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The Relationship Between Morphological Changes of Lens Epithelial Cells and Intraocular Lens Optic Material

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Abstract: To examine the morphological changes of lens epithelial cells (LECs) occurring directly beneath and at regions contacting various intraocular lens (IOL) optic materials, human LECs were cultured on human anterior lens capsules and were further incubated upon placing above the cells lens optics made of polymethylmethacrylate, silicone, and soft acrylic material. Observations as to the morphological changes of LECs under phase-contrast microscope and scanning electron microscope were performed on the 14th day of incubation. Gatherings of LECs were observed at regions contacting the soft acrylic material under phase-contrast microscope, and gatherings of LECs were observed accurately at the same regions mentioned above under scanning electron microscope. On the other hand, LECs in contact with two other optic materials did not show morphological changes. The results suggest that LECs attached to and proliferated on not only the anterior lens capsules but also the soft acrylic IOL optics. The model used in this study may be useful in studying the relationship between cellular movement of LECs and IOL optic material. **Jpn J Ophthalmol 1998;42:46–50** © 1998 Japanese Ophthalmological Society

Key Words: Gathering of lens epithelial cells, human lens epithelial cell, intraocular lens, phase-contrast microscope, scanning electron microscope.

Introduction

While intraocular lens (IOL) implantation has become the method of choice today for restoring postoperative vision following cataract extraction, its procedure continues to undergo improvement. New types of IOLs are also constantly introduced in an attempt to provide better surgical outcome. Soft-material or foldable IOLs made of silicone or soft acrylic material, which were developed for small-incision cataract surgery aimed to minimize postoperative astigmatism and provide early recovery, significantly contributed in disseminating the small-incision sutureless method.[1–4] As to the postoperative results after making use of silicone IOL or soft acrylic IOL, it was reported that the frequency of occurrence of postoperative posterior capsule opacification was different between cases making use of silicone IOL and cases making use of soft acrylic IOL.[5] It is possible that the different frequency of occurrence of postoperative posterior capsule opacification mentioned above was caused by the differences of cellular movement of lens epithelial cells (LECs) proliferating onto the posterior capsule. Therefore, in this study, differences of cellular movement of LECs to IOL optics made of different materials using the cell culture system were examined.

Materials and Methods

Anterior lens capsules adhering to LECs were obtained following anterior capsulotomy during cataract surgery from patients ranging in age from 42 to 78 years. To detach the sheets of LECs, the capsules were treated for 60 minutes at 37°C with Dispase II (Godo Shusei, Tokyo, Japan), 2000 protease units/mL in concentration, adjusted using Eagle's minimum essential medium (MEM) (Nissui Seiyaku, Tokyo, Japan), which was supplemented with bovine fetal serum of 12% concentration (Gibco Laboratories, Life Technologies, Inc., Grand Island, NY, USA). The sheets of detached LECs were next collected and placed onto the center of a 35-mm-diameter

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Table 1. Composition and Power of Intraocular Lens Optics Used

Material	Power
Polymethylmethacrylate	+20.0 Diopters
Silicone	+20.0 Diopters
Soft acrylic material	+20.0 Diopters

plastic culture dish (Falcon 3001) filled with 2.0 mL of 12% MEM to be incubated for 7 days in an incubator at 5% CO_2 and 95% air, 100% humidity, and 37°C (LNA-IIIDH, Tabai, Osaka, Japan). The medium was changed every 3 days.

The remaining anterior lens capsules deprived of LECs were washed thoroughly with Ca^{2+}, Mg^{2+}-free phosphate buffered saline (PBS). Fifteen 35-mm-diameter plastic culture dishes, each containing at its center a capsule placed on the side not having adhered LECs prior to their detachment, were prepared and incubated in the dark for 7 days.

Following 7 days of incubation, LEC sheets were treated with trypsin (Mochida Pharmaceutical, Tokyo, Japan) of 1000 units/mL in concentration to isolate each cell; 1×10^4 cells were next mixed in 40 μL of 12% MEM, covering the capsules at the center of each dish, and were again incubated.

On the first day of incubation, upon confirming cell adhesion on all capsules using the phase-contrast microscope (DIAPHOT-TMD, Nikon, Tokyo, Japan), IOLs were placed face down above the cells in 15 dishes, and the cells were further incubated with 500 μL of 12% MEM medium. Fifteen IOLs were used in this study. Five IOLs had optics made of polymethylmethacrylate (PMMA), 5 IOLs had optics made of silicone, and 5 IOLs had optics made of

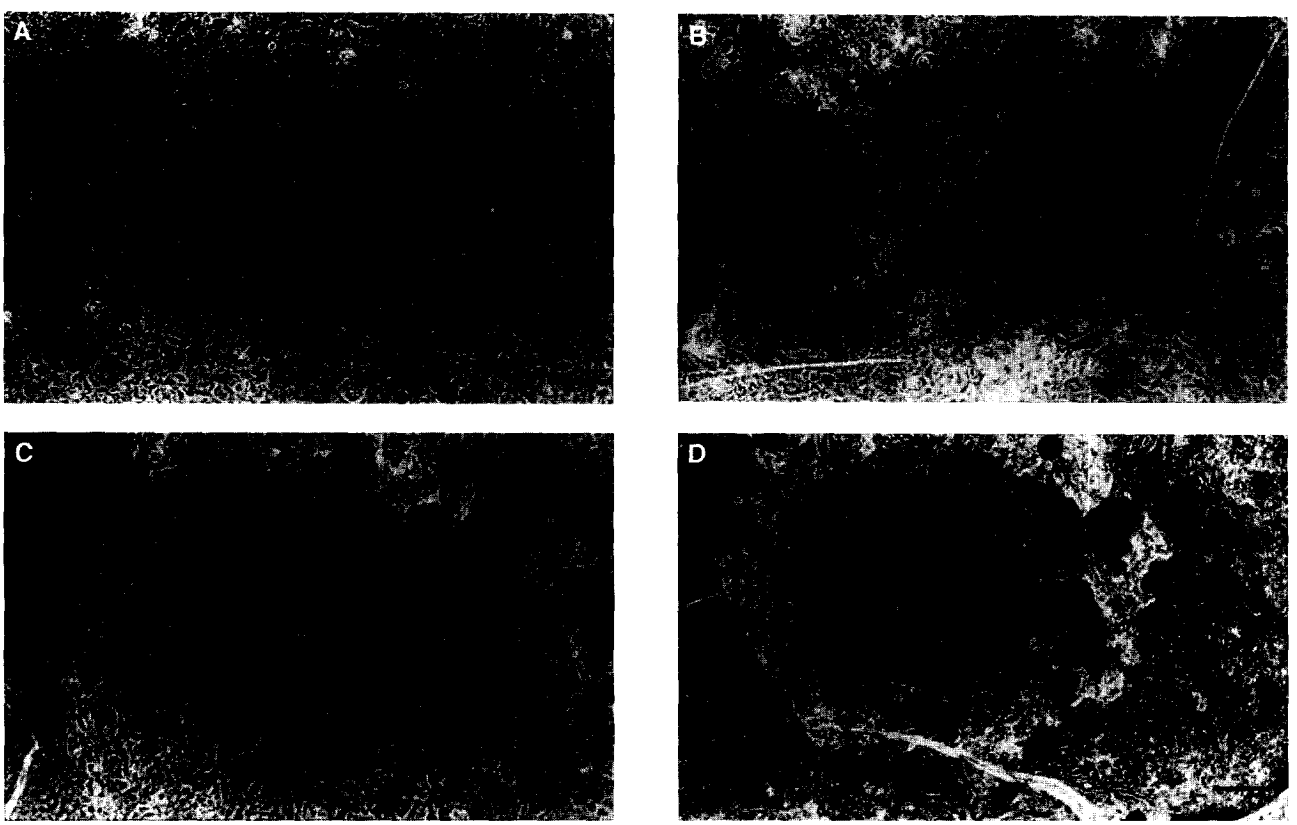

Figure 1. (**A**) Cellular morphology of lens epithelial cells (LECs) in the control groups (bar = 230 μm). (**B**) Cellular morphology of LECs after removing the intraocular lens (IOL). Arrows indicate that the LECs had been observed beneath the IOL, and arrowheads indicate that the LECs had been observed at regions contacting the optics (bar = 230 μm). (**C**) Cellular morphology of LECs after removing the IOL. Arrows indicate that the LECs had been observed beneath the IOL, and arrowheads indicate that the LECs had been observed at regions contacting the optics (bar = 230 μm). (**D**) Cellular morphology of LECs after removing the IOL. Arrows indicate that the LECs had been observed beneath the IOL, and arrowheads indicate that the LECs had been observed at regions contacting the optics (bar = 230 μm).

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soft acrylic material (Table 1). Fourteen days after incubation, LECs directly below and at regions in contact with each optic were observed using the phase-contrast microscope to determine which optics cause morphological changes of LECs. On the other hand, the cellular morphology of 1×10^4 cells cultured on the capsules without IOLs were observed using the phase-contrast microscope on day 14 of incubation as a control.

On day 14 of incubation, all IOLs were removed from the capsules, and morphology of cells attaching to the capsules after removing the optics were observed using the phase-contrast microscope.

For evaluating the morphological changes of the LECs at regions contacting the optics, all removed IOLs having remaining LECs on the optics were gently washed with PBS supplemented with Ca^{2+} and Mg^{2+}. The cells adhering to the optics were next fixed with 0.5% glutaraldehyde, and adhering LECs of each sample were observed under a JSM-840A model scanning electron microscope (Nihondenshi Co., Tokyo, Japan) after they had undergone sputter coating with gold using an IB-3 model (Eicoengineering Co., Tokyo, Japan).

Results

The following observations of cellular morphology on day 14 of incubation were made using a phase-contrast microscope:

1. *Control groups:* The cultured LECs were observed uniformly, and the gatherings of LECs were not observed in the control groups. (Figure 1A).
2. *PMMA IOLs:* The PMMA IOLs were removed from the capsules in all cultures to examine for the cellular morphology beneath the IOL optics and at regions contacting the IOL optics. The gatherings of LECs were not observed in all cultures of both regions beneath the IOL optics and regions contacting the IOL optics (Figure 1B).
3. *Silicone IOLs:* Silicone IOLs were removed from the capsules in all cultures to examine for the cellular morphology beneath the IOL optics and at regions contacting the IOL optics. The gatherings of LECs were not observed in all cultures of both regions beneath the IOL optics and regions contacting the IOL optics (Figure 1C).
4. *Soft acrylic material IOLs:* All three cultures disclosed gatherings of LECs at regions contacting the optics. On the other hand, gatherings of LECs were not observed at regions beneath the IOL optics (Figure 1D). However, as the gatherings of LECs were not clear under the low magnification using the phase-contrast microscope, the gatherings of LECs existing at regions contacting the optics were observed under the higher magnification. As a result, the gatherings of LECs were observed clearly (Figure 2).

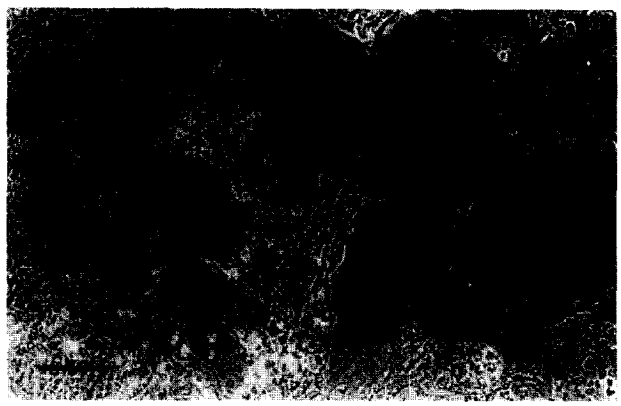

Figure 2. Gatherings of lens epithelial cells (LECs), indicated by the arrows, were observed clearly at regions contacting the optics. The arrowhead indicates the region having LECs that migrated and extended toward the optic. The asterisk indicates the region having LECs that existed beneath the optic (bar = 50 μm).

The following observations of cellular morphology were made using a scanning electron microscope:

1. *PMMA IOLs:* As to the cellular morphology of LECs that existed at regions contacting the IOL optics, the findings indicating cell–cell adhesion were observed in all cases. However, the gatherings of LECs were not observed (Figure 3A).
2. *Silicone IOLs:* As to the cellular morphology of LECs that existed at regions contacting the IOL optics, some expanding LECs were observed in all cases, However, the gatherings of LECs were not observed (Figure 3B).
3. *Soft acrylic material IOLs:* The gatherings of LECs were observed accurately at regions contacting the IOL optics in all cases (Figure 3C).

Discussion

This study obtained human anterior lens capsules adhering to LECs during cataract surgery; the cells were isolated and incubated on the capsules, followed by incubation of three types of IOL optic materials placed above these cells. Using the phase-contrast microscope, the cells directly below and at regions contacting the optics were examined for any morphological changes and the influence of different

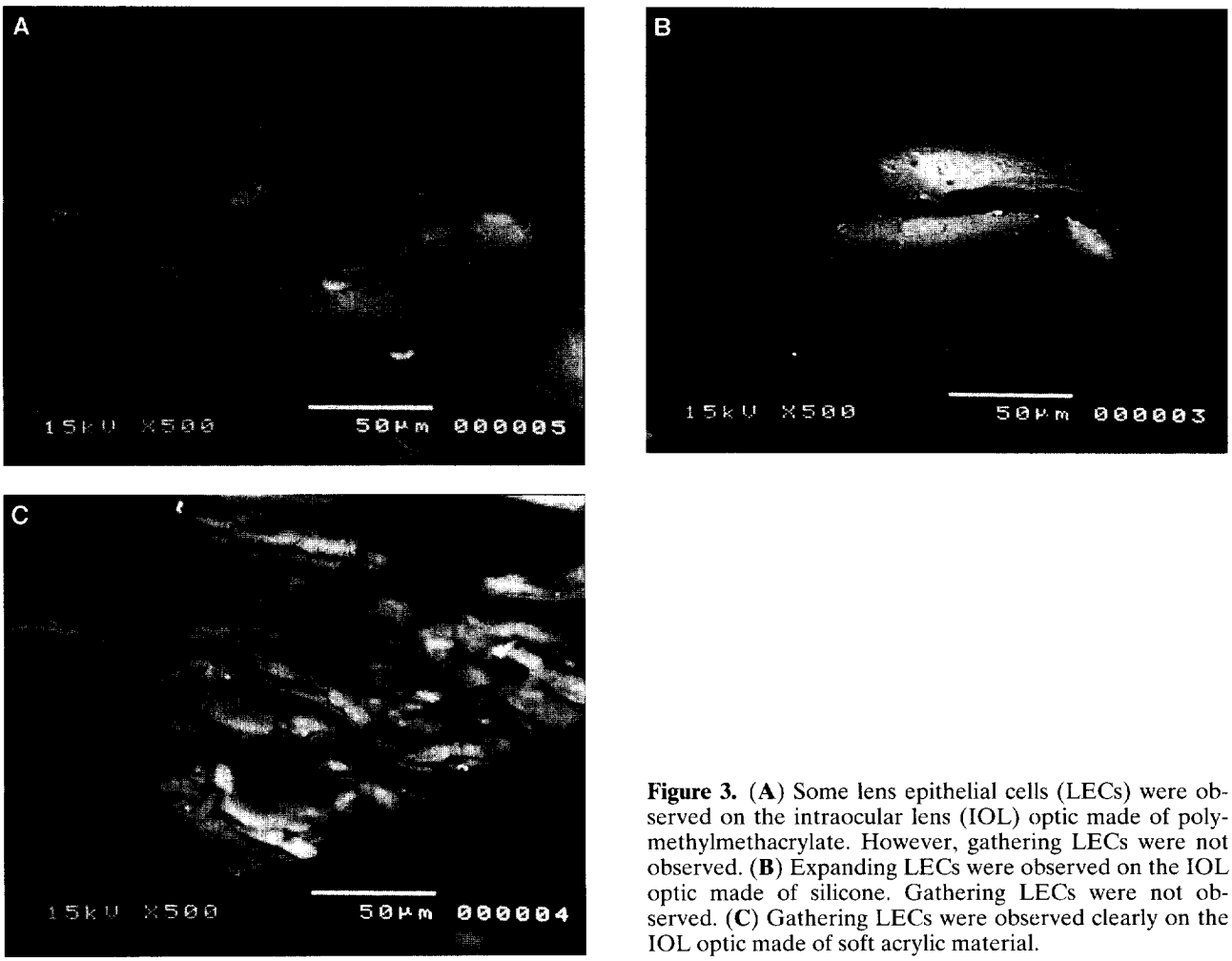

Figure 3. (**A**) Some lens epithelial cells (LECs) were observed on the intraocular lens (IOL) optic made of polymethylmethacrylate. However, gathering LECs were not observed. (**B**) Expanding LECs were observed on the IOL optic made of silicone. Gathering LECs were not observed. (**C**) Gathering LECs were observed clearly on the IOL optic made of soft acrylic material.

optic materials on LEC behavior. At regions where the LECs contacted the optics, LECs reacted differently to various optic materials. The gatherings of LECs were observed on day 14 of incubation with soft acrylic material IOLs under phase-contrast microscope, and gatherings of LECs were observed accurately on the soft acrylic material IOLs under scanning electron microscope. On the other hand, these findings were not observed on day 14 of incubation with PMMA IOLs and silicone IOLs. So, what caused the differences in LEC behavior when coming into contact with different optic materials? The adhesion rate of LECs to different optic materials has previously been reported.[6]

That result indicated that soft acrylic material IOLs showed a greater LEC adhesion rate than those of other materials. From the result mentioned above, reasons as to why LECs that existed at regions contacting the IOL optics made of soft acrylic material gathered toward each other may be inferred.

Compared to PMMA and silicone IOLs, the soft acrylic IOL placed on the anterior lens capsule-culturing LECs demonstrated more adherence of LECs beneath and at regions contacting the optic, which is understandable when considering the nature of the soft acrylic material, and this property is believed to increase with time. On the other hand, because some LECs on the anterior lens capsule do not contact the lens, one should expect to see these cells migrate and extend toward the optic. It may be hypothesized, however, that these cellular migrations are arrested at regions where the cells come into contact with the soft acrylic material due to the following reason.

Assume that LECs existing beneath and at the edge of the optic easily attach to the lens material and continue to increase in adherence; these cells will prohibit the peripheral cells from migrating and extending toward the lens center, eventually causing them to gather at the edge of the lens to migrate and

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extend onto the optic. So, how do we make good use of this characteristic point of the IOL optics made of soft acrylic material? Until now, lower frequency of postoperative posterior lens capsule opacification after making use of soft acrylic material IOLs compared with those after making use of IOLs made of other materials was reported.[5] In fact, the frequency of occurrence of postoperative posterior lens capsule opacification after making use of soft acrylic IOLs was 4.7%, and that after making use of silicone IOLs or PMMA IOLs was 29.8% or 27.5% in the hospital where I worked.

In this study, LECs were cultured on anterior lens capsules and placed onto IOLs made of different biomaterials to study the morphological changes of the cells with time. In actual clinical situations, however, a larger area of the optic and the posterior lens capsule is believed to be in contact when a biconvex lens is used. If this is the case, then the regions where LECs from the anterior capsule migrate and extend toward the lens edge contact the IOL optic are close to the equator. That is to say, after the soft acrylic material IOL was implanted in the capsular bag, residual LECs migrating and extending on the posterior capsule contacted the IOL optic at regions near the equator, and, most likely, LECs existing at the edge of the optic attached to the lens material and continued to increase in adherence. Hence, the gatherings of LECs were formed in these regions, and the migration and extension of LECs toward the lens center were prohibited. This may be one of the reasons for the low incidence of Nd:YAG capsulotomy or postcataract formation. Until now, although there were a lot of clinical reports documenting the biocompatibility of IOLs,[7–13] reports discussing (from a cell biological standpoint using a cell culture system) the relationship among materials of IOLs, cellular movement of LECs from human cataractous lenses, and lens capsule were few.[14,15] Therefore, the findings of this study provide useful information when considering selection of materials of IOLs.

References

1. Steinert RF, Brint SF, White SM, et al. Astigmatism after small incision cataract surgery: A prospective, randomized, multicenter comparison of 4- and 6.5-mm incisions. Ophthalmology 1991;98:417–24.
2. Brint SF, Ostrick DM, Bran JE. Keratometric cylinder and visual performance following phacoemulsification and implantation with silicone small-incision of poly (methyl methacrylate) intraocular lenses. J Cataract Refract Surg 1991;17:32–6.
3. Martin RG, Sanders DR, Van Der Karr MA, et al. Effect of small incision intraocular lens surgery on postoperative inflammation and astigmatism. A study of the AMO SI-18NB small incision lens. 1992;18:51–5.
4. Leen MM, Ho CC, Yanoff M. Association between surgically-induced astigmatism and cataract incision size in the early postoperative period. Ophthalmic Surg 1993;24:586–92.
5. Oshika T. Comparison of foldable and small diameter optic PMMA intraocular lenses for small incision cataract surgery. Jpn J Ophthalmic Surg 1994;7:21–34.
6. Majima K. An evaluation of the biocompatibility of intraocular lenses. Ophthalmic Surg Lasers 1996;27:946–51.
7. Balyeat HD, Nordquist RE, Lerner MP, et al. Comparison of endothelial damage produced by control and surface modified poly methyl methacrylate intraocular lenses. J Cataract Refract Surg 1989;15:491–4.
8. Chelly Y, Buchen MS, Scott C, et al. Evaluation of the biocompatibility and fixation of a new silicone intraocular lens in the feline model. J Cataract Refract Surg 1989;15:545–53.
9. Hafstrand A. Evidence for an increased biocompatibility of heparin surface modified (HSM) PMMA intraocular lenses. Implant in Ophthalmology 1990;4:35–9.
10. Michael A, Rupert M. Cellular invasion on hydrogel and poly (methyl methacrylate) implants. J Cataract Refract Surg 1991; 17:744–9.
11. Zetterstrom C, Lundvall A. Exfoliation syndrome and heparin surface modified intraocular lenses. Acta Ophthalmol 1992;70:91–5.
12. Milazzo S, Sigot LMF, Borhan M, et al. In vitro organotypic culture method to evaluate the biocompatibility of heparin-surface modified intraocular lenses. J Cataract Refract Surg 1994;20:638–42.
13. Oshika T, Susuki Y, Kizaki H, Yaguchi S. Two year clinical study of a soft acrylic intraocular lens. J Cataract Refract Surg 1996;22:104–9.
14. Nagamoto T. Postoperative proliferation of lens epithelial cells in vitro. Journal of the Eye (Atarashii Ganka) 1993; 10:1619–23.
15. Liu CSC, Wormstone IM, Duncan G, Marcantonio JM, Webb SF, Davies PD. Invest Ophthalmol Vis Sci 1996;37:906–14.