of a peripheral iridectomy. Correct in-the-bag placement of the lenses, as well as lens centration, was verified at the end of the procedure. Postoperative topical therapy included combination antibiotics/steroid ointment (neomycin and polymyxin B sulfates and dexamethasone) during the first postoperative week and topical prednisolone acetate drops during the second postoperative week.

All eyes were evaluated by slitlamp examination and scored for ocular inflammatory response at 1, 3, 4, 5, and 6 weeks. This was assessed on a scale of 0 to 3 with steps of 1 (0 = absent; 1 = mild; 2 = moderate; 3 = severe reaction) for flare and cells. Photographs were taken for documentation with a camera fitted to the slitlamp. Retroillumination images with the pupil fully dilated were obtained for the purpose of qualitative photographic documentation regarding IOL fixation, centration, rotation, and tilt, as well as ACO, ILO, and PCO formation.

After a follow-up of 6 weeks, the animals were anesthetized and killed. Their globes were enucleated and placed in 10% neutral buffered formalin for at least 24 hours. Gross examination of the anterior segments from a posterior view was performed to analyze capsular bag opacification (ACO, ILO, peripheral PCO, central PCO, and Soemmering's ring formation). The intensity of ACO, central and peripheral PCO, and Soemmering's ring formation was qualitatively scored from grades 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). The protrusion of regenerative/proliferative material between the lenses' optics (ILO) was noted according to the extension (relation to the center of the interlenticular space from 0 to 3; none, periphery, paracentral area, and central area, respectively) and area from 0 to 4 (number of quadrants). Other parameters analyzed from a posterior view included capsulorhexis coverage of the anterior IOL optic (noted in degrees) and presence/absence of IOL decentration. Results from the 3 groups were statistically compared.[11]

The globes were then sectioned and processed for standard light microscopy and stained with hematoxylin and eosin (H&E), periodic acid-Schiff, and Masson's trichrome stains.

RESULTS

Minimal bleeding was observed in some of the eyes implanted with study lenses that received a peripheral iridectomy at the end of the procedure. The implantation procedures were otherwise uneventful. The presence of fibrin between the optics in some of the eyes in all groups was observed at the 1-week examination. The amount of fibrin progressively decreased and generally disappeared by the 4-week examination. The piggyback groups (especially the silicone-plate group) showed more decentration of the posterior lens in relation to the anterior lens. This could be observed at the 1-week examination. The right eye of 1 rabbit implanted with the Synchrony lens (rabbit number 2) and the right eye of 1 rabbit implanted with a pair of silicone-plate lenses (rabbit number 10) developed postoperative endophthalmitis, and these 2 eyes were excluded from the study.

In the study group, no differences were observed between the eyes having and not having a peripheral iridectomy. With

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the exception of the eye presenting with endophthalmitis (no peripheral iridectomy), the postoperative course of the other eyes in this group was uneventful. Giant cells were observed on the surface of some lenses in all groups, especially from the 4-week examination on (and more prominently on the silicone lenses). Soemmering's ring formation started to appear more prominent at the 3-week examination. At that time, the proliferating material could be seen protruding between the piggyback lenses, especially the AcrySof lenses. It was interesting to observe that in the eyes in this group, the proliferating material started to protrude in the interlenticular space at the level of the optic–haptic junctions.

Table 1 summarizes the means and standard deviations of the parameters analyzed post-mortem from the posterior view of the anterior segment, as well as the results of the statistical analysis of the same parameters. The parameters showing statistically significant differences between the 2 groups were the following: central PCO, ILO extension (quadrants), ILO extension × ILO quadrants, and capsulorhexis coverage. Pairwise post comparisons regarding ILO extension and ILO extension × ILO quadrants showed that the differences between the study group and the pair of silicone-plate group were not significant. The differences between the pair of AcrySof lenses and the study lens ($P = .0008$, ILO extension and $P = .002$, ILO extension × ILO quadrants) or the pair of silicone-plate lenses ($P = .002$, ILO extension and $P = .001$, ILO extension × ILO quadrants) were statistically significant. Figures 1 through 3 show representative slitlamp and corresponding gross photographs from the posterior view of eyes in the 3 different groups.

Histopathologic analysis of serial sections obtained from each eye confirmed the findings from the gross analysis of the anterior segments from a posterior view in terms of capsular bag proliferation. The IOLs were dissolved during the preparation for histopathological examination, but in some sections, an outline of the lenses could be observed. A prominent peripheral Soemmering's ring formation was observed in most eyes in all groups, which is not uncommon with the rabbit model. In some sections, an extension of the proliferating material from the Soemmering's ring onto the posterior capsule, causing PCO, and sometimes within the interlenticular space, causing ILO, was seen. This later was especially observed in the group of piggyback AcrySof lenses. All the capsular bags appeared expanded in the histologic sections, but this was more prominent in the eyes implanted with the silicone lenses (especially the Synchrony lens). No signs of untoward inflammation or toxicity to intraocular structures were observed in any section. Figures 4 through 6 show representative photomicrographs of sections of eyes in the 3 groups.

DISCUSSION

Previous studies of ILO formation demonstrate that this complication is particularly related to in-the-bag implantation of 2 hydrophobic acrylic lenses (with adhesive properties) through a relatively small capsulorhexis.[5–10] Implantation of the posterior lens in the capsular bag and the anterior lens in the sulcus has been suggested for ILO prevention.[8] Pathologic evaluation of the ILO cases demonstrated that the material opacifying the interlenticular space is composed of regenerative/proliferative cortex material and lens epithelial cells, with a pathogenesis similar to that of PCO formation.[6,8–10] In the rabbit model described here, ILO was significantly associated with the pair of AcrySof lenses, while the least amounts were observed with the silicone lenses (especially with the study lens). Gross and histopathologic evaluation confirmed that the material opacifying the interlenticular space originated from proliferative cortical material within Soemmering's ring.

Although Soemmering's ring formation was similar in the 3 groups, the material within it generally did not

Table 1. Parameters analyzed from a posterior or Miyake-Apple view.

Parameter	Synchrony	IOL Plate (Pair)	AcrySof (Pair)	*P* Value*
Central PCO	0.27 ± 0.36	1.11 ± 0.78	1.2 ± 1.11	.0152 (S)
Peripheral PCO	0.55 ± 0.46	1.22 ± 1.09	1.4 ± 1.04	.1772 (NS)
SRI × SRA	4.11 ± 2.75	1.66 ± 1.87	3.2 ± 2.04	.0557 (NS)
ACO	0	0.22 ± 0.44	0.1 ± 0.31	.325 (NS)
ILO extension	0.38 ± 0.48	0.55 ± 0.72	1.8 ± 0.78	.0013 (S)
ILOe × ILOq	0.61 ± 0.85	0.55 ± 0.72	3.4 ± 2.22	.0023 (S)
Capsulorhexis coverage	215.55 ± 66.16	108.88 ± 114.93	75 ± 86.05	.0113 (S)

Means ± MD
ACO = anterior capsule opacification; ILO = interlenticular opacification; ILOq = interlenticular opacification quadrants; NS = not significant; PCO = posterior capsule opacification; S = significant; SRI × SRA = Soemmering's ring intensity × Soemmering's ring area
*Kruskal-Wallis test

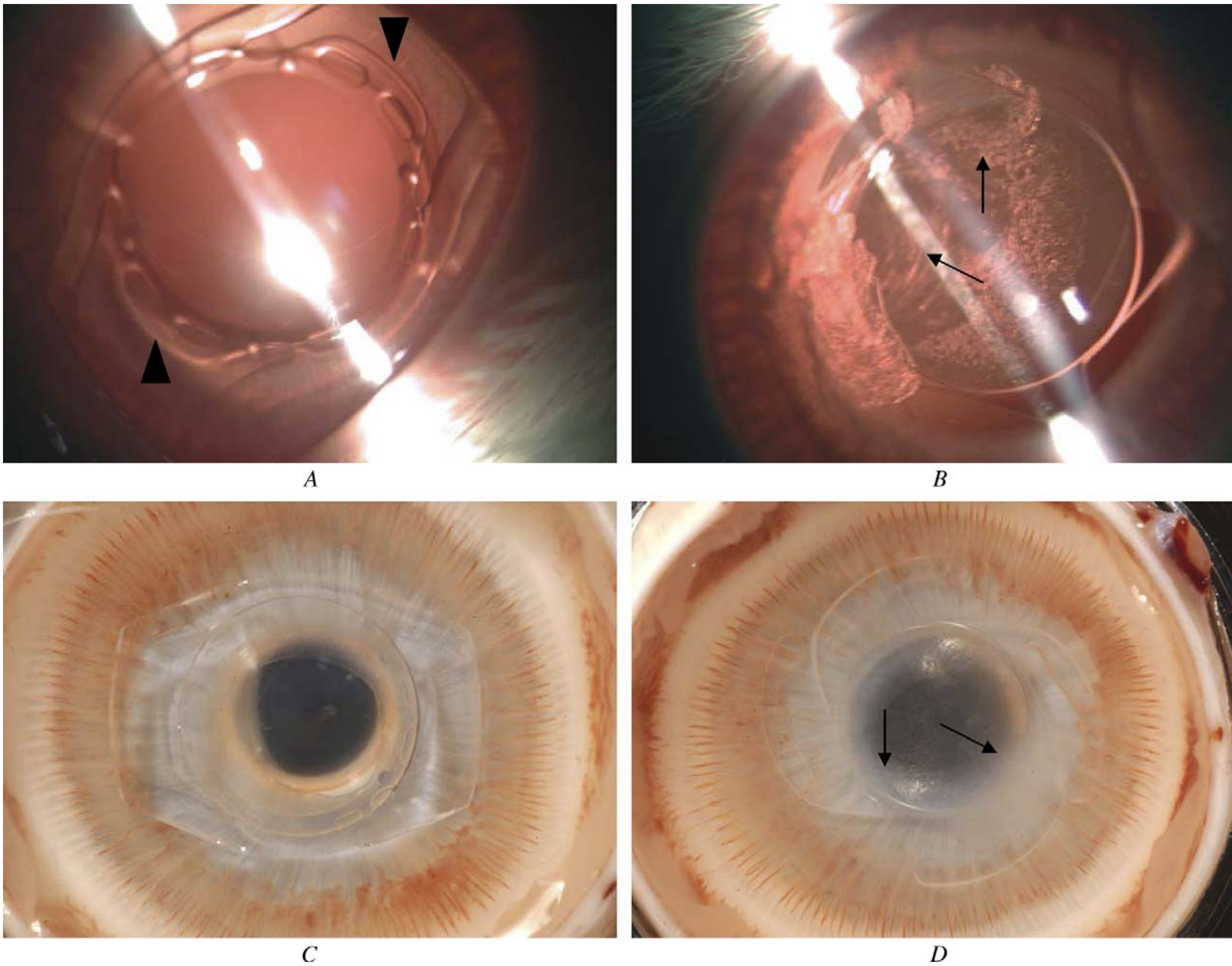
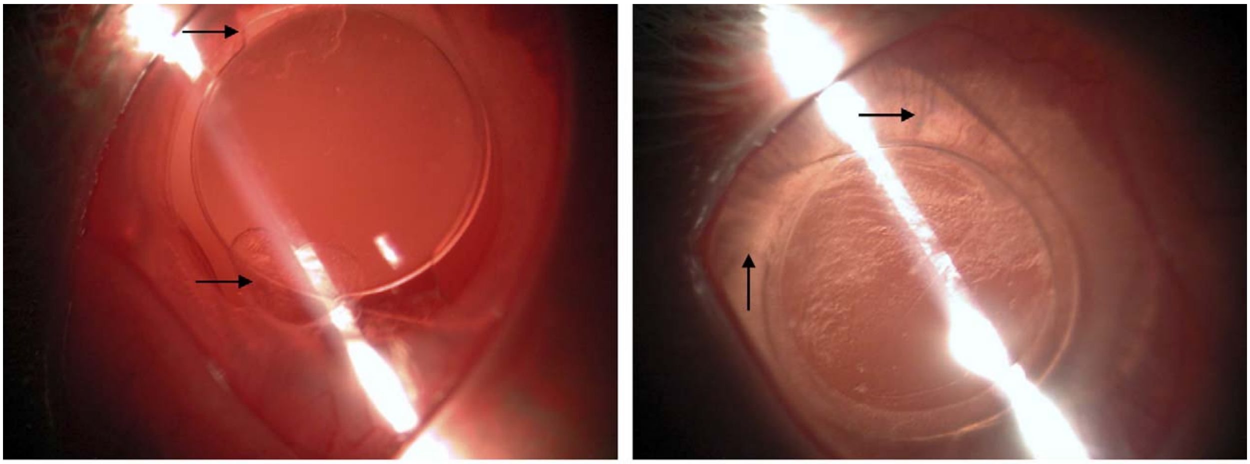


Figure 1. Slitlamp photographs taken 6 weeks postoperatively (*A* and *B*) and corresponding gross photographs obtained post-mortem (posterior or Miyake-Apple view, *C* and *D*). The photographs are from both eyes of the same rabbit (number 1). No capsular bag opacification is observed in the eye implanted with the study lens. Posterior capsule opacification as well as interlenticular opacification (arrows) can be observed in the eye implanted with the AcrySof piggyback pair. The arrowheads in *A* show the lateral expansions of the anterior optic of the study lens, which lift up the anterior capsule, minimizing its contact with the anterior optic surface.

progress beyond the level of the optic edges with the study lens. It has to be noted that the rabbit eye does not accommodate. Therefore, in the human situation, it is expected that the thickness of the interlenticular space will experience dynamic changes, as a function of efforts of accommodation. Whether this will influence the outcome of postoperative ILO formation needs to be assessed in clinical studies. In a series of 25 patients implanted with the Synchrony lens and followed for 12 months, no ILO formation was observed (I.L.Ossma-Gomez, MD, et al., "Synchrony Dual-Optic Accommodating IOL: One-Year Follow-Up," presented at the ASCRS Symposium on Cataract, IOL, and Refractive Surgery, Washington, DC, USA, April 2005).

In this study, the pairs of silicone-plate lenses were oriented perpendicularly to each other. This was done because of the observations of Joel Shugar, MD, who has not seen ILO formation after placing pairs of plate-haptic silicone lenses in the capsular bag with the haptics 90 degrees apart (L.J. Rongé, "Preventing Problems with Piggyback IOLs," EyeNet, June 2002, pages 21–22). In the current study in rabbit eyes, the degree of ILO formation with the pair of plate lenses was intermediate between the degree with the study lens and with the pair of AcrySof lenses (but not significantly higher than the study lenses). The decentration of the posterior lens in relation to the anterior lens, generally observed in these rabbit eyes, may have influenced the outcome of ILO by creating easier access of the proliferating material to the interlenticular space.

During the clinical follow-up of the rabbits, our impression was that in at least 7 of the 10 eyes implanted



A B

Figure 2. Slitlamp photographs taken 6 weeks postoperatively (*A* and *B*). The photographs are from 2 eyes implanted with an AcrySof piggyback pair (rabbit numbers 7 and 9, respectively). The arrows indicate the optic–haptic junctions that appeared to be the site of the beginning of IOL formation.

with the pair of AcrySof lenses, ILO formation started at the level of the optic–haptic junctions. This appears to confirm previous observations in rabbit studies, in which the optic–haptic junctions of this single-piece hydrophobic acrylic design and those of a single-piece hydrophilic acrylic design were the sites of the beginning of ingrowth of material causing PCO.[12–14]

In our previous rabbit study of the Synchrony lens,[4] postoperative lens dislocation into the anterior chamber and pupillary block syndrome were observed in some eyes of the study group, which was relieved by the performance of a peripheral iridectomy. In our current study, no differences were observed between the eyes having and those not having a peripheral iridectomy. With the exception of the right eye of rabbit number 2, which had endophthalmitis (no peripheral iridectomy), the postoperative course of the other eyes in this group was uneventful. One possible explanation for this is a modification of the design of the lens since the previous study. As noted in Figure 1, *A*, the lateral expansions of the anterior optic of the study lens, which are supposed to lift up the anterior capsule, minimizing its contact with the anterior optic surface, now have large holes to allow more fluid flow.

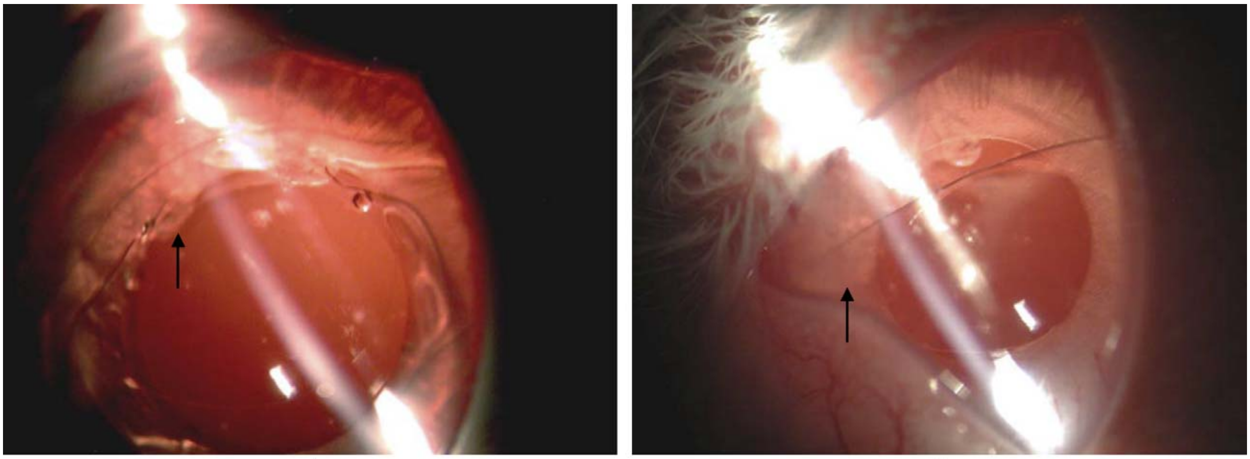


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Figure 3. Slitlamp photographs taken 6 weeks postoperatively (*A* and *B*). The photographs are from an eye implanted with a study lens (rabbit number 13, *A*) and an eye with a silicone-plate piggyback pair (rabbit number 12, *B*). The beginning of protrusion of the material within Soemmering's ring into the interlenticular space (ILO) can be seen in both eyes (arrows), more prominently in the eye with the silicone-plate lenses (*B*). In this eye, the posterior lens is decentered in relation to the anterior lens. Note the presence of cell deposits (giant cells) on the surfaces of the lenses in both eyes.

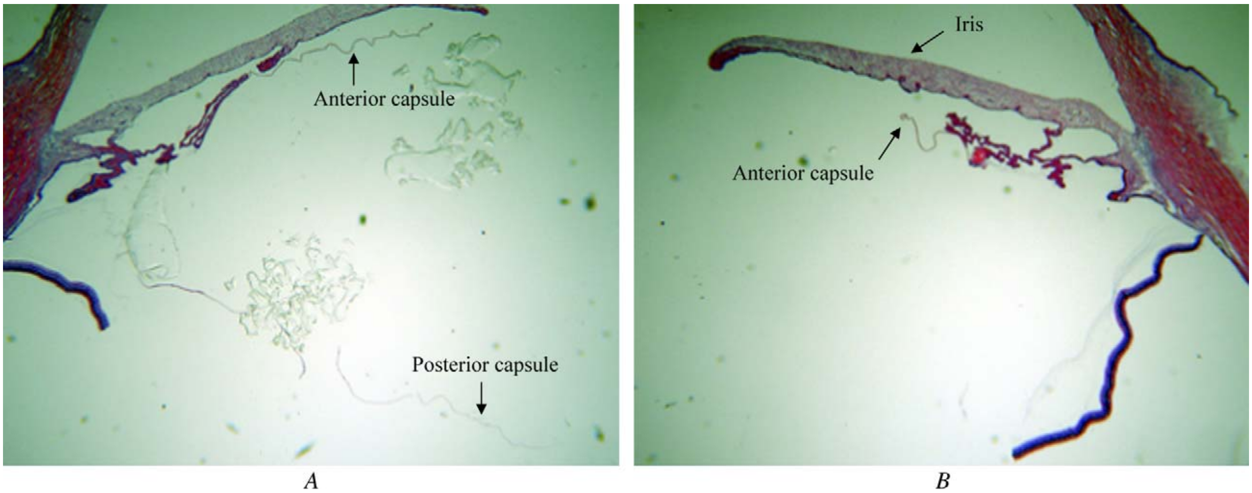

Figure 4. Photomicrographs of a histologic section cut from an eye implanted with the study lens (rabbit number 1, left eye). *A* and *B* show the left and right side of the section, respectively (H&E stain; original magnification ×20). No opacification within the capsular bag, which is very expanded, can be observed.

No significant ACO was observed in any group, including the silicone-plate group. This is in contrast to our previous rabbit study in which significant ACO, as well as contraction of the capsulorhexis opening, was observed in the eyes implanted with a single silicone-plate lens.[4] In a study by Hara et al.[15] of spring-loaded lenses, IOLs with anteroposterior lengths of 4.0 and 8.0 mm were implanted in rabbit eyes. Rabbit eyes receiving the thin (4.0 mm) spring-loaded lenses had opacified anterior capsules over the entire area, while rabbit eyes receiving thick (8.0 mm) spring-loaded lenses retained transparent anterior capsules. The authors postulate that the anterior capsules retained their transparency in the eyes implanted with thick spring-loaded lenses because of mechanical compression against the lens epithelial cells. Expansion of the capsular bag with a possible mechanical effect by implantation of 2 silicone-plate lenses might partly explain the differences in ACO observed in both of the studies.

Reassessment of factors leading to ILO formation is important because of the development of dual-optic IOLs and also because piggyback implantation for correction of residual refractive errors appears to be increasing in

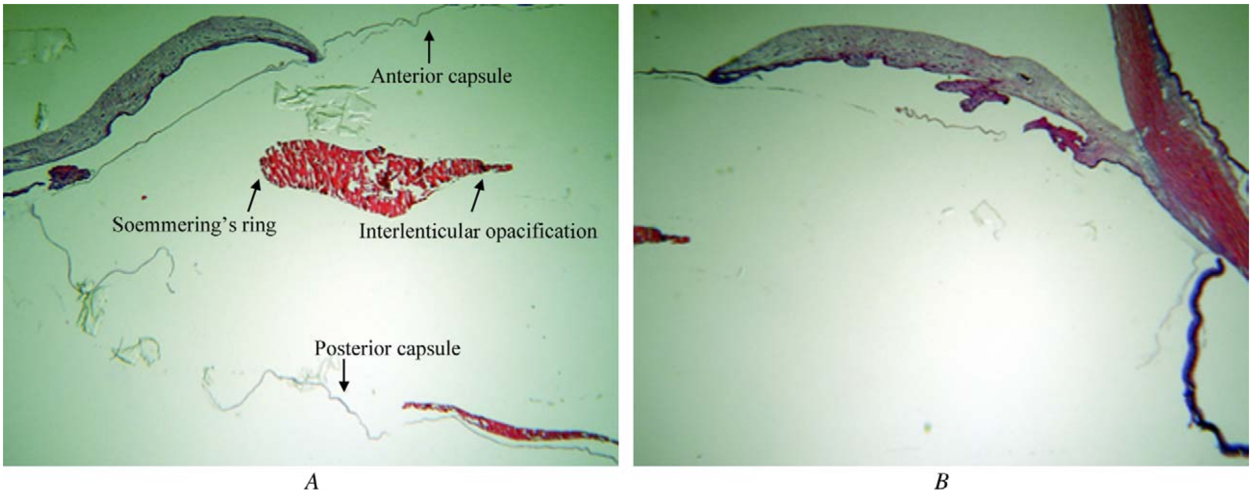

Figure 5. Photomicrographs of a histologic section cut from an eye implanted with a pair of silicone- plate lenses (rabbit number 5, left eye). *A* and *B* show the left and right side of the section, respectively (H&E stain; original magnification ×20). On the left side, the beginning of protrusion of the material within the Soemmering's ring into the interlenticular space can be seen. Proliferation on the central posterior capsule can also be observed. The capsular bag appears very expanded.

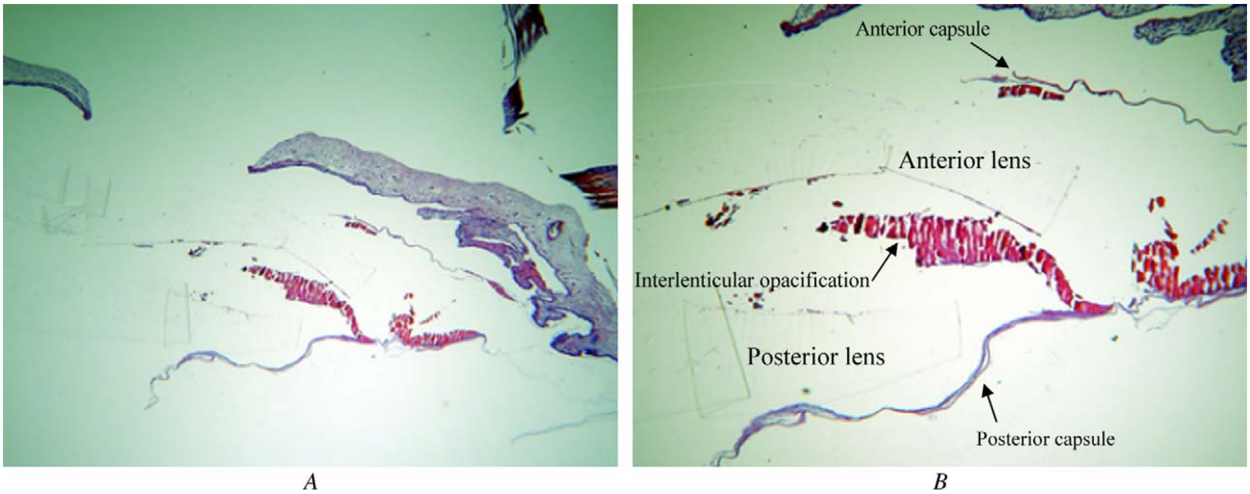

Figure 6. Photomicrographs of a histologic section cut from an eye implanted with a pair of AcrySof lenses (rabbit number 5, right eye). *A* and *B* show the right side of the section (H&E stain; original magnification ×20 and ×100, respectively). In this section, although the lenses were dissolved during the processing, their outline can be clearly observed. Note that the material within the Soemmering's ring protrudes into the interlenticular space. A fibrous proliferation onto the central posterior capsule can also be observed. The degree of capsular bag expansion appears to be less than that in Figures 4 and 5.

popularity.[16] We cannot forget that complete filling of the capsular bag by regenerating/proliferating lens material can occur in the rabbit eye if a long enough follow-up is observed.[17] The regeneration/proliferation of the material is also accelerated, and 6 to 8 weeks in the rabbit eye correspond to approximately 2 years in the human eye. Although this makes the rabbit model suitable for evaluation of proliferation within the capsular bag in relatively short periods of time, the results of this study need to be confirmed by clinical studies with long follow-ups.

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