



34 *Posterior Capsule Opacification: Experimental and Clinical Studies and Factors for Prevention*

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- Overview
- Background
- Reasons to Eradicate Posterior Capsule Opacification
- Etiopathogenesis
- Lens Epithelial Cells Proliferation: Role of Growth Factors
- Clinical Manifestations and Treatment
- Surgical and Implant Related Factors for Prevention of Posterior Capsule Opacification
- Confirmation of Surgical and Implant Related Factors in the Laboratory and Clinical Studies

- Pharmacological Prevention of Posterior Capsule Opacification
- Sealed Capsule Irrigation for Maintaining Postoperative Capsular Bag Transparency
- Removal of Lens Epithelial Cells using AquaLase® Liquefaction Device
- Summary and Conclusions

OVERVIEW

Posterior capsule opacification (PCO, secondary cataract, after cataract) is a nagging complication of cataract-intraocular lens (IOL) surgery since the beginning of extracapsular cataract surgery (ECCE) and IOL implantation. PCO needs to be eliminated since deleterious sequelae of this complication occur and Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG) laser treatment now constitutes a major and unnecessary financial burden on the health care system. A successful expansion of ECCE-IOL surgery in the developing world depends on eradication of PCO, since patient follow-up is difficult and access

to the Nd:YAG laser is not widely available. Advances in the surgical techniques, IOL designs/biomaterials have been instrumental in gradual, and unnoticed decrease in the incidence of the PCO. We strongly believe that the overall incidence of PCO and hence the incidence of Nd:YAG laser posterior capsulotomy is now rapidly decreasing from rates as high as 50 percent in the 1980s-early 1990s to less than 10 percent in the developed World. Our 2 decades of active research and information derived from other experimental and clinical studies from several other centers have revealed that the tools, surgical procedures, skills and appropriate IOLs designs are now available to significantly reduce this complication.

BACKGROUND

Opacification of the posterior capsule caused by postoperative proliferation of cells in the capsular bag remains the most frequent complication of cataract-intraocular lens (IOL) surgery (Figure 34.1).^{1,2} In addition to classic posterior capsule opacification (PCO, secondary cataract, after cataract), postoperative lens epithelial cell (LEC) proliferation is also involved in the pathogenesis of anterior capsule opacification/fibrosis (ACO) and interlenticular opacification (ILO).³⁻⁶ Secondary cataract (PCO) has been recognized since the origin of extracapsular cataract surgery (ECCE) and was noted by Sir Harold Ridley in his first IOL implantations.^{7,8} It was particularly common and severe in the early days of IOL surgery (in late 1970s and early 1980s) when the importance of cortical clean-up was less appreciated. Through the 1980s and early 1990s, the incidence of PCO ranged between 25-50 percent.⁹ PCO is a major problem in pediatric cataract surgery where the incidence approached 100 percent.¹⁰⁻¹²

One of the crowning achievements of modern cataract surgery has been a gradual, almost unnoticed decrease in the incidence of this complication. Our data at present show that with modern techniques and IOLs, the expected rate of PCO and the need for subsequent Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG) laser posterior capsulotomy rate is decreasing to single digit (less than 10%).^{13,14}

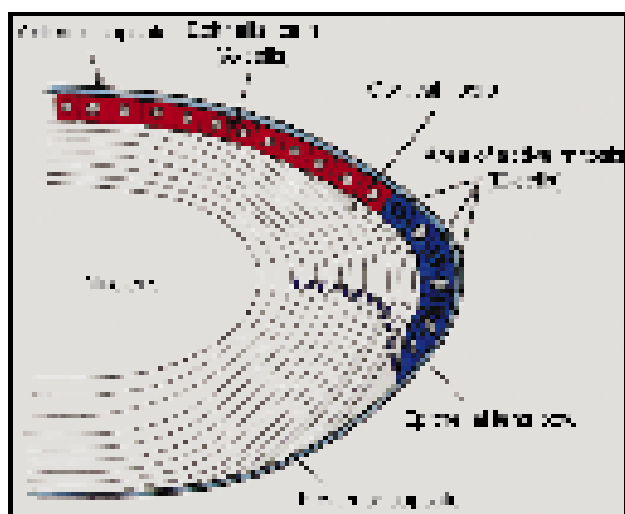
In this chapter, we review the etiopathogenesis, experimental and clinical studies and propose surgical and

implant-related factors for PCO prevention. Careful application and utilization of these factors by surgeons can genuinely lead in the direction of virtual eradication of secondary cataract, the second most common cause of visual loss worldwide. Most of the information provided in this review is based on several experimental studies on the pathogenesis and treatment of PCO in our laboratory during past 20 years, and after compiling information derived from other experimental and clinical studies from several centers worldwide. It is hoped that this discussion provides relevant information and guidance regarding PCO and its prevention and that it will increase surgeons' awareness of the various tools now available to eradicate this complication.

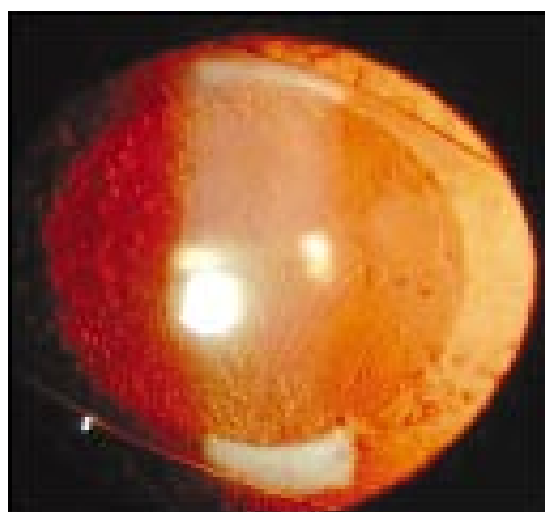
REASONS TO ERADICATE POSTERIOR CAPSULE OPACIFICATION

Although cataract is the most common cause of blindness in the world, after-cataract (PCO or secondary cataract) is an extremely common cause as well. Jan GF Worst, MD has stated- "*the most meaningful development in intraocular implant research in the next five years will be effective prevention of secondary cataract formation*" (International Intraocular Implant Club Report, Vol. 1, No. 2, January, 1999). Eradication of PCO following ECCE has major medical and financial implications:

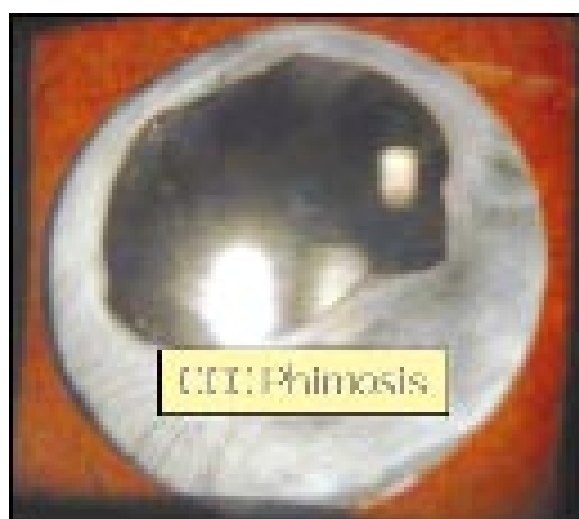
- A. Nd: YAG laser secondary posterior capsulotomy, can be associated with significant complications. Potential problems including IOL optic damage/pitting, postoperative intraocular pressure elevation, cystoid macular edema, retinal detachment, and IOL subluxation.¹⁵⁻¹⁸
- B. Dense PCO and secondary membrane formation is particularly common following pediatric IOL implantation.¹⁰⁻¹² A delay in diagnosis can cause irreparable amblyopia.
- C. PCO represents a significant cost to the US health care system. Nd:YAG laser treatments of almost one million patients per year have cost up to \$250 million annually.⁹
- D. A posterior capsulotomy can increase the risk of posterior segment complications in high myopes and patients with uveitis, glaucoma, and diabetic retinopathy.



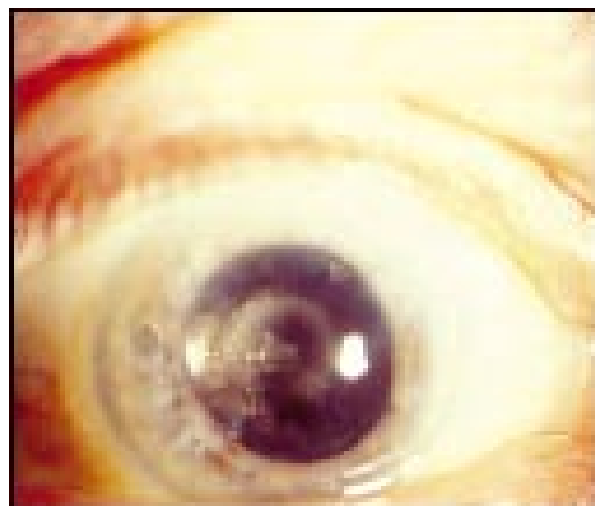
A



B



C



D

FIGURES 34.1A to D: Postoperative proliferation of lens epithelial cells can also lead to postoperative opacification of capsular bag secondary to development of anterior capsule opacification/fibrosis (ACO) and interlenticular opacification (ILO). (A) Schematic illustration of the microscopic anatomy of the lens and the capsular bag, showing the “A” cells of the anterior epithelium and the “E” cells, the important germinal epithelial cells of the equatorial lens bow. The primary cells of origin for posterior capsule opacification (PCO) are the mitotic germinal cells of the epithelial lens bow. These cells normally migrate centrally from the lens equator and contribute to formation of the nucleus or epinucleus throughout life. In pathologic states, they tend to migrate posteriorly to form such lesions as a posterior subcapsular cataract, as well as postoperative PCO following ECCE. (B-D) Clinical photograph showing PCO, capsular phimosis and ILO

- E. PCO of even a mild degree can decrease near acuity through a multifocal IOL, and may interfere with the function of refractive/accommodating IOL designs.
- F. A significant incidence of PCO means that cataract surgery, alone, may not restore lasting sight to the 25 million people worldwide who are blind from cataract.¹⁹

- G. Finally, a successful expansion of ECCE-IOL surgery in the developing world depends on eradication, or at least diminishing of PCO, since patient follow-up is difficult and access to the Nd:YAG laser is not widely available.¹⁹

ETIOPATHOGENESIS

In the normal crystalline lens, the LECs are confined to the anterior surface at the equatorial region and the equatorial lens bow. This single row of cuboidal cells can be divided into two different biological zones (Figure 34.1):

- A. The anterior-central zone (corresponding to the zone of the anterior lens capsule) consists of a monolayer of flat cuboidal, epithelial cells with minimal mitotic activity. In response to a variety of stimuli, the anterior epithelial cells (“A” cells) proliferate and undergo fibrous metaplasia. This has been called “pseudofibrous metaplasia” by Font and Brownstein.²⁰
- B. The second zone is important in the pathogenesis of “pearl” formation. This layer is a continuation of anterior lens cells around the equator, forming the equatorial lens bow (“E” cells). Unlike within the A-cell layer, cell mitoses, division, and multiplication are quite active in this region. New lens fibers are continuously produced in this zone throughout life.

In addition to classic PCO, postoperative LEC proliferation is also involved in the pathogenesis of other entities, such as anterior capsule opacification/fibrosis (ACO)^{3,4} and ILO; a more recently described complication related to piggyback IOLs.^{5,6} Thus, there are three distinct anatomic locations within the capsular bag where clinically significant opacification may occur postoperatively (Figure 34.1). Ophthalmic researchers are now developing surgical techniques/devices not only to eliminate PCO, but also to eliminate capsular bag opacification, secondary to proliferation of LECs.

Although both types of cells (from the anterior central zone and from the equatorial lens bow) have the potential to produce visually significant opacification, most cases of classic PCO are caused by proliferation of the equatorial cells. The term posterior capsule opacification is actually a misnomer. It is not the capsule which opacifies. Rather, an opaque



FIGURE 34.2: Gross photograph from behind (Miyake-Apple posterior photographic technique) of a human eye obtained postmortem showing massive overgrowth of a Soemmering's ring over the lens optic. This has created a “pearl form” of total PCO. This lens was asymmetrically fixated. The left haptic is in the capsular bag. The right haptic (not visible) is in the ciliary sulcus

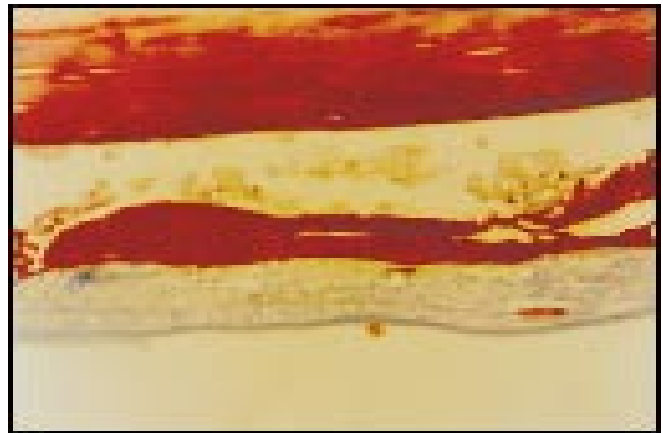
membrane develops as retained cells proliferate and migrate onto the posterior capsular surface.

The opacification usually takes one of two morphologic forms. One form consists of capsular **pearls**, which can consist of clusters of swollen, opacified epithelial “pearls” or clusters of posteriorly migrated equatorial epithelial (E) cells (bladder or Wedl cells) (Figure 34.2). It is probable that both LEC types can also contribute to the **fibrous** form of opacification. Anterior epithelial (A) cells are probably important in the pathogenesis of fibrosis PCO, since the primary type of response of these cells is to undergo fibrous metaplasia. Although the preferred type of growth of the equatorial epithelial (E) cells is in the direction of bloated, swollen, bullous-like bladder (Wedl) cells, these also may contribute to formation of the fibrous form of PCO by undergoing a fibrous metaplasia. This is a particularly common occurrence in cataracts in developing world settings where cataract surgery has been delayed for many years, and where posterior subcapsular cataracts have turned into fibrous plaques (Figure 34.3).²¹

Capsulorhexis contraction (capsular phimosis) is an important complication related to extreme fibrous proliferation of the anterior capsule.²⁻⁴ Capsular



A



B



C

FIGURES 34.3A to C: A less common form of PCO seen commonly in the developing world consists of a so-called *fibrous plaque*. This is sometimes noticed immediately after performing ECCE, and is sometimes termed “acute” PCO. This represents a pseudofibrous metaplasia of a very long-standing posterior subcapsular cataract. It usually occurs as a result of delayed treatment and is therefore common in the developing world. (A) This Figure illustrates a human eye obtained postmortem (Miyake-Apple posterior photographic technique) showing an example of a posterior subcapsular plaque. (B) Photomicrographs of posterior subcapsular fibrous plaques. The fibrous plaque is the light blue-staining material adjacent to the posterior capsule (below). A plaque this thin probably does not cause severe visual difficulties. (C) A much thicker plaque (blue-staining region) representing a lesion that could be of clinical significance (Masson’s trichrome stain, X150)

phimosis can be avoided by not making the capsulorhexis too small. In general, a diameter less than 5.5 mm is undesirable.

In contrast to the lesions of the anterior (A cells) capsule that cause phenomena related to fibrosis, the E cells of the equatorial lens bow (Figure 34.1A) tend to form cells that differentiate toward pearls (bladder cells) and cortex. Equatorial cells (E-cells) are also responsible for formation of a Soemmering’s ring. The Soemmering’s ring, a dumb-bell or donut shaped lesion that often forms following any type of rupture of the anterior capsule, was first described in connection with ocular trauma. The pathogenetic basis of a Soemmering’s ring is rupture of the anterior

lens capsule with extrusion of nuclear and some central lens material. The extruded cortical remnants then transform into Elschnig pearls (Figure 34.2). It is not widely appreciated that a Soemmering’s ring forms virtually every time that any form of ECCE is done, whether manual, automated or with phacoemulsification. This material is derived from proliferation of the epithelial cells (E-cells) of the equatorial lens bow. We have noted that these cells have the capability to proliferate and migrate posteriorly across the visual axis, thereby opacifying the posterior capsular. Because the Soemmering’s ring is a direct precursor to PCO, surgeons should strive to prevent its formation.

Cells types other than lens epithelial cells may be involved in PCO. As ECCE is always associated with some breakdown of the blood-aqueous barrier, inflammatory cells, erythrocytes, and many other inflammatory mediators may be released into the aqueous humor. The severity of this inflammatory response may be exacerbated by the IOL. This foreign body elicits a three-stage immune response that involves many different cell types, including polymorphonuclear leukocytes, giant cells, and fibroblasts. Collagen deposition onto the IOL and onto the capsule may cause opacities and fine wrinkles to form in the posterior capsule. In most cases, however, this inflammatory response is clinically insignificant. Iris melanocytes also have been shown to adhere to and migrate over the anterior surface of the posterior capsule.

LENS EPITHELIAL CELLS PROLIFERATION: ROLE OF GROWTH FACTORS

Cataract surgery causes major changes in the ocular environment. Not only because of breakdown of the blood aqueous barrier, as mentioned above, but also through the release/activation of endogenous cytokines and growth factors from endogenous sources during wound healing. Aqueous and vitreous humors are rich in growth and regulatory factors and there is now abundant evidence that differences in the distribution of such factors between aqueous and vitreous compartments determine normal lens polarity and growth patterns; that is, factors in the vitreous environment promote the differentiation of fiber cells whereas the aqueous factors promote epithelial differentiation and growth.²²

The lens itself expresses members of major growth factor families and a variety of growth factor receptors and molecules involved in a range of signaling pathways.²³ Studies over the last couple of decades have mostly concentrated on identifying the factor(s) that controls the differentiation of lens epithelial cells into fibers and there is now compelling evidence that members of the FGF growth factor family are required for induction of this process.²² Recent studies have also indicated that the Wnt growth factor family plays a key role in promoting the differentiation of the epithelial sheet.²⁴ However, in relation to PCO, the most interesting studies have been on the transforming growth factor-beta (TGF β) family.²⁵



FIGURE 34.4: Shows a diagrammatic representation of the effects of TGF β on lens epithelial cells. TGF β induces epithelial cells to lose their normal apical-basal polarity and multilayer to form plaques of cells that deposit large amounts of extracellular matrix. The morphological and molecular markers of lens epithelial cells are replaced by markers for myofibroblastic/fibroblastic cells. These include cytoskeletal components, α -smooth muscle actin and desmin, as well as extracellular matrix molecules, collagen types I and III, fibronectin and tenascin. This process is known as epithelial mesenchymal transition

TGF β is abundant in the lens, and the surrounding ocular media.²⁶ The effects of TGF β on lens cells were initially studied in rats using epithelial explants and whole lens cultures. TGF β induces lens epithelial cells to commit to a differentiation pathway that is distinct from that seen in the normal lens. In cultured lenses, TGF β induces the formation of subcapsular opacities.²⁷ These correspond to plaques of spindle-shaped cells that contain α -smooth muscle actin and desmin, and accumulations of extracellular matrix that include collagen types I and III, fibronectin and tenascin.²⁸ TGF β also induces localized wrinkling of the capsule in epithelial explants and cultured lenses.^{27,29} Similarly, overexpression of TGF β in transgenic mice also results in the development of anterior subcapsular fibrotic plaques that grow progressively with age.^{28,30} These studies clearly show that TGF β disrupts the normal lens epithelial architecture and induces an epithelial-mesenchymal transition that is a central feature of the fibrotic growth that results in opacification and disturbed vision (Figure 34.4).

Similar patterns of aberrant growth and differentiation are found in subcapsular cataracts in humans. Following eye trauma, surgery, or associated with other disorders (e.g. atopic dermatitis and retinitis pigmentosa), anterior subcapsular cataracts (ASC) can arise.³¹ These exhibit similar fibrotic changes to that

described for PCO. In this form of cataract in humans it also appears that members of the TGF β family initiate the epithelial mesenchymal transition that is a central feature of this condition. In addition, it appears that an initial TGF β insult induces connective tissue growth factor, TGF β -inducible gene-H3 and other autocrine signaling pathways, including endogenous TGF β signaling, that promotes the progressive fibrosis that leads to cataract.^{25,32,33}

As TGF β is expressed by lens cells and the ocular media have abundant supplies, TGF β bioavailability must be tightly regulated, otherwise all lenses would develop cataract. It appears that there may be multiple levels of TGF β regulation. For example, it is well-known that TGF β is generally produced in a latent form that requires conversion to the mature (active) form. In addition, the ocular media, particularly vitreous, normally contain molecule(s) that inhibit active TGF β and block its cataract-inducing effects.³² The sensitivity of lens cells to TGF β may also be modulated by many factors. For example, studies with rats have shown that estrogen can protect the lens from TGF β -induced cataract.³⁵ This is consistent with epidemiological studies that report female hormones may help prevent or slow the development of some forms of cataract.³⁶

In summary, during cataract surgery many growth factors are upregulated and/or activated in the lens and the ocular media. Not only does this disturb the normal distribution and activity of factors in the aqueous and vitreous compartments that are critical for determining normal growth patterns, but additional events such as activation of latent stores of TGF β in the ocular media result in the induction of aberrant growth and differentiation in the lens. Clearly procedures that reduce the trauma of cataract surgery will be beneficial, as this will minimize disruption of the growth factor composition in and around the lens. A better understanding of lens cells biology also opens up possibilities of introducing molecules that will effectively kill residual lens cells. In addition, blockers of TGF β could be included in irrigation solutions during surgery, and as coatings of IOLs, to ensure that any residual lens cells do not undergo epithelial mesenchymal transition, but rather maintain a normal epithelial phenotype.

CLINICAL MANIFESTATIONS AND TREATMENT

The interval between surgery and PCO varies widely, ranging anywhere from three months to four years after the surgery. Although the causes of PCO are multifactorial as reported in several studies.^{9,37,38} There is an inverse correlation with age. Young age is a significant risk factor for PCO, and its occurrence is a virtual certainty in pediatric patients.¹⁰⁻¹²

Visual symptoms do not always correlate to the observed amount of PCO. Some patients with significant PCO on slit lamp examination are relatively asymptomatic while others have significant symptoms with mild apparent haze, which is reversed by capsulotomy.³⁹

Visually significant PCO usually managed by creating an opening within the opaque capsule using the Nd: YAG laser. A surgical posterior capsulotomy may be indicated in children for dense PCO associated with secondary membrane formation. The technical details, parameters, preoperative and postoperative treatment, complications and recommendations for surgical and Nd: YAG laser posterior capsulotomy are discussed in literature¹⁵⁻¹⁸ and not covered in this chapter. In brief, indications for Nd: YAG laser capsulotomy include: presence of a thickened capsule leading to functional impairment of vision, and the need to evaluate and treat posterior segment pathology. However, caution should be exercised if there is any signs suggestive of intraocular inflammation, raised intraocular pressure, macular edema, and a predisposition to retinal detachment (e.g. high myopia). As mentioned before Nd: YAG laser posterior capsulotomy may be rarely associated with complications such as transient rise in intraocular pressure, enhanced risk of retinal detachment, which is particularly marked in axial myopia, cystoid macular edema, IOL subluxation, lens optic damage/pitting, exacerbation of local endophthalmitis, and vitreous prolapse into the anterior chamber and anterior hyaloid disruption.

SURGICAL AND IMPLANT RELATED FACTORS FOR PREVENTION OF POSTERIOR CAPSULE OPACIFICATION

Based upon our 20 years research experience on evaluation of ca. 17,500 IOL related specimens (7523 human eyes obtained postmortem; 6127 eyes

Table 34.1: Factors that significantly influence the formation of PCO. Three factors are related to the type and quality of surgery and three are related to IOL biomaterial/design

3 Surgery-Related Factors "Capsular" Surgery	3 IOL-Related Factors "Ideal" IOL
1. Hydrodissection-enhanced cortical clean-up	1. Biocompatible IOL to reduce stimulation of cellular proliferation
2. In-the-bag fixation	2. Maximal IOL optic- posterior capsule contact with angulated haptics, "adhesive" biomaterial to create a "shrink wrap" of the capsule
3. Small capsulorhexis with anterior capsular edge on the IOL surface to sequester the capsular bag (shrink wrap the capsule around the IOL optic).	3. IOL optic geometry a square, truncated edge for 360 degrees

implanted with rigid lenses and 1396 eyes implanted with foldable lenses) using Miyake-Apple technique, and published studies from our Center and other Centers,^{1,9,13,14,19,40-45} we can review the principles of PCO prevention. These measures can be divided into two categories. One strategy is to minimize the number of retained/regenerated cells and cortex (including the Soemmering's ring) through thorough cortical clean-up. The second strategy is to prevent the remaining cells from migrating posteriorly. The edge of the IOL optic is critical in the formation of such a physical barrier.

We have identified three surgery-related factors and three IOL-related factors that are particularly important in the prevention of PCO (Table 34.1).⁴⁰⁻⁴⁵

Surgery-Related Factors to Reduce PCO

Hydrodissection-Enhanced Cortical Clean-up

A very important and underrated surgical step is hydrodissection. Dr I Howard Fine perfected and popularized this technique and coined the term cortical cleaving hydrodissection.⁴⁶ Until fairly recently, many surgeons had a rather fatalistic attitude regarding removal of lens cortex and cells during ECCE - either manual or automated - or with phacoemulsification. A common opinion was that removing all or even most equatorial cells from the bag is impossible. PCO was

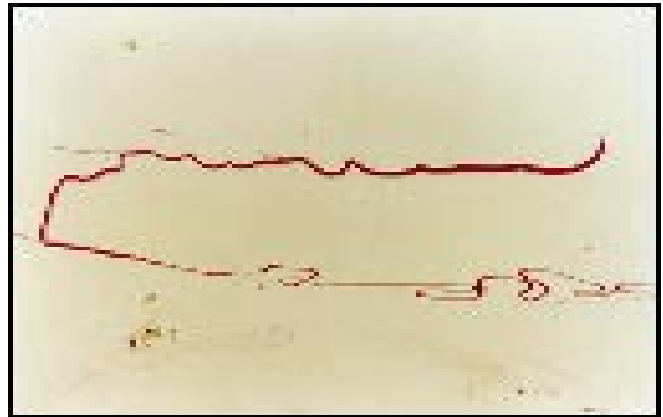
therefore considered an inevitable complication. This conclusion arose, in part, because PCO occurred in up to 50% of cases.

The necessary tenting up of the anterior capsule during subcapsular (or cortical cleaving) hydrodissection is best achieved by using a cannula with a bend at the tip allowing a flow of fluid toward the capsule to efficiently separate capsule from cortex (Figure 34.5). By freeing and rotating the lens nucleus, hydrodissection facilitates lens nucleus and cortex removal without zonular-capsular rupture.⁴⁷ We now know from autopsy and experimental studies that thorough cortical and cellular clean-up from the capsular bag can be accomplished in most cases.⁴² Use of hydrodissection during cataract surgery allowed more efficient removal of cortex and LECs, (which in turn reduces PCO), when compared to control eyes where hydrodissection was not utilized (Figures 34.5).⁴² A successfully performed cortical cleaving hydrodissection provides an easy way to remove the entire lens cortex as well as nucleus. Occasionally, this can even occur without the need for cortical aspiration with a separate irrigation/aspiration instrument.

Surgeons use balanced salt solution (Alcon Inc., Fort Worth, TX., USA) while performing cortical cleaving hydrodissection. Recent experimental animal studies from our Center have shown that use of preservative-free lidocaine 1 percent during hydrodissection may diminish the amount of live LECs by facilitating cortical clean-up, by loosening the desmosomal area of cell-cell adhesion with decreased cellular adherence, or by a direct toxic effect.⁴⁸ Corneal endothelial toxicity continues to be a major concern of using hypo-osmolar agents (to loosen the cell-cell adhesion) during hydrodissection or any step of cataract surgery, in absence of a sealed capsular bag. However, it is now possible to irrigate the entire capsular bag using an injection-molded silicone disposable innovative device known as Perfect Capsule™ (Milvella Pty. Ltd., Sydney, Australia). Sealed capsule irrigation (SCI) isolates the internal lens capsule, and facilitates removal of residual cortical material as well as lens epithelial cells, and thus prevents/delays capsular bag opacification.^{49,50} The SCI technique is pioneered by one of us (AJM), and discussed in details in later part of this chapter.



A



B



C

FIGURES 34.5A to C: In our laboratory studies on human eyes obtained postmortem, we were pleasantly surprised that with copious hydrodissection and meticulous cortical clean-up, most cortex and most if not all lens epithelial cells from the equator (E cells) could be removed when compared to eyes without hydrodissection. (A) Gross photograph of experimental surgery on a human cadaver eye from Anterior (surgeon's) view showing the technique of subcapsular hydrodissection (cortical cleaving hydrodissection). Note that the 27-gauge bent cannula is immediately under the edge of the capsulorhexis. (B) Photomicrograph of the lens capsular bag of one of the eye that underwent experimental cataract surgery associated with copious hydrodissection. Note excellent removal of lens material and E cells—a very clear capsular bag. (Periodic acid-Schiff stain, original magnification $\times 750$). (C) Photomicrograph of a sagittal view of a crystalline lens without hydrodissection in human cadaver eyes. Note residual cortical material and equatorial lens epithelial cells. (Periodic acid-Schiff stain, original magnification $250\times$)

In-The-Bag (Capsular) IOL Fixation

The hallmark of modern cataract surgery is the achievement of consistent and secure in-the-bag (capsular) fixation (Table 34.1). The most obvious advantage of in-the-bag fixation is the accomplishment of good optic centration and sequestration of the IOL from adjacent uveal tissues. Numerous other advantages have been described elsewhere.^{51,52} However, it is not often appreciated that this is also extremely important in reducing the amount of PCO.

One desired goal of in-the-bag fixation is enhancing the IOL optic barrier effect, which is functional and maximal when the lens optic is fully in-the-bag with direct contact with the posterior

capsule. In case one or both haptics are not placed in the bag, a potential space is created, allowing an avenue for cells to grow posteriorly toward the visual axis. The reader may recall the barrier ridge IOL design devised by Kenneth Hoffer in the 1980s, which did not function sufficiently at the time.⁹ The reason was not a problem with the concept or the IOLs themselves, but rather that only about 30 percent of posterior chamber IOLs were implanted inside the bag at the time.

With nonphaco ECCE in-the-bag fixation of IOLs occurs about 60 percent of the time. One explanation is that many cases combined rigid design IOLs with can-opener anterior capsulotomies. Secure and permanent in-the-bag fixation only occurred in

approximately 60 percent of cases.⁴⁰ However, when considering modern foldable lens implantation, the number rapidly rises to over 90 percent. It is not the foldable IOL itself, or even the small incision in and of itself that provides this positive result, but rather the fact that successful foldable IOL insertion generally requires meticulous surgery, with the necessity of performing a continuous curvilinear capsulorhexis (CCC) and secures implantation of both IOL loops in the bag.⁴⁰

Capsulorhexis Edge on IOL Surface

A less obvious, but significant addition to precise in-the-bag fixation, is creating a CCC diameter slightly smaller than that of the IOL optic. For example, if the IOL optic were 6.0 mm, the capsulorhexis diameter would ideally be slightly smaller, perhaps 5.0-5.5 mm. This places the cut anterior capsule edge on the anterior surface of the optic, providing a tight fit (analogous to a “shrink wrap”) and helping to sequester the optic in the capsular bag from the surrounding aqueous humor (Table 34.1). This mechanism may support protecting the milieu within the capsule from at least some potentially deleterious factors within the aqueous, especially some macromolecules, and some inflammatory mediators. The concept of capsular sequestration based on the CCC size and shape is subtle, but more and more surgeons appear to be applying this principle and seeing its advantages.

Implant-related Factors to Reduce PCO

In addition to the three above-mentioned surgery-related factors we will describe briefly the three IOL-related factors, which in our opinion play an important role in the eradication of PCO.

IOL Biocompatibility

Lens material biocompatibility (Table 34.1) is an often-misunderstood term. It can be defined by many criteria, e.g. the ability to inhibit stimulation of epithelial cellular proliferation.³⁸ The less the cell proliferation the lower the chance for secondary cataract formation. In our large series of postmortem human eyes, the Alcon AcrySof[®] IOLs presented with minimal to absent Soemmering’s ring formation, PCO and ACO (Figure 34.6).^{1-4,13,14,41,51} In addition, the



FIGURE 34.6: Among 9 different types of rigid and foldable lens designs studies in pseudophakic human eyes, hydrophobic acrylic IOLs had the lowest PCO formation and therefore the Nd: YAG laser posterior capsulotomy rates. The lowest PCO score was confirmed by gross and histological evaluation. (A) Human eye obtained postmortem, Miyake-Apple posterior photographic technique of a single-piece hydrophobic acrylic optic/haptics (Alcon AcrySof[®]) PC-IOL showing a symmetric fixation and excellent centration. The surgical technique was excellent and there is virtually no retained/regenerative material (Soemmering’s ring). This obviously represents good cortical clean-up, and also suggests good biocompatibility with minimal proliferation. (B) A 3-piece acrylic optic/PMMA haptics (Alcon AcrySof[®]) showing a good example of excellent cortical clean-up, and also suggesting good biocompatibility, with minimal cellular proliferation

amount of cell proliferation is greatly influenced by surgical factors, such as copious cortical clean-up. Furthermore, the time factor also plays a role, such as the duration of the implant in the eye. Additional long-term studies are required to assess the overall role of “biocompatibility” in the pathogenesis of PCO.

Maximal IOL Optic-Posterior Capsule Contact

Other contributing factors in reducing PCO are posterior angulation of the IOL haptic and posterior convexity of the optic (Table 34.1). This is due to the creation of a “shrink wrap”, a tight fit of the posterior capsule against the back of the IOL optic. The relative “stickiness” of the IOL optic biomaterial probably helps producing an adhesion between the capsule and IOL optic. There is preliminary evidence that the hydrophobic acrylic IOL biomaterial provides enhanced capsular adhesion, or “bioadhesion”.⁵⁴⁻⁵⁶ This will require further study.

Barrier Effect of the IOL Optic

The IOL optic barrier effect (Table 34.1), plays an important role as a second line of defense against PCO, especially in cases where retained cortex and cells remain following ECCE. The concept of the barrier effect goes back to the original Ridley lens.⁸ If accurately implanted in the capsular bag, it provided an excellent barrier effect, with almost complete filling of the capsular bag and contact of the posterior IOL optic to the posterior capsule (“no space, no cells”). A lens with one or both haptics “out-of-the-bag” has much less of a chance to produce a barrier effect. Indeed, the IOL optic’s barrier function has been one of the main reasons that PC-IOLs implanted after ECCE throughout the decades did not produce an unacceptably high incidence of florid PCO.

A subtle difference between classic optics with a round tapered edge and optics with a square truncated edge became evident recently (Table 34.1). The effect of a square-edge optic design as a barrier was first discussed by Nishi et al^{57,58} in articles related to PCO. In a clinicopathological study, our laboratory was the first to confirm this phenomenon in human eyes (Figure 34.7).^{32,33} We reported our results of a large histopathological analysis covering the IOL barrier effect, with special reference to the efficacy of the truncated edge (Figure 34.7). A truncated, square-edged optic rim appears to cause a complete blockade of cells at the optic edge, preventing epithelial ingrowth over the posterior capsule.⁶⁰⁻⁶⁷ The enhanced barrier effect of this particular edge geometry provides another supplemental factor, in addition to the five above-mentioned factors, that has



FIGURE 34.7: Even when a significant Soemmering’s ring remains in the eye, a square truncated edge such as what exists on the AcrySof® IOL provides a second line of defense against cortical ingrowth. Other IOLs with square or truncated optic edges include the Ciba Mentor MemoryLens™, the Staar Surgical/Bausch and Lomb Surgical elastimide-polyimide silicone design, the Pfizer CeeOn Edge™ 911 silicone IOL, Advanced Medical Optics Sensar OptiEdge™ and plate haptic IOLs. (A) Gross photograph from behind (Miyake-Apple posterior photographic technique) of a human eye obtained postmortem containing an AcrySof® IOL. Some cortical remnants (a Soemmering’s ring) remain peripherally but the optical zone remains totally cell free, with no encroachment of cells past the edge of the IOL optic. (B) Photomicrograph of an eye in which an Alcon AcrySof® IOL was implanted. Clean-up was not complete and a Soemmering’s ring resulted. However, the Soemmering’s ring remnants (red) were blocked by the square optic edge, leaving the posterior capsule cell-free. (Masson’s trichrome stain, original magnification × 100)

significantly diminished the overall incidence of clinical PCO.

Our past studies,^{13,14} demonstrated that the original, three-piece MA60 AcrySof® (Alcon Inc., Fort

Worth, TX) IOL successfully combined these three IOL-related factors (Table 34.1, Figures 34.6 and 34.7) in a way that produced a major PCO advantage. Other manufacturers have begun to incorporate these PCO preventing features, such as a sharp, or squared-posterior edge. The Cee-On 911™ silicone IOL (Pfizer Inc., New York, NY) was the first silicone IOL to feature a squared edge. The Sensar™ hydrophobic acrylic (Advanced Medical Optics Inc., Santa Ana, CA) and Clariflex™ silicone (Advanced Medical Optics Inc, Santa Ana, CA) IOLs now feature a sharp posterior edge, combined with a rounded anterior edge. Modification in the Centerflex® one-piece hydrophilic IOL design (Rayner Inc., Hove East Sussex, UK) has been incorporated to prevent cellular ingrowth at the broad optic-haptic junction. The modified profile provides a square edge (barrier, ridge, wall) for 360 degrees around the lens optic (enhanced square edge), eliminating the potential defect (Figure 34.8). This further minimizes the ingrowth of migrating LECs toward the visual axis.

A major disadvantage of the truncated edge is the production of clinical visual aberrations, such as glare, halos and crescents.⁶⁸ Subtle changes in manufacturing are now helping alleviate glare and other optical complications. Figure 34.9 illustrates scanning electron microscopy of the single-piece AcrySof® (SA30AL) IOL showing the square (truncated) edge of the optic that had a matte (velvet) appearance, a feature that may minimize edge glare and other visual phenomena. Another example of design modification include introduction of Sensar OpticEdge™ IOL manufactured by Advanced Medical Optics. This IOL has squared posterior edge and a round anterior edge (Figure 34.10). Therefore, it avoids the optical dysphotopsias, while retaining the PCO beneficial squared posterior edge.

CONFIRMATION OF SURGICAL AND IMPLANT RELATED FACTORS IN THE LABORATORY AND CLINICAL STUDIES

Laboratory Analysis of Nd: YAG Posterior Capsulotomy Rates in Pseudophakic Human Eyes Obtained Postmortem

Review of literature,^{9,37,38,55-67} experimental studies from our center,^{14,32,33,44,45} and a complete analysis of our large series of eyes obtained postmortem^{1-4,13,51} has

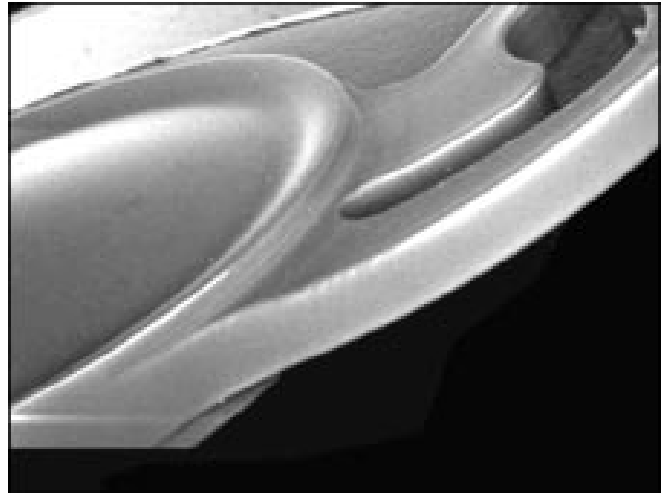


FIGURE 34.8: Scanning electron photograph obtained at the level of the optic-haptic junction of the Rayner Centerflex™ one-piece hydrophilic IOL. This profile provides a square edge (barrier, ridge, wall) for 360 degrees around the lens optic, eliminating the potential defect. The round tapered edge of classic one-piece IOL design at the optic edge that subtends the optic-haptic junction represents a theoretical “Achilles’ heel” in which when ingrowing cells may bypass the desired barrier

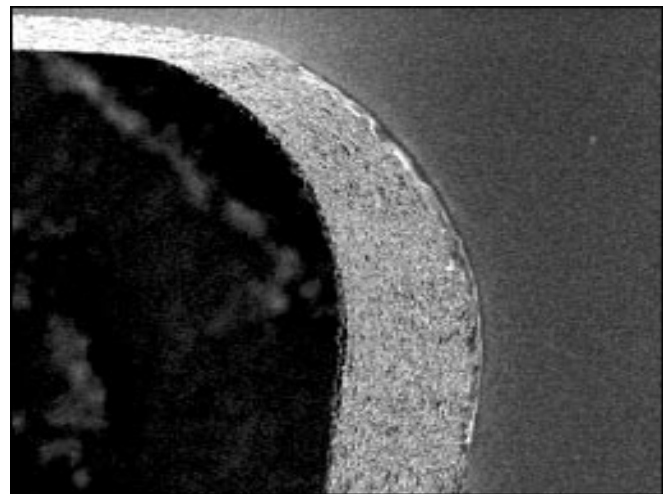


FIGURE 34.9: Scanning electron microscopy of the single-piece AcrySof® (SA30AL) IOL showed excellent surface finish. Note the square (truncated) edge of the optic that had a matte (velvet) appearance, a feature that may minimize edge glare and other visual phenomena. A well-fabricated square or truncated haptic edge was demonstrated

helped us develop the above-mentioned six factors that we believe greatly contribute to the reduction of PCO. Furthermore, an analysis of Nd: YAG laser posterior capsulotomy rates among 9 commonly used IOL models has led us to the optimistic conclusion that

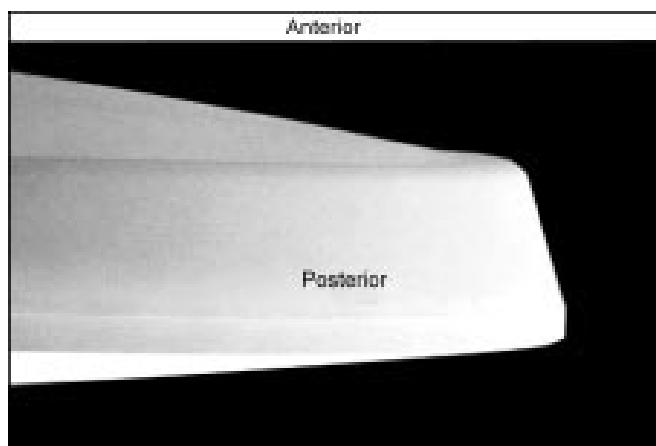


FIGURE 34.10: Scanning electron microscopy of the advanced medical optics sensor OpticEdge™ IOL design. Note the rounded anterior edge that scatters the light thus reducing the internal reflection. The sloping side edge minimizes potential for edge glare and the square posterior edge facilitates 360 degree capsular seal

the incidence of PCO is rapidly diminishing, at least in the industrialized world. Table 34.2 shows the ranking of the Nd: YAG laser posterior capsulotomy rates (%) evaluated in a total of 7523 pseudophakic human eye obtained postmortem (between January 1988 to July 2002) at our Center. Note the lowest percentage of Nd: YAG laser posterior capsulotomy (at the top) and the relatively older, (rigid lenses and early foldable lens designs) had shown higher ND: YAG laser posterior capsulotomy rate (shown at the bottom of the table [unpublished data]). The three lenses with the lowest posterior capsulotomy rates

ranging between 0 percent and 12.20 percent are modern designs, mostly implanted after 1992 in contrast to the remaining 6 lenses with the higher rates ranging between 20.2 percent and 31.5 percent. These were all older designs, already in the database prior to 1992. In order to evaluate the influence of lens quality vs. the influence of the surgical technique on the PCO/ Nd: YAG laser posterior capsulotomy rates, it is useful to follow a trend-line over a long-term period. Under optimal conditions, but not possible in this analysis, the information should be viewed considering the age and the duration of each implant. One of the important limitation in most of the studies of pseudophakic human eyes obtained postmortem from our Center,^{1-4,13,51} was lack of detailed information such as dates of IOL implantation or the time between implantation and death. These details were difficult to determine due to ethical considerations. These variables are going to factor out over time as larger numbers are obtained and the trend “time line” is extended.¹³

Tracking the trend “time lines” for each lens design will be necessary to help rule out other factors in addition to the duration of each implant in the eye (for example, the quality of surgery) in order to properly assess the differences among the IOLs. Various surgeons’ criteria for Nd: YAG laser capsulotomy (e.g. aggressive, conservative) also plays a role in the rate. Nevertheless surgeons’ criteria, surgical technique, and implant duration will become equalized as the number of accessions and the duration of the study increases.

Table 34.2: Tabulation of Nd: YAG laser capsulotomy rates on 9 different IOL types between January 1988 up to July 2002. These are listed with the highest Nd: YAG laser posterior capsulotomy rates below. Note that the rigid IOL optic designs had the highest rates. The newly introduced foldable IOL designs had the Nd: YAG laser posterior capsulotomy in single digits (less than 10%)

IOL	Total	Nd:YAG	YAG%
1 PC All-Acrylic (AcrySof)	14	0	0%
3 PC Acrylic-PMMA (AcrySof)	470	22	4.70%
3 PC Silicone-PMMA	148	18	12.20%
1 PC Silicone Plate, Large Hole	109	22	20.20%
3 PC Silicone-Polyimide	91	20	22.00%
1 PC Silicone Plate, Small Hole	155	36	23.20%
3 PC Silicone-Prolene	409	97	23.70%
3 PC PMMA (Rigid)	3781	1158	30.60%
1 PC All-PMMA (Rigid)	2346	738	31.50%
All Lenses since 1/88	7523	2111	28.10%
Foldable lenses	1396	215	15.40%
Rigid Lenses	6127	1896	30.90%

Confirmation of the Six Factors in Clinical Studies

We would like to cite 3 studies that confirm the advantage of applying one or more surgical/IOL related factors to prevent or delay PCO formation. Firstly, a clinical study, by Ram, Pandey, Apple, and associates⁶⁹ confirmed previous pathological studies demonstrating the importance of in-the-bag fixation of posterior chamber (PC) IOLs (both rigid and foldable) in reducing the incidence of PCO. This is true for both standard ECCE and phacoemulsification. This study comprised 278 eyes of 263 patients having ECCE and 318 eyes of 297 patients having phacoemulsification with PC IOL implantation. The presence of visually significant PCO (a decrease in Snellen visual acuity of 2 or more lines) and IOL haptic fixation were evaluated postoperatively using slit lamp biomicroscopy. Haptic position was noted as in-the-bag (B-B), 1 haptic in the bag and 1 in the sulcus (bag-sulcus [B-S]), or both haptics out of the bag (sulcus-sulcus [S-S]). In addition, the rate of visually significant PCO was compared among 3 IOL biomaterials: polymethyl methacrylate, silicone, and hydrophobic acrylic. Visually significant PCO occurred in 42.45 percent of eyes having ECCE and 19.18 percent of eyes having phacoemulsification ($P < .001$, chi-square test) after a mean follow-up of 2.4 years \pm 0.7 (SD). In both groups, visually significant PCO was significantly less in eyes with B-B fixation than in those with B-S or S-S fixation ($P < .001$). The rate of visually significant PCO in all eyes in the phacoemulsification group with B-B fixation was low (11.90%) and was significantly lower in eyes with a hydrophobic acrylic IOL (2.22%; $P < .05$, chi-square test). The results of this study suggested in-the-bag PC IOL fixation reduces the incidence of PCO. Thorough removal of lens substance, including hydrodissection-assisted cortical clean-up, and in-the-bag PC IOL fixation seem to be the most important surgical factors in reducing PCO, regardless of surgical procedure or IOL type used.

Ravalico and associates⁷⁰ determined the ideal capsulorhexis size for minimizing the incidence of PCO. These authors retrospectively evaluated 107 patients who had extracapsular cataract extraction with capsulorhexis and capsular bag IOL implantation. The PCO site (central, paracentral, and peripheral) and degree (mild, moderate, and severe) were evaluated

in relation to the capsulorhexis edge location relative to the IOL optic. Patients were divided into three groups. Group 1: capsulorhexis free edge located on the IOL optic for 360 degrees; Group 2: capsulorhexis free edge located asymmetrically on and peripherally to the IOL optic; Group 3: capsulorhexis free edge located peripherally to IOL optic for 360 degrees. The results of this study demonstrated that, in Groups 1 and 2, the capsular transparency was higher than in Group 3 ($P < .04$). Central opacification percentage was lower in Group 1 than in Groups 2 and 3 ($P < .04$). These authors concluded that capsulorhexis with a slightly smaller diameter than the IOL optic appears to be better than a large-size capsulorhexis in reducing the incidence of PCO.

T. Akahoshi, MD, reported his experience of three-piece AcrySof[®] IOL implantation in more than 17,000 human eyes in Japan. The incidence of YAG capsulotomy has been found to be 1.19 percent (207 out of 17,329) after 75 months of follow-up period. Among the cases treated with Nd: YAG laser, 81.2 percent had an eccentric and incomplete coverage of the lens optic by the anterior capsulorhexis margin. In 8.2 percent of the cases, the anterior capsule margin was on the optic edge and in 10.6 percent of the cases it was completely outside. Long-term follow-up revealed that the incidence of after cataract formation in three-piece AcrySof[®] IOLs is extremely low. The size and position of the CCC, however, seems to be one of the most important factors to reduce the YAG capsulotomy rate. (T Akahoshi, MD Clear corneal cataract surgery and AcrySof[®] implantation. Presented in the ASCRS Symposium on Cataract, IOL and Refractive Surgery, Boston, MA, April 28, 2001).

PHARMACOLOGICAL PREVENTION OF POSTERIOR CAPSULE OPACIFICATION

Intraocular application of pharmacologic agents has also been investigated by several authors as a means to prevent PCO.⁷¹⁻⁷⁶ The idea was to selectively destroy the LECs and avoid toxic side effects on other intraocular tissues such as the sensitive corneal endothelium. Pharmacologic agents being investigated include cancer chemotherapeutic drugs (e.g. antimetabolites such as methotrexate, mitomycin, daunomycin, 5-FU, colchicine, and daunorubicin), anti-inflammatory substances, hypo-osmolar drugs, and immunological agents.

We designed an intracapsular ring to prevent capsular bag contraction and also to inhibit LECs proliferation and metaplasia by sustained release of 5-FU.⁷⁷⁻⁷⁹ The effects of the intracapsular ring on the prevention of PCO was prospectively studied by analyzing postmortem ocular specimens macroscopically using Miyake-Apple technique^{81,82} and histologically. We also evaluated the toxic effects of 5-FU on the corneal endothelium, capsular bag and retina of rabbits.⁷⁷ Results of this study suggested that implantation of intracapsular ring may prevent central PCO after cataract surgery by mechanically blocking migration of lens epithelial cells towards the central visual axis. The potential pharmacological effect of 5-FU for PCO prevention was not demonstrated in this experimental study.⁷⁷

Toxicity to corneal endothelium and other ocular structure remains one of the major concern for using cancer chemotherapeutic drugs, anti-inflammatory substances, hypo-osmolar drugs, and immunological agents, when intralenticular compartment is in direct contact with anterior chamber. However, with the development of a *SCI device*, it is now possible to precisely deliver the pharmacological/ hypo-osmolar agents to the lens epithelial cells within the capsular bag, while minimizing the potential for collateral ocular damage.^{49,50}

SEALED CAPSULE IRRIGATION FOR MAINTAINING POSTOPERATIVE CAPSULAR BAG TRANSPARENCY

Sealed Capsule Irrigation (SCI) device may allow the isolated safe delivery of pharmacologic agents into the capsular bag following cataract surgery (Figure 34.11).^{49,50} Developed by one of the co-author (AJM), SCI is a form of Sealed Irrigation System applied to the internal eye, and may be applied elsewhere to the body. In the eye, the technique of capsular bag irrigation may be used with pharmacologic agents to target LECs, eliminate PCO and help maintain capsular bag transparency. We consider that SCI should meet the following requirements: it should be minimally invasive, be easy to use, fit through a small incision, be relatively inexpensive, provide a repeatable seal with the lens capsule, and be not add significantly to the duration of routine cataract surgery.

The intact human lens capsule is functionally a separate compartment within the eye. Once breached,

the intralenticular compartment becomes continuous with the anterior chamber and the rest of the eye. However, since intact capsulorhexis is now routinely performed, we devised a technique to reseal the capsular bag following lens removal. By resealing the capsular bag, we re-compartmentalize the lens and allow for the selective irrigation of the internal contents of the capsular bag.

The SCI device called Perfect Capsule™ (Milvella Pty. Ltd., Sydney, Australia), which is made from biomedical grade soft silicone, allows the surgeon to reseal the capsular bag. The device consists of a rounded plate containing a suction ring, which abuts the anterior capsule, and an extension arm that passes through a phacoemulsification wound. This extension arm carries a vacuum channel which supplies vacuum to the suction ring, and a combined irrigation and aspiration channel. The irrigation and aspiration channels allow for communication between the sealed capsular bag and the external eye.

We have performed initial testing of a 1st generation device on postmortem porcine lens capsules and demonstrated its effectiveness for sealed capsule irrigation.⁴⁹ We have further refined the device to its current third generation form, to incorporate changes which would allow it to be used in small incision cataract surgery, and address the potential risk of pseudosuction, which would result in loss of sealing of the capsular bag. We considered the properties of the adult capsule to be less elastic than the pediatric capsule, and less prone to pseudosuction. The device was modified to contain a vacuum manifold within the suction ring that ensures no focal occlusion of the suction ring is possible at any point, and that the vacuum is evenly distributed to the entire ring.

In performing product validation of this third generation device, 13 randomly chosen devices were subjected to testing on pig capsule. In all cases, the devices sealed the capsule using vacuum generated by a 20 mL lockable syringe resulting in a maximal vacuum pressure of greater than 700 mmHg on application, with no evidence of pseudosuction with less than 2.5 percent reduction in vacuum pressure over a 1 minute period. One of these devices was then selected for repeat testing for a period of 10 minutes with less than 5 percent reduction in vacuum at 10 minutes.

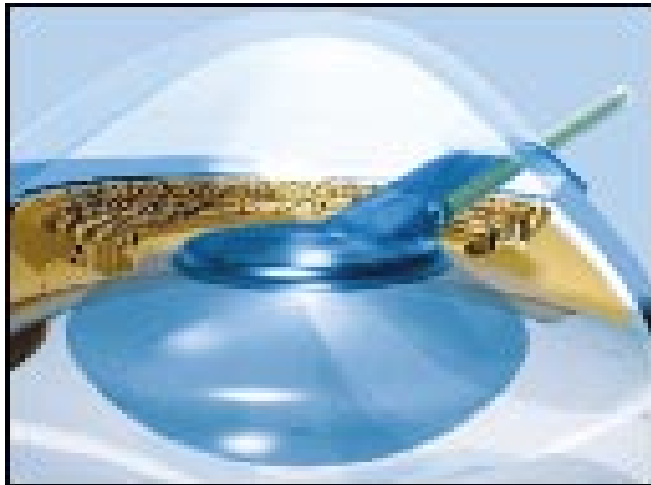
We are continuing to demonstrate that selective capsular bag irrigation can be performed in animals



A



B



C



D

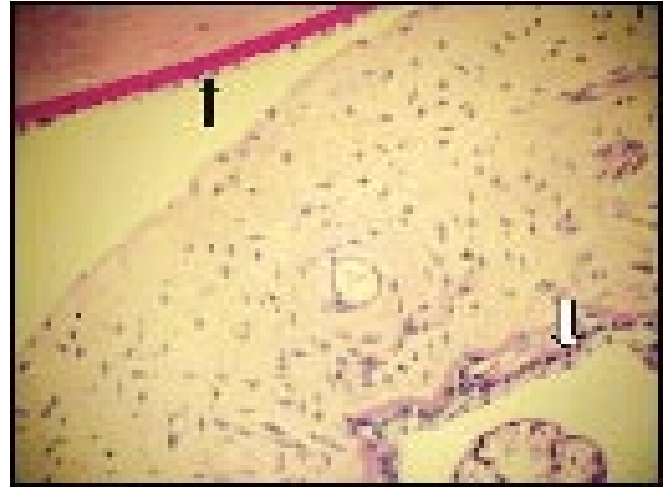
FIGURES 34.11A to D: Schematic diagrams illustrating the concept of sealed capsule irrigating device (Perfect Capsule,TM Milvella Pty. Ltd., Sydney, Australia). This device is designed to hold the capsular bag by means of a toroidal suction ring connected to a locking suction syringe. An irrigation /aspiration port allows fluids to be injected through the device into the empty capsule, significantly reducing the concentration of irrigation fluid able to contact other ocular structures and thus perform sealed capsule irrigation. (A) Sealed capsule irrigation device viewed from the top. It consists of a round plate that seals against the capsule and an extension arm that passes outside the wound to provide to the internal lens capsule. (B) Sealed capsule irrigation device is folded and inserted through a 3-mm incision. (C) Sealed capsule irrigation device is placed onto the capsular bag and vacuum-activated by a syringe. (D) Internal irrigation of the capsular bag using sealed capsule irrigation device

and humans. In a rabbit study,⁵⁰ we assessed the ability to deliver a nonspecific extremely toxic agent directly to the LECs postcrystalline lens removal, and assessed the eyes histologically for evidence of collateral damage (Figures 34.12 to 34.14). A total of 6 New Zealand White rabbit eyes were selected. The eyes were divided into 3 groups of 4 eyes. All eyes underwent phacoaspiration of the crystalline lens via

a 3.2 mm corneal incision. Group 1 eyes were used as control. In Group 2 eyes, the capsular bag was irrigated with 1% Triton X-100 and demineralized water for injection (DWI) for 5 minutes. In Group 3 eyes, the capsular bag was isolated from the anterior segment using the Perfect CapsuleTM. Immediately after the surgery, all (6) rabbits were humanly euthanized. The enucleated eyes were immediately



A



B



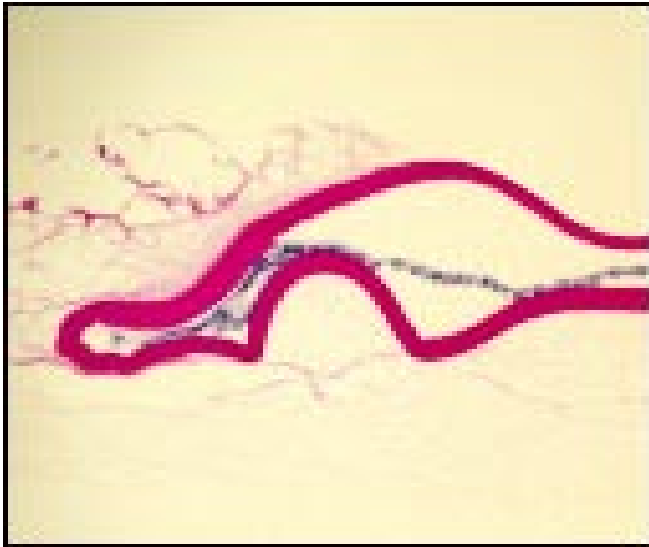
C

FIGURES 34.12A to C: Histological findings of the rabbit eyes in group 1 (phacoaspiration surgery without any treatment, control group). (A) Photomicrograph showing the capsular bag. Note the presence of residual viable LECs within the capsular bag. (Periodic acid-Schiff stain, original magnification x40). (B) Photomicrograph showing healthy corneal endothelial cells and posterior iris epithelium. (Periodic acid-Schiff stain, original magnification x40). (C) Photomicrograph showing undamaged retinal tissue and epithelium. There is postmortem artefactual detachment at the ora serata. (Periodic acid-Schiff stain, original magnification x40)

fixed in 10 percent neutral buffered formalin and histological analysis was performed to assess the corneal endothelium, iris, and retina. The capsular bag was also assessed and residual equatorial LECs were evaluated. There was no intraoperative complication in any eye. The capsular bag was sealed and inflated under SCI, Perfect Capsule™ in all treatment eyes in Group 3. Histological evaluation revealed no evidence of any collateral damage in Group 1 (control, group) and Group 3 (with SCI) (Figures 34.12 and 34.14). Significant histological damage to the cornea, iris and peripheral retina was noted in Group 2 eyes, which underwent irrigation with DWI and Triton X-100 (without SCI) (Figure 34.13). Histological evaluation of capsular bag

suggests presence of LECs in Group 1 (control group) and Group 2 (without SCI) (Figures 34.12 and 34.13). In the presence of SCI, Triton X-100 caused almost complete destruction of LECs in the capsular bag (Figure 34.14). Result of this pilot study suggest that SCI allows selective delivery of toxic agents directly into the capsular bag preventing collateral damage to surrounding intraocular structures in a rabbit eye. The SCI device kept the capsular bag well-inflated intraoperatively and therefore it may allow the isolated safe delivery of pharmacological agents into the capsular bag during cataract surgery.

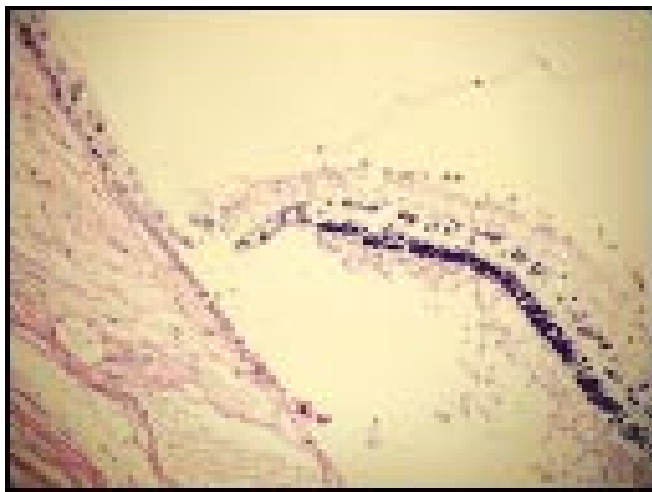
We have recently completed a 1-year follow-up on a total of 9 human eyes underwent cataract-IOL surgery using SCI with distilled water and silicone



A



B



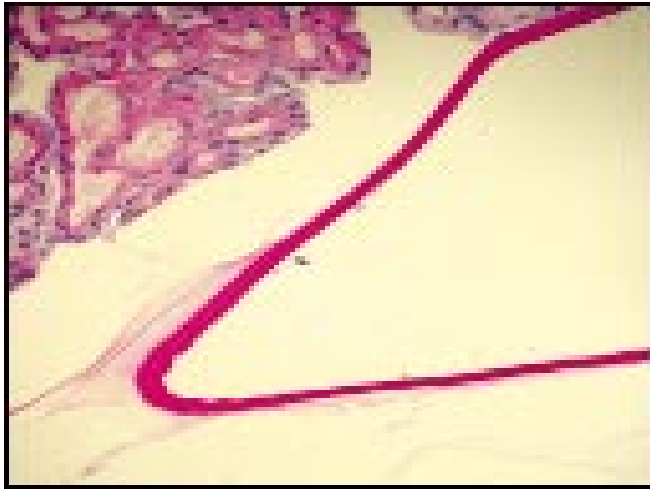
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FIGURES 34.13A to C: Histological findings of the rabbit eyes in group 2 (phacoaspiration surgery and non-selective irrigation of the capsular bag with DWI and TTX-100 without SCI). (A) Photomicrograph showing the collapsed fornices of the capsular bag. Note the presence of viable LECs at the anterior and equatorial region of the capsular bag. (Periodic acid-Schiff stain, original magnification x40). (B) Photomicrograph showing almost total loss of corneal endothelial cells, with bare Descemet's membrane. There is a loss of integrity of posterior iris epithelium (Periodic acid-Schiff stain, original magnification x40). (C) Photomicrograph of the peripheral retina showing significant disorganization of the retinal tissue and epithelium. (Periodic acid-Schiff stain, original magnification x40)

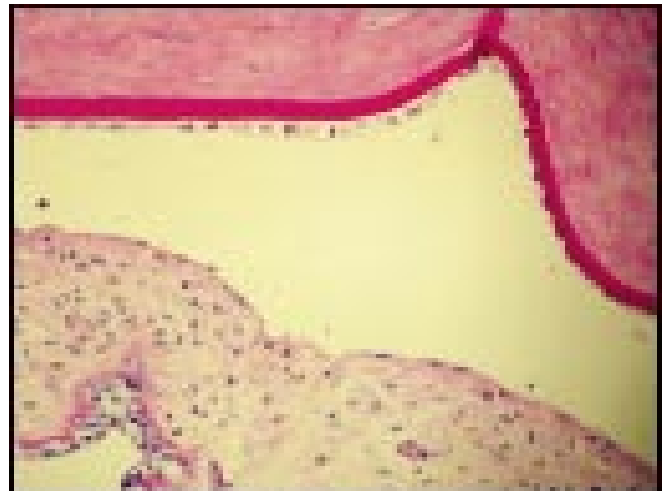
lenses (SI40NB, Clariflex®, Advanced Medical Optics, Santa Ana, CA, USA). A control group of 9 eyes, underwent cataract surgery with implantation of silicone lenses, without SCI. All eyes in the treatment Group, underwent internal irrigation of the capsular bag using 20cc of distilled water for 60 seconds to 90 seconds using the Perfect Capsule,™. Fluorescein sodium (0.01%) or trypan blue (0.01%) was used to identify any leakage into the anterior chamber during the SCI procedure (Figure 34.15). Slit lamp biomicroscopic examination was performed at 1 day, 1 week, 3, 6, and 12 months to evaluate anterior capsule opacification (ACO), capsular folds/wrinkling, capsular phimosis, and posterior capsule opacification

(PCO) (area/severity). Intraoperatively, there was no visible leakage of fluorescein sodium/trypan blue dyes into the anterior chamber during SCI in all eyes in Group AA and AS, indicative of effective seal provided by the SCI device. Follow-up examination at 6 and 12 months demonstrated a significant reduction in ACO in all eyes, which had undergone SCI with distilled water treatment in comparison to control eyes (Figures 34.16 to 34.20). In addition, the degree of capsular phimosis was significantly reduced in treatment group, compared to control groups.

Using SCI technique, targeting of lens epithelial cells to prevent PCO can be safely conducted using precise delivery of known doses of pharmacologic



A



B



C

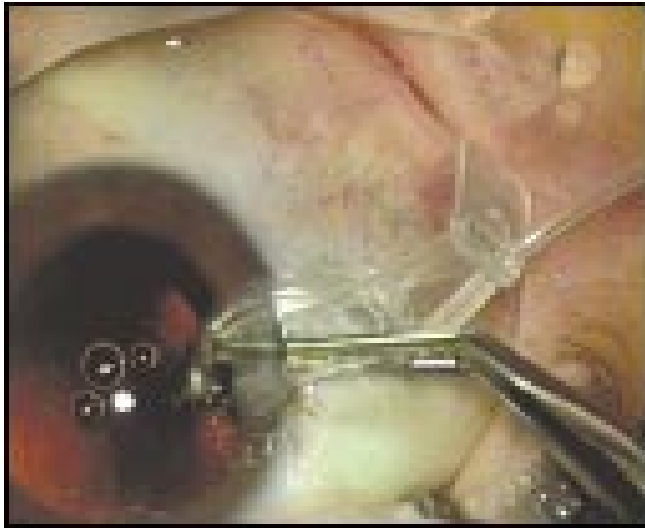
FIGURES 34.14A to C: Histological findings of the rabbit eyes in Group 3 (phacoaspiration surgery and selective irrigation of the capsular bag with DWI and TTX-100 with SCI). (A) Photomicrograph showing the capsular bag. Note the absence of viable LECs within the capsular fornices. Some nuclear remnants are visible lying on the capsule (Periodic acid-Schiff stain, original magnification $\times 40$). (B) Photomicrograph showing healthy corneal endothelial cells and posterior iris epithelium. (Periodic acid-Schiff stain, original magnification $\times 40$). (C) Photomicrograph showing undamaged peripheral retinal tissue and epithelium. (Periodic acid-Schiff stain, original magnification $\times 40$)

agents, with much less fear of toxicity to surrounding intraocular structures. This method may be utilized to eliminate or modulate LEC activity after cataract surgery, which may lead to less postoperative inflammation and a theoretical reduction in the risk of postoperative cystoid macular edema, reduced anterior and posterior capsule opacification, and allow for definitive implantation of multifocal and accommodative lenses so that the treatment of presbyopia may finally become a reality (Figure 34.21). Clinical studies will be needed to test efficacy of SCI during pediatric cataract surgery. Theoretically, SCI may be helpful to elimination of LECs and therefore avoid the PCO/secondary membrane formation postoperatively. It may obviate the need for primary posterior capsulotomy with anterior vitrectomy intraoperatively.

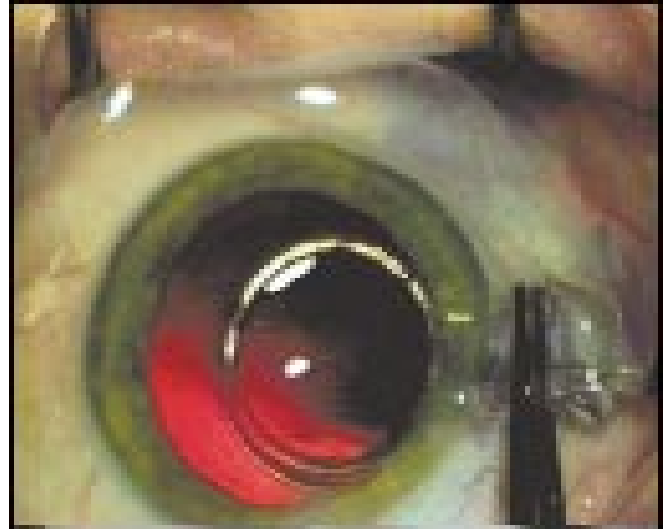
REMOVAL OF LENS EPITHELIAL CELLS USING AQUALASE® LIQUEFACTION DEVICE

AquaLase® Liquefaction Device is a new advancement in lens removal technology which is a part of the newly introduced Infiniti™ Vision System (Alcon Inc., Fort Worth, Tx, USA).⁸² The AquaLase® liquefaction hand-piece proved to be effective to remove nuclear cataracts of up to grade 2 with reasonable efficiency and this technology may have applications in polishing the capsule, removing lens equatorial cells thus minimizing the postoperative cellular proliferation of the LECs, thus minimizing or eliminating the risk of capsular bag fibrosis (ACO/PCO).

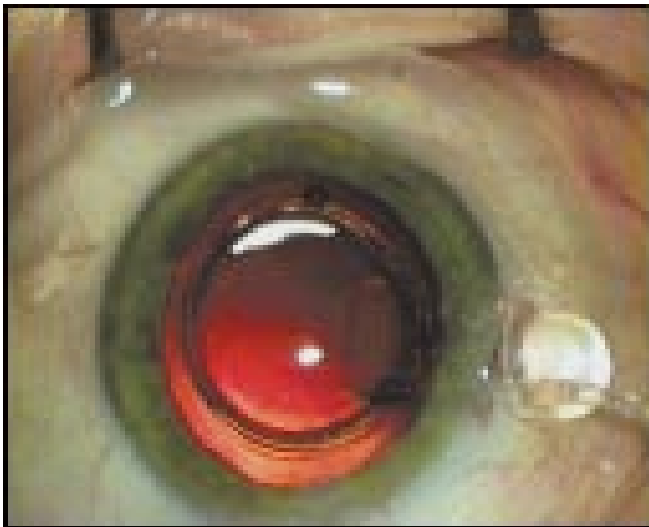
The AquaLase® tip is composed of a soft polymer and has soft, rounded edges. This design makes the



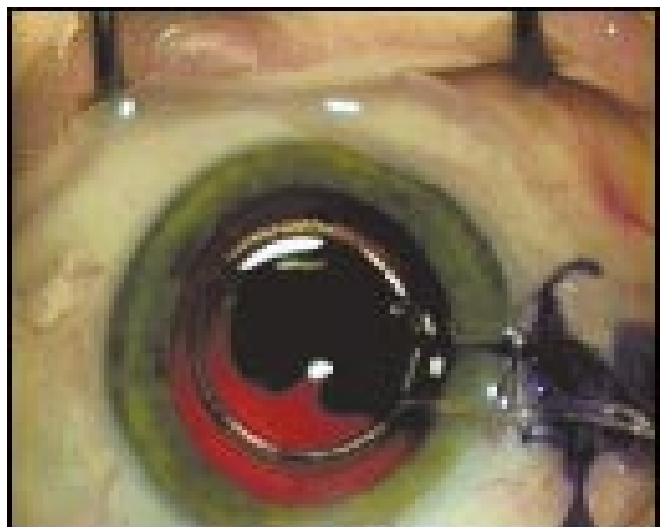
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D

FIGURES 34.15A to D: Clinical photographs showing insertion and capsular irrigation being performed in a human eye using sealed capsule irrigation (SCI, Perfect Capsule™). (A) Because the device is soft, it folds easily and can be inserted through a 3.2 to 3.5 mm incision using Kelman-McPherson forceps (Katena Products, Inc., Denville, NJ, USA) following phacoemulsification. (B and C) The SCI device unfolds instantly in the anterior chamber, resting on the cut edge of the anterior capsule (capsulorhexis margin). (D) The seal and capsule integrity can be tested by inflating the capsule with BSS®, and confirmed with nonleakage of trypan blue (VisionBlue™, DORC, Zuidland, the Netherlands) from the sealed capsular bag to the anterior chamber

instrument more capsule-friendly than metal ultrasound tips. The AquaLase® hand piece propels small pulses of balanced saline solution (BSS®) warmed to 57°C to liquefy lens material just inside the aspiration port of the tip. The BSS pulses are delivered at a maximum rate of 50 Hz, and the surgeon controls the magnitude of the pulses with the Infiniti™ foot pedal.

SUMMARY AND CONCLUSIONS

The tools, surgical procedures, skills, and appropriate IOLs are now available to eradicate PCO. Continued motivation to apply the 6 factors noted in this article, the efficacy of which have been further suggested in a recent study⁵⁴, will help diminish this final major complication of cataract-IOL surgery exactly fifty

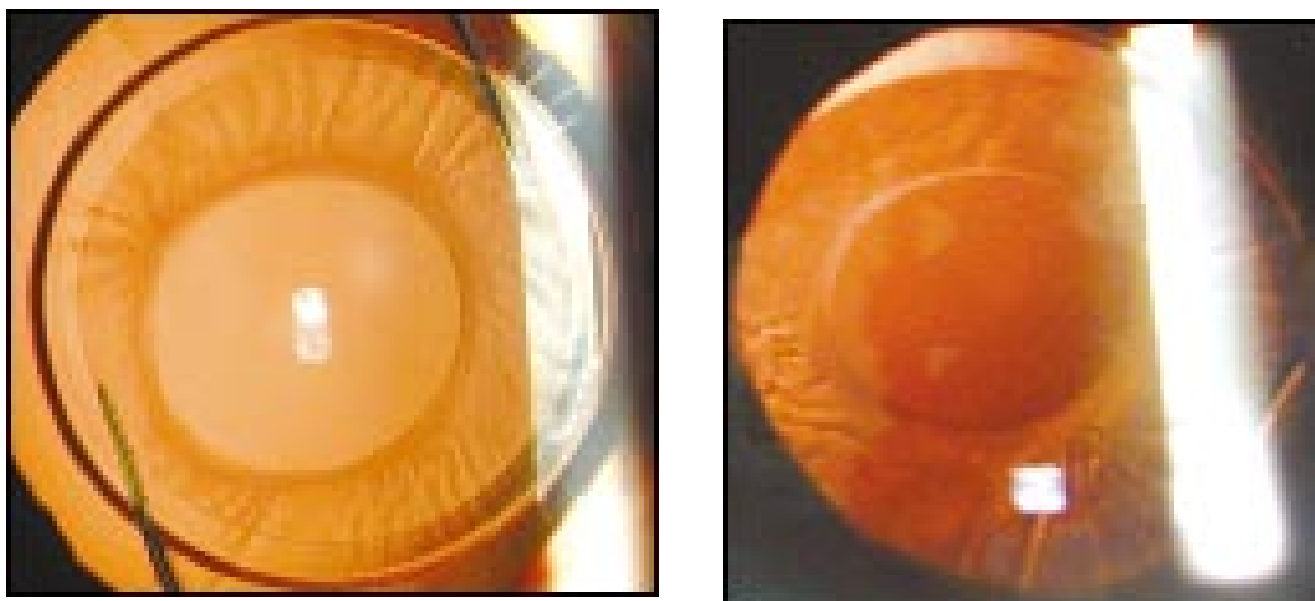


FIGURE 34.16: Slit lamp photograph of control eyes, implanted with silicone IOL designs, after 6 months follow-up. Note the mild anterior capsule opacification associated with some wrinkling and mild capsular phimosis. The posterior capsule appears nonopacified

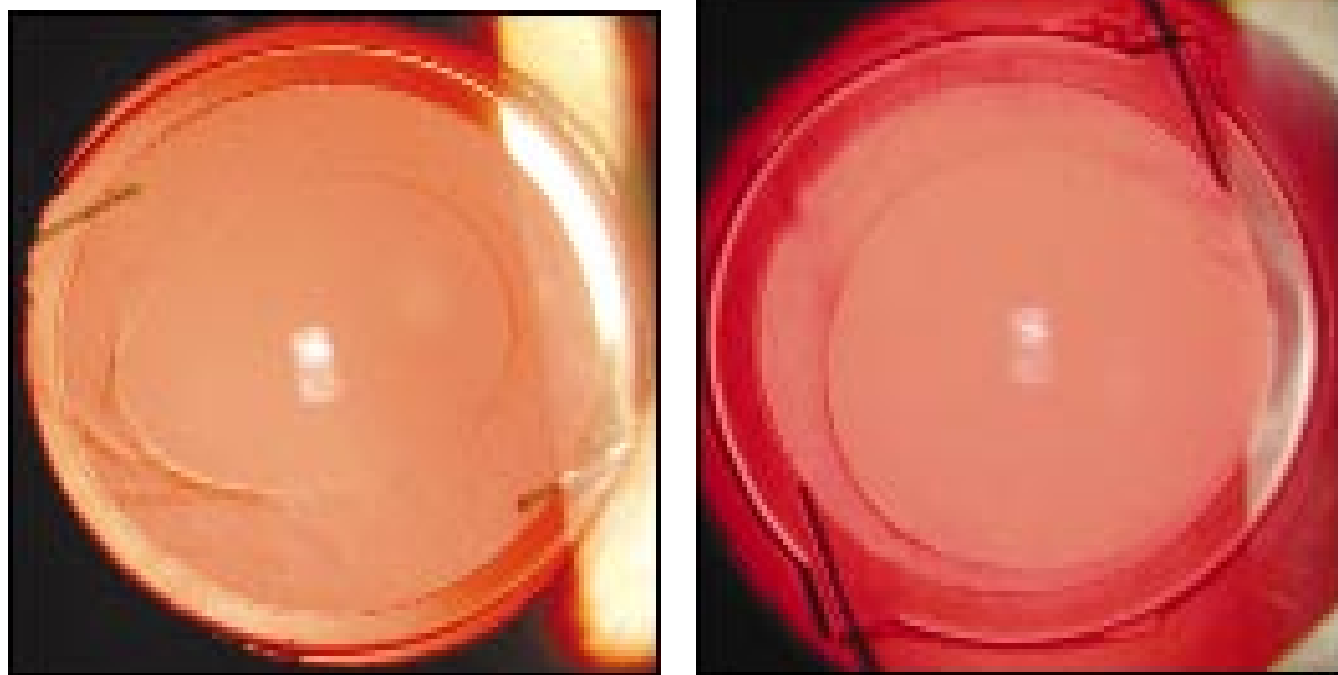


FIGURE 34.17: Slit lamp photograph of treatment of eyes, implanted with silicone IOL designs, after 6 months of follow-up. Note the clear anterior capsule with absence of wrinkling. Note the posterior capsule is clean at this stage. However, long-term follow-up will be undertaken to draw definitive conclusion on efficacy of SCI to reduce or eliminate the PCO

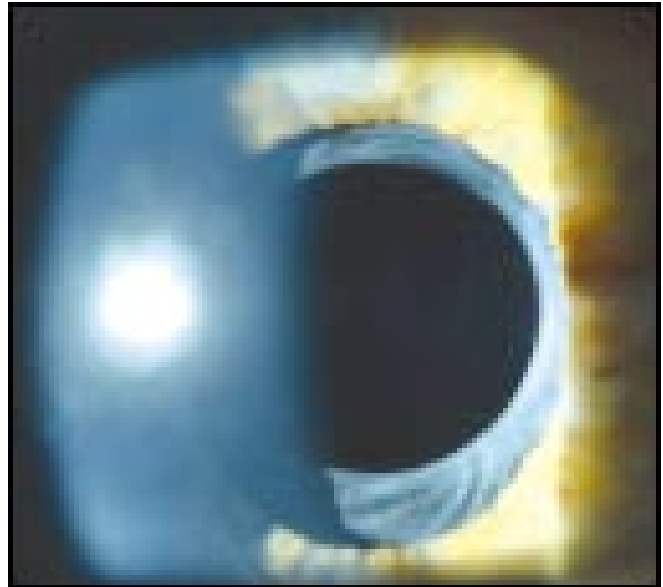
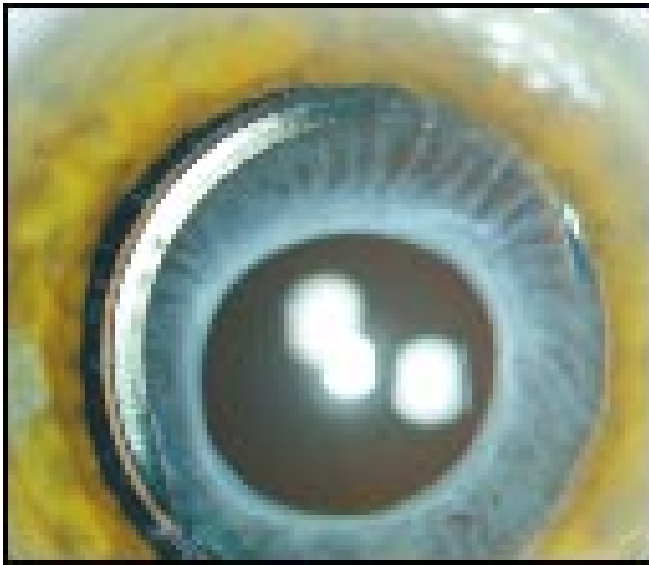


FIGURE 34.18: Slit lamp photograph of control eyes, implanted with silicone IOL designs, after 12 months of follow-up. Note the moderate anterior capsule opacification at CCC opening associate with wrinkling/folds of the anterior lens capsule. The CCC opening is progressively constricted (capsular phimosis)

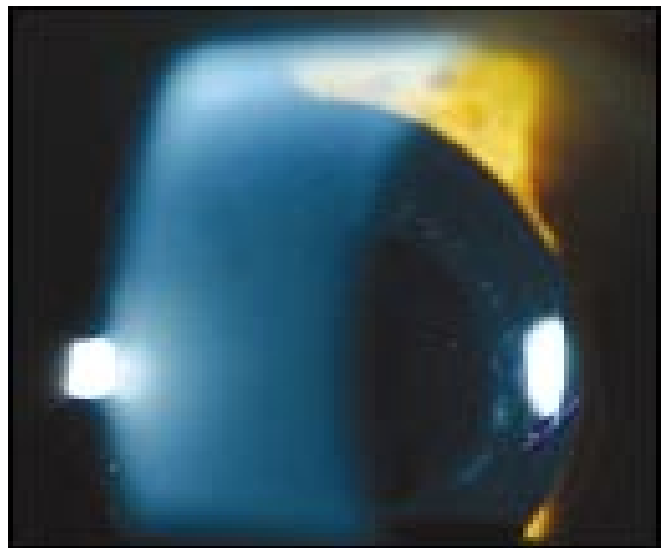
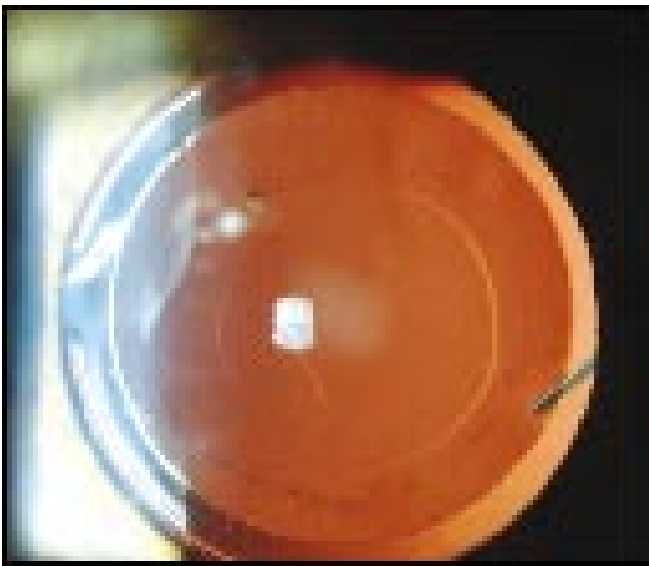


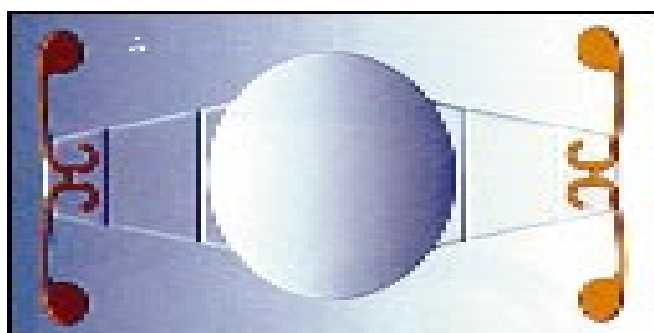
FIGURE 34.19: Slit lamp photograph of treatment of eyes, implanted with silicone IOL designs, after 12 months of follow-up. Note the clear anterior and posterior capsules. Focal areas of minimal anterior capsule opacity at the CCC margin can be seen, which may corresponds to the vacuum ring of Perfect Capsule™ in close approximation to capsulorhexis margin

years after Sir Ridley's first encounter with this complication. A major reduction of Nd: YAG laser capsulotomy rates towards single digits is now possible because of application of aforementioned surgical factors and factors related to modern lens

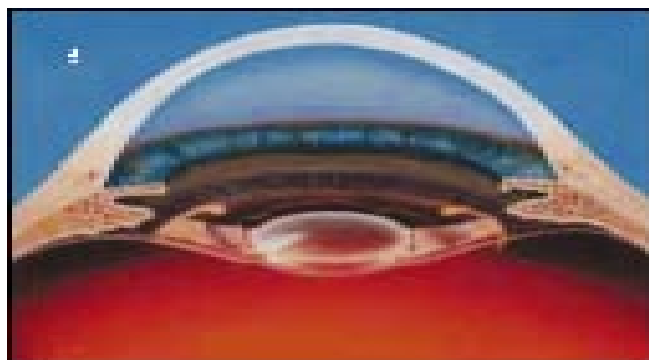
designs/biomaterials- at least in the industrialized world. This will obviously be of great benefit to patients in achieving improved long-term results and avoidance of Nd: YAG laser capsulotomy complications. Eradication of the Nd: YAG laser



FIGURE 34.20: Slit lamp photograph of treatment of eyes, implanted with silicone IOL design, after 12 months of follow-up. Note the clear anterior capsule with focal area of mild to moderate anterior capsule opacity at the CCC margin, which may correspond to the vacuum ring of PerfectCapsule™ in close approximation to capsulorhexis margin



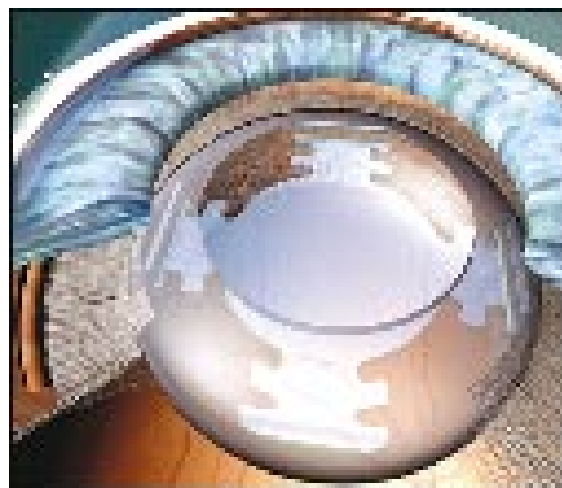
A



B



C



D

FIGURES 34.21A to D: PCO and any form of intracapsular cellular proliferation must be avoided if modern phacorefractive, including “piggybacks” and multifocal and accommodative IOLs are to succeed. The Figure 34.21 illustrates some of the accommodative lenses, which are underinvestigations. (A) The C and C CrystaLens™. (B) Schematic illustration of the C and C CrystaLens™ IOL in the eye. (C) Dual-optic intraocular accommodating system (Synchrony™ IOL manufactured by Visiogen Inc.). (D) Schematic drawing of the Akkommodative 1 CU lens in the capsular bag

procedure will help control what has been the one of the most expensive costs to the health care system. To date one cannot precisely determine the relative proportion or contribution of IOL design vs. surgical techniques to the decrease of Nd: YAG laser rates observed here. However, this could be possible with continuing analysis including annual updates and increasing numbers of pseudophakic autopsy eyes.

In summary, we have ascertained various factors that help bring about the very positive conclusion that surgeons now have the sufficient tools and appropriate IOLs to help reduce the incidence of PCO. The recent advent of SCI is a significant step to eliminate PCO and to maintain long-term capsular bag clarity that is necessary for success of accommodative/refractive lenses. The SCI will also be helpful for maintaining the long-term clear visual axis in pediatric cataract-IOL surgery. However, further experimental studies and multicentric clinical trials are necessary to test its efficacy.

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