Evaluation of posterior capsule opacification using a new posterior view method in rabbits

Single-piece acrylic versus 3-piece acrylic intraocular lens

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PURPOSE: To introduce a new procedure for evaluating posterior capsule opacification (PCO) in rabbit eyes and to perform a comparative study of the single-piece and 3-piece acrylic intraocular lenses (IOLs) on PCO using the new evaluation method.

SETTING: Jinshikai Medical Foundation, Nishi Eye Hospital, Osaka, Japan.

METHODS: A single-piece or 3-piece acrylic IOL was implanted in 1 eye and the other in the contralateral eye of 5 rabbits. Three weeks after surgery, PCO was scored by Evaluation of Posterior Capsule Opacification (EPCO) in posterior view. Before the posterior view was photographed, the anterior capsule was removed from the whole optic area to eliminate disturbing anterior capsule opacification (ACO) for the PCO evaluation.

RESULTS: Posterior capsule opacification could be well observed and viewed in the posterior view so that it could be scored by EPCO without confusion with ACO. The mean PCO score of the single-piece and 3-piece acrylic IOLs was 3.12 $\pm$ 0.19 and 2.41 $\pm$ 0.70, respectively (P<.05 and P = .03, respectively).

CONCLUSION: The removal of ACO allowed scoring of PCO by EPCO in rabbit eyes. The single-piece acrylic IOL showed singnificantly more PCO than the 3-piece acrylic IOL at least 3 weeks after surgery in rabbits.

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Recently, the most frequent postoperative complication after cataract surgery, posterior capsule opacification (PCO), has been reduced significantly by the sharp-edged intraocular lens (IOL).[1–8] Posterior capsule opacification, however, cannot be completely prevented and remains an important issue to be solved. The preventive effect of an IOL on PCO has been well known. We have pointed out the importance of matching design or material of the corresponding IOLs that were investigated.[9] While the role of material on the preventive effect could not be clarified clearly, 1 of the roles of design could be definitively proven as the sharp-edged optic formed a sharp posterior capsular bend that inhibited migration of lens epithelial cells (LEC) onto the posterior capsule. Since a sharp capsular bend was always seen in the eyes that received an IOL with sharp optic edges regardless of material,[1–3,9] the formation of sharp discontinuous capsular bend is the key for understanding the preventive effect of an IOL on PCO.

Besides the sharp optic edge, many other IOL-related factors, such as haptic length and angulation, single-piece or 3-piece IOL, optic size, optic thickness, and material,

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may be involved for the capsular bend formation. The relationship between IOL and capsule in size may also be an important factor. Thus, to clarify how each of these factors participates in the capsular bend formation is important to further optimize the PCO-preventive effect of an IOL.

In our previous study of how optic size is related to the preventive effect,[10] we showed that bulky haptics, such as those of the single-piece AcrySof IOL, and large optics hampered capsular adhesion, and particularly at the haptic root, resulted in abundant PCO. That study suggested that 3-piece acrylic IOLs might be superior to single-piece acrylic IOLs because of the reduction of PCO. In this paper, we compared the PCO-preventive effect between the single-piece acrylic and 3-piece acrylic IOLs, with particular attention to capsular bend formation at the haptic root.

SUBJECTS AND METHODS

Five pigmented Dutch rabbits (all weighed about 1.0 to 1.1 kg) were used for the study. All animal procedures were performed in compliance with the ARVO Statement for Use of Animals in an Ophthalmic and Vision Research.

Surgical Technique

The rabbits were anesthetized as reported previously.[1] Lens material was removed using phacoemulsification in an identical manner. Special care was taken to make a well-centered capsulorhexis approximately 3.5 to 4.0 mm in diameter to ensure that the anterior capsule edge was entirely apposed to the IOL optic. This was confirmed carefully under the operating microscope at the end of surgery in all rabbits. A single-piece acrylic IOL with a 6.0 mm optic (AcrySof SA) or 3-piece acrylic IOL with a 6.0 mm optic (AcrySof MA) was implanted in 1 eye, while the other was implanted in the contralateral eye. Heparin sodium 1000 U was added to the infusion solution of 500 mL to prevent fibrin formation during surgery. At the end of surgery, a mixture of 0.1 mL of dexamethasone (20 mg/mL) and 0.1 mL of gentamicin (40 mg/mL) was applied subconjunctivally and atropine sulfate eyedrop was instilled. No medication was given postoperatively.

Evaluation of Posterior Capsule Opacification

Three weeks after surgery, all animals were killed as described previously[1] and both eyes were enucleated. A small incision was made at the peripheral cornea and equatorial sclera of the enucleated eye so that neutral buffered formalin 10% could be infused into the globe to sufficiently fix the intraocular tissues for at least 48 hours. The PCO was evaluated by posterior view and histopathological section at the haptic root. The section was so determined that haptic angle, it passed the optic-cutting both haptics.

Posterior View

Because anterior capsule opacification (ACO) is generally disturbing for the observation and evaluation of PCO in the posterior view, ACO was removed from the anterior optic surface before evaluating PCO.

After the cornea was cropped near the limbus and the posterior globe near the pars plana in the remaining middle portion of the globe containing the IOL and the capsular bag, a radial incision was made from the pupillary margin toward the iris root. Then, the iris was removed by circumferencial cutting at its root and kept aside. The anterior capsule including the fibrotic continuous curvilinear capsulorhexis (CCC) was removed by a fine forceps. First, an attempt was made to incise the capsule at the anterior optic edge with a sharp razor blade, but this failed to cut the capsule unless the blade was pressed down hard against the optic. To prevent crushing the tissue structure underneath the IOL, a forceps was used. Part of the fibrotic CCC was first fastened, then pulled very gently. The capsule congruous to the CCC almost spontaneously tore along the outline, allowing the fibrotic CCC to be easily and entirely removed. Then, the remaining anterior capsule leaf was removed by tearing with the forceps, taking care that the tear did not run into the capsule over the optic edge. Finally, the ragged margin of the anterior capsule at the anterior optic edge was torn off with the forceps piece by piece. Then, the iris was placed on the original site. The PCO was observed under a microscope in the magnification 1× to 2× and photographed by a digital camera for microscopic documentation (DS-L1 and DS-5M, Nikon Instech Co. Ltd.), while the object was illuminated by a halogen fiber-optic light source.

Evaluation of Overall Posterior Capsule Opacification by EPCO

Each digital photograph of the posterior view was then submitted to the evaluation of PCO using the Evaluation of Posterior Capsule Opacification (EPCO) system.[11] The individual PCO score was calculated by multiplying the density of the opacification, graded from 0 to 4, by the fraction of capsule area within the optic area, according to the instruction.

Histopathological Examination

After the specimens (the remaining anterior segment containing the IOL and capsular bag without the iris and anterior capsule now) were sufficiently washed with distilled water and dehydrated with ethanol, they were placed in 100 mL of Technovit 7100 cold polymerizing resin (resin contained no agent for immunohistochemical section) for embedding (Heraeus Kulzer GmbH) and hardening agent I (contained in the kit, Kulzer Histo-Technik) for 60 minutes at room temperature. The specimens were then washed with distilled water. This procedure was repeated twice. The specimens were placed in Histoform Q (Teflon-embedding mold; Kulzer Co GmbH). The Technovit 7100 containing 1g of hardening agent II instead of agent I was injected into the Histoform Q as casting material. After 12 hours, the hardened block was removed from Histoform Q and sliced into 10 to 13 μm thick sections with a rotary microtome. The sliced specimens were immersed in distilled water and then gently placed on glass slides with a fine forceps. After drying, the specimens were stained with toluidine blue 10% or hematoxylin–eosin.

The capsule bending effect was evaluated using 4 grades as reported previously[3]: no effect (–), detectable (+), obvious (++), and distinct (+++). The grade was based on how distinctly the capsular bend was created by the optic edge and the amount of LECs that migrated over the optic edge further toward the posterior capsule.

RESULTS

After the iris was removed, it was confirmed that all eyes exhibited circumferential capsule–optic overlap without secondary retraction of the CCC rim behind the posterior optic in any case.

Posterior View

Comparison of the Posterior View Before and After Removal of the Anterior Capsule Opacification

Before removal of ACO, PCO could be differentiated from ACO only under a microscope with special attention, but not in the digital photographs. After removal of ACO, which precluded the exact observation of PCO in the posterior view, PCO could be well and clearly observed under a microscope and in the digital photographs so that PCO could be readily evaluated by EPCO in a digital photograph (Figure 1).

Gross Observation of Posterior Capsule Opacification

In a gross view, an extensive and intensive PCO area was remarkable in the eyes that received a single-piece AcrySof IOL. In 3 rabbits, PCO was more intense in the eye that received single-piece AcrySof IOL (Figure 1, rabbit 1; rabbits 2 and 4).

Posterior Capsule Opacification at the Haptic Root

In the eye with the single-piece AcrySof IOL, a very intensive LEC migration from the haptic root area in the optic–haptic angle was observed in all rabbits, at least at 1 haptic in rabbits 2 and 4, and at both haptics in rabbits 1, 3, (Figure 2) and 5, whereas such finding was observed just in rabbit 3 at 1 haptic with the 3-piece AcrySof IOL.

Posterior Capsule Opacification Score by EPCO

The density of the opacification and the corresponding capsule area could be easily defined, and the individual PCO score were calculated (Figure 3). In all rabbits, the PCO score was higher with single-piece AcrySof IOL (Table 1). The mean PCO score with single-piece AcrySof and 3-piece AcrySof IOLs was 3.12 $\pm$ 0.19 and 2.41 $\pm$ 0.70, respectively. Thus, the mean PCO score was significantly lower in the eyes with the 3-piece AcrySof IOL (Student t test, $P<.05$).

Histopathological Examinations

The edge effect is shown in Table 1. With the 3-piece AcrySof IOL, the capsular bending effect was obviously formed in all eyes except in rabbits 3 and 5; it was practically not present with all rabbits that received the single-piece AcrySof IOL (Figure 4).

DISCUSSION

The early and precise evaluation of PCO is important to compare different means for preventing PCO. Recently, several clinical methods have been developed for this purpose.[11–13] However, these clinical methods for humans can hardly be applied to rabbits because of the difficulty in taking retroillumination photographs of a good quality. Miosis and synechias that inevitably occur in rabbit eyes also

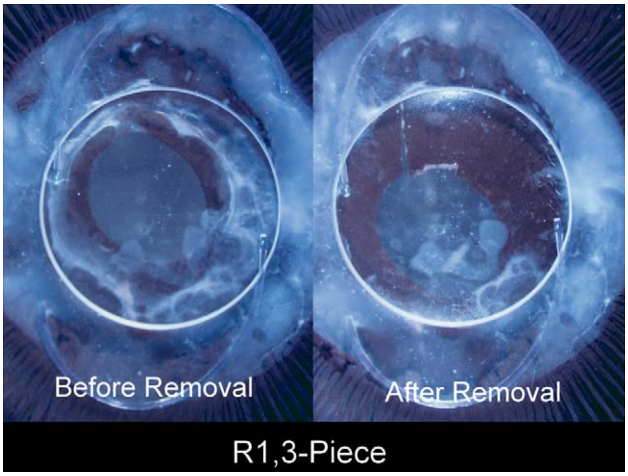

Figure 1. Posterior view of rabbit 1 before and after removal of the anterior capsule from the whole optic surface area. After removal, the opacified area on the optic showed merely PCO.

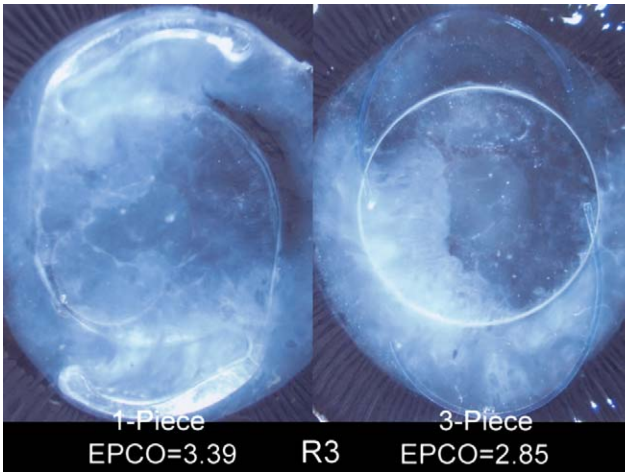

Figure 2. Posterior view of rabbit 3 after removal of the anterior capsule. Note that massive LECs had migrated from both haptic roots with the single-piece AcrySof IOL. The PCO is obviously noted more with the single-piece AcrySof IOL.

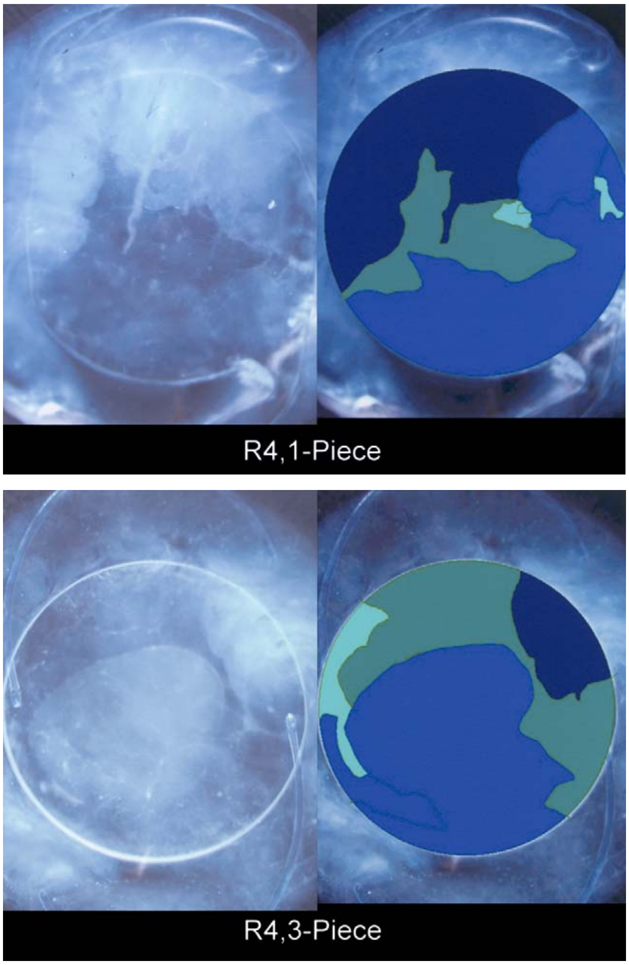

Figure 3. The PCO score by EPCO in rabbit 4. The PCO is distinctly noted more with the single-piece AcrySof IOL. Note a massive and intensive LEC migration at the upper haptic root with the single-piece AcrySof IOL.

impede the procedure. Therefore, the evaluation of PCO in rabbits had always been performed in the enucleated eye.

However, ACO always disturbed the view on PCO in the posterior view and impaired the exact and precise evaluation of PCO. After removal of the opacified anterior capsule, PCO could be clearly observed in the posterior view and PCO could be easily scored by EPCO in the digital photograph. Our concern was to alter the posterior capsule structure due to the manipulation to the opacified anterior capsule and its removal. However, histopathology showed that posterior capsule structure was apparently unharmed. The anterior capsule cannot be observed, but it does not matter because the posterior capsular bend can be observed at the posterior optic edge, which is relevant for the evaluation of the preventive effect of an IOL on PCO. The method of scoring PCO by EPCO appeared to have been established, as it is increasingly used clinically. We believe

Table 1. Posterior capsule opacification score by EPCO and capsular bending effect in histopathological sections.

			Equatorial Capsular Bend	
Rabbit	PCO	EPCO Score	Side 1	Side 2
1	Single-piece	2.90	+	–
	3-piece	1.17	+++	+++
2	Single-piece	3.12	–	–
	3-piece	2.76	–	++
3	Single-piece	3.39	–	–
	3-piece	2.85	–	+
4	Single-piece	3.21	+	–
	3-piece	2.66	++	++
5	Single-piece	2.98	+	–
	3-piece	2.60	+	–
Mean	Single-piece	3.12 ± 0.19		
Mean	3-piece	2.41 ± 0.70		($P<.05$)

Side 1 and Side 2: The 2 equatorial sides of a capsular section
PCO = posterior capsule opacification

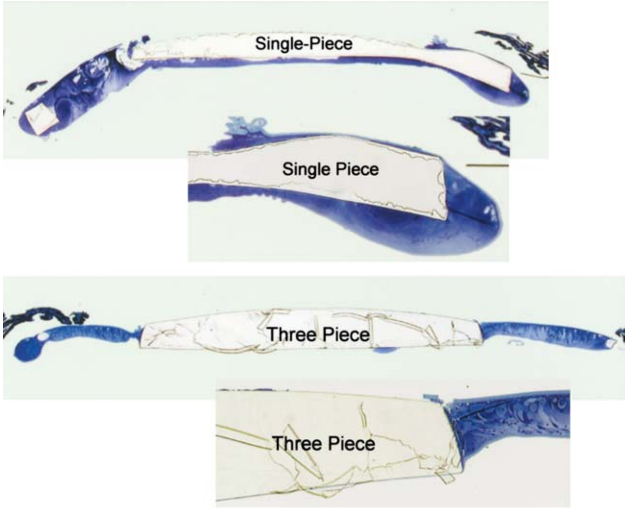

Figure 4. Histopathological findings of the posterior capsule of rabbit 1. With the single-piece AcrySof IOL, the capsular adhesion between the anterior and posterior capsules or the capsular bend was not present (*top*). Note the distinct capsular bending at the posterior sharp edge of the 3-piece AcrySof IOL (*bottom*).

that our procedure of the PCO evaluation could be a well established standard method for animal and post-mortem human PCO studies.

The results have shown that the 3-piece acrylic IOL was superior to the single-piece acrylic IOL in the EPCO score, thus indicating PCO reduction, as suggested in our former study,[10] at least 3 weeks after surgery in rabbit eyes.

To prevent LECs from migrating onto the posterior capsule, formation of the capsular bend at the entire posterior optic edge is important. For the bend formation, adhesion between the anterior and posterior capsules is an important and prerequisite process.[14] With the single-piece AcrySof IOL, there is less free space between the optic and haptic for the adhesion of the anterior and posterior capsules, particularly at the haptic root, so that the prerequisite of the bend formation did not take place. Additionally, there is no posterior optic edge at the haptic root because the haptic is as thick as the optic, which prevented the capsule from forming a bend (Figure 5).

In this study, a very intensive LEC migration from the haptic root area was observed in all rabbits at 1 or both haptics of the single-piece AcrySof IOL. This is in accordance with the above consideration, although the capsular bend formation was not obvious in some eyes that received the 3-piece AcrySof IOL, and migration of a considerable amount of LECs, although fewer than that in eyes with

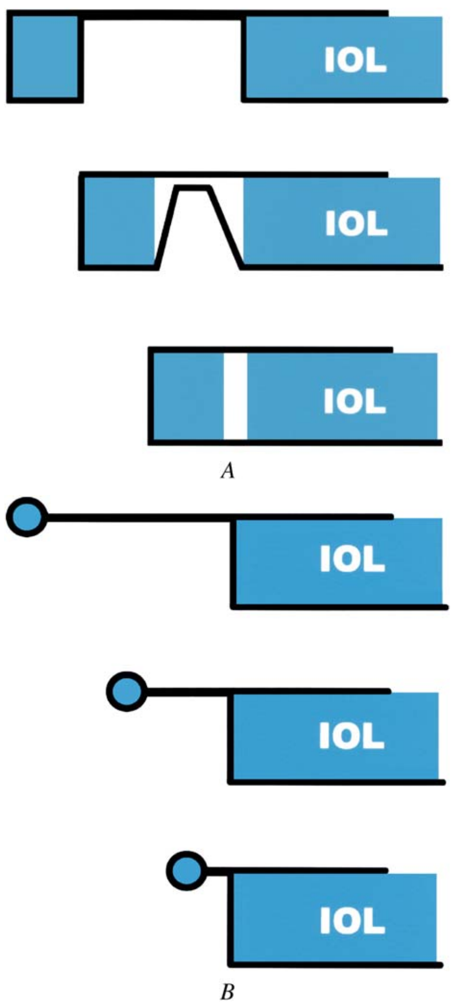

Figure 5. Capsular adhesion and bend formation at the haptic root in the single-piece and 3-piece AcrySof IOL. Capsular bend can be formed with the 3-piece AcrySof IOL thanks to the thin haptic, while with the single-piece AcrySof haptic, bulky and as thick as the optic, will hinder the capsular adhesion and therefore the bend formation in the haptic-optic angle.

the single-piece AcrySof IOL, was seen in these eyes. The rabbits used were young, and LECs, therefore, proliferated excessively and breached the capsular bend. Despite this excessive LEC proliferation, there was a significant difference between the 2 types of IOLs, which may have resulted from the difference in the haptic design and the degree of capsule bend formation.

There are still fewer clinical reports on the preventive effect of the single-piece AcrySof IOL. A report of 1 case[15] in which LEC had migrated at the haptic root 3 years after surgery suggests the possible failure of the capsular bend formation there. Bender et al.[16] reported that the PCO score was slightly higher with the single-piece AcrySof IOL, but there was no significant difference compared with the 3-piece AcrySof IOL in a 1-year follow-up. Nejima et al.[17] reported in a prospective randomized comparison between the single-piece and 3-piece AcrySof IOLs that while there was no statistically significant difference in PCO measurements, there was a tendency toward greater PCO in the single-piece AcrySof group. Wallin and coauthors[18] reported in a retrospective study of 75 patients that single-piece AcrySof IOLs were associated with more PCO, and the neodymium:YAG laser capsulotomy rate was higher, but the incidence did not reach statistical significance in this small study. In their prospective randomized study, Sacu et al.[19] reported that there was a significant difference between the single-piece and 3-piece AcrySof IOLs in terms of the AQUA score (PCO score) after 1 year. After 2 years, the difference became insignificant due to LEC regression. Studies with a greater population and longer follow-up period are needed.

In conclusion, a new method for the PCO evaluation, in which the posterior view is performed after removal of the anterior capsule, enables us to clearly observe and score PCO using EPCO system in enucleated rabbit eyes. An experimental comparison of the single-piece and 3-piece AcrySof IOL revealed that PCO score by EPCO was significantly greater with the single-piece AcrySof IOL 3 weeks after surgery in rabbits. This should be eventually proven by clinical studies.

REFERENCES

1. Nishi O, Nishi K. Preventing posterior capsule opacification by creating a discontinuous sharp bend in the capsule. J Cataract Refract Surg 1999; 25:521–526
2. Nishi O, Nishi K, Akura J, et al. Effect of round-edged acrylic intraocular lenses on preventing posterior capsule opacification. J Cataract Refract Surg 2001; 27:608–613
3. Nishi O, Nishi K, Wickstrom K. Preventing lens epithelial cell migration using intraocular lenses with sharp rectangular optic edges. J Cataract Refract Surg 2000; 26:1543–1549
4. Abela-Formanek C, Amon M, Schild G, et al. Uveal and capsular biocompatibility of hydrophilic acrylic, hydrophobic acrylic, and silicone intraocular lenses. J Cataract Refract Surg 2002; 28:50–61

5. Auffarth GU, Golescu A, Becker KA, et al. Quantification of posterior capsule opacification with round and sharp edge intraocular lenses. Ophthalmology 2003; 110:772–780
6. Buehl W, Findl O, Menapace R, et al. Effect of an acrylic intraocular lens with a sharp posterior optic edge on posterior capsule opacification. J Cataract Refract Surg 2002; 28:1105–1111
7. Kruger AJ, Schauersberger J, Abela C, et al. Two year results: sharp versus rounded optic edges on silicone lenses. J Cataract Refract Surg 2000; 26:566–570
8. Schauersberger J, Amon M, Kruger A, et al. Comparison of the biocompatibility of 2 foldable intraocular lenses with sharp optic edges. J Cataract Refract Surg 2001; 27:1579–1585
9. Nishi O. Posterior capsule opacification. Part I. Experimental investigations. J Cataract Refract Surgery 1999; 25:106–117
10. Nishi O, Nishi K. Effect of the optic size of a single-piece acrylic intraocular lens on posterior capsule opacification. J Cataract Refract Surg 2003; 29:348–353
11. Tetz MR, Auffuhrt GU, Sperker M, et al. Photographic image analysis system of posterior capsule opacification. J Cataract Refract Surg 1997; 23:1515–1520
12. Barman SA, Hollik EJ, Boyce JF. Quantification of posterior capsule opacification in digital images after cataract surgery. Invest Ophthalmol Vis Sci 2000; 41:3882–3892
13. Findl O, Buehl W, Siegl H, Pinz A. Removal of reflections in the photographic assessment of PCO by fusion of digital retroillumination images. Invest Ophthalmol Vis Sci 2003; 44:275–280
14. Nishi O, Nishi K, Akura J. Speed of capsular bend formation at the optic edge of acrylic, silicone, and poly(methyl methacrylate) lenses. J Cataract Refract Surg 2002; 28:431–437
15. Sugita M, Kato S, Sugita G, Oshika T. Migration of lens epithelial cells through haptic root of single-piece acrylic-foldable intraocular lens. Am J Ophthalmol 2004; 37:377–379
16. Bender LE, Nimsgern C, Jose R, et al. Effect of 1-piece and 3-piece AcrySof intraocular lenses on the development of posterior capsule opacification after cataract surgery. J Cataract Refract Surg 2004; 30: 786–789
17. Nejima R, Miyata K, Honbou M, et al. A prospective, randomized comparison of single and three piece acrylic foldable intraocular lenses. Br J Ophthalmol 2004; 88:746–749
18. Wallin TR, Hinckley M, Nilson C, et al. A clinical comparison of single-piece and three-piece truncated hydrophobic acrylic intraocular lenses. Am J Ophthalmol 2003; 136:614–619
19. Sacu S, Findl O, Menapace R, et al. Comparison of posterior capsule opacification between the 1-piece and 3-piece Acrysof intraocular lenses: Two-year results of a randomized trial. Ophthalmology 2004; 111:1840–1846