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Ophthalmology Times

CLINICAL NEWS & ANALYSIS

SPECIAL REPORT
ADVANCES IN GLAUCOMA

MYOPIC LASIK WFG ABLATIONS
+ POINT/COUNTERPOINT 'IDEAL' DME THERAPY

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Editorial

THE ELEMENTS OF SUCCESS

By Peter J. McDonnell, MD

The country of Brazil has changed dramatically in the past two decades. After emerging from a military government, successive democratically elected governments have overseen dramatic economic growth—Brazil is 5th or 6th in terms of gross domestic product—with an unemployment rate lower than the United States, plus the emergence of an extremely large middle class. With this success comes greater demand for health-care services.

My friend, Mauro, is an ophthalmologist in the largest city (by population) in the Western Hemisphere.

*(See story on page 4 : **Editorial**)*

Cataract

3 STRATEGIES FOR TRAUMATIC CATARACT

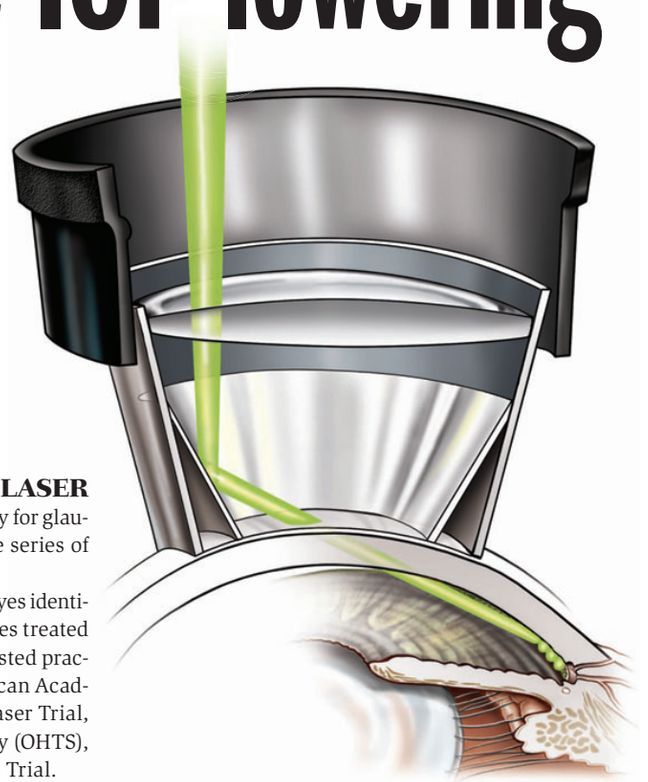
DURHAM, NC :: **MANAGING TRAUMATIC CATARACTS** in children requires attention to three issues when implanting an IOL: the timing of the implantation, the lens type, and the IOL calculations, said Edward G. Buckley MD. However, there are several controversies regarding IOL implantation in children.

*(See story on page 30 : **Traumatic**)*

SLT as standard for first-line IOP lowering

Large retrospective analysis supports approach for reducing pressure with durable benefit

By Cheryl Guttman Krader;
Reviewed by Lawrence F. Jindra, MD



NEW YORK :: **THE SUCCESS OF SELECTIVE LASER** trabeculoplasty (SLT) as a primary therapy for glaucoma is supported by a review of a large series of eyes with long-term follow-up.

The analysis included data from 1,983 eyes identified from a consecutive series of 4,048 eyes treated with SLT over a period of 10 years. Suggested practice guidelines were used from the American Academy of Ophthalmology, the Glaucoma Laser Trial, the Ocular Hypertension Treatment Study (OHTS), and the Early Management of Glaucoma Trial.

All patients had a minimum follow-up of 2 months. Average follow-up for the 1,983 eyes was 917 days.

Mean IOP was 18.1 mm Hg prior to SLT, and it decreased to 12.8 mm Hg (–29%) at last follow-up.

*(Continues on page 21 : **SLT**)*

Applications for SLT therapy

Selective laser trabeculoplasty (SLT) is a highly effective approach for first-line glaucoma therapy. It is also effective as adjunct therapy with drugs, and as alternative therapy when drugs or surgery fail. Most importantly, SLT enables ophthalmologists to manage patients' glaucoma treatment without the compliance issues and side effects associated with drug therapy.

(Figure courtesy of Ellex)

Proven Technology. Proven Results.

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2500+ of your colleagues can't be wrong. Choose SLT technology from Ellex.

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Offering superior energy control, a sharp-edged aiming beam and the fastest firing rate at 3 shots per second, Ellex's proprietary SLT technology allows you to visualise the TM in greater detail, perform procedures faster and with improved accuracy – delivering better patient outcomes.

*JA. Donnelly, EM. Miglino, Jindra LF. Selective Laser Trabeculoplasty as Primary Therapy in Patients With Glaucoma: Ten-Year Experience. Poster presented at: American Society of Cataract and Refractive Surgeons (ASCRS); 2013, San Francisco.

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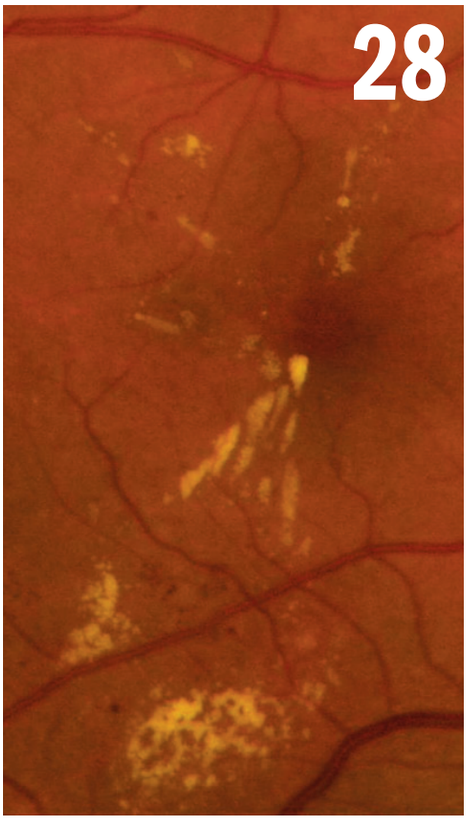

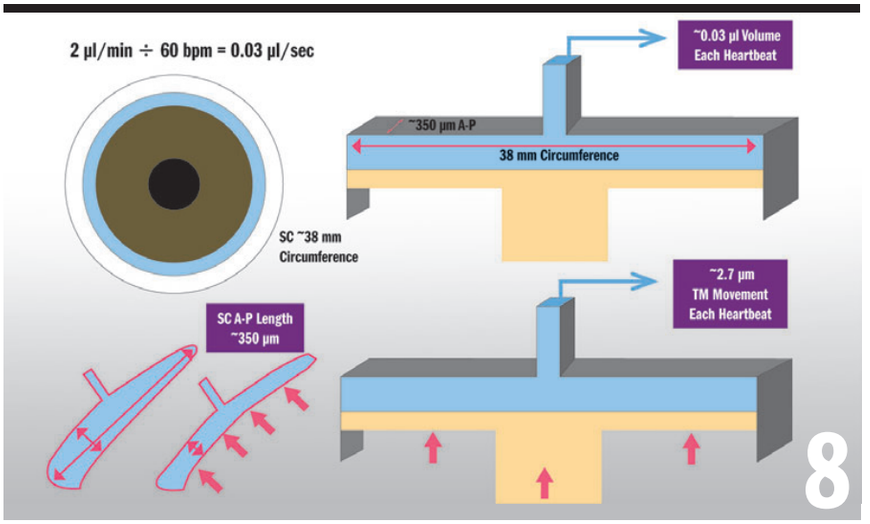

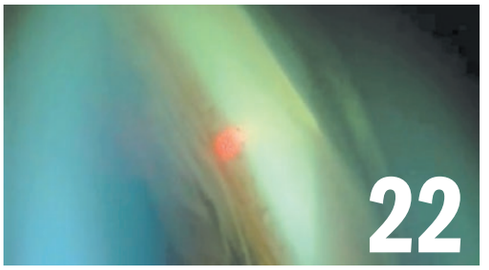

Neuro-Ophthalmology

Retina

Cataract

Refractive

Practice Management

Special Report GLAUCOMA

The elements of success

Technology may be important, but employees are the real key

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*.

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"I am not led. I lead."
—Motto of the city of São Paulo, Brazil

THE COUNTRY OF BRAZIL has changed dramatically in the past two decades. After emerging from a military government, successive democratically elected governments have overseen dramatic economic growth—Brazil is 5th or 6th in terms of gross domestic product—with an unemployment rate lower than the United States, plus the emergence of an extremely large middle class. With this success comes greater demand for health-care services.

My friend, Mauro, is an ophthalmologist in the largest city (by population) in the Western Hemisphere. In 2010, he opened the first large eye hospital in this city of 16 million-plus people. By all measures, this hospital has been a great success.

From 2010 to 2012, surgeries increased by 68%, emergency referrals by 600%, routine exams by 376%, and ophthalmologists using the hospital grew from 13 in 2010 to 198 in 2012. Any eye hospital in the United States would be delighted with such numbers.

Among Mauro's elements of success:

- **Assembly-line efficiency**
- **Strict quality norms**
- **Brand recognition**
- **Standardization**
- **Consistency**
- **Ruthless cost control**
- **Economies of scale that accompany high volume**

"What is the key element that explains your success?" I asked my friend.

"Having the best technology is important," he said, "but the real key is having the best people."

INVESTING IN EMPLOYEES

Mauro has devoted a lot of attention to attracting and retaining the best employees for his hospital. He has a formal orientation program to train employees as they join, and continuing education for everyone. Every employee is to have a career plan within the organization.

The educational programs are intended not simply to enhance the skill level of employees, but also to help them feel that they are engaging in personal development.

"Our goal is not to get them to perform a little better, but to encourage critical thinking and problem solving," he said.

Educational programs must have excellent trainers, mix employees from different areas of the hospital, be less than 2 hours in length, and be formally assessed and improved with time.

Trainers are required to make sure their sessions are informative, interesting, and participatory. Teamwork is emphasized.

Mauro regularly measures employee satisfaction to determine the effectiveness of various employee development and retention initiatives.

In his research of the literature, he finds that an overall satisfaction score of 45% is considered quite high, and his hospital has exceeded this with a score of 65%.

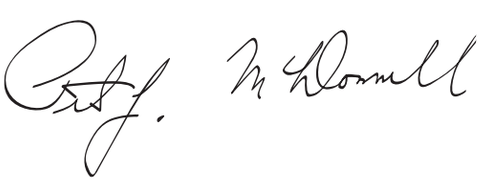
Also, he has found that employee satisfaction scores are correlated with age. Employees aged fewer than 30 years consistently report lower satisfaction scores than do older workers.

In the largest country of South America, as in the largest of North America, there is the belief that younger people—and younger physicians—have a different approach to work and work-life balance. People in Mauro's position must recognize and respond to that reality.

LESSONS TO LEARN

What can we ophthalmologists in the wealthiest country in the Western Hemisphere learn from the success of ophthalmic institutions in other countries with different cultures, histories, and degrees of wealth? A great deal, I believe.

As downward pressure on health-care reimbursement continues in the United States, the institutions that survive and thrive will be the ones that adopt many of Mauro's strategies. ■



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Ophthalmology Times *Mission Statement*

*Ophthalmology Time*s is a physician-driven publication that disseminates news and information of a clinical, socioeconomic, and political nature in a timely and accurate manner for members of the ophthalmic community.

In partnership with our readers, we will achieve mutual success by:

- Being a forum for ophthalmologists to communicate their clinical knowledge, insights, and discoveries.
- Providing management information that allows ophthalmologists to improve and expand their practices.
- Addressing political and socioeconomic issues that may either assist or hinder the ophthalmic community, and reporting those issues and their potential outcomes to our readers.

In Brief

In memoriam

GLAUCOMA RESEARCHER DR. BERNARD BECKER DIES

ST. LOUIS :: **BERNARD BECKER, MD,** chairman of the ophthalmology department at the Washington University School of Medicine in St. Louis for 35 years, has died.

Dr. Becker, 93, passed away Aug. 28 at his home in St. Louis after a battle with lung cancer.


Dr. Becker

Dr. Becker was known for discovering one of the first treatments for glaucoma—a drug called acetazolamide used to decrease pressure in the brain. He determined the drug could also be used to decrease pressure in the eyes.

From 1953 to 1988, Dr. Becker helped Washington University build its Department of Ophthalmology and Visual Arts. He was also one of the founders of the Association for Research in Vision and Ophthalmology, and helped establish the National Eye Institute.

In 1995, Washington University renamed its medical library in his honor.

Dr. Becker grew up in Brooklyn, NY, and graduated from Princeton University and Harvard Medical School. He was also an army psychiatrist during World War II.

Following the war, Dr. Becker trained in ophthalmology at Johns Hopkins University.

Dr. Becker has received many awards, including the American Academy of Ophthalmology's highest honor. He has also co-written the first two editions of "Diagnosis and Therapy of the Glaucomas."

Washington University is planning a memorial service for Dr. Becker, who donated his body to the university's school of medicine.

Aflibercept indication

REGENERON INJECTION GAINS EUROPEAN APPROVAL

TARRYTOWN, NY :: **REGENERON PHARMACEUTICALS'** new treatment for visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO) has been approved by the European Commission.

Aflibercept (Eylea) was approved in the United States for the treatment of neovascular (wet) age-related macular degeneration (AMD) in 2011, and for macular edema following CRVO in 2012.

"We are pleased with the approval of (aflibercept) in the European Union in a second indication," said George D. Yancopoulos, MD, PhD, chief scientific officer of Regeneron and president of Regeneron Laboratories. "Our phase III studies showed that (aflibercept) improved visual outcomes significantly. . . . This additional approval of (aflibercept) is great news for patients in Europe."

Aflibercept has also been approved in Europe, Japan, Australia, and in several other countries for use in wet AMD and in selected countries in South American for macular edema following CRVO.

CLARIFICATION The first installment of the new "Gloves Off with Gulani" series will begin in the Oct. 1 issue of *Ophthalmology Times.* Missed the series introduction? Go to *http://bit.ly/15memRo.*

HEADLINES YOU MIGHT HAVE MISSED

AS SEEN IN *Ophthalmology Times*' weekly eReport. Sign up at *http://www.modernmedicine.com/OphthalmologyTimes/enewssignup*

CMS CLEARS RETINAL PROSTHESIS SYSTEM

SECOND SIGHT MEDICAL PRODUCTS' retinal prosthesis system has been approved by the Centers for Medicare and Medicaid Services for both inpatient and outpatient settings of care payments beginning Oct. 1.
http://bit.ly/14gaM8H

INSITE VISION EARNS PATENT ISSUANCE

INSITE VISION INC.'S DRUG DELIVERY SYSTEM has received a patent from the U.S. Patent and Trademark Office. The patent will provide utility-composition of matter protection until 2029 for InSite Vision's DuraSite 2 for both its delivery system and drugs.
http://bit.ly/1anYtLa

VMA TREATMENT OK'D IN CANADA

HEALTH CANADA HAS CLEARED ThromboGenics NV's treatment for symptomatic vitreomacular adhesion. Canada is now the first market where ocriplasmin (Jetrea) is approved outside the United States and Europe.
http://bit.ly/12lU5r8

On Twitter

Recent hashtags *Ophthalmology Times* has used on **twitter.com/OphthTimes**

#ophthalmology
#eyecare
#astigmatism
#retina
#AMD
#myopia
#eyehealth
#cataract
#dryeye
#dispensing
#optical
#AMD

Digital App

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

Video

See how an iPhone can be used in place of a traditional slit lamp camera. Go to *http://bit.ly/15mzBCL*

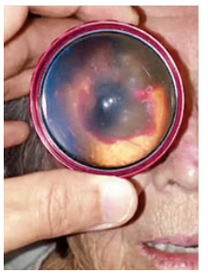

Photo of Dr. Becker courtesy of the American Academy of Ophthalmology

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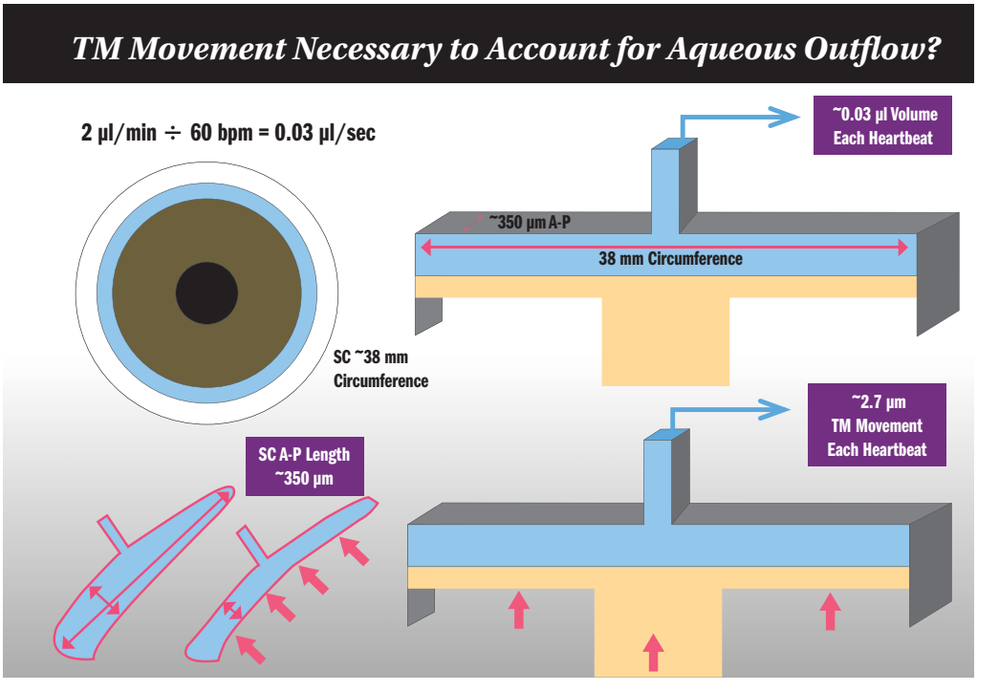
EXPRESS®
Glaucoma Filtration Device

CAUTION: Federal law restricts this device to sale by or on the order of a physician.
INDICATION: The EX-PRESS® Glaucoma Filtration Device is intended to reduce intraocular pressure in glaucoma patients where medical and conventional surgical treatments have failed.
GUIDANCE REGARDING THE SELECTION OF THE APPROPRIATE VERSION: Prior clinical studies were not designed to compare between the various versions of the EX-PRESS® Glaucoma Filtration Device. The selection of the appropriate version is according to the doctor's discretion.
CONTRAINDICATIONS: The use of this device is contraindicated if one or more of the following conditions exist:
- Presence of ocular disease such as uveitis, ocular infection, severe dry eye, severe blepharitis.
- Pre-existing ocular or systemic pathology that, in the opinion of the surgeon, is likely to cause postoperative complications following implantation of the device.
- Patients diagnosed with angle closure glaucoma.

WARNINGS/PRECAUTIONS:
- The surgeon should be familiar with the instructions for use.
- The integrity of the package should be examined prior to use and the device should not be used if the package is damaged and sterility is compromised.
- This device is for single use only.
- MRI of the head is permitted, however not recommended, in the first two weeks post implantation.

ATTENTION: Reference the Directions for Use labeling for a complete listing of indications, warnings, precautions, complications and adverse events.



(FIGURE 1) **Aqueous outflow from Schlemm's canal (SC) is pulsatile, being dependent on trabecular meshwork (TM) motion with optical coherence tomography measurements indicating the TM motion is adequate to account for all of aqueous outflow. (A-P is anterior-posterior SC length.** *(Figure courtesy of Murray Johnstone, MD)*

A NON-INVASIVE LOOK AT TRABECULAR MESHWORK

How novel OCT platform detects and measures motion, may advance glaucoma research and patient care

By Cheryl Guttman Krader; *Reviewed by Murray Johnstone, MD*

take-home

- **An investigational non-invasive imaging tool—phase-sensitive optical coherence tomography—can be used to detect and measure movement of the trabecular meshwork in vivo.**

SEATTLE ::

Phase-sensitive optical coherence tomography (PhS-OCT) for in vivo evaluation is a promising tool for advancing glaucoma research and patient care, according to findings from a human study presented by Murray Johnstone, MD.

The investigational device—developed by Ruikang Wang, PhD, professor of bioengineering, University of Washington, Seattle—has resolution at the nanometer scale and moves OCT technology, which is limited to structural imaging, to a new realm involving characterization of motion and function.

PhS-OCT was highly sensitive for detecting trabecular meshwork motion, according to results of an initial laboratory study involving enucleated primate eyes. The study also showed the tissue movement correlated to a simulated cardiac pulse with amplitude trabecular motion sufficient to account for aqueous outflow.

EXAMINING THE HUMAN STUDY

A second study using PhS-OCT was then conducted in 10 human adults to investigate pulse-induced trabecular meshwork motion, said Dr. Johnstone, clinical professor of ophthalmology, University of Washington.


Dr. Johnstone

As in the animal study, PhS-OCT was highly sensitive for detecting trabecular meshwork motion.

Analyses of the trabecular meshwork tissue motion wave, in relation to the digital pulsimetry wave, showed a high correlation between trabecular meshwork wave minima and digital pulse peaks. The research also showed PhS-OCT could be used to measure velocity of the trabecular meshwork motion and the strain rate.

"This technology opens a new window into understanding abnormalities of trabecular meshwork biomechanics leading to glaucoma," Dr. Johnstone said. "It will eventually revolutionize our approaches to glaucoma management."

EVALUATING NEED FOR TRABECULAR MESHWORK

Interest in developing technology for evaluating trabecular meshwork motion derives from revised concepts about aqueous outflow and resistance.

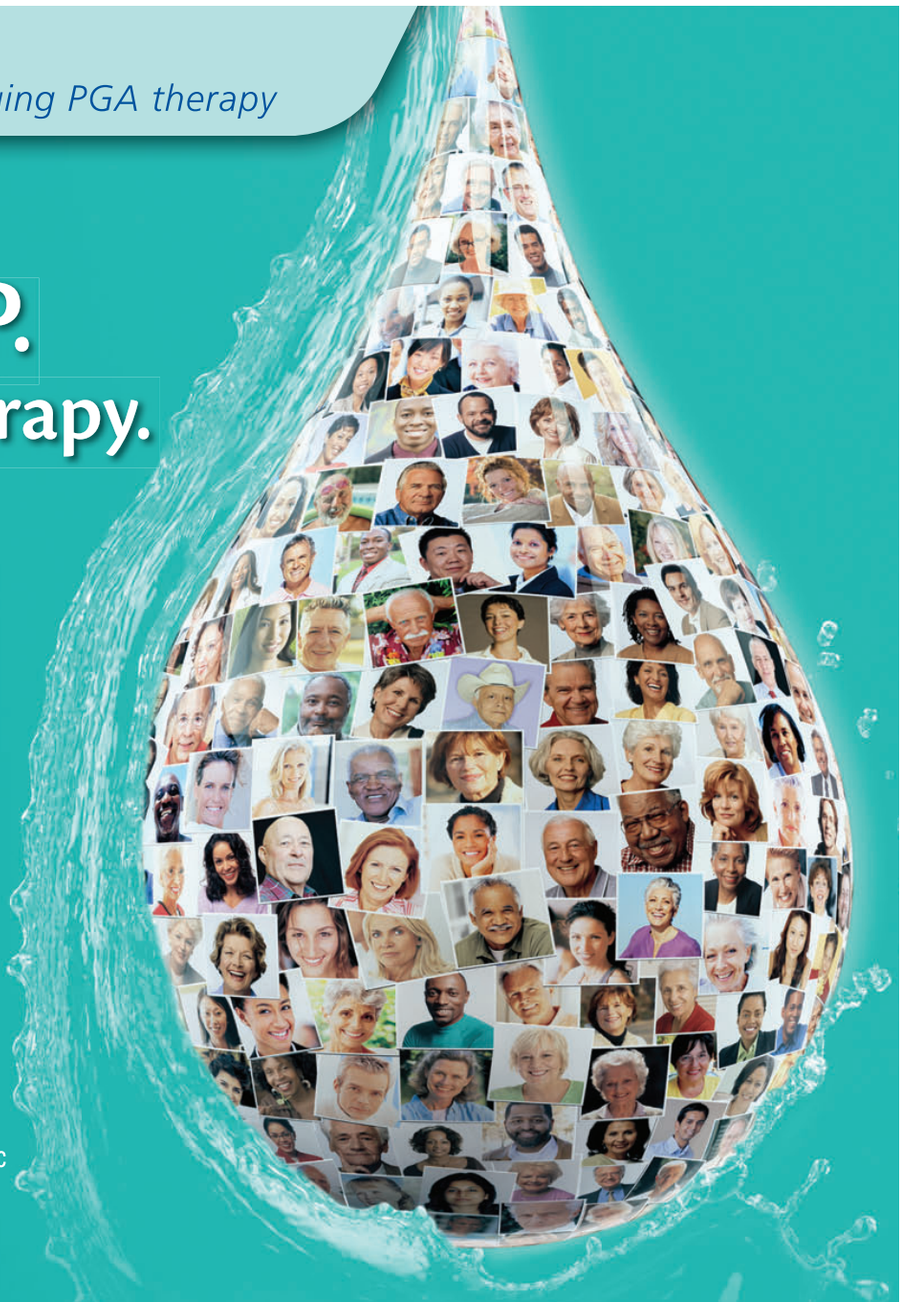
Whereas initial work by Morton Grant, MD, posited that the trabecular meshwork acted as a rigid, restrictive filter creating resistance, additional research demonstrated that the tissue was highly compliant. This indicated that movement of the trabecular meshwork becomes appositional with the external wall of Schlemm's canal and represented the most important source of resistance.

Findings from histological studies provided support for this concept, but direct evidence of trabecular meshwork motion in vivo was lacking until the development of PhS-OCT.

Continues on page 15 : ***Non-invasive***

For patients starting or changing PGA therapy

Drop IOP.
Keep monotherapy.



Indication: LUMIGAN® (bimatoprost ophthalmic solution) 0.01% is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Important Safety Information

Warnings and Precautions: LUMIGAN® causes changes to pigmented tissues, mostly increased pigmentation of the iris, eyelid, and eyelashes as long as LUMIGAN® is administered. Iris color change may not be noticeable for several months to years. After discontinuation of bimatoprost, iris pigmentation is likely to be permanent, while eyelid and eyelash changes have been reported to be reversible in some patients. Patients should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

LUMIGAN® should be used with caution in patients with active intraocular inflammation (eg, uveitis) because the inflammation may be exacerbated. Macular edema, including cystoid macular edema, has been reported with LUMIGAN®. LUMIGAN® should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Adverse Reactions: The most common (25%-45%) adverse event with LUMIGAN® was conjunctival hyperemia. Approximately 0.5% to 3% of patients discontinued therapy due to conjunctival hyperemia. Other common events (> 10%) included growth of eyelashes and ocular pruritus.

Please see Brief Summary of the full Prescribing Information on adjacent page.

Write it RIGHT 0.01%

LUMIGAN® 0.01%
(bimatoprost ophthalmic solution) 0.01%

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(bimatoprost ophthalmic solution)

Brief Summary—Please see the LUMIGAN® 0.01% and 0.03% package insert for full Prescribing Information.

INDICATIONS AND USAGE

LUMIGAN® 0.01% and 0.03% (bimatoprost ophthalmic solution) is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Pigmentation: Bimatoprost ophthalmic solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as bimatoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of bimatoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes: LUMIGAN® 0.01% and 0.03% may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation: LUMIGAN® 0.01% and 0.03% should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost ophthalmic solution. **LUMIGAN®** 0.01% and 0.03% should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Angle-closure, Inflammatory, or Neovascular Glaucoma: LUMIGAN® 0.01% and 0.03% has not been evaluated for the treatment of angle-closure, inflammatory or neovascular glaucoma.

Bacterial Keratitis: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use With Contact Lenses: Contact lenses should be removed prior to instillation of **LUMIGAN®** 0.01% and 0.03% and may be reinserted 15 minutes following its administration.

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 rates in the clinical studies of another drug and may not reflect the rates observed in practice.

In clinical studies with bimatoprost ophthalmic solutions (0.01% or 0.03%) the most common adverse reaction was conjunctival hyperemia (range 25%–45%). Approximately 0.5% to 3% of patients discontinued therapy due to conjunctival hyperemia with 0.01% or 0.03% bimatoprost ophthalmic solutions. Other common reactions (>10%) included growth of eyelashes, and ocular pruritus.

Additional ocular adverse reactions (reported in 1 to 10% of patients) with bimatoprost ophthalmic solutions included ocular dryness, visual disturbance, ocular burning, foreign body sensation, eye pain, pigmentation of the periocular skin, blepharitis, cataract, superficial punctate keratitis, periorbital erythema, ocular irritation, eyelash darkening, eye discharge, tearing, photophobia, allergic conjunctivitis, asthenopia, increases in iris pigmentation, conjunctival edema, conjunctival hemorrhage, and abnormal hair growth. Intraocular inflammation, reported as iritis, was reported in less than 1% of patients.

Systemic adverse reactions reported in approximately 10% of patients with bimatoprost ophthalmic solutions were infections (primarily colds and upper respiratory tract infections). Other systemic adverse reactions (reported in 1 to 5% of patients) included headaches, abnormal liver function tests, and asthenia.

Postmarketing Experience: The following reactions have been identified during postmarketing use of **LUMIGAN®** 0.01% and 0.03% 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 **LUMIGAN®** or a combination of these factors, include: dizziness, eyelid edema, hypertension, nausea, and periorbital and lid changes associated with a deepening of the eyelid sulcus.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C

Teratogenic effects: In embryo/fetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 33 or 97 times, respectively, the maximum intended human exposure based on blood AUC levels.

At doses at least 41 times the maximum intended human exposure based on blood AUC levels, the gestation length was reduced in the dams, the incidence of dead fetuses, late resorptions, peri- and postnatal pup mortality was increased, and pup body weights were reduced.

There are no adequate and well-controlled studies of **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) administration in pregnant women. Because animal reproductive studies are not always predictive of human response **LUMIGAN®** should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether **LUMIGAN®** 0.01% and 0.03% is excreted in human milk, although in animal studies, bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when **LUMIGAN®** is administered to a nursing woman.

Pediatric Use: Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

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

Hepatic Impairment: In patients with a history of liver disease or abnormal ALT, AST and/or bilirubin at baseline, bimatoprost 0.03% had no adverse effect on liver function over 48 months.

OVERDOSAGE

No information is available on overdosage in humans. If overdose with **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) occurs, treatment should be symptomatic.

In oral (by gavage) mouse and rat studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m2 is at least 70 times higher than the accidental dose of one bottle of **LUMIGAN®** 0.03% for a 10 kg child.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage at doses of up to 2 mg/kg/day and 1 mg/kg/day respectively (at least 192 and 291 times the recommended human exposure based on blood AUC levels respectively) for 104 weeks.

Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the *in vivo* mouse micronucleus tests.

Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day (at least 103 times the recommended human exposure based on blood AUC levels).

PATIENT COUNSELING INFORMATION

Potential for Pigmentation: Patients should be advised about the potential for increased brown pigmentation of the iris, which may be permanent. Patients should also be informed about the possibility of eyelid skin darkening, which may be reversible after discontinuation of **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution).

Potential for Eyelash Changes: Patients should also be informed of the possibility of eyelash and vellus hair changes in the treated eye during treatment with **LUMIGAN®** 0.01% and 0.03%. These changes may result in a disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are usually reversible upon discontinuation of treatment.

Handling the Container: Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When to Seek Physician Advice: Patients should also be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of **LUMIGAN®** 0.01% and 0.03%.

Use with Contact Lenses: Patients should be advised that **LUMIGAN®** 0.01% and 0.03% contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of **LUMIGAN®** and may be reinserted 15 minutes following its administration.

Use with Other Ophthalmic Drugs: Patients should be advised that if more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

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Controlling circadian IOP fluctuation

Neurons may offer novel glaucoma therapeutic target, animal study results show

By Cheryl Guttman Krader; *Reviewed by Brian C. Samuels, MD, PhD*

INDIANAPOLIS ::

A POSSIBLE ROLE FOR a specific type of hypothalamic neuron in mediating circadian variations in IOP has been identified, according to research findings presented by Brian C. Samuels, MD, PhD.

Dr. Samuels

The study, which was conducted in an animal model, was approached from the perspective that the condition is a neurologic disease, rather than one involving only the eye. The focus was on the effects of neurons containing orexin neuropeptides located in the dorsomedial/periformical hypothalamus (DMH/PeF).

Chemical stimulation of this region of the hypothalamus results in increases in heart rate, blood pressure, IOP, intracranial pressure (ICP), and the translaminar pressure gradient, said Dr. Samuels, assistant professor of ophthalmology, Indiana University School of Medicine, Indianapolis.

take-home

- **Research shows circadian variations in IOP can be regulated by orexin-containing neurons located in the hypothalamus.**

EXAMINING THE STUDY

Knowing that the DMH/PeF is rich in orexin-containing neurons that have been shown to regulate circadian rhythmicity of various physiological processes—and that IOP displays circadian patterns—it was investigated to find if orexin-containing neurons may also regulate circadian fluctuations in IOP and ICP.

For the study, responses to chemical stimulation of the hypothalamus were evaluated when animals were pre-treated with an orexin receptor antagonist or vehicle control.

Increases in IOP were found and ICP induced by chemical stimulation were significantly attenuated by orexin receptor antagonist pretreatment in a dose-dependent fashion.

Vital sign monitoring showed no attenuation of the increases in the animals' heart rate or blood pressure.

"We are excited about these initial findings, considering fluctuation in IOP is a known independent risk factor for glaucoma progression and because recent work has shown an aberrancy in the translaminar gradient in patients with glaucoma," Dr. Samuels said.

"However, additional research is needed to establish the efficacy and safety of orexin antagonists as a clinical approach to stabilizing IOP, ICP, and the translaminar pressure gradient," he said.

The orexin antagonist used in the study was supplied by Merck and is a derivative of a compound that has been investigated as a treatment for insomnia in a phase III study.

Because there is already clinical trial data demonstrating an acceptable safety profile for orexin receptor antagonists—together with their oral mode of administration—enhance interest in investigating this class of drugs as novel therapy for glaucoma.

"The availability of human safety data makes an orexin antagonist well-positioned for entering clinical trials as a potential treatment for glaucoma, assuming there are positive efficacy findings from further animal studies," Dr. Samuels said. "Considering how poorly patients [with glaucoma] comply with use of their topical medications, perhaps an orally administered drug would be beneficial."

LOOKING TO THE FUTURE

The next step, Dr. Samuels said, will be to describe the afferent and efferent pathways for the orexin-containing neurons, as well as characterizing the pharmacology of orexin antagonists that are selective for type 1 or type 2 receptors.

"Like the parent molecule and other orexin antagonists in clinical trials, the compound we tested in this animal study was a dual orexin receptor antagonist that affects both type 1 and type 2 orexin receptors," he said. "We would like to determine if there may be any efficacy and/or safety advantages of an agent that specifically targets just one receptor subtype." ■

BRIAN C. SAMUELS, MD, PHD

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Dr. Samuels receives speaking honoraria from Merck, but it is not related to this research. He holds a patent for the use of orexin antagonists for the treatment of glaucoma. The patent has not been optioned by outside companies and Dr. Samuels is not currently receiving payments for the patent.

Ellex's SLT technology launches in U.S.

ADELAIDE, AUSTRALIA ::

ELLEX MEDICAL LASERS LTD. announced the launch of its proprietary selective laser trabeculoplasty (SLT) technology in the United States.

The launch comes following the expiration of a patent held by Massachusetts General Hospital (sub-licensed to Lumenis), which prevented Ellex from selling its SLT technology in the United States, the company said in a prepared statement.

SLT advanced laser therapy, which is non-invasive and non-thermal, stimulates a natural healing response in the eye to treat glaucoma.

"[SLT] also overcomes the compliance issues and side effects of anti-glaucoma medications, which have long plagued physicians and patients alike," according to Tom Spurling, chief executive officer of Ellex.

As a highly effective approach for first-line glaucoma treatment, SLT can also be used as an adjunct therapy with medications and as alternative therapy when medications or surgery fail

Ellex's SLT platform is available in Tango SLT/YAG combination laser and Solo SLT laser. ■

Special Report) **GLAUCOMA**

Phaco + microinvasive glaucoma surgery safe, effective

Study results show the procedure reduces medication burden in eyes with IOP

By Cheryl Guttman Krader; *Reviewed by Steven D. Vold, MD*

FAYETTEVILLE, AR ::

IMPLANTATION OF AN INVESTIGATIONAL supraciliary micro-stent (CyPass Micro-Stent, Transcend Medical) combined with phacoemulsification in patients with mild-to-moderate open-angle glaucoma is safe and controls IOP, according to study results presented by Steven D. Vold, MD.

Dr. Vold

The CyPass Clinical Experience study (CyCLE) is a multicenter, interventional European clinical trial that enrolled 248 patients with Shaffer Grade III or IV glaucoma undergoing phacoemulsification with micro-stent implantation and has planned follow-up to 3 years.

THE FINDINGS

The results focus on 2 years of follow-up from a cohort of 136 patients that entered the study on 1 to 2 medications, said Dr. Vold, founder and chief executive officer, Vold Vision, Fayetteville, AR.

Among 85 patients with IOP controlled at <21 mm Hg at baseline, IOP remained stable after surgery, but the need for IOP medication was significantly reduced.

At baseline, mean IOP was 16.4 mm Hg and patients were using an average of 2.0 medications daily. There were 59 patients in the subgroup evaluated at 2 years, at which time mean IOP was 16.1 mm Hg, while mean daily medication use had decreased ~50% to just 1.1.

There were 51 patients who had IOP ≥21 mm Hg at baseline. This subgroup had a mean baseline IOP of 25.5 mm Hg and a 35% reduction at 1 year to 15.8 mm Hg, along with a >50% reduction in mean daily medication use from 2.2 to 1.0.

EXAMINING SAFETY

"The safety of this glaucoma procedure was also very impressive as there were no serious complications," Dr. Vold said. "Now, we are waiting for results from the randomized, controlled FDA IDE study (COMPASS) to substantiate the long-term efficacy and benefit of the combined procedure over cataract surgery alone."

The safety review showed there were no cases of:

- Hypotony maculopathy
- Suprachoroidal hemorrhage
- Retinal detachment
- Other retinal complications
- Iris atrophy
- Endophthalmitis

The device explantation rate and repositioning rate were each 0.7%.

Obstruction of the device was the most common adverse event (8.8%), followed by endothelial touch (3.7%), elevated IOP lasting >1 month (2.9%), transient hyphema lasting <1 month (1.5%), and iritis persisting >1 month (0.7%).

There were no cases of best-corrected visual acuity loss related to the device.

(FIGURE 1) The supraciliary micro-stent (CyPass Micro-Stent, Transcend Medical), as shown in position. *(Images courtesy of Steven D. Vold, MD)*

HOW IT WORKS

The supraciliary micro-stent reduces IOP by increasing aqueous outflow toward the suprachoroidal space. It is made of a non-degradable, biocompatible polyimide material, measures 6.35 mm in length, and has a 300-µm internal lumen.

The micro-stent is implanted in a microinvasive glaucoma procedure using an ab interno approach through a 1.5-mm clear corneal incision or other size phaco incision. The procedure spares conjunctiva and sclera, and also preserves the trabecular meshwork, so that laser and incisional surgery procedures can be performed in the future if necessary.

Dr. Vold said insertion of the device using a gonio lens (Vold Gonio Lens, Transcend Medical) he developed specifically for use in the procedure could also be used.

"This lens can be held in either hand, and as one of its advantages, it minimizes any need for tilting the surgical microscope," Dr. Vold said. "It features a stabilization ring that prevents the eye from moving, giving the surgeon increased control, and it has a floating lens that minimizes pressure on the cornea, which can lead to image distortion." ■

take-home

- **Data from 2 years of follow-up from a case series of patients with open-angle glaucoma show implantation of an investigational supraciliary micro-stent has IOP- and medication-reducing benefits in eyes.**

STEVEN D. VOLD, MD
E: *svold@voldvision.com*
Dr. Vold is a consultant to Transcend Medical.

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INDICATION AND DOSING

PATADAY® Solution is a mast cell stabilizer indicated for the treatment of ocular itching associated with allergic conjunctivitis. The recommended dose is one drop in each affected eye once a day.

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PATADAY® Solution is for topical ocular use only. It is not for injection or oral use.

To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep the bottle tightly closed when not in use.

Patients should be advised not to wear contact lenses if their eyes are red.

PATADAY® Solution should not be used to treat contact lens-related irritation. The preservative in PATADAY® Solution, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and **whose eyes are not red** should be instructed to wait at least ten minutes after instilling PATADAY® Solution before they insert their contact lenses.

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%.

For additional information about PATADAY® Solution, please refer to the brief summary of prescribing information on adjacent page.

References: 1. IMS Health, IMS National Prescription Audit™, August 2010 to December 2012, USC 61500 OPHTH ANTI-ALLERGY. **2**. PATADAY® Solution package insert. **3**. Formulary data provided by Pinsonault Associates, LLC, PathfinderRx, April 2013.

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Special Report) **GLAUCOMA**

Novel glaucoma agent rivals standard therapy

Latanoprostene bunod may produce greater reductions in IOP than latanoprost ophthalmic solution in study

By Roxanne Nelson; *Reviewed by L. Jay Katz, MD*

PHILADELPHIA ::

A NEW DRUG SHOWS potential as a therapy for glaucoma, according to study results showing that it performed better than a standard therapy.

Treatment with latanoprostene bunod 0.024% resulted in significantly greater reductions in mean diurnal IOP than with latanoprost ophthalmic solution in patients with open-angle glaucoma (OAG) or ocular hypertension.

"(However, the drug) is not yet FDA approved," said L. Jay Katz, MD, director of the Glaucoma Service, Wills Eye Institute and professor of ophthalmology, Thomas Jefferson University, Philadelphia. "Latanoprost is the most commonly used glaucoma medication."

Latanoprostene bunod is a nitric oxide-donating prostaglandin F2-alpha analog that is currently in development for the treatment of glaucoma and ocular hypertension. It is intended for the reduction of IOP in patients with elevated pressure due to glaucoma or ocular hypertension.

take-home

Latanoprostene bunod is a probable new drug for the treatment of glaucoma that seems to be well tolerated and potent in lowering IOP.

EXAMINING THE STUDY

Results of the study were very promising, said Dr. Katz, noting that the drug has the potential to be a first-line agent if confirmed in larger clinical trials.

In this study, latanoprostene bunod 0.024% was compared with latanoprost 0.005% ophthalmic solution in a randomized trial.

The goal was to assess the efficacy of the agent in reducing and maintaining mean diurnal IOP for up to 29 days in patients with OAG or ocular hypertension, and its performance against a standard therapy.

The study participants were randomly assigned to either latanoprostene bunod 0.024% (n = 83) or latanoprost 0.005% ophthalmic solution (n = 82). All patients had an IOP ≥26 and ≤32 mm Hg and a diagnosis of OAG or ocular hypertension.

The two groups had similar demographics. The mean age of the patients was 61 years, 77.6% were white, and 66.7% were women.

In addition, almost one-half (43%) were treatment naïve at enrollment. Patients received their drug dosage once a day in the evening for a total of 28 days. Evaluations for safety and efficacy occurred on days 7, 14, 28, and 29.

Efficacy assessments included evaluating the mean diurnal IOP and the proportion of patients who were able to maintain a mean diurnal IOP at ≤18 mm Hg.

For safety assessment, the researchers measured adverse events, best-corrected visual acuity, ocular tolerability, ocular signs, and vital signs. An analysis of covariance model with fixed-effect terms was performed, and for measuring changes from baseline IOP, t-tests were performed for all treatment groups.

THE FINDINGS

Results showed that at days 7, 14, and 28, there were statistically greater reductions in mean diurnal IOP for patients treated with latanoprostene bunod 0.024%, as compared with latanoprost 0.005% at day 7 (8.3 versus 7.3 mm Hg, respectively; $p = 0.0325$), day 14 (8.9 versus 7.7 mm Hg; $p = 0.0145$), and day 28 (9 versus 7.8 mm Hg; $p = 0.0051$).

There were significantly more patients who received latanoprostene bunod 0.024% that had a study eye mean diurnal IOP ≤18 mm Hg at days 7 ($p = 0.0057$), 14 ($p = 0.0464$), 28 ($p = 0.0061$), and 29 ($p = 0.026$), as compared with those who received latanoprost 0.005%.

All adverse events related to the treatment were mild or moderate in severity, and the percentages of patients with conjunctival hyperemia were similar across both treatment groups.

Latanoprostene bunod 0.024% produced significantly greater reductions (~1 mm Hg) in mean diurnal IOP for up to 29 days as compared with latanoprost 0.005%. ■

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

NON-INVASIVE

(Continued from page 8)

"Color velocity maps obtained with this technology show the trabecular meshwork in motion, changing configuration as it moves outward toward the external wall of Schlemm's canal during systole, then rebounds toward the anterior chamber during diastole," Dr. Johnstone said.

By providing information about issue motion, he said, PhS-OCT provides an objective measurement of trabecular meshwork tissue elasticity and compliance, and thus its ability to control IOP.

"Just as HbA1c measurements provide a better indication of diabetes control than random blood glucose testing," Dr. Johnstone said, "measuring the biomechanical properties of the trabecular meshwork to determine the function of the outflow system may prove to be a better assessment tool than IOP for evaluating eyes with glaucoma and their response to treatment."

POSSIBLE CLINICAL APPLICATIONS

PhS-OCT may also be used to guide medical and surgical therapy decisions.

Ocular hypotensive medications that increase pulsatile aqueous outflow (i.e., miotics, adrenergics, prostaglandin analogues) exert their effects on trabecular meshwork motion and occur very quickly, he said. Thus, in-office PhS-OCT might be used to determine if a patient will be a responder following test dose administration.

The ability to characterize trabecular meshwork motion at different sites could also be useful for guiding optimal placement of stent devices used in microinvasive glaucoma surgical procedures.

The technology might be applied as a non-invasive method to determine whether patients are good candidates for canaloplasty, Dr. Johnstone said.

Canaloplasty pioneer, Robert Stegmann, MD, has shown that response after canaloplasty can be predicted by the ability of intraoperative provocative gonioscopy to cause Schlemm's canal blood reflux—a surrogate for trabecular meshwork motion.

"PhS-OCT might allow screening of canaloplasty candidates without going to the operating room, and it might also allow us to select better candidates for laser trabeculoplasty or ab interno trabeculotomy," Dr. Johnstone said. ■

MURRAY JOHNSTONE, MD
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Dr. Johnstone has financial interests with Alcon Laboratories, Allergan, Cascade Ophthalmics, Healionics, Sensimed, and the University of Washington Center for Commercialization.

Microshunt OAG trial given approval by FDA

From Staff Reports

MIAMI ::

INNFOCUS INC. HAS RECEIVED authorization from the FDA to begin the phase I trial of the InnFocus MicroShunt to treat open-angle glaucoma (OAG).

The trial will be the first to use trabeculectomy with mitomycin C as a study control, according to the company.

"We believe that the excellent clinical results achieved by [this shunt] in earlier clinical evaluations indicate that the device will perform well against the current gold standard of trabeculectomy," said Leonard Pinchuk, PhD, president of InnFocus.

An ongoing study, now in its third year in the Dominican Republic, shows that the device can lower IOP by 50% to 60% with the average pressure residing between 10 and 12 mm Hg.

"This is particularly important in view of many well-documented studies showing that reducing pressure below 14 mm Hg arrests progression of the disease," Dr. Pinchuk said.

About 90% of the patients' pressures are below 14 mm Hg and similar numbers of patients are totally off glaucoma medication, he said.

"The key to our success is our proprietary biomaterial which demonstrates a clinically insignificant foreign body reaction in the eye," Dr. Pinchuk said.

InnFocus has also announced a $13.4 million financing led by HOYA and Saints Capital Everest. ■

Special Report) **GLAUCOMA**

Lack of data fuels glaucoma shunt study

Mean IOP and success rates similar between device, trabeculectomy groups after 1 year

By Cheryl Guttman Krader; *Reviewed by Yvonne M. Buys, MD*

TORONTO ::

A COMPARISON OF GUARDED implantation of a glaucoma filtration device (Ex-PRESS P-50, Alcon Laboratories) with standard trabeculectomy shows no between-group differences in IOP reduction or safety outcomes, according to results from 1 year of follow-up in a prospective, randomized study.

The device-based procedure was associated with faster visual recovery, but its use carried a higher cost, according to Yvonne M. Buys, MD.

Dr. Buys

The study enrolled 64 consecutive patients with open-angle glaucoma who were scheduled to undergo filtration surgery because IOP was uncontrolled on maximally tolerated medical therapy.

The device was implanted under a scleral flap, and both surgeries were performed using intraoperative mitomycin-C 0.4 mg/ml for 2 minutes. Sixty-one of the 64 patients were evaluated at 1 year.

"The surgical procedure for its implantation has several potential advantages, including a short-learning curve, consistency, and less tissue manipulation," said Dr. Buys, professor, Department of Ophthalmology and Vision Sciences, University of Toronto.

STUDY MOTIVATION

The miniature glaucoma shunt has been available since 2002. However, a lack of evidence-based data on its outcomes motivated researchers to undertake this study, according to Dr. Buys.

"In our study, only cost emerged as a major factor differentiating between the two procedures through 1 year," she said. "However, the faster visual recovery after the miniature shunt procedure compared with trabeculectomy is an interesting difference that deserves further study, and longer follow-up is certainly needed."

IOP was analyzed as the primary efficacy outcome measure for the randomized trial. Mean IOP was similar in the shunt and trabeculectomy groups at baseline (22.6 and 22 mm Hg, respectively) and at all follow-up visits, which were scheduled at 1 day, 1 and 2 weeks, and 1, 2, 3, 4, 6, and 12 months.

At 1 year, mean IOP was 11 mm Hg in the shunt group and 10 mm Hg in the trabeculectomy eyes.

The rate of complete success—defined as IOP between 5 and 18 mm Hg with a ≥20% reduction from baseline without medication—was higher in the miniature shunt group compared with the trabeculectomy eyes, 71% versus 57%. The difference, however, was not statistically significant.

Mean logMAR visual acuity decreased significantly immediately after surgery in both groups and then began to improve.

In the trabeculectomy group, best mean visual acuity after surgery was not achieved until 2 months after surgery, but it worsened thereafter. Mean visual acuity was significantly below the baseline level at all follow-up visits.

In the miniature shunt group, mean visual acuity never returned to baseline, but it did recover to a level that was no longer significantly different from baseline by 1 month after surgery and was stable thereafter.

At 1 year, both groups had a median visual acuity loss from baseline of 1 Snellen line. However, the proportion of eyes with a >2 line loss of visual acuity was significantly higher in the trabeculectomy group than in the miniature shunt eyes, 30% versus 3%.

Four of the nine eyes in the trabeculectomy group that lost more than 2 Snellen lines were due to reasons not directly related to the surgery, Dr. Buys noted.

Other secondary outcomes included number of glaucoma medications, complications, need for additional procedures, bleb morphology, central corneal thickness, endothelial cell count, and surgical time, and there were no significant differences between study groups in any of these endpoints.

COST CONSIDERATIONS

Economic analysis took into account the costs of surgery and follow-up care through 1 year. Postoperative cost was lower for the shunt group than for the trabeculectomy eyes by about $125. However, due to the cost of the device, the total cost per case through 1 year was nearly $1,000 more for the shunt procedure.

Dr. Buys noted that at the time the study was launched, there was a single published report of a randomized controlled study comparing the miniature glaucoma shunt with trabeculectomy. While it reported significantly greater success in the device group after 1 year, by 3 years and continuing through 5 years of follow-up, there was no difference between groups.

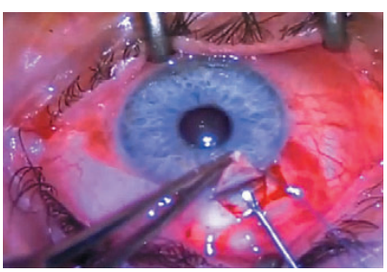
"Subsequently, another prospective, randomized study was published that compared the two procedures in fellow eyes of patients with bilateral glaucoma," Dr. Buys said. "While this study found the success rate was significantly higher for the miniature shunt after a mean follow-up of almost 2 years, it enrolled only 15 patients of which 3 dropped out.

"Our study enrollment surpassed our target sample size of 52 patients, which was the number needed to detect a 2-mm Hg difference in IOP between groups with 80% power," she said. "Now we are looking at our data from follow-up at 2 and 3 years." ■

take-home

A prospective study randomly assigned 64 patients with open-angle glaucoma to surgery with a miniature glaucoma shunt or standard trabeculectomy, both with mitomycin-C.

SURGICAL TECHNIQUE



VIDEO To view a surgical technique showing the glaucoma shunt implanted under a scleral flap, go to **http://bit.ly/15YLnk3**. *(Video courtesy of Yvonne M. Buys, MD)*

YVONNE M. BUYS, MD

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Dr. Buys received some of the devices used in the study at no charge from Alcon Canada and I-Med, and has received speaking fees from Alcon for unrelated topics.

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IMPORTANT RISK INFORMATION ABOUT PROLENSA™

Indications and Usage
PROLENSA™ (bromfenac ophthalmic solution) 0.07% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.

Dosage and Administration
Instill one drop into the affected eye once daily beginning 1 day prior to surgery, continued on the day of surgery, and through the first 14 days post surgery.

Please see brief summary of full Prescribing Information on adjacent page.

References: 1. PROLENSA™ Prescribing Information, April 2013. **2.** Data on file, Bausch & Lomb Incorporated. **3.** Baklayan GA, Patterson HM, Song CK, Gow JA, McNamara TR. 24-hour evaluation of the ocular distribution of ^{14}C-labeled bromfenac following topical instillation into the eyes of New Zealand White rabbits. *J Ocul Pharmacol Ther.* 2008;24(4):392-398.

BAUSCH + LOMB

Warnings and Precautions
- Sulfite allergic reactions
- Slow or delayed healing
- Potential for cross-sensitivity
- Increased bleeding of ocular tissues
- Corneal effects, including keratitis
- Contact lens wear

Adverse Reactions
The most commonly reported adverse reactions in 3%-8% of patients were anterior chamber inflammation, foreign body sensation, eye pain, photophobia, and blurred vision.

PROLENSA™
(bromfenac ophthalmic solution) 0.07%

INDICATIONS AND USAGE

PROLENSA (bromfenac ophthalmic solution) 0.07% is indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.

DOSAGE AND ADMINISTRATION

Recommended Dosing

One drop of PROLENSA ophthalmic solution should be applied to the affected eye once daily beginning 1 day prior to cataract surgery, continued on the day of surgery, and through the first 14 days of the postoperative period.

Use with Other Topical Ophthalmic Medications

PROLENSA ophthalmic solution may be administered in conjunction with other topical ophthalmic medications such as alpha-agonists, beta-blockers, carbonic anhydrase inhibitors, cycloplegics, and mydriatics. Drops should be administered at least 5 minutes apart.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Sulfite Allergic Reactions

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

Slow or Delayed Healing

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

Potential for Cross-Sensitivity

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including bromfenac. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

Increased Bleeding Time

With some NSAIDs, including bromfenac, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

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

Keratitis and Corneal Reactions

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

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

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

Contact Lens Wear

PROLENSA should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of PROLENSA. The preservative in PROLENSA, benzalkonium chloride may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of PROLENSA.

ADVERSE REACTIONS

Clinical Trial Experience

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

The most commonly reported adverse reactions following use of PROLENSA following cataract surgery include: anterior chamber inflammation, foreign body sensation, eye pain, photophobia and vision blurred. These reactions were reported in 3 to 8% of patients.

USE IN SPECIFIC POPULATIONS

Pregnancy

Treatment of rats at oral doses up to 0.9 mg/kg/day (systemic exposure 90 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and rabbits at oral doses up to 7.5 mg/kg/day (150 times the predicted human systemic exposure) produced no treatment-related malformations in reproduction studies. However, embryo-fetal lethality and maternal toxicity were produced in rats and rabbits at 0.9 mg/kg/day and 7.5 mg/kg/day, respectively. In rats, bromfenac treatment caused delayed parturition at 0.3 mg/kg/day (30 times the predicted human exposure), and caused dystocia, increased neonatal mortality and reduced postnatal growth at 0.9 mg/kg/day.

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

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

Nursing Mothers

Caution should be exercised when PROLENSA is administered to a nursing woman.

Pediatric Use

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

Geriatric Use

There is no evidence that the efficacy or safety profiles for PROLENSA differ in patients 70 years of age and older compared to younger adult patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis and Impairment of Fertility

Long-term carcinogenicity studies in rats and mice given oral doses of bromfenac up to 0.6 mg/kg/day (systemic exposure 30 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and 5 mg/kg/day (340 times the predicted human systemic exposure), respectively, revealed no significant increases in tumor incidence.

Bromfenac did not show mutagenic potential in various mutagenicity studies, including the reverse mutation, chromosomal aberration, and micronucleus tests.

Bromfenac did not impair fertility when administered orally to male and female rats at doses up to 0.9 mg/kg/day and 0.3 mg/kg/day, respectively (systemic exposure 90 and 30 times the predicted human exposure, respectively).

PATIENT COUNSELING INFORMATION

Slowed or Delayed Healing

Advise patients of the possibility that slow or delayed healing may occur while using NSAIDs.

Sterility of Dropper Tip

Advise patients to replace bottle cap after using and to not touch dropper tip to any surface, as this may contaminate the contents.

Advise patients that a single bottle of PROLENSA, be used to treat only one eye.

Concomitant Use of Contact Lenses

Advise patients to remove contact lenses prior to instillation of PROLENSA. The preservative in PROLENSA, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of PROLENSA.

Concomitant Topical Ocular Therapy

If more than one topical ophthalmic medication is being used, the medicines should be administered at least 5 minutes apart

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When fixed-combination is viable option

Brinzolamide-brimonidine may benefit patients who have contraindications to beta-blocker

By Cheryl Guttman Krader; *Reviewed by Jess T. Whitson, MD*

DALLAS ::

THE NEW FIXED-COMBINATION agent of brinzolamide 1%–brimonidine 0.2% (Simbrinza Suspension, Alcon Laboratories) is a safe and effective option for lowering IOP in patients with glaucoma or ocular hypertension uncontrolled on monotherapy.

The medication also brings the benefits of fixed-combination therapy to individuals who have contraindications to a beta-blocker, said Jess T. Whitson, MD.


Dr. Whitson

Dr. Whitson is professor of ophthalmology, University of Texas Southwestern Medical Center, Dallas, and the lead author of a recently published paper (*Clin Ophthalmol.* 2013;7:1053-1060) presenting the 6-month results from one of the two pivotal clinical trials that led to FDA approval of brinzolamide-brimonidine.

The randomized study began with a 3-month, double-masked phase comparing three times-daily treatment with brinzolamide-brimonidine against the carbonic anhydrase inhibitor (brinzolamide) or alpha-agonist (brimonidine) alone. After 3 months, mean IOP at all measured time points (8 a.m., 10 a.m., 3 p.m., and 5 p.m.) was significantly lower in patients using the fixed-combination than in the monotherapy groups.

The study was continued for a 3-month safety extension. At 6 months, mean IOP was stable in all treatment groups. No new or increased safety signals emerged.

After 6 months in the fixed-combination group, percent IOP reduction from baseline ranged from 20% at trough to 30.7% at peak.

"There is a large pool of potential candidates for a fixed-combination IOP-lowering agent," Dr. Whitson said. "Recent studies and national drug plan prescription data show that as many as 40% of patients with glaucoma are [taking] more than one medication to control IOP."

take-home

- **A new fixed-combination of brinzolamide-brimonidine is a safe and effective option for lowering IOP in patients who are not candidates for a beta-blocker.**

WHY FIXED-COMBINATION MAY BE BEST OPTION

There are many reasons to choose a fixed-combination for these individuals.

Patient compliance may be enhanced because of the simplicity of instilling one drop instead of two and by the lower cost of having just one co-payment.

"In addition, a fixed-combination avoids the potential for drop washout if patients do not wait a sufficient time between instilling their medications, and its use lessens ocular surface exposure to preservatives like benzalkonium chloride," Dr. Whitson said.

However, there has been a need for a beta-blocker-free fixed-combination, since cardiac and pulmonary conditions—which are contraindications to an ophthalmic beta-blocker—are prevalent in the elderly population of patients being treated for ocular hypertension and glaucoma.

The new combination of brinzolamide plus brimonidine meets this need, Dr. Whitson noted.

> 'As many as 40% of patients with glaucoma are [taking] more than one medication to control IOP.'
>
> — Jess T. Whitson, MD

PIVOTAL TRIAL

The pivotal trial randomly assigned 690 patients with ocular hypertension or open-angle glaucoma. Eligible participants underwent a washout period ranging from 5 to 28 days, depending on what medication(s) they were taking. The patients had to have IOP at two consecutive visits ranging from 24 to 36 mm Hg at 8 a.m. and from 21 to 36 mm Hg at 10 a.m.

Patients were instructed to administer the medication at 8 a.m., 3 p.m., and 10 p.m., and returned for follow-up visits after 2 weeks, 6 weeks, 3 months, and 6 months.

Data on adverse events and from pulse rate and blood pressure monitoring demonstrated that the fixed-combination had good systemic safety. Local ocular adverse events accounted for the majority of adverse event reports in all groups.

The types of adverse events reported were those expected based on experience with brinzolamide and brimonidine, Dr. Whitson noted.

Use of brinzolamide alone or in combination was associated with all cases of blurred vision and nearly all reports of dysgeusia, whereas use of brimonidine alone or in combination was associated with all or nearly all cases of conjunctivitis, dry mouth, and ocular allergy.

"This 6-month study has a relatively short duration, and some cases of allergy or other adverse events may only develop over longer-term use," Dr. Whitson said.

Seventy-two of 77 patients who discontinued study participation because of an adverse event were using brimonidine either alone (34 patients) or as the fixed-combination (38 patients).

There were no serious treatment-related adverse events in any study group. ■

Do you use a fixed-combination therapy for patients with glaucoma? Weigh in at **Facebook.com/OphthalmologyTimes.**

JESS T. WHITSON, MD

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Dr. Whitson is on the speaker's bureau for Alcon Laboratories, Allergan, Merck, and Sucampo.

Special Report) **GLAUCOMA**

Topical tactics for the ocular surface

How preservatives in topical ophthalmic medications may have adverse consequences

By Fred Gebhart; *Reviewed by Douglas Rhee, MD*

BOSTON ::

PRESERVATIVES IN TOPICAL ophthalmic medications are not benign, but may have adverse consequences for the ocular surface, the success of bleb-dependent procedures, and the trabecular meshwork.

"There is excellent evidence in the literature to support the claim that alternatively preserved and non-preserved medications are more gentle than medications preserved with benzalkonium chloride," said Douglas Rhee, MD, associate professor of ophthalmology, Harvard Medical School, Boston.

(***Editor's Note:*** *Dr. Rhee has recently been named Chairman of Ophthalmology and Visual Sciences at Case Western Reserve University School of Medicine and University Hospitals' Case Medical Center, Cleveland, where he is expected to start this month.)*

Topical ophthalmic medications typically come in three forms, he said.

- **The most common formulation uses benzalkonium chloride as a preservative. These medications are usually less expensive compared with other formulations and are the agents preferred—and sometimes required—by third-party payers.**
- **Alternatively preserved medications typically use one of two preservatives: Purite, which is a stabilized oxychloro complex containing oxygen, sodium, and chlorine free radicals, and SofZia, which is an ionic buffer containing borate, worbitol, polylene, glycol, and zinc.**
- **Preservative-free formulations are often referred to as non-preserved medications.**

PRESERVATIVE VERSUS NON-PRESERVED DRUGS

There is ample evidence to consider medications that are not preserved or are preserved with alternative agents as being more gentle to ocular tissues, Dr. Rhee said.

However, the evidence is less convincing when it comes to the potential effect of preservatives on bleb-dependent trabeculectomies and the trabecular meshwork.

The primary factor is that ophthalmic drugs can have adverse effects on ocular tissue.

"It is certainly true that pharmacologic agents themselves have an effect on ocular tissues," Dr. Rhee said. "That drug-related effect is unavoidable, at least when you are using a topical delivery system.

"We may eventually get around surface disease issues and trabeculectomy issues by going to a different, non-topical delivery route, but those systems are still in development and testing," he said.

Various in vitro studies have confirmed that benzalkonium chloride can cause inflammation in the conjunctiva and that it is lethal to trabecular meshwork cells—both as a single agent and as a preservative in ophthalmic medications.

"There is very good evidence that preservatives, or at least benzalkonium chloride, does have a deleterious effect on the ocular surface," Dr. Rhee said. "Whether there is a difference in ocular surface disease between non-preserved medication and alternatively preserved medications is less clear—there is not a lot of evidence either way—but when it comes to benzalkonium chloride, the evidence of ocular surface disease is convincing.

"There is little question, based on my own clinical experience, that alternatively preserved and non-preserved agents are more gentle, better tolerated, and induce fewer symptomatic side effects compared with the same drugs preserved with benzalkonium chloride," he said.

There is also evidence that preserved topical medication can reduce the success rate of trabeculectomy surgeries that use a filtering bleb.

The problem is that benzalkonium chloride increases inflammation in the conjunctiva, Dr. Rhee said.

Topical ophthalmic medications also induce inflammation in the conjunctiva.

LOOKING FURTHER

The degree of inflammation that is due to the medications versus the inflammatory effects of preservatives is difficult to tease out. However, rabbits treated with non-preserved timolol had less conjunctival inflammation than similar rabbits given preserved timolol.

Those experimental findings support clinical observations that patients treated with non-preserved timolol for more than 1 year had more normal cytology than similar patients treated with preserved latanoprost or timolol.

"There is excellent evidence that topically delivered glaucoma medications—preserved and possibly non-preserved—cause an increase in conjunctival inflammation," Dr. Rhee said. "That has been shown using impression cytology, confocal microscopy, and conjunctival biopsy. The major confounder is the pharmacologic agents themselves."

The good news is pre-treating with topical corticosteroids before surgery may reverse inflammation and increase success rates for bleb-dependent trabeculectomies, he said.

Blebless procedures—such as ab interno trabeculectomy, laser trabeculoplasty, tube shunt, trabecular micro-bypass stent (iStent, Glaukos) or similar device implantation, and endoscopic cyclophotocoagulation—are less affected by conjunctival inflammation.

Evidence suggesting that intraocular benzalkonium chloride contributes to trabecular meshwork pathology is less convincing.

In vitro exposure to benzalkonium chloride and other preservatives kill cultured trabecular meshwork cells in a dose-dependent manner.

Dr. Rhee and others are actively investigating the potential in vivo effects of preservatives on the trabecular meshwork.

"If it is feasible clinically and economically, there is convincing evidence that non-preserved and alternatively preserved medications are better than benzalkonium chloride-preserved medications, because they are more gentle and better tolerated," he said. "Reducing those side effects is an important positive step, because side effects are a major barrier to adherence." ■

take-home

- **Ophthalmologists need to weigh the evidence regarding the best use for medications that are non-preserved, alternatively preserved, or benzalkonium chloride-preserved.**

DOUGLAS RHEE, MD

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Dr. Rhee is an ad hoc consultant to Aerie Pharmaceuticals, Alcon Laboratories, Allergan, Johnson & Johnson, Merck, and Santen and has research relationships with Alcon, Aquesys, and Merck.

SLT

(Continued from page 1)

PROBABILITY OF SUCCESS

Based on criteria for defining success—a decrease in IOP and subsequent maintenance below goal IOP without any need for hypotensive medication, repeat SLT, or filtration/shunt surgery—the cumulative probability of success of SLT as primary therapy was 97% at 1 year, 92% at 5 years, and still 90% at years 7 through 10.

Dr. Jindra

"The Glaucoma Laser Trial established the efficacy of laser trabeculoplasty in lowering IOP in previously untreated patients, while results from the OHTS and Early Manifest Glaucoma Trial established the efficacy of early and effective treatment to preserve long-term visual function in [patients with] glaucoma," said Lawrence F. Jindra, MD, co-author of the study and chief emeritus, Winthrop University Hospital and assistant clinical professor of ophthalmology, Columbia University, New York.

The findings build on these studies in demonstrating SLT produces significant IOP lowering and with durable benefit, he said.

"Further study of SLT in controlled trials is indicated," Dr. Jindra said. "But given the amount of data and experience on SLT, we believe that prescribing medications instead of SLT for primary treatment of glaucoma today is analogous to performing intracapsular cataract extraction rather than phacoemulsification. It can be done, but why would you?"

(Continues on page 22 : ***Safety*** *)*

SLT OVER THE LONG TERM

VIDEO In this video interview, Lawrence F. Jindra, MD, shares his long-term results for SLT when used as a primary, secondary, and replacement therapy. Go to **http://bit.ly/17PkFNs.** *(Video courtesy of Ellex)*

OT OphthalmologyTimes.com *ONLINE EXCLUSIVE*

SLT: A NEW STANDARD IN GLAUCOMA TREATMENT

AS SOCIETY CONTINUES to become more technologically advanced and patient expectations grow alongside, there is no better time for physicians to rework the antiquated eyedrop-centered glaucoma treatment regime. SLT offers the treatment efficacy and convenience patients today need and stands to give the 1970s-based management of glaucoma a long-awaited shake-up in the 2010s, suggests Lawrence F. Jindra, MD. Go to http://bit.ly/17PkFNs.

Special Report) **GLAUCOMA**

SAFETY

(*Continued from page 21*)

Dr. Jindra also commented on safety of SLT, noting it is not "argon laser trabeculoplasty-lite."

SLT—performed using a Q-switched, frequency-doubled (532 nm), low-energy Nd:YAG laser—targets melanocytes in the trabecular meshwork. The treatment induces a biologic response that involves release of cytokines that trigger macrophage recruitment and other changes leading to reduction in IOP.

SLT is distinctly different from argon laser trabeculoplasty, and it requires the surgeon to make and accept an intellectual and practical paradigm shift, according to Dr. Jindra.

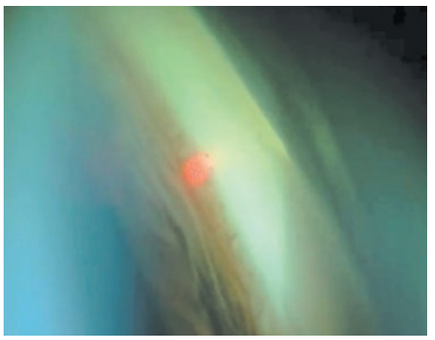
"SLT has less energy than the average laser used to scan groceries at the checkout," he said. "So it treats the trabecular meshwork without causing thermal or coagulative damage, without producing peripheral anterior synechiae, but allowing for clinically effective repeatability." ■

take-home

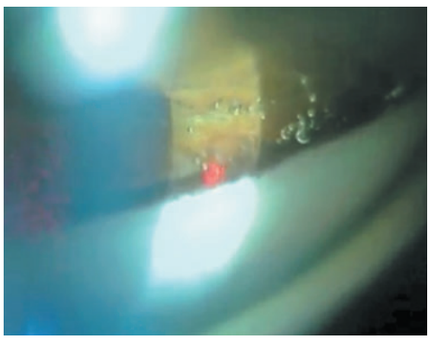
In an analysis of almost 2,000 eyes treated with selective laser trabeculoplasty as primary therapy for glaucoma, mean IOP decreased 29% and the cumulative probability of success at 10 years was 90%.

LAWRENCE F. JINDRA, MD
E: *drlfjind@optonline.net*

Dr. Jindra has received honoraria from Ellex Corp. in the past year.



SLT Treatment Protocol
SLT is a relatively quick and easy outpatient procedure. During treatment about 100 confluent spots are applied along meshwork to treat a 360° angle.



Energy Selection
After the threshold level is found (the point at which mini-bubble formation occurs), the energy level is decreased in 0.1 mJs steps as treatment continues until bubble formation ceases. This energy is then used for treatment.
(Images courtesy of Ellex)

GRF receives largest bequest in its history

SAN FRANCISCO ::
THE GLAUCOMA RESEARCH FOUNDATION (GRF) has received a $3 million bequest, the largest gift in its history.

The bequest, which was given by Henry Adolph Sutro, DDS, of Oakland, CA, was made in honor of his ophthalmologist, Andrew G. Iwach, MD.

Dr. Iwach is the executive director of the Glaucoma Center of San Francisco and board chairman of GRF.

"We are incredibly grateful to Dr. Sutro for this remarkable gift," said Thomas M. Brunner, president and chief executive officer of GRF.

"His thoughtful contribution in honor of Dr. Iwach is particularly meaningful—as it is a testament to the quality and excellence of the care and compassion Dr. Iwach provides to all of his patients," Brunner added.

The bequest will establish the Dr. Henry A. Sutro Family Grant for Research and the Drs. Henry and Frederick Sutro Memorial Lecture.

The lecture will be held each year at the Glaucoma 360° annual meeting. It was created to promote innovation in glaucoma therapy, as well as continuing education program for clinicians to highlight the latest advances in glaucoma management.

MIGS with stents may benefit OAG

By Lynda Charters

SAN FRANCISCO ::
PATIENTS WITH OPEN-ANGLE GLAUCOMA (OAG) had a significant reduction in IOP and did not require anti-glaucoma medications over 1 year postoperatively when micro-invasive glaucoma surgery (MIGS) was performed, according to interim results for a MIGS study group that were reported by David F. Chang, MD.

The surgery, in which two first-generation trabecular micro-bypass stents (iStent, Glaukos) were implanted as the only treatment, appeared effective for treating OAG, which was uncontrolled by one anti-glaucoma medication.

The MIGS study group consisted of subjects at the Malayan Center in Yerevan, Armenia. Patients who were phakic or pseudophakic (n = 39) with OAG and treated with one medication were included.

All patients had a cup-to-disc ratio of 0.9 or less and IOP between 18 and 30 mm Hg. After a medication washout period, the preoperative IOP ranged from 22 to 38 mm Hg.

One-year efficacy endpoints were IOP reduction without anti-glaucoma mediations of 20% or more, an IOP of 18 mm Hg or lower without medication, and mean change in IOP.

In the 39 eyes followed for 1 year, compared with baseline, mean IOP reduction overall was 44%: 67% of eyes had a reduction of 40% or more, 85% had a reduction of 30% or more, and 92% of eyes met the primary endpoint of an IOP reduction of 20% or more.

At the 1-year evaluation, 92% of eyes met the secondary endpoint of postoperative IOP of 18 mm Hg or lower without medication and 77% of eyes had an IOP of 15 mm Hg or lower without medication. BCVA remained the same or improved in 35 of 39 eyes. At 1 year, 74% had 20/40 or better visual acuity, compared with 67% preoperatively.

"In the United States, the (trabecular micro-bypass stent) is only approved as a combined procedure with phaco, and it is therefore hard to know how much of any resulting IOP lowering is due to cataract surgery alone," Dr. Change said. The iStent is FDA-approved in the United States, CE marked in Europe, and has medical device approval in Canada. ■

Tracking visual loss in MS

Time-domain OCT used to determine if thinning of retinal nerve fiber layer continued

By Lynda Charters; *Reviewed by Stephen Moster, MS*

TAKE-HOME

- ***Patients with multiple sclerosis seem to have visual loss and progressive thinning of the retinal nerve fiber layer over time, according to a longitudinal study.***

PHILADELPHIA ::

Visual loss and progressive thinning of the retinal nerve fiber layer (RNFL) occur over time in patients with multiple sclerosis (MS), according to results from a longitudinal study of visual function and optical coherence tomography (OCT).

"Axonal and neuronal loss are common in (the disease) and have been shown pathologically in the anterior visual pathway, even in patients with no history of optic neuritis," said Stephen Moster, MS.


Moster

"The introduction of OCT has allowed researchers to capture the structure/function correlations in MS and has brought the anterior visual pathway to the forefront as a model for testing new therapies," said Moster, a fourth-year medical student at the University of Pennsylvania, Philadelphia.

Data from the longitudinal study showed that baseline RNFL in the eyes of patients with MS was 91 µm compared with 104 µm in healthy controls.

The initial 3-year study showed significant progressive RNFL thinning from baseline to 3 years.

Using time-domain OCT, Moster and colleagues extended the study to determine if the RNFL thinning continued and was associated with visual loss in patients with MS.

ABOUT THE STUDY

In this multicenter study, patients were followed every 6 to 12 months after baseline evaluation. Patients underwent high- and low-contrast acuity testing and measurement of the RNFL (Stratus OCT-3, Carl Zeiss Meditec).

The study included 196 patients (mean age, 44 years; 379 eyes). Three-quarters of patients were women. More than 80% had the relapsing/remitting form of MS. Forty-three percent of patients had a history of optic neuritis.

Results showed a trend in RNFL thinning over time (Figure 1).

"Notably, the trend continued past the 3-year time point and did not level off," he said.

Compared with baseline, at 5 to 7 years the RNFL decreased by –9.2 µm ($p < 0.001$).

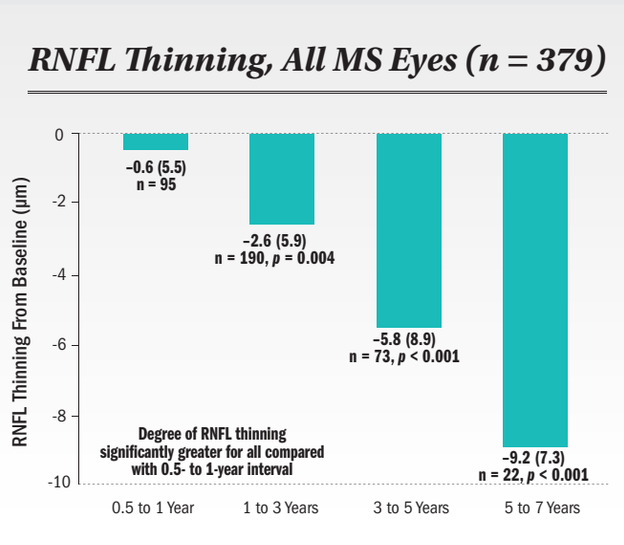
An evaluation of the subgroup of 153 eyes of patients with a history of optic neuritis also indicated the same trend in thinning of the RNFL. The same thinning was seen in the eyes of patients without a history of optic neuritis.

"When we compared the amount of RNFL thinning between eyes with and without a history of optic neuritis, there was no significant difference in the amount of thinning between the two groups," Moster said.

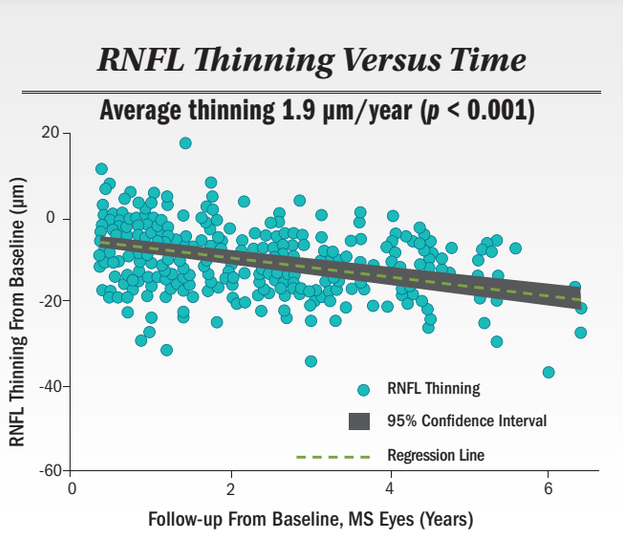
Thinning of the RNFL progressed by an average of about 1.9 µm annually at the 7-year time point, which agreed with the rate of progression at 3 years (Figure 2).

In healthy controls, the annual rate of RNFL thinning was about 0.16 µm.

"These results indicated that there is a steady subclinical axonal loss in the anterior visual pathway in patients with MS that continues beyond 3 years," Moster said.



(FIGURE 1) **Patients were followed every 6 to 12 months after baseline evaluation. Compared with baseline, at 5 to 7 years the retinal nerve fiber layer decreased by –9.2 µm ($p < 0.001$).**



(FIGURE 2) **Thinning of the retinal nerve fiber layer progressed by an average of ~1.9 µm annually at the 7-year time point, agreeing with the rate of progression at 3 years.** *(Figures courtesy of Stephen Moster, MS)*

The percentage of eyes in patients with RNFL loss also increased from 19% at 1 to 2 years after baseline to 56% at 5 to 7 years after baseline.

A history of optic neuritis was not predictive of the amount of RNFL thinning over time.

VISUAL ACUITY

Regarding visual acuity loss, researchers found that eyes with greater visual loss had greater RNFL thinning. The percentage of eyes with visual loss by low-contrast visual acuity testing increased from 7% during the early years of follow-up to 40% from 5 to 7 years after baseline.

A notable finding was that eyes of patients with visual loss over time did not have differences in the baseline RNFL thickness compared with the eyes of patients with steady vision, Moster said.

"Eyes with low-contrast visual loss over time had significant ($p < 0.001$) differences in the amount of thinning of the RNFL over time compared with eyes with steady vision," Moster said.

Based on these findings, the study concluded that visual loss and thinning of the RNFL occur as a function of time in MS, and that there is a steady decrease in the RNFL thickness over time—suggesting progressive axonal loss in the anterior visual pathway that continues beyond 3 years after baseline.

The study findings also supported the use of OCT and low-contrast visual acuity testing in MS trials. ■

STEPHEN MOSTER, MS

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Moster has no financial interest in the subject matter. Research is supported by the National MS Society, National Eye Institute, McNeill Foundation, and DADs Foundation.

Retinal imaging may reveal stroke risk

From Staff Reports

SINGAPORE ::

A RETINAL EXAMINATION MAY be valuable for the assessment of stroke risk in patients with hypertension, suggests findings from a recent study.

"The retina provides information on the status of blood vessels in the brain," said Mohammad Kamran Ikram, MD, PhD, lead author of the study and assistant professor, Singapore Eye Research Institute, Department of Ophthalmology and Memory Aging & Cognition Centre, National University of Singapore.

However, Dr. Ikram noted that it is too early to recommend changes in clinical practice. Other studies need to confirm the findings and examine whether retinal imaging can be useful in providing additional information about stroke risk in people with high blood pressure.

Researchers tracked stroke occurrence for an average 13 years in 2,907 patients with high blood pressure who had not previously experienced a stroke. Damage to the retinal blood vessels attributed to hypertension (hypertensive retinopathy) evident on the imaging was scored as none, mild, or moderate/severe.

They found the risk of stroke was 35% higher in those with mild hypertensive retinopathy and 137% higher in those with moderate or severe hypertensive retinopathy.

Even in patients taking medication and achieving good blood pressure control, the risk of a blood clot was 96% higher in those with mild hypertensive retinopathy and 198% higher in those with moderate or severe hypertensive retinopathy.

The study was published Aug. 12 in the journal *Hypertension*. ■

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Release Date: September 1, 2013
Expiration Date: September 1, 2014

Learning Objectives

- Describe recent guideline protocols for diagnosing dry eye disease (DED), classifying DED severity, and differentiating underlying etiologies of DED
- List the current recommendations for the treatment and follow-up of DED by level of severity and underlying etiologies

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The Vicious Cycle of Dry Eye Disease

Byron, a 63-year-old farmer with rosacea, comes to your office approximately 3 years after being diagnosed with dry eye secondary to meibomian gland dysfunction. Since the initial diagnosis, his symptoms had been well controlled with topical cyclosporine 0.05% and lid hygiene. However, the recent exacerbation of his dry eye-related visual discomfort and photophobia have made it difficult for Byron to work outdoors. It is important to note that Byron is also being treated for rheumatoid arthritis (RA), with a regimen of oral prednisone and methotrexate.

To understand the complex nature of the vicious cycle of dry eye disease (DED), it may help to envision the disorder as a disturbance of the lacrimal functional unit, an integrated system that includes the lacrimal glands, the ocular surface (cornea, conjunctiva, and meibomian glands), the lids, and the sensory and motor nerves that connect to these structures. When functioning properly, the lacrimal functional unit helps to preserve the integrity of the tear film, the transparency of the cornea, and the quality of the visual image produced by the anterior-most interface in the eye's optical system.[1]

DED varies in duration, severity, and cause. In most patients, it is marked by symptoms of ocular irritation and periods of blurred vision but is typically not sight-threatening. However, DED that is left untreated and becomes severe can lead to rare but serious complications, such as corneal damage (scarring, thinning, neovascularization, or ulceration), ocular surface keratinization, and severe loss of vision.[2]

In order to improve quality of life for patients with DED, strategies that stimulate tear production, maintain the quality of the ocular surface epithelium, and inhibit inflammatory factors that impair tear production are recommended. Initiating such strategies early in the course of the disease and recognizing that patients with DED secondary to a chronic systemic condition (see Table 1) or ongoing, exacerbating medication will need to incorporate such strategies beyond the time of initial symptom relief may prevent potentially serious complications of DED.[1]

Additional CME Opportunity

For further details about Byron, including insight into his long-term treatment plan and possible complications, check out our separate CME activity at www.iche.edu/dryeyecase2

Hyperosmolarity is Key

One of the principal intrinsic causes of chronic evaporative dry eye is meibomian gland dysfunction (MGD), which leads to an unstable tear film lipid layer, allowing excessive tear evaporation (for more on MGD, see last month's article in this CME series). This excessive evaporation leads to an increase in the osmolarity of the tear film. Hyperosmolarity may also be caused by dysfunction of the lacrimal secretory glands, which can occur, for instance, with RA and/or Sjögren's syndrome.[2] Whatever the cause or causes, hyperosmolarity is regarded as a central mechanism of dry eye, causing inflammation of and damage to the ocular surface, leading to symptom onset.[1]

Hyperosmolarity and instability of the tear film are drivers of the core mechanisms of DED. Hyperosmolarity leads to inflammation of the ocular surface and the release of inflammatory mediators into the tear film. The damage to the epithelium that results from this inflammation, including apoptosis, loss of goblet cells, and disruption of mucin production, leads to tear film instability, which further elevates tear osmolarity. This is the vicious cycle of DED.[1,3]

Conditions Contributing to Chronic Dry Eye Disease[2] (Table 1)

Conditions	Examples
Chronic viral infections	HIV, hepatitis C
Neurological conditions	Parkinson's disease, Bell's palsy, trigeminal neuralgia
Systemic medications	Antihistamines, diuretics, hormones/hormone antagonists, antidepressants, anticholinergic drugs, beta-adrenergic antagonists, cardiac antiarrhythmic drugs
Systemic inflammatory diseases	Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, scleroderma
Dermatological diseases	Rosacea
Allergic conjunctivitis	

Diagnostic Workup

Diagnostic workup of the patient with DED should include a careful ocular and systemic history, external examination, visual acuity measurement, and slit-lamp exam. Examination of the lids should include meibomian gland expression to assess the functioning quality of the secretions. Tests should include tear breakup time to evaluate tear-film stability, ocular surface staining with vital dyes (rose bengal, lissamine green, or fluorescein) to evaluate ocular surface disease, and Schirmer's and fluorescein clearance tests to evaluate tear production and clearance. These tests can help to determine whether the cause of an individual patient's dry eye is an aqueous deficiency, excessive evaporation, or a mixture of both.[2]

A relatively new addition to the diagnostic arsenal is tear osmolarity testing, which has been shown to be more sensitive than other tests for grading the severity of DED.[2,4] In one commercially available "lab-on-a-chip" test, which requires a tear sample of only 50 nL, a measurement of 316 mOsmol/L or greater is considered hyperosmolar, and an inter-eye difference greater than 8 mOsmol/L is indicative of dry eye.[5] Reduction in osmolarity over time appears to precede symptomatic improvement.[6]

Another promising lab-on-a-chip technology measures the level in the tears of matrix metalloproteinase-9 (MMP-9), an inflammatory marker that is elevated in DED.[7] This technology has received regulatory approval in Europe and Canada, but not yet in the United States. Utilization of these and other objective tests for diagnosis and follow-up of dry eye patients may improve the future management of DED.

Multifactorial Treatment Approach

DED can have multiple contributory factors, and it is therefore important to address as many as possible with appropriate therapy. Tear supplements may bring temporary relief, but these are palliative and not sufficient as a sole treatment modality, especially in patients with chronic DED. Patient education regarding the causes and chronic nature of the individual's particular form of DED is vital for successful management.[2]

For DED due to evaporative tear loss, effective therapies include environmental modifications and moisture chamber spectacles; eyelid therapy to address blepharitis and meibomianitis; artificial tear supplements, gels, and ointments; omega-3 fatty acid supplementation; and a tetracycline antibiotic to address meibomianitis and rosacea.[2,8]

In patients with severe DED, more aggressive treatments may be considered. These include systemic cholinergic agonists, systemic anti-inflammatory agents, mucolytic agents, autologous serum tears, and permanent punctal occlusion. In the most severe cases, surgical correction of eyelid abnormalities or tarsorrhaphy may be necessary.[2,8]

Emerging Treatments for Dry Eye Disease (Table 2)

Treatment	Action
LipiFlow® Thermal Pulsation System[13]	Applies controlled heat to the upper and lower inner eyelids, along with pulsation to evacuate meibomian glands
Maskin® Meibomian Gland Intraductal Probes and Tubes[14]	Provides symptomatic relief for patients with obstructive MGD
Rebamipide ophthalmic suspension 2%[15] (Regulatory approval in Japan, but not in the U.S.)	Mucin secretagogue improved objective dry eye-related signs and subjective ocular symptoms in a phase 3 trial
Topical anakinra 2.5%[16]	IL-1 antagonist significantly reduced symptoms in patients with dry eye in a phase 1/2 trial
Diquafosol ophthalmic solution 3%[17] (Regulatory approval in Japan, but not in the U.S.)	Secretagogue had high clinical efficacy and was well tolerated with a good safety profile in a phase 3 trial
Recombinant human serum albumin[18]	Topical compound, RU-101: phase 2 trial has begun enrolling patients
Recombinant hyaluronic acid[19]	Preclinical work has been presented

IL=interleukin, MGD=meibomian gland dysfunction

The Role of Inflammation

Because inflammation plays a central role in the pathogenesis of DED, anti-inflammatory therapies have become a mainstay of treatment. These include topical corticosteroids, cyclosporine ophthalmic emulsion, and tetracycline derivatives.[1-3,8] Topical steroids and cyclosporine are the anti-inflammatory agents most frequently prescribed for DED.[2]

Topical corticosteroids reduce symptoms of ocular irritation and decrease fluorescein staining. Short courses of topical steroids at infrequent intervals can help suppress inflammation and related irritation, but patients must be monitored for ocular complications of steroid use, such as cataract formation, elevation of intraocular pressure, and corneal melting.[2]

Topical cyclosporine has been shown in clinical trials to decrease **subjective** measures of DED, such as the need for artificial tears and symptoms of blurred vision, as well as **objective** measures, such as corneal fluorescein staining and anesthetized Schirmer test values.[8] In addition, artificial tears prepared from autologous serum can improve symptoms in most patients and help heal persistent epithelial defects associated with DED.[2]

Reversing the Dry Eye Cascade

One result of the disruption of the lacrimal functional unit in DED may be dysfunction in the underlying corneal nerves. Inflammation on the ocular surface can interfere with the normal neural connections that drive the tear reflex. If this type of nerve damage has occurred in a patient with moderate DED, it is possible that successful therapy may paradoxically appear to be making the patient worse. That is, when therapy begins to reverse the dry eye cascade and restore function to the ocular surface nerves, the patient may once again become sensitive to the irritation caused by DED. If this is the case, increased patient complaints of irritation may actually indicate an improvement in the dry eye condition. It is hoped that these new symptoms will eventually diminish as the patient continues to improve.[9,10]

A number of new treatment options for DED are now on the horizon. Several of these are listed in Table 2.

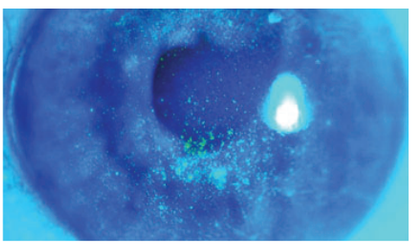

Image showing severe corneal staining in a patient with RA

Conclusion

DED is a complex disease that can require multifactorial treatment. Effective diagnosis depends on recognition of the presence of aqueous deficient and/or evaporative components, and management must address all aspects of the disease. As the multifaceted nature of dry eye is increasingly recognized, new diagnostic modalities and treatments are emerging to help clinicians better manage the individual manifestations of DED present in each patient.

Claiming Credit

Please go to www.iche.edu/dryeye2 to claim AMA credit. A complete set of references can be found online.

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DEFINING THE 'IDEAL' DME TREATMENT

POINT

Laser treatment necessary for DME

Subthreshold micropulse laser preferred over conventional laser

By Cheryl Guttman Krader; *Reviewed by Victor Chong, MD*

TAKE-HOME

- ***Lasers continue to have a place in the treatment of diabetic macular edema with foveal involvement, despite the advent of anti-vascular endothelial growth factor therapy.***

OXFORD, ENGLAND ::

Laser treatment—specifically, subthreshold micropulse laser treatment—has an important role in the management of diabetic macular edema (DME), according to Victor Chong, MD.

"Historically, it was thought direct coagulation of the microaneurysms was the goal for laser treatment," said Dr. Chong, department director, Oxford Eye Hospital, Oxford University Hospitals, Oxford, England.

Dr. Chong

Now researchers know that the target is retinal pigment epithelium cells—not the retina—and that absorption of the laser energy by those cells changes the microenvironment, leading to closure of microaneurysms and reduction of edema, Dr. Chong said.

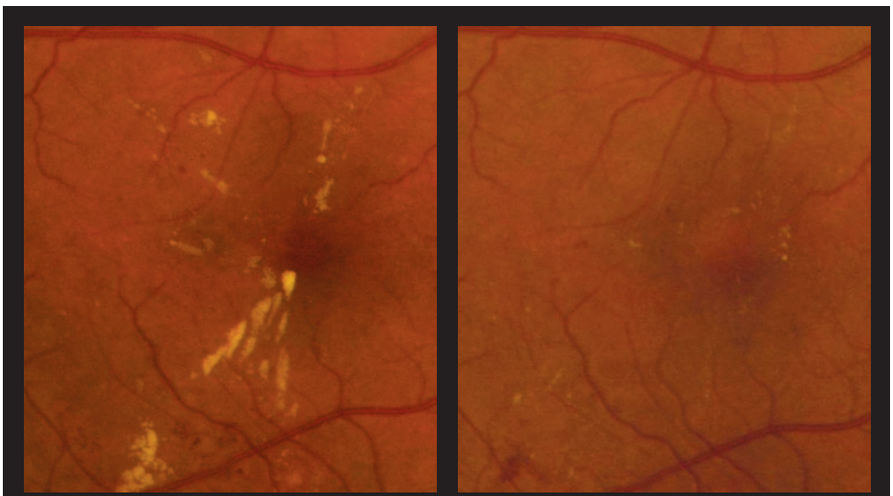
"If one is going to use a laser, it needs to be asked: Why would you want to scar the retina?" he said. "Subthreshold micropulse laser [treatment] delivers enough energy to produce the desired effect—but delivers the energy in pulses so there is less collateral retinal damage and no visible damage."

ROLE OF LASER PHOTOCOAGULATION FOR DME

Laser photocoagulation is still recognized as the standard of care when the fovea is not involved, Dr. Chong said.

However, data from the RESTORE study support a place for laser treatment in eyes of patients with visual impairment, secondary to foveal involvement with DME. In the study, patients were randomly assigned to treatment with:

- **Ranibizumab (Lucentis, Genentech) plus sham laser.**
- **Ranibizumab plus active (not deferred) laser.**
- **Or, sham injection with active laser.**



PRE- AND POST-LASER Defending the role of subthreshold micropulse laser, Victor Chong, MD, reviewed randomized, controlled clinical trial evidence supporting laser treatment for diabetic macular edema. Shown here are images preoperatively (left) and 12 months postoperatively (right) with subthreshold micropulse laser treatment. *(Images courtesy of Victor Chong, MD)*

With patients' eyes categorized into three subgroups contingent on baseline retinal thickness, it was clear that the anti-vascular endothelial growth factor (VEGF) treatment was best in the subgroup with the thickest retinas (>400 µm on time-domain optical coherence tomography), Dr. Chong said.

However, any benefit of anti-VEGF injection over laser monotherapy was minimal in eyes with retinal thickness of 300 µm or less.

Another subgroup analysis in RESTORE grouped eyes by whether they had prior laser treatment. Though the differences between treatment arms were not statistically significant, within the subgroup that had prior laser, mean change in best-corrected visual acuity (BCVA) from baseline to 12 months was greater in patients treated with ranibizumab alone than in those receiving ranibizumab plus laser, 7.6 versus 4.5 letters, respectively.

However, among the non-treated eyes, BCVA gain was greater for the group treated with both ranibizumab and laser than for those receiving ranibizumab monotherapy, 8 versus 5.9 letters, respectively.

"Eyes with prior laser treatment joined the study as laser treatment failures, and so it is not surprising to find in that situation [the] laser treatment did not add much value to ranibizumab," Dr. Chong said. "However, the outcomes were reversed for eyes with no prior laser treatment."

FURTHER EVIDENCE

Results from the DRCR.net protocol I study show that even with ranibizumab injections, laser treatment is often needed.

Over the study period of 3 years, 46% of eyes treated with ranibizumab with deferred laser still needed laser treatment. This was despite

Continues on page 29 : ***Necessary***

DEFINING THE 'IDEAL' DME TREATMENT

COUNTERPOINT

Factors limit subthreshold laser for DME

Why laser treatment currently not an important therapeutic modality

By Cheryl Guttman Krader; *Reviewed by Lloyd Paul Aiello, MD, PhD*

TAKE-HOME

- ***Presenting an opposing view, Dr. Aiello reviews efficacy and practical limitations of subthreshold laser treatment for diabetic macular edema.***

BOSTON ::

The answer to the question of whether subthreshold laser treatment is an important treatment for diabetic macular edema (DME) is "not at this time," according to Lloyd Paul Aiello, MD, PhD.

"The concept that subthreshold laser treatment may not cause substantial or permanent structural changes in the retina is attractive," said Dr. Aiello, professor of ophthalmology, Harvard Medical School, Boston. "However, there are multiple factors that limit the importance of this treatment in the current management of DME."

EFFICACY AND SAFETY OF LASER PHOTOCOAGULATION

The benefit of focal/grid laser treatment for DME, Dr. Aiello said, is not as rapid or great as what can be achieved with anti-vascular endothelial growth factor (VEGF) injections.

Nevertheless, patients can achieve significant gains in vision and reductions in central subfield thickness over time, and without substantive visual sequelae from the laser treatment.

There have also been relatively few randomized controlled trials investigating this technique for treatment of DME, Dr. Aiello said.

The results from those reported do not indicate subthreshold laser treatment provides any major visual acuity improvement compared with standard laser approaches.

The subthreshold laser treatment also has some practical limitations—it is difficult to tell where the treatment was performed, and therefore difficult to assess treatment adequacy, location, efficacy, or re-treatment areas, he said.

The availability of nondestructive, pharmacological approaches for treating DME is another issue to consider.

As shown by results from the phase III RISE and RIDE studies investigating ranibizumab (Lucentis, Genentech), anti-VEGF injection results in marked visual improvement in the large majority of patients with DME.

In addition, outcomes from the DRCR.net protocol I study indicate that adding laser when initiating anti-VEGF therapy may not be beneficial in the long term.

In the latter study, patients randomly assigned to anti-VEGF injection with prompt laser had a significantly lower visual outcome at 3 years than those assigned to anti-VEGF therapy with deferred laser.

DRCR.net protocol I results also showed more than one-half of eyes in the anti-VEGF plus deferred laser group (54%) received no laser treatment by the end of 3 years.

"If the idea for using subthreshold treatment is to laser as little as possible, it then begs the question: Why laser at all?" said Dr. Aiello, who is also director, Section of Eye Research and director, Beetham Eye Institute, Joslin Diabetes Center, Boston. "Indeed, as seen in DRCR.net protocol I, we are finding with anti-VEGF therapy that the need for laser is markedly reduced."

Current laser technology works for treating DME with no major sequelae, whereas subthreshold laser is difficult to visualize, has limited randomized trial data to support its use, and no clear evidence at this time that it provides a better visual acuity outcome.

The need for focal/grid laser treatment has also been reduced by the emergence of VEGF inhibition and steroids, Dr. Aiello said.

"Therefore, the answer to the question of whether subthreshold laser is currently an important treatment for DME has to be 'no'," he said. ■

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Dr. Aiello is a consultant to Genentech and scientific founder of Kalvista, which is developing pharmaceutical treatment for diabetic macular edema. He has no financial interest or competing financial interest in any laser technology.

NECESSARY

(Continued from page 28)

receiving 14 intravitreal injections at a cost of about $28,000 over time (based on drug cost of about $2,000 per injection, not including surgeon and facility fees).

Considering about one-half of the eyes entered into the trial had previous laser treatment, more than 70% of the ranibizumab-treated eyes had laser treatment at some point during 3 years, even in the deferred laser group, according to Dr. Chong.

"If you are saying laser is not important in the anti-VEGF era, it is like spending $30,000 to buy a car and being told that about half of the time you need to do something else to keep it working, but that something else is not important," Dr. Chong said.

Not having a micropulse laser, Dr. Chong said, is a common reason retina specialists give for not performing subthreshold micropulse laser treatment for DME. However, he noted that anyone who has a transpupillary thermotherapy laser in fact has a micropulse laser because it is the same 810 diode laser. ■

VICTOR CHONG, MD

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Dr. Chong is a consultant for Iridex and Novartis, a speaker for Quantel, and receives donated equipment from Iridex and Quantel.

3 strategies for managing traumatic cataract in children

Timing, IOL type, and lens calculations are important factors to recognize for pediatrics

By Lynda Charters; *Reviewed by Edward G. Buckley, MD*

TAKE-HOME

- ***There are several vital components surgeons need to take into consideration when treating children who have traumatic cataracts.***

DURHAM, NC ::

Managing traumatic cataracts in children requires attention to three issues when implanting an IOL: namely, the timing of the implantation, the type of lens, and the IOL calculations, according to Edward G. Buckley MD.

However, there are several controversies regarding IOL implantation in children.


Dr. Buckley

Whether to implant the IOL in the sulcus or capsule, if the surgery is primary or secondary, and how to deal with the lack of capsular support are some of the concerns, said Dr. Buckley, professor of ophthalmology and pediatrics and vice dean of medical education, Duke University School of Medicine, Durham, NC.

TIMING

As a general rule in terms of the timing for IOL implantation, Dr. Buckley said, "the later, the better."

If surgery in a patient's inflamed eye can be avoided, the clinician will experience that:

- **The procedure will be easier.**
- **The cornea will be clearer.**
- **The tissue will be less reactive.**
- **The IOL calculations will be more accurate.**
- **There is a better chance of in-the-bag placement.**
- **There will be fewer postoperative issues.**

The surgeon must determine if the IOL is inserted during the primary surgery or during a secondary procedure.

"The answer depends on the anterior chamber," Dr. Buckley said. "If the chamber is not in good shape after the initial surgery, waiting is likely a better option to avoid a rocky postoperative course with further complications.

"The general rule is: When in doubt, don't do it," he said.

No long-term data suggest a difference regarding capsular implantation or sulcus fixation in children with traumatic cataract.

"Exerting heroic efforts to put the IOL in the bag is probably not a good idea, especially in the presence of a poor anterior segment," he said.

IOL TYPES

There are two IOL options for use in children.

- **A single-piece polymethylmethacrylate (PMMA) lens is the hallmark IOL for use in inflamed eyes, Dr. Buckley said. This lens is implanted through a 7-mm incision and is more suitable in the sulcus.**

- **Other lenses include an acrylic, single-piece IOL (AcrySof IOL MA60AC, Alcon Laboratories) that is foldable and implantable through a 4-mm incision and another model (SA60AT, Alcon) that is injectable through a 2.75-mm incision.**

The SA60AT IOL is by far the lens of choice by 93.3% of pediatric ophthalmologists for in-the-bag fixation, and not for implantation in the sulcus, he noted.

The MA60AC IOL should be considered for eyes with a great deal of inflammation.

When sulcus fixation is desired, a three-piece acrylic lens or a one-piece PMMA lens is the best choice, he said.

To determine if a PMMA lens can be implanted in the sulcus, surgeons need to find the degree of optic support that is available, Dr. Buckley said.

If the capsule can support the optic, a MA60AC IOL is "perfectly satisfactory," he said.

In the absence of optic support, a PMMA lens may be a better choice, because it is sufficiently rigid to achieve adequate support.

Inflammation is an important factor when choosing the appropriate lens in these cases.

Acrylic IOLs can develop a great deal of deposits and are not a good choice in an eye that may have severe inflammation.

PMMA IOLs, however, are easier to clean than acrylic lenses.

In the absence of adequate capsular support, the surgeon is faced with the choice of an anterior chamber lens or suturing a lens in the posterior chamber.

"In children, the anterior chamber IOLs do not have a good track record because of pupil problems, persistent inflammation, hyphema, and glaucoma," Dr. Buckley said.

A new lens (Artisan Iris Clip Lens, Ophtec) may be advantageous, but the long-term performance is unknown.

IOLs that are sutured in place are associated with complications during the initial surgery.

The long-term safety is a question that centers around the 10-0 Prolene suture material, which tends to break (average time to breakage, 6 years) in up to 33% of patients, according to Dr. Buckley. This can be avoided by using 9-0 Prolene.

IOL CALCULATIONS

There is a myopic shift in children over time that extends into the teen years.

"Surgeons need to consider the myopic shift ahead of time," Dr. Buckley said. "The eye should be undercorrected early to avoid very high myopia later."

The formula used to calculate IOL powers does not matter.

"Because timing is an issue, waiting until the eye is 'quiet' is best," he said. "The IOL type depends on the implant location, which dictates the optimal lens material.

"The myopic shift must be considered when doing the IOL calculations," Dr. Buckley said. ■

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

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How WFG ablations compare

No clear patient preference for wavefront-guided excimer lasers for myopic LASIK

By Fred Gebhart; *Reviewed by Edward E. Manche, MD*

TAKE-HOME

- ***In a comparison of two wavefront-guided excimer lasers, one platform provides better clinical results on some measures but cannot image certain eyes. The other system can image nearly all eyes, but has slightly less robust clinical results, research suggests.***

STANFORD, CA ::

Multiple trials suggest that wavefront-guided (WFG) excimer ablations yield better results for myopic LASIK than wavefront-optimized (WFO) procedures.

But how do WFG platform results compare?

A recent head-to-head comparison found that though one system (WaveLight Allegretto Wave Eye-Q 400 Hz, Alcon Laboratories) produced slightly better results for some clinical outcome measures than a similar excimer platform (VISX CustomVue S4 IR, Abbott Medical Optics [AMO]), the latter was easier to use and could be used on eyes that the first unit could not image.

Dr. Manche

"The take home is that you had excellent safety in both groups," said lead author Edward E. Manche, MD, director of refractive and cornea surgery and professor of ophthalmology, Byers Eye Institute, Stanford University School of Medicine, Stanford, CA.

"No eyes lost more than 1 line of best-corrected visual acuity (BCVA)," Dr. Manche said. "We had gains in both groups that were essentially equivalent, with almost 50% gaining 1 or more lines of BCVA.

"It's very difficult to obtain good quality images on the Allegretto," he said. "You can only image about three-quarters of eyes . . . preoperatively. Postoperatively, it was even more difficult."

Dr. Manche has conducted a number of prior studies using both WFG and WFO platforms from multiple manufacturers.

"What we've found . . . was that WFG ablations yielded better results than WFO on both the VISX and the Allegretto," he said. "If WFG is better than WFO on both machines, it was only logical to compare WFG ablations."

The prospective, randomized, contralateral study treated both eyes in 50 subjects, a total of 100 eyes. One eye of each patient had WFG LASIK with the Allegretto laser, whereas the contralateral eye had WFG LASIK with the CustomVue laser. Eyes were randomly assigned by ocular dominance, and all LASIK flaps were constructed using a 150-kHz femtosecond laser (IntraLase iFS, AMO).

Eyes were closely matched by age, gender, and most visual measurements. The only statistically significant difference was slightly worse myopia in the CustomVue group, –4.18 D compared with –3.89 D in the Allegretto group.

SIMILARITIES, DIFFERENCES

One year after surgery, the two groups were statistically identical in terms of residual spherical equivalent and residual cylinder, Dr. Manche noted. There were significant differences, however, in higher-order aberrations at 1 month ($p = 0.04$) and at 12 months ($p = 0.01$).

The Allegretto eyes went from 0.38 µm preoperatively to 0.33 µm after surgery compared with 0.37 µm preoperatively in CustomVue eyes to 0.40 µm after surgery. Trefoil was reduced by similar amounts in both groups. Coma was unchanged in the Allegretto group and increased slightly in the CustomVue group. Spherical aberration decreased in the Allegretto group and increased in the CustomVue group.

Predictability was better in the Allegretto group at 3 months ($p = 0.04$), 6 months ($p = 0.02$), and 12 months ($p = 0.04$).

Best uncorrected visual acuity was similar in the two groups at 1 month, 3 months, and 12 months, but was significantly better in the Allegretto group at 6 months ($p = 0.04$). There was no statistically significant difference in BCVA between the two groups.

Subjective clarity presented the biggest difference between groups. Patients judged their Allegretto-treated eyes better both during the day ($p = 0.005$) and at night ($p = 0.001$) compared with their CustomVue-treated eyes.

PATIENT, PHYSICIAN PREFERENCES

There was no clear patient preference for one platform over the other. About 23% of patients preferred both the Allegretto and CustomVue lasers, just under 45% had no preference, and the balance were unsure which they preferred.

Though the Allegretto laser offered statistically significantly better outcomes on several measures, patients themselves had no preference for one treatment over the other, Dr. Manche said.

The two surgeons, however, had very clear preferences.

"We imaged the patients on both machines preoperatively and postoperatively," he said.

Preoperatively, the surgeons obtained images of 100% of eyes on an aberrometer (VISX WaveScan, AMO), but could only obtain images on 70% to 75% of eyes on another aberrometer (Allegretto Allegro Analyzer, Alcon).

"It is very difficult to obtain good quality images on the Allegro Analyzer, and the ones we obtained often took an extremely long time," Dr. Manche said. "Most people who use the Allegretto use the WFO treatment ablations, because the Allegro Anayzer is difficult to use."

That may put clinicians in a bind, he explained. The Allegretto produces better results for certain clinical outcome meaures, but imaging can be difficult to impossible. The CustomVue results are slightly lower for certain outcome measures, but imaging rarely fails, he noted.

"I do 100% WFG procedures," Dr. Manche said. "If I can't image [eyes of patients] on the Allegretto Allegro Analyzer, I [use] the VISX WaveScan. The VISX WaveScan can image almost anyone, with the exception of patients with very small pupils or corneal scarring. It is an extremely robust system." ■

Discuss the merits of wavefront-guided ablations at **Facebook.com/OphthalmologyTimes.**

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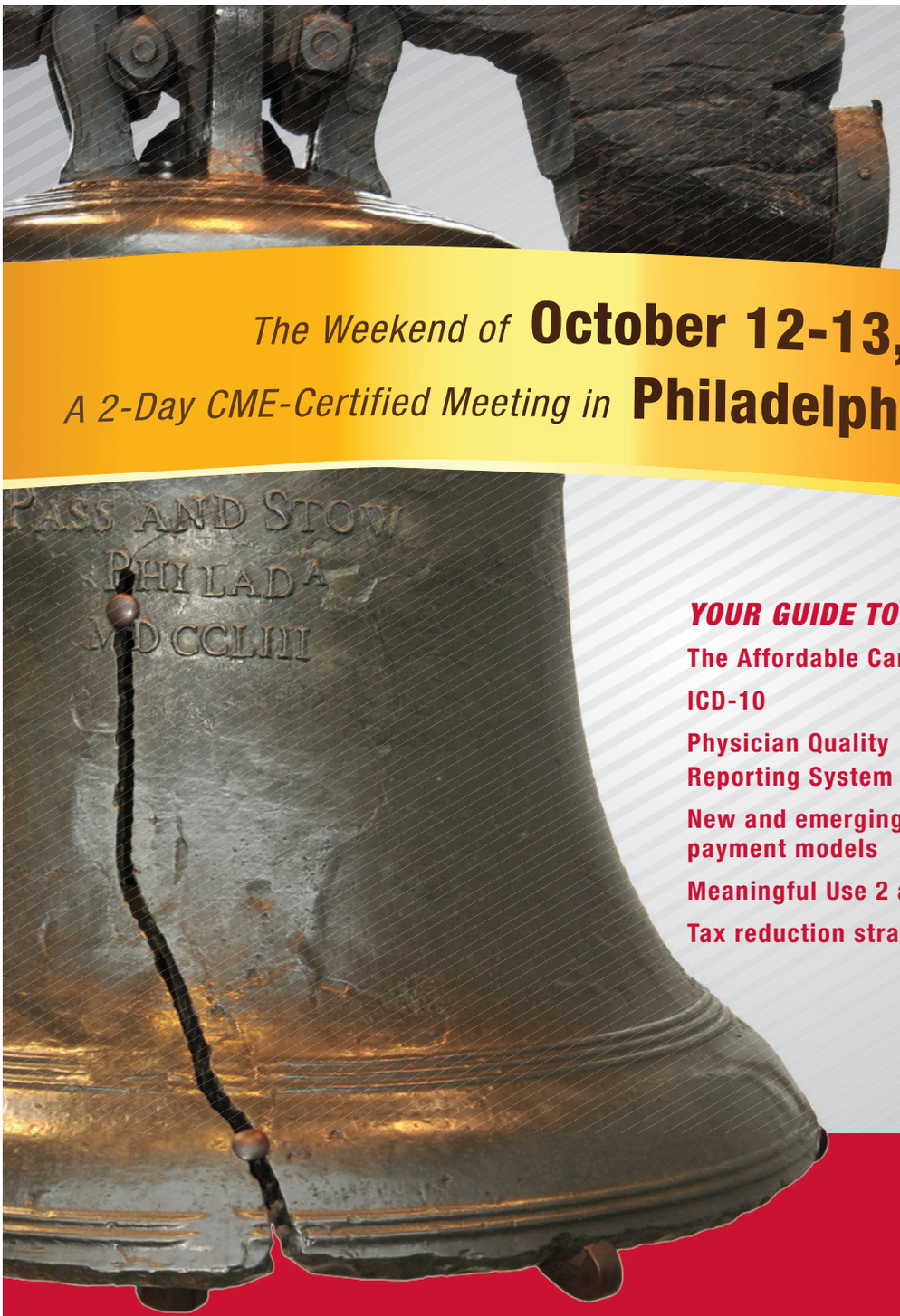
Dr. Manche has no financial disclosures that relate to this story.



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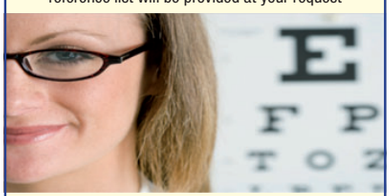

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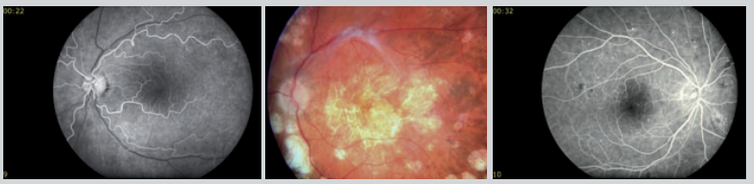

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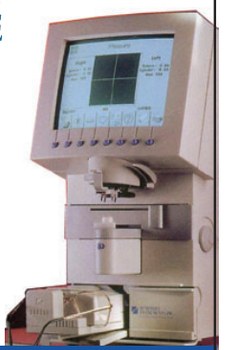

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Taking one for the team

When putting others before self for the good of the group can have meaningful outcomes

Putting It In View *By Dianna E. Graves, COMT, BS Ed*

TAKE-HOME

- ***The act of willingly making a sacrifice for the benefit of others can reap rewards both in the short and long term.***

Recently, we needed to add a new lead technician to the group. We have seven clinics located throughout the St. Paul area, and the leads are in charge of running their respective clinic.

A lead technician works to ensure that:

- **The technical staff is running up to speed and working as a team.**
- **The clinics are clean and safe for patients.**
- **The day is coordinated with the staffs at the front desk and in optical to ensure that all goes smoothly and calmly—or as calmly as it potentially can be.**

By nature, some days are just whirlwinds and other days are gentle breezes.

A couple of months ago, one of our current lead technicians from a busy two-physician office asked for a break from the action. She requested to be moved from her lead role in order to go back to the general technician population and give her brain a rest.

Losing a lead technician, even for a rest, can be very disruptive. However, I would rather let this technician relax a bit and be "just a tech" than to insist he or she stay in the role, burn out, and then possibly leave the practice.

Thus we began a search of the current staff for the next lead.

SEARCHING FOR THE PERFECT LEAD

This is not an easy endeavor. Though all of the technicians in our group have laudable skills and talents, being a lead is a different breed of technician.

I felt we had two technicians who had demonstrated they had matured enough in the past year to be groomed to become the next lead.

As in the past, I would have spoke to the candidates, discussed the potential of training to be a lead, and waited for the reaction.

I have seen every possible reaction when potentially moving a technician into a role outside of his or her comfort level—whether it be diagnostics, minor procedures, or being the lead. Reactions can range from:

- **Elation to absolute terror**
- **Instant megalomaniac**
- **The often-witnessed sullen behavior because they don't want be in charge–even though for years they have stated they could do it better!**

For some reason, this time I spoke to three of our seasoned leads and asked what they thought of my choices. Two agreed with my selections, whereas the other, Patti, went 180° and threw another name in the hat.

RUNNING INTO TROUBLE

Patti felt that a third technician, Mandy, was the best candidate.

This sent me hurtling back to a day about 7 months ago, when Mandy walked in my office and declared she wanted to be given a chance to step up to a leadership role.

She felt she had matured enough to do so and it was time for me to consider making her a lead when I had the next opportunity.

I was willing to give her a chance, but now I had a problem.

I needed one of the smaller, one-physician clinics to put her in so she could train and learn—without being blown away by trying to run one of the manic and larger two- or three-physician clinics.

So where's the problem?

The lead who recommended Mandy had the clinic where I needed Mandy to go!

Patti would need to leave so that Mandy could call it her own. Patti was going to have to go to our newest clinic that was a two-physician clinic and very busy.

CRISIS AVERTED

I went over one morning to share the news with Patti, but she was already aware of the problem.

"So, it's not too late. Should we choose one of the other technicians and wait a bit more on Mandy?" I asked her.

"I can't believe I am saying this—but, no," Patti said. "[Mandy] is ready and I guess she should have my clinic so she can get a good start under her belt. I will go to Sara's clinic and run it while she is gone. Then can we revisit it down the line when things are settled down?"

> 'Being a lead is a different breed of technician.'
>
> — Dianna E. Graves, COMT, BS Ed

In that moment, Patti had matured above and beyond by taking one for the team and continuing to push for her teammate to be the next lead—even if it meant disrupting her whole work life for a while. I was quietly so proud of Patti for stepping up into that situation for the good of the group.

And it stayed in the back of my mind—until last week.

NOT THE ONLY ONE

I was watching the evening news and saw a story about Lance Cpl. Bradley O'Keefe who had been injured while on duty in Afghanistan. He had finally been reunited with his black labrador retriever, Earl, whose training was in bomb detection.

Earl was a hero because he saved 13 members of O'Keefe's Army unit. The dog has alerted them to a hidden explosive nearby just before it was set off by an unknown enemy soldier.

O'Keefe was seriously injured by the blast and was sent back home to the United

Continues on page 38 : ***For the team***

FOR THE TEAM

(Continued from page 37)

States, whereas Earl was sent back to another unit to continue service.

While recovering, O'Keefe had lost hope of ever seeing his former partner again, until his step-sister intervened on a mission of her own to track down Earl and reunite him with her brother.

After a long year of looking, his sister was finally able to locate Earl.

When the military began to downsize its K-9 corps, Earl was transferred to the United States.

Earl eventually was sent to Rhode Island, where he was assigned to Trooper Damien Maddox.

One of Earl's and Maddox's missions was responding to the Boston marathon bombings to sweep for any additional explosives.

Even though Earl had been partnered with Maddox—and might have worked 4 or 5 more years with him—when O'Keefe's sister called and told the Rhode Island police chief of her brother's story, the final decision was delegated to Maddox, who agreed without hesitation.

"O'Keefe needs Earl more than I do," said Maddox, as he gave Earl's leash to O'Keefe.

O'Keefe and Earl were finally reunited at the Rhode Island State Police headquarters, where O'Keefe received a Purple Heart for his injuries in Afghanistan.

There are many forms of taking one for the team—from O'Keefe's injuries serving his country to Maddox returning his partner back to O'Keefe.

Of course, last but not least, there's Patti giving up her clinic so someone else could shine

Who says there are no heroes left? ■

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