Phacodonesis and a Subluxated Crystalline Lens

BY EHUD I. ASSIA, MD; STEVEN DEWEY, MD; RICHARD J. MACKOOL, MD; MARK PACKER, MD; DEVESH K. VARMA, MD; AND IQBAL IKE K. AHMED, MD

CASE PRESENTATION

A 67-year-old female presents for a cataract surgical evaluation. Her ocular history is significant for advanced proliferative diabetic retinopathy and open-angle glaucoma. She is status post scatter photocoagulation in both eyes, and a local retina specialist says the patient may eventually require pars plana vitrectomy. There is no rubeosis. The patient is being treated for glaucoma (0.9 cup-to-disc ratio and mild visual field loss), and her IOP is currently controlled on three topical medications.

An examination reveals a BCVA of 20/100 OD and 20/200 OS. Significant bilateral nuclear sclerosis with phacodonesis is present (Figure 1). After pupillary dilation, the inferior edge of the crystalline lens is visible for 180º (Figure 2). The patient has no obvious physical traits suggestive of Marfan's or Weill-Marchesani syndrome, and she denies trauma.

How would you approach the cataract surgery?

Figure 1. In both eyes, a 3+ nuclear sclerotic lens appears to be superiorly subluxated. No vitreous prolapse is present.

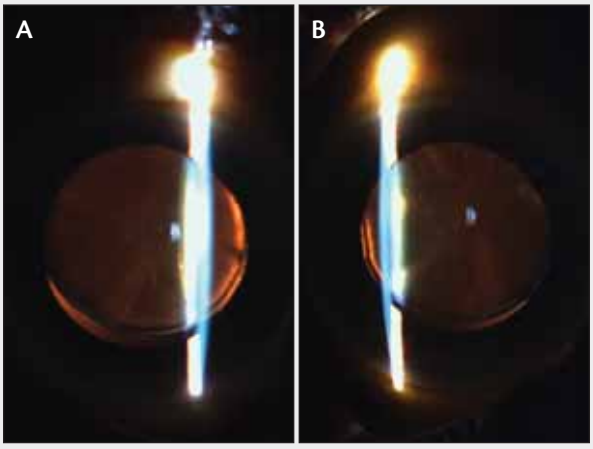


Figure 2. Retroillumination images of the patient's right (A) and left (B) crystalline lenses show their inferior edge for greater than 180º.

(Figures 1 and 2 courtesy of Tal Raviv, MD.)

EHUD I. ASSIA, MD

The combination of advanced glaucoma and phacodonesis with lens subluxation suggests pseudoexfoliation (PXF) syndrome, which needs to be ruled out. Another potential cause is high myopia, in which significant phacodonesis is not uncommon. Cataract extraction is certainly indicated, not only to remove the opaque media but also because of the patient's glaucoma. Anterior displacement of the unstable lens may play a role in the high IOP, and removal of the crystalline lens is often associated with decreased pressure.

Intracapsular cataract extraction and the implantation of either an ACIOL (angle or iris supported) or a suture-fixated PCIOL are valid options. My preference, however, would be to preserve the posterior capsule by fixating the lens capsule to the scleral wall. The Cionni Rings for Sclera Fixation and the Ahmed Capsular Tension Segments (CTS) (both from Morcher GmbH, Stuttgart, Germany; distributed in the United States by FCI Ophthalmics, Marshfield Hills, MA) were shown to be highly effective for fixation of the capsular bag to the scleral wall.

I have developed with Hanita Lenses (Kibbutz Hanita, Israel) an alternative device, the AssiAnchor (not available in the United States), which clips to the anterior capsule

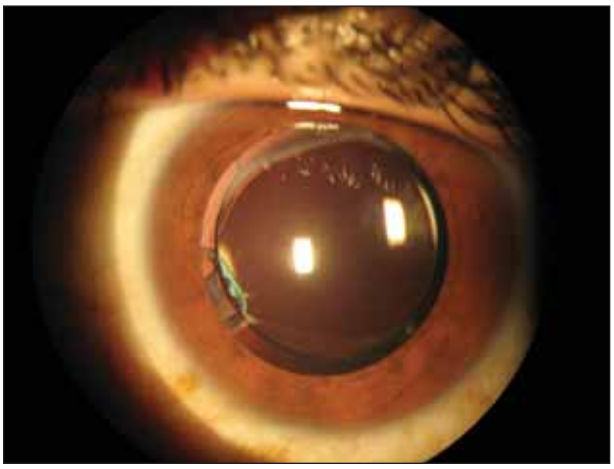
and is sutured to the scleral wall[1,2] (Figure 3). After the lens is stabilized by the AssiAnchor, the surgeon performs phacoemulsification in the conventional manner. A capsular tension ring (CTR) may also be inserted to preserve the round contour of the capsular equator. My clinical experience (11 patients, 12 anchors) has been encouraging, and final follow-up (more than 2 years for four patients) revealed stable and central capsule-fixated IOLs in all eyes. This patient's diabetic retinopathy should be well controlled prior to surgery to minimize postoperative macular edema.

STEVEN DEWEY, MD

The youth of this patient highlights the complexity of the case. Under most circumstances, I would recommend an ACIOL as a perfectly acceptable option for an eye with zonular laxity. I would not change this decision for mild glaucoma or well-controlled diabetes. The presented "gestalt" of this patient, however, suggests a high risk for worsening glaucomatous visual field loss and increasing diabetic ischemic disease, with rubeosis a significant possibility. These issues are relative contraindications for an angle-fixated ACIOL. The choice is therefore between an iris-fixated or a scleral-sutured PCIOL. I would defer the decision until after removing the cataract. The IOL would need to be acrylic with rounded edges at potential points of contact with uveal tissue. Due to potential problems with centration, the lens should be spherical or neutrally aspheric.

The specific technical aspect of the surgery is whether the capsule is capable of providing long-term assistance in the fixation of the IOL. As a general rule, I use a CTR at the start of a case only in the presence of significant phacodonesis, but I do not use a CTR if the lens is relatively stable despite the apparent zonular defect. If the zonules prove more resilient and remain intact with a gentle phacoemulsification (large capsulorhexis with either a supracapsular flip or, preferably, a well-controlled chop to preserve the zonules as much as possible), then the extent of the zonular abnormality can be assessed. If fewer than 3 to 4 clock hours are impaired, a CTR alone may be reasonable. More than 4 but fewer than 6 clock hours calls for scleral fixation in the region of zonular laxity, with a Cionni Ring for Sclera Fixation, a Henderson Capsular Tension Ring (Morcher GmbH; distributed in the United States by FCI Ophthalmics), or an Ahmed CTS. Otherwise, I would keep all incisions anterior to the limbus to preserve the conjunctiva.

If the zonules appeared pathologic and the lens seemed to be unstable as the case began, I would place retractors from the Mackool Cataract Support System (Duckworth & Kent Ltd., Hertfordshire, United Kingdom) as I performed the capsulorhexis. In this situation, the capsule would not likely help support the IOL, and iris-suture fixation would probably be the best option to minimize surgical trauma and spare the conjunctiva. Whether the capsule is useful or likely to be a nuisance could be decided at that point. I would carefully remove the ophthalmic viscosurgical device (OVD) at the end of the case.



(Courtesy of Ehud I. Assia, MD.)

Figure 3. The surgeon fixates the capsular bag to the scleral wall with the AssiAnchor in a case of large posttraumatic zonular dialysis (6 to 10 o'clock). The anterior capsule is clipped between the two lateral arms (located behind the capsule) and the central rod, positioned in front of the capsule, and sutured to the scleral wall.

My preference would be to pretreat this patient with Avastin or Lucentis (both from Genentech, Inc., South San Francisco, CA) and to administer intravitreal triamcinolone acetonide (only 1 mg) at the end of the case to minimize the impact of her diabetic condition.

RICHARD J. MACKOOL, MD

I would administer a peribulbar block and create a superior primary incision. Next, I would inject Viscoat (Alcon Laboratories, Inc., Fort Worth, TX) into the region of absent zonule, stain the anterior capsule with trypan blue, and completely fill the anterior chamber with additional viscoelastic. I would then perform the capsulorhexis and insert at least five retractors from the Mackool Cataract Support System before phacoemulsification. The retractors should be inserted at 45° intervals where the zonule is absent and at 90° intervals where there is evidence of possible zonular laxity. I would insert a standard CTR and then place an Ahmed CTS in the inferior capsular fornix and suture it to the sclera. If the superior zonule were not adequate, I would use two Ahmed CTS. After removing the Cataract Support System's retractors, I would perform endoscopic cyclophotocoagulation (ECP) for at least 270° using the E2 Microprobe Laser and Endoscopy System

(Endo Optiks, Little Silver, NJ). Insertion of the IOL into the capsular sac would complete the procedure.

I would carefully monitor the IOP for 3 to 4 hours due to the eye's advanced glaucomatous optic nerve damage. To reduce the possibility of a significant IOP spike, one could administer Miostat (Alcon Laboratories, Inc.) intraoperatively, ensure the complete removal of viscoelastic material, instill topical antiglaucoma medications at the end of the procedure, and administer oral acetazolamide.

MARK PACKER, MD

There are several points of diagnostic interest in this case. First is the etiology of the lens subluxation. In the absence of any evidence of a systemic disease (including PXF), previous surgery, or trauma, one might assume simple ectopia lentis. Also intriguing is the patient's potential acuity based on macular function, given her history of diabetic retinopathy. A potential acuity test would help set reasonable expectations on the part of the patient for cataract extraction. Posterior segment optical coherence tomography, perhaps already performed by the retina colleague mentioned, would help define the anatomical status of the macula. Finally, the severity of glaucoma and degree of its control would affect my surgical decisions. The number of medications and the presence of field loss suggest to me that adjunctive ECP at the time of cataract surgery might be indicated. The decision to perform ECP would depend on the target IOP and the likelihood of the patient's ongoing adherence to medical therapy.

I would use my standard infection prophylaxis with a preoperative topical fluoroquinolone antibiotic and my routine preoperative anti-inflammatory protocol with a topical steroid and nonsteroidal anti-inflammatory drug beginning 3 days before surgery.

In the absence of vitreous prolapse, I would construct two trapezoidal single-plane incisions (each 1.4 mm internally) in the superior and inferior temporal quadrants in preparation for a biaxial microincisional approach to phacoemulsification. After filling the anterior chamber with a dispersive OVD, I would initiate the capsulorhexis centrally with a pinch-type forceps and complete the tear with a spiral-out technique (going inferiorly first).

After gentle hydrodissection, the insertion of a CTR distributes the equatorial forces on the bag and centers the lens. Depending on the degree of phacodonesis, a Cionni Ring for Sclera Fixation is probably necessary here. I would pass each arm of a 10–0 or 9–0 Prolene suture (Ethicon Inc., Somerville, NJ) through the eyelet of the ring and then into the eye, under the iris, and out through a Hoffman pocket-type incision inferiorly. I would then rotate the ring into the capsule.[3] Because a vertical chopping technique applies minimal force to the zonule, it would permit pha-

Vigamox®

(moxifloxacin hydrochloride ophthalmic solution) 0.5% as base

DESCRIPTION: VIGAMOX® (moxifloxacin HCl ophthalmic solution) 0.5% is a sterile ophthalmic solution. It is an 8-methoxy fluoroquinolone anti-infective for topical ophthalmic use.

CLINICAL PHARMACOLOGY:
Microbiology:
The following *in vitro* data are also available, **but their clinical significance in ophthalmic infections is unknown.** The safety and effectiveness of VIGAMOX® solution in treating ophthalmological infections due to these microorganisms have not been established in adequate and well-controlled trials.

The following organisms are considered susceptible when evaluated using systemic breakpoints. However, a correlation between the *in vitro* systemic breakpoint and ophthalmological efficacy has not been established. The list of organisms is provided as guidance only in assessing the potential treatment of conjunctival infections. Moxifloxacin exhibits *in vitro* minimal inhibitory concentrations (MICs) of 2 µg/ml or less (systemic susceptible breakpoint) against most (≥ 90%) strains of the following ocular pathogens.

Aerobic Gram-positive microorganisms:
Listeria monocytogenes
Streptococcus mitis
Staphylococcus saprophyticus
Streptococcus pyogenes
Streptococcus agalactiae
Streptococcus Group C, G and F

Aerobic Gram-negative microorganisms:
Acinetobacter baumannii
Acinetobacter calcoaceticus
Citrobacter freundii
Citrobacter koseri
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Klebsiella oxytoca
Klebsiella pneumoniae
Moraxella catarrhalis
Morganella morganii
Neisseria gonorrhoeae
Proteus mirabilis
Proteus vulgaris
Pseudomonas stutzeri

Anaerobic microorganisms:
Clostridium perfringens
Fusobacterium species
Prevotella species
Propionibacterium acnes

Other microorganisms:
Chlamydia pneumoniae
Legionella pneumophila
Mycobacterium avium
Mycobacterium marinum
Mycoplasma pneumoniae

Clinical Studies:
In two randomized, double-masked, multicenter, controlled clinical trials in which patients were dosed 3 times a day for 4 days, VIGAMOX® solution produced clinical cures on day 5-6 in 66% to 69% of patients treated for bacterial conjunctivitis. Microbiological success rates for the eradication of the baseline pathogens ranged from 84% to 94%. Please note that microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

INDICATIONS AND USAGE: VIGAMOX® solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

Aerobic Gram-positive microorganisms:
Corynebacterium species*
*Micrococcus luteus**
Staphylococcus aureus
Staphylococcus epidermidis
Staphylococcus haemolyticus
Staphylococcus hominis
*Staphylococcus warneri**
Streptococcus pneumoniae
Streptococcus viridans group

Aerobic Gram-negative microorganisms:
*Acinetobacter lwoffii**
Haemophilus influenzae
*Haemophilus parainfluenzae**

Other microorganisms:
Chlamydia trachomatis

*Efficacy for this organism was studied in fewer than 10 infections.

CONTRAINDICATIONS: VIGAMOX® solution is contraindicated in patients with a history of hypersensitivity to moxifloxacin, to other quinolones, or to any of the components in this medication.

WARNINGS:
NOT FOR INJECTION.

VIGAMOX® solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

In patients receiving systemically administered quinolones, including moxifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to moxifloxacin occurs, discontinue use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

PRECAUTIONS:
General: As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information for Patients: Avoid contaminating the applicator tip with material from the eye, fingers or other source.

Systemically administered quinolones including moxifloxacin have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

Drug Interactions: Drug-drug interaction studies have not been conducted with VIGAMOX® solution. *In vitro* studies indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2 indicating that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these cytochrome P450 isozymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed. However, in an accelerated study with initiators and promoters, moxifloxacin was not carcinogenic in rats following up to 38 weeks of oral dosing at 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose for a 50 kg person, on a mg/kg basis).

Moxifloxacin was not mutagenic in four bacterial strains used in the Ames *Salmonella* reversion assay. As with other quinolones, the positive response observed with moxifloxacin in strain TA 102 using the same assay may be due to the inhibition of DNA gyrase. Moxifloxacin was not mutagenic in the CHO/HGPRT mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when v79 cells were used. Moxifloxacin was clastogenic in the v79 chromosome aberration assay, but it did not induce unscheduled DNA synthesis in cultured rat hepatocytes. There was no evidence of genotoxicity *in vivo* in a micronucleus test or a dominant lethal test in mice.

Moxifloxacin had no effect on fertility in male and female rats at oral doses as high as 500 mg/kg/day, approximately 21,700 times the highest recommended total daily human ophthalmic dose. At 500 mg/kg orally there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.

Pregnancy: Teratogenic Effects.
Pregnancy Category C: Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis at oral doses as high as 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose); however, decreased fetal body weights and slightly delayed fetal skeletal development were observed. There was no evidence of teratogenicity when pregnant Cynomolgus monkeys were given oral doses as high as 100 mg/kg/day (approximately 4,300 times the highest recommended total daily human ophthalmic dose). An increased incidence of smaller fetuses was observed at 100 mg/kg/day.

Since there are no adequate and well-controlled studies in pregnant women, VIGAMOX® solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Moxifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when VIGAMOX® solution is administered to a nursing mother.

Pediatric Use: The safety and effectiveness of VIGAMOX® solution in infants below 1 year of age have not been established.

There is no evidence that the ophthalmic administration of VIGAMOX® solution has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

Geriatric Use: No overall differences in safety and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS:
The most frequently reported ocular adverse events were conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage, and tearing. These events occurred in approximately 1-6% of patients.

Nonocular adverse events reported at a rate of 1-4% were fever, increased cough, infection, otitis media, pharyngitis, rash, and rhinitis.

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(Figures 4 and 5 courtesy of Iqbal Ike K. Ahmed, MD, FRCS(C).)

Figure 4. The Ahmed Capsular Tension Segment.

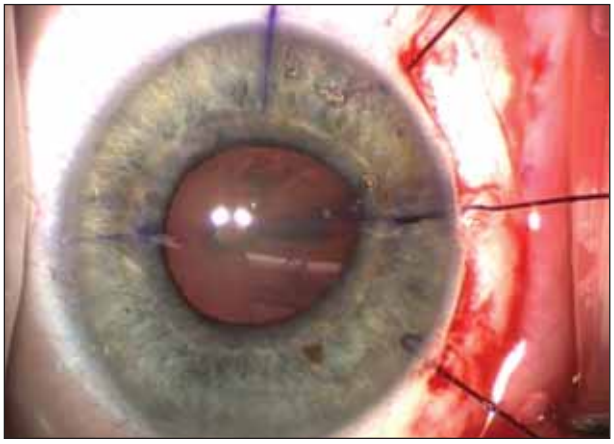


Figure 5. An iris hook is inverted and placed through the eyelet of the CTS to support the capsule at its equator.

coemulsification of this dense nucleus without damage to the capsule. Cortical cleanup would be facilitated by gentle tangential aspiration and biaxial I/A (which would allow a direct approach to 360º of the capsule).

I would favor a three-piece, monofocal, hydrophobic acrylic, square-posterior-edge IOL in this case. This IOL would provide a defense against capsular contraction, a high-quality image, and resistance to posterior capsular opacification (as well as compatibility with silicone oil). The IOL's insertion would require a 2.8-mm temporal clear corneal incision. I would gladly perform limbal relaxing incisions if indicated for the correction of preexisting keratometric astigmatism (if with the rule, the inferior incision could be incorporated into the construction of the Hoffman pocket).

After the IOL's implantation, I would perform ECP on 270º of the ciliary epithelium, thoroughly aspirate all of the OVD, and use stromal hydration to seal the incisions. Depending on the IOP on the first day after surgery, I would have the patient continue using one or two of her glaucoma medications and then re-evaluate her in a couple of weeks.

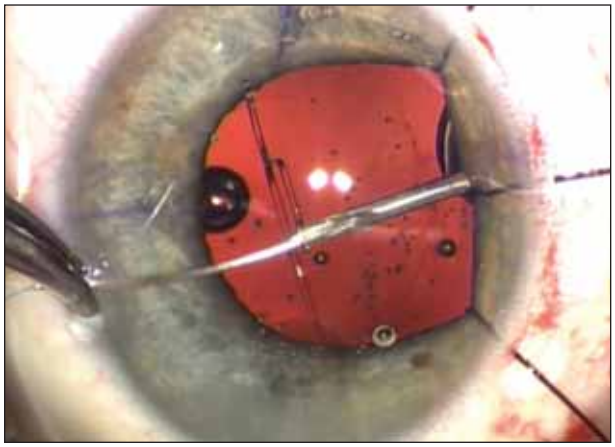
An early follow-up visit with the retina specialist would be a good idea. The perioperative injection of a vascular endothelial growth factor inhibitor might be indicated to forestall the development of macular edema or the resurgence of neovascularization.

DEVESH K. VARMA, MD, AND IQBAL IKE K. AHMED, MD

Before approaching surgery, we would fully explore the systemic causes of the lens' subluxation, because they may present risks for anesthesia. PXF typically causes inferior subluxation, but in the context of underlying glaucoma, PXF should also be considered, because this patient could be at risk of postoperative IOP spikes. The IOP might be slightly lower after cataract surgery alone, but because of her advanced cupping and need for three medications to maintain IOP control, the surgeon could consider a combined glaucoma-cataract procedure. In addition, given her advanced proliferative diabetic retinopathy, the patient would benefit from a preoperative retinal evaluation and treatment of any macular edema.

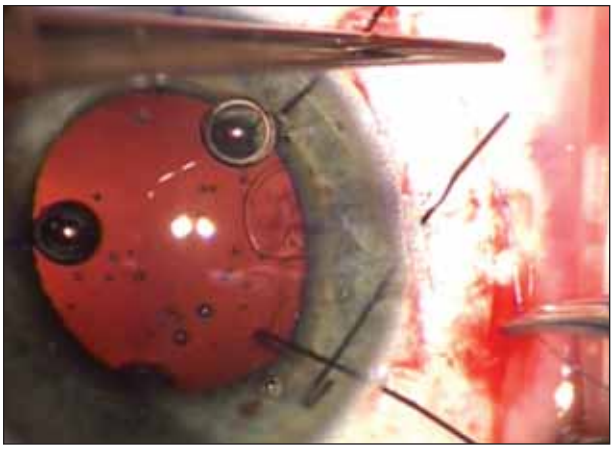
This patient likely has isolated ectopia lentis, a diffuse zonulopathy. Zonular loss may therefore extend farther than the 180º visible in the retroillumination photographs.

We would implant a single-piece, foldable acrylic IOL in the bag, with support provided by a combination of a CTR and one or two Ahmed CTS, sutured to the sclera using an implantation technique previously described[4] (Figure 4). The generous use of an OVD and strict avoidance of a shallow anterior chamber throughout the case would be key to preventing vitreous from prolapsing anteriorly. We would perform the capsulorhexis with the support of iris hooks on its margin inferiorly, and we would carefully leave an adequate shelf of intact anterior capsule for the future placement of a CTS. Next, we would insert a CTR after viscodissection to facilitate later cortical removal. Under OVD protection, the CTS would be introduced into the bag inferiorly and retracted by one iris hook passed through its



(Courtesy of Iqbal Ike K. Ahmed, MD, FRCS(C).)

Figure 6. The surgeon docks a 9–0 Prolene suture that has been passed through the eyelet of the CTS within the lumen of a 26-gauge needle introduced through a scleral groove.



(Courtesy of Iqbal Ike K. Ahmed, MD, FRCSC.)

Figure 7. The surgeon positions a CTS by adjusting tension on the suture.

central eyelet (Figure 5). The remaining iris hooks could then be removed.

With the capsule supported at its equator by the CTS, we would complete phacoemulsification using a zonule-friendly chopping technique, followed by cortical removal and implantation of a foldable acrylic lens. We would then release the iris hook and temporarily move the CTS to the central anterior chamber to facilitate suture fixation. We would create an inferior limbal peritomy and partial-thickness scleral groove. Next, we would expand the inferior sulcus with an OVD to prevent capsular trauma during the suturing of the CTS to the sclera. A 26-gauge needle on a viscoelastic syringe would be passed through the scleral groove into the sulcus and advanced centrally. A double-armed 9–0 Prolene suture with a CIF-4 needle (straightened with two needle drivers) (Ethicon Inc.) would be introduced through the temporal corneal incision, passed through the eyelet of the CTS, and docked into the lumen of the 26-gauge needle (Figure 6). The docked needle complex would be withdrawn through the scleral groove, and the process would be repeated with the second arm of the suture (without its passing through the eyelet of the CTS).

We would then place the CTS back in the capsular bag and tie the suture externally using a slipknot, with its tension adjusted to achieve a centered IOL (Figure 7). Using a Sinskey hook, we would bury the knot in the sclera. If needed, a second CTS could be implanted, 180º from the first segment. After withdrawing the OVD via a dry-aspiration technique, we would suture the incisions to avoid inadvertent shallowing of the anterior chamber and vitreous prolapse.

If the capsular bag became unusable, alternative strategies include iris or scleral suture fixation of a PCIOL, enclavation of the Artisan IOL (Ophtec BV, Groningen Netherlands), or an ACIOL. ■

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