Ophthalmology Times®
CUTTING-EDGE ADVANCEMENTS
October 1, 2013 VOL. 38, NO. 19
CLINICAL DIAGNOSIS | SURGERY | DRUG THERAPY

OphthalmologyTimes.com
FOLLOW US ONLINE:

Practice Management

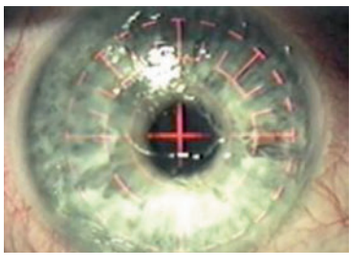
REVISITING THE RUCKUS OVER RUC

PHYSICIANS WHO TREAT MEDICARE patients instinctively know that there's a process involved in setting payment rates for services and a committee that's responsible for the task.

Lately, some industry observers have characterized the group—the American Medical Association (AMA)/Specialty Society Relative Value Scale Update Committee (RUC)—with one of two extremes.

*(See story on page 41 : **RUC role**)*

Surgery



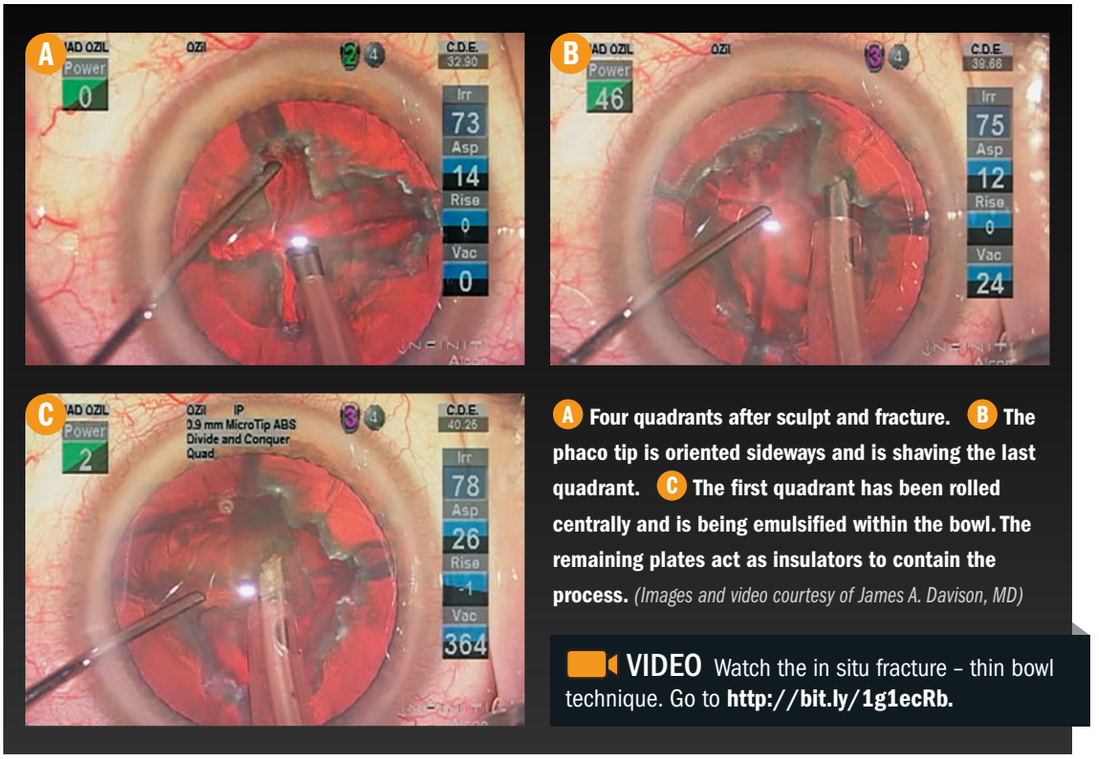
MULTIFOCAL IOL NIGHTMARE: BACK TO 20/20

JACKSONVILLE, FL :: **WHEN PRACTICED AS AN ART FORM**, full-spectrum refractive surgery not only can address virgin eyes with all levels of ametropia, but it also can reverse and correct complex and complicated cases back to 20/20 vision, according to Arun C. Gulani, MD.

*(See story on page 18 : **Gloves Off**)*

IN SITU SCULPTING enhances cataract surgery

Approach uses longitudinal phacoemulsification to groove nucleus as per a divide-and-conquer technique for hard cataracts



A Four quadrants after sculpt and fracture. B The phaco tip is oriented sideways and is shaving the last quadrant. C The first quadrant has been rolled centrally and is being emulsified within the bowl. The remaining plates act as insulators to contain the process. *(Images and video courtesy of James A. Davison, MD)*

VIDEO Watch the in situ fracture – thin bowl technique. Go to **http://bit.ly/1g1ecRb.**

By Cheryl Guttman Krader;
Reviewed by James A. Davison, MD, FACS

MARSHALLTOWN, IA ::
THE IN SITU fracture – thin bowl technique is a safe and effective method for removing hard cataracts, according to James A. Davison, MD, FACS.

The approach uses longitudinal phacoemulsification to groove the nucleus as per a divide-and-conquer technique, according to Dr. Davison, who specializes in cataract and refractive surgery at the Wolfe Eye Clinic, Marshalltown, IA.

However, while still working within the capsular bag, the surgeon continues to sculpt the nucleus into a thin bowl, creating two-dimensional plates that are drawn into the anterior central bowl for removal using either longitudinal phacoemulsification or a torsional/vacuum triggered longitudinal strategy.

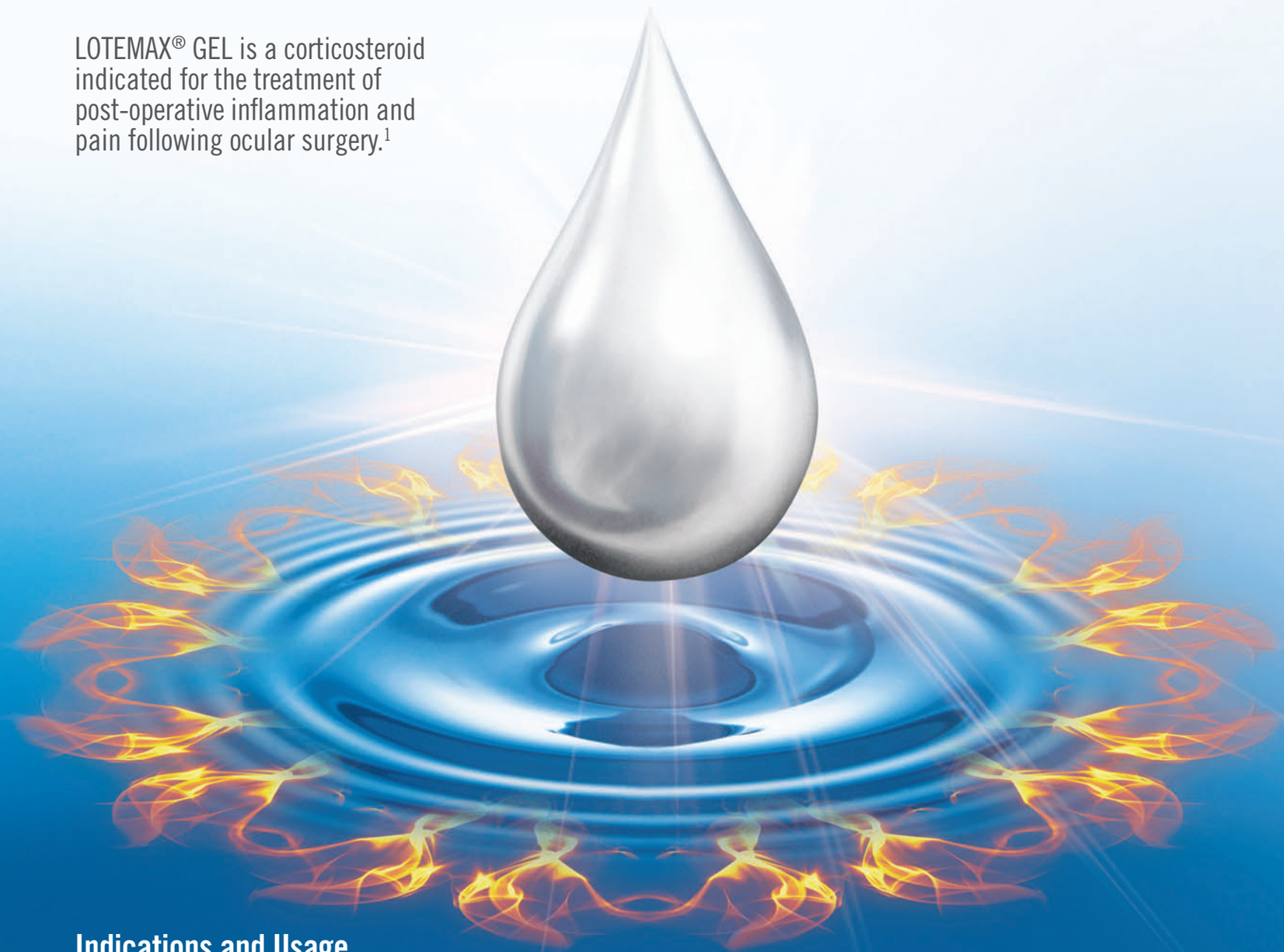
Surgery for hard cataracts using the in situ fracture – thin bowl technique has been associated with few complications and a lower endothelial cell loss rate compared with the chop technique, which is popular with about half of surgeons in the United States, Dr. Davison said.

"Many surgeons routinely use the chop technique,

*(Continues on page 20 : **In situ technique**)*

LOTEMAX® GEL— UNIQUE FORMULATION DESIGNED TO

LOTEMAX® GEL is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.[1]



Indications and Usage

- LOTEMAX® GEL is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery

Important Risk Information about LOTEMAX® GEL

- LOTEMAX® GEL is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures
- Intraocular pressure (IOP) increase—Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored
- Cataracts—Use of corticosteroids may result in posterior subcapsular cataract formation
- Delayed healing—Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation and occurrence of perforations in those with diseases causing corneal and scleral thinning. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification
- Bacterial infections—Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infection. In acute purulent conditions, steroids may mask infection or enhance existing infections
- Viral infections—Use of corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and exacerbate the severity of many viral infections of the eye (herpes simplex)

CONTROL INFLAMMATION

FIRST IN CLASS* GEL DROP

FORMULATED FOR POWER IN EVERY GEL DROP

- MUCOADHESIVE TECHNOLOGY—
  Engineered to adhere to the ocular surface[1-3]
- DOSE UNIFORMITY—
  No shaking required to resuspend drug[1,4,5]
- LOW PRESERVATIVE AND TWO
  KNOWN MOISTURIZERS[1,2,4,6]

PROVEN EFFICACY AND ESTABLISHED SAFETY

- PROVEN EFFICACY IN POST-OPERATIVE
  INFLAMMATION[1,2,4]
- LOW INCIDENCE OF SIGNIFICANT IOP ELEVATIONS—
  Similar to vehicle[2]

Specify LOTEMAX® GEL dispense as written when prescribing

LOTEMAX® GEL
1-2 drops qid for 2 weeks

- Fungal infections—Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use
- Contact lens wear—Patients should not wear contact lenses when using LOTEMAX® GEL
- The most common ocular adverse drug reactions were anterior chamber inflammation (5%), eye pain (2%) and foreign body sensation (2%)

Please see brief summary of full prescribing information on next page.

*Ophthalmic corticosteroid.

References: 1. LOTEMAX GEL Prescribing Information, September 2012. **2.** Fong R, Leitritz M, Siou-Mermet R, Erb T. Loteprednol etabonate gel 0.5% for postoperative pain and inflammation after cataract surgery: results of a multicenter trial. *Clin Ophthalmol.* 2012;6:1113-1124. **3.** Shaikh R, Singh TRR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. *J Pharm Bioallied Sci.* 2011;3(1):89-100. **4.** Data on file, Bausch & Lomb Incorporated. **5.** Coffey MJ, Davio SR. Viscoelastic and sedimentation characterization of loteprednol etabonate ophthalmic gel, 0.5%. Poster presented at: Association for Research in Vision and Ophthalmology (ARVO); May 6-10, 2012; Fort Lauderdale, FL. Poster #6283/D1143. **6.** Lotemax Prescribing Information, April 2006.

BAUSCH+LOMB

LOTEMAX® GEL
loteprednol etabonate
ophthalmic gel 0.5%

BAUSCH + LOMB

LOTEMAX®

loteprednol etabonate
ophthalmic gel 0.5%

Brief Summary: Based on full prescribing information.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb at 1-800-323-0000 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

INDICATIONS AND USAGE

LOTEMAX is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once to fill tip before instilling drops.

Apply one to two drops of LOTEMAX into the conjunctival sac of the affected eye four times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period.

CONTRAINDICATIONS

LOTEMAX, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

WARNINGS AND PRECAUTIONS

Intraocular Pressure (IOP) Increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.

Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Bacterial Infections

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

Viral Infections

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungal Infections

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

Contact Lens Wear

Patients should not wear contact lenses during their course of therapy with LOTEMAX.

ADVERSE REACTIONS

Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with infrequent optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, delayed wound healing and secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

The most common adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%), and foreign body sensation (2%).

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects: Pregnancy Category C.

Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocele, abnormal left common carotid artery, and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (35 times the maximum daily clinical dose), a dose which caused no maternal toxicity. The no-observed-effect-level (NOEL) for these effects was 0.5 mg/kg/day (6 times the maximum daily clinical dose). Oral treatment of rats during organogenesis resulted in teratogenicity (absent innominate artery at ≥5 mg/kg/day doses, and cleft palate and umbilical hernia at ≥50 mg/kg/day) and embryotoxicity (increased post-implantation losses at 100 mg/kg/day and decreased fetal body weight and skeletal ossification with ≥50 mg/kg/day). Treatment of rats with 0.5 mg/kg/day (6 times the maximum clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥5 mg/kg/day.

Oral exposure of female rats to 50 mg/kg/day of loteprednol etabonate from the start of the fetal period through the end of lactation, a maternally toxic treatment regimen (significantly decreased body weight gain), gave rise to decreased growth and survival, and retarded development in the offspring during lactation; the NOEL for these effects was 5 mg/kg/day. Loteprednol etabonate had no effect on the duration of gestation or parturition when administered orally to pregnant rats at doses up to 50 mg/kg/day during the fetal period.

There are no adequate and well controlled studies in pregnant women. LOTEMAX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemic steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when LOTEMAX is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment Of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in a chromosome aberration test in human lymphocytes, or *in vivo* in the single dose mouse micronucleus assay. Treatment of male and female rats with up to 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (600 and 300 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

PATIENT COUNSELING INFORMATION

Administration

Invert closed bottle and shake once to fill tip before instilling drops.

Risk of Contamination

Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the gel.

Contact Lens Wear

Patients should be advised not to wear contact lenses when using LOTEMAX.

Risk of Secondary Infection

If pain develops, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician.

FOR MORE DETAILED INFORMATION, PLEASE READ THE PRESCRIBING INFORMATION.

Bausch & Lomb Incorporated
Tampa, Florida 33637 USA
US Patent No. 5,800,807

Official publication sponsor of International Vision Expo & Conference New York, International Vision Expo & Conference Las Vegas

How to Contact Ophthalmology Times

Editorial
24950 Country Club Blvd.,
Suite 200
North Olmsted, OH 44070-5351
440/243-8100
FAX: 440/756-5227

Subscription Services
Toll-Free: 888/527-7008 or
218/740-6477
FAX: 218/740-6417

Advertising
485 Route 1 South
Building F, Suite 210,
Iselin, NJ 08830-3009
732/596-0276
FAX: 732/596-0003

Production
131 W. First St.
Duluth, MN 55802-2065
800/346-0085
FAX: 218/740-7223,
218/740-6576

Ophthalmology Times *Mission Statement*

Ophthalmology Times is a physician-driven media brand that presents cutting-edge advancements and analysis from around the world in surgery, drug therapy, technology, and clinical diagnosis to elevate the delivery of progressive eye health from physician to patient.

Ophthalmology Times' vision is to be the leading content resource for ophthalmologists.

Through its multifaceted content channels, *Ophthalmology Times* will assist physicians with the tools and knowledge necessary to provide advanced quality patient care in the global world of medicine.

A cutting-edge focus

Introducing a sharpened vision for innovation, insights, discoveries

By Peter J. McDonnell, MD

director of the Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, and chief medical editor of *Ophthalmology Times*.

He can be reached at 727 Maumenee Building 600 N. Wolfe St. Baltimore, MD 21287-9278
Phone: 443/287-1511 Fax: 443/287-1514
E-mail: pmcdonn1@jhmi.edu

"The only thing that is constant is change."
—Heraclitus, Greek philosopher in 500 BC

HERACLITUS WAS KNOWN FOR his doctrine of change being central to the cosmos. Like Heraclitus' universe, ophthalmology is constantly in a state of change. Always has been, always will. We're seeing more and more shifts in how ophthalmologists practice medicine—and that transformation will undoubtedly continue as we advance through the 21st century.

Ophthalmology is already facing many transitions in social, patient, and professional demographics—how we treat patients, even how we perform surgery. This is becoming more evident as new technology emerges.

All this change makes it difficult for ophthalmologists to stay on top of cutting-edge advancements. Aside from the clinic, readers also are challenged by the multitude of peer-reviewed content and other publications to find the latest advancements in the field.

Understanding these challenges, *Ophthalmology Times* is retooling its editorial direction, transitioning from a clinical newsmagazine to a resource that will explore the innovative concepts, insights, and discoveries in ophthalmology.

Beginning with this issue, *Ophthalmology Times* will present cutting-edge advancements from around the world in four distinct categories:

- ***Surgery*** **will highlight the latest surgical techniques and technology across all subspecialties of ophthalmology, especially cataract, refractive, glaucoma, and retina.**
- ***Drug therapy*** **will keep readers connected to the latest pharmaceutical advancements, with updates to existing drugs and those pharmaceuticals making their way through the clinical pipeline.**
- ***Clinical diagnosis*** **will update readers on the latest treatments and therapies in clinical care.**
- ***Technology*** **will spotlight the new products and scientific ingenuity that surface from labs of industry and exhibit halls of major ophthalmic meetings.**

The driving force behind this new direction is the *Ophthalmology Times* Editorial Advisory Board (EAB). The board consists of more than 50 of the most innovative and influential ophthalmologists.

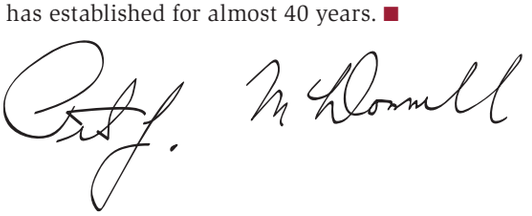
Their expertise, knowledge, and leadership will identify the innovations that continually permeate ophthalmology. The EAB will engage more with readers by providing articles about clinical advances and technologies, as well as opinion articles and clinical perspective and analysis within the various subspecialties.

Readers can expect to see more articles from physicians and other key opinion leaders. *Ophthalmology Times* also has developed new columns and added new editors to its existing columns. Physician-to-physician articles will also drive additional content through *Ophthalmology Times*' digital channels with videos, podcasts, and online article exclusives.

Finally, with new direction comes a new mission for *Ophthalmology Times*. The publication's new mission statement reflects these changes as we move into the digital age—today and in the future:

- ***Ophthalmology Times*** **is a physician-driven media brand that presents cutting-edge advancements and analysis from around the world in surgery, drug therapy, technology, and clinical diagnosis to elevate the delivery of progressive eye health from physician to patient.**
- ***Ophthalmology Times*****' vision is to be the leading content resource for ophthalmologists.**
- **Through its multifaceted content channels, *Ophthalmology Times* will assist physicians with the tools and knowledge necessary to provide advanced quality patient care in the global world of medicine.**

Ophthalmology Times has been a physician-driven media brand. This new direction will only solidify the editorial forum and build on the editorial success that *Ophthalmology Times* has established for almost 40 years. ■



Ophthalmology Times
OCTOBER 1, 2013 ■ VOL. 38, NO. 19

For the treatment of elevated IOP

UNLOCK TREATMENT POSSIBILITIES

SIMBRINZA™ Suspension provided additional 1-3 mm Hg IOP lowering compared to the individual components[1]

- IOP measured at 8 AM, 10 AM, 3 PM, and 5 PM was reduced by **21-35%** at Month 3[2-4]
- Efficacy proven in two pivotal Phase 3 randomized, multicenter, double-masked, parallel-group, 3-month, 3-arm, contribution-of-elements studies[2,3]
- The most frequently reported adverse reactions (3-7%) in a six month clinical trial were eye irritation, eye allergy, conjunctivitis, blurred vision, dysgeusia (bad taste), conjunctivitis allergic, eye pruritus, and dry mouth[5]
- Only available beta-blocker-free fixed combination[2,3]

INDICATIONS AND USAGE

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination indicated in the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

Dosage and Administration

The recommended dose is one drop of SIMBRINZA™ Suspension in the affected eye(s) three times daily. Shake well before use. SIMBRINZA™ Suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

IMPORTANT SAFETY INFORMATION

Contraindications

SIMBRINZA™ Suspension is contraindicated in patients who are hypersensitive to any component of this product and neonates and infants under the age of 2 years.

Warnings and Precautions

Sulfonamide Hypersensitivity Reactions—Brinzolamide is a sulfonamide, and although administered topically, is absorbed systemically. Sulfonamide attributable adverse reactions may occur. Fatalities have occurred due to severe reactions to sulfonamides. Sensitization may recur when a sulfonamide is readministered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

Corneal Endothelium—There is an increased potential for developing corneal edema in patients with low endothelial cell counts.

Severe Hepatic or Renal Impairment (CrCl <30 mL/min)—SIMBRINZA™ Suspension has not been specifically studied in these patients and is not recommended.

Adverse Reactions

In two clinical trials of 3 months' duration with SIMBRINZA™ Suspension, the most frequent reactions associated with its use occurring in approximately 3-5% of patients in descending order of incidence included: blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Adverse reaction rates with SIMBRINZA™ Suspension were comparable to those of the individual components. Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA™ Suspension patients.

Drug Interactions—Consider the following when prescribing SIMBRINZA™ Suspension:

Concomitant administration with oral carbonic anhydrase inhibitors is not recommended due to the potential additive effect. Use with high-dose salicylate may result in acid-base and electrolyte alterations. Use with CNS depressants may result in an additive or potentiating effect. Use with antihypertensives/cardiac glycosides may result in additive or potentiating effect on lowering blood pressure. Use with tricyclic antidepressants may blunt the hypotensive effect of systemic clonidine and it is unknown if use with this class of drugs interferes with IOP lowering. Use with monoamine oxidase inhibitors may result in increased hypotension.

For additional information about SIMBRINZA™ Suspension, please see Brief Summary of full Prescribing Information on adjacent page.

Learn more at myalcon.com/simbrinza

SIMBRINZA™
(brinzolamide/brimonidine
tartrate ophthalmic suspension)
1%/0.2%

ONE BOTTLE. MANY POSSIBILITIES.

References: 1. SIMBRINZA™ Suspension Package Insert. **2.** Katz G, DuBiner H, Samples J, et al. Three-month randomized trial of fixed-combination brinzolamide, 1%, and brimonidine, 0.2% [published online ahead of print April 11, 2013]. *JAMA Ophthalmol.* doi:10.1001/jamaophthalmol.2013.188. **3.** Nguyen QH, McMenemy MG, Realini T, et al. Phase 3 randomized 3-month trial with an ongoing 3-month safety extension of fixed-combination brinzolamide 1%/brimonidine 0.2%. *J Ocul Pharmacol Ther.* 2013;29(3):
290-297. **4.** Data on file, 2013. **5.** Whitson JT, Realini T, Nguyen QH, McMenemy MG, Goode SM. Six-month results from a Phase III randomized trial of fixed-combination brinzolamide 1% + brimonidine 0.2% versus brinzolamide or brimonidine monotherapy in glaucoma or ocular hypertension. *Clin Ophthalmol.* 2013;7:1053-1060.

Alcon
a Novartis company

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination of a carbonic anhydrase inhibitor and an alpha 2 adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop of SIMBRINZA™ Suspension in the affected eye(s) three times daily. Shake well before use. SIMBRINZA™ Suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

DOSAGE FORMS AND STRENGTHS

Suspension containing 10 mg/mL brinzolamide and 2 mg/mL brimonidine tartrate.

CONTRAINDICATIONS

Hypersensitivity - SIMBRINZA™ Suspension is contraindicated in patients who are hypersensitive to any component of this product.

Neonates and Infants (under the age of 2 years) - SIMBRINZA™ Suspension is contraindicated in neonates and infants (under the age of 2 years*) see Use in Specific Populations*

WARNINGS AND PRECAUTIONS

Sulfonamide Hypersensitivity Reactions - SIMBRINZA™ Suspension contains brinzolamide, a sulfonamide, and although administered topically is absorbed systemically. Therefore, the same types of adverse reactions that are attributable to sulfonamides may occur with topical administration of SIMBRINZA™ Suspension. Fatalities have occurred due to severe reactions to sulfonamides including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Sensitization may recur when a sulfonamide is re-administered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation *[see Patient Counseling Information]*

Corneal Endothelium - Carbonic anhydrase activity has been observed in both the cytoplasm and around the plasma membranes of the corneal endothelium. There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Caution should be used when prescribing SIMBRINZA™ Suspension to this group of patients.

Severe Renal Impairment - SIMBRINZA™ Suspension has not been specifically studied in patients with severe renal impairment (CrCl $<$ 30 mL/min). Since brinzolamide and its metabolite are excreted predominantly by the kidney, SIMBRINZA™ Suspension is not recommended in such patients.

Acute Angle-Closure Glaucoma - The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. SIMBRINZA™ Suspension has not been studied in patients with acute angle-closure glaucoma.

Contact Lens Wear - The preservative in SIMBRINZA™, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA™ Suspension but may be reinserted 15 minutes after instillation *[see Patient Counseling Information]*.

Severe Cardiovascular Disease - Brimonidine tartrate, a component of SIMBRINZA™ Suspension, has a less than 5% mean decrease in blood pressure 2 hours after dosing in clinical studies; caution should be exercised in treating patients with severe cardiovascular disease.

Severe Hepatic Impairment - Because brimonidine tartrate, a component of SIMBRINZA™ Suspension, has not been studied in patients with hepatic impairment, caution should be exercised in such patients.

Potentiation of Vascular Insufficiency - Brimonidine tartrate, a component of SIMBRINZA™ Suspension, may potentiate syndromes associated with vascular insufficiency. SIMBRINZA™ Suspension should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangitis obliterans.

Contamination of Topical Ophthalmic Products After Use - There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers have been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface *[see Patient Counseling Information]*.

ADVERSE REACTIONS

Clinical Studies Experience - Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to the rates in the clinical studies of another drug and may not reflect the rates observed in practice.

SIMBRINZA™ Suspension - In two clinical trials of 3 months duration 435 patients were treated with SIMBRINZA™ Suspension, and 915 were treated with the two individual components. The most frequently reported adverse reactions in patients treated with SIMBRINZA™ Suspension occurring in approximately 3 to 5% of patients in descending order of incidence were blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Rates of adverse reactions reported with the individual components were comparable. Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA™ Suspension patients.

Other adverse reactions that have been reported with the individual components during clinical trials are listed below.

Brinzolamide 1% - In clinical studies of brinzolamide ophthalmic suspension 1%, the most frequently reported adverse reactions reported in 5 to 10% of patients were blurred vision and bitter, sour or unusual taste. Adverse reactions occurring in 1 to 5% of patients were blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular discharge, ocular discomfort, ocular keratitis, ocular pain, ocular pruritus and rhinitis.

The following adverse reactions were reported at an incidence below 1%: allergic reactions, alopecia, chest pain, conjunctivitis, diarrhea, diplopia, dizziness, dry mouth, dyspnea, dyspepsia, eye fatigue, hypertonia, keratoconjunctivitis, keratopathy, kidney pain, lid margin crusting or sticky sensation, nausea, pharyngitis, tearing and urticaria.

Brimonidine Tartrate 0.2% - In clinical studies of brimonidine tartrate 0.2%, adverse reactions occurring in approximately 10 to 30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus.

Reactions occurring in approximately 3 to 9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain.

The following adverse reactions were reported in less than 3% of the patients: lid crusting, conjunctival hemorrhage, abnormal taste, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitations/arrhythmias, nasal dryness and syncope.

Postmarketing Experience - The following reactions have been identified during postmarketing use of brimonidine tartrate ophthalmic solutions in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to brimonidine tartrate ophthalmic solutions, or a combination of these factors, include: bradycardia, hypersensitivity, iritis, keratoconjunctivitis sicca, miosis, nausea, skin reactions (including erythema, eyelid pruritus, rash, and vasodilation), and tachycardia.

Apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solutions *[see Contraindications]*.

DRUG INTERACTIONS

Oral Carbonic Anhydrase Inhibitors - There is a potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition in patients receiving an oral carbonic anhydrase inhibitor and brinzolamide ophthalmic suspension 1%, a component of SIMBRINZA™ Suspension. The concomitant administration of SIMBRINZA™ Suspension and oral carbonic anhydrase inhibitors is not recommended.

High-Dose Salicylate Therapy - Carbonic anhydrase inhibitors may produce acid-base and electrolyte alterations. These alterations were not reported in the clinical trials with brinzolamide ophthalmic suspension 1%. However, in patients treated with oral carbonic anhydrase inhibitors, rare instances of acid-base alterations have occurred with high-dose salicylate therapy. Therefore, the potential for such drug interactions should be considered in patients receiving SIMBRINZA™ Suspension.

CNS Depressants - Although specific drug interaction studies have not been conducted with SIMBRINZA™, the possibility of an additive or potentiating effect with CNS depressants (alcohol, opiates, barbiturates, sedatives, or anesthetics) should be considered.

Antihypertensives/Cardiac Glycosides - Because brimonidine tartrate, a component of SIMBRINZA™ Suspension, may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with SIMBRINZA™ Suspension is advised.

Tricyclic Antidepressants - Tricyclic antidepressants have been reported to blunt the hypotensive effect of systemic clonidine. It is not known whether the concurrent use of these agents with SIMBRINZA™ Suspension in humans can lead to resulting interference with the IOP lowering effect. Caution is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

Monoamine Oxidase Inhibitors - Monoamine oxidase (MAO) inhibitors may theoretically interfere with the metabolism of brimonidine tartrate and potentially result in an increased systemic side-effect such as hypotension. Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

USE IN SPECIFIC POPULATIONS

Pregnancy - *Pregnancy Category C:* Developmental toxicity studies with brinzolamide in rabbits at oral doses of 1, 3, and 6 mg/kg/day (20, 60, and 120 times the recommended human ophthalmic dose) produced maternal toxicity at 6 mg/kg/day and a significant increase in the number of fetal variations, such as accessory skull bones, which was only slightly higher than the historic value at 1 and 6 mg/kg. In rats, statistically decreased body weights of fetuses from dams receiving oral doses of 18 mg/kg/day (180 times the recommended human ophthalmic dose) during gestation were proportional to the reduced maternal weight gain, with no statistically significant effects on organ or tissue development. Increases in unossified sternebrae, reduced ossification of the skull, and unossified hyoid that occurred at 6 and 18 mg/kg were not statistically significant. No treatment-related malformations were seen. Following oral administration of ^{14}C-brinzolamide to pregnant rats, radioactivity was found to cross the placenta and was present in the fetal tissues and blood.

Developmental toxicity studies performed in rats with oral doses of 0.66 mg brimonidine base/kg revealed no evidence of harm to the fetus. Dosing at this level resulted in a plasma drug concentration approximately 100 times higher than that seen in humans at the recommended human ophthalmic dose. In animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent.

There are no adequate and well-controlled studies in pregnant women. SIMBRINZA™ Suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers - In a study of brinzolamide in lactating rats, decreases in body weight gain in offspring at an oral dose of 15 mg/kg/day (150 times the recommended human ophthalmic dose) were observed during lactation. No other effects were observed. However, following oral administration of ^{14}C-brinzolamide to lactating rats, radioactivity was found in milk at concentrations below those in the blood and plasma. In animal studies, brimonidine was excreted in breast milk.

It is not known whether brinzolamide and brimonidine tartrate are excreted in human milk following topical ocular administration. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use - The individual component, brinzolamide, has been studied in pediatric glaucoma patients 4 weeks to 5 years of age. The individual component, brimonidine tartrate, has been studied in pediatric patients 2 to 7 years old. Somnolence (50-83%) and decreased alertness was seen in patients 2 to 6 years old. SIMBRINZA™ Suspension is contraindicated in children under the age of 2 years *[see Contraindications]*.

Geriatric Use - No overall differences in safety or effectiveness have been observed between elderly and adult patients.

OVERDOSAGE

Although no human data are available, electrolyte imbalance, development of an acidotic state, and possible nervous system effects may occur following an oral overdose of brinzolamide. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

Very limited information exists on accidental ingestion of brimonidine in adults; the only adverse event reported to date has been hypotension. Symptoms of brimonidine overdose have been reported in neonates, infants, and children receiving brimonidine as part of medical treatment of congenital glaucoma or by accidental oral ingestion. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

PATIENT COUNSELING INFORMATION

Sulfonamide Reactions - Advise patients that if serious or unusual ocular or systemic reactions or signs of hypersensitivity occur, they should discontinue the use of the product and consult their physician.

Temporary Blurred Vision - Vision may be temporarily blurred following dosing with SIMBRINZA™ Suspension. Care should be exercised in operating machinery or driving a motor vehicle.

Effect on Ability to Drive and Use Machinery - As with other drugs in this class, SIMBRINZA™ Suspension may cause fatigue and/or drowsiness in some patients. Caution patients who engage in hazardous activities of the potential for a decrease in mental alertness.

Avoiding Contamination of the Product - Instruct patients that ocular solutions, if handled improperly or if the tip of the dispensing container contacts the eye or surrounding structures, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions *[see Warnings and Precautions]*. Always replace the cap after using. If solution changes color or becomes cloudy, do not use. Do not use the product after the expiration date marked on the bottle.

Intercurrent Ocular Conditions - Advise patients that if they have ocular surgery or develop an intercurrent ocular condition (e.g., trauma or infection), they should immediately seek their physician's advice concerning the continued use of the present multidose container.

Concomitant Topical Ocular Therapy - If more than one topical ophthalmic drug is being used, the drugs should be administered at least five minutes apart.

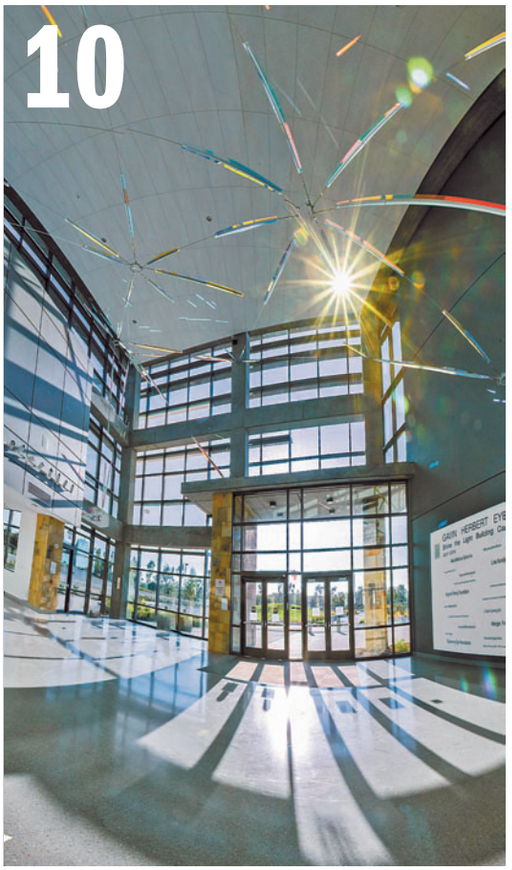
Contact Lens Wear - The preservative in SIMBRINZA™, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA™ Suspension, but may be reinserted 15 minutes after instillation.

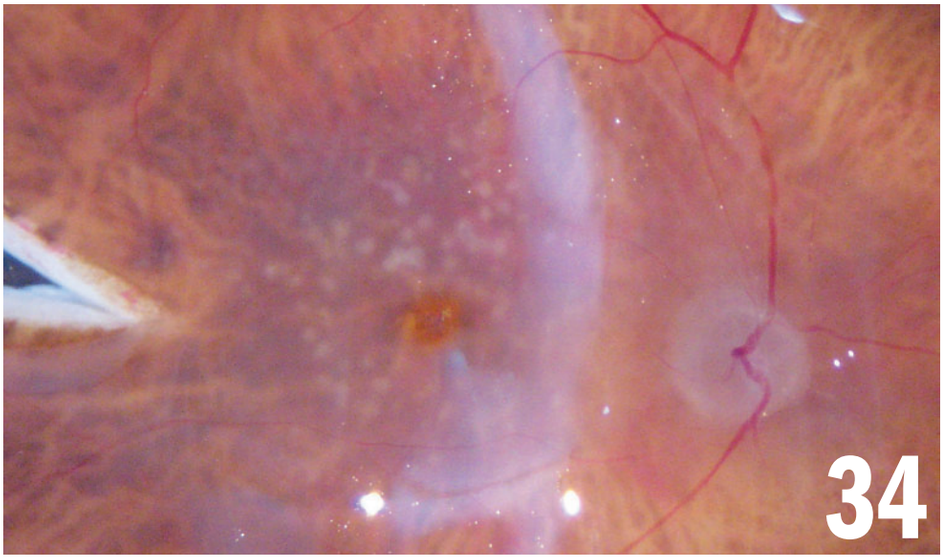
U.S. Patent No:
6,316,441

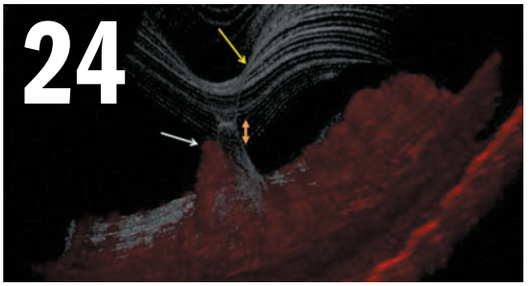
ALCON LABORATORIES, INC.
Fort Worth, Texas 76134 USA
1-800-757-9195
alcon.medinfo@alcon.com

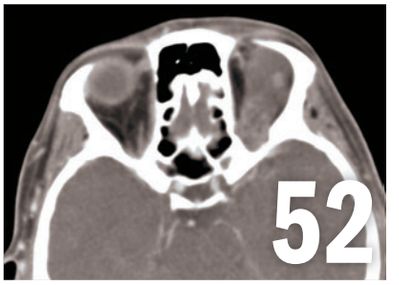
Alcon®

a Novartis company









Drug Therapy

Surgery

In Every Issue

Clinical Diagnosis

Technology

Special Report on page 24
RETINA

Practice Management

Grand Rounds

UC Irvine unveils new eye health institute

Center specializes in innovative research, technology, and educational programing

By Rose Schneider, *Content Specialist,* Ophthalmology Times

The Gavin Herbert Eye Institute, part of UC Irvine Health, moved into its new 70,000-square-foot home on the UC Irvine campus in September. The building includes 34 patient exam rooms with the latest in optical equipment, the first campus outpatient surgery center, a dedicated pediatric examination area, an optical shop, faculty offices, and conference space.
(Photos courtesy of UC Irvine Health/Photos by Cy Kuckenbaker)

IRVINE, CA ::

More than 10 years in the making, the Gavin Herbert Eye Institute has opened its doors at the University of California (UC), Irvine campus.

The $39 million, 70,000-square-foot institute, which opened in September, was built in order to provide cutting-edge technologies, educational programs, and research to amplify visual health for its patients, said James Mazzo, chairman of the Gavin Herbert Eye Institute steering committee.


Mazzo

Eye-care professionals at the center provide treatments across all specialties of ophthalmology and offer comprehensive eye care ranging from annual screening exams to complex surgeries, as well as access to clinical trials.

There are 24 physicians, surgeons, and researchers at the institute.

"Its premise is based on research, . . . leading-edge research," said Mazzo, who is also a UC Irvine Foundation trustee and operating partner with Versant Ventures, a Newport Beach-based venture capital firm.

Studying treatments—such as stem cell therapies to preserve and restore eyesight for patients with retinitis pigmentosa and age-related macular degeneration, as well as a vaccine for ocular herpes—are just some of the research components the institute will focus on, according to UC Irvine.

TAKE-HOME

The new, 70,000-square-foot eye health institute, which was funded entirely by community philanthropy, opened in September at the University of California, Irvine campus.

The institute will have a corneal tissue bank on site as well, which Mazzo said is "very unique" for an eye institution.

"I doubt many teaching institutes in our field have (a corneal tissue bank)," he said.

All of these components, Mazzo said, are "the key differentiating factors" that make the Gavin Herbert Eye Institute stand out among the nation's other eye health institutions.

"At the end of the day, we deal with debilitating eye diseases. No one wants the loss of vision, because it reduces their independence," he said. "The ability to improve eyesight, the ability to have people maintain their independence, the ability to find cures, is really the critical nature (for why) we need research."

TECHNOLOGY AND LAYOUT

Another aspect of the new building is its innovative technology and construction make-up, which Roger Steinert, MD, said aims at optimizing effective patient care.

Dr. Steinert

"The new institute created an opportunity for us to take the technology—in the sense of equipment—and combine it with what we've learned about efficient patient care and effective education all in one building," said Dr. Steinert, who is the institute's founding director.

Those innovations range from newly designed and managed operating rooms to the latest diagnostic, imaging, and laser treatment technology on the market, said Dr. Steinert, who is also chairman of the UC Irvine Department of Ophthalmology, Irving H. Leopold Professor of Ophthalmology, and professor of biomedical engineering.

New technology, he said, includes high-definition (HD) video, which ophthalmologists use to record their surgeries and that is automatically stored for up to 3 months for future examination or case studies, and can be edited by surgeons in their offices. The new system also allows those surgeries to be broadcast live in HD internally into teaching spaces at the institute for students, as well as on the Internet.

There is touchscreen equipment in every room throughout the institute as well, such as controls for lighting, music, and microscopes.

To optimize patients' experience at the institute, Dr. Steinert said the main clinic floor tracks all patients through electronic records so "patients can feel confident about the security and portability of their records."

The floor plan was also designed to be "user friendly," he said, so patients can better navigate through the building.

"It's extremely exciting to have the opportunity to create this type of environment," Dr. Steinert said.

FEATURES

AMBULATORY SURGERY center with two operating suites and a laser cataract procedure room

8,000-square-foot eye clinic with multiple laser procedure rooms and cutting-edge diagnostic imaging technology

TRANSLATIONAL CLINICAL research center for innovative therapy trials

THIRTY-FOUR exam rooms, four of which are dedicated to pediatrics

LASIK refractive surgery center

OCULOFACIAL PLASTIC surgery center with dedicated procedure room

MORE THAN 1,500 square feet of conference and educational space

OPTICAL SHOP with one full-time optometrist, one part-time optometrist, and two opticians

A suspended dichroic glass sculpture, created by Portland, OR-based artist Ed Carpenter, animates the Gavin Herbert Eye Institute lobby through its interaction with natural and artificial light. This arrangement yields views from all three floors of the building, creating a feeling of light play that reinforces the institute's mission to enhance eye health and performance.

BACKSTORY

The institute began as an idea 11 years ago, when Mazzo—along with several colleagues who later formed the institute's steering committee—decided there was a "need to create a leading institute here in Orange County," Mazzo said.

"We have Orange County here with so many (eye-care) companies, but there wasn't really any teaching institution or research facility we found that coordinated our efforts," Mazzo said. "We really wanted something in our backyard."

While he believes the new institute's innovative focus on research is one of its best qualities, Mazzo said the ability to raise $39 million through philanthropy alone to build the institute will be remembered as an achievement.

"It's sure to be a hallmark," he said. "The university donated the land, but we didn't get any public money for construction. Every dollar given to us was all through philanthropy."

Major donors include: Gavin Herbert, founder and chairman emeritus of Allergan—who provided the initial naming gift in 2007—Abbott Medical Optics Inc., the Alcon Foundation, the Allergan Foundation, and Bausch + Lomb.

"We're obviously quite proud of what everybody has contributed, both in time and money. It's been going on now for 10 years," he said. "We're all in this business and we love what we do . . . it's a great feeling."

LOOKING TOWARD THE FUTURE

Both Mazzo and Dr. Steinert said they could not be more excited the institute is finally open.

"It's a bit surreal after 10 years," Mazzo said. "It's definitely something that I'm very proud to be a part of."

Though the building is finished and patients are now being seen, Mazzo insisted there is still more work ahead.

"Any research facility is never done," he said.

Looking at where industry and the eye institute may intersect on research, Mazzo said, he anticipates there will be more efforts in retina, glaucoma, dry eye, presbyopia, and other debilitating diseases.

Since the building is also a teaching facility, Mazzo said there will be a focus on expanding that programming as well.

"The more young ophthalmologists we create, the better," he said.

Mazzo also hopes to expand the institute's reach overseas.

"We can cross-fertilize and have a big impact beyond Orange County, beyond California, beyond the United States, and have a world impact," he said. ■

JAMES MAZZO

E: *jmazzo@acufocus.com*

Mazzo currently serves as chairman and chief executive officer of Versant portfolio company AcuFocus, which specializes in corneal inlays.

ROGER STEINERT, MD

E: *steinert@uci.edu*

Dr. Steinert did not indicate any proprietary interest in the subject matter.

Women spread wings in eye care

Ten years later: Progress is realized, but further steps must be taken to continue gowth

The OWL Quarterly **By Marsha D. Link, PhD**

TAKE-HOME

- ***As Ophthalmic Women Leaders marks its 10th anniversary, the organization celebrates the milestones and challenges ahead.***

IN THE PROFESSIONAL world, there's never been an easy path for women to tread. Fortunately, women today are afforded opportunities that never existed for their mothers, aunts, and grandmothers.

Unfortunately, it would be disingenuous to claim that we've arrived at our destination. One need not look further than recent data to see that—while great strides have been made in advancing women's careers—stark inequality still exists.

As of 2011, women's median annual earnings (for full-time, year-round workers) across the entire workforce represented only 77% of their male counterparts. This represents a pay gap of 23%—nearly an entire quarter's worth of disparity.[1]

Among chief executive officers (CEOs), women in top-earning positions at S&P 500 companies accounted for only 8% of positions and faced, on average, an 18% pay gap.[2]

Additional statistics reinforce this trend: women represent 46.9% of the American labor force, but only 14.3% of executive officers, 16.6% of board members, 8.1% of top earners, and 4.2% of CEOs.[3]

ENTER OWL

Ten years ago, my colleagues at Ophthalmic Women Leaders (OWL) founded this organization to address the same reality in the world of ophthalmology.

Tamara Swanson, then working for Heidelberg Engineering, observed a group of men networking at a conference and realizing a vacuum existed for women when it came to this type of industry support. Not content to accept this as a product of the way things were, Tamara—together with Jan Beiting, Jaci Lindstrom, Jane Aguirre, Adrienne Graves, PhD, and Marguerite McDonald, MD—set out to bring to fruition the dream of creating a support network for women in the ophthalmic space.

When OWL was launched, its advisory board included almost every woman CEO in ophthalmology. Ten years later, I'm proud to say that twenty are presidents or CEOs of their respective companies.

As a result, OWL has spread its wings beyond social support—such as networking events and cocktail hours—to offer its members strong, educational leadership programs designed to advance the role of women in the ophthalmic professional world.

Perhaps Jan Beiting, OWL's current president, said it best when she explained that OWL "brings people together and fosters peer-to-peer learning," often realized through educational activities such as webinars (of which OWL hosts several, on a range of topics), but also through "observing women I admire, working with them on OWL projects, and becoming involved in informal mentoring relationships."

As the incoming president, I see OWL as more relevant now than ever. Our growth over the past decade has, in many ways, cleared the path for women to advance in ophthalmology and beyond.

But even the best-cleared path leaves room for improvement. It's time to lay down the proverbial stones that will lift our organization and its members in the decade ahead.

ENHANCEMENT, ENGAGEMENT, AND ENERGY

OWL is a place for women to grow, develop, and determine our own destiny—tangible actions that can be achieved with the help of three Es: enhancement, engagement, and energy.

We will enhance by continuously improving the educational assets we have in place; our content-rich website (*www.owlsite.org*) and impactful webinars, for one, but also our signature receptions at AAO and ASCRS and networking events at ARVO, ESCRS, and Hawaiian Eye.

We will engage members and encourage them to share their stories; not just about how OWL has provided them support, but how they have provided support or mentorship to other women, both within and outside of ophthalmology.

In our journey ahead, we will remain energetic, connecting with members about their wants and needs, creating new programs, activities, and content designed to enrich their professional and personal lives.

Despite the great headway we've made, both men and women continue to perceive men as the breadwinners or providers. I believe that unless an honest, ongoing dialogue between professional men and women is established, progress will continue to stall.

OWL's core values—leadership, advancement, and community—can play a major role in empowering women to approach this dialogue with the confidence and skills necessary to achieve parity. If we as an organization affect ophthalmology in a meaningful way, our actions will resonate, bettering the careers and lives of professional women in a multitude of industries.

We haven't reached our destination, but we are certainly at a crossroads. Our members—executives, surgeons, administrators, technicians, members of the media, marketers, researchers, medical educators, and others—have positioned this organization to make a real change in our industry and beyond.

Looking back on the past 10 years, I am proud of what we've accomplished. Looking forward at the next 10, I am ecstatic. ■

References

1. American Association of University Women. The simple truth about the gender pay gap. 2013. *http://www.aauw.org/resource/the-simple-truth-about-the-gender-pay-gap/*
2. Bloomberg. Best-paid women in S&P 500 settle for less remuneration. Aug. 13, 2013. *http://www.bloomberg.com/news/2013-08-13/best-paid-women-in-s-p-500-settle-for-less-with-18-gender-gap.html*
3. Catalyst Research. U.S. women in business. July 1, 2013. *http://www.catalyst.org/knowledge/us-women-business*

MARSHA D. LINK, PHD, *is the incoming president of Ophthalmic Women Leaders. She is the founder and principal of Link Consulting, a professional training and coaching firm with a strong heritage in health-care based in Orange County, CA. She may be reached at marshalink@4link.biz.*

tango™

Introducing Tango™... your partner for SLT, capsulotomy and iridotomy procedures.

Switch Between SLT and YAG at the Touch of a Button

Designed to make procedures as efficient as possible, Tango's proprietary dual-mode laser cavity allows you to instantly switch between SLT and YAG.

Optimized for Anterior Segment Viewing

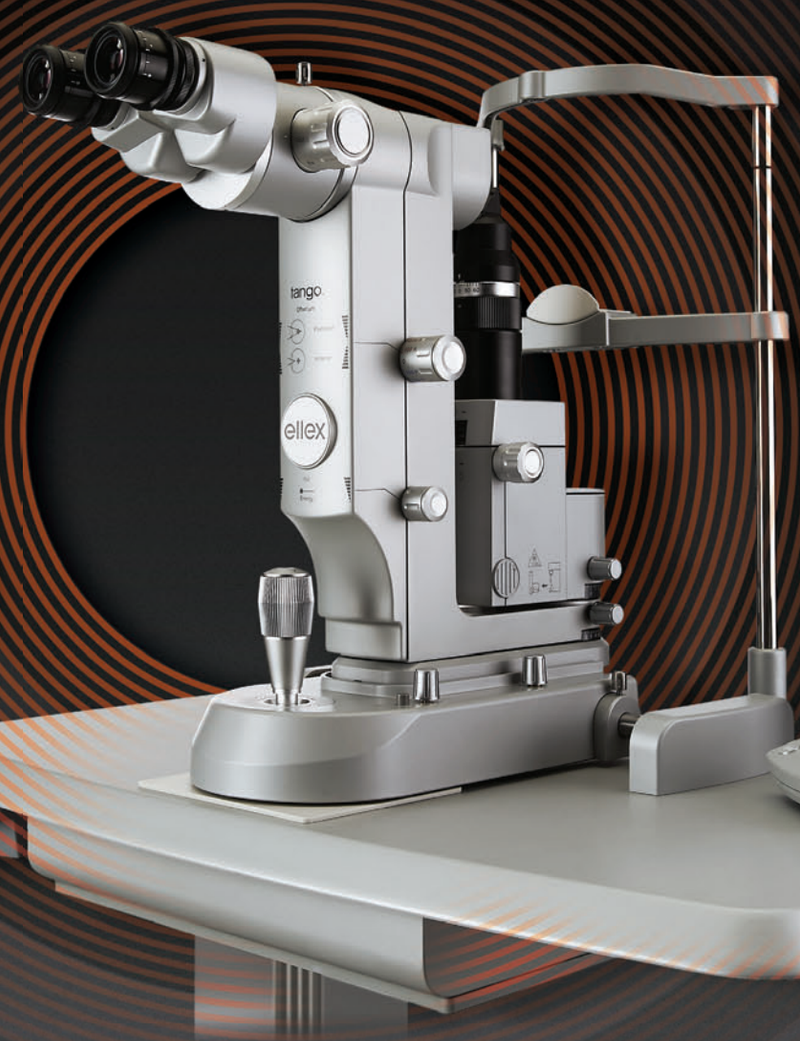
A custom-built optical system provides a more natural stereoscopic view and brighter, clearer illumination of the TM.

IOL-Friendly Photodisruption

Tango's proprietary optical breakdown design allows you to cut tissue more effectively using fewer shots and less cumulative energy – making it ideal for use with the latest generation IOLs.

Faster Treatment

With the industry's fastest firing rate at 3 shots per second, Tango™ allows you to perform quick SLT and YAG treatments.



ellex

Tango™ combines a full-featured SLT laser for highly accurate glaucoma treatment with a precise, powerful YAG laser designed to perform capsulotomy and iridotomy treatments at ultra-low energy levels. Ellex's proprietary SLT technology is also available in the SLT-only configuration Solo™.

www.ellex.com
855 767-5784

It's time to Tango! Preview Tango™ SLT/YAG laser at AAO Exhibit #1117.

Sustained drug delivery may transform glaucoma

Advances could make administering medications to eye easier, while enhancing adherence

By Fred Gebhart; *Reviewed by Ike Ahmed, MD*

TAKE-HOME

- ***Glaucoma treatment is poised to become a more interventional discipline with the introduction of sustained-release drug delivery devices.***

TORONTO ::

Perspectives on the treatment of glaucoma are shifting.

Direct intervention in glaucoma is about to become the norm. Instead of prescribing eye drops and hoping for adherence, ophthalmologists will soon be placing sustained-release drug delivery devices on and in the eye to ensure appropriate transmission.


Dr. Ahmed

"We will be seeing a transformation in the next 5 years of how medications are given and glaucoma is treated," said Ike Ahmed, MD, assistant professor, University of Toronto. "This is part of the whole transition of glaucoma treatment from a very medication-heavy specialty to an interventionist specialty.

"The term I like to use is interventional glaucoma, where we are placing devices like microstents—using microinvasive glaucoma surgery (MIGS)—(while also) injecting medications and placing sustained-release drug depots to provide good medium-term medication delivery . . . we are on the precipice of this transition," he said.

The development of these devices is driven largely by clinical need.

Clinicians already have multiple classes of efficacious topical medications, but effectiveness is lagging. Even with the best of intentions, topical agents are difficult to administer.

If the patient is accurate in saying that he or she applies eye drops at the appropriate time, there is no way to assess whether the drops were administered properly. Even so, there is no way to assess whether the drops spread across the ocular surface as expected and needed for therapeutic activity.

"There is a huge upside with the introduction and use of drug delivery devices to address the many shortcomings of topical medications," Dr. Ahmed said. "We have four or five classes of highly effective drugs available . . . we just have to find ways to deliver them more effectively."

EXAMINING THE EVIDENCE

The goals of sustained-release drug delivery are clear in that the devices:

- **Ensure the drug is delivered to the site of action.**
- **Reduce the side effects of topical drops.**
- **Improve adherence.**
- **Improve clinical outcomes.**

Recent research found that 73% of patients are willing to undergo subconjunctival injections every 3 months, and 86% are willing to accept higher costs than current treatments.

Patients who admit to non-adherence and those who are taking more medications and/or higher frequency of dosing are the most willing to accept ocular injections and increased costs, he said.

The current generation of topical medications has just one route of administration—onto the ocular surface.

SUSTAINED-RELEASE DEVICES

Sustained-release devices in development are designed to exploit at least six different routes:

- **The ocular surface.**
- **The sclera.**
- **The anterior chamber.**
- **The subconjunctival and suprachoroidal spaces.**
- **Intravitreally.**

These multiple routes of administration offer various roles in therapy.

Sustained-release devices are an obvious choice, Dr. Ahmed said, for any patient who has problems with adherence. They also show promise for patients who are intolerant of topical agents or show significant side effects.

Device delivery could also be used to improve therapeutic outcomes in patients whose disease cannot be managed with topical agents, as an adjunct to MIGS or as a tool to delay incisional surgery.

Sustained-release devices are more invasive than topical agents, Dr. Ahmed said, but they also offer longer duration of effect with a single application, more reliable dosing, and reduced toxicities.

Devices currently in clinical trials and under development fall into two broad categories: surface therapies and injectables.

"I see ocular surface therapies, punctal plugs, ocular surface inserts, and contact lenses as more likely to be approved sooner," Dr. Ahmed said. "Some of the injectable technologies are 3 or 4 years from approval, at least in the United States. . . . The less invasive ocular surface technologies are at a different level of scrutiny."

It is important to question who would pay for these devices if and when they are approved, Dr. Ahmed said, because the devices would be more costly than topical agents—at least initially.

The reimbursement key, however, is to focus on cost-effectiveness.

"There are potential savings to using these more invasive techniques in terms of getting (the) drug where it needs to be with longer duration of activity," Dr. Ahmed said. "But once we get into the cost-effectiveness analysis, I think we are going to see some substantial savings." ■

IKE AHMED, MD

E: *ikeahmed@mac.com*

Dr. Ahmed is a consultant for or receives research grants/speaker honoraria from Allergan, Liquidia Technology, and other device manufacturers.

OptiMedica is now part of Abbott Medical Optics.

More Experts. More Insights. More Solutions.

Join us at the Abbott Medical Optics Speakers Forum at the 2013 AAO Annual Meeting

Saturday, November 16th

- 10:15 am–10:45 am
  New Phaco Techniques for Laser Cataract Surgery
  Tal Raviv MD – Moderator
  William Culbertson MD, Robert Rivera MD
- 11:00 am–11:45 am
  IOL Customization and Premium Lens Design for High-Quality Visual Outcomes
  Roger Steinert MD – Moderator
  Daniel Chang MD, Jessica Ciralsky MD
- 12:00 pm–12:45 pm
  Innovation in Laser Cataract Surgery With the Catalys® Precision Laser System
  William Wiley MD – Moderator
  Burkhard Dick MD, PhD; Shachar Tauber MD
- 1:00 pm–1:45 pm
  Optimizing Premium IOL Outcomes With Laser Cataract Surgery
  Mark Blecher MD – Moderator
  Shamik Bafna MD, Jason Jones MD
- 2:00 pm–3:00 pm
  Surgical Surprises: Pearls for Managing Complicated Cases
  David Chang MD – Moderator
  Steven Dewey MD, Sam Garg MD, David Yan MD

Sunday, November 17th

- 10:30 am–11:15 am
  Successful Management of Astigmatic Correction With a New Toric IOL
  Doug Koch MD – Moderator
  Ike Ahmed MD, Elizabeth Yeu MD
- 11:30 am–12:15 pm
  The Business Case and Workflow Integration for Laser Cataract Surgery
  Subba Gollamudi MD – Moderator
  James Khodabakhsh MD, Mike Mann MD
- 1:00 pm–1:45 pm
  Evaluating the Cornea and Ocular Surface: Keys to Successful Surgical Outcomes
  Kenneth Greenberg MD – Moderator
  Sandy Feldman MD, James Loden MD
- 2:00 pm–2:45 pm
  Expanding Your Refractive Cataract Practice With Premium IOLs
  Kerry Assil MD – Moderator
  Elizabeth Davis MD, Keith Walter MD
- 3:00 pm–3:45 pm
  The Advantages of Using the Liquid Optics Interface in Laser Cataract Surgery
  Jonathan Talamo MD – Moderator
  Lisa Arbisser MD, Barry Seibel MD

Visit Booth 1326

Important Safety Information

INDICATION: The OptiMedica® Catalys™ Precision Laser System is indicated for use in patients undergoing cataract surgery for removal of the crystalline lens. Intended uses in cataract surgery include anterior capsulotomy, phacofragmentation, and the creation of single plane and multi-plane arc cuts/incisions in the cornea, each of which may be performed either individually or consecutively during the same procedure. **ADVERSE EFFECTS:** Complications associated with the Catalys® System include mild Petechiae and subconjunctival hemorrhage due to vacuum pressure of the Liquid Optics™ Interface suction ring. Potential complications and adverse events include those generally associated with the performance of capsulotomy and lens fragmentation, or creation of a partial-thickness or full-thickness cut or incision of the cornea. **CAUTION:** Federal law (USA) restricts this device to sale by or on the order of a physician. The system should be used only by qualified physicians who have extensive knowledge of the use of this device and have been trained and certified by OptiMedica.

Visit **www.AbbottMedicalOptics.com/forums** to register early and organize your conference calendar*

*Speakers subject to change. Booth presentations are not affiliated with the official program of the meeting.

Abbott Medical Optics

Reducing the need for postoperative eye drops

Protocol addresses adherence, financial impact among large numbers of patients

By James P. Gills MD; *Special to* Ophthalmology Times

TAKE-HOME

- ***One ophthalmologist proposes a practice-changing opportunity to eliminate the use of eye drops after cataract surgery.***

TARPON SPRINGS, FL ::
IN A COMMON SCENARIO, eye drops prescribed for patients following cataract surgery typically include antibiotics, steroids, and non-steroidal anti-inflammatory drugs (NSAIDs).

The eye drops may be prescribed for up to 6 or 8 weeks, or longer in certain cases. In addition, adherence may be difficult for patients in regard to getting the drops into the eye(s), as well as monetary considerations.

Up until recently, the majority of telephone calls we received from postoperative patients were related to eye drop schedules—how and when to use them and refilling prescriptions.

Now, we seldom receive calls from patients regarding their eye drop schedule or refill requests.

A Korean study by Kim, Yang, Lee, and Park showed the effect of retrobulbar sub-Tenon's injections of triamcinolone acetate (TA) on the progression of diabetic retinopathy after cataract surgery.[1]

A single dose of 40 mg/1 ml of TA decreased macular edema postoperatively for about 3 weeks and reduced the thickness of the retina to less than preoperative thickness for 6 weeks. This suggests that the effectiveness of the medicine is about 6 weeks.

None of the patients in this study had an elevation in IOP with the retrobulbar TA injections being placed behind the equator/retrobulbar space. This suggests that sub-Tenon's injected posteriorly are not associated with IOP rises.

Many people have injected out of the 6 mm zone of the limbus and have not had pressure rises.

For years, drug-delivery implants have been studied by various companies in an effort to eliminate the need for postoperative drops. Though these implants are available, they are expensive and not reimbursable by Medicare.

We currently have a study in South Africa that consists of a 1 × 2 mm implant that is inserted into the capsule at the time of cataract surgery which will allow an NSAID to be slowly released through the eye over 7 weeks.

Other companies have used various forms of biodegradable delayed drug delivery systems to treat many forms of eye diseases. Although it appears that intraocular drug delivery implants may be preferred, they are not approved by the FDA or reimbursable by insurance companies.

Therefore, my protocol consists of 1.2 cc of triamcinolone acetate injected sub-Tenon's equatorial/retrobulbar. I have done this in more than 10,000 cases since August 2009, which is the basis of this article.

DATA

Patients receive medical screening to determine whether they were taking anticoagulants, have retinal disease, or have any other conditions or considerations.

If patients have diabetic retinopathy or macular degeneration, they may have the additional use of non-steroidals along with the retrobulbar kenalog. These patients are followed and checked with photo stress tests, optical coherence tomography (OCT), and visual acuity. About 1% of patients need added eye drops after the initial kenalog.

Thus, 85% to 95% of patients will receive 1.2 cc of subconjunctival kenalog in the superior nasal quadrant right above the medial rectus muscle going through the upper edge of the conjunctival fold or caruncle. This allows the kenalog to be placed essentially at the equator of the eye 1 mm above the medial rectus muscle.

Prior to instilling this, we use Xylocaine gel once before surgery and again just prior to the injection.

We also give a mixture of vancomycin, ceftazidime, and dexamethasone (1/10th of the therapeutic dose) in the anterior chamber at the end of the case.

Both the Mackool Eye Center and St. Luke's have done 75,000 cases without endophthalmitis with the use of intraocular antibiotics.

COMMENT

This method does shift a greater responsibility upon the physician. Injecting the sub-Tenon's area requires the surgeon to be able to pick up the conjunctiva and tenons, know exactly where the sub-Tenon's area is, and inject under it.

Precision is of the utmost importance as it is easy to penetrate the globe if you are not used to doing this type of work. Several extremely good surgeons have started doing this but they ended up penetrating the globe so they gave up the injections.

> We have done **10,000** routine cataract surgery cases with sub-Tenon's triamcinolone acetate 1.2 cc injections and have eliminated the need for eye drops.

It is important to develop a technique where you can pick up the tenons and have the needle go so the sharp part is vertical to the sclera and let the needle ride right along the crest of the sclera without catching or obstruction in the "feel" of the needle as it passes over the sclera. After the needle is mostly embedded to the area of the equator, the kenalog can be administered.

It has been known for years that if steroids are injected away from the trabecular meshwork, it will not cause an IOP rise. We have had fewer pressure rises with kenalog equatorially/retrobulbarly than we had with drops (less than one-fourth of 1%).

It has become a rarity to expect either endophthalmitis or pressure rises in our postoperative period. This added benefit of cataract surgery falls on the surgeon and is something that should only be done by those who feel they can actually benefit the patient more by

this. Some physicians will not want to do this because of the time and the associated risk.

We have had fewer problems with kenalog injections than with local drops. With drops we have seen keratitis, corneal melts, and many other problems that we rarely observe anymore. We rarely see a medication keratitis with the equatorial/retrobulbar triamcinolone acetate and the postoperative period is extremely uneventful for both patient and physician.

This is presented as a continuation of use of retrobulbar injections of steroids that began more than 50 year ago. At that time, depomedrol was used. Kenalog injections are the "in-between" stage of delivery of medicine.

Most ophthalmologists would prefer an implant be available that can be inserted in the eye at the time of surgery to deliver medications; one with exactly the right dose and one that is reimbursable from insurance.

In the first years that we were doing sub-Tenon's injections of kenalog we tried injecting various ways. We found that patients who were taking anticoagulants had the potential to bleed more than those who were not. Therefore, we do not perform injections on patients taking anticoagulants.

For patients with diabetic retinopathy and macular degeneration we review OCT images for any evidence of significant elevation of the retina due to either condition. The use of intraocular anti-vascular endothelial growth factor drugs and/or steroids may be used in the week prior to surgery to decrease the elevation, OCT images may be repeated and reviewed before and after surgery, and medications given accordingly. The exact way to treat patients with chronic diabetic retinopathy is yet to be ascertained; whether with injections or photocoagulation.

Another option that has been thought beneficial is chronic non-steroidal medications given over a period of years. This needs to be worked out and shown to be a significant return on investment capital. Time will tell whether intravitreal injections, photocoagulation or topical drops is the best form of therapy for each parameter.

At this point, patients have accepted the treatment of subconjunctival triamcinolone acetate because they save about $400 per eye on postoperative medications.

The next important factor is compliance. Patients do not have to worry about putting the drops in their eyes on time. There are many elderly patients that have a disability or live alone and do not have anyone to help them with this task so the kenalog injections allow them to have the medication they need without the added stress of adhering to a drop regimen.

The popularity of this among the patients has slowly grown. I call my patients the day after surgery to check on them and it is interesting that one of things they always marvel at is the fact that they do not have to use drops for several weeks after surgery like many of their neighbors did.

SUMMARY

We have done 10,000 routine cataract surgery cases with sub-Tenon's triamcinolone acetate 1.2 cc injections—mostly superior nasally in patients who are not taking blood thinners at the time of surgery—and thus, have eliminated the need for eye drops.

The only drops we use are lubricants to help with dry eyes after surgery.

Therefore, we will continue to use this regime until intraocular implants are available that will have a non-steroidal and eliminate the need for postoperative drops. It is also possible that the implant can be incorporated with an antibiotic so that we will not have to use our concoction for anterior chamber antibiotics as well. ■

Reference

1. Kim SY, Yang J, Lee YC, Park YH. Effect of a single intraoperative sub-tenon injection of triamcinolone acetonide on the progression of diabetic retinopathy and visual outcomes after cataract surgery. *J Cataract Refract Surg.* 2008;34:823-826.

JAMES P. GILLS, MD, *is founder and director of St. Luke's Cataract and Laser Institute, Tarpon Springs, FL. He did not indicate a financial interest in the subject matter. Readers may contact Dr. Gills at jgills@stlukeseye.com or 727/938-2020.*

On Twitter

Follow *Ophthalmology Times* on Twitter for the latest news and advancements in ophthalmology **@OphthTimes**

@OphthTimes Konan debuts its new Chart2020 v5 visual acuity and #ocular performance testing software #visionexpo #ophthalmology

@OphthTimes Transitions Optical has launched new responsive adaptive lenses, Transitions Signature VII lenses with Chromea7 tech #VisionExpo

@OphthTimes @LENSAR has secured $87M in financing to support market expansion of its laser #cataract surgery system: http://on.wsj.com/16JUgRF

While attending the American Academy of Ophthalmology meeting, stay connected by using and following **#aao13** and **#aao130T**.

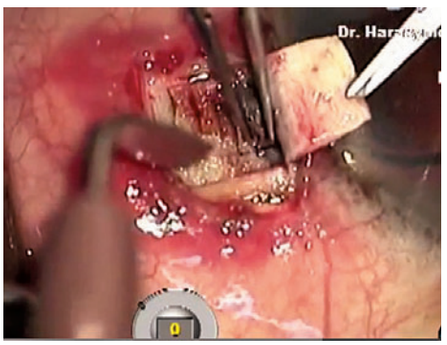
Digital App

Introducing the *Ophthalmology Times* app for iPad and iPhone. Download it for free today at *OphthalmologyTimes.com/OTapp.*

eReport

Sign up for *Ophthalmology Times'* weekly eReport at *http://bit.ly/XjksXX.*

Video



To see how use of a shunt device may augment deep sclerectomy, go to *http://bit.ly/13IaCBS*

Facebook

Like *Ophthalmology Times* at **Facebook.com/OphthalmologyTimes.**

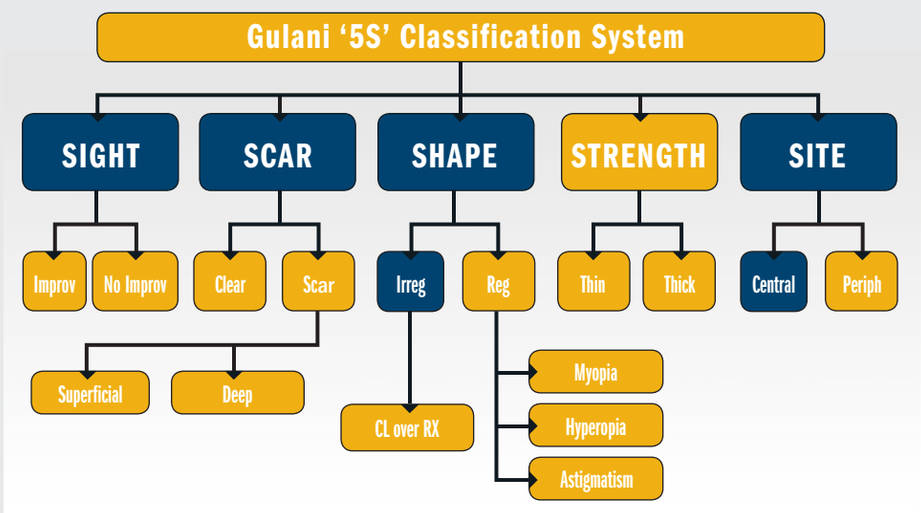
Multifocal IOL nightmare: Reversed to 20/20

Refractive surgery can truly come to its own rescue in complex, complicated cases

Gloves Off with Gulani ***By Arun C. Gulani, MD***

Editor's Note: Ophthalmology Times *presents this first installment of the new "Gloves Off with Gulani" column that applies Dr. Gulani's concept of Corneoplastique—a super-specialty of LASIK, custom cataract, corneal, and full-spectrum vision refractive surgery—to this multifocal IOL nightmare case study in which a 73-year-old female patient's vision was reversed to 20/20.*

The next "Gloves Off with Gulani" column will feature the case study: Taming the devil—LASIK ectasia back to 20/20.



Using this 5S system, note that the Sight (vision), Scar, Shape (irregular), and Site (central) are affected. In this case, since Strength is normal, the surgeon would need to peel off the scar with simultaneous laser refractive ablation (not PTK) in order to measure the patient's actual refractive error. The present refractive error is a play of the corneal scar. Once the true refractive error is obtained, then it can be accurately corrected.

JACKSONVILLE, FL ::

When practiced as an art, full-spectrum refractive surgery not only can address virgin eyes with all levels of ametropia, but it also can reverse and correct complex and complicated cases back to 20/20 vision.

I will share with you a case study that demonstrates how using Corneoplastique principles and applying the "5S" system in practically any refractive situation (corneal/lens/anterior segment)—no matter how complex or complicated—can be successful.

The patient is a 73-year-old white female with a history of IOL implant (AcrySof ReSTOR model SN60D3, Alcon Laboratories) and YAG posterior capsulotomy (YAG PC) done by another surgeon. She was referred to me with corneal scar from multiple laser vision surgery attempts, poor vision, and an angry demeanor, ready to sue her surgeon.

DETAILED PATIENT HISTORY WITH HER SURGEON

In 2005, the patient underwent lens implantation in the left eye, with a preoperative refraction of +2.25 –0. 5 × 70, with a +22 D lens. This resulted in vision of 20/40 and near vision of J2. She was never happy with her vision. One year later, she presented again to her surgeon with vision of 20/40, and she was still not seeing clearly. Her refraction at this time was +1.25 Sph best corrected to 20/25.

Her physician did photorefractive keratectomy (PRK) in April 2006, aiming to correct 1 D sphere as a refractive input. Two months later, the patient presented with 20/80 vision with corneal haze, a refraction of +2.50 –1.00 × 105, best corrected to 20/40, but with double/distorted vision. One month later, the patient was still unhappy with vision of 20/100. Refraction now was +4.50 –0.75 × 90, best corrected to 20/25 (distorted).

Her surgeon now proceeded to perform a repeat PRK for 4 D spherical refractive error. The patient's vision never improved, however, and remained unhappy with her results. She presented again 4 months later, with vision of 20/60 (with double and distorted vision), and a refraction of +2.25 –1.00 × 180. The patient was referred to me by her physician 3 months later.

APPROACH WITH APPROPRIATE MINDSET

My approach and stance in every case referred to me with bad outcomes is always the same: How do we take what we have and lead this to "perfect" vision?

Perhaps the point of paramount importance here is the mindset. We should not think we are doing the patient or referring surgeon a favor by merely attempting to help, and being satisfied with any improvement, however mediocre.

Rather, we should approach such scenarios with an attempt to take the baton from where we received it and run with it to the finish line of 20/20 or the patient's best vision potential (BVP) and therefore truly help the patient and their surgeon.

The first step in the repair of such situations includes restoring patient trust with the initial surgeon, and gaining confidence in you, presuming that the referring surgeon has confirmed that they would prefer that you proceed.

BESIVANCE® (besifloxacin ophthalmic suspension) 0.6%: A Powerful Option for the Treatment of Bacterial Conjunctivitis

Penny A. Asbell, MD, FACS, MBA

ABSTRACT Appropriate treatment of bacterial conjunctivitis serves to shorten the clinical course of disease, reduce symptoms, abbreviate the period of contagion, and reduce time lost from school or work.[1,2] Furthermore, treatment with an effective agent can reduce the slight risk for more serious complications.[2] Introduced in 2009, besifloxacin ophthalmic suspension 0.6% (BESIVANCE®) is broad-spectrum, topical fluoroquinolone with high potency and balanced affinity for bacterial DNA gyrase and topoisomerase IV.[3-5] BESIVANCE® is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria: *Aerococcus viridans**, CDC coryneform group G, *Corynebacterium pseudodiphtheriticum**, *Corynebacterium striatum**, *Haemophilus influenzae*, *Moraxella catarrhalis**, *Moraxella lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis**, *Staphylococcus lugdunensis**, *Staphylococcus warneri**, *Streptococcus mitis* group, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus salivarius**.

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

In vitro studies have found that common bacterial conjunctivitis pathogens, including antibiotic-resistant strains, are susceptible to BESIVANCE®; and in clinical trials BESIVANCE® has demonstrated safety and robust efficacy against typical bacterial conjunctivitis pathogens.[6,7] Use of a mucoadhesive polymer in the BESIVANCE® formulation increases residence time of the antimicrobial on the ocular surface and contributes to its pharmacokinetic/pharmacodynamic profile.[8] Formulated for use only as a topical antibiotic, besifloxacin has not been used in internal medicine or agriculture, which may decrease selection pressure for resistance to the drug.[9]

See Important Risk Information about BESIVANCE®.

Introduction

Each year, more than 4 million Americans suffer from bacterial conjunctivitis, and many of them seek medical attention.[10] An estimated 1% to 4% of primary care consultations are for acute red eye, and there is evidence that the majority of those cases are caused by bacterial conjunctivitis.[10,11]

Prospective studies utilizing conjunctival culture found that most cases of acute conjunctivitis in children were bacterial in origin.[1,11] Interestingly, physicians have been found to underestimate the prevalence of bacterial conjunctivitis in relation to other causes of an acute red eye.[1]

Patients with acute bacterial conjunctivitis characteristically experience tearing, ocular surface irritation, marked redness, and the presence of mucopurulent discharge that can be copious and lead to matting of the lash cilia. To prevent spreading the infection to others, patients are frequently required to stay home from work or school. While the prognosis is generally favorable—60% of cases resolve spontaneously within 2 weeks—bacterial conjunctivitis carries a small (but not zero) risk of progressing to keratitis, particularly in patients carrying large numbers of bacteria and/or an epithelial defect.[11] Furthermore, infection with a difficult-to-treat pathogen such as *Pseudomonas aeruginosa* carries a higher risk for adverse outcomes (Figure 1).[2]

Important Risk Information for BESIVANCE®

- BESIVANCE® is for topical ophthalmic use only, and should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.
- As with other anti-infectives, prolonged use of BESIVANCE® may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy.
- Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with BESIVANCE®.
- The most common adverse event reported in 2% of patients treated with BESIVANCE® was conjunctival redness. Other adverse events reported in patients receiving BESIVANCE® occurring in approximately 1–2% of patients included: blurred vision, eye pain, eye irritation, eye pruritus and headache.
- BESIVANCE® is not intended to be administered systemically. Quinolones administered systemically have been associated with hypersensitivity reactions, even following a single dose. Patients should be advised to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.
- Safety and effectiveness in infants below one year of age have not been established.

Please see the full prescribing information for BESIVANCE® on page 4.

Microbiology

Since bacterial conjunctivitis is typically treated without culturing the eye, selection of an appropriate treatment requires knowledge of the most likely etiologic agents and their susceptibilities. Pathogens commonly implicated in bacterial conjunctivitis include typical commensal flora of the skin and nasopharynx, including such gram-positive organisms as *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Streptococcus pneumoniae*; and gram negatives *Moraxella catarrhalis* and *Haemophilus influenzae*.[9] *P. aeruginosa* is a common cause of infection among contact lens wearers.[2]

An important challenge in the management of bacterial conjunctivitis is antimicrobial resistance.

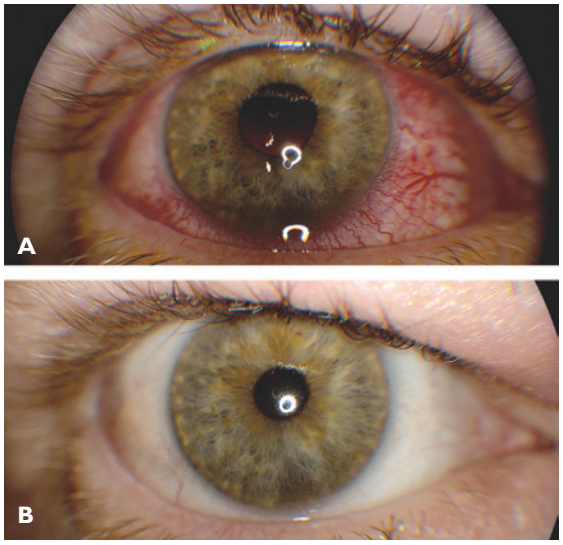


Figure 1 (a) Eye with confirmed bacterial conjunctivitis due to *P. aeruginosa*. (b) The same eye after 1 week of therapy with BESIVANCE® TID.

Resistance

Clinicians who treat external ocular disease have been somewhat protected from problems associated with antibiotic resistance due to the unique pharmacokinetics of topically administered ophthalmic drugs—which can typically achieve concentrations at the site of infection far greater than systemic drugs.

However, even among ocular infections, rates of resistance to commonly used antibiotics are increasing rapidly; and resistant pathogens have been linked to treatment failure.[9] It is therefore important that ophthalmologists keep abreast of the changing status of antibiotic resistance.

The study designated Ocular TRUST (for Tracking Resistance in the US Today) reported nationwide antibiotic susceptibility patterns of three key ocular pathogens—*S. aureus*, *S. pneumoniae*, and *H. influenzae*—to multiple classes of ophthalmic antibiotics.[12] Ocular TRUST found that, despite widespread use of fluoroquinolones in medicine and veterinary settings, and consequently high resistance selection pressure, the fluoroquinolones remained the most consistently effective class of antibiotic against *S. pneumoniae*, *H. influenzae*, and methicillin-susceptible *S. aureus* (MSSA) ocular isolates.[12]

Of particular concern, however, is the emergence of multidrug resistant gram-positive pathogens, including methicillin-resistant *S. aureus* (MRSA) and methicillin resistant *S. epidermidis* (MRSE). According to the Ocular TRUST study and others, MRSA is becoming increasingly resistant to multiple antibiotics.[12] Ocular isolates from the 2009 ARMOR (Antibiotic Resistance Monitoring in Ocular microoRganisms) showed similar patterns of multidrug resistance among MRSA.[13] ARMOR also revealed high rates of resistance among ocular MRSE isolates, and high levels of multidrug resistance among staphylococci and *Pseudomonas* strains.[13]

Potency

Antibiotic potency is typically quantified in terms of the minimum inhibitory concentration (MIC), the lowest concentration of a drug able to inhibit the growth of a bacterial isolate.[14] To describe the potency of a drug against a bacterial *species*, we use the MIC_{50} and MIC_{90}, the concentrations of antibiotic necessary to inhibit the growth of 50% and 90%, respectively, of different bacterial isolates of the same species. While low MIC values indicate that low concentrations of drug will be required to effect bacterial inhibition, the clinical significance of in vitro data has not been established.[14]

To date, besifloxacin has demonstrated excellent in vitro potency against gram-positive ocular pathogens. For example, three large clinical studies of BESIVANCE® for the treatment of bacterial conjunctivitis demonstrated low MICs against all clinical isolates (MIC_{50} = 0.06 and MIC_{90} = 0.25 mg/mL).[6] In these studies, a total of 1324 bacterial pathogens representing more

A 42-year-old man requested an emergency ophthalmology visit due to symptoms of "pink eye" that were affecting his ability to work. The patient reported a 2-day history of redness, irritation, and a thickened discharge from his right eye. Upon awakening, his eyelid was matted shut. His left eye felt normal and seemed to be unaffected. He reported no contact with anyone who had pink eye at home or work. He wore glasses for distance; otherwise he had no significant ocular or medical history.

Examination of his right eye revealed a best corrected visual acuity of 20/30. Slit lamp examination showed trace lid swelling, 2+ conjunctival injection, and mucopurulent discharge. The eye tested negative for the presence of adenovirus. The cornea and anterior segment appeared normal. The left eye was correctable to 20/20, and slit lamp exam was normal.

The patient was diagnosed with acute bacterial conjunctivitis in the right eye. BESIVANCE® (besifloxacin ophthalmic solution) 0.6% was prescribed and the patient instructed to instill one drop in the affected eye 3 times a day (4 to 12 hours apart) for 7 days. Seen 3 days later, the patient was significantly improved. He was instructed to continue BESIVANCE® to the end of the initial 7-day period and then discontinue.

Please see Important Risk Information on page 1 and the full prescribing information for BESIVANCE® on page 4.

than 70 species were isolated.[6]

Besifloxacin also demonstrated strong activity against MRSA, including ciprofloxacin-resistant strains.[6] Indeed, clinical research has demonstrated rapid microbial eradication by besifloxacin in cases of bacterial conjunctivitis culture-positive for MRSA and MRSE—even where the cultured isolates were found to be concurrently resistant to ciprofloxacin.[15] Microbial eradication does not always correlate with clinical outcomes in antiinfective trials. In this study, the MIC_{90} values for besifloxacin were found to be 2 mg/mL against ciprofloxacin-resistant MRSA isolates, and 4 mg/mL against ciprofloxacin-resistant MRSE isolates.[15]

The Besifloxacin Molecule

The besifloxacin molecule represents an evolution of the topical ocular fluoroquinolone family. Fluoroquinolones work by binding two enzymes critical for DNA bacterial replication: DNA gyrase (topoisomerase II) and topoisomerase IV.[5] The original quinolones predominantly targeted DNA gyrase, which gave them good activity against replication of gram-negative organisms.[5] Subsequent generations have had better activity against topoisomerase IV, which expands the spectrum of coverage against gram-positive organisms.[5]

BESIVANCE® has two halogen atoms on the quinolone backbone: a fluorine (common to all fluoroquinolones) and a chlorine at carbon 8. This imparts a balanced and increased affinity for both DNA gyrase and topoisomerase IV, enhancing besifloxacin's overall potency.[3,4] Targeting both enzymes relatively equally also means that two mutations would be required for the development of substantial resistance.[5]

Treating Bacterial Conjunctivitis

Since suspected bacterial conjunctivitis cases are not routinely cultured, empirical therapy should be broad-spectrum, covering as many as possible of the common gram-positive and gram-negative pathogens known to cause bacterial conjunctivitis. In addition, treatment efficacy may be enhanced by the use of a potent antibiotic that resides for a significant period on the ocular surface.

BESIVANCE® satisfies each of these criteria and several others. Its broad spectrum of coverage includes gram-positive and gram-negative pathogens that commonly cause bacterial conjunctivitis. BESIVANCE® has demonstrated potency against worrisome pathogens such as MRSA, MRSE, and *P. aeruginosa*.[6] BESIVANCE® (besifloxacin ophthalmic suspension) 0.6% is also formulated with a mucoadhesive polymer.[8] Studies have shown that this suspension allows for prolonged surface contact with the eye compared to antibiotics formulated in aqueous solutions.[16]

Finally, BESIVANCE® has an established safety profile and is a potent agent for the treatment of bacterial conjunctivitis.

Penny A. Asbell, MD, FACS, MBA, is professor of ophthalmology, director of cornea and refractive services, and cornea fellowship director in the department of ophthalmology of the Mount Sinai School of Medicine in New York, NY.

References

1. Patel PB, Diaz MCG, Bennett JE, Attia MW. Clinical features of bacterial conjunctivitis in children. *Acad Emerg Med* 2007;14:1-5.
2. Silverstein BE, Morris TW, Gearinger LS, Decory HH, Comstock TL. Besifloxacin ophthalmic suspension 0.6% in the treatment of bacterial conjunctivitis patients with *Pseudomonas aeruginosa* infections. *Clin Ophthalmol.* 2012;6:1987-96.
3. Sanfilippo CM, Hesje CK, Haas W, Morris TW. Topoisomerase mutations that are associated with high-level resistance to earlier fluoroquinolones in *Staphylococcus aureus* have less effect on the antibacterial activity of besifloxacin. *Chemotherapy.* 2011;57:363-71.
4. Cambau E, Matrat S, Pan X, et al. Target specificity of the new fluoroquinolone besifloxacin in Streptococcus pneumoniae, Staphylococcus aureus, and Escherichia coli. *J Antimicrob Chemother.* 2009;63(3):443-50.
5. Bearden DT, Danziger LH. Mechanism of action and resistance to quinolones. *Pharmacotherapy.* 2001;21(10)(Suppl):224S-32S.
6. Haas W, Gearinger LS, Usner DW, et al. Integrated analysis of three bacterial conjunctivitis trials of besifloxacin ophthalmic suspension, 0.6%: etiology of bacterial conjunctivitis and antibacterial susceptibility profile. *Clin Ophthalmol.* 2011 Sept;5:1369-79.
7. Tepedino ME, Heller WH, Usner DW, et al. Phase III efficacy and safety study of besifloxacin ophthalmic suspension 0.6% in the treatment of bacterial conjunctivitis. *Curr Med Res Opin*. 2009;25:1159-69.
8. O'Brien TP. Besifloxacin ophthalmic suspension, 0.6%: a novel topical fluoroquinolone for bacterial conjunctivitis. *Adv Ther*. 2012;29:473-90.
9. Karpecki P, Paterno MR, Comstock TL. Limitations of current antibiotics for the treatment of bacterial conjunctivitis. *Optom Vis Sci*. 2010;87:908-19.
10. Smith AF, Waycaster C. Estimate of the direct and indirect annual cost of bacterial conjunctivitis in the United States. *BMC Ophthalmol.* 2009;9:13. Available at: http://www.biomedcentral.com/content/pdf/1471-2415-9-13.pdf.
11. Hovding G. Acute bacterial conjunctivitis. *Acta Ophthalmol*. 2008;86:5-17.
12. Asbell PA, Colby KA, Deng S, McDonnell P, Meisler DM, Raizman MB, Sheppard JD Jr, Sahm DF. Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates. *Am J Ophthalmol.* 2008;145:951-8
13. Haas W, Pillar CM, Torres M, Morris TW, Sahm DF. Monitoring antibiotic resistance in ocular microorganisms: results from the Antibiotic Resistance Monitoring in Ocular micRorganisms (ARMOR) 2009 surveillance study. *Am J Ophthalmol.* 2011;152:567-74.
14. Kowalski RP, Yates KA, Romanowski EG, et al. An ophthalmologist's guide to understanding antibiotic susceptibility and minimum inhibitory concentration data. *Ophthalmology*. 2005;112:1987-91.
15. DeCory HH, Comstock TL, Gearinger LS, Morris TW. Clinical efficacy of besifloxacin ophthalmic suspension, 0.6% against MRSA and MRSE. Poster presented at the annual meeting of the Association for Research in Vision and Ophthalmology; Fort Lauderdale, FL; May 6-10, 2012.
16. Proksch JW, Granvil CP, Siou-Mermet R, et al. Ocular pharmacokinetics of besifloxacin following topical administration to rabbits, monkeys, and humans. *J Ocul Pharmacol Ther.* 2009;25:335-43.

BAUSCH+LOMB
Besivance®
besifloxacin ophthalmic suspension, 0.6%

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Besivance safely and effectively. See full prescribing information for Besivance.

Besivance® (besifloxacin ophthalmic suspension) 0.6%
Sterile topical ophthalmic drops
Initial U.S. Approval: 2009

---------- RECENT MAJOR CHANGES ----------
Indications and Usage (1) 09/2012
---------- INDICATIONS AND USAGE ----------
Besivance® (besifloxacin ophthalmic suspension) 0.6%, is a quinolone antimicrobial indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria:
*Aerococcus viridans**, CDC coryneform group G, *Corynebacterium pseudodiphtheriticum**, *Corynebacterium striatum**, *Haemophilus influenzae*, *Moraxella catarrhalis**, *Moraxella lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis**, *Staphylococcus lugdunensis**, *Staphylococcus warneri**, *Streptococcus mitis* group, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus salivarius**
*Efficacy for this organism was studied in fewer than 10 infections. (1)

---------- DOSAGE AND ADMINISTRATION----------
Instill one drop in the affected eye(s) 3 times a day, four to twelve hours apart for 7 days. (2)
---------- DOSAGE FORMS AND STRENGTHS----------
7.5 mL size bottle filled with 5 mL of besifloxacin ophthalmic suspension, 0.6% (3)
----------CONTRAINDICATIONS----------
None (4)
----------WARNINGS AND PRECAUTIONS ----------
Topical Ophthalmic Use Only. (5.1)
Growth of Resistant Organisms with Prolonged Use. (5.2)
Avoidance of Contact Lenses. Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance. (5.3)
---------- ADVERSE REACTIONS ----------
The most common adverse reaction reported in 2% of patients treated with Besivance was conjunctival redness. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb Incorporated at 1-800-323-0000 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION
Revised: 09/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Besivance® (besifloxacin ophthalmic suspension) 0.6%, is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria:
*Aerococcus viridans**
CDC coryneform group G
*Corynebacterium pseudodiphtheriticum**
*Corynebacterium striatum**
Haemophilus influenzae
*Moraxella catarrhalis**
*Moraxella lacunata**
*Pseudomonas aeruginosa**
Staphylococcus aureus
Staphylococcus epidermidis
*Staphylococcus hominis**
*Staphylococcus lugdunensis**
*Staphylococcus warneri**
Streptococcus mitis group
Streptococcus oralis
Streptococcus pneumoniae
*Streptococcus salivarius**
*Efficacy for this organism was studied in fewer than 10 infections.

2 DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once before use.
Instill one drop in the affected eye(s) 3 times a day, four to twelve hours apart for 7 days.

3 DOSAGE FORMS AND STRENGTHS

7.5 mL bottle filled with 5 mL of besifloxacin ophthalmic suspension, 0.6%.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Topical Ophthalmic Use Only

NOT FOR INJECTION INTO THE EYE.
Besivance is for topical ophthalmic use only, and should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

5.2 Growth of Resistant Organisms with Prolonged Use

As with other anti-infectives, prolonged use of Besivance (besifloxacin ophthalmic suspension) 0.6% may result in overgrowth of non-susceptible organisms, including fungi. If super-infection 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.

5.3 Avoidance of Contact Lenses

Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance.

6 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in one clinical trial of a drug cannot be directly compared with the rates in the clinical trials of the same or another drug and may not reflect the rates observed in practice.
The data described below reflect exposure to Besivance in approximately 1,000 patients between 1 and 98 years old with clinical signs and symptoms of bacterial conjunctivitis.
The most frequently reported ocular adverse reaction was conjunctival redness, reported in approximately 2% of patients.
Other adverse reactions reported in patients receiving Besivance occuring in approximately 1-2% of patients included: blurred vision, eye pain, eye irritation, eye pruritus and headache.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C.
Oral doses of besifloxacin up to 1000 mg/kg/day were not associated with visceral or skeletal malformations in rat pups in a study of embryo-fetal development, although this dose was associated with maternal toxicity (reduced body weight gain and food consumption) and maternal mortality. Increased post-implantation loss, decreased fetal body weights, and decreased fetal ossification were also observed. At this dose, the mean C_{max} in the rat dams was approximately 20 mcg/mL, >45,000 times the mean plasma concentrations measured in humans. The No Observed Adverse Effect Level (NOAEL) for this embryo-fetal development study was 100 mg/kg/day (C_{max}, 5 mcg/mL, >11,000 times the mean plasma concentrations measured in humans).
In a prenatal and postnatal development study in rats, the NOAELs for both fetal and maternal toxicity were also 100 mg/kg/day. At 1000 mg/kg/day, the pups weighed significantly less than controls and had a reduced neonatal survival rate. Attainment of developmental landmarks and sexual maturation were delayed, although surviving pups from this dose group that were reared to maturity did not demonstrate deficits in behavior, including activity, learning and memory, and their reproductive capacity appeared normal.
Since there are no adequate and well-controlled studies in pregnant women, Besivance should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

Besifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when Besivance is administered to a nursing mother.

8.4 Pediatric Use

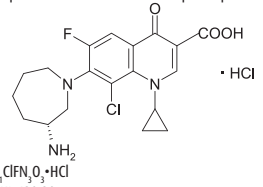
The safety and effectiveness of Besivance® in infants below one year of age have not been established. The efficacy of Besivance in treating bacterial conjunctivitis in pediatric patients one year or older has been demonstrated in controlled clinical trials *[see CLINICAL STUDIES (14)]*.
There is no evidence that the ophthalmic administration of quinolones has any effect on weight bearing joints, even though systemic administration of some quinolones has been shown to cause arthropathy in immature animals.

8.5 Geriatric Use

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

11 DESCRIPTION

Besivance (besifloxacin ophthalmic suspension) 0.6%, is a sterile ophthalmic suspension of besifloxacin formulated with DuraSite®† (polycarbophil, edetate disodium dihydrate and sodium chloride). Each mL of Besivance contains 6.63 mg besifloxacin hydrochloride equivalent to 6 mg besifloxacin base. It is an 8-chloro fluoroquinolone anti-infective for topical ophthalmic use.



$C_{19}H_{21}ClFN_3O_3 \cdot HCl$
Mol Wt 430.30
Chemical Name: (+)-7-[(3R)-3-aminohexahydro-1H-azepin-1-yl]-8-chloro-1- cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.
Besifloxacin hydrochloride is a white to pale yellowish-white powder.

Each mL Contains:
Active: besifloxacin 0.6% (6 mg/mL);
Preservative: benzalkonium chloride 0.01%
Inactives: polycarbophil, mannitol, poloxamer 407, sodium chloride, edetate disodium dihydrate, sodium hydroxide and water for injection.
Besivance is an isotonic suspension with an osmolality of approximately 290 mOsm/kg.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Besifloxacin is a fluoroquinolone antibacterial *[see CLINICAL PHARMACOLOGY (12.4)]*.

12.3 Pharmacokinetics

Plasma concentrations of besifloxacin were measured in adult patients with suspected bacterial conjunctivitis who received Besivance bilaterally three times a day (16 doses total). Following the first and last dose, the maximum plasma besifloxacin concentration in each patient was less than 1.3 ng/mL. The mean besifloxacin C_{max} was 0.37 ng/mL on day 1 and 0.43 ng/mL on day 6. The average elimination half-life of besifloxacin in plasma following multiple dosing was estimated to be 7 hours.

12.4 Microbiology

Besifloxacin is an 8-chloro fluoroquinolone with a N-1 cyclopropyl group. The compound has activity against Gram-positive and Gram-negative bacteria due to the inhibition of both bacterial DNA gyrase and topoisomerase IV. DNA gyrase is an essential enzyme required for replication, transcription and repair of bacterial DNA. Topoisomerase IV is an essential enzyme required for partitioning of the chromosomal DNA during bacterial cell division. Besifloxacin is bactericidal with minimum bactericidal concentrations (MBCs) generally within one dilution of the minimum inhibitory concentrations (MICs).
The mechanism of action of fluoroquinolones, including besifloxacin, is different from that of aminoglycoside, macrolide, and β-lactam antibiotics. Therefore, besifloxacin may be active against pathogens that are resistant to these antibiotics and these antibiotics may be active against pathogens that are resistant to besifloxacin. *In vitro* studies demonstrated cross-resistance between besifloxacin and some fluoroquinolones.
In vitro resistance to besifloxacin develops via multiple-step mutations and occurs at a general frequency of < 3.3×10^{-10} for *Staphylococcus aureus* and < 7×10^{-10} for *Streptococcus pneumoniae*.
Besifloxacin has been shown to be active against most isolates of the following bacteria both *in vitro* and in conjunctival infections treated in clinical trials as described in the INDICATIONS AND USAGE section:
*Aerococcus viridans**, CDC coryneform group G, *Corynebacterium pseudodiphtheriticum**, *C. striatum**, *Haemophilus influenzae*, *Moraxella catarrhalis**, *M. lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus*, *S. epidermidis*, *S. hominis**, *S. lugdunensis**, *S. warneri**, *Streptococcus mitis* group, *S. oralis*, *S. pneumoniae*, *S. salivarius**
*Efficacy for this organism was studied in fewer than 10 infections.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to determine the carcinogenic potential of besifloxacin have not been performed.
No *in vitro* mutagenic activity of besifloxacin was observed in an Ames test (up to 3.33 mcg/plate) on bacterial tester strains *Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and *Escherichia coli* WP2uvrA. However, it was mutagenic in *S. typhimurium* strain TA102 and *E. coli* strain WP2(pKM101). Positive responses in these strains have been observed with other quinolones and are likely related to topoisomerase inhibition.
Besifloxacin induced chromosomal aberrations in CHO cells *in vitro* and it was positive in an *in vivo* mouse micronucleus assay at oral doses ≥ 1500 mg/kg. Besifloxacin did not induce unscheduled DNA synthesis in hepatocytes cultured from rats given the test compound up to 2,000 mg/kg by the oral route. In a fertility and early embryonic development study in rats, besifloxacin did not impair the fertility of male or female rats at oral doses of up to 500 mg/kg/day. This is over 10,000 times higher than the recommended total daily human ophthalmic dose.

14 CLINICAL STUDIES

In a randomized, double-masked, vehicle controlled, multicenter clinical trial, in which patients 1-98 years of age were dosed 3 times a day for 5 days, Besivance was superior to its vehicle in patients with bacterial conjunctivitis. Clinical resolution was achieved in 45% (90/198) for the Besivance treated group versus 33% (63/191) for the vehicle treated group (difference 12%, 95% CI 3% - 22%). Microbiological outcomes demonstrated a statistically significant eradication rate for causative pathogens of 91% (181/198) for the Besivance treated group versus 60% (114/191) for the vehicle treated group (difference 31%, 95% CI 23% - 40%). Microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

16 HOW SUPPLIED/STORAGE AND HANDLING

Besivance® (besifloxacin ophthalmic suspension) 0.6%, is supplied as a sterile ophthalmic suspension in a white low density polyethylene (LDPE) bottle with a controlled dropper tip and tan polypropylene cap. Tamper evidence is provided with a shrink band around the cap and neck area of the package.

5 mL in 7.5 mL bottle
NDC 24208-446-05

Storage:

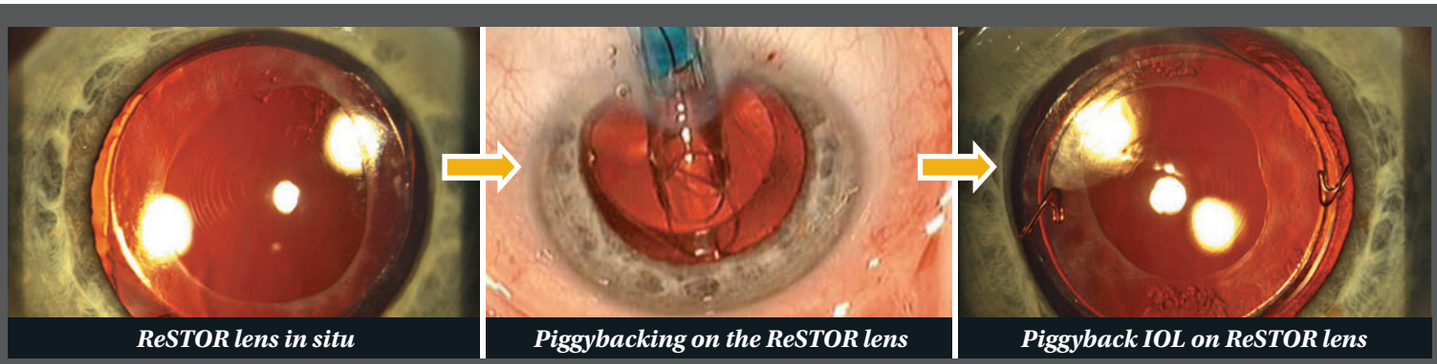
Store at 15°-25°C (59°-77°F). Protect from Light. Invert closed bottle and shake once before use.

17 PATIENT COUNSELING INFORMATION

Patients should be advised to avoid contaminating the applicator tip with material from the eye, fingers or other source.
Although Besivance is not intended to be administered systemically, quinolones administered systemically have been associated with hypersensitivity reactions, even following a single dose. Patients should be advised to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.
Patients should be told that although it is common to feel better early in the course of the therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Besivance or other antibacterial drugs in the future.
Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance.
Patients should be advised to thoroughly wash hands prior to using Besivance.
Patients should be instructed to invert closed bottle (upside down) and shake once before each use. Remove cap with bottle still in the inverted position. Tilt head back, and with bottle inverted, gently squeeze bottle to instill one drop into the affected eye(s).

Manufactured by: Bausch & Lomb Incorporated
Tampa, Florida 33637

9142605(flat)
9142705(folded)



ReSTOR lens in situ | *Piggybacking on the ReSTOR lens* | *Piggyback IOL on ReSTOR lens*

Stage II, Piggyback Lens: Given the patient's past YAG PC opening by her surgeon and presently detected high hyperopia, a piggyback IOL was planned on top of the ReSTOR lens. This surgery was executed with simultaneous surgical PI. Final refraction of –0.50 –0.50 × 002 OS with Vsc of 20/20 at distance and near.

Always listen to the patient. In most cases, the patient's anger will stem from the surgeon having not listened/admitted to the problem, or not reacting to it as important and failing to provide options.

Reassure the patient that outcomes like these are possible with the best of surgeons. Involve them in making a logical plan to follow. Make them a team player with you in the journey of vision correction. Remember, no patient wants any more surgery after such outcomes.

The Corneoplastique mindset calls for the least interventional techniques, which must qualify as brief, topical, aesthetically pleasing, visually promising, and still maintaining patient candidacy for any back-up surgery, such as penetrating keratoplasty.

APPLY THE 5S SYSTEM

The backbone behind technique selection and plan formation is the 5S classification system: Sight, Scar, Shape, Strength, and Site. This algorithm makes any complex case scenario simple to understand and treat effectively.

Using the 5S system on this patient, we find that the Sight (vision) is affected adversely, there is a Scar, Shape is irregular, and central cornea Site is affected. Strength is not involved, as the cornea is neither too thin nor thick. Given that the patient had Sight, we must do something. Since Strength is normal in this case, we do not need any corneal building or stabilizing surgery (i.e., lamellar keratoplasty, corneal ring implants, cross linking etc.), but must centrally (Site) address the Scar and Shape.

Remember that the refraction in these "on cornea" cases is a camouflage; therefore, we need to determine this patient's real refraction. The single surgery that can do all of these is excimer laser myopic PRK.

Under the excimer laser, I proceeded with manual epithelial debridement to study the scar underneath and found slivers of plastic wrap-like scar layers; I have seen this consistent look in multiple PRK scars that I have corrected. Gently and patiently peel these scars off the cornea in toto.

My pearl here is never to use sharp instruments or blades and always let the cornea be a resistance-guided platform. This same principle can be used for Salzmann's nodules, epithelial ingrowth, pterygium head removal, etc., to reveal a near-smooth stromal bed underneath.

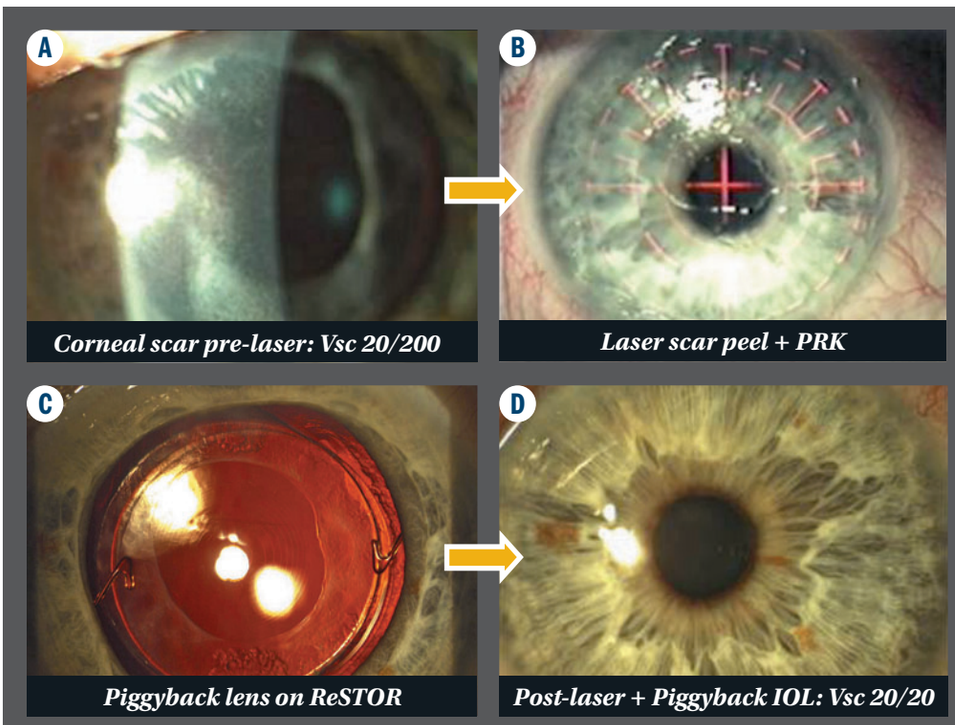
The excimer laser (VISX, Abbott Medical Optics) was programmed for a –3 D large zone, myopic ablation and mitomycin C (0.02%) was used on a weck cel centrally to be copiously washed off after a minute.

Standard PRK regimen of eye drops was followed, and a bandage contact lens was placed on this eye.

As the patient healed, her cornea healed and cleared completely, and her best-corrected vision (20/25) was measurable, with a refraction of +6.00 –0.25 × 170 best corrected to a clear and appreciable 20/25 Vsc.

I followed her at regular intervals to determine stability and also to allow her to decide whether she wanted to proceed with the planned stage 2 lens-based procedure. Seven months postoperatively, she proved good stability and had a clear cornea. I had her simulate her vision with the stable refraction using a soft contact lens, and she appreciated 20/25 vision and was very happy.

Continues on page 23 : ***Reversed to 20/20***



Corneal scar pre-laser: Vsc 20/200 | *Laser scar peel + PRK*

Piggyback lens on ReSTOR | *Post-laser + Piggyback IOL: Vsc 20/20*

Summary of results: This patient—who was very angry with her surgeon and also mentally depressed with her poor vision—is now delighted with her outcomes. She remembers only two, staged, very brief, topical procedures resulting in her vision recovery to 20/20. *(Images courtesy of Arun C. Gulani, MD)*

STATEMENT OF OWNERSHIP, MANAGEMENT, AND CIRCULATION
(Requester Publications Only)
(Required by 39 USC 3685)

1. **Publication Title:** Ophthalmology Times
2. **Publication Number:** 0193-032X
3. **Filing Date:** 9/30/13
4. **Issue Frequency:** Twice Monthly
5. **Number of Issues Published Annually:** 24
6. **Annual Subscription Price (if any):** **$200.00**
7. **Complete Mailing Address of Known Office of Publication:** 131 West First Street, Duluth, St. Louis County, Minnesota 55802-2065
   Contact Person: Wendy Bong **Telephone:** 218-740-7244
8. **Complete Mailing Address of Headquarters or General Business Office of Publisher:**
   2501 Colorado Avenue, Suite 280, Santa Monica, CA 90404
9. **Full Names and Complete Mailing Addresses of Group Publisher:** Leonardo Avila, 485F US Hwy 1S, Suite 210, Iselin, NJ 08830
   Group Content Director: Mark L. Dlugoss, Great Northern Corporate Center II, 24950 Country Club Blvd., North Olmsted, OH 44070
   Content Channel Director: Sheryl Stevenson, Great Northern Corporate Center II, 24950 Country Club Blvd., North Olmsted, OH 44070
10. **This publication is owned by:** Advanstar Communications Inc., 2501 Colorado Avenue, Suite 280, Santa Monica, CA 90404. The sole shareholder of Advanstar Communications Inc. is: Advanstar, Inc., whose mailing address is 2501 Colorado Avenue, Suite 280, Santa Monica, CA 90404.
11. Advanstar Communications Inc. is a borrower under Credit Agreements dated June 6, 2013, with various lenders as named therein from time to time. As of June 6, 2013, the agent for the lenders is: Goldman Sachs Lending Partners LLC, Administrative Agent, 30 Hudson St, 4th Floor, Jersey City, NJ 07302.
12. **Does Not Apply**
13. **Publication Title:** Ophthalmology Times
14. **Issue Date for Circulation Data Below:** August 15, 2013
15. **Extent and Nature of Circulation**

		Average No. Copies Each Issue During Preceding 12 Months	No. Copies of Single Issue Published Nearest to Filing Date
A.	**Total Number of Copies**	20,241	19,588
B.	**Legitimate Paid and/or Requested Distribution**		
1.	**Outside County Paid/ Requested Mail Subscriptions Stated on PS Form 3541**	13,054	12,333
2.	**In-County Paid/Requested Mail Subscriptions Stated on PS Form 3541**	0	0
3.	**Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Paid or Requested Distribution Outside USPS**	604	585
4.	**Requested Copies Distributed by Other Mail Classes Through the USPS**	0	0
C.	**Total Paid and /or Requested Circulation** (Sum of 15b (1), (2), (3), and (4))	13,657	12,918
D.	**Non-requested Distribution**		
1.	**Outside County Non-requested Copies Stated on PS Form 3541**	5,571	5,856
2.	**In-County Non-requested Copies Stated on PS Form 3541**	0	0
3.	**Non-requested Copies Distributed Through the USPS by Other Classes of Mail**	0	0
4.	**Non-requested Copies Distributed Outside the Mail**	826	643
E.	**Total Non-requested Distribution** (Sum of 15d (1), (2), (3) and (4))	6,397	6,499
F.	**Total Distribution** (Sum of 15c and e)	20,055	19,417
G.	**Copies not Distributed**	186	171
H.	**Total** (Sum of 15f and g)	20,241	19,588
I.	**Percent Paid and/or Requested Circulation**	68.10%	66.53%

16. ☐ **Total circulation includes electronic copies. Report circulation on PS Form 3526-X worksheet.**
17. **Publication of Statement of Ownership for a Requester Publication is required and will be printed in the October 1st issue of this publication.**
    Name and Title of Editor, Publisher, Business Manager, or Owner: Christine Shappell, Audience Development Director
    Signature:

Date: 09/30/13
I certify that the statements made by me above are correct and complete.

Christine Shappell

IN SITU TECHNIQUE

(Continued from page 1)

TAKE-HOME

The in situ fracture – thin bowl technique is designed to reduce the risk of corneal endothelial damage when removing hard cataracts. Clinical study data show that it works.

but that may be a disadvantaged approach with hard cataracts. It brings large chunks of hard nuclear material up into the iris plane and anterior chamber where it can abrade the corneal endothelium," Dr. Davison said.

"Reducing the nucleus to thin plates first before centralizing the material in the higher vacuum and aspiration rate quadrant removal mode makes surgery for hard cataracts, faster, easier, and ultimately healthier for the eye," he added.

EVALUATION OF TECHNIQUE

To evaluate the in situ fracture – thin bowl technique, Dr. Davison conducted a prospective study that included 56 consecutive eyes with hard cataract (LOCS III NC > 3.8). Surgery was performed using a phacoemulsification platform (Infiniti Vision System, Alcon Laboratories) through a 2.4-mm incision. The in situ fracture – thin bowl technique was used in all cases, but the eyes were randomly assigned to quadrant removal using either a longitudinal tip motion or a torsional/vacuum triggered longitudinal tip motion (OZil Intelligent Phaco, Alcon).

Outcomes assessed included intraoperative complications and change in endothelial cell density (ECD) measurements from preoperative to 3 months after surgery.

The only intraoperative complication in the study was the development of a whitened thermal effect at the corneal incision in one eye that underwent quadrant removal with longitudinal tip motion, and the incision was closed at the end of the case with a single "X" pattern 10-0 nylon suture.

At 3 months after surgery, the mean % decrease in corneal ECD was 5.9% for the longitudinal group and 2.7% for the torsional/vacuum triggered longitudinal group, which was a statistically insignificant difference.

"The outcome in both groups compares very favorably with other techniques for removing hard cataracts," said Dr. Davison, citing a study in which ECD decreased 15.7% among eyes with hard cataracts using a chop technique. ■

JAMES A. DAVISON, MD
E: *jdavison@wolfeclinic.com*
Dr. Davison is a paid consultant to Alcon Laboratories, but has no financial interest in any of the devices or techniques presented.

FDA panel favorably votes for ReSure Sealant

BEDFORD, MA ::
OCULAR THERAPEUTIX INC.'S ReSure Sealant has been declared safe and effective for the management of clear corneal wound leaks following cataract surgery by the FDA's ophthalmic devices panel.

To make the determination, the panel reviewed data from a 488 patient-controlled, multicenter, randomized, prospective clinical trial of the medical device.

For the primary endpoint of prevention of wound leaks within the first 7 days postoperatively, the study found the sealant demonstrated statistical superiority over sutures—having successfully prevented would leaks in 95.9% of cases, compared with sutures at a rate of 65.9%. Use of the sealant was also found to be associated with fewer adverse events when compared with suture and was well tolerated by patients.

"Prior to device application, nearly half of all clear corneal wounds spontaneously leaked in the trial, while the majority of remaining incisions leaked with minimal provocation," said Amar Sawhney, president and chief executive officer of Ocular Therapeutix Inc. "Suturing has so far been the best definitive recourse for treating leaking wounds, however, in this trial the (sealant) was demonstrated to be superior to sutures." ■

WELCOME TO THE ERA OF CENTURION®

Optimize every moment of your cataract removal procedure with the NEW CENTURION® Vision System.

Active Fluidics™

Automatically optimizes chamber stability by allowing surgeons to customize and control IOP throughout the procedure.

Balanced Energy™

Enhances cataract emulsification efficiency using OZil® Intelligent Phaco and the new INTREPID® Balanced Tip design.

Applied Integration™

Designed to work seamlessly with other Alcon technologies for an integrated cataract procedure experience.

Learn more about the new era of cataract procedures. Visit MyAlcon.com.

Alcon®
a Novartis company

CENTURION®
VISION SYSTEM

For important safety information, please see adjacent page.

Plasma blade rivals femtosecond laser

Tool offers advantages, adjunctive uses, cost effectiveness for capsulotomy creation

By Cheryl Guttman Krader; *Reviewed by Richard J. Fugo, MD, PhD*

NORRISTOWN, PA ::

THOUGH A PLASMA ablation incising device (Fugo Plasma Blade, MediSURG Research & Management Corp.) and femtosecond laser are fraternal technologies with enormous synergistic capabilities for use in cataract surgery, they are distinctly different, said Richard J. Fugo, MD, PhD.

Dr. Fugo

"Both . . . allow surgeons to create a perfectly round capsulotomy, but each has its own advantages and additional applications," said Dr. Fugo, chief executive officer, MediSurg, Norristown, PA. "Surgeons should recognize that the (blade) represents not only an alternative tool for creating a precise capsulotomy, but offers the ability to salvage femtosecond procedures that have not gone as planned."

Dr. Fugo is the ophthalmologist-inventor of the plasma blade.

Both devices, he said, create capsulotomy by plasma ablation. For example, transferred energy shatters the molecular lattice structure of the capsule and causes transient formation of a microscopic plasma in the tissue. In fact, the FDA used the plasma blade as the predicate unit to approve femtosecond lasers for capsulotomy.

DIFFERENCES

However, the plasma blade create s a "postage-stamp capsulotomy" in which the rim is characterized by a series of wavelets, Dr. Fugo said, whereas the femtosecond laser creates a smooth-edged capsulotomy.

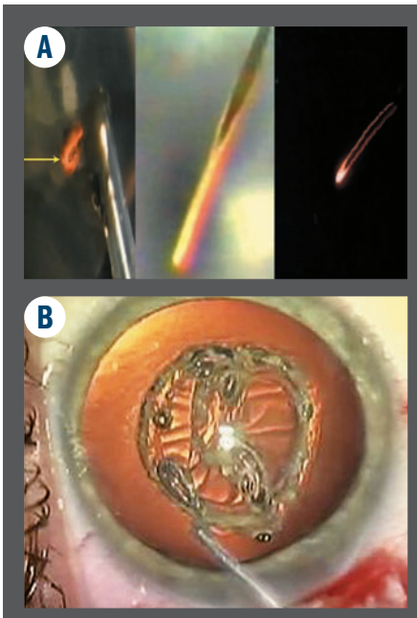
"As noted in research1 performed by the late David Apple, MD, the postage-stamp rim geometry is desirable for its strength and stability that make it resistant to radial tears," Dr. Fugo said.

Also in contrast to the femtosecond laser, the plasma blade can be used to perform capsulotomy easily, even with a highly fibrotic capsule and regardless of pupil size.

"Using the femtosecond laser, the capsulotomy diameter can be no larger than 2 mm less than the pupil diameter," Dr. Fugo said. "For example, if the pupil enlarges only to 6 mm, the largest possible capsulotomy is only 4 mm."

Since plasma blade capsulotomy is performed after entering the eye, surgeons can first enlarge non-dilating pupils using various stretching techniques or devices. However, it can also be done without performing any of those maneuvers, he said, as the surgeon can simply slip the handheld probe's ultrathin cutting filament under the iris.

"I find that I perform capsulotomy by ablating under the iris in about 40% of cases," Dr. Fugo said. "The cutting filament is not within the surgeon's view with this technique, but it can be easily done by any surgeon who has used the (plasma blade) to perform about 20 standard capsulotomies."



A High magnification of the activated Fugo plasma blade ablation filament with three image filter levels.

B A 10-second completed Fugo plasma blade capsulotomy: the Fugo blade thin probe enters through the keratome incision inferiorly and is connected to a handpiece held by the surgeon. *(Images courtesy of Richard J. Fugo, MD, PhD)*

Since capsulotomy using the plasma blade is created during the main surgical procedure after the keratome incision is made, surgeons can also easily revise the capsulotomy size or shape. The device can also be used to perform a primary posterior capsulotomy, like what is done in pediatric eyes.

The plasma blade also offers a tool for salvaging cases where anterior capsule rim tears or posterior capsule tears develop.

In these situations, the device is used to ablate plasma quickly and safely around the entire capsule tear. It can also be used to ablate

Continues on page 23 : ***Plasma blade***

PLASMA BLADE

(Continued from page 22)

safely and complete an incomplete femtosecond laser-created capsulotomy, as well as enlarge or modify the shape of a femtosecond capsulotomy.

"Even if the surgeon must turn to the (plasma blade) in one in 20 cases where the femtosecond laser was used for capsulotomy, it represents a valuable parachute that will allow the surgeon to face the patient with a smile rather than with bad news," Dr. Fugo said.

"Therefore, it has positive implications for the surgeon's emotional well-being, as well as possible medicolegal ramifications," Dr. Fugo continued.

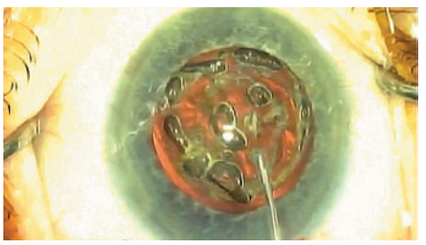
Both the plasma blade and femtosecond laser offer versatility, but their capabilities differ, and there are obvious differences between them in affordability and physical features. Femtosecond lasers have other applications for cataract surgery—and some platforms can be used to make a LASIK flap or for other corneal applications—whereas the plasma blade also has FDA approvals for peripheral iridotomy and glaucoma filtering surgery.

In contrast to femtosecond lasers that have a fixed-floor console powered by AC wall current and cost hundreds of thousands of dollars, the plasma blade is a portable device that weighs only around 5 lbs., runs on "C" cell flashlight batteries, and sells for less than $25,000. ■

Reference

- Izak AM, Werner L, Pandey SK, Apple DJ, Izak MGJ. Analysis of the capsule edge after Fugo plasma blade capsulotomy, continuous curvilinear capsulorhexis, and can-opener capsulotomy. *J Cataract Refract Surg.* 2004;30:2606–2261.

BENEFITS OF PLASMA BLADE



VIDEO To learn more about some of the advantages associated with use of the Fugo plasma blade in cataract surgery, especially when used in conjunction with the femtosecond laser, go to **http://bit.ly/GzKsNU.**
(Video courtesy of Richard J. Fugo, MD, PhD)

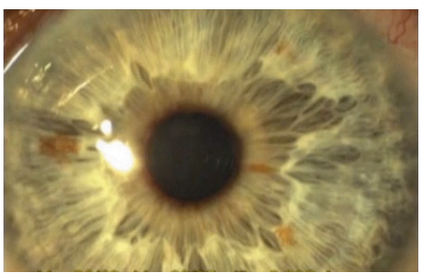
RICHARD J. FUGO, MD, PHD
E: *medisurgltd@yahoo.com*
Dr. Fugo has a financial interest in the subject matter.

REVERSED TO 20/20

(Continued from page 19)

Given her real and stable refractive error of +6.00 sphere and the previous YAG PC opening by her surgeon—excluding IOL exchange as an option—I planned for a piggyback IOL on top of her previously implanted lens. Through the patient's previous incision, I implanted a piggyback lens (AQ2010V, STAAR Surgical) of 9 D with a simultaneous surgical iridectomy. This resulted in 20/20 vision at distance and near, with a residual refractive error of –0.50 –0.50 × 002.

REVERSING BACK TO 20/20



VIDEO To view more on this case study about multifocal lens nightmare reversal, go to **http://bit.ly/1aIILHC.**
(Video courtesy of Arun C. Gulani, MD)

IN THE END ZONE

In this case, since the patient's strength was normal, we needed to peel off the scar with simultaneous laser refractive ablation (PRK not phototherapeutic keratectomy) in order to measure her actual refractive error.

The presence of refractive error is a play of her corneal scar. Once we have the true refractive error, we can accurately correct it.

My advice in complex cases, such as this, is: Do not give it a complex name that will scare you or the patient into planning for a mediocre outcome.

Break it down into an optical challenge with a vision goal and use surgical technique and technology as a means to get there.

The road map is provided by the 5S system, which results in the patient and you mutually enjoying the journey to their BVP.

This patient—who was very angry with her surgeon and also mentally depressed with her poor vision—is now delighted with her outcomes. She remembers only two, staged, very brief, topical procedures resulting in her vision recovery to 20/20.

We maintained all principles of Corneoplastique surgery in that the procedures selected were topical, brief, aesthetically pleasing, and visually promising. Also, had they not worked, she could still have a corneal transplant/lens exchange.

Today, this patient is 6 years' postoperative and continues to enjoy her vision at distance and near. ■

References

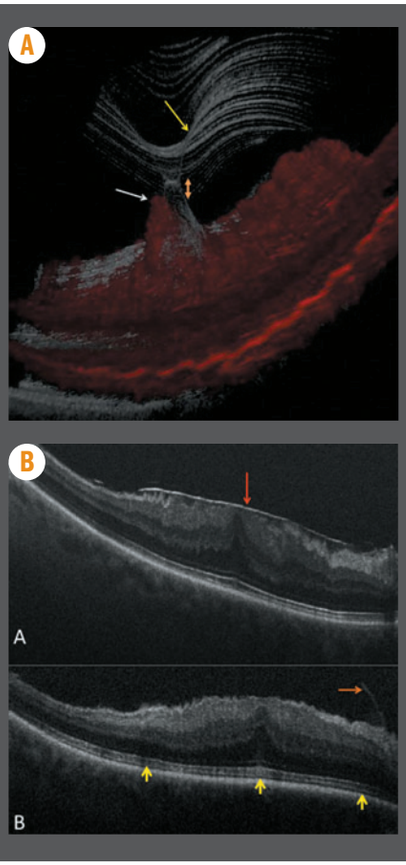
- Gulani AC. Shaping the future and reshaping the past: The art of vision surgery. In: Afshari N, Copeland R, eds. Textbook of Cornea and Refractive Surgery. 1st ed. J.P. Publishers; 2013:1252-1273.
- Bansal J, Gulani AC. Excimer laser enhancements after multifocal IOLs. In: Hovanesian J, ed. Textbook of Premium Cataract Surgery: A Step By Step Guide. 1st ed. Thorofare, NJ: Slack Inc.; 2012:135-145.
- Donnenfeld E, Gulani AC. Femtosecond laser for astigmatism correction during cataract surgery. J.P. Publishers; 2012:155-161;21.
- Gulani AC. Using excimer laser PRK—not PTK—for corneal scars: Straight to 20/20 vision. *Advanced Ocular Care.* 2012(Sept/Oct); Volume:1-3.
- Gulani AC. Algorithm addresses corneal scarring. Ophthalmology Times. Nov. 30, 2011. *http://ophthalmologytimes.modernmedicine.com/ophthalmologytimes/news/modernmedicine/modern-medicine-news/algorithm-addresses-corneal-scarring.* Accessed Sept. 25, 2013.
- Gulani AC. Pentacam technology in LASIK. *Corneal Refractive Surgery in Video Atlas of Ophthalmic Surgery.* XVII. (2). 2008.
- Gulani AC. Corneoplastique. *Video Journal of Ophthalmology.* III. 2007.
- Gulani AC. Principles of surgical treatment of irregular astigmatism in unstable corneas. Text book of irregular astigmatisum. Diagnosis and treatment. Thorofare, NJ. Slack Inc., 2007:251-261.
- Gulani AC. Corneoplastique. Techniques in ophthalmology. 5(1);11-20:2007.
- Gulani AC. Corneoplastique. *Video Journal of Cataract and Refractive Surgery.* XXII. Issue 3, 2006.

ARUN C. GULANI, MD, *is founder and chief surgeon of the Gulani Vision Institute, Jacksonville, FL. He has no financial disclosures relevant to the subject matter.*

PIONEERING EFFORTS

Intraoperative OCT useful tool during vitreoretinal surgery, according to new study

By Michelle Dalton, ELS; *Reviewed by Justis P. Ehlers, MD*



A Three-dimensional reconstruction of vitreomacular traction intraoperative OCT scan revealing the configuration immediately prior to lifting the hyaloid (gray) and immediately after removing the hyaloid (red overlay). Prominent foveal traction is noted with vitreous traction (yellow arrow). Following release of traction there is decrease in central foveal thickness (orange arrow) and continuity of the inner retinal contour (white).

B Intraoperative OCT showing prominent epiretinal membrane prior to peeling (red arrow). Following membrane peeling expansion of the IS/OS (i.e., ellipsoid zone) to retinal pigment epithelial distance is noted with increased subretinal hyporeflectivity (yellow arrows). Residual membrane is noted at the optic nerve head (orange). *(Images courtesy of Justis P. Ehlers, MD)*

CLEVELAND ::

Optical coherence tomography (OCT) can be successfully used during vitreoretinal surgery and can provide significant information about various milestones throughout the surgery, said Justis P. Ehlers, MD.

"Anatomic visualization with intraoperative OCT (iOCT) provides live feedback to the surgeon," said Dr. Ehlers, assistant professor, Vitreoretinal Service, Cole Eye Institute, Cleveland Clinic. "It's a unique opportunity to understand the underlying pathophysiology of surgical ophthalmic diseases."

The Prospective Intraoperative and Perioperative Ophthalmic ImagiNg with Optical CoherEncE TomogRaphy (PIONEER) Study prospectively enrolled 394 eyes of patients undergoing ophthalmic surgery to assess its feasibility and use in anterior and vitreoretinal surgery, Dr. Ehlers said.

Of those 394 eyes, 196 were vitreoretinal surgeries, most of which were for macular surgical diseases.

Over the course of the first 18 months of the ongoing study, six vitreoretinal surgeons and five anterior segment surgeons used a microscope-mounted portable spectral-domain OCT probe (Envisu SDOIS, Bioptigen) to acquire images during the surgeries.

Most eyes (n = 149; 76%) were pseudophakic; 40 eyes (20%) were phakic and seven eyes (4%) were aphakic.

In the vitreoretinal arm of the study, epiretinal membrane and full thickness macular hole were the most frequent indications with 73 eyes (37%) and 42 eyes (21%), respectively.

Other diagnoses included retinal detachment and proliferative diabetic retinopathy/traction retinal detachment (31 and 27 eyes, respectively). The remaining eyes underwent surgery for vitreomacular traction, vitreous hemorrhage, subretinal hemorrhage, and endophthalmitis.

Successful iOCT imaging was obtained in 188 eyes (96%), and added anywhere from 65 seconds to 4 minutes to the procedure.

"Using the microscope-mounted system, the surgeon would stop surgery, position the device for aiming, and acquire the image," Dr. Ehlers said. "In the future, utilizing a microscope integrated system, the surgeon could potentially image without even stopping the surgery."

The investigators obtained multiple images at each session, typically requiring about 65 seconds to position, aim, and acquire the first image. Although adverse events occurred during the various surgeries (e.g., elevated IOP), none was determined to be specifically related to the OCT scan acquisition, Dr. Ehlers said.

REAL-WORLD FEEDBACK

Using a surgeon feedback questionnaire, it was determined that if the surgeon was unsure whether membrane peeling was complete, iOCT gave the definitive answer in 97% of cases, Dr. Ehlers said.

In cases where surgeons believed the surgical objectives were achieved and membrane peeling was complete, iOCT revealed residual membranes that the surgeons determined required peeling due to foveal proximity in 8% of cases, he said.

Novel findings included:

- **Subclinical alterations in the foveal architecture.**
- **Increased subretinal hyporeflectivity following ILM peeling.**
- **Focal architectural changes at the surgical manipulation site.**

Analysis of the iOCT images showed significant expansion in the subretinal hyporeflective band following membrane peeling,

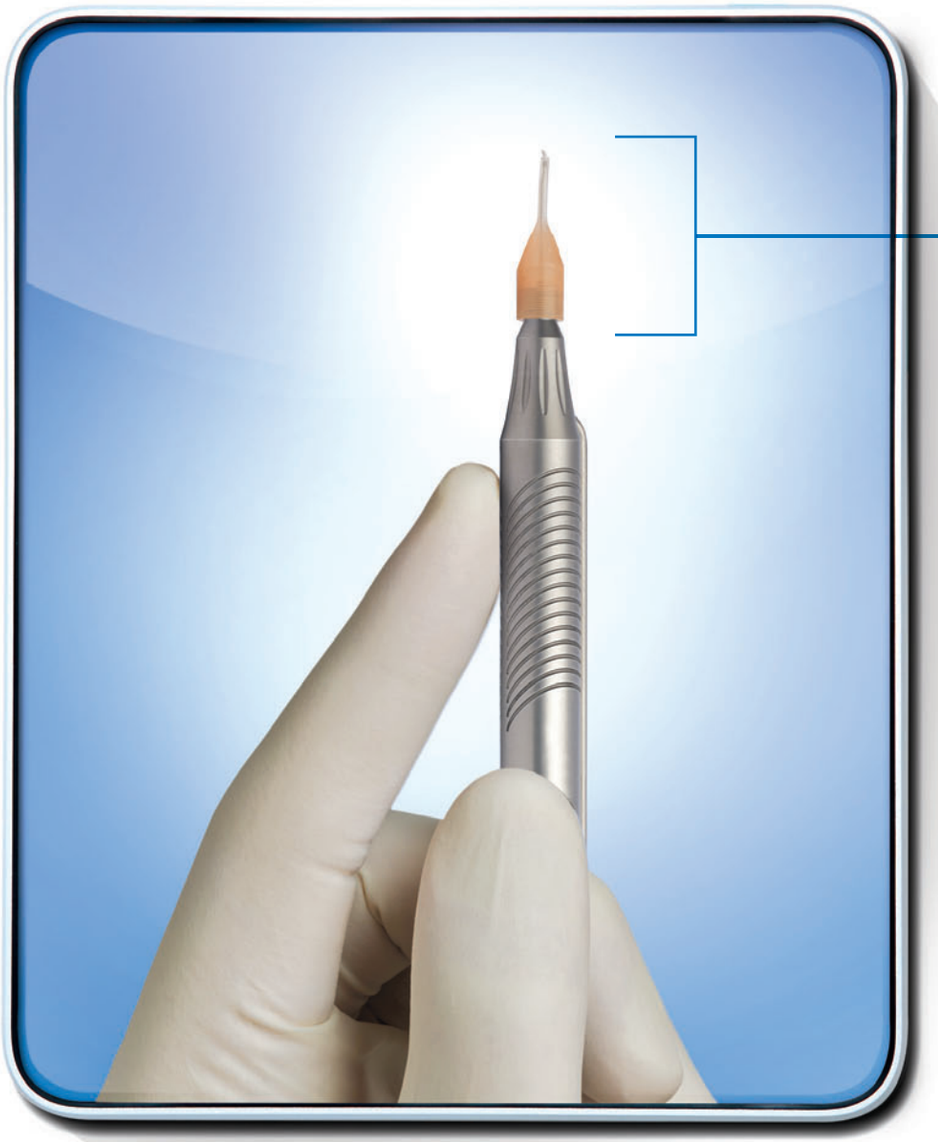
Continues on page 28 : ***Pioneer***

DO YOU PREFER

THERMAL PROTECTION

— OR —

PHACO PERFORMANCE?



Protect your procedures with INTREPID® Tips and Sleeves.

YES.

Experience uncompromising cataract micro procedure performance with phaco tips engineered to enhance OZil® technology, improve surgical efficiency and increase protection.[1,2] Combine with INTREPID® Ultra and Nano Infusion Sleeves for a superior thermal safety profile.[1]

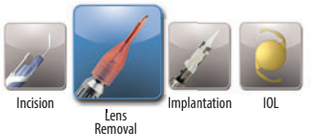
To learn more about INTREPID® Tips and Sleeves as part of the comprehensive INTREPID® System, contact your local Alcon representative.

1. Jun B. Thermal study of longitudinal and torsional ultrasound phacoemulsification: tracking the temperature of the corneal surface, incision, and handpiece. *J Cataract Refract Surg*. 2010;36(5):832-837.
2. Davison J. Cumulative tip travel and implied followability of longitudinal and torsional phacoemulsification. *J Cataract Refract Surg*. June 2008;34.

Alcon®

a Novartis company

Do more through less.™



INTREPID® micro-coaxial system

For important safety information, please see adjacent page.

Determining ocriplasmin success

Certain attributes of patients lead to better results when using new therapy, study shows

By Michelle Dalton, ELS; *Reviewed by Tarek S. Hassan, MD*

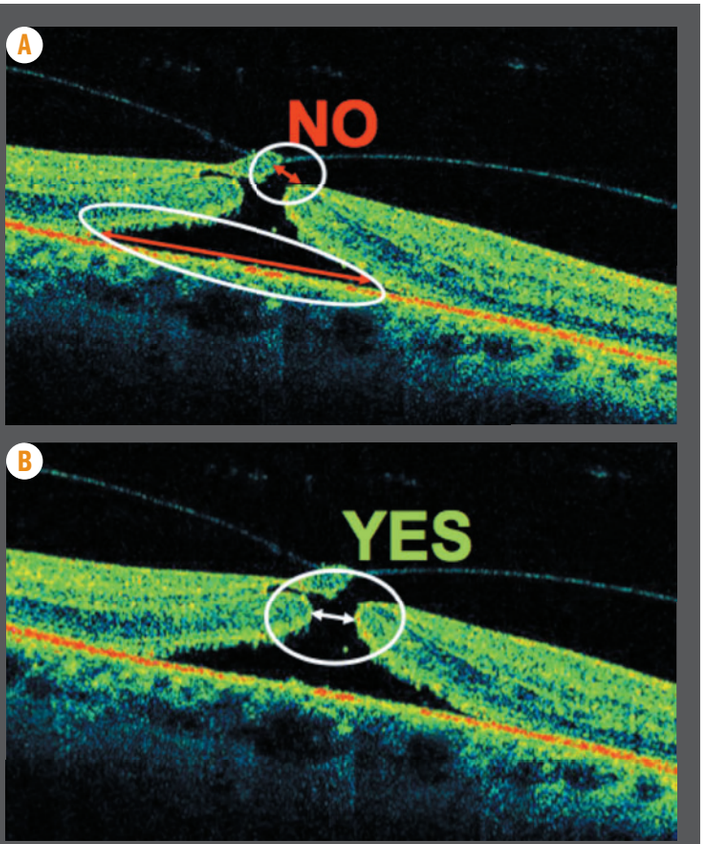
ROYAL OAK, MI ::

UNDERSTANDING THE pre-treatment characteristics of patients who have had successful outcomes following intravitreal injections of ocriplasmin for macular holes and vitreomacular adhesion (VMA) may ultimately lead to improved patient management, said Tarek S. Hassan, MD.

Dr. Hassan

Before last year's approval of ocriplasmin (Jetrea, ThromboGenics), the primary treatments for symptomatic VMA were either observation or vitrectomy with separation of the posterior hyaloid.

Enter ocriplasmin, a fibrinolytic enzyme which targets fibronectin, laminin, and collagen to induce both vitreous liquefaction and separation of the vitreous from the internal limiting membrane (PVD), said Dr. Hassan, professor of ophthalmology, Oakland University William Beaumont School of Medicine, and partner, Associated Retinal Consultants, Royal Oak, MI.



FTMH diameter: Positive predictor of macular hole closure

KEY MEASUREMENT: Smallest diameter at aperture of the hole, roughly parallel to the retinal pigment epithelium. *(Images courtesy of Tarek S. Hassan, MD)*

The Microplasmin for Intravitreous Injection-Traction Release without Surgical Treatment (MIVI-TRUST) studies randomly assigned patients to intravitreal injections of either ocriplasmin 125 µg or placebo in a 2:1 ratio (MIVI-006, United States only), or 3:1 (MIVI-007, Europe and United States) to evaluate the primary endpoint of pharmacologic VMA resolution at day 28.

Secondary endpoints included: the development of a total posterior vitreous detachment at day 28; nonsurgical closure of full thickness macular hole; visual acuity changes of more than 2 or 3 lines of visual acuity; need for vitrectomy; and improvement in the VFQ-25 assessment.

MIVI-006 enrolled 464 patients, MIVI-007 enrolled 188 patients.

"This was a large cohort study—652 eyes were treated with a single injection," Dr. Hassan said.

Overall, 26.5% of those treated with ocriplasmin had complete VMA resolution at day 28, compared with only 10.1% of those in the sham arm.

PREDICTIVE BASELINE FEATURES

The investigators then looked at baseline features that might be

Continues on page 28 : ***VMA therapy***

DO YOU PREFER

EXTREMELY SMOOTH

OR

EXTREMELY SAFE?*

YES.

Part of the INTREPID® System, single-use polymer I/A handpieces and tips deliver a smooth surface for IOL repositioning and rotation. Plus, unique non-metal I/A tip technology is designed to eliminate sharp edges for added safety and assurance.*

To learn more about the uncompromising cataract micro performance of INTREPID® Polymer I/A Handpieces and Tips, talk to your local Alcon representative.

Experience smooth procedures with INTREPID® Polymer I/A Handpieces and Tips.

*Non-metal I/A material compared to metal I/A material.

Alcon®

a Novartis company

Do more through less.™

INTREPID® micro-coaxial system

For important safety information, please see adjacent page.

VMA THERAPY

(Continued from page 26)

predictive of pharmacologic resolution, he said.

Non-ocular characteristics analyzed included: age, gender, race, body mass index, and expected need for vitrectomy.

The ocular characteristics included: size of the full thickness macular hole, VMA diameter, lens status, epiretinal membrane, diabetic retinopathy, and best-corrected visual acuity.

"What we found was that patients in younger age groups had a higher rate of improvement," Dr. Hassan said.

A total of 47.5% of patients in the ocriplasmin group who were under 65 years old (n = 80) had complete VMA resolution at day 28, compared with 29% in the 65-to-75-year-old group (n = 207) and 14.1% in the 75-plus-year-old group (n = 177).

Those rates of resolution were at least double—and in the oldest group, almost triple—the rates of resolution in the placebo group.

If the VMA diameter was under 1,500 µm (n = 314), 34.7% achieved VMA resolution at day 28.

Similarly, 37.4% of those without epiretinal membrane in the ocriplasmin arm had VMA resolution at day 28, compared with only 14.3% of the placebo group.

take-home

- **A new agent aimed at treating symptomatic vitreomacular adhesion may lead to variable outcomes based on several pre-treatment patient characteristics.**

For the 106 patients with a full thickness macular hole of 400 µm and VMA at baseline, 50% achieved full resolution at day 28, compared with 25.5% of those in the placebo group (n = 47).

"We need to continue to assess these parameters as we seek to further determine how we can gain the most success using ocriplasmin treatment," he said.

Dr. Hassan noted that it was important to identify holes with a diameter of 400 µm or less by taking the measurement at the smallest diameter at the aperture of the hole that is parallel to the retinal pigment epithelium, and not at the top (most anterior aspect) or bottom (most posterior aspect) of the hole.

Baseline diameter was "a positive predictor of macular hole closure," he said.

If the baseline full thickness macular hole was no more than 400 µm, 48.8% of those in the ocriplasmin group (n = 86) had pharmacologic closure at month 6. This was compared with 18.2% of the 44 patients in the placebo group.

Overall, phakic patients fared better than pseudophakes as 34.2% of phakic eyes in the ocriplasmin arm achieved VMA resolution at day 28, compared with 13.4% of pseudophakic eyes following ocriplasmin injection.

We hope to more fully determine which patients would be most likely to benefit from ocriplasmin treatment by assessing combinations of independent baseline factors that can be correlated, he said.

"Short of being able to use a crystal ball, we don't know for certain which patients will benefit," Dr. Hassan said. "These subgroup analyses, however, are getting us one step closer to gaining such an understanding." ■

TAREK S. HASSAN, MD

P: *248/288-2280*

Dr. Hassan is a consultant and speaker for ThromboGenics but declares no financial interest in ocriplasmin.

PIONEER

(Continued from page 24)

suggesting increased distance between the ellipsoid zone (i.e., IS/OS junction) and the retinal pigment epithelium, Dr. Ehlers said.

The system utilized for PIONEER was a SD-OCT engine. Time-domain OCT has both quality and speed issues, making it of limited utility for the purposes of this study, he said.

"(However), swept source OCT may have a significant role in the future and we are actively looking at this in our research labs at the Ophthalmic Imaging Center at Cleveland Clinic and through a collaborative biomedical research partnership NIH grant with Duke University in partnership with Cynthia Toth, MD, and Joseph Izatt, PhD," Dr. Ehlers said.

"Swept source would provide an even better acquisition speed, as well as a much greater scan depth that allows for visualization, not only at the retinal surface but also in the vitreous," Dr. Ehlers said, "which may be particularly useful for intraoperative applications, such as visualizing instrument-tissue interactions."

PIONEER does have some limitations, he added. As it currently exists, the OCT system—though mounted on the microscope—is optically separate from the microscope, which does not allow for the visualization of the instrument-tissue interaction, he said.

"The Cole Eye iOCT research team, including Yuankai Tao, PhD, has developed an integrated system that is currently undergoing laboratory testing," he said. "(Clearly), more research is needed to delineate functional and anatomic correlates and surgical outcomes." ■

JUSTIS P. EHLERS, MD

P: *216/636-0183*

Dr. Ehlers receives royalties and has intellectual property rights with Bioptigen.

DO YOU PREFER

INNOVATIVE SOLUTIONS

— OR AN —

INTEGRATED SYSTEM?

The INTREPID® System puts integrated performance at your fingertips.

YES.

Accept no compromises. The INTREPID® System delivers a portfolio of proven tools that seamlessly work together, so you can pursue cataract micro surgery with confidence.

To learn more about the INTREPID® System, contact your Alcon representative.

Alcon®

a Novartis company

Do more through less.™

INTREPID® micro-coaxial system

For important safety information, please see adjacent page.

SMD therapy effective for CSC

Laser rivals low-fluence photodynamic therapy for central serous chorioretinopathy

By Roxanne Nelson; *Reviewed by Joan Giralt, MD*

BARCELONA, SPAIN :: **SUBTHRESHOLD DIODE MICROPULSE** (SDM) laser may be more effective than standard therapy for patients with chronic central serous chorioretinopathy (CSC), according to Joan Giralt, MD.

While still preliminary, data from a new study—authored by Dr. Giralt—has found that SDM is more effective, less expensive, and safer than low-fluence photodynamic therapy (PDT). It also has the therapeutic benefits of PDT without the iatrogenic damage.

PDT is thus far the only treatment in patients with chronic CSC that is very close to the fovea, said Dr. Giralt, Department of Ophthalmology, Hospital Clinic de Barcelona, Universidad de Barcelona, Spain.

"If it is away from the fovea, then it can be treated with the traditional laser," Dr. Giralt said. "PDT can damage the retinal epithelium."

CSC is characterized by leakage of fluid in the center of the retina, which, in turn, can lead to a blister or serous detachment in the macula. The result could be vision distortions and decreased visual acuity.

In the majority of acute cases, resolution is spontaneous. However, visual symptoms may persist despite resolution. For a small number of patients, it will develop into chronic CSC—which is arbitrarily defined by the presence of subretinal fluid for period that exceeds 3 months.

Chronic CSC can lead to significant visual impairment, and treatment options include: laser photocoagulation, PDT, antivascular endothelial growth factor treatment, acetazolamide, and finasteride.

Traditional laser therapy carries a risk of residual vision defects due to laser-induced scarring. PDT with verteporfin has been shown to be effective in chronic CSC by improving visual acuity and reducing subretinal fluid. Complications such as secondary choroidal neovascularization, persistent choriocapillaris hypoperfusion, and pigmentary retinal pigment epithelium changes in the areas treated have been reported, however.

take-home

- **Subthreshold diode micropulse laser seems to be a more economical, safer, and effective treatment of chronic central serous chorioretinopathy compared with low-fluence photodynamic therapy.**

ABOUT THE STUDY

Dr. Giralt and colleagues conducted a retrospective, comparative, interventional case series analysis of 36 eyes of 36 patients with chronic CSC.

None of the participants experienced a spontaneous resolution of neuroepithelial serous detachment, which was confirmed by optical coherence tomography (OCT) and fluorescein. All patients in the study had experienced the onset of their condition more than 6 months ago, and all underwent either SDM or PDT. Best-corrected visual acuity (BCVA) and OCT were evaluated before beginning treatment and during the clinic follow-up.

All of the patients in the SDM group received photocoagulation treatment that was performed with 810-nm infrared dioxide laser. For patients receiving PDT, verteporfin with half-fluence at a rate of 25J/cm^2, and an intensity of 300mW/cm^2 was delivered for 83 seconds to the area of choroidal hyperperfusion.

The authors evaluated 20 eyes in the SDM group and 16 eyes in the PDT group, and found that all of the patients had an anatomical and functional improvement after their treatment, except for two patients who had undergone PDT.

Among patients in the SDM group, average BCVA improvement was 0.39 ± 0.22 with a central foveal thickness decrease of 210.1 ± 77.6 µm. The re-treatment rate in this group was 0.45, and the clinical follow-up was 13.5 ± 6 months.

In the PDT group, the average BCVA improvement was 0.20 ± 0.30, and the central foveal thickness decrease was 102 ± 761µm. The re-treatment rate was 0.19, and the clinical follow-up period was 20.4 ± 14.2 months.

"There were no complications with the SMD treatment and the results were better," Dr. Giralt said. "SMD is available and should be considered for this complication."

Preliminary results show that SDM is the better option for this indication, Dr. Giralt said. Treatments for chronic CSC are still evolving, and more research is needed. ■

JOAN GIRALT, MD
E: *Jgiralt@clinic.ub.es*

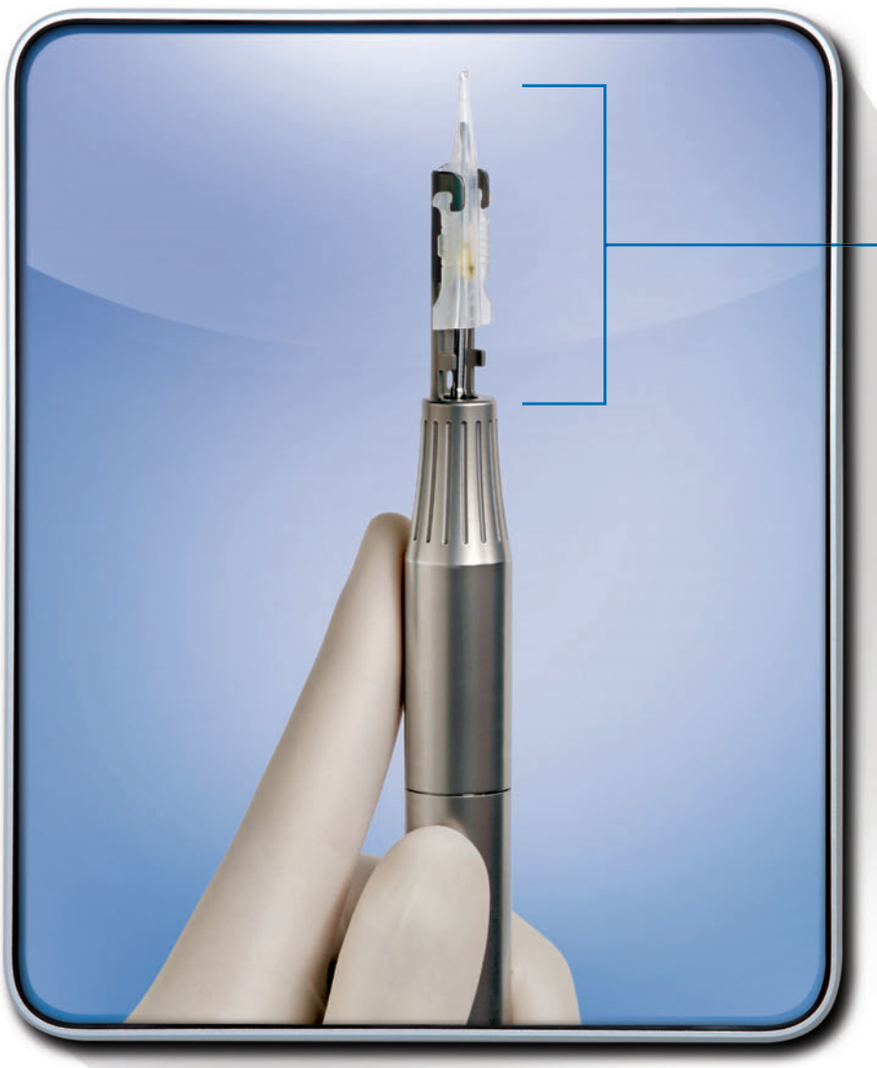
Dr. Giralt has no financial interest in the subject matter.

DO YOU PREFER

MORE CONTROL

— OR —

MORE CONSISTENCY?



Automated lens delivery with the INTREPID® AutoSert® IOL Injector.

YES.

Achieve smoother, more controlled IOL delivery for smaller incision sizes with the fully automated INTREPID® AutoSert® IOL Injector. An ideal solution for MICS procedures, the INTREPID® AutoSert® IOL Injector optimizes surgical control while helping to minimize wound disruption and trauma.

To learn how the INTREPID® AutoSert® IOL Injector can help improve your surgical outcomes, talk to your local Alcon representative.

1. Johansson, C. Comparison of Motorized IOL Insertion to Traditional Manual IOL Delivery. ASCRS Presentation, 2011.
2. Allen, D. Experience with Electro-Assisted IOL Injection Device. ASCRS Presentation, 2011.

Do more through less.™

INTREPID®
micro-coaxial system

Alcon®

a Novartis company

For important safety information, please see adjacent page.

Genetic testing shows promise in predicting AMD progression

Clinicians may be able to use genetic testing in conjunction with a phenotypic evaluation

By Michelle Dalton, ELS; *Reviewed by Lawrence J. Singerman, MD, FACS, FICS*

CLEVELAND ::

COMBINING BOTH GENETIC testing and phenotypic evaluations in patients with drusen can more accurately determine which patients are likely to develop advanced age-related macular degeneration (AMD), said Lawrence J. Singerman, MD, FACS, FICS.


Dr. Singerman

"Most patients are referred to us too late, after their AMD has progressed," said Dr. Singerman, founder of Retina Associates of Cleveland.

"We know from many years' experience that over half of patients with AMD are referred to retinal specialists for evaluation when their first eye has vision of 20/70 or worse," he said. "We now know that we can preserve much better vision in over 90% of patients when we see them early enough."

The earlier that primary eyecare physicians can identify and refer patients who are at a high risk for developing advanced AMD, the more likely AMD-related vision loss can be minimized, Dr. Singerman said.

In addition to genetic testing, Dr. Singerman said he evaluates the back of the eye for the phenotype of characteristics for AMD.

"Genetic testing in no way replaces phenotypic examination of the eyes," he said. "We learned many years ago—in large part based on studies from another NEI-sponsored study, the Macular Photocoagulation Study—that patients with larger drusen, confluent drusen, and pigmentary disturbance have a higher risk of progression from early to late stage AMD."

Other, more recent studies have identified other variables associated with increased risk, he said, including:

- **Patient age at presentation.**
- **Smoking history.**
- **Body mass in addition to genetic risk factors.**

take-home

New study results show using genetic testing and phenotypic evaluations together in patients with drusen can increase the likelihood of determining who may develop advanced AMD.

CHANGING PERSPECTIVES

Genetic testing is still somewhat controversial, Dr. Singerman said.

As recently as November 2012, the American Academy of Ophthalmology discouraged genetic testing for AMD.

"There's still some controversy about genetic testing, but it's decreasing," Dr. Singerman said.

With a current treatment burden on both physicians and patients, Dr. Singerman said it is important to decide which patients need to be seen every 3 months and which patients can be seen once a year.

The current genetic testing is divided into five risk categories. Based on where a patient falls on the five-point scale, "we're doing a better job of deciding how often to see a patient than we can do with just a phenotypic evaluation alone," he said.

Also, using a combination will further the emphasis on personalized medicine, Dr. Singerman added.

For instance, others have shown the combination of retinal phenotype and genetics yielded an area under the ROC curve for 5-year and 10-year risk of 0.80 and 0.82, respectively, he said, which indicate the superiority of a combination of clinical and genetic data in risk prediction.[1]

HIGH PROGRESSION RATE

The genetic component in macular degeneration appears to be much stronger than it is in many other diseases, Dr. Singerman said.

"What we're just bringing out now is that in macular degeneration, the genetic testing has a good correlation with the outcomes," he explained. "Those with a higher

genetic risk develop more advanced disease earlier in life.

"We know from the Age-Related Eye Disease Study (AREDS) that we can reduce the risk of going from intermediate to late AMD by an average of 25%," Dr. Singerman added, which thus led to further investigation into genetic components in the AREDS population.

A recent study found specific vitamins and minerals are more likely to reduce the likelihood of progression in people with specific genetic components. Some are more likely to benefit from the complete AREDS formulation, whereas other are more likely to benefit from vitamins alone or zinc alone.[2]

'Genetic testing can help retinal specialists personalize their recommendations for vitamins and minerals.' — *Lawrence J. Singerman, MD, FACS, FICS*

Those authors estimated using the genotype-directed therapy that the pharmacogenetic analysis (Vita Risk, ArcticDx) provides would have more than doubled the reduction in AMD progression rates for a subset of 995 patients who took AREDS formula supplements to help prevent the progression to advanced AMD.[2]

"I believe that the value of genetic testing is greatly supported by this paper, and that, over time, these results are likely to minimize controversy and increase the number of ophthalmologists who will find it helpful for their patients," Dr. Singerman said. "Genetic testing can help retinal specialists personalize their recommendations for vitamins and minerals so that we're likely to reduce progression to advanced AMD in a higher percentage of patients than when we offer the AREDS formulation to all patients with intermediate AMD." ■

References

1. Yu Y, Reynolds R, Rosner B, Daly MJ, Seddon JM. Prospective assessment of genetic effects on progression to different stages of age-related macular degeneration using multistate Markov models. Invest *Ophthalmol Vis Sci.* 2012;53:1548-1556.
2. Awh CC, Lane AM, Hawken S, Zanke B, Kim IK. CFH and ARMS2 genetic polymorphisms predict response to antioxidants and zinc in patients with age-related macular degeneration. *Ophthalmology.* 2013 Aug 20. pii: S0161-6420(13)00679-9. doi:10.1016/j.ophtha.2013.07.039. [Epub ahead of print]

LAWRENCE J. SINGERMAN, MD, FACS, FICS
P: *216/831-5700*
Dr. Singerman is a member of the advisory board of ArcticDx and receives honoraria and stock options.

Understanding genetic risk factors for AMD

Ocular tissue research may help explain why some eyes are more susceptible to disease

Eye on Research **By Robert F. Mullins, MS, PhD,** *Special to* Ophthalmology Times

TAKE-HOME

- ***A better understanding of how genetic risk factors influence the trajectory of age-related macular degeneration may be key to solving the puzzles of this disease. Ocular tissue research may play a role in that process.***

The clinical community now has some very effective anti-vascular endothelial growth factor drugs for managing neovascular membranes in age-related macular degeneration (AMD).

However, there is little recourse for patients with geographic atrophy—in part because we do not yet understand what causes retinal cells to become damaged and die in the dry form of AMD.

Ideally, not only would we like to be able to treat both forms of AMD, but also to intervene earlier in the disease, before there is irreparable damage.

A better understanding of how genetic risk factors influence the trajectory of AMD may be key to solving the puzzles of this disease.

Already, many millions of dollars have been spent in identifying genetic risks for AMD, and with some very positive results.

We now have a long list of genetic variations associated with AMD.

However, little is known about how these polymorphisms or mutations increase risk or how they might affect disease severity or progression.

My laboratory is exploring how genetic variations might predispose the choriocapillaris endothelial cells to become abnormally activated in wet AMD or damaged in dry AMD, in order to determine how we can arrest these processes.

We have been able to study many of these genetic variations in mice. However, one of the major risk factors for AMD is a haplotype on chromosome 10q that includes the ARMS2 gene.

This interesting gene, unfortunately, has no ortholog outside primates.

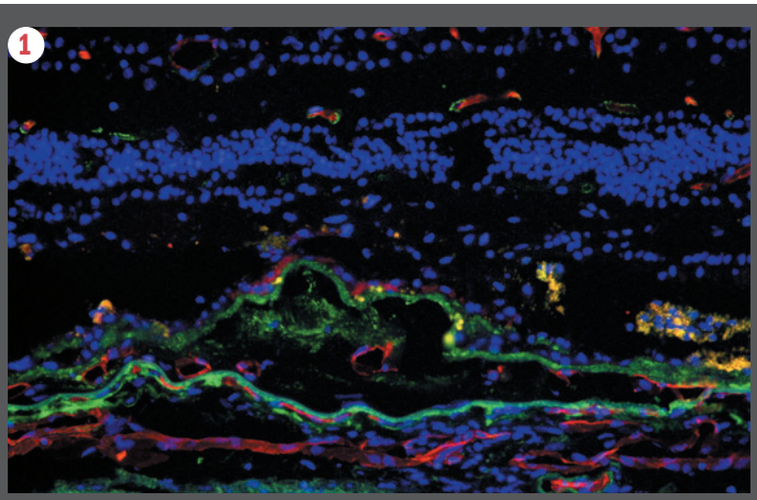
To study the biochemistry of ARMS2—that is, how the ARMS2 risk factor changes the behavior of cells and expression of genes in the macula—we need to analyze cellular proteins and ribonucleic acid (RNA) from human retinal tissue.

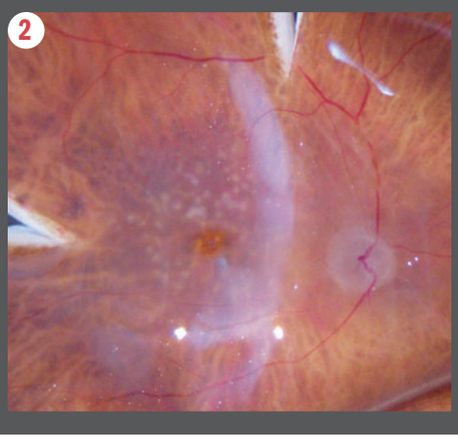
Unlike DNA—which is extremely stable and can be taken from Neanderthal bones or 4,000-year-old mummies—RNA survives only for a few hours after death, so it is challenging to study. Once obtained, though, we can use commercially available chips or deep sequencing to study the expression of 25,000 genes relatively easily all at once.

> ‘We need to analyze cellular proteins and ribonucleic acid from human retinal tissue.’
>
> — Robert F. Mullins, MS, PhD

AMD AND THE COMPLEMENT SYSTEM

We know that genetic variations in the complement factor H (CFH) gene are associated with an elevated risk of early AMD, geographic atrophy, and choroidal neovascularization (Figure 1 on Page 35).





(Figure 1) Immunofluorescence analysis of an eye with neovascular age-related macular degeneration shows abnormal blood vessels (red) that have invaded Bruch's membrane. Green fluorescence shows the distribution of complement complexes in this histology sample.

(Figure 2) Gross photo of a human eye prior to genotyping and histology preparation. *(Images courtesy of Robert F. Mullins, MS, PhD)*

The complement system is protective in humans—it helps kill harmful fungi and microbes and prepare them for removal—but when it goes awry it can quickly overwhelm and damage "bystander" cells.

Data from human genetics, histopathology, and animal models have long suggested a major role for the complement system in the development of AMD.

CFH itself is an inhibitor that works to keep the complement system in check. What we suspect is that in eyes with a polymorphism that prevents CFH from functioning correctly, the complement system starts destroying retinal cells.

In seeking to figure out where to intervene in the complement pathway, we have been studying the membrane attack complex (MAC).

The MAC is a funnel-shaped, cell-perforating complex of proteins. In aging human eyes, the MAC is deposited around the choriocapillaris (Figure 1).

Most of it is in the choroid[1] and there is more MAC in the macular region of the retina than in the extramacular regions.[2] We sought to determine whether eyes from donors with the high-risk genotype—with two copies of the AMD-associated polymorphism—exhibited altered levels of MAC in the choroid compared with eyes with a low-risk genotype.

To accomplish this, proteins were extracted from the retinal pigment epithelium (RPE) and choroid of 18 donors (10 low-risk and 8 high-risk) and levels of MAC were assessed.

We found that MAC levels were 69% higher in the high-risk eyes than in the low-risk eyes ($p < 0.05$), independent of whether the eyes showed signs of early AMD.[3]

This is evidence that high-risk CFH genotypes may affect AMD risk by increased deposition of MAC around the aging choriocapillaris, thereby leading to increased injury and death of choriocapillaris endothelial cells.

Research into the complement system represents just one of the ways that human donor eyes can be used to make new discoveries about retinal cell biology. The hope is that donor tissue can also be used to help translate cell biology findings into new therapeutic approaches.

For example, if complement genes—or some other factor that we have yet to

Continues on page 37 : ***Risk factors***

How wavefront aberrometry can help improve toric IOL outcomes

Access to technology among practitioners may change standard of care for astigmatism

By Fred Gebhart; *Reviewed by Robert J. Cionni, MD*

TAKE-HOME

- ***Using wavefront technology in place of conventional corneal measurements and nomograms for selection and placement of toric IOLs can improve patient outcomes.***

SALT LAKE CITY ::
CLINICIANS CAN IMPROVE postoperative outcomes for patients with astigmatism who receive toric IOLs by adding a wavefront aberrometer to the standard operative workflow.


Dr. Cionni

"We clearly get better results using an intraoperative wavefront aberrometer—more accurate results—compared [with] conventional techniques for toric IOL selection and placement," said Robert J. Cionni, MD, medical director, The Eye Institute of Utah and adjunct clinical professor, at The University of Utah Moran Eye Center, Salt Lake City.

"Indeed, I no longer will implant a toric IOL without guidance from an aberrometer," Dr. Cionni continued. "Up until the introduction of aberrometry, we typically have utilized calculations and nomograms that point us to the best result for the average of a group of patients. Now, by utilizing aberrometry, we can determine the best answer for each individual patient."

OUTCOMES COULD BE IMPROVED

Results of a recent study do not yet change the standard of care for toric IOL implants, Dr. Cionni noted.

However, the data offer clear evidence that outcomes achieved using conventional techniques can be significantly improved.

The study looked at 65 eyes that had at least 1.5 D of preoperative keratometric astigmatism. All of the patients were scheduled for cataract surgery with the implantation of a toric IOL. The initial cylinder power was selected based on standard measurements of anterior corneal curvature and a standard toric IOL nomogram. The steep axis was marked prior to surgery in keeping with standard procedures.

After phaco, the aphakic refraction was measured (ORA System, WaveTec Vision). The aberrometer was used to verify the magnitude and axis of refractive astigmatism and to determine the optimal cylinder power and axis for the lens to be implanted.

After the final lens selection, the diagnostic system was used for pseudophakic measurements and the IOL was rotated to the optimal axis using the device as a guide for final placement. A final measurement was taken to confirm correct positioning.

For most patients, 36 eyes (55%), ORA recommended a cylinder power other than the power calculated using standard methods. ORA recommended a decrease in power for 27 eyes and an increase for 9 eyes.

"Usually these changes were just one magnitude power difference, representing 0.75 D," Dr. Cionni said. "But in five cases there was a decrease of 2.25 D and another case with an increase of 2.25 D. If the aberrometer was right, these recommendations would mean the difference in having to do a second procedure because we had used the wrong implant the first time."

The difference, he explained, is that standard methodology is based on anterior corneal curvature.

Posterior curvature is poorly understood and not typically measured, nor are other potential sources of aberration.

CLOSER LOOK AT MEASUREMENTS

Comparing preoperative keratometric astigmatism with aphakic refractive astigmatism measured using the diagnostic device confirmed recent results presented by Doug Koch, MD—suggesting that traditional methods tend to underestimate against-the-rule astigmatism and overestimate with-the-rule astigmatism, Dr. Cionni continued.

Wavefront aberrometry is able to take into account posterior corneal curvature, which appears to average about 0.5 D different from anterior corneal curvature measurements.

Pre- and postoperative measurements confirm that aberrometry can improve outcomes.

The mean preoperative astigmatism was 2.01 D ± 1.04 D.

The mean postoperative refractive astigmatism was 0.33 D ± 0.35 D.

Though this was not a head-to-head comparison of conventional technique versus wavefront aberrometry, historical data on 244 eyes provide a useful comparison.

The mean ORA postoperative refractive astigmatism of 0.33 D compared with a postoperative mean of 0.55 D in historical controls. The average cylinder reduction for ORA patients was 84% compared with 62.4% reduction for historical data.

Just over half of ORA eyes (54%) had postoperative refractive astigmatism of 0.25 D or less. More than three-quarters of ORA eyes (78%) had 0.5 D or less postoperative refractive astigmatism compared with 62% of historical eyes.

Nearly all ORA eyes (98%) had 1 D or less of postoperative refractive astigmatism compared with 88% of historical eyes.

SEEKING A 'STANDARD OF CARE'

Many ophthalmologists who implant toric IOLs do not utilize a wavefront aberrometer, said Dr. Cionni, noting that the standard of care for astigmatism will not and cannot change until more practitioners have access to the technology.

"I truly believe that I would be doing my patients a disservice if I didn't use an aberrometer when placing a toric implant," Dr. Cionni said. "The bottom line is that when we looked at results using aberrometry-guided placement of toric implants compared [with] the historical method, the aberrometer was significantly better." ■

ROBERT J. CIONNI, MD
E: *rcionni@theeyeinstitute.com*
Dr. Cionni is a paid consultant for WaveTec Vision.

RISK FACTORS

(*Continued from page 35*)

identify—are always present at too high a level in eyes with early AMD, perhaps a drug that alters levels of that genetic factor can protect the cells.

ONGOING NEED FOR TISSUE

Another use for donor tissue lies in the area of therapeutic stem cell research.

We now understand that choroidal abnormalities—including choriocapillaris endothelial cell loss—occur very early in AMD, which suggests that the utility of injecting RPE stem cells on top of damaged or dead choroidal vascular cells may not be very high. Donor tissue will be needed to both guide the stem cell experiments in different disease states and to help us understand how to optimize delivery of stem cells so they do help to preserve vision.

Gathering donor tissue that is fresh enough and of high enough quality to be useful for research requires a tremendous and well-coordinated effort.

We have been fortunate to be able to work closely with the Iowa Eye Bank to collect more than 1,300 donor eyes since 2004. One of our lab members is always on pager duty so that tissue can be received and processed at any time of the day or night.

The donor eyes are photographed (Figure 2 on Page 35), dissected, and preserved in a standardized fashion to maximize their value to a range of scientists at the University of Iowa Institute for Vision Research studying AMD, glaucoma, diabetic retinopathy, and other conditions.

This is an unusual commitment, both from the eye bank and the university. Most eye banks around the country have not been as focused on providing research tissue within short death-to-preservation times, perhaps because end users have also not been as willing to accept tissue at inconvenient times.

With organizations—such as the Iowa Lions Eye Bank in Iowa City and the Lions Eye Institute for Transplant and Research in Tampa, FL, which says it dedicates about 40% of its tissue to research—we can make tremendous progress in understanding genetic risk factors for AMD.

The gift of ocular tissue is such a valuable one. It is very exciting that through the generosity of donors and their families, not only can we transplant corneas to help individuals see, but we also can conduct research that will one day help millions of people avoid vision loss from AMD. ■

About this series

EYE ON RESEARCH is a quarterly series of articles highlighting cutting-edge ophthalmic research with the potential to have a significant effect on vision and ocular health worldwide. The series is supported by the Lions Eye Institute for Transplant and Research Inc. (LEITR), a nonprofit organization dedicated to the recovery, evaluation, and distribution of eye tissue for transplantation, research, and education. Located in Tampa, FL, LEITR is the only combined eye bank and ocular research center in the world. LEITR provides fresh donor globes, corneas, lenses, trabecular meshwork, and other tissues from diseased and healthy human eyes, often within 4 to 6 hours of death, to researchers for immediate use in their own labs or in its onsite research facility. For more information, contact *info@LionsEyeInstitute.org* or visit *LionsEyeInstitute.org*.

References

1. Seth A, Cui J, To E, et al. Complement-associated deposits in the human retina. *Invest Ophthalmol Vis Sci*. 2008;49:743-750.
2. Hageman GS, Anderson DH, Johnson LV, et al. A common haplotype in the complement regulatory gene factor H (HF1/CFH) predisposes individuals to age-related macular degeneration. *Proc Natl Acad Sci USA*. 2005;102:7227-7232.
3. Mullins RF, Dewald AD, Streb LM, et al. Elevated membrane attack complex in human choroid with high-risk complement factor H genotypes. *Exp Eye Res*. 2011;93:565-567.

ROBERT F. MULLINS, MS, PHD, *is associate professor of ophthalmology and visual sciences, associate professor of molecular physiology and biophysics, and the Hansjoerg EJW Kolder, MD, PhD, Professor in Best Disease Research at the University of Iowa Carver College of Medicine and the University's Institute for Vision Research, Iowa City. Readers may contact Dr. Mullins at robert-mullins@uiowa.edu or 319/335-8222.*

Ethnic variations factor into OAG

Diagnosis may be improved by suitability of screening program to patient population

By Cheryl Guttman Krader

GUANGZHOU, CHINA ::

VARIOUS ISSUES IMPACT the effectiveness of population screening for open-angle glaucoma (OAG).

However, use of ethnicity-specific normative databases for structural tests may improve their diagnostic performance, said Mingguang He, MD, PhD.

"Available evidence indicates that [more than] 50% of OAG in industrialized countries is undetected," said Dr. He, deputy director and professor, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, Peoples Republic of China. "Identification of these people is a challenge and indicates the need for screening tests that are accurate, and reproducible."

Data from a study by Quigley et al. highlight the variation in OAG prevalence among different ethnic groups.

Age-specific prevalence of the disease was highest in Africa and Latin America, followed by China. The prevalence was similar in India, Japan, and Europe.

CONSIDERATIONS ON SCREENING METHOD

No one diagnostic test is considered a gold standard for OAG diagnosis.

Whereas optic disc stereo assessment for optic disc damage and standard automated perimetry to identify visual field loss represent the usual methods employed in clinical trials, the best criterion may be progressive change in the optic nerve, Dr. He said.

A number of structural tests exist for assessing the optic disc and retinal nerve fiber layer (RNFL), and there are also several methods to assess function.

Results of a study published in 2005 by Wollstein et al. evaluating the diagnostic efficacy of these different techniques and technologies indicated that optical coherence tomography was better than frequency-doubling technology (FDT) and scanning laser polarimetry followed by short-wave automated perimetry.

In a systematic review and meta-analysis of screening tests for detecting OAG, Mowatt et al. concluded FDT, oculokinetic perimetry, and scanning laser tomography were the most promising tests.

WEIGHING EFFICACY

The efficacy of a screening test must be considered in the context of population prevalence, he noted.

Assuming a test has 95% sensitivity and specificity—even in a population where the prevalence of glaucoma is relatively high, such as among older Africans and Latin Americans where the prevalence is about 5%—the test would still have a 50% false positive rate.

If used in a population where the prevalence of OAG is only 3% (e.g., Chinese), the false positive rate is 72%, and when the prevalence rate drops to 2%, as in older Japanese, European, and Indian cohorts, the false positive rate rises to 84%.

"These false positive rates represent the proportion of screened individuals who will be referred unnecessarily for health care," Dr. He said.

Further complicating the effectiveness of community screening is a high proportion of undiagnosed OAG in the population is mild disease. Distribution data on structural features show there is a lot of overlap between these individuals and the eyes of normal persons without glaucoma.

"Looking at RNFL thickness, for example, it is easy to differentiate eyes with advanced glaucoma from those that are 'super normal,' " Dr. He said. "However, it can be challenging to separate early glaucoma from normal eyes . . . (which) will result in a lot of false positives and false negatives."

The databases for some structural diagnostic platforms are also based on "normal" eyes defined using arbitrary criterion, but what is normal may differ in different ethnic groups.

However, after adjusting for the latter, there were no significant ethnicity-related differences for other disc parameters.

Dr. He said the latest generation of a retinal tomographer (Heidelberg Retina Tomograph III, Heidelberg Engineering) integrates data from various ethnic groups in its normative database and that research using this platform with the Moorfields regression analysis and glaucoma probability score found that it performed similarly in detecting glaucoma across different ethnicities. ■

MINGGUANG HE, MD, PHD
E: *mingguang_he@yahoo.com*
Dr. He has no financial interest in any of the products discussed.

Device upgrade eases refraction

Redesigned auto kerato-refractometer provides multiple enhancements, integration

New Product Focus **By Cheryl Guttman Krader**

OAKLAND, NJ ::

THE NEW KR-800 Auto Kerato-Refractometer (Topcon Medical Systems) builds on established technology with new features and an enhanced design that increases ease of use and office integration.

"This latest generation of auto refractors retains Topcon's proven rotary prism technology known to deliver dependably accurate keratometric and refraction measurements," said David Biggins, senior product manager–refraction, Topcon Medical Systems, Oakland, NJ.

"However, the system has been rebuilt into a smaller footprint with an improved user interface, a new motorized joystick mechanism, and expanded options for automated data transfer to electronic medical records (EMRs)," Biggins added.

The new KR-800 Auto Kerato-Refractometer is designed to increase ease of use and office integration. *(Image courtesy of Topcon Medical Systems)*

A new, 8.5-inch color touchscreen panel replaces the old black-and-white display found on previous Topcon auto kerato-refractometers. The new LCD screen provides the operator with a broader array of information as it fully displays the refractive and keratometry readings for both eyes and the number of measurements taken.

"The easy-to-read icons on the touchscreen display also give the operator improved control of the unit during the measurement process," Biggins said.

IMPROVED CONTROL

The new device uses the same fixation target as its predecessor that limits accommodation to increase the accuracy of the reading. The new model also allows the operator to adjust the length of fogging time in order to overcome accommodation in younger patients.

A new motorized mechanism makes joystick operation easier, quieter, and more responsive than the previous design. With its new electronics, the KR-800 is also more compact and about 23% lighter than its predecessor, which makes alignment smoother and easier.

"The improved measuring process of the KR-800 allows for stable, accurate results, and the new ergonomic design affords operators a better view of the patient so they can more readily detect facial movements that can influence the measurements," Biggins said.

Like its predecessor, the new KR-800 features a serial port (RS-232). A new feature with the KR-800 is LAN connectivity that allows for direct integration with other Topcon instruments, including the CV-5000S Automated Vision Tester, or with the office network, allowing incorporation of the data into the patient's EMR.

Users can also purchase an optional Bluetooth module if they desire a wireless connection. The KR-800 also has a built-in easy-to-load printer that lets users print measurement results. ■

Automated IOL insertion technology helps improve surgical precision

Device allows for 'quicker and slicker' procedures, increasing surgeon satisfaction

By Fred Gebhart; *Reviewed by Richard J. Mackool, MD*

TAKE-HOME

- ***A one-handed IOL insertion device allows for smoother, less traumatic lens insertions even in difficult incisions and eyes.***

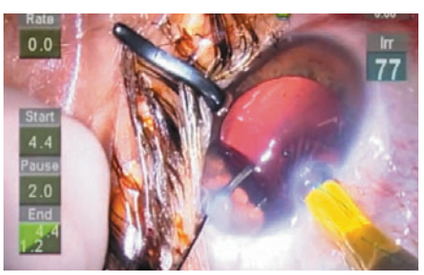
ASTORIA, NY :: **INSERTING AN INTRAOCULAR** lens can be tricky.

Traditional technology—which was a practical technique in an era when incisions were large and there was room for error—requires two hands to position and control the injection device. If the eye depositioned slightly during insertion, there was room for recovery. However, as incisions shrink to 2.75, 2.4, and 2.2 mm, the margin for error shrinks, too.

Dr. Mackool

"If you are using two hands on the injector, you don't have any extra hands to reposition the globe or the implant," said Richard J. Mackool, MD, Mackool Eye Institute, Astoria, NY. "If the eye gets decentered, you cannot see quite as well and you cannot control where the implant is going quite as accurately. You cannot be as precise as you want."

AUTOMATED LENS INSERTION



VIDEO To view an example of a case using the automated IOL insertion device technology, go to **http://bit.ly/16nGBh0.** *(Video courtesy of Richard J. Mackool, MD)*

An automated insertion device (Intrepid AutoSert IOL Injector, Alcon Laboratories) restores that lost precision.

ABOUT THE DEVICE

The one-handed device can be programmed for completely automated IOL insertion or controlled manually by a foot pedal.

"The capsulorhexis might be a little small, the incision might be a little tight, and you still want the lens to be inserted into the capsular sac as atraumatically as possible," Dr. Mackool said. "The [device] makes those difficult insertions easier."

Current trends in cataract surgery make an automated insertion device more attractive, Dr. Mackool said.

As surgical incisions continue to shrink, automated solutions will become more appealing. Though there is a certain degree of resistance to using ever-smaller incisions, biomechanical factors favor smaller, less invasive procedures.

A familiar 2.75-mm incision can produce half a diopter of flattening, Dr. Mackool said. The degree of flattening varies from 0 to 0.5 D from eye to eye with little predictability, however.

"If your patient has 1 D of astigmatism and you are using an astigmatic IOL, you've got an unpredictable 0.5 D range of astigmatic effect from your incision alone" he said. "Half of your potential correction is lost before you even insert the IOL, nobody wants that kind of unpredictable outcome.

"Smaller and smaller incisions are a bigger and bigger part of accurate cataract refractive surgery, and the [device] supports the kind of high-precision surgery we all want to perform," Dr. Mackool said. "It lets you work through a smaller incision and it helps you be more precise in every eye you work on."

IMPORTANCE OF DEVICE

It is not clear if the new device makes a significant difference in long-term patient outcomes, he noted, but automated lens insertion does make a difference in perioperative complication rates and surgeon satisfaction.

"The real change in satisfaction is with surgeons," he said. "Surgeons know when they are doing a quick and slick job and when they are struggling, and the reality, is that even when you are struggling to position a lens, things usually turn out okay. Maybe there is a little more postoperative iritis, but that generally goes away and it's not a big deal.

"But every now and again it is a big deal, because if you inject a ciliary focus lens behind the capsule, you'd better be a real expert," Dr. Mackool said. "Repositioning that lens to the proper location is not an easy thing to do and it is those traumatic insertions that cause problems later."

The cataract surgery ideal, Dr. Mackool said, is to complete the procedure without the eye noticing that it has been invaded. The incision and cataract removal should be:

- **Atraumatic.**
- **Fluidics should not be altered.**
- **Ultrasound should be minimized.**
- **Nothing should touch the iris.**

"If you have to struggle with the insertion and manipulate the lens into position, you are more likely to bump the iris and end up with iritis," he said. "The more iritis you get, the greater the risk of macular edema you get. It's a series of cascading events and the most effective way to stop the cascade is to prevent that initiating event."

This is one more way to make cataract surgery and IOL implantation more precise, using a smaller incision so you get a better astigmatic result, Dr. Mackool said.

Because the surgery is more precise, less postoperative inflammation occurs, he said.

The eyes with postoperative inflammation do not see as well and as soon compared with eyes that endured less procedural trauma.

"[The device] helps you work quicker and slicker with less trauma," Dr. Mackool said. ■

RICHARD J. MACKOOL, MD
P: *718/728-3400* **E:** *mackooleye@aol.com*
Dr. Mackool is a consultant to Alcon Laboratories.

Revisiting ruckus over RUC

What physicians need to know about aim of Relative Value Scale Update Committee

By Scott Baltic

TAKE-HOME

A physician committee that helps set Medicare rates for specific procedures is under the spotlight. Are the accusations of price-fixing fair, and are there better alternatives?

Physicians who treat Medicare patients instinctively know that there's a process involved in setting payment rates for services and a committee that's responsible for the task.

Lately, some industry observers have characterized the group—the American Medical Association (AMA)/Specialty Society Relative Value Scale Update Committee (RUC) (*http://bit.ly/ksGjWm*)—with one of two extremes:

- **As an obscure committee that holds three boring meetings each year to do tedious evaluations that help the Centers for Medicare and Medicaid Services (CMS) set Medicare rates for physician reimbursements; or**

- **As a secretive, highly politicized group that wields enormous influence over physician reimbursements—from both Medicare and private insurers—that also has conflicting interests and little oversight.**

The answer might be somewhere in the middle, but it depends on who you talk to. According to AMA, RUC makes annual recommendations to CMS regarding new and revised physician services and performs broad reviews of the Resource-Based Relative Value Scale (RBRVS) every 5 years. RBRVS is a function that weighs physicians' services relative to their value and time investment in order to arrive at a benchmark for compensation on behalf of the Medicare program.

It's not actual dollar figures, but *relative values.*

What is most important to note is the broad influence RUC has on how much physicians get paid both in the Medicare program directly and in the private market. Though the committee makes recommendations for relative value, those recommendations carry great weight as industry-wide benchmarks for actual-dollar payment rates.

Those who participate in the RUC and those who are critics of it have polarizing views, and there is a need to discover RUC's role in the real world of health care, both today and for the future. It is hoped that this article produces more light than heat, which might be an improvement over recent mainstream media coverage that over the past few years has explained, and to varying extents, excoriated the RUC.

For example, an article in the Feb. 20, 2007 *Annals of Internal Medicine* (*http://bit.ly/18TOnPY*) discussing the income gap between primary-care and medical specialties took the committee to task for failing to do more to close that gap. Specifically, the article blamed the over-representation of specialty physicians on the RUC for the lower incomes of primary-care providers (PCPs). The article did note other factors, however, such as private insurers "reimbursing specialists at large percentages and primary care providers at small percentages over Medicare rates."

Perhaps the most vilifying headline appeared with a July/August 2013 article in *Washington Monthly:* "Special Deal: The shadowy cartel of doctors that controls Medicare" (*http://bit.ly/1auB1g1*). It and other articles are clear on a number of criticisms.

CRITICS: There is weak representation of primary care on RUC, therefore RUC is skewed in favor of specialists.

Taken as a whole, the negative articles criticize RUC based largely on the same perceptions. Much of the focus specifically falls on the committee's purported effects on reimbursements for PCPs.

The committee is in fact heavier on medical specialists than PCPs by headcount, which at least encourages the ongoing tendency for procedural CPT codes to be reimbursed more generously than cognitive codes, such as those for patient Evaluation and Management (E/M). And since PCPs tend to engage in a higher proportion of activities that fall under E/M codes, a related criticism is that the updating process undervalues the work of PCPs.

Even so, there are also persistent issues around payments for procedural codes versus those for cognitive codes.

"RUC represents that tension, but it doesn't define it," said David Muhlestein, director of research for health-care consultants Leavitt Partners LLC.

RUC: Primary care compensation is increasing appropriately.

From 1991 to 2011, the portion of Medicare money paid to primary care increased from 37% to 43% while the portion going to surgical specialties dropped from 32% to 21%, according to William L. Rich III, MD, FACS, medical director of health policy for the American Academy of Ophthalmology and former RUC chairman.

Similarly, reimbursement for routine office visits with established patients (E/M code 99213) has risen from $32 to $66 since 1995, he said.

"There has been a redistribution of valuation by the RUC," said Dr. Rich. "There has been an absolute shift of dollars to primary care, appropriately."

He adds that in the past two years and on its own initiative, RUC has added valuations for care coordination, team education, and phone calls.

There are still, however, "some distortions" in pay, he said. Cardiology, gastroenterology, and orthopedic/spine surgery, for example, "pay substantially more than primary care or general surgery."

Glen Stream, MD, past president and former board chairman of the American Academy of Family Physicians (AAFP), counters that though the tide is turning back toward primary care, it's only "to a small and inadequate degree."

He points out that the common codes (E/M 99213 and 99214, which includes moderate-complexity medical decision making) are also embedded into many codes for surgical procedures, such as for preoperative and follow-up visits. Therefore, increasing the pay for common codes helps PCPs less than might initially seem the case.

AAFP has recommended to CMS that the

Continues on page 42 : ***What RUC does***

WHAT RUC DOES

(Continued from page 41)

agency create primary-care–specific E/M codes. The academy's position is that evaluation and management work in primary care is more demanding and complex than in specialties, especially with an aging population that often presents with multiple or chronic conditions.

But the whole idea behind RUC and its value determinations is to arrive at relatively fair compensation for time and skill. Each CPT code—created exclusively by AMA to document healthcare services for the purpose of reimbursement—has a Relative Value Unit (RVU) assigned to it. When the RVU is multiplied by a conversion factor and a geographical adjustment, it creates the compensation for a particular service.

RVU numbers are translated into actual reimbursement dollars by the CMS conversion factor, which is flat, or the same for all specialties, said Barbara S. Levy, MD, the current RUC chairwoman and vice president of health policy for the American College of Obstetricians and Gynecologists. She adds that private insurers' conversion factors are affected by market forces, such as the availability of a given specialty in a certain area, and so aren't necessarily flat.

Although it's not the only formula, private insurers often use Medicare rates as a baseline for their separately negotiated rates with providers. Market forces, quality programs, pay for performance and other factors figure in as well.

CRITICS: **Service time metrics can become out-of-date with medical advances.**

Other criticisms of the RUC cover a wide range of issues. For example, the amount of time attributed to many procedures has remained high even as the procedures have advanced to become more routine and to require less of the physician's time than previously documented.

The *Washington Post* article (*http://wapo.st/1bT9Eud*) noted that 78 physicians in Florida had—on paper—performed at least 24 hours worth of procedures in a single work day based on RVU figures, which would be clearly impossible in the real world. And reportedly, certain ophthalmologists performed 30 to 40 procedures in a single day, which would have been 30-plus hours worth of work based on RVU figures.

RUC: **The numbers must be examined in context.**

In a press release shortly after the article appeared (*http://bit.ly//17yJ5al*), the AMA stated that it had asked to see the magazine's cited data for the Florida physicians, but that the documentation was not provided. Regarding the ophthalmologists, the association noted that the procedures cited appeared to have included LASIK, for which RVU values have never been determined, because the procedure is not covered by Medicare.

As to the system not addressing procedures that have become more efficient, Dr. Rich said that over a 10-year period, he went from doing three cataract surgeries in about seven hours to doing 10, but his reimbursement per surgery declined significantly. The Medicare reimbursement for cataract surgery was $941 in 1995 and is $578 currently (figures not adjusted for inflation), Dr. Rich said.

CRITICS: **RVU numbers assigned to procedures always go up.**

Reimbursement just keeps growing over time, say the critics. A *Washington Post* analysis of records for 5,700 procedures reportedly showed that work RVUs are seven times likelier to increase than to fall.

RUC: **The values are relative.**

The AMA and RUC have repeatedly emphasized that the RBRVS and its updates are based on relative values. In other words, if everything is inflated by a similar factor, the RVU figures are still valid, compared with each other. And RUC leadership insists that the committee's RVU recommendations are largely in line with each other in those relative relationships.

It's a common misperception that RUC is somehow jacking up physicians' fees in absolute terms, according to AMA. With the various steps between an RVU allocation by the RUC and a final dollar figure in the following year's Physician Fee Schedule, accusations of "price-fixing" are off the mark.

"The RUC does not control revenue," Dr. Rich said, "it just determines valuation."

Further, Dr. Rich said, since 2010, RUC has reviewed 1,553 codes. Of those, only 5% increased, 43% decreased, 34% stayed the same and 18% are still under review. Most of the redistribution of value was to primary care, he said.

CRITICS: **There is overvaluation of certain procedures.**

Overvaluation encourages overuse, not only under Medicare, but under private insurance, too. Many insurers use the RBRVS as a baseline for their own payment scales, with some using a percentage of Medicare payment—such as 125%—as a final rate. This "Medicare spillover" effect does exist, Muhlestein said. Medicare is the payer with the most clout, and its rates do indeed influence private insurers.

RUC: **The RBRVS as administered by the CMS is budget-neutral, as reflected by annual adjustments in the conversion factor.**

The amount that Medicare spends on physician fees, even fees per patient, continues to rise drastically, of course, but that's being driven by other factors, such as utilization increasing overall.

As for private insurers, the RUC has no control over whether they use the RBRVS values or whether or how they modify them.

CRITICS: **CMS essentially rubber-stamps the RUC's recommendations.**

Historically, CMS has approved more than 90% of RUC recommendations. The raw numbers are hard to argue with, but the reasons for them are hotly debated. Many question whether new payment models will force CMS to push back on some of the RUC determinations.

RUC: **The committee is doing its job well.**

The fact that CMS accepts the vast majority of the committee's recommendations is an indication of how carefully and fairly the RUC does its job, according to AMA.

In addition, RUC leadership points to the fact that CMS "listens to every debate," said Dr. Rich. So what the committee does and how it does it is completely transparent to CMS.

Dr. Stream does agree that CMS has been "more discerning" lately about accepting the RUC's valuations.

CRITICS: **RUC is 'secretive.'**

In not publishing the results of RVU votes and in requiring a broad nondisclosure agreement from any non-members allowed to attend a meeting, RUC appears to be less than transparent in its decision-making process.

The lack of transparency engenders much of the distrust of the committee, said Dr. Stream, who adds that the AAFP has pushed for more transparency within RUC and outside of it.

Medicare is becoming somewhat more open about what it pays providers since a federal judge lifted a 1979 injunction that prohibited CMS from disclosing Medicare payments. In May, CMS released hospital charge data for 100 common procedures (*http://go.cms.gov/16WaMfH*), but physicians remain divided on the issue of making the information public.

The biggest favor RUC could do for itself would be more transparency, agrees Muhlestein.

RUC: Some information is better kept within the committee.

RUC meetings are closed for good reasons, principally that new CPT codes requiring an RVU recommendation often involve new medical devices, and RUC doesn't want its deliberations to become fodder for the stock market.

"They [CMS] don't want Wall Street responding to the debates in that room," said Dr. Rich.

The AMA also notes that RUC meetings typically are attended by 300 people, so the attendees hardly comprise a small, clandestine "cartel."

TRANSFORMING RUC FROM THE INSIDE

So, is the RUC deservedly as controversial as mainstream media portrays? Or is it more of a lightning rod for a variety of contentious, persistent issues around Medicare reimbursements specifically and concerns around fee-for-service payments generally?

In a September post on the American College of Physicians' ACP Internist blog (*http://blog.acpinternist.org*), Robert M. Centor, MD, FACP, an academic general internist and associate dean at the University of Alabama School of Medicine, writes: ". . . the RUC did not create the system. They try hard to balance a system that is designed to achieve the wrong outcomes. The RUC has become a very easy and attractive kicking post, but the problem comes from the idea of resource-based relative value units . . ."

He goes on to say he does not blame RUC. Although it is not perfect, members are working to patch a flawed concept.

And RUC leadership has been moving to address at least a couple of the concerns highlighted by recent media coverage. For example, one allegation has been that RUC members vote in blocs and that the surgeons or other specialties agree to vote in concert.

Around 1999 and 2000, Dr. Levy said, "there were factions" that would meet separately the night before a meeting to plan their votes, but both she and Dr. Rich worked hard to drive that attitude out.

Dr. Levy said she tells RUC members, "When you sit on the RUC, you're representing the house of medicine," not a particular society or specialty.

"People are not voting in blocs," currently, she said, adding, "most of our votes are overwhelming. Generally it's not close."

One way she and Dr. Rich brought about a cultural shift, Dr. Levy said, was procedural. The typical agenda book for a RUC meeting is massive—about 2,000 to 3,000 pages—so this material is now divided up and assigned to advance reviewers who are from specialties different than the specific codes they're reviewing. These reviewers also become the lead commenters on those codes during the meeting.

The result has been more-informed discussion, Dr. Levy said. "People don't come in as fearful."

In another change, Dr. Levy said, RUC votes will be published for the first time after CMS publishes its final rule—likely in November. The votes will be reported only as totals for and against a given RVU assignment, however, not as individual voting records.

"We have to have" that level of anonymity, said Dr. Levy. She doesn't want to risk RUC members being punished for voting against their specialty society's narrow interests, which she said happens commonly.

Continues on page 44 : ***Committee***

How RUC determines the value of health care

How much is an annual physical exam worth, compared with cataract surgery? What about a well-baby visit, versus a colonoscopy?

These questions are neither trivial nor easy to answer, and the decades-long road to the current American Medical Association (AMA)/Specialty Society Relative Value Scale Update Committee (RUC) illustrates that.

For some years after Medicare began in 1965, reimbursements were based on physicians' historic "usual, customary, and reasonable" charges. Even with various ceilings on annual increases, something better was needed. In the mid-1980s, Congress directed the Health Care Financing Administration (HCFA) to find it.

Over the next few years, a team led by William Hsiao, PhD, a Harvard economist, devised what eventually took shape as the Resource-Based Relative Value Scale (RBRVS). The RBRVS was enacted into law as part of the Omnibus Budget Reconciliation Act of 1989 and took effect at the start of 1992.

The currency of the RBRVS is the Relative Value Unit (RVU), with each covered medical procedure being assigned a certain RVU number. In theory, procedures that take longer, or require more skill, or require more equipment, and so forth, are assigned higher RVU numbers.

However, some group or structure clearly was needed to update the initial RBRVS values, so the AMA essentially volunteered to form a group that would take on that task, at no cost to the federal government.

The result was the RUC, created in 1991, which is made up of representatives from the AMA itself, the American Osteopathic Association and 21 or more professional groups for medical specialties.

The RUC supplies updated RVU numbers for various CPT codes, along with new RVU totals for new CPT codes, to HCFA's successor, the Centers for Medicare and Medicaid Services (CMS).

It's up to CMS to accept or reject the RUC's values, but historically the agency has accepted more than 90% of them. CMS also applies a conversion factor (currently 34.0230), which turns the RVU figures into actual reimbursable dollar amounts. And there's also a geographic adjustment.

The RUC "represents the entire medical profession," according to the AMA, "with 21 of its 31 members appointed by major national medical specialty societies . . . ." Four additional seats rotate on a 2-year basis, with two reserved for an internal medicine subspecialty, one for a primary-care representative, and one for any other specialty.

A two-thirds vote of the 28 voting members of the RUC is needed to accept an RVU recommendation.

The Total RVU components are Work RVU, Practice Expense RVU and Professional Liability Insurance RVU. The RUC submits information to CMS for components such as clinical staff type/time, medical supplies and medical equipment for the Practice Expense RVU.

Four aspects are considered for every service: time, technical skill, mental effort and judgment, and iatrogenic risk, explained William L. Rich III, MD, FACS, a former RUC chairman and currently medical director of health policy for the American Academy of Ophthalmology.

The work can be extremely detailed, said Barbara S. Levy, MD, the current RUC chair.

"We get into the weeds so far, we argue about tenths of a point, a minute here or there, one band-aid or two," she said.

By now, the RUC has a substantial history, and AMA reports costs among participating specialty societies and the volunteer physicians total about $7 million each year.

Nonetheless, some of those who are knowledgeable about the RBRVS updating process say that letting the AMA run it was a bad idea from the get-go.

Hsiao, for one, said that RUC is biased, mainly because of two factors: politics and lack of scientifically sound processes.

First, he said, the AMA, "a political organization of organized medicine," "uses unsound methods to produce biased results in favor of particular specialties, without any oversight by any unbiased scientific or government agency."

Second, Hsaio said, the AMA "does not have the in-house technical expertise to produce objective and scientifically sound RBRVS updates. AMA has little interest to do that. The updating of RBRVS has become a tool for AMA to gain the political support of selected specialties."

Is there a better way?

Hsiao concedes that physicians have to make up most of the RUC membership, but the process should be re-evaluated.

The more important question, he said, is: "What rules are set for RUC on methods and data to be used to determine the RBRVS?"

As payment reform takes shape in Medicare and the private market, no doubt RUC will need to respond to the changing needs of the industry.

—Scott Baltic

COMMITTEE

(Continued from page 43)

The RBRVS update process is based entirely on effort, so it's lacking any elements connected with health outcomes or the value to a patient of a procedure or E/M. RUC's leadership and outside observers agree—although it's an improvement—the change is unlikely to happen any time soon.

Physician payments should be based to an extent on effort, as they currently are, said Roy Poses, MD, a clinical associate professor of medicine at Brown University, an internist and blogger (*http://hcrenewal.blogspot.com*) who has followed the RUC for half a dozen years. But the most important thing to add to the RBRVS, he said, would be "some measure of value for the patient … Ideally, effectiveness ought to be part of it."

"The problem is, that's really hard to measure," he added. "Right now, I don't think we know enough" about outcomes.

When the RUC was established, there was supposed to be a valuation proposition to it, Dr. Rich said, but the committee didn't have such tools in 1989.

"We're starting to find ways to measure value to the patient," such as quality-of-life scores or patient-related outcomes, he said.

Dr. Levy said that if she could recommend changes to RBRVS, she'd like to add factors for relative patient benefit, as shown by outcomes research, and add a factor for cost-effectiveness.

By law, however, the only factors that can be considered in the RBRVS are work, practice expenses, and malpractice insurance expenses, along with "a bit of a geographic modifier," said Dr. Levy. As a result, the RUC can't yet consider a procedure's value to the patient or to society.

TRANSFORMING RUC FROM THE OUTSIDE

Section 3134 of the Affordable Care Act mandates that CMS establish a process to validate RVUs of Physician Fee Schedule services, and the agency has contracted with the Urban Institute and the RAND Corp. to do so.

The Urban Institute project is intended to give CMS a way to review proposed work RVUs, assess how reasonable they are in terms of external data, and ensure that the overall RBRVS fee schedule is internally consistent within families of services and specialties. The project will examine the work RVUs for 100 services in the Physician Fee Schedule. Clinical

Continues on page 46 : ***Fee schedule***

Presbyopes: The Real Cost of Not having a Femtosecond Laser

2013 Eyecare Webinar Series

Featuring Jeffrey Machat, MD.

- Fundamentals: Understanding the technology and how to sell it to your patients
- Economics: How to make it work for your practice
- Comparative Data: What you need to understand
- Femto Procedures: Not just for LASIK, the role for presbyopia and cataract surgery

Register Today

October 16th, 2013 | 7PM EST

October 17th, 2013 | 9PM EST

https://vts.inxpo.com/Launch/QReg.htm?ShowKey=16507/print

Ophthalmology Times
CLINICAL NEWS & ANALYSIS

Sponsored by
ziemer
OPHTHALMOLOGY

FEE SCHEDULE

(Continued from page 44)

panels made up of physicians from a range of specialties will review the new data regarding the time necessary to perform specific services and procedures.

Over a two-year period, the RAND project will build a validation model to predict work RVUs and their time and intensity components. "The model design will be informed by the statistical methodologies and approach used to develop the initial work RVUs and to identify potentially misvalued procedures under current RUC and CMS processes," according to RAND. CMS will provide a sample of CPT codes to test the model.

One of the issues underlying these efforts seems to be the question of who would be better qualified to determine physician work values than the physicians themselves? To put it another way: Could a body substantially different from RUC do the same job, but better?

Dr. Levy is skeptical, noting that almost everyone on RUC is a practicing physician. She questions how a non-physician could set RVUs, particularly the aspects of a procedure's intensity and the potential harm that might result.

She said she would be more optimistic about changing other aspects of Medicare payment policy. For example, there's a policy related to implantable defibrillators. Costing more than $100,000 installed, the devices are indicated only for congestive heart failure, but their use has over time been extended to other conditions without supporting evidence.

CMS has tried to rein in the extended use, she said, "but they get tremendous pressure" from Congress.

Health services researchers originally developed the RVU concept, so presumably they would be qualified to do RUC's work, said Muhlestein, though he isn't aware of any significant current research efforts along this line.

"It's hard to get non-physicians really interested" in this kind of work, he adds.

On one hand, Muhlestein explains, the reported $7 million that the AMA spends annually to operate RUC is roughly one ten-thousandth of the about $60 billion a year that Medicare pays for physicians fees, so more effort in ensuring that RVU allocations are accurate wouldn't be a big hit on the federal budget.

On the other hand, he points out, Congress has never given CMS the resources to replace or supplement the RUC.

Calling RUC's procedures "complicated and opaque," Brown University's Dr. Poses said RBRVS should be updated by a formal federal advisory committee whose members are appointed by the federal government; which accepts open, public comments; and which includes "some representation by patients and taxpayers." He envisions something along the lines of the Patient-Centered Outcomes Research Institute, whose board includes representatives from patient-advocacy groups.

A potential step in the direction that Muhlestein and Dr. Poses suggest was taken in June, when U.S. Rep. Jim McDermott (D-WA) introduced a bill that would create a new panel to oversee the RUC.

In a press release, McDermott's office said the RUC "is unevenly weighted by procedural specialists over PCPs and relies heavily on anecdotal and self-serving survey evidence, rather than forensic data."

"Medicare certainly needs clinical expertise in order to fairly set reimbursements, but an outside organization . . . needs checks and balances," McDermott said. "No matter how well-intentioned, structural biases are inevitable and we're seeing that effect as new doctors flock toward specialty care and away from primary care."

McDermott is a psychiatrist as well as the ranking member of the House Ways and Means Subcommittee on Health.

Based on a recommendation from the Medicare Payment Advisory Committee, the Accuracy in Medicare Physician Payment Act of 2013 introduced by McDermott in June would establish a panel of independent experts within CMS "to identify distortions in the fee schedule and develop evidence to justify more accurate updates."

The panel's members would include patient representatives, and the group would be subject to the Federal Advisory Committee Act, which requires such bodies to hold open meetings and publish their minutes.

Under the bill, Medicare could continue to request work from the RUC, but the new panel would both initiate such requests and review the RUC's work.

THE FUTURE OF THE RBRVS

It's clear that RUC is, for better or worse, handcuffed to the RBRVS, which was built on a fee-for-service model. With or without major changes, what might the future hold for the RBRVS?

Even within group practices, accountable care organizations (ACOs) and other care models, rewards need to be divvied up somehow, said Dr. Rich, either by RVU or some equivalent, and the current RVU assignments are already very commonly used for such purposes.

"These are not going away. They're always going to be needed," he said, even if the FFS model fades somewhat.

Levy adds that in addition to being part of how ACOs apportion salaries, the RBRVS is likely to be part of any bundled-payment valuations.

The RVU is "the default standard" for such purposes, Muhlestein agrees. He notes that Leavitt Partners' Center for Accountable Care Intelligence has been tracking ACOs and their payment arrangements for about three years and concludes that most contracts are still fee-for-service based. In addition, the ACOs in the Medicare Shared Savings Program are all based on FFS, he said.

Catalyst for Payment Reform (CPR), a national, not-for-profit collaborative of large employers, in March found that 10.9% of commercial healthcare payments today are tied to value rather than volume.

The biggest take-away from the current controversy about RBRVS and its updates, Muhlestein said, is simply that "RUC is still very relevant and will be relevant for a long time." ■

Current composition of RUC

- Chairperson+
- American Medical Association Representative
- CPT Editorial Panel Representative+
- American Osteopathic Association Representative
- Health Care Professionals Advisory Committee Representative
- Practice Expense Review Committee Representative+
- Anesthesiology
- Cardiology
- Dermatology
- Emergency Medicine
- Family Medicine
- General Surgery
- Geriatric Medicine
- Infectious Disease*
- Internal Medicine
- Neurology
- Neurosurgery
- Obstetrics/Gynecology
- Oncology/Hematology*
- Ophthalmology
- Orthopaedic Surgery
- Otolaryngology
- Pathology
- Pediatrics
- Pediatric Surgery*
- Plastic Surgery
- Primary Care*
- Psychiatry
- Radiology
- Thoracic Surgery
- Urology

+Indicates non-voting member
**Indicates rotating seat*

Source: American Medical Association

5 steps to help create an estate plan

Devising a plan may seem daunting, but many tools exist to make the process easier

Money Matters *By John J. Grande, CFP; Traudy F. Grande, CFP; and John S. Grande, CFP*

TAKE-HOME

- ***Though many put off estate planning because it can be difficult, there are several tips to follow that can make the process less stressful.***

WHEN IT COMES to estate planning, procrastinating is easy. The task of getting one's financial house in order can seem daunting and the topic uncomfortable. In fact, while the majority of Americans believe that all adults should have an estate plan, only 44% have actually created one, according to a 2011 LexisNexis survey.[1]

Unplanned estates may be left to wind their way through probate court, leaving state law to determine the disposition of assets.

"The time to devise an estate plan is now, if you haven't already," says John Padberg, vice president of Life Event Services and Estate Planning, Wells Fargo Advisors.

Many people equate estate plans with wills, he said, but a well-thought-out structure involves much more.

Tools—such as living trusts and financial and health-care powers of attorney—can help trusted professionals and family members manage your affairs if you cannot.

Planning does not need to be stressful, and the results often confer the comfort of knowing assets will be distributed in an orderly way.

Padberg offered five steps to help create an estate plan to accomplish that goal:

1 FIND AN EXPERIENCED ESTATE-PLANNING ATTORNEY

It takes specialized expertise to create a plan that includes all the necessary elements and meets specific needs. A solid estate plan will likely consist of several documents, which may include the following:

- **A will, which states how individually owned assets are to be distributed upon death.**
- **A living will, which communicates your wishes regarding life-prolonging medical treatments.**
- **Powers of attorney, which designate another individual to handle financial or health-care matters if you are incapacitated.**
- **Revocable trusts, which can be useful in avoiding the probate process in states where probate is burdensome, and can be altered or canceled according to your wishes.**

Creating a well-designed plan will require input from both an attorney and a financial advisor. A financial advisor may be able to provide some options for legal assistance, if you do not yet have an estate planning attorney.

2 ASSESS YOUR ASSETS

Before drafting an estate plan, ask a financial advisor to prepare a financial net worth statement. This will give a clear sense of what you are working with.

Also, review the beneficiaries listed on critical documents, such as life insurance policies and retirement plans. Beneficiary designations determine how those assets will be distributed, Padberg cautioned, so you want the named beneficiaries to reflect—and not undermine—your intentions.

3 DEFINE YOUR GOALS

An estate plan is also an opportunity to direct how wealth will be passed on to the next generation.

For instance, leaving a large sum to a child or young adult may create long-term issues if that individual lacks the skills or maturity to manage such a windfall. Ask a financial advisor about trusts that might be established to control the distribution of inherited funds.

To bequeath money to a charity, ask a financial advisor and estate planning attorney about the many charitable giving strategies that are available. He or she can offer guidance on choosing the technique that best fits your philanthropic goals.

4 DETERMINE YOUR TAX LIABILITY

Under the fiscal cliff agreement enacted in early 2013, individual estates worth $5.25 million or less can avoid federal estate taxes. Amounts that exceed the exclusion amount are taxed at a rate of 40%.

Work with a financial advisor to determine current estate tax liability and project any future liability. Consider the impact those taxes might have on how you wish to pass assets on to the family.

"The planning will be different—and more sophisticated—if you're planning for a tax bill," Padberg said.

5 UPDATE YOUR PLAN

Life is about change, so it's crucial to make sure instructions are always current.

That means updating an estate plan whenever you experience a major life event, such as a new baby or a marriage. Otherwise, not only will the plan fail to contemplate new circumstances the way you want, but it could also increase the potential for outside challenges.

Ambiguity and conflicts about intentions could have a disastrous effect on family, Padberg said, so preventing them is important. ■

Reference

1. EZLaw survey finds most Americans recognize the importance of a will or estate planning, yet few have necessary documents in place. LexisNexis, 19 July 2011. *https://www.lexisnexis.com/media/press-release.aspx?id=1311095221427043*

JOHN J. GRANDE, CFP®; TRAUDY F. GRANDE, CFP®; AND JOHN S. GRANDE, CFP® *are co-editors of Money Matters. They are owners of Grande Financial Services Inc., Oakhurst, NJ, and registered principals of Wells Fargo Advisors Financial Network Inc., member FINRA/SIPC.*

The Grandes lecture at Johns Hopkins University School of Medicine, and they advise ophthalmologists across the country on a diverse range of investment and financial matters. Readers may submit their financial questions to them at 800/722-1258 or e-mail john.s.grande@wfafinet.com. Readers also may access the Grande's website at www.grandefinancialservices.com

EHR brings tangible benefits

How it's possible to operate an ophthalmology practice electronically and efficiently

By Gregg J. Berdy, MD, FACS, *Special to* Ophthalmology Times

TAKE-HOME

- ***For one ophthalmology practice, implementing an electronic health record system has increased the workflow productivity of the office and enabled the practice to operate at a more efficient level.***

MY ASSOCIATES AND I contemplated implementing an electronic health record (EHR) system for our practice more than a decade ago.

However, we did not seriously consider it until the passing of the Health Information Technology for Economic Clinical Health (HITECH) Act, part of the American Recovery and Reinvestment Act of 2009. Under the HITECH Act, physicians were required to implement an EHR technology.

Accordingly, we began interviewing EHR companies to determine the best fit for our practice.

DECIDING ON AN EHR SYSTEM

We wanted an EHR system specific to our ophthalmic practice. None of the systems seemed to make sense to us, until we met with certified EHR specialists from our chosen vendor (ManagementPlus).

The vendor's staff was approachable and took the time to decipher what we needed as ophthalmologists.

We had many questions about the challenges inherent in developing templates, as well as the regulations required by Medicare and Medicaid. Although this vendor does provide generic, template-style formats, its specialists were able to guide our software implementation and help customize the EHR system to our practice's unique workflow and examinations.

The specialists helped develop templates with specific dropdown menus that allow us not only to communicate to our scribes in an organized manner, but also to interpret data better and print it out in a narrative form for sending referral letters.

CUSTOMIZING THE EHR

We purchased our ophthalmology-specific EHR software in 2011 and began to upgrade our practice with new computers and video monitors.

During the course of the following year, my colleagues and I—along with the EHR specialists—went through the database templates, section by section. Our physicians, technicians, front-desk staff, and optometrists invested hundreds of hours in customizing dropdown menus for external eye disorders, glaucoma, corneal, and retinal diseases, and added images for drawing capabilities, diagnosis codes, and verbiage specific to our practice.

The finished product is the result of a collaborative process and more than a year's worth of work among physicians, front-desk staff, and technicians.

Our practice has been established for more than 20 years, with 51,000 patients in the database and about 16,000 active patients. My colleagues and I decided that we were not going to cut back temporarily on patient flow and suffer a loss of income when we implemented the EHR system.

At first, its implementation slowed us down, and patients were not receptive. We explained how the implementation is a meticulous process and the system would be back to speed shortly. Fortunately, most patients understood what we were trying to accomplish and they accepted prolonged wait times.

Initially, we were only adding new patients' records to the EHR, but now we are entering all patient records in the system.

BENEFITS

As a cornea specialist, I like to use photographs to demonstrate patients' diseases of the cornea or anterior segment. Each of our 10 exam lanes has dual 27" diagonal high-definition screens—one is used for our scribe, and the other is used for patient data (e.g., visual fields) and pictures.

Each physician uses a tablet (iPad, Apple) to access patient narratives for the day. Being able to display a retinal or corneal photograph or a visual field on a large-screen display provides the opportunity to discuss with the patient diseases, such as glaucoma, diabetic retinopathy, age-related macular degeneration, corneal ulcers, meibomian gland dysfunction, and dry eye.

Patients are impressed by the technology and the ability to see their problem—it is a great educational tool.

Instead of flipping through sheets of paper, we now can present data effectively to and communicate with patients and their families.

When a patient can see lissamine green staining of the conjunctiva, purulent secretions from meibomian glands, retinal hemorrhages, or a visual field defect, it is much easier for the patient to understand the effect of the disease.

The EHR system has also saved time spent on dictating letters to referring physicians. I used to dictate 10 letters a day. Dictating for each patient took 4 to 5 minutes, so I spent about 1 hour a day dictating.

We have developed our narrative to read like a letter, which prints out on our letterhead. We can send the letter via a secure electronic facsimile program to referring doctors at the conclusion of the patient's examination.

We used to employ a transcriptionist who had a 1-week turnaround time. At best, I would be able to send a letter 7 days after seeing a patient. Now, the letter is sent and received before the patient has checked out from our office.

CONCLUSION

I never expected that implementing an EHR system would mean the practice would become completely paperless. As a busy surgical practice, we probably will continue to print copies of surgical patient notes, including refractions and astigmatism axes, printouts of topographies (Orbscan, Bausch + Lomb), and calculations from the biometer (IOLMaster 500, Carl Zeiss Meditec) to have when we are in the operating room.

Ultimately, EHR has increased the workflow productivity of the office and allowed us to operate the practice at a more efficient level. ■

GREGG J. BERDY, MD, *is in practice with Ophthalmology Associates and is an assistant professor of clinical ophthalmology, Department of Ophthalmology and Visual Science, Washington University School of Medicine, both in St. Louis, MO. He acknowledged no financial interest in the products or companies mentioned. Dr. Berdy may be reached at gregg.berdy@youreyedoc.com.*

INNOVATIVE • ENTERTAINING • INTERACTIVE

THE EYES HAVE IT

OPTIMIZING THE MANAGEMENT AND TREATMENT OF

DIABETIC MACULAR EDEMA AND AGE-RELATED MACULAR DEGENERATION

SATURDAY, NOVEMBER 16

6:30-7:00 PM
Registration & Reception

7:00-8:30 PM
Educational Session

MARRIOTT CONVENTION CENTER

859 Convention Center Blvd.
New Orleans, LA

THIS EVENT IS NOT AFFILIATED WITH THE 2013 AAO ANNUAL MEETING.

Provided as an educational service of the Institute for Continuing Healthcare Education. This activity is supported by an educational grant from Genentech

---

FACULTY

DAVID BOYER, MD (CHAIR)
Clinical Professor of Ophthalmology
University of Southern California
Keck School of Medicine
Los Angeles, CA

JEFFREY S. HEIER, MD
Director, Vitreoretinal Service
Ophthalmic Consultants of Boston
Boston, MA

MICHAEL S. IP, MD
Associate Professor
University of Wisconsin
Department of Ophthalmology
and Visual Sciences
Madison, WI

2 EASY WAYS TO REGISTER

WEB: To reserve your place for this activity, register online at www.iche.edu/eyes2013

ONSITE: You may also register onsite before the start of the activity.

There is no registration fee for attending this program.

Food and beverages will be provided.

LEARNING OBJECTIVES

1. Summarize existing data on the available agents used to treat DME and AMD
2. Discuss the evidence supporting current guideline recommendations for the diagnosis and treatment of DME and AMD
3. Describe the mechanisms of action of novel agents used in the treatment of DME and AMD

TARGET AUDIENCE

The primary target audience for these activities is comprised of retinal specialists, although the education will be appropriate for comprehensive ophthalmologists who manage and treat patients with DME and AMD.

ACCREDITATION STATEMENT

The Institute for Continuing Healthcare Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Institute designates this educational activity for a maximum of 1.5 *AMA PRA Category 1 Credit(s)™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

When is it okay to share a secret?

Determine what the secret is about and the potential consequences of hearing it

Putting It In View *By Dianna E. Graves, COMT, BS Ed*

TAKE-HOME

- ***It is inevitable that staff will develop secrets and gossip. Be aware of how to manage these situations and know when to step away, because of the possible ramifications from learning what was said.***

AMERICAN NOVELIST E.W. Howe once said: "A man who can keep a secret may be wise, but not half as wise as the man with no secrets to keep." My mother also told me: "If two people know a secret—then it isn't a secret anymore!"

As my staff size continues to grow, the times I am burdened with being told a secret increase exponentially. It may involve:

- Third-party scuttlebutt regarding someone thinking about looking at another practice for a career change.
- Someone having issues with another staff member and the OK Corral will be re-enacted Friday at high noon, otherwise known as a catfight in the lunchroom.
- Or, in the worst case, there's the secret that is actually more serious, and may have consequences to all involved, especially the secret teller.

I keep reminding my staff that managers and administrators are people—we like to laugh, have fun, and be part of the gang, and being part of the gang means being entrusted with secrets from time to time. But safekeeping a secret is a burdensome task—and frankly, is no real favor, or fun, for anyone.

SECRET AS GOSSIP

In most cases, the predominance of secrets passing around the clinic at any given time is actually better described as gossip.

Someone talking smack about another often ruffles many feathers. Most of the time the comments are unfounded, but they still are hurtful to the recipient nonetheless.

When I hear it, I try to stop them quickly by gently chiding the gossiper with, "Oh, I thought you had something really good."

Why listen at all? Because sometimes behind all the smoke, there's a little something to it and I need to be aware of the repercussions that will eventually come.

Though these secrets are irritating at best, they need to be watched and downplayed to prevent future issues. I look at them as necessary evils, but only as irritating information.

SECRET AS WARNING

The person directly involved in the gossip usually tells "warning bell" secrets to you.

For example, Patti comes to your office and announces that she and her husband are thinking of opening a business and are probably going to do it at the first of the year—if all goes right. She really doesn't want to leave, and actually after the business opens, she is planning to come back part-time. If that doesn't work, she will need to find some place willing to let her work on her terms.

"Please don't tell anyone, I want to do that when the time is right, but wanted you to know up front," Patti said.

Ten minutes into the conversation Patti informs you she has only told two doctors and two other technicians that she trusts. Oh, and let's not forget her recent posting on Facebook last night.

These are more serious secrets.

First, Patti is leveraging this gossip as an ultimatum to get something down the line in her favor. Second, she's literally told you—without resigning—that she is probably leaving, thereby throwing you in a staff-seeking/planning mode. She is sharing a secret, while already leaking it to others and the social media, so when it becomes part of the gossip mill, it looks like it is you who has betrayed her trust!

Lastly, when the time comes to leave, you are the bad guy because you won't fight for her and allow her back part-time.

These are dangerous to mortal secrets, because no matter what, you lose. Don't play into them, but heed them alertly! Though we all want to be confided in, some secrets should not be shared with your manager.

I had a staff member awhile back come into the office asking if she could talk with me, something was bothering her.

Donna's face looked like she had swallowed six lemons.

Before she sat down, I said, "Before you begin, remember who you are talking to."

I wanted her to share, and obviously by looking at her she needed to, but I couldn't promise to do nothing without knowing the problem. Some secrets need to be acted on. After listening to half of the story, this one needed to be acted on drastically.

Donna had been given a secret to keep by Pam, and was told not to tell anyone. They both knew it was wrong not to tell. Keeping the secret was making them feel guilty and as complicit as the one who had done the initial deed. Because of the secret pact and rules, they were now both caught in something they needed help getting out of.

By being tattletales, they would probably be ostracized by others. In essence, by doing the right thing, they would probably be hurt in the aftermath.

Now I had a problem. As a manager, I had to act on the information, but I needed to protect them from the consequences.

I finally figured out a relatively simple way of keeping Donna and Pam out of the loop while still initiating changes that would prevent this from happening again. When changes occur, they will affect the wrongdoers and it should be slightly obvious to those involved that something has happened, but the secret sharers will be protected.

These types of secrets—while far and few apart—are nerve wracking and dilemma full. They are secrets to beware of at all costs, because not only do they affect the staff, but they now also affect you. By telling you, they have now made you duplicit!

The next time someone wants to share a secret, gently place your hands firmly over both ears, run to your office, and lock the door! ■

DIANNA E. GRAVES, COMT, BS ED, *is clinical services manager at St. Paul Eye Clinic PA, in Woodbury, MN. Graves is a graduate of the School of Ophthalmic Medical Technology, St. Paul, MN, and has been a member of its teaching faculty since 1983. She can be reached at dgraves@stpauleye.com.*

iTech

Building the Ophthalmic Tech's Community of Practice

modernmedicine.com/iTech

Resource Center for Technician Education

WEB EXCLUSIVE CONTENT

Related Articles | Continuing Education | Clinical Tools & Tips

iTech provides educational presentations and information for ophthalmic and optometric technicians, helping them work effectively with their doctors to enhance the practice.

Brought to you by Ophthalmology Times & Optometry Times

Patient has recurrent redness, pain of left eye

Woman presents with proptosis and eyelid numbness: What is the diagnosis?

By Audrey C. Ko, MD, Basil K. Williams, MD, Rebecca A. Shields, MD, Sander R. Dubovy, MD, and Wendy W. Lee, MD, MS;
Bascom Palmer Eye Institute Grand Rounds Editors: Jonathan S. Chang, MD and Aleksandra V. Rachitskaya, MD

TAKE-HOME

- ***A female aged 38 years presents with recurrent redness, pain, blurry vision, and protrusion of the left eye. An exam was remarkable for mild proptosis. What is the differential diagnosis?***

A female aged 38 years presented to the Bascom Palmer Eye Institute emergency room with a 1-week history of recurrent episodes of redness and pain of the left eye.

She also reported protrusion of the left eye, and pain with left lateral gaze without diplopia.

Review of symptoms was positive for mild heat and cold intolerance, but otherwise negative.

The patient's medical, surgical, and family histories were unremarkable.

EXAMINATION

The patient's best-corrected vision was 20/20 and 20/25 in the right and left eyes, respectively. Her pupils were equal, round, and reactive without a relative afferent pupillary defect.

IOP, confrontational visual fields, and ocular motility were within normal limits.

Hertel measurements were 16 and 20 mm of the right and left eyes, respectively.

The patient had full-color plates of both eyes and no red desaturation.

Eyelid and corneal sensations were within normal limits.

Slit lamp and dilated fundus exam were unremarkable, with normal appearing optic nerves without pallor or edema, and no retinal striae.

DIAGNOSTIC COURSE

The finding of proptosis is concerning for an orbital mass.

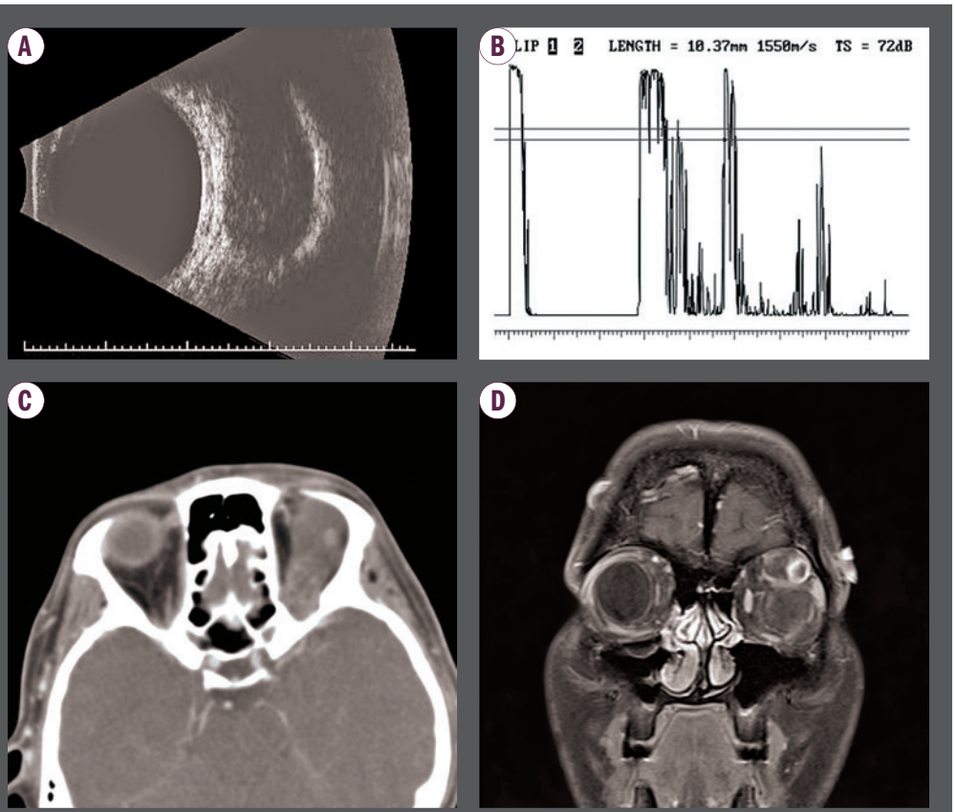


Figure 1

A B Contact B-scan and diagnostic A-scan ultrasound examination of the left orbit showed a well-defined extraconal mass between the levator and the orbital roof. The mass was firm and regularly structured with few septae and low reflectivity. There was no evidence of vascularity.

C Computed tomography scan of the orbits with contrast showed a well-circumscribed, extraconal, oval-shaped mass with heterogeneous enhancement.

D Magnetic resonance imaging of the orbits with gadolinium showed a heterogenous enhancing mass in the superior left orbit that measured 4.8 × 1.2 × 2.1 cm.

(Figures A and B courtesy of Bernadete Ayres, MD; Figures C and D courtesy of Wendy Lee, MD, MS)

The differential diagnosis is broad and includes inflammatory (idiopathic orbital inflammatory syndrome, thyroid eye disease, sarcoid, vasculitis), vascular (carotid cavernous fistula, cavernous hemangioma), neoplastic (cavernous hemangioma, glioma, meningioma, rhabdomyosarcoma, neurofibroma), metastatic (breast, lung, or prostate), lymphoid (lymphoma, benign reactive lymphoid hyperplasia), infectious (abscess, cellulitis), and other etiologies (mucocele, dermoid cyst, epidermoid cyst).

Imaging studies were obtained (Figure 1).

Continues on page 56 : ***Schwannoma***

For Products & Services advertising information, contact: **Karen Gerome** at 800-225-4569, ext 2670 • Fax 440-756-5271 • Email: kgerome@advanstar.com
For Recruitment advertising information, contact: **Joanna Shippoli** at 800-225-4569, ext 2615 • Fax 440-756-5271 • Email: jshippoli@advanstar.com

PRODUCTS & SERVICES

BILLING SERVICES

PM Medical Billing & Consulting

Exclusive Ophthalmology Billers
Expert Ophthalmology Billers
Excellent Ophthalmology Billers
Triple E = Everything gets Paid

Concentrating on one Specialty makes the difference.

We are a Nationwide Ophthalmology Billing Service. We have been in business over twenty years. Our staff consists of billers who are certified Ophthalmic Techs, Ophthalmic assistants, and fundus photographers who are dual certified ophthalmic coders and billers. This combination of clinical backgrounds in ophthalmology with the certified coding degree is the ideal combination of expertise that you need to dramatically increase your revenue. We will get you paid on every procedure every single time. No more bundling, downcoding or denials…

Primary, Secondary, Tertiary and Patient Billing
Relentless and meticulous follow up.

- Experts in Forensic Billing .Specializing in old AR cleanup
- Credentialing and Re credentialing our Specialty. We have a separate Credentialing Department who has cultivated years of contacts to expedite the process as well as getting providers on plans that are technically closed.
- We can offer you our own Practice Management software at no cost to you or we can VPN into your system if that is what you prefer.
- Totally Hippa compliant. We are certified Hippa and have invested in the most secure Hippa connection that Google and Cisco use.
- Monthly custom reports provided.

We presently work on all of the following Practice Management systems :

NextGen, MD Office, Centricity, Medisoft, Office Mate, MD Intellus, Medware, Medcomp, Management Plus, ADS, Revolution EHR, EyeMd EMR, Next Tec, Open Practice Solutions , Cerner Works and more….

All of our clients were paid the PQRI and E-prescribe bonuses and we are ready for the ICD-10 change

Our staff has years of Attendance at AAO and ASCRS and attends all ongoing Ophthalmology billing and Practice Management continuing education classes. We are always knowledgeable and prepared for all government and commercial changes.

On staff MBA consultants

Call today to schedule a free on site consultation.

We will travel to you anytime to evaluate your AR and show you how we can dramatically increase your Revenue.

Call toll free at 1-888-PM-BILLING (1-888-762-4554)
Email: pmmedbill@aol.com
Web: www.pmophthalmologybilling.com
24 hours: 516-830-1500

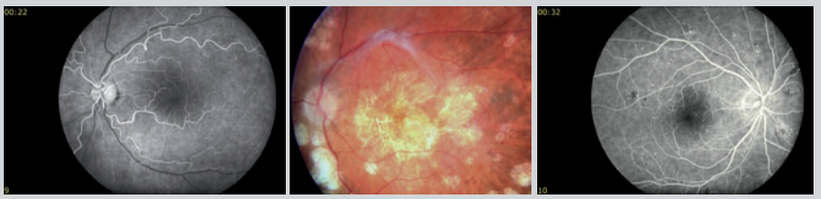
VISIT US AT THE AAO TRADE SHOW, AT BOOTH NUMBER 1721

Our Prestigious National Ophthalmology Clients reference list will be provided at your request

PM (Practice Management) Billing will keep an EYE on your Billing so you can keep an EYE on your patients.

DIGITAL IMAGING

DOES YOUR DIGITAL IMAGING SYSTEM CAPTURE IMPRESSIVE 21MP IMAGES?



FUNDUS PHOTO DOES!

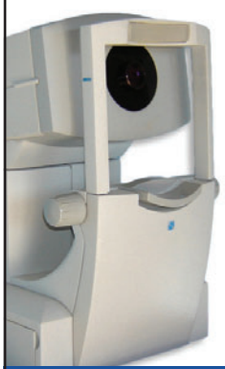
Learn more at www.itsthisgood.com 314.533.6000

EQUIPMENT

YES YOU CAN STILL GET THEM!!

Humphrey HARK 599 with Glare - Lens Analyzer 350 & 360
ECA has calibration systems, loaner and units in stock!

HUMPHREY 599 w/Glare



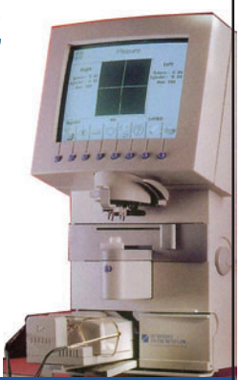
EYE CARE ALLIANCE
800-328-2020
www.eyecarealliance.com

Refurbished Units with Warranties In Stock

Full Repair and Refurbishment Services

CALL FOR A FREE ESTIMATE

LENS ANALYZER



We will also buy your HARK 599 and LA 350/360 - Call for a quote today!

PRODUCTS & SERVICES

EQUIPMENT

LASERS

PRACTICE FOR SALE

NATIONAL

NEW YORK

RECRUITMENT

INTERNATIONAL

Repeating an ad ***ENSURES*** it will be seen and remembered!

SCHWANNOMA

(Continued from page 52)

An ocular ultrasound showed a well-defined extraconal mass extending from the orbital rim to the apex superiorly.

The mass was minimally enhancing on CT of the orbits and did not demonstrate any bony erosion.

The MRI was consistent with these findings, showing a minimally enhancing mass in the superior orbit. A Humphrey Visual Field 30-2 did not show any evidence of visual field loss.

The next step in management was a biopsy of the mass, which was performed via a left anterior orbitotomy. The results were non-diagnostic.

Since the patient was asymptomatic and there were no signs of visual compromise, observation versus surgical resection was discussed with the patient and she elected for observation.

Two years later, the patient presented with left orbital pain that had worsened significantly over a 1-week period. Exam showed normal visual acuity, no afferent papillary defect, and no restriction.

However, compared with her previous exam, she had increased proptosis with Hertel measurements of 16 and 23 mm of the right and left eyes, respectively.

The patient also had new onset of decreased sensation along the left medial canthus and medial and lateral upper eyelid with intact corneal sensation, which was suggestive of extension of the mass into the superior orbital fissure, outside of the annulus of Zinn.

Repeat ocular ultrasound, CT of the orbits, and MRI of the orbits again showed a minimally enhancing mass located in the superior orbit that now extended through the superior orbital fissure. Due to concern for gradual compression and compromise of the optic nerve, the mass was removed via a left superior craniotomy.

The morphologic features of the pathology specimen were that of a schwannoma (Figure 2 on Page 57).

Physical examination did not reveal any café au lait spots, axillary or inguinal freckling, or nodules. Postoperatively, the patient initially had diplopia with upgaze that resolved within 3 months.

Schwannomas which are also known as neurilemomas—typically affect young and middle-aged adults and have a slight female predominance.

A repeat MRI of the orbits was negative for recurrence at 6 months.

DISCUSSION

Schwannomas—which are also known as neurilemomas—typically affect young and middle-aged adults and have a slight female predominance.

Although they are common peripheral nerve tumors that typically affect sensory nerves, they are infrequently found in the head and neck region and account for 1% to 4% of orbital tumors.

In decreasing order of frequency, orbital schwannomas typically affect the ophthalmic branch (V1) of the trigeminal nerve, fol-

OPHTHALMOLOGY TIMES (Print ISSN 0193-032X, Digital ISSN 2150-7333) is published semi-monthly (24 issues yearly) by Advanstar Communications Inc., 131 W First Street, Duluth, MN 55802-2065. Subscription rates: $200 for one year in the United States & Possessions, Canada and Mexico; all other countries $263 for one year. Pricing includes air-expedited service. Single copies (prepaid only): $13 in the United States & Possessions, Canada and Mexico; $20 all other countries. Back issues, if available are $25 in the U.S. $ Possessions; $30 in Canada and Mexico; $35 in all other countries. Include $6.50 per order plus $2 per additional copy for U.S. postage and handling. If shipping outside the U.S., include an additional $10 per order plus $5 per additional copy. **Periodicals postage paid** at Duluth, MN 55806 and additional mailing offices. **POSTMASTER:** Please send address changes to OPHTHALMOLOGY TIMES, P.O. Box 6009, Duluth, MN 55806-6009. Canadian G.S.T. number: R-124213133RT001, Publications Mail Agreement Number 40612608. Return undeliverable Canadian addresses to: IMEX Global Solutions PO Box 25542 London, ON N6C 6B2 CANADA. Printed in the U.S.A.

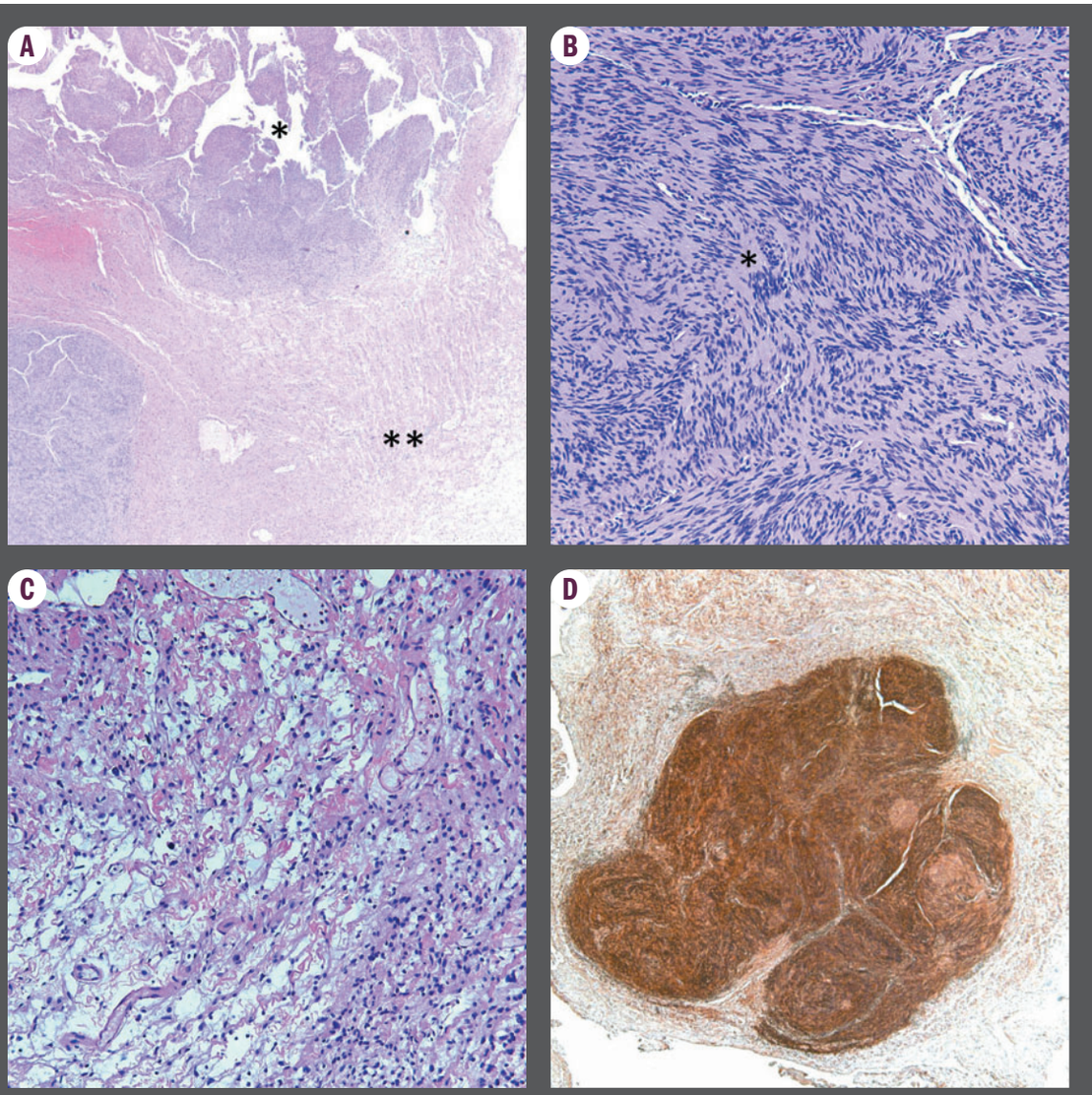


Figure 2—Schwannoma

A Hematoxylin and eosin stain at 40× magnification showing both Antoni A (single asterisk) and Antoni B (double asterisk) pattern at low power.

B Hematoxylin and eosin stain at 200× magnification demonstrating the Antoni A pattern, which appears as interlacing cords, whorls, and palisades of cells. Verocay bodies are also present (single asterisk).

C Hematoxylin and eosin stain at 200× magnification demonstrating Antoni B pattern, which appears as stellate cells within a mucoid stroma.

D Positive S-100 stain at 40× magnification demonstrating neural origin. *(Figures A to D courtesy of Sander R. Dubovy, MD)*

lowed by the supraorbital and supratrochlear nerves, and less commonly the infraorbital nerve.

Schwannomas are of neural crest origin and demonstrate proliferations of Schwann cells that are encapsulated by perineurium.

Histologically, these tumors are comprised of cells demonstrating both a dense proliferation of schwann cells in an Antoni A pattern, and also a loose proliferation of schwann cells with mucoid stroma in an Antoni B pattern (Figure 2).

They also stain positively for S-100 and vimentin.

These tumors are well-encapsulated and fusiform in shape, and are usually slow-growing and noninvasive.

Although they are considered a relatively benign lesion, they can cause pain, motor limitations, and compression of the optic nerve.

Asymptomatic lesions that are not causing visual symptoms may be observed, but surgical resection is recommended when there is risk of optic nerve compromise.

Postoperatively, patients need to be monitored at regular intervals for recurrence.

Additionally, these tumors are associated with neurofibromatosis type 1 in 2% to 18% of patients and may undergo malignant transformation.

Therefore, systemic workup is recommended in patients with orbital schwannoma.

CONCLUSION

Orbital schwannomas are relatively benign lesions and can be observed.

However, patients need regular monitoring for signs of optic nerve compression and surgical resection is recommended once vision is affected or if the patient starts exhibiting functional problems related to the mass.

References

- Cantore WA. Neural orbital tumors. *Curr Opin Ophthalmol.* 2000;11:367–571.
- Gunduz K, Shields CL, Gunalp I, Erden E, Shields JA. Orbital schwannoma: Correlation of magnetic resonance imaging and pathologic findings. *Graefes Arch Clin Exp Ophthalmol.* 2003;241:593–597.
- Rootman J, Goldberg C, Robertson W. Primary orbital schwannomas. *Br J Ophthalmol.* 1982;66:194–204.
- Yanoff M and Sassani JW. Ocular pathology. 6th edition. Mosby: China, 2009.

Have you encountered schwannoma in ophthalmic practice? Or have an interesting case study to share? Join the discussion at **Facebook.com/Ophthalmology Times.**

JETREA™
(ocriplasmin)
Intravitreal Injection, 2.5 mg/mL

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

Please see the JETREA® package insert for full Prescribing Information.

1 INDICATIONS AND USAGE
JETREA is a proteolytic enzyme indicated for the treatment of symptomatic vitreomacular adhesion.

2 DOSAGE AND ADMINISTRATION
2.1 General Dosing Information
Must be diluted before use. For single-use ophthalmic intravitreal injection only. JETREA must only be administered by a qualified physician.

2.2 Dosing
The recommended dose is 0.125 mg (0.1 mL of the diluted solution) administered by intravitreal injection to the affected eye once as a single dose.

2.3 Preparation for Administration
Remove the vial (2.5 mg/mL corresponding to 0.5 mg ocriplasmin) from the freezer and allow to thaw at room temperature (within a few minutes). Once completely thawed, remove the protective polypropylene flip-off cap from the vial. The top of the vial should be disinfected with an alcohol wipe. Using aseptic technique, add 0.2 mL of 0.9% w/v Sodium Chloride Injection, USP (sterile, preservative-free) into the JETREA vial and gently swirl the vial until the solutions are mixed.

Visually inspect the vial for particulate matter. Only a clear, colorless solution without visible particles should be used. Using aseptic technique, withdraw all of the diluted solution using a sterile #19 gauge needle (slightly tilt the vial to ease withdrawal) and discard the needle after withdrawal of the vial contents. Do not use this needle for the intravitreal injection.

Replace the needle with a sterile #30 gauge needle, carefully expel the air bubbles and excess drug from the syringe and adjust the dose to the 0.1 mL mark on the syringe (corresponding to 0.125 mg ocriplasmin). THE SOLUTION SHOULD BE USED IMMEDIATELY AS IT CONTAINS NO PRESERVATIVES. Discard the vial and any unused portion of the diluted solution after single use.

2.4 Administration and Monitoring
The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include the use of sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad spectrum microbiocide should be administered according to standard medical practice.

The injection needle should be inserted 3.5 - 4.0 mm posterior to the limbus aiming towards the center of the vitreous cavity, avoiding the horizontal meridian. The injection volume of 0.1 mL is then delivered into the mid-vitreous.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurred or decreased vision) without delay *[see Patient Counseling Information]*.

Each vial should only be used to provide a single injection for the treatment of a single eye. If the contralateral eye requires treatment, a new vial should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, and injection needles should be changed before JETREA is administered to the other eye, however, treatment with JETREA in the other eye is not recommended within 7 days of the initial injection in order to monitor the post-injection course including the potential for decreased vision in the injected eye.

Repeated administration of JETREA in the same eye is not recommended *[see Nonclinical Toxicology]*.

After injection, any unused product must be discarded.

No special dosage modification is required for any of the populations that have been studied (e.g. gender, elderly).

3 DOSAGE FORMS AND STRENGTHS
Single-use glass vial containing JETREA 0.5 mg in 0.2 mL solution for intravitreal injection (2.5 mg/mL).

4 CONTRAINDICATIONS
None

5 WARNINGS AND PRECAUTIONS
5.1 Decreased Vision
A decrease of ≥ 3 line of best corrected visual acuity (BCVA) was experienced by 5.6% of patients treated with JETREA and 3.2% of patients treated with vehicle in the controlled trials *[see Clinical Studies]*.

The majority of these decreases in vision were due to progression of the condition with traction and many required surgical intervention. Patients should be monitored appropriately *[see Dosage and Administration]*.

5.2 Intravitreal Injection Procedure Associated Effects
Intravitreal injections are associated with intraocular inflammation / infection, intraocular hemorrhage and increased intraocular pressure (IOP). In the controlled trials, intraocular inflammation occurred in 7.1% of patients injected with JETREA vs. 3.7% of patients injected with vehicle. Most of the post-injection intraocular inflammation events were mild and transient. Intraocular hemorrhage occurred in 2.4% vs. 3.7% of patients injected with JETREA vs. vehicle, respectively. Increased intraocular pressure occurred in 4.1% vs. 5.3% of patients injected with JETREA vs. vehicle, respectively.

5.3 Potential for Lens Subluxation
One case of lens subluxation was reported in a patient who received an intravitreal injection of 0.175 mg (1.4 times higher than the recommended dose). Lens subluxation was observed in three animal species (monkey, rabbit, minipig) following a single intravitreal injection that achieved vitreous concentrations of ocriplasmin 1.4 times higher than achieved with the recommended treatment dose. Administration of a second intravitreal dose in monkeys, 28 days apart, produced lens subluxation in 100% of the treated eyes *[see Nonclinical Toxicology]*.

5.4 Retinal Breaks
In the controlled trials, the incidence of retinal detachment was 0.9% in the JETREA group and 1.6% in the vehicle group, while the incidence of retinal tear (without detachment) was 1.1% in the JETREA group and 2.7% in the vehicle group. Most of these events occurred during or after vitrectomy in both groups. The incidence of retinal detachment that occurred pre-vitrectomy was 0.4% in the JETREA group and none in the vehicle group, while the incidence of retinal tear (without detachment) that occurred pre-vitrectomy was none in the JETREA group and 0.5% in the vehicle group.

5.5 Dyschromatopsia
Dyschromatopsia (generally described as yellowish vision) was reported in 2% of all patients injected with JETREA. In approximately half of these dyschromatopsia cases there were also electroretinographic (ERG) changes reported (a- and b-wave amplitude decrease).

6 ADVERSE REACTIONS
The following adverse reactions are described below and elsewhere in the labeling:

- Decreased Vision *[see Warnings and Precautions]*
- Intravitreal Injection Procedure Associated Effects *[see Warnings and Precautions and Dosage and Administration]*
- Potential for Lens Subluxation *[see Warnings and Precautions]*
- Retinal Breaks *[see Warnings and Precautions and Dosage and Administration]*

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates in one clinical trial of a drug cannot be directly compared with rates in the clinical trials of the same or another drug and may not reflect the rates observed in practice.

Approximately 800 patients have been treated with an intravitreal injection of JETREA. Of these, 465 patients received an intravitreal injection of ocriplasmin 0.125 mg (187 patients received vehicle) in the 2 vehicle-controlled studies (Study 1 and Study 2).

The most common adverse reactions (incidence 5% - 20% listed in descending order of frequency) in the vehicle-controlled clinical studies were: vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment, and retinal edema.

Less common adverse reactions observed in the studies at a frequency of 2% - < 5% in patients treated with JETREA included macular edema, increased intraocular pressure, anterior chamber cell, photophobia, vitreous detachment, ocular discomfort, iritis, cataract, dry eye, metamorphopsia, conjunctival hyperemia, and retinal degeneration.

Dyschromatopsia was reported in 2% of patients injected with JETREA, with the majority of cases reported from two uncontrolled clinical studies. In approximately half of these dyschromatopsia cases there were also electroretinographic (ERG) changes reported (a- and b-wave amplitude decrease).

6.2 Immunogenicity
As with all therapeutic proteins, there is potential for immunogenicity. Immunogenicity for this product has not been evaluated.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy: Teratogenic Effects
Pregnancy Category C. Animal reproduction studies have not been conducted with ocriplasmin. There are no adequate and well-controlled studies of ocriplasmin in pregnant women. It is not known whether ocriplasmin can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. The systemic exposure to ocriplasmin is expected to be low after intravitreal injection of a single 0.125 mg dose. Assuming 100% systemic absorption (and a plasma volume of 2700 mL), the estimated plasma concentration is 46 ng/mL. JETREA should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers
It is not known whether ocriplasmin is excreted in human milk. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when JETREA is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
In the clinical studies, 384 and 145 patients were ≥ 65 years and of these 192 and 73 patients were ≥ 75 years in the JETREA and vehicle groups respectively. No significant differences in efficacy or safety were seen with increasing age in these studies.

10 OVERDOSAGE
The clinical data on the effects of JETREA overdose are limited. One case of accidental overdose of 0.250 mg ocriplasmin (twice the recommended dose) was reported to be associated with inflammation and a decrease in visual acuity.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
No carcinogenicity, mutagenicity or reproductive and developmental toxicity studies were conducted with ocriplasmin.

13.2 Animal Toxicology and/or Pharmacology
The ocular toxicity of ocriplasmin after a single intravitreal dose has been evaluated in rabbits, monkeys and minipigs. Ocriplasmin induced an inflammatory response and transient ERG changes in rabbits and monkeys, which tended to resolve over time. Lens subluxation was observed in the 3 species at ocriplasmin concentrations in the vitreous at or above 41 mcg/mL, a concentration 1.4-fold above the intended clinical concentration in the vitreous of 29 mcg/mL. Intraocular hemorrhage was observed in rabbits and monkeys.

A second intravitreal administration of ocriplasmin (28 days apart) in monkeys at doses of 75 mcg/eye (41 mcg/mL vitreous) or 125 mcg/eye (68 mcg/mL vitreous) was associated with lens subluxation in all ocriplasmin treated eyes. Sustained increases in IOP occurred in two animals with lens subluxation. Microscopic findings in the eye included vitreous liquefaction, degeneration/disruption of the hyaloideo-capsular ligament (with loss of ciliary zonular fibers), lens degeneration, mononuclear cell infiltration of the vitreous, and vacuolation of the retinal inner nuclear cell layer. These doses are 1.4-fold and 2.3-fold the intended clinical concentration in the vitreous of 29 mcg/mL, respectively.

14 CLINICAL STUDIES
The efficacy and safety of JETREA was demonstrated in two multicenter, randomized, double masked, vehicle-controlled, 6 month studies in patients with symptomatic vitreomacular adhesion (VMA). A total of 652 patients (JETREA 464, vehicle 188) were randomized in these 2 studies. Randomization was 2:1 (JETREA:vehicle) in Study 1 and 3:1 in Study 2.

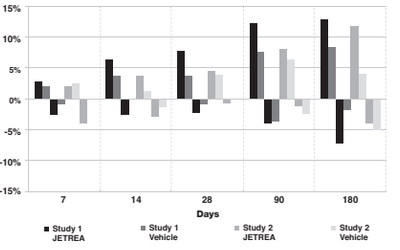
Patients were treated with a single injection of JETREA or vehicle. In both of the studies, the proportion of patients who achieved VMA resolution at Day 28 (i.e., achieved success on the primary endpoint) was significantly higher in the ocriplasmin group compared with the vehicle group through Month 6.

The number of patients with at least 3 lines increase in visual acuity was numerically higher in the ocriplasmin group compared to vehicle in both trials, however, the number of patients with at least a 3 lines decrease in visual acuity was also higher in the ocriplasmin group in one of the studies (Table 1 and Figure 1).

Table 1: Categorical Change from Baseline in BCVA at Month 6, Irrespective of Vitrectomy (Study 1 and Study 2)

Study 1			
	JETREA	Vehicle	Difference
	N=219	N=107	(95% CI)
≥ 3 line Improvement in BCVA			
Month 6	28 (12.8%)	9 (8.4%)	4.4 (-2.5, 11.2)
> 3 line Worsening in BCVA			
Month 6	16 (7.3%)	2 (1.9%)	5.4 (1.1, 9.7)
Study 2			
	JETREA	Vehicle	Difference
	N=245	N=81	(95% CI)
≥ 3 line Improvement in BCVA			
Month 6	29 (11.8%)	3 (3.8%)	8.1 (2.3, 13.9)
> 3 line Worsening in BCVA			
Month 6	10 (4.1%)	4 (5.0%)	-0.9 (-6.3, 4.5)

Figure 1: Percentage of Patients with Gain or Loss of ≥ 3 Lines of BCVA at Protocol-Specified Visits



16 HOW SUPPLIED/STORAGE AND HANDLING
Each vial of JETREA contains 0.5 mg ocriplasmin in 0.2 mL citric-buffered solution (2.5 mg/mL). JETREA is supplied in a 2 mL glass vial with a latex free rubber stopper. Vials are for single use only.

Storage
Store frozen at or below -4°F (-20°C). Protect the vials from light by storing in the original package until time of use.

17 PATIENT COUNSELING INFORMATION
In the days following JETREA administration, patients are at risk of developing intraocular inflammation/infection. Advise patients to seek immediate care from an ophthalmologist if the eye becomes red, sensitive to light, painful, or develops a change in vision *[see Warnings and Precautions]*.

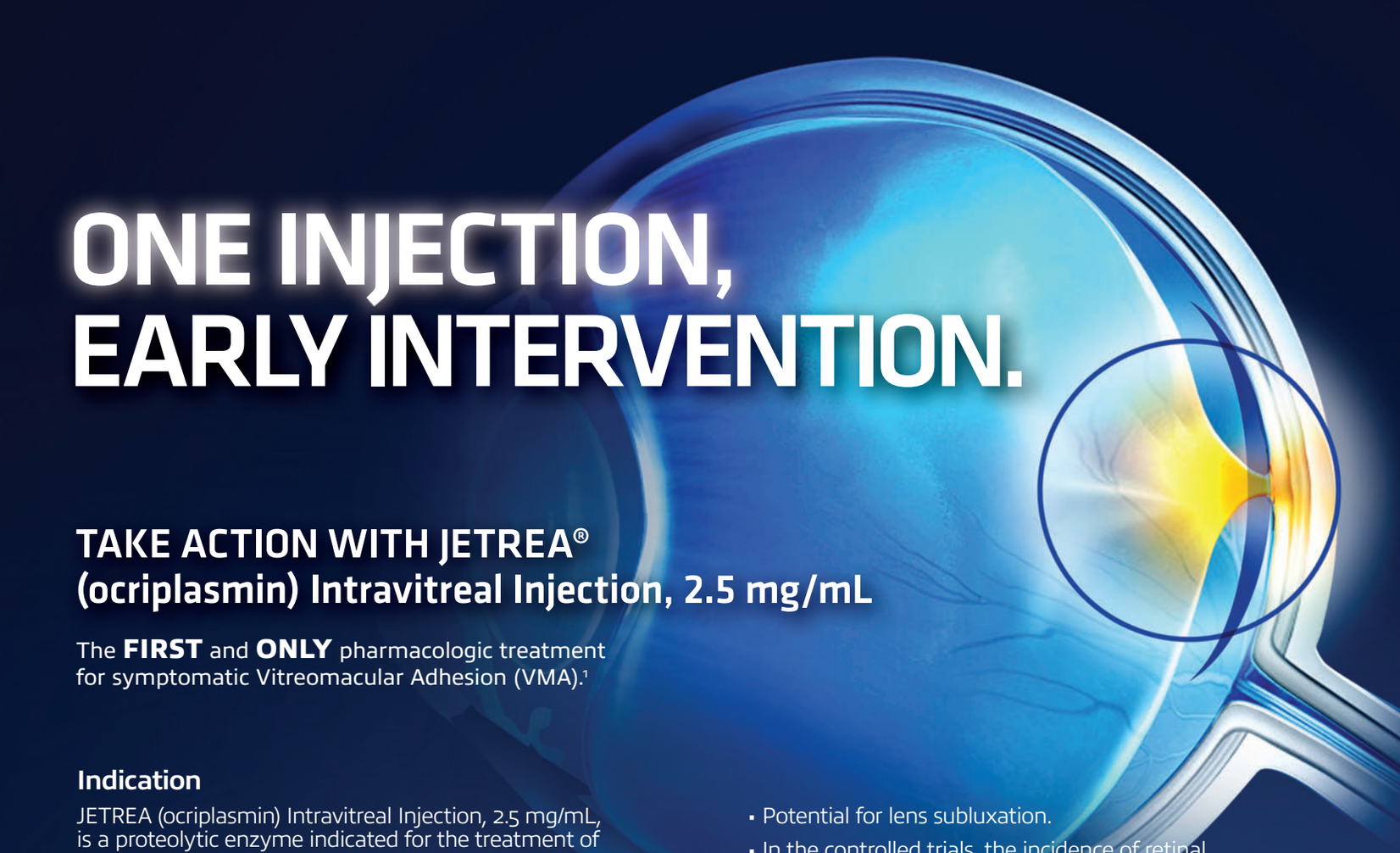
Patients may experience temporary visual impairment after receiving an intravitreal injection of JETREA *[see Warnings and Precautions]*. Advise patients to not drive or operate heavy machinery until this visual impairment has resolved. If visual impairment persists or decreases further, advise patients to seek care from an ophthalmologist.

Manufactured for:
ThromboGenics, Inc.
101 Wood Avenue South, 6th Floor
Iselin, NJ 08830

U.S. License Number: 1866

Version 1.0
Initial U.S. Approval: 2012
ThromboGenics U.S. patents: 7,445,775; 7,547,435; 7,914,783 and other pending patents.

05/13 OCRVMA0072 PI G



ONE INJECTION, EARLY INTERVENTION.

TAKE ACTION WITH JETREA®
(ocriplasmin) Intravitreal Injection, 2.5 mg/mL

The **FIRST** and **ONLY** pharmacologic treatment for symptomatic Vitreomacular Adhesion (VMA).[1]

Indication

JETREA (ocriplasmin) Intravitreal Injection, 2.5 mg/mL, is a proteolytic enzyme indicated for the treatment of symptomatic vitreomacular adhesion.

Important Safety Information

Warnings and Precautions

- A decrease of ≥ 3 lines of best-corrected visual acuity (BCVA) was experienced by 5.6% of patients treated with JETREA and 3.2% of patients treated with vehicle in the controlled trials. The majority of these decreases in vision were due to progression of the condition with traction and many required surgical intervention. Patients should be monitored appropriately.
- Intravitreal injections are associated with intraocular inflammation/infection, intraocular hemorrhage and increased intraocular pressure (IOP). Patients should be monitored and instructed to report any symptoms without delay. In the controlled trials, intraocular inflammation occurred in 7.1% of patients injected with JETREA vs 3.7% of patients injected with vehicle. Most of the post-injection intraocular inflammation events were mild and transient. If the contralateral eye requires treatment with JETREA, it is not recommended within 7 days of the initial injection in order to monitor the post-injection course in the injected eye.
- Potential for lens subluxation.
- In the controlled trials, the incidence of retinal detachment was 0.9% in the JETREA group and 1.6% in the vehicle group, while the incidence of retinal tear (without detachment) was 1.1% in the JETREA group and 2.7% in the vehicle group. Most of these events occurred during or after vitrectomy in both groups.
- Dyschromatopsia (generally described as yellowish vision) was reported in 2% of all patients injected with JETREA. In approximately half of these dyschromatopsia cases there were also electroretinographic (ERG) changes reported (a- and b-wave amplitude decrease).

Adverse Reactions

- The most commonly reported reactions (≥ 5%) in patients treated with JETREA were vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment, and retinal edema.

VISIT **JETREACARE.COM** FOR REIMBURSEMENT AND ORDERING INFORMATION

LEARN MORE AT JETREA.COM

Please see Brief Summary of full Prescribing Information on adjacent page.

ThromboGenics®

JETREA™
(ocriplasmin)
Intravitreal Injection, 2.5 mg/mL

Reference: 1. JETREA [package insert]. Iselin, NJ: ThromboGenics, Inc.; 2012.

05/13 OCRVMA0072 JA1 G

References
1. Christensen MT, Blackie CA, Korb DR, et al. An evaluation of the performance of a novel lubricant eye drop. Poster D692 presented at: The Association for Research in Vision and Ophthalmology Annual Meeting; May 2-6, 2010; Fort Lauderdale, FL. **2.** Davitt WF, Bloomenstein M, Christensen M, et al. Efficacy in patients with dry eye after treatment with a new lubricant eye drop formulation. *J Ocul Pharmacol Ther.* 2010;26(4):347-353. **3.** Data on file, Alcon. **4.** Wojtowica JC., et al. Pilot, Prospective, Randomized, Double-masked, Placebo-controlled Clinical Trial of an Omega-3 Supplement for Dry Eye. *Cornea* 2011:30(3) 308-314. **5.** Geerling G., et al. The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on Management and Treatment of Meibomian Gland Dysfunction. IOVS 2011:52(4).

Systane® Family of Products

Surface Protection and More

Alcon®
a Novartis company

 10/12 SYS13100JAD