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The Effect of Polymethylmethacrylate and AcrySof Intraocular Lenses on the Posterior Capsule in Patients with a Large Capsulorrhexis

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Purpose: We have previously shown that patients who have a capsulorrhexis larger than the diameter of a polymethylmethacrylate (PMMA) intraocular lens (IOL) rapidly develop increased posterior capsule opacification (PCO), in effect, producing an example of enhanced PCO. This study focuses on the influence of AcrySof IOLs on this process.

Methods: Phacoemulsification was performed on two groups of patients. The first consisted of 38 patients with a large capsulorrhexis of 6–7 mm who received a 5.5-mm PMMA IOL. The second group of 32 patients had identical surgery and a 5.5-mm MA30 AcrySof IOL was implanted. On days 1,14, 28, 90, 180, and 360, high resolution digitized retroillumination images were taken of the posterior capsule. The PCO area was measured by image analysis at 90, 180, and 360 days. Wrinkling of the posterior capsule was determined at 90 days, and the progression or regression of lens epithelial cell (LEC) proliferation was established by examination of serial images at 28 and 180 days.

Results: At 90 days, 79% of the patients with PMMA IOLs had moderate to severe wrinkling of the posterior capsule, whereas the patients with AcrySof IOLs had none ($P < .001$). The percentage of PCO area was 69% for the PMMA IOLs and 24% for the AcrySof IOL group at 360 days ($P < .0001$). In the PMMA group, LEC progression occurred in 77%, LEC growth was stable in 15%, and LEC regression occurred in only 8%, compared to 69% of patients with AcrySof IOLs ($P < .0001$).

Conclusions: In patients with a rhexis larger than the IOL, AcrySof IOLs potentially can prevent capsular wrinkling and cause less PCO than a PMMA IOL with a similar rhexis size. The LEC regression occurs with AcrySof between 28 and 180 days. The reasons for this are discussed. **Jpn J Ophthalmol 2001;45:348–354** © 2001 Japanese Ophthalmological Society

Key Words: Cataract surgery, intraocular lens, lens epithelial cell, posterior capsule opacification.

Introduction

Following cataract surgery and posterior chamber intraocular lens (IOL) implantation, posterior capsule opacification (PCO) occurs in up to 50% of cases.[1] This becomes clinically significant when the residual lens epithelial cells (LEC) migrate or undergo fibrous metaplasia and encroach on the visual axis, causing patients to experience blurring and glare by light scatter. Apart from the medical complications of laser capsulotomy, PCO also has social and economic adverse effects; in 1993 Nd:YAG laser capsulotomy cost the Medicare program in the United States $250 million.[2] There is, therefore, considerable interest in studying ways of preventing PCO.

It has been shown that capsulorrhexis size has a clinically significant effect on PCO.[3,4] In a study that compared capsulorrhexis size in patients using the same size of polymethylmethacrylate (PMMA) IOL, there was significantly more capsular wrinkling and PCO in the patients when the rhexis was larger than the IOL optic. An IOL, therefore, with the rhexis ly-

Laboratory Investigation

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ing off the optic can be regarded as an example of accelerated PCO.

The aim of this study was to compare the effect of a 5.5-mm optic size PMMA IOL with the 5.5-mm optic size MA30 AcrySof lens in patients with a capsulorrhexis larger than the IOL diameter. The resolution of our imaging system has also enabled us to follow the cellular changes of LEC growth on the posterior capsules in patients fitted with both these types of IOL.[5]

Materials and Methods

Following approval from the St. Thomas' Hospital Ethics Committee, two groups of patients were recruited concurrently between September 1996 and November 1997. All patients were seen preoperatively by the same clinician. Inclusion criterion was the presence of senile cataract in an otherwise normal eye in patients over 55 years of age. Exclusion criteria were a history of any previous ocular disease, intraocular surgery, laser treatment, diabetes requiring medical control, glaucoma, previous uveitis, or posterior segment pathology that would preclude a postoperative vision of 20/40 or better. Patients using topical medications (apart from lubricants) were excluded. Patients who had cataract surgery on the contralateral eye in the previous 4 months were excluded as well as those who were unable to give informed consent.

All patients had phacoemulsification with continuous curvilinear capsulorrhexis (CCC), performed by a single surgeon (EJH) using peribulbar anesthesia. The surgical technique and medication were standard. A temporal clear corneal section was made and the anterior chamber was reformed with Healon (Pharmacia, Uppsala, Sweden). A large CCC of between 6 and 7 mm was performed with a bent needle. The nucleus was removed by phaco-chop technique and soft lens material was removed by irrigation-aspiration with balanced salt solution (BSS, Alcon, Fort Worth, TX, USA) containing vancomycin (concentration 10 mg/L) and epinephrine (1:100000, 1 ml/L). No attempt was made to remove LECs by polishing the anterior capsule. The bag was reformed with Healon and the section enlarged. The first group received a 5.5-mm one-piece PMMA IOL (Pharmacia model 812A), which was inserted in the bag (Group 1) and the second group received a foldable 5.5-mm three-piece AcrySof (MA30BM, Alcon) IOL (Group 2). Healon was removed by irrigation aspiration with BSS. Corneal incisions were sutured where necessary. Any surgical complications such as capsulorrhexis rim tear, zonular dehiscence, posterior capsule rupture, or vitreous loss led to patient exclusion from the study. Postoperatively all patients used Maxitrol drops (neomycin, polymixin, and dexamethasone 0.1%, Alcon) four times a day for 1 month. No nonsteroidal anti-inflammatory preparation was used pre-, peri-, or postoperatively. Postoperatively all IOLs were confirmed to have in-the-bag placement.

At surgery it can be difficult to ensure that the CCC is concentric with the implant and so postoperatively a large CCC was defined as a rhexis greater than 6 mm in diameter with the anterior capsular flap touching the IOL surface for less than one quadrant on the first day postoperatively. High resolution digitized retroillumination images of the posterior capsule were taken at days 1, 14, 28, 90, 180, and 360 postoperatively using a custom-built digitized retroillumination camera system.[5] The percentage area of PCO at 90, 180, and 360 days, in each image, was calculated objectively using dedicated software that produces a segmentation of the image using a directional variance operator based on the texture of the image.[6] The area of measurement that was chosen was that part of the posterior capsule that was behind the IOL optic. Any part of the capsule outside this area was excluded from analysis.

At 90 days, wrinkling of the posterior capsule was graded for each patient separately using the retroillumination images displayed on a monitor. They were graded as none, mild, moderate, or severe, depending on the number of quadrants of wrinkles observed. Mild wrinkling meant in only one quadrant, moderate in two, and severe was wrinkling in three or four quadrants.

The presence or absence of LECs on the posterior capsule was determined at 28 days. Progression or regression of LEC migration and growth was then established by examination of serial images at 28 and 180 days postoperatively.

Thirty-eight patients were recruited in group 1 with a large CCC and PMMA IOL. Four patients were excluded because the rhexis was found to lie in contact with the IOL for more than one quadrant on day 1. In the 34 that were included, the rhexis lay off the IOL in all quadrants in 20 patients (52.6%) and touched one quadrant in 14 patients (36.8%). All 34 patients were available for follow-up, except one who was too ill to attend at 28, 90, and 180 days.

Thirty-two patients were enrolled in group 2, with a large CCC and MA30 AcrySof IOL. Three patients were excluded because the capsulorrhexis lay eccentrically on the IOL optic for more than one

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quadrant. In the others the capsulorrhexis lay completely off the IOL in 19 patients (61%) and touched one quadrant in 10 patients (32%). All were available for image analysis at 28, 90, 180, and 360 days. The average age was 73 in group 1 and 74 in group 2. There was no difference between the two groups in age and sex distribution.

Statistical Methods

The difference between groups 1 and 2 was analyzed using a chi-square test for posterior capsular wrinkling and LEC regression, and unpaired *t*-test for percentage of PCO area.

Results

Percentage Area of Posterior Capsular Opacification

The average area of PCO as determined by our image analysis is shown in Figure 1. The AcrySof group had significantly less PCO than the PMMA group. At 360 days the mean percentage of PCO area was 24% (95% confidence interval: 18.5–29.0) for the AcrySof group and 69% (52.5–73.0) for the PMMA group ($P < .0001$).

Posterior Capsule Wrinkling

The degree of posterior capsular wrinkling was strikingly different between the AcrySof and PMMA groups (Figure 2). At 90 days, moderate to severe wrinkling was seen in 27 (79%) patients with PMMA lenses, as compared to none in patients with AcrySof IOLs. There was mild wrinkling in 6 AcrySof patients (21%) ($P < .0001$); 23 (79%) patients with AcrySof lenses had no posterior capsule wrinkling. Examples of images of a PMMA lens are shown in Figures 3a,b. An example of an AcrySof lens showing no wrinkling is shown in Figure 4a and an example showing mild wrinkling is shown in Figure 4b.

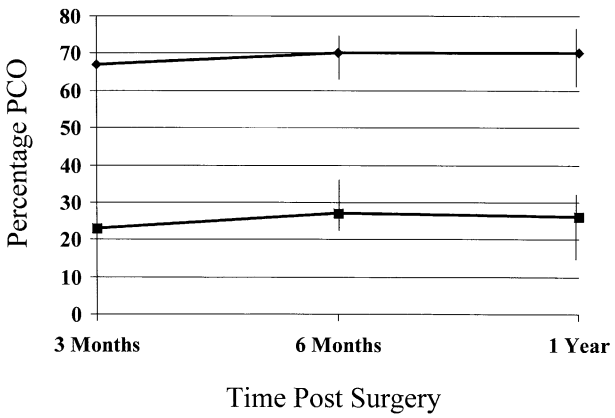

Figure 1. Mean percentage of posterior capsule opacification area in patients with polymethylmethacrylate (PMMA) and AcrySof IOLs and large capsulorrhexis (vertical bars indicate 95% confidence interval) ◆: PMMA, ■: AcrySof.

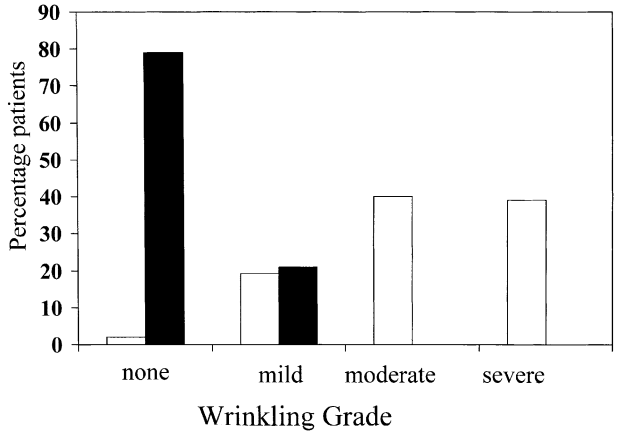

Figure 2. Grade of posterior capsule wrinkling at 90 days postoperatively. □: polymethylmethacrylate, ■: AcrySof.

Lens Epithelial Cell Changes

The imaging system we used has a high degree of resolution (25000 pixels/mm) and the presence of LECs on the posterior capsule (independent of area of cover) could be determined in all patients. In both groups all patients had some LECs present on the posterior capsule at 28 days, although the PMMA group had more. Analysis of subsequent images at 180 days showed that in the PMMA group, 26 (77%) patients had continuing LEC progression, in 5 (15%) LEC growth was stable, and in 3 (8%) there was minor regression on some areas of the capsule (Figure 5). In contrast, 20 (69%) patients with AcrySof IOLs showed subsequent LEC regression, 3 (10%) showed progression, and in 6 (21%) growth was stable. There was significantly more regression in patients with AcrySof IOLs than in those with PMMA IOLs ($P < .0001$). An example of an AcrySof lens showing LEC regression is shown in Figure 6.

Visual Acuity and Contrast Sensitivity

Following exclusion of 4 patients from group 1, and 2 from group 2, because they developed age-related macular degeneration, both groups had good average Log_{Mar} visual acuities at 1 year: 0.00 (Snellen equivalent = 6/6) for the PMMA group and 0.02 (Snellen equivalent = 6/6) for the AcrySof group ($P =$

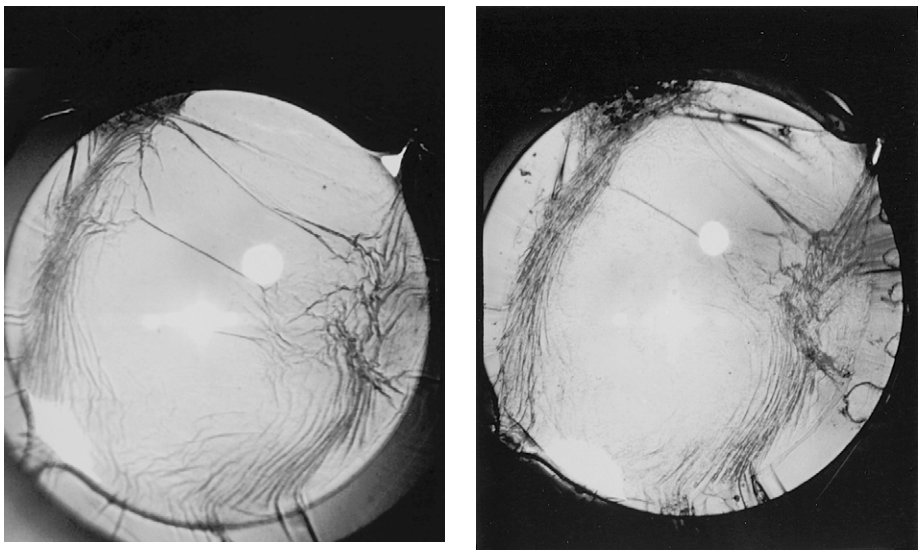

Figure 3. (**left**) A 5.5-mm polymethylmethacrylate intraocular lens (IOL) at 90 days showing fine folds and wrinkling of posterior capsule. (**right**) At 180 days fine lens epithelial cell (LEC) ingrowth can be seen.

NS). The average Pelli-Robson contrast sensitivity was 1.49 for the PMMA group and 1.50 for the Acrysof group (P = NS). Despite the absence of statistical differences in visual function between the two groups, 3 patients in the PMMA group had clinically significant PCO that required Nd:YAG laser capsulotomy. None of the patients in the AcrySof group required Nd:YAG lasertreatment for posterior capsule opacification.

Discussion

Patients with a PMMA IOL and a rhexis that is larger than the diameter of the IOL optic have more PCO and worse vision by 1-year postoperatively in comparison to patients with the same PMMA IOL and a rhexis totally on the anterior IOL surface.[3] The probable explanation is that the anterior capsular LECs have the ability to transform into myofibroblasts,[7–9] and a large CCC allows the anterior and posterior capsular flaps to come into contact, allowing these LECs to migrate onto the posterior capsule producing fibrotic changes. Conversely, a small "on the IOL" rhexis keeps the anterior and posterior capsules separated, allowing peripheral equatorial LECs better access.

This study showed that in patients with a rhexis larger than the IOL diameter, AcrySof IOLs behaved differently in the eye compared to PMMA IOLs with a rhexis of similar size, preventing the early fibrotic changes that sometimes occur with PMMA IOLs. The significant increase in PCO seen with the PMMA IOLs at 1 year in comparison to the AcrySof IOLs was not, however, associated with significant differences in either visual acuity or contrast sensitivity at this time, although this might be expected to occur with time.

With the high resolution of our imaging system, we could observe the changes in LEC migration. In vitro studies have shown that LEC migration starts within days of surgery[9–11] and using our imaging system, patterns of LEC growth on the posterior capsule are easily detectable on the human posterior capsule in vivo in the first few weeks postoperatively. In this study, all patients had a capsulorrhexis larger than the IOL optic and had some LECs present on the posterior capsule at 30 days postoperatively, although eyes with AcrySof IOLs had fewer cells present. This is in contrast to our experience with AcrySof IOLs in eyes with a rhexis edge lying on the anterior surface of the IOL, where the posterior capsule is often acellular at this time. In eyes with PMMA IOLs the LEC growth progressed in 77% of patients by 3 and 6 months, remained stable in 15% and areas of cellular regression were seen in only 8%. In contrast there was a dramatic difference in the patients with AcrySof IOLs; regression of LEC growth was seen in 69% of patients ($P <$ .0001), only 10% showed progression, and in 21% growth remained stable. Thus, the LECs present on posterior capsules at 3 months had a tendency to progress with PMMA IOLs and regress with AcrySof lenses. In an earlier study comparing LEC growth on the posterior capsule with PMMA, silicone, and AcrySof IOLs, where the rhexis size was smaller in relation to the IOL optic, we found that only 46% of patients with Acrysof IOLs had LECs on the posterior capsule at 3 months postopera-

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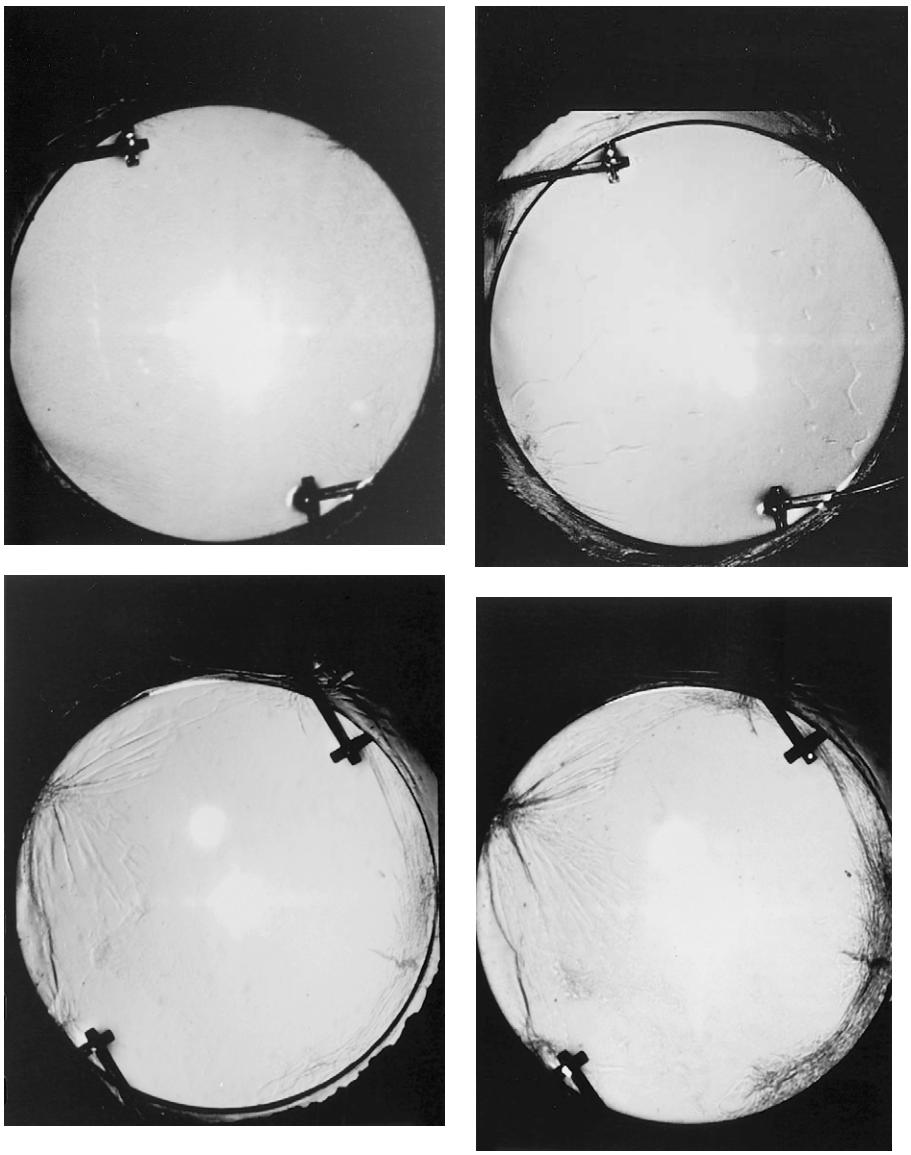

Figure 4. A 5.5-mm AcrySof intraocular lens (IOL) at 90 (**top left**) and 180 days (**top right**) postoperatively showing no wrinkling of posterior capsule. Another AcrySof IOL at 90 (**bottom left**) and 180 days (**bottom right**) postoperatively. Mild folding in capsule can be seen superiorly associated with lens epithelial cell (LEC) ingrowth. Wrinkling remains much the same at 180 days (**bottom right**) although LEC changes are more marked.

tively.[12] Of these patients, cellular regression was seen in 83% with AcrySof IOLs compared to 8% with PMMA lenses. The amount of LEC regression in patients with AcrySof IOLs was greater than in this present study, which is probably explained by the difference in the IOL optic diameter (6 mm compared to 5.5 mm) and area of rhexis contact: it appears that the AcrySof IOL provides a more efficient barrier to LEC migration when the rhexis lies on the anterior IOL surface than off it.

Posterior capsule opacification is influenced by many factors and ideally protocols should be designed to examine the influence of a single factor. This is not usually possible in clinical studies, as different lens materials must, by definition, have different designs. Studies have shown that AcrySof IOLs are effective in maintaining clearer posterior capsules than IOLs made of other materials.[13–15] A fundamental difference between the AcrySof and PMMA IOLs in this study was the edge profile of the lens optic; the optic size was constant. The AcrySof had a squared edge, whereas the PMMA, a round-edge design. Recent experimental[16,17] work has shown that square-edged profiles can prevent LEC migration onto the posterior capsule. This may explain why the eyes with AcrySof IOLs develop less PCO and capsule wrinkling. It does not, however, explain the phenomenon of LEC regression with AcrySof IOLs. AcrySof is a copolymer of phenylethyl acrylate and phenylethyl methacrylate

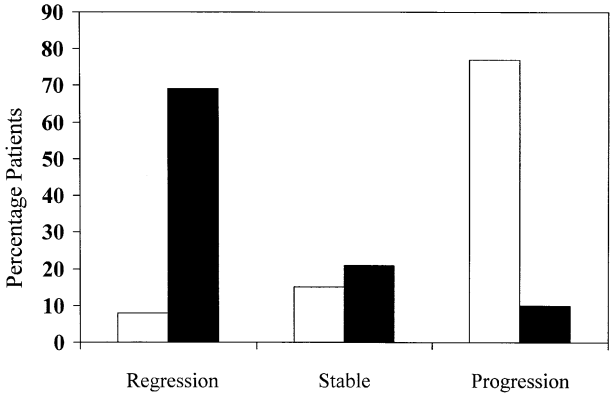

Figure 5. Fate of lens epithelial cells on the posterior capsule between 28 and 180 days postoperatively. □: polymethylmethacrylate, ■: AcrySof

cross-linked with 1.4 butanediol diacrylate. AcrySof contains exceedingly low levels of extractable monomer and the plastic itself is not toxic to LECs. These IOLs have a sticky surface and adhere to collagen and the lens capsule more than PMMA and silicone IOLs.[18,19] In vitro fibronectin is deposited in greater amounts on AcrySof IOLs in comparison to PMMA[20,21] and we have postulated that this may produce bio-adhesion as well as physical adhesion between the IOL optic and the posterior capsule. Such adhesion could explain the greater stability of the anterior capsule on the anterior IOL surface seen with AcrySof IOLs[22] and may contribute to the mechanism of LEC regression. This seems to take several weeks to fully develop, as LECs appear and increase on the posterior capsule in the first few weeks postoperatively. We postulate that during this time LEC migration can occur, but once capsule-to-IOL adhesion is established, access of nutrients and growth factors may become restricted to the migrated LECs, making them die of malnutrition.

This study has shown that in patients with a large capsulorrhexis the cellular changes in the posterior capsule following surgery are markedly different, depending on whether patients are given AcrySof or PMMA IOLs. The debate on whether these differences are primarily due to variations in surgical technique, IOL design, or IOL material is still in progress.

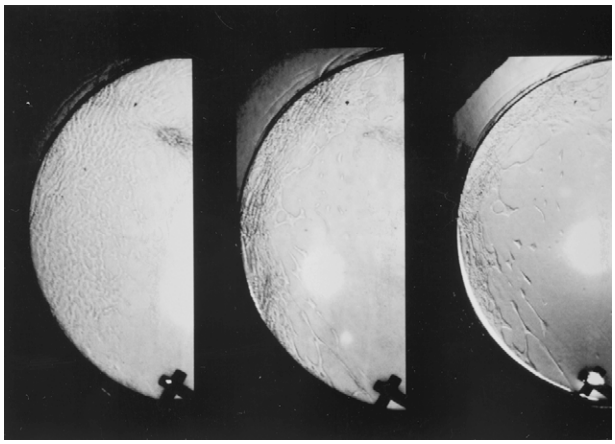

Figure 6. Regions of AcrySof intraocular lens at 28, 90, and 180 days postoperatively (left: 28 days, center: 90 days, right: 180 days). At 28 days fine reticular cellular growth can be seen on posterior capsule. There is marked regression of this cellular pattern between 28 and 90 days which shows only minor changes at 180 days.

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