

# Improving Visibility Inside the Eye

Surgical strategies for achieving complete cortical cleanup and removal of lens epithelial cells during cataract surgery.

BY SURESH K. PANDEY, MD; E. JOHN MILVERTON, MBBS, DO, FRANZCO, FRCOPHTH;  
AND ANTHONY J. MALOOF, MBBS, MBIOMEDE, FRANZCO, FRACS

**P**ostoperative opacification of the capsular bag remains the most common complication following pediatric and adult cataract and lens implant surgery.<sup>1-3</sup> It occurs from the proliferation and migration of the lens epithelial cells present on the anterior and equatorial inner surfaces of the capsular bag and within the residual cortex and/or cortical fibers. The complication can be subclassified as anterior, equatorial, or posterior capsular opacification.<sup>1,2</sup>

It is possible to obtain a 360° view of the peripheral capsular bag (capsular fornices) in postmortem eyes using an oblique or side view by creating a uveoscleral window<sup>4</sup> or using the Miyake-Apple posterior video/photographic technique.<sup>5,6</sup> In living eyes, however, it is impossible to visualize the peripheral capsular bag, which is hidden by the iris root. As a result, it is difficult to remove the residual cortex, cortical fibers, and cells within the capsular fornices under direct visualization with a surgical microscope (Figure 1).

We conducted a two-part study intended to highlight surgical strategies for achieving complete cortical cleanup and the removal of lens epithelial cells. In the first part, we proposed a novel technique that uses a fiber-optic endoscope for intraoperatively visualizing the capsular fornices for the presence or absence of residual cortex/cortical fibers during cataract surgery. In the second part, we presented an experimental study evaluating the effect of distilled water for irrigation on the lens epithelial cells present on the anterior-capsulectomy (capsulorhexis) specimens.

## PART 1: THE INTRAOPERATIVE VISUALIZATION OF THE CAPSULAR FORNICES

### Materials and Methods

Six eyes with age-related cataract (without any ocular and/or systemic pathology) underwent routine phaco surgery. We used a standard surgical technique (capsu-

lorhexis creation, hydrodissection, hydrodelineation, nuclear rotation and emulsification, I/A, and lens implantation) in all cases. Immediately after concluding I/A and prior to implanting the IOL, we inserted a fiber-optic endoscope (Endo Optiks, Little Silver, NJ) into the anterior chamber and capsular bag in order to examine the capsular fornices for the presence or absence of residual cortex/cortical fibers (Figure 2).

## PART 2: DISTILLED WATER FOR IRRIGATION

We obtained the anterior-capsulotomy specimens (approximately 4.5 to 5.0mm) from six routine cataract surgeries. After completing the capsulorhexis, we placed the excised anterior capsules on the anterior surface of the cornea and gently rinsed them with BSS (Alcon

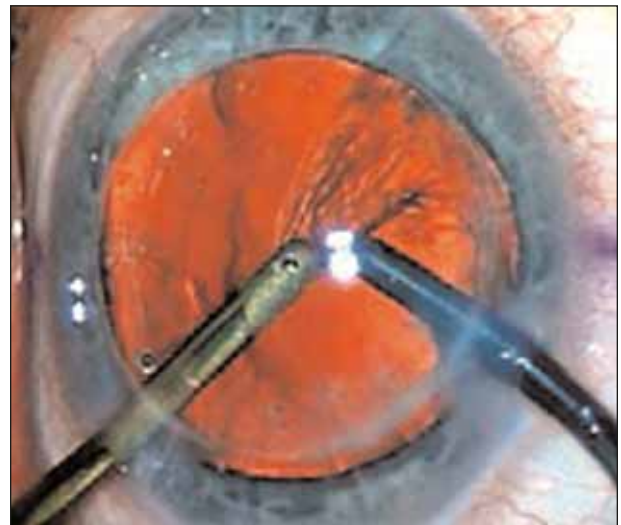


Figure 1. The iris root obscures the view of the peripheral capsular bag (capsular fornices) and thereby makes it difficult to remove the residual cortex and cortical fibers under a surgical microscope.



Figure 2. One of the researchers inserts a fiber-optic endoscope in the anterior chamber and capsular bag to examine the capsular fornices in order to confirm the presence or absence of residual cortex and cortical fibers. The capsular bag appears clean when viewed through a surgical microscope.

Laboratories, Inc., Fort Worth, TX) to remove any residual viscoelastic. We then transferred the capsules to plastic vials (BD Ophthalmic Systems, Franklin Lakes, NJ) containing minimal essential media (M-199) for culture. Then, we transferred the plastic vials containing the specimens from the OR to the laboratory. We placed the capsulorhexis specimens within a culture plate containing minimal essential media (M-199) and fixated them to the plate using metallic pins to avoid their displacement during irrigation with distilled water. We oriented the specimens in the culture plate such that the posterior surface of the anterior capsule containing lens epithelial cells faced anteriorly.

We placed the culture plate on the phase-contrast microscope and selected an area containing viable lens epithelial cells. We used a digital timer to note the time of the cells' treatment with distilled water. We used approximately 30mL of distilled water (Baxter Healthcare Pty. Ltd., Old Toongabbie, New South Wales, Australia) to irrigate the lens epithelial cells present on the fixated anterior capsule. During the initial experiments, we performed irrigation for a maximum of 2 minutes. We also stained the cultures with 0.001% trypan blue solution in order to confirm that the cells were not viable.

## RESULTS

### Examination of the Capsular Fornices

No intraoperative complications occurred. The capsular bag appeared to be clean when viewed through the surgical microscope (Figure 2). Endoscope-assisted visu-

#### Brief Summary of Prescribing Information

##### STERILE

##### Indications and Usage:

XIBROM ophthalmic solution is indicated for the treatment of postoperative inflammation in patients who have undergone cataract extraction.

##### Contraindications:

XIBROM ophthalmic solution is contraindicated in patients with known hypersensitivity to any ingredient in the formulation.

##### Warnings:

Contains sodium sulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs. With some NSAIDs, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

##### Precautions:

##### General:

All topical nonsteroidal anti-inflammatory drugs (NSAIDs) may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs and should be closely monitored for corneal health.

Postmarketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Postmarketing experience with topical NSAIDs also suggests that use more than 24 hours prior to surgery or use beyond 14 days post surgery may increase patient risk for the occurrence and severity of corneal adverse events.

It is recommended that XIBROM ophthalmic solution be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

##### Information for Patients:

XIBROM ophthalmic solution should not be administered while wearing contact lenses.

##### Carcinogenesis, Mutagenesis, Impairment of Fertility:

Long-term carcinogenicity studies in rats and mice given oral doses of bromfenac: up to 0.6 mg/kg/day (360 times the recommended human ophthalmic dose [RHOD] of 1.67 µg/kg in 60 kg person on a mg/kg basis, assuming 100% absorbed) and 5.0 mg/kg/day (3000 times RHOD), respectively revealed no significant increases in tumor incidence. Bromfenac did not show mutagenic potential in various mutagenicity studies, including the reverse mutation, chromosomal aberration, and micronucleus tests.

Bromfenac did not impair fertility when administered orally to male and female rats at doses up to 0.9 mg/kg/day and 0.3 mg/kg/day, respectively (540 and 180 times RHOD, respectively).

##### Pregnancy: Teratogenic Effects: Pregnancy Category C.

Reproduction studies performed in rats at oral doses up to 0.9 mg/kg/day (540 times RHOD) and in rabbits at oral doses up to 7.5 mg/kg/day (4500 times RHOD) revealed no evidence of teratogenicity due to bromfenac. However, 0.9mg/kg/day in rats caused embryo-fetal lethality, increased neonatal mortality, and reduced postnatal growth. Pregnant rabbits treated with 7.5 mg/kg/day caused increased post-implantation loss.

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

##### Non-Teratogenic Effects:

Because of the known effects of prostaglandin biosynthesis-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), the use of XIBROM ophthalmic solution during late pregnancy should be avoided.

##### Nursing Mothers:

Caution should be exercised when XIBROM ophthalmic solution is administered to a nursing woman.

##### Pediatric Use:

Safety and efficacy in pediatric patients below the age of 18 have not been established.

##### Geriatric Use:

There is no evidence that the efficacy or safety profiles for XIBROM differ in patients 65 years of age and older compared to younger adult patients.

##### Adverse Reactions:

The most commonly reported adverse experiences reported following use of XIBROM after cataract surgery include: abnormal sensation in eye, conjunctival hyperemia, eye irritation (including burning/stinging), eye pain, eye pruritus, eye redness, headache, and ititis. These events were reported in 2-7% of patients.

##### Clinical Practice:

The following events have been identified during postmarketing use of bromfenac ophthalmic solution 0.09% in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The events, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to topical bromfenac ophthalmic solution 0.09%, or a combination of these factors, include corneal erosion, corneal perforation, corneal thinning, and epithelial breakdown (see PRECAUTIONS, General).

##### Dosage and Administration:

For the treatment of postoperative inflammation in patients who have undergone cataract extraction, one drop of XIBROM ophthalmic solution should be applied to the affected eye(s) two times daily beginning 24 hours after cataract surgery and continuing through the first 2 weeks of the postoperative period.

##### How Supplied:

XIBROM™ (bromfenac ophthalmic solution) 0.09% is supplied in a white LDPE plastic squeeze bottle with a 15 mm LDPE white dropper-tip and 15 mm polypropylene gray cap as follows:  
NDC 67425-004-50 5 mL in 10 cc container

##### Storage

Store at 15-25°C (59-77°F)

##### Rx Only

Manufactured for: ISTA Pharmaceuticals, Inc., Irvine, CA 92618

by: Bausch & Lomb Incorporated, Tampa, FL 33637

Under license from: Senju Pharmaceutical Co., Ltd., Osaka, Japan 541-0046

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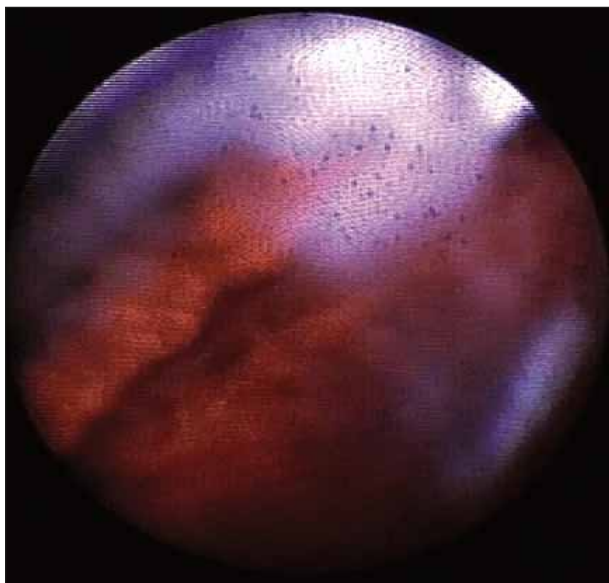


Figure 3. Endoscope-assisted visualization shows a degree of residual cortex and cortical fibers within the nasal quadrant of the capsular fornices.

alization of the capsular fornices, however, suggested a varying degree of residual cortex/fibers/lens epithelial cells in all cases (Figure 3).

We were able to remove the residual cortex and cortical fibers using bimanual and/or coaxial I/A with or without the capsular vacuum setting (Legacy phacoemulsification system; Alcon Laboratories, Inc.). We could also see the anterior capsulorhexis through the endoscope. The anterior capsule and capsular bag had a slight blue tinge, probably due to the presence of lens epithelial cells. Figure 2 illustrates the absence of residual cortex/cortical fibers when viewed through the surgical microscope after we performed cortical cleanup using automated I/A. Endoscopic-assisted visualization of the capsular fornices of the same specimen, however, revealed the presence of residual cortex and cortical fibers in the inferonasal quadrant of the capsular bag (Figure 3).

Using automated I/A with and without the capsular vacuum setting, we carefully attempted to clean the residual cortical material and cortical strands from the inferonasal quadrant of the capsular fornices. We then reinserted the endoscope to confirm the presence or absence of residual cortex. We were able to clean the residual cortical material and cortical strands from the capsular fornices (Figure 4).

### Effect of Irrigation

The lens epithelial cells had been completely lysed in five cases after being exposed to distilled water for irriga-

tion for 120 seconds. The lysis of lens epithelial cells was incomplete in one specimen in which few cortical fibers were present. We saw the earliest microscopic evidence of cellular lysis after 30 seconds of exposure to irrigation with distilled water. At this stage, we had stained the cell nuclei with trypan blue, which was suggestive of a cell that was not viable. The nucleus became swollen and stained densely with trypan blue as time progressed to 120 seconds (Figure 5).

### DISCUSSION

Owing to the localization deep in the fornix of the capsular bag, the residual cortex and germinative lens epithelial cells may escape complete removal during I/A. Thorough cleanup of cortical fibers and the successful removal of potent pre-equatorial germinative cells in significant quantities remain the basis for reducing capsular bag opacification.

Endoscopic-assisted visualization of the capsular fornices suggested the presence of varying amounts of residual cortex/fibers/lens epithelial cells within the capsular fornices during routine cataract surgery, even in cases handled by an experienced surgeon. Experimental studies in rabbit and human eyes have suggested that the retained residual cortex in the capsular bag can harbor mitotically active lens epithelial cells.<sup>7-9</sup>

Lens cortex may also act as a barrier against the osmotic effect of irrigation with distilled water on the lens epithelial cells, as observed in one capsulectomy specimen in our *in vitro* study. The presence of residual cor-

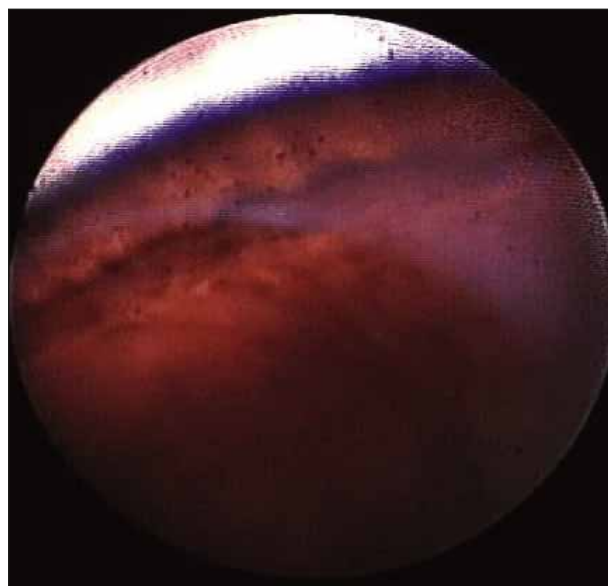


Figure 4. An endoscopic view of the capsular fornices after the capsular bag was cleaned using automated I/A with and without the capsular vacuum setting shows the absence of cortical material and lens fibers from the capsular fornices.

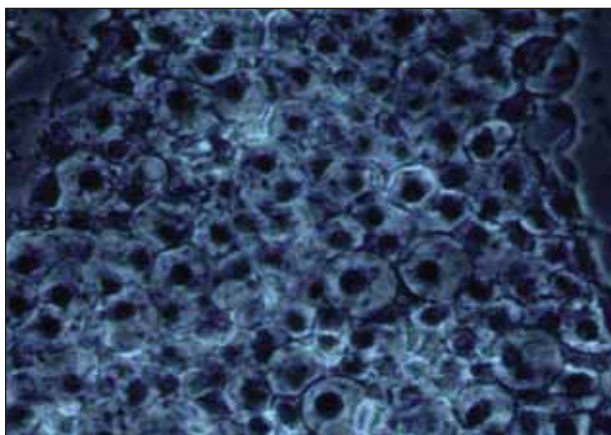


Figure 5. Lysis of lens epithelial cells occurs after treatment with demineralized distilled water. The swollen nuclei were stained densely with trypan blue after 120 seconds of irrigation with distilled water.

tex and fibers may be attributed to the incomplete lysis of the lens epithelial cells in the clinical setting when using a sealed-capsule irrigation technique (Perfectcapsule; Milvella Pty. Ltd., Sydney, Australia).<sup>10</sup> Studies have also suggested that the presence of residual cortex may lead to the breach of the capsular bend's formation with time.<sup>11</sup> This phenomenon may result in visually significant posterior capsular opacification, even after the implantation of a square-edged lens.<sup>11</sup>

The selective irrigation of distilled water into the human capsular bag is now possible using the Perfectcapsule Sealed Capsule Irrigation (Milvella Pty. Ltd.) device, which allows the isolation of lens epithelial cells and positive pressure inflation of the capsular bag intraoperatively.<sup>10</sup> We have demonstrated the lysis of the lens epithelial cells using distilled-water irrigation in a laboratory setting. In spite of complete lysis of the lens epithelial cells in an in vitro setting, there can be some variation in the clinical settings during the use of distilled water with the Perfectcapsule device—differences that may influence the efficacy of irrigation. These variations are (1) the presence of residual cortex within the capsular fornices, (2) the presence of viscoelastic in the capsular bag, and (3) the role of the inflammatory mediators secondary to disruption of the blood-aqueous barrier during cataract surgery.

In summary, endoscopic-assisted visualization of the capsular bag suggests the presence of residual cortex/fibers within the capsular fornices, despite a clean appearance of the capsular bag under the operating microscope. Our in vitro study demonstrated the complete lysis of residual lens epithelial cells present on the anterior lens capsule using irrigation with distilled water. The cap-

sular bag's opacification is a multifactorial process. Thorough cortical cleanup and removal of lens epithelial cells are critical for maintaining the capsular bag's transparency, which is important for a long-term, successful visual outcome with injectable, accommodative, refractive, and new-technology lens implants. ■

Anthony J. Maloof, MBBS, MBIomedE, FRANZCO, FRACS, is a member of the Intraocular Implant Unit, Sydney Eye Hospital, and Director of Ophthalmic Surgery at the Western Sydney Eye Hospital in Westmead, New South Wales, Australia. He holds a financial interest in the Perfectcapsule. Dr. Maloof may be reached at +61 2 9845 6972; [drmaloof@cornea-eyeplastics.com.au](mailto:drmaloof@cornea-eyeplastics.com.au).



John E. Milverton, MBBS, DO, FRANZCO, FRCOphth, is Chairman of the Intraocular Implant Unit, Sydney Eye Hospital. He holds a financial interest in the Perfectcapsule. Dr. Milverton may be reached at +61 2 9382 7433; [milvertonj@sesahs.nsw.gov.au](mailto:milvertonj@sesahs.nsw.gov.au).



Suresh K. Pandey, MD, is Assistant Professor for the John A. Moran Eye Center at University of Utah Health Sciences in Salt Lake City and is affiliated with the Intraocular Implant Unit, Sydney Eye Hospital, Save Sight Institute, University of Sydney. He states that he holds no financial interest in the products or companies mentioned herein. Dr. Pandey may be reached at +61 2 9382 7111; [suresh.pandey@gmail.com](mailto:suresh.pandey@gmail.com) or [suresh.pandey@hsc.utah.edu](mailto:suresh.pandey@hsc.utah.edu).



1. Pandey SK, Apple DJ, Werner L, et al. Posterior capsule opacification: a review of the aetopathogenesis, experimental and clinical studies and factors for prevention. *Indian J Ophthalmol.* 2004;52:99-112.
2. Werner L, Apple DJ, Pandey SK. Postoperative proliferation of anterior and equatorial lens epithelial cells: a comparison between various foldable IOL designs. In: Buratto L, Osher R, Masket S, eds. *Cataract Surgery in Complicated Cases*. Thorofare, NJ: Slack Inc.; 2000: 399-417.
3. Pandey SK, Wilson ME, Trivedi RH, et al. Pediatric cataract surgery and intraocular lens implantation: current techniques, complications and management. *Int Ophthalmol Clin.* 2001;41:175-196.
4. Assia EI, Apple DJ. Side-view analysis of the lens. I. The crystalline lens and the evacuated bag. *Arch Ophthalmol.* 1992;110:1:89-93.
5. Miyake K, Miyake C. Intraoperative posterior chamber lens haptic fixation in the human cadaver eye. *Ophthalmic Surg.* 1985;16:230-236.
6. Apple DJ, Lim ES, Morgan RC, et al. Preparation and study of human eyes obtained post-mortem with the Miyake posterior photographic technique. *Ophthalmology.* 1990;97:810-816.
7. Peng Q, Apple DJ, Visessook N, et al. Surgical prevention of posterior capsule opacification. Part 2: enhancement of cortical cleanup by focusing on hydrodissection. *J Cataract Refract Surg.* 2000;26:2:188-197.
8. Peng Q, Visessook N, Apple DJ, et al. Surgical prevention of posterior capsule opacification. Part 3: intraocular lens optic barrier effect as a second line of defense. *J Cataract Refract Surg.* 2000;26:198-213.
9. Maloof A, Pandey SK, Neilson G, et al. Selective death of lens epithelial cells using demineralized water and Triton X-100 with PerfectCapsule™ sealed capsule irrigation: a histological study in rabbit eyes. *Arch Ophthalmol.* In press.
10. Maloof AJ, Neilson G, Milverton EJ, Pandey SK. Selective and specific targeting of lens epithelial cells during cataract surgery using sealed-capsule irrigation. *J Cataract Refract Surg.* 2003;29:1566-1568.
11. Dewey SH, Werner L, Apple DJ, et al. Cellular proliferation and Soemmerings ring: the long-term threat to capsule clarity. Video presented at: The ASCRS/ASOA Symposium on Cataract, IOL, and Refractive Surgery; May 2-3, 2004; San Diego, CA.