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Effect of Posterior Convexity of Intraocular Lenses on Lens Epithelial Cell Migration

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Purpose: To investigate in vitro how the posterior convexity of an intraocular lens (IOL) affected the migration of lens epithelial cells (LECs) under its optic.

Methods: Porcine LECs were cultured for 9 days with polymethylmethacrylate (PMMA) IOLs in a cell culture chamber insert containing a collagen membrane on which the IOLs were implanted. The central sagittal optic depths of the implanted IOLs were 0, 0.158, 0.303, and 0.452 mm. The migration of LECs was observed with an inverted phase microscope. The cell-free area under the IOL optic, where LECs had not migrated, was measured.

Results: As time elapsed, LECs migrated onto the collagen membrane beneath the IOL optics from the periphery to the central area in a concentric fashion in all IOL configurations. At 5 days in culture, the greater central sagittal optic depths of the IOL optic were associated with wider cell-free areas ($P = .0108$). At 9 days in culture, LECs almost completely covered the collagen membrane under IOLs with 0-, 0.158- and 0.303-mm central sagittal optic depth whereas the cell-free area under the 0.452-mm IOL was 4.3 ± 3.0% ($P = .0029$).

Conclusions: The posterior convexity of an IOL optic has an inhibitory effect on LEC migration under the optic. However, this inhibition had little effect after 9 days in culture. **Jpn J Ophthalmol 2003;47:332–337** © 2003 Japanese Ophthalmological Society

Key Words: Cell migration in vitro, intraocular lens, lens epithelial cells, posterior convexity.

Introduction

Following cataract surgery, residual lens epithelial cells (LECs) proliferate and migrate from the peripheral posterior capsular bag into the space between the posterior capsule and the optic of the intraocular lens (IOL). These LECs produce posterior capsule opacification (PCO),[1–4] a common complication causing decreased visual acuity after cataract surgery.[1] Patients with PCO who are treated with an Nd: YAG laser to remove a central region of the opacified posterior capsule usually recover their visual acuity, but this procedure is costly and uncommonly results in severe complications such as retinal detachment and secondary glaucoma.[1,5,6]

The design of an IOL influences the incidence of PCO,[1] and the configuration of the posterior surface of the IOL is believed to affect LEC migration.[1,7–10] The posterior convexity has an inhibitory effect because the summit of the curved surface of the IOL makes stronger contact with the posterior capsule than a planar surface (the "no space, no cells" theory).[1] While the convex design of the posterior optic has been reported to decrease the incidence of PCO,[7–10] Yamada et al[11] reported that the planar design also decreases the incidence. Disagreement between these studies may be attributed to confounding variables arising in clinical trials. Details of LEC migration are difficult to determine in patients by slit-lamp examination in vivo, while PCO in patients and even in experimental animals may be influenced by a variety of factors such as age, surgical procedure, and postoperative inflammation.[12,13] Because the degree of convexity protrusion of IOLs is related to IOL power, the convexity of IOLs implanted in each patient differs according to the optical power required.

Given the limitations of in vivo studies, various kinds of in vitro models have been developed.[12–17] These studies revealed that the IOL affects LEC migration under its optic.

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However, quantitative examination of LEC migration has not been carried out. We recently developed a simple in vitro system to facilitate quantitative examination of LEC migration under the IOL optic.[18] This model consists of a cell culture chamber insert containing a collagen membrane, on which the IOL can be implanted. LECs were cultured in this model, and their migration was observed using an inverted phase microscope. To examine whether the posterior convexity of an IOL has an inhibitory effect on the migration of LECs, LECs were cultured with IOLs having various posterior convexities.

Materials and Methods

Porcine LECs obtained as described previously[19] were cultured in a humidified atmosphere of 5% CO_2 and 95% air at 37ºC in a MED 10 medium, consisting of F-12 nutrient mixture (Life Technologies, Gaithersburg, MD, USA), 10% fetal bovine serum (FBS; Bioserum, Victoria, Australia), 0.15% sodium bicarbonate solution (Life Technologies), 50 units/mL penicillin (Life Technologies), and 50 µg/mL streptomycin (Life Technologies). LECs in primary culture were harvested using a solution of trypsin-EDTA (Life Technologies) for use in the following experiments. All procedures were carried out in accordance with the guidelines in the Association for Research in Vision and Ophthalmology Resolution on the Use of Animals in Research.

Migration of LECs under the IOL optic was evaluated in the culture model previously reported.[18] In brief, the model consisted of a cell culture chamber insert with a diameter of 10 mm that contained a collagen membrane (Kokencollagen CM-24; Funakoshi, Tokyo). The insert was placed in a 35-mm dish (Becton Dickinson Labware, Franklin Lakes, NJ, USA). The collagen membrane consisted of atherocollagen that had been extracted from the insoluble collagen of bovine dermis; substances of low molecular weight such as amino acids and glucose can penetrate this membrane. A 200-µL volume of MED 10 was added to the insert, and 3 mL of MED 10 was added to the dish, which then was incubated in 5% CO_2 at 37ºC for 24 hours. Following incubation, the IOL was implanted into the insert. Since the haptics were hooked to the bottom of the insert wall, the IOL optic pushed the collagen membrane downward, with slight stretching of the membrane. In this manner, the IOL optic was fitted to the collagen membrane. Two hours later, 100 µL of a suspension of porcine LEC (10000 cells/insert) was added.

Characteristics and physical parameters of the IOLs used in this study are shown in Table 1. These IOLs included a convex-plano IOL with +20 diopters (D) (UY-5TE; HOYA Healthcare, Tokyo) and biconvex IOLs (UY-5TEB; HOYA) with +8.5, +16.0, or +22.0 D. The material and design of these IOLs were identical except for configuration of the anterior and posterior surface of the optic. All optics were 6.5 mm in diameter. Central sagittal optic depths (the perpendicular distance between the summit of the posterior curved surface and the peripheral posterior rim; Figure 1) of these IOLs were 0 mm for the convex-plano IOL, 0.158 mm for the biconvex IOL with +8.5 D, 0.303 mm for the biconvex IOL with +16.0 D, and 0.452 mm for the biconvex IOL with +22.0 D. These IOLs had undergone ‘‘tumble-polishing’’, in which all parts of the IOL are polished equally in a tumbling barrel, producing a rounded optic edge.

Table 1. Characteristics of Implanted Intraocular Lenses (IOLs)

	Central Sagittal Optic Depth (mm)			
Characteristic	0	0.158	0.303	0.452
Configuration	Convex-plano	Biconvex	Biconvex	Biconvex
Power (diopters)	+20.0	+8.5	+16.0	+22.0
Optic material	PMMA	PMMA	PMMA	PMMA
Optic diameter (mm)	6.5	6.5	6.5	6.5
Radius of curvature of posterior surface (mm)	–	33.50	17.58	11.91
Area of posterior surface (mm^2)	33.18	33.26	33.47	33.87
Configuration	Convex-plano	Biconvex	Biconvex	Biconvex
Haptic material	Polypropylene	Polypropylene	Polypropylene	Polypropylene
Haptic angle	5º	5º	5º	5º
Overall diameter (mm)	13.5	13.5	13.5	13.5
Weight (mg)	27.6	17.4	23.5	27.9

PMMA: polymethylmethacrylate.

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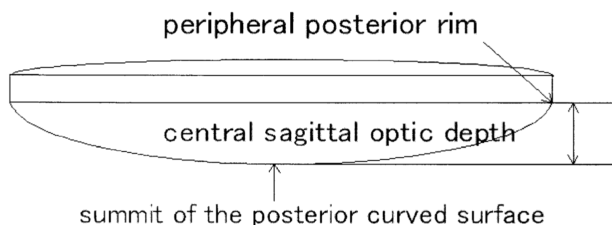

Figure 1. Schematic drawing of an intraocular lens. Central sagittal optic depth is the perpendicular distance between the summit of the posterior curved surface and the peripheral posterior rim.

Migration of the LECs under the IOL optic was observed and photographed using an inverted phase microscope over a 9-day period. The extent of the cell-free area where the LECs had failed to migrate beneath the IOL optic (Figures 2A and 2B), and the extent of cell-occupied areas, where LEC had migrated, were measured using NIH Image 1.47 software (developed by the US National Institutes of Health, Bethesda, MD, USA), and expressed as a percentage relative to the area of the entire IOL optic. However, when biconvex IOLs were implanted, the cell-free or cell-occupied areas measured in a planar field with inverted phase microscope were slightly smaller than the real area because of the indentation of the collagen membrane caused by the convexity of the posterior surface. Therefore, a corrected cell-occupied area was calculated using the following formula when a biconvex IOL was implanted:

$$\text{Corrected cell} - \text{occupied area} = 2\pi r_p\left[h - (r_p - \sqrt{r_p^2 - r_{cf}^2})\right],$$

where h is the central sagittal optic depth of the IOL, r_p is the radius curvature of the posterior surface of IOL; and

$$r_{cf}: \text{the radius of the cell-free area} = \text{radius of IOL optic} \times \sqrt{\text{cell} - \text{free area}(\%) \div 100}.$$

Data are presented as the mean ± SD for four wells. Differences were evaluated by one-way analysis of variance (ANOVA) and Fisher's protected least significant difference test. A level of $P < .05$ was accepted as indicating statistical significance.

Results

Within 24 hours after plating, most LECs attached directly to the peripheral collagen membrane where no IOL optic was present. LECs had begun to migrate into the space between the collagen membrane and the IOL optic at 24 hours after plating. No difference was noted in the mode of LEC migration under each IOL. There was no optic edge on any polymethylmethacrylate (PMMA) IOLs implanted in this study which blocked completely the migration of LECs. LECs continued to migrate onto the collagen membrane beneath the IOL optic from the periphery to the central area in a concentric fashion as time elapsed (Figures 3 A-D).

LECs had not completely covered the collagen membrane under any IOL at 5 days in culture (Figures 4A and 4B). However, LECs in all inserts of an IOL with a 0-mm central sagittal optic depth (4/4) and in one insert

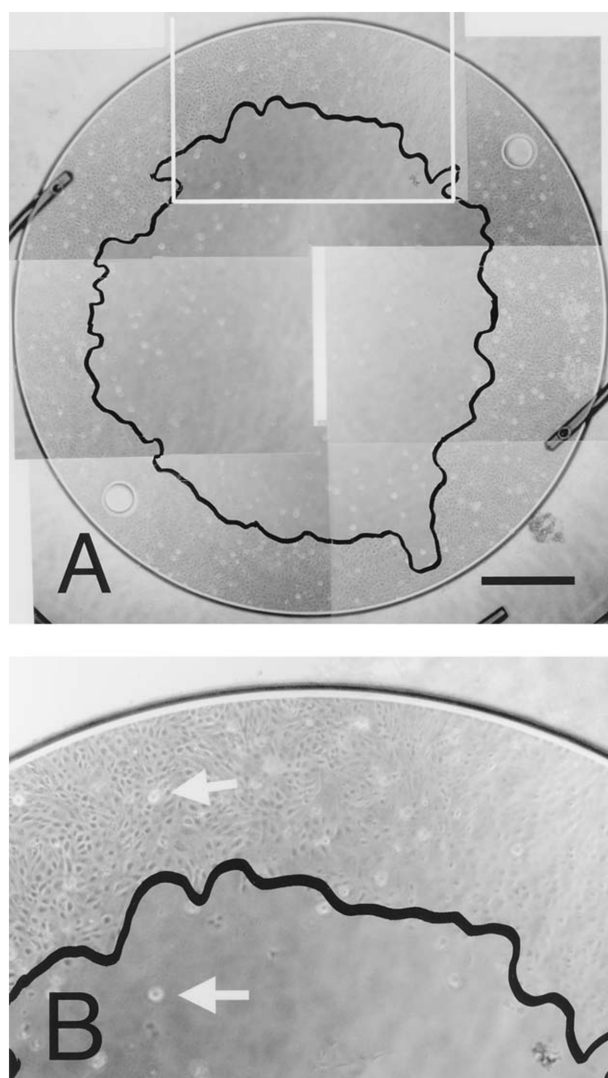

Figure 2. Photographs of lens epithelial cells (LECs) obtained using a phase microscope to show migration beneath an intraocular lens (IOL) optic. The area enclosed within the black line in A indicates the cell-free area where LECs have not migrated. Bar = 1 mm. B shows a higher magnification of A. Some LECs (arrows) attached to the upper surface of the IOL optic are out of focus.

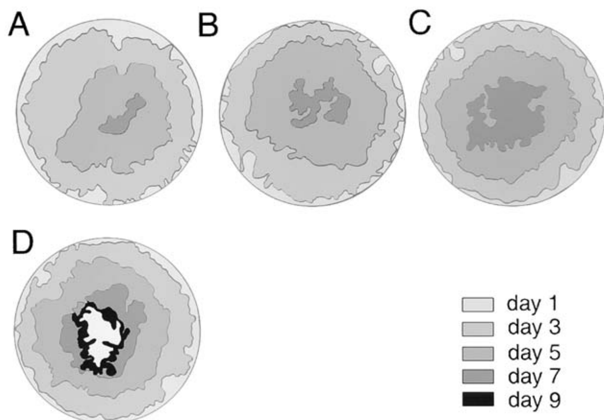

Figure 3. LEC migration under IOLs with central sagittal optic depths of 0 (A), 0.158 (B), 0.303 (C), and 0.452 mm (D). In A to D, migration of LEC occurred from the periphery to the central area in a concentric fashion. The IOLs showed no blockade of LEC migration at the optic edge. LECs completely covered the collagen membrane under IOLs with 0- (A), 0.158- (B), and 0.303-mm (C) central sagittal optic depth, but not under IOLs with a 0.452-mm central sagittal optic depth (D).

of an IOL with a 0.158-mm central sagittal optic depth (1/4) completely covered the collagen membrane at 6 days of culture, reducing the cell-free area to 0%. Such confluent LECs could no longer migrate. Therefore, cell-free areas at 5 days of culture were used to examine the effect of convexity. Cell-free areas under IOLs with greater central sagittal optic depth were wider. LEC migration was inhibited in proportion to the central sagittal optic depth of the IOL (Figure 4B). However, a possibility existed that the indentation of the collagen membrane by the convexity of the posterior surface might have brought about a spurious difference, since IOLs with greater central sagittal optic depth had a wider area of collagen membrane under the optic. Corrected cell-occupied areas therefore were calculated. IOLs with greater central sagittal optic depth had smaller corrected cell-occupied areas (Figure 5).

At 9 days in culture, LECs almost completely covered collagen membranes under IOLs with 0-, 0.158- and 0.303-mm central sagittal optic depths (cell-free areas: 0.0 ± 0.0%, 0.14 ± 0.28%, 0.0 ± 0.0%, respectively) while LECs could not completely cover the collagen membrane under IOLs with a 0.452-mm central sagittal optic depth. The cell-free area under these IOLs was 4.3 ± 3.0% (P = .0029; ANOVA, Figure 4A).

Discussion

In this study LECs were found to migrate through the space between the posterior surface of the IOL optic and the collagen membrane. This LEC migration was affected by the configuration of the posterior surface of the IOL. IOLs with greater central sagittal optic depth inhibited LEC migration more effectively. However, at 9 days in culture, LECs almost completely covered the collagen membrane under IOLs with central sagittal optic depths of 0, 0.158 and 0.303 mm. The cell-free area under IOLs with a 0.452-mm central sagittal optic depth was only 4.3 ± 3.0% at 9 days in culture.

Although LECs could not completely cover the collagen membrane under IOLs with a 0.452-mm central sagittal optic depth at 9 days in culture, collagen membranes

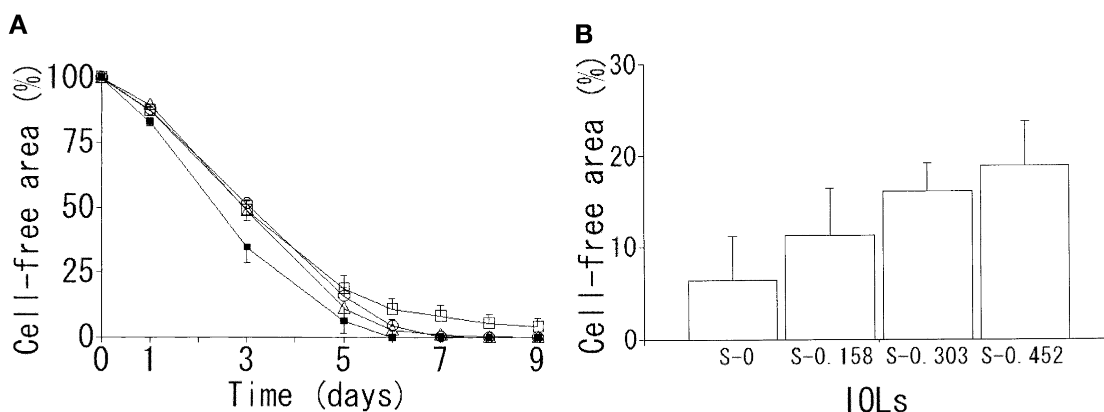

Figure 4. IOL type and overall cell-free area. (A) time course of changes in cell-free area beneath the following IOL optics: central sagittal optic depth of 0 mm (solid squares), 0.158 mm (open triangles), 0.303 mm (open circles), and 0.452 mm (open squares).(B) influence of IOLs on cell-free area (P = .108; one-way ANOVA). Areas were measured on day 5. Significant differences were detected between the areas under IOLs with central sagittal optic depths of 0 mm and 0.303 or 0.452 mm and between the areas under IOLs with central sagittal optic depths of 0.158 mm and 0.452 mm. For A and B, values are the mean ± SD for four culture preparations.

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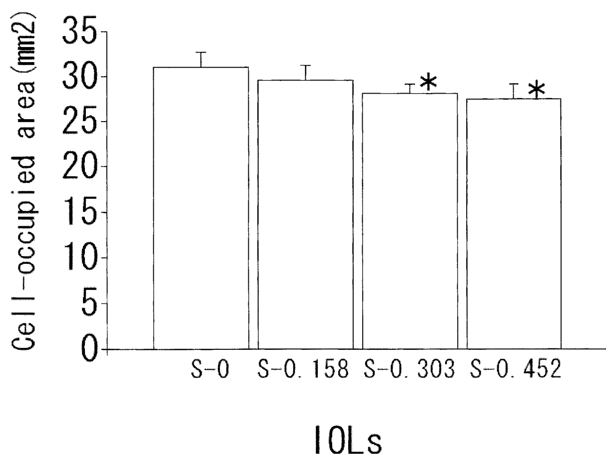

Figure 5. Influence of IOLs on the corrected cell-occupied area ($P = .0282$; one-way ANOVA). Areas measured on day 5 were corrected by using a calculation formula as described in the text. Significant differences were detected between the corrected cell-occupied area under IOLs with central sagittal optic depths of 0 mm and 0.303 or 0.452 mm. Values are the mean ± SD for four culture preparations.

under the other three types of IOLs were fully occupied by LECs. Thus the convexity of the posterior surface of the IOL optic showed only a weak inhibitory effect on LEC migration. We previously reported that cell-free areas under IOLs with a sharp edge (acrylic, 41.1 ± 8.0%; sharp-edged convex-plano PMMA, 60.9 ± 39.0%), were significantly larger than the cell-free areas under IOLs with a round edge (silicone, 0.0 ± 0.0%; round-edged biconvex PMMA, 1.5 ± 1.2%) at 10 days in culture using the same in vitro model.[18] Accordingly, a sharp edge may act as a barrier to LEC migration. Nagata et al[20] reported that most eyes with sharp-edged IOLs, either biconvex or convex-plano, had clear posterior capsules, while patients with round-edged IOLs showed a marked tendency toward PCO. These findings also suggested that the effect of convexity of the posterior surface of the IOL optic was relatively slight, and that other factors such as edge sharpness of IOL optic[18,20–22] or optic material[18,23,24] may be more important for preventing PCO.

Ninn-Penderson et al[25] reported that the frequency of Nd: YAG laser posterior capsulotomy for PCO was not related to preoperative axial length among eyes implanted with posterior-convex IOLs. Because the IOL power needed for correction of eyes with shorter axial length is greater, IOLs implanted in these eyes would be more convex. Therefore, although other factors might have masked the effect of posterior convexity, the effect of posterior convexity appeared to be slight.

In this study, IOLs with greater central sagittal optic depth inhibited LEC migration more effectively. The weight of a biconvex IOL with greater central sagittal optic depth is greater. Because a heavy IOL would press more forcefully on the collagen membrane than a light IOL, differences in IOL weight could affect LEC migration. In this study, the weight of the lightest IOL was 17.4 mg (a biconvex IOL with a 0.158-mm central sagittal optic depth), while one of the heaviest IOLs weighed 27.9 mg (a biconvex IOL with a 0.452-mm central sagittal optic depth). However, because the specific gravity of PMMA is 1.18, the effective weight difference in the medium was only about 2 mg. Moreover, a convex-plano IOL with a 0-mm central sagittal optic depth weighed 27.6 mg, nearly the same as a biconvex IOL with a 0.452-mm central sagittal optic depth. This convex-plano IOL inhibited LEC migration less effectively than a biconvex IOL with a 0.158-mm central sagittal optic depth (17.4 mg). These findings suggest that the effect of pressure from the weight of IOL was only slight.

In our model, the collagen membrane of the cell culture insert can be stretched to fit the posterior surface of the IOL, whether this surface is flat or convex. However, in vivo, because the posterior lens capsule is curved, a planar surface of an IOL might be more difficult to fit to the posterior lens capsule. This difference between our collagen membrane and the posterior lens capsule might have caused underestimation of the effect of posterior convexity.

The optic edge of IOLs may have had limited blocking effect on LEC migration because of the rounded optic edge. Using an in vitro model, in which LECs remaining in the lens capsular bag were cultured with the IOLs, Nagamoto et al[13] found that the optic edge of a convex-plano PMMA IOL blocked migration of LEC more effectively than the optic edge of a biconvex PMMA IOL. However, these authors did not examine the effect of configuration on LEC migration after LECs had migrated beyond the IOL optic edge. In our present study, blocking of LEC migration by the edge of either convex-plano or biconvex optics was not observed. Had the optic edge blocked LEC migration, the effect of posterior convexity might have been masked.

In conclusion, using an in vitro model, we found that the posterior convexity of an IOL optic had an inhibitory effect on LEC migration under the optic. However, this effect was not strong, and the cell-free area was minimal after 9 days in culture, even with an IOL having a central sagittal optic depth of 0.452 mm. In preventing PCO, the material and edge sharpness of an IOL optic may be more important than posterior convexity.

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