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specialist Ian Crozier, MD, made medical headlines twice in recent months—first as one of the critically ill healthcare workers transported from West Africa to the United States after being diagnosed with acute Ebola virus disease (EVD), and again when the live virus was found in his aqueous humor weeks after he had been declared free of the disease.

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“Even though the acute outbreak status has improved significantly and has faded from media attention, there are still thousands of survivors who require ongoing care for their ophthalmologic issues as well as their systemic issues,” said Dr. Yeh, associate professor of ophthalmology, Emory Eye Center.

“In addition, their focus is on disseminating ways that we can strategize how we can not only screen patients but provide a higher level of care for potential uveitis outbreaks of a larger magnitude,” he added. “In addition, their focus is on disseminat-
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In This Issue

6 EDITORIAL

12 FOCAL POINTS

43 MARKETPLACE

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Beware venom ophthalmia
An ophthalmologist’s guide for avoiding spitting snakes

By Peter J. McDonnell, MD
director of the Willer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, and chief medical editor of Ophthalmology Times.

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THINGS THAT STRIKE terror in the hearts of many Americans—spiders, earthquakes, Ebola virus disease, and politicians with plans to “fix” healthcare—don’t faze me much. But, for as long as I can remember, I have had this visceral negative reaction to snakes.

This strong objection to these fusable reptiles was recently reinforced when I learned the story of Bayan Chungsang. He served in Kublai Khan’s army as it invaded China in the 13th century. In the cinematic version of the story, Genghis Khan orders that the man be blinded as a punishment for defying the Khan’s orders. Subsequently known to Marco Polo as “Bayan Hundred Eyes,” he became a general who led his troops with great success on the battlefield.

The way in which he is blinded is remarkable. His captors hold a cobra in front of him, and the snake spits fluid into the eyes of the prisoner who cries out in pain. The result is scarred and inflamed lids and bilaterally opaque corneas. Why do snakes inject venom into some animals and spit at others? According to scientists, they inject and eat small animals while they spit at larger animals perceived as threats but too large to eat. Pretty logical. So, what have we learned?

First, snakes are disgusting.

Second, if you find yourself face to face with a cobra, presume that you are small enough to eat—and experience convinces me that most ophthalmologists (no offense intended) are not—it is about to spit at your eyes. Refuse to look at it and close your eyes or put on goggles. Consider diverting its attention by holding your phone to the side at arm’s length while it plays an Adele video on YouTube—apparently no living thing can resist watching that lady sing.

Third, if someone comes into your office complaining of cobra venom in his or her eyes, immediate copious lavage and measures to support epithelial healing and limit ulceration are appropriate.2 Restorative measures such as limbic skin grafting and use of amniotic membrane to limit ulceration and promote repair—akin to those employed in patients with bad chemical burns—might obviate the need for eventual keratoplasty or keratoprosthesis.

corneal tissue destruction and scarring in rabbit corneas first treated with spitting cobra venom.

The snakes are accurate. One scientist wearing goggles tested the snakes. From a distance of 6 feet the Mozambique snake hit the investigator’s eyes 10 out of 10 times, whereas the black-necked spitting cobra was on target eight of 10 times. This spitting is instinctive, with the little rascals documented to spit at herpetologists (the scientists who study snakes) literally at the moment they emerge from their shells.

References

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ADVERSE EVENTS: Possible adverse events include loss of best spectacle corrected visual acuity (BSCVA), serious Transient Light Sensitivity Syndrome, serious primary open angle glaucoma, mislocated flap, melting of the flap, severe glare, and severe dry eyes. Complications can include corneal edema, epithelial ingrowth, diffuse lamellar keratitis, foreign body sensation, and pain.

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DETERMINING THE COST OF A HUMAN LIFE

I ENJOYED READING a recent editorial by Peter J. McDonnell, MD ("What’s the cost of a human life? Ophthalmology Times, Dec. 2015; bit.ly/1PSvoHt). I agree that no one could prove Dr. McDonnell wrong if he asserted that the correct percentage of gross domestic product (GDP) to spend on healthcare is 25%. In fact, I would even assert that no percentage could be proved “incorrect.”

The amount of GDP spent on healthcare is a collective choice we make as a country. It is true one more dollar spent in healthcare is one dollar less to be spent elsewhere. But then this is true for every dollar spent, in healthcare or not.

‘The amount of GDP spent on healthcare is a collective choice we make as a country.’
—Sheridan Lam, MD

Obviously, the growth of the healthcare sector of economy can only reach 100% of GDP, but this is true for every sector of the U.S. economy. Somewhere between 0% and 100%, we Americans would conclude that the benefit from one additional dollar spent in healthcare is less than the benefit from that dollar could be spent elsewhere.

At this point, the growth in healthcare spending would cease.

I do not see any problem in athletes or CEOs being paid in the millions. If the sport fans or shareholders are willing to shell out the cash, who am I to say what the correct levels of compensation ought to be? If one does not like watching Kobe Bryant play, he or she can turn off the television, or if he or she does not like Marissa Mayer as the CEO of Yahoo!, he or she can sell his or her stock in Yahoo! or mount a hostile takeover.

This is American free enterprise. You vote by spending or not spending your dollar.

Unfortunately, in healthcare, each consumer does not spend his or her own money but someone else’s. To each American healthcare consumer, it makes economic sense to consume more healthcare than what he or she has paid in as health insurance premiums. Furthermore, the doctor is not compelled to explain to the patient (the healthcare consumer) the economic cost of the care he or she is prescribing, because the patient does not bear the total cost of the care (assuming all goes well). Under our current system, I believe that the growth of the healthcare should top off, when any additional dollar paid in premium can no long purchase a dollar worth of healthcare.

Lastly, what is the cost of human life? That’s easy. I assume that Dr. McDonnell drives or takes public transportation to work every day. The compensation he receives has to worth more than the risk he takes with his life while driving or riding the bus or the train to work. Otherwise, he would get out of bed in the morning (at least, not for going to work).

In theory, the Wilter Eye Institute can keep on lowering Dr. McDonnell’s salary until he decides he no longer wants to take the risk with his life every morning to get himself to work (among other minor stresses of being a chairman).

This would be the cost of his human life (in current annualized basis).
—Sheridan Lam, MD

BOARD RECERTIFICATION: A THING OF THE PAST?

WITH GREAT INTEREST, I read the editorial by Peter J. McDonnell, MD, about how board recertification, as it is presently demanded, may become a thing of the past ("What have you learned? Ophthalmology Times, Oct. 1, 2015; bit.ly/1NAwWuH). Being in the first group of ophthalmologists with a “time-limited board certification,” I am sure I express the opinion of most that recertification (MOC) must stop.

The majority of the medical community is against MOC. What a novel idea for Dr. McDonnell to suggest that the American Academy of Ophthalmology, after 23 years, would conduct a survey of its dues-paying members as to their opinion on such an important and wide-reaching topic.

I anxiously will be checking my inbox.
—Bill Marks, MD

Atlanta
A 67-YEAR-OLD AFRICAN American male presented to the ophthalmology clinic after referral from an outside optometrist. He was seen previously for a 4-month history of red eye by two outside optometrists, diagnosed with filamentary keratitis, and given tobramycin/dexamethasone ophthalmic suspension 0.3%/0.05%.

His medical history was significant for hypertension and a history of prostate cancer. His medications included hypertensive medi-
cines and aspirin.

He denied any ocular history except soft contact lens wear for the past 24 years with average daily wear of 12 to 16 hours a day. He denied any ocular insult, did not use eye drops prior to presentation to the optometrist, or any family history of ocular diseases. He gave no history of severe allergic reactions, rash, autoimmune diseases, radiation, or any other cancers.

**EXAMINATION**

At the time of presentation, ocular examination showed a best-corrected visual acuity of 20/30 in both eyes with ability to pinhole down to 20/20 in the right eye and 20/25 in the left. Pupils, motility, and IOP were unremarkable.

Anterior examination revealed pannus superiority and 1+ guttae in both eyes. In the left eye, opaque epithelium arising from the superior limbus was observed to cover the visual axis and involve 70% of the cornea. Similar findings were present to a lesser degree in the right eye.

Late-fluorescein staining with a “whorl-like” pattern was demonstrated bilaterally.

**DISCUSSION AND DIAGNOSIS**

This patient exhibited classic findings of limbal stem cell deficiency (LSCD). Given his extensive contact lens history and lack of any other ocular etiologies, he was diagnosed with soft contact lens-induced limbal stem cell deficiency (SCL-LSCD).

SCL-LSCD is a poorly understood cause of LSCD. Its prevalence among SCL patients and SCL wearers is unknown with one cite stating 15% and 4%, respectively.1,3

SCL-LSCD is a well-known ophthalmologic disease. Common etiologies include Stevens-Johnson syndrome, chemical/thermal insult, radiation, mitomycin C, surgically induced, and aniridia.1,3

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Common symptoms of SCL-LSCD are de-
increased vision ranging from 20/25 to HM, photophobia, pain, redness, and tearing. These patients may also be asymptomatic; diagnosed during routine examination.1,3

Clinical findings are similar to those found in LSCD. The corneal epithelium demonstrates a dull and irregular reflex with opaque and variable thickness. A “streaming” appearance of the epithelium may be appreciated. The classic sign of late-fluorescein staining is present in all cases elicited due to the increased permeability of abnormal conjunctivalized epithelial cells.1,3 Superior involvement is present in all patients with SCL-LSCD with some degree of bilateral involvement.

All patients who exhibit SCL-LSCD are found to have worn soft contact lens daily. The average use at time of diagnosis is from 14.1 to 17.6 years (range 1 to 30 years) and 10 to 16.25 hours daily.1,3 Women are more affected than men accounting for 67% to 93%.1,3

The pathogenesis of SCL-LSCD is poorly understood. Mechanical friction of the SCL on the limbus may induce damage to the limbal stem cells. Hypoxia from the SCL may induce destruction. Thimerosal, a preservative used in SCL disinfecting solution, has also been associated with limbal stem cell failure.4

However, it is unknown why among the millions of SCL wearers, the diagnosis of SCL-LSCD is not more common. A “two-hit hypothesis” has been proposed suggesting that these patients are predisposed with co-existing ocular diseases (e.g., rosacea, conjunctivitis, low serum Vit A) or prior ocular insult (e.g., exposure to thimerosal).2

Often SCL-LSCD presents in patients with no other ocular diseases or risk factors.1,3

Management of SCL-LSCD is similar to the treatment of LSCD with the exception of indefinite cessation of SCL wear. Mild cases may resolve or stabilize with termination of SCL wear, preservative free artificial tears, and steroid drops. Adjunctive measures, such as warm compresses, lid scrubs, punctual occlusions, and autologous serum eye drops, may be used to promote ocular surface health.

Topical cyclosporine has been successful in continuing anti-inflammatory activity as steroids are tapered.

Vitamin A and scleral lenses have also been used with good success in recalcitrant cases.1,5

Epithelial debridement of conjunctivalized cornea is another successfully employed technique.6-7 Amniotic membrane has been used for partial-LSCD patients and shown to be successful in eyes with up to 330° of LSCD involvement.8-9

A number of other surgical options are available for SCL-LSCD.10-11 Conjunctival limbal autograft (CLAU) should be discouraged as both eyes almost always exhibit some extent of LSCD.

Living-related conjunctival limbal allograft (LR-CLAL) and keratolimbal allograft (KLAU—cadaveric donor) are two possible options with proven success. Both procedures, however, commit the patient to life-long use of systemic immunosuppressant.

Cultured limbal epithelial transplantation (CLET) is a relatively new promising technique. Donor epithelium may come from autologous, living-relative, cadaveric, or autologous oral mucosa epithelium and cultured to provide donor corneal epithelium. It has been used successfully in a limited number of cases.10 Among all these treatments, the most important is the indefinite cessation of soft contact lens use. With the cessation of SCL and artificial tears alone, 22% to 61% of SCL-LSCD resolved or stabilized.1,5 The addition of a steroid eye drop increased the percentage to 89% to 100%.1,1,5

Another study reported failure of conservative treatment in all eyes with all patients requiring surgery.2 Their diagnosis of SCL-LSCD, however, included only severe LSCD patients with greater than 6 clock hours of LSCD. Regardless of treatment method, visual and symptomatic prognosis is very good in this population with the majority achieving 20/30 or better vision.1,3,5

Our patient was instructed to immediately stop contact lens wear and use preservative-free artificial tears QID and Pred Forte QID. By 2 weeks, his clinical exam stabilized, redness improved, and vision stabilized.

CONCLUSIONS

It is difficult to predict which patients will develop SCL-LSCD. Therefore, all SCL patients should be encouraged to undergo routine ophthalmologic examination. One should always consider this disease when presented with a SCL-wearing patient with vague complaints, as early and correct diagnosis may reverse the damage with conservative measures alone.

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Dr. David Apple’s legacy endures through laboratory

Dr. Gerd Auffarth continues pioneering IOL work; advances ophthalmic research into clinic

By Vanessa Caceres; Reviewed by Gerd U. Auffarth, MD, FEBO

Before his death in 2011, David J. Apple, MD, was exalted within ophthalmology for his tireless investigation of IOLs.

Were he alive today, Dr. Apple would likely feel heartened by how his work has been carried on by Gerd U. Auffarth, MD, FEBO, who is now director of The David J. Apple International Laboratory for Ocular Pathology at the University of Heidelberg, Germany.

Dr. Auffarth was a fellow under Dr. Apple—a group nicknamed the “Apple Korps”—and traveled numerous times to the United States so the two could continue research with each other. When Dr. Apple died from tongue cancer in 2011, his widow, Ann, spoke with Dr. Auffarth about the possibility of continuing on her husband’s work. Dr. Auffarth was ready for the challenge.

Once they made arrangements, the Apple Lab was transferred from Charleston, SC, to Germany with about 300 boxes of material that had to be unloaded, checked, stored, and set up, Dr. Auffarth said. He also had to invest in special equipment, such as bench machines, and hire optical engineers and other staff members.

**E V O L U T I O N  O F  T H E  L A B**

Under Dr. Auffarth’s guidance, the laboratory has expanded research capabilities so that its findings can eventually reach the clinic.

The laboratory continues to evaluate explanted IOLs from autopsy eyes. Europe is an ideal place for those kinds of evaluations due to the sheer number of IOL types used there, Dr. Auffarth said.

“We evaluate them not only in terms of different materials and pathologies, but also optical design, where we can do an evaluation on the optical bench, visual quality, and so on,” he said.

The laboratory has joined forces with nearby Max Planck Institute for Polymer Research, Mainz, Germany, for some of the work. Additionally, the laboratory sometimes collaborates with companies that produce IOL materials. With evolving technology, researchers at the laboratory are able to take a closer look at the capsular bag, continuing the work achieved through the Miyake-Apple technique.

“There are new techniques that can isolate the capsular bag to see it from above and behind,” Dr. Auffarth said. “There are high-speed cameras where you see in a fraction of a second how the haptic unfolds.”

The behavior of the capsular bag can now be visualized, analyzed, placed in a computer, and further evaluated with mathematical simulations, he explained.

The laboratory also evaluates newer technology and approaches, such as femtosecond laser use for cataract surgery, the distribution of pharmacological agents in the vitreous body after intravitreal injections, and fluidics in the aqueous humor and the impact on IOP.

With Dr. Auffarth’s background as a clinician, he believes it is crucial to connect research with the clinic.

“David was more of a pathologist,” he said. “We’re trying to get circulation into other areas. I think the lab needs translation into the clinic.”

Staff members also stay busy presenting and publishing papers, with about 17 publications related to the laboratory since its establishment in Germany, and more on the way, Dr. Auffarth said.

There are 8 to 10 people who work regularly at the laboratory, including a professor, post-doctoral students, an optical engineer, and an optometrist.

If Dr. Apple could see the laboratory today, Dr. Auffarth is certain that his friend and colleague would be proud.

“He’d love it,” Dr. Auffarth said. “He loved to work and chat with young people.”

For more information about The David J Apple International Laboratory for Ocular Pathology, go to http://djapplelab.com/

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Dr. Auffarth did not indicate any financial interest in the subject matter.
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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 hypHEMA) 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 be closely monitored for corneal health.

Post-marketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal derangement, 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® ophthalmic solution 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 estimated human systemic exposure) 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® ophthalmic solution, 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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ing more knowledge about this disease and to have discussions about complicated scenarios that are novel.”

Other issues that are ongoing for Ebola survivors who have already lost so much are mental health issues, psychosocial stressors, problems with pregnancy, arthritis, and arthralgia, Dr. Yeh noted.

**Ocular Symptoms Present**

Dr. Crozier, who had been working in an Ebola treatment unit in Sierra Leone, was treated for 40 days then discharged when blood and urine tests for the virus were negative. But 14 weeks after his initial diagnosis, he developed ocular symptoms.

As his condition worsened, Dr. Yeh and Jessica G. Shantha, MD, from the Emory Eye Center, along with infectious disease physicians from the Emory University Hospital Serious Communicable Diseases Unit, intervened with procedures including a paracentesis of the anterior chamber.

“That led to the identification of live Ebola virus in the eye both by culture and also by molecular testing,” Dr. Yeh said.

Dr. Crozier was treated with a combination of oral, topical, and local corticosteroids and an oral antiviral medication. His symptoms improved over several months, and he subsequently has returned to Liberia and Sierra Leone to continue his volunteer work with Ebola survivors.

**Managing Ocular Complications**

One discovery from this case that will be useful in managing the ocular complications of EVD was that conjunctival and tear film samples taken both before and after the anterior chamber paracentesis tested negative for the virus.

This has implications for the clinical examination of Ebola survivors from an infection control and precaution guidance standpoint, but more invasive procedures are still being vetted in terms of the right way to proceed for ophthalmologists abroad,” Dr. Yeh said.

“The prevalence of the persistence of the Ebola virus in intraocular fluid is still unknown,” he said. “Further study is needed.”

Emory physicians seized the opportunity of this unprecedented case to launch research and outreach efforts. During the critical treatment stages, they were unsure whether the case was an outlier or whether other Ebola patients and survivors had similar complications.

“We looked in the literature and found some case reports of Ebola-associated uveitis, so we thought this might be a real problem,” said Dr. Shantha, who was then an ophthalmology resident and is currently a medical retina fellow at the Retina Consultants of Hawaii.

“We started to reach out to various ophthalmic, non-governmental organizations in Liberia and Sierra Leone to see if anyone had seen this aggressive, sight-threatening panuveitis, but also, as Dr. Crozier got better, we thought that the lessons we learned could be translated and help with the care of survivors in West Africa,” Dr. Shantha said.

In collaboration with lead clinician John Fankhauser, MD, and providers from Serving in Mission/Eternal Love Winning Africa Hospital and other organizations, Drs. Yeh, Shantha, Crozier, and Brent Hayek traveled to Monrovia, Liberia, to set up a mobile clinic and examine Ebola survivors.

“We noted different ocular complications, including cranial nerve problems, optic neuropathy, and the most common finding, uveitis, in less than 25% of patients,” Dr. Shantha said. “We realized that uveitis is an issue and is something that providers in West Africa need to be aware of.

“In addition, since we found Ebola virus in the ocular fluid of Dr. Crozier, we wanted to be sure that ophthalmic providers were aware of these findings because this could potentially be a source of an outbreak and a source of exposure for patients and ophthalmic providers,” Dr. Shantha said.

Contact between Emory physicians and providers and organizations abroad has continued, including a trip to Sierra Leone in the summer of 2015 to bring supplies, provide treatment protocols, screen and manage patients, and hold educational programs.

Other organizations including Partners in Health, Medecins Sans Frontieres, Ministry of Health and Sanitation, and in-country eye care providers are providing ongoing ophthalmic care for thousands of Ebola survivors in West Africa. Further trips to West Africa are being planned.

In addition, groups such as the World Health Organization are developing guidelines for care and follow-up of Ebola survivors.

**Take-Home**

- The unexpected discovery of viable Ebola virus in the eye of a patient who had recovered from the systemic disease has strengthened efforts to learn more about ophthalmic and systemic complications of Ebola survivors and has translated to management and follow-up strategies in West Africa.
Acrylic conformers effective in congenital anophthalmia

By Laird Harrison; Reviewed by Thomas E. Johnson, MD

Treatment requires close collaboration among patient, ophthalmologist, ocularist

By Laird Harrison

FITTING PATIENTS who have congenital anophthalmia or extreme microphthalmia with successively larger acrylic conformers can prepare space for ocular prostheses with minimal complications, said Thomas E. Johnson, MD.

“This works as well as, if not better than, a lot of the other techniques that have been used or reported,” said Dr. Johnson, professor of clinical ophthalmology, Bascom Palmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore.

Anophthalmia is extremely rare, affecting only 0.18 to 0.4 in 10,000 births. Microphthalmia is only slightly more common, affecting about 1.5 in 10,000. Causes include genetic disorders; gestational infections, such as toxoplasmosis, rubella and some strains of influenza; gestational exposure to thalidomide or x-rays; or gestational vitamin A deficiency, Dr. Johnson said. In the absence of a normal eye, sockets will not expand properly leading to a disfigured appearance.

Treatment “is mainly cosmetic,” he said. “It helps patients with their esteem to be able to wear an artificial eye and look normal.”

Ophthalmologists have used a variety of techniques to avoid this problem. One approach is a surgically implanted hydrogel ball implant that expands by osmosis of fluid in the socket, reaching about 10 times their original volume in 2 to 6 weeks. Hydrogel balls are surgically replaced with successively larger sizes.

Such devices have been available for about 20 years, but do not always provide the desired results, Dr. Johnson said. “There have been reported complications, including migration,” he said.

Another approach is a saline tissue expander implanted into the deep socket using titanium T-plate fixation at the lateral orbital rim. This requires surgery and multiple computed tomography (CT) scans. Inserting the device sometimes disrupts the important lateral canthus.

Dermis fat grafting can also expand the orbit. Typically the graft is placed around age 4 to 5 years. Drawbacks include unpredictable growth, atrophy, and poor socket elasticity that prevent the socket from responding well to future prosthetic enlargement. Other ophthalmologists have attacked the problem using surgery, including canthotomy and osteotomies, but this also can leave scars and may expose the patient to radiation from CT scans increasing the risk of leukemia and brain cancer.

In addition, some research suggests that repeated use of general anesthesia can impair a child’s cognitive development.

Using Acrylic Expanders

By contrast, Dr. Johnson described a series of 8 patients in whom he and his colleagues treated 14 sockets with acrylic expanders. These patients did not need surgery until they reached a mean age of 5.73 years when an adult-sized orbital implant was placed.

Of these patients, two required further surgery, in both cases to graft mucous membrane. In one case, the surgery was needed because of a car accident.

“In the other, we may have been too aggressive” in expanding the socket rapidly, he said.

The risk of adverse events from the conformers is small, he said. Acrylic is very inert and very few people develop allergies to it.

Dr. Johnson first became aware of the possibility of using acrylic conformers in 1997 when he read an article by Merritt and Trawnick in the Journal of Ophthalmic Prosthetics describing a similar approach.

While living in Saudi Arabia, Dr. Johnson collaborated with an ocularist, Yasser Bataineh, who was skilled in creating such acrylic conformers for these patients. Bataineh moved to Florida, and when Dr. Johnson took a position there at Bascom Palmer, the two resumed their collaboration. In their series of patients, they placed an average of about 20 successively larger conformers in each socket before implanting an orbital implant.

“The conformers start out flat and become progressively more rounded. Convexities on their posterior aspect stimulate an indentation in the socket called the pit.

“We think this pit plays a role in causing the socket expansion,” Dr. Johnson said. “In some of these other techniques the pit may not be respected, and that’s why we think the expansion may not be as good.”

One of the biggest challenges in the procedure is expanding the eyelids, Dr. Johnson said.

“One needs to expand the eyelids to hold the ocular prosthesis, and you also need to expand the boney orbit, because if you don’t, the patient will end up with a constricted socket with the inability to wear a prosthesis,” he said.

This approach works best with motivated parents because both the physician and the ocularist must see the patient frequently, he said.

“If they lose their conformer they have to come in fairly quickly,” he said. “You need to have very dedicated parents.”

Bilateral cases are easier to treat than unilateral ones because it can be difficult to exactly match the size of a natural eye with a prosthesis.

“Symmetry is very important in facial appearance,” he added.

The treatment requires a team approach. A geneticist and pediatrician should see the patient at the outset to determine whether other systemic abnormalities may result in comorbidities that must be managed.

“Then it’s a very close collaboration between the ophthalmologist and the ocularist,” said Dr. Johnson. “You have to work with an excellent ocularist who is very patient with children.”

TAKE-HOME

Acrylic expanders may be an option for the management of patients with congenital anophthalmos and microphthalmos.

Dr. Johnson

This article was adapted from Dr. Johnson’s delivery of the Ruedemann Lecture at the 2015 meeting of the American Academy of Ophthalmology. Dr. Johnson has no financial disclosures.
For patients with decreased tear production presumed to be due to ocular inflammation associated with Chronic Dry Eye

THE DRY EYE TREATMENT SHE NEEDS TODAY. BECAUSE TOMORROW MATTERS.

RESTASIS® twice a day, every day, helps patients experience increased tear production

Increased tear production was seen at 6 months.1

Indication and Usage
RESTASIS® (cyclosporine ophthalmic emulsion) 0.05% is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.

Important Safety Information

Contraindications
RESTASIS® is contraindicated in patients with known or suspected hypersensitivity to any of the ingredients in the formulation.

Warnings and Precautions
Potential for Eye Injury and Contamination: To avoid the potential for eye injury and contamination, individuals prescribed RESTASIS® should not touch the vial tip to their eye or other surfaces.

Use With Contact Lenses: RESTASIS® should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to the administration of the emulsion. Lenses may be reinserted 15 minutes following administration of RESTASIS® ophthalmic emulsion.

Adverse Reactions
In clinical trials, the most common adverse reaction following the use of RESTASIS® was ocular burning (upon instillation)—17%. Other reactions reported in 1% to 5% of patients included conjunctival hyperemia, discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging, and visual disturbance (most often blurring).

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

Reference: 1. RESTASIS® Prescribing Information.
A single injection of a gene therapy construct rAAV.sFlt-1 for advanced age-related macular degeneration (AMD) has shown safety and efficacy through 3 years in a small cohort, said Ian J. Constable, MBBS.

The investigator-initiated study (supported by Avanlanche Biotechnologies) has 3-year data from a phase I/IIa study on rAAV.sFlt-1. Prof. Constable noted the idea was that this single injection might be able to continuously secrete a therapeutic protein over an extended period to avoid the need for frequent injections in the neovascular AMD patient.

“Three-year follow-up from the phase I/IIa trial of rAAV.sFlt-1 has shown safety and efficacy through 3 years in a small cohort, said Ian J. Constable, MBBS.

The gene construct injection was done at day 7 coupled with vitrectomy. Patients were randomly assigned (3:1) to receive either 1 × 10^10 vector genomes (vg; low-dose rAAV.sFlt-1 group) or 1 × 10^11 vg (high-dose rAAV.sFlt-1 group), or no gene-therapy treatment (control group). All subjects had monthly assessments and received ranibizumab rescue injections as mandated by optical coherence swirling, loss of corrected vision, or fluorescein angiography.

Results published in 2015 on the first eight treated subjects “showed that at 1 year in the pilot study there was no loss of vision and there were minimal or no rescues required. Likewise, the center point thickness which was reduced with the booster doses at the beginning was largely maintained, although the retinal thickness was still above normal in some of the cases,” Prof. Constable said.

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INJECTION

(Continued from page 18)

corrected visual acuity (BCVA) of 36.5 letters (range, 28 to 56). The median center point thickness was 549 μm.

None of the eight enrolled patients were treatment-naïve, and the number of previous anti-vascular endothelial growth factor doses ranged from 1 to 29, with a mean of 11.5. A post-hoc analysis of the images indicated established sequelae—seven patients (88%) had subretinal fibrosis, and five (63%) had pigment epithelial detachment.

Six patients had long-term data at 18 months, and four have 36-month data (two patients dropped out at months 18 and 21 due to advancing Alzheimer’s disease). Although there were ocular adverse events, they occurred early and did not affect vision, Prof. Constable said. “There were no treatment-related ocular adverse events observed between the 12- and 36-month period,” he said. “Likewise, we encountered no systemic adverse events attributable to the gene therapy up to the 36-month exit point.”

Vector shedding was seen early (day 3) in two patients, but was absent at Day 21 and beyond. No associated virus antibodies were found at baseline in one of the two, and rose in the other, but were not associated with the number of rescue injections.

“Visual acuity was maintained,” he said. “During the period up to 18 months, there was a modest decrease in visual acuity in 3 out of 4 patients who were followed out to 36 months. The center point thickness was reduced by a mean of 186 μm at 12 months and 179 μm in the 4 remaining patients at 36 months.”

At both 12 and 18 months, there were very few rescue treatments in the high-dose group, but one patient in the low-dose group underwent an additional four rescue injections in year 3.

“Our overall impression is that per-protocol dictates an injection away from the macula, so maybe we’re undertreating these patients,” he said. “We’ve certainly seen no patient lose vision from geographic atrophy.”

Ongoing debate remains regarding the best place to inject—off-center eliminates the potential for disrupting the fibrotic macula, and the literature is beginning to show damage is limited by detaching the macula with a subretinal injection, Prof. Constable said.

“It may be that we will have to transflect a larger area; this is but one of the factors stopping us from moving directly onto a phase IIb study,” he said.

Instead, the group will be re-evaluating where to inject in a primate experiment.

OTHER CONSIDERATIONS

There is “good laboratory evidence” that peeling the internal limiting membrane (ILM) increases the transfer across the retina, but “there are new subtypes of AAV that seem to penetrate the ILM and get through better and it may be that one can still do it just with an injection and without the vitrectomy or peeling the ILM or indeed injecting under the retina with some of the new subtypes,” Prof. Constable said. “We simply don’t know.”

However, in this study all enrolled patients had posterior vitreous detachment to meet the safety requirements.

Prof. Constable added choroidal atrophy is an area the researchers will continue to monitor with the enlarged 40 patient cohort. Because of their advanced disease, some patients already had geographic atrophy and some in whom the geographic atrophy increased slightly.

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Instead, the group will be re-evaluating where to inject in a primate experiment.

Dr. Joel Schuman appointed chairman, NYU Langone Medical Center

CLINICIAN-SCIENTIST Joel S. Schuman, MD—whose work has led to significant advances in the detection and treatment of glaucoma—was appointed chairman, Department of Ophthalmology, NYU Langone Medical Center, New York, effective Jan. 1.

Dr. Schuman joins NYU Langone following a career at the University of Pittsburgh School of Medicine, where he was a distinguished professor and chairman of ophthalmology, and the director of the UPMC Eye Center. Dr. Schuman also held appointments at the university’s McGowan Institute for Regenerative Medicine, the Center for the Neural Basis of Cognition, and as professor of bioengineering at the Swanson School of Engineering.

A National Institutes of Health-funded researcher, Dr. Schuman and his colleagues were the first to discover a molecular marker for glaucoma, according to a prepared statement from NYU Langone Medical Center.

To aid in early detection, Dr. Schuman was a member of the team that developed a ground-breaking medical imaging procedure (optical coherence tomography), the statement said. Dr. Schuman and coworkers continue to improve this technology which has revolutionized research and treatment in the field.

After graduating cum laude with a bachelor of arts in psychology from Columbia University, Dr. Schuman received his medical degree from Mount Sinai School of Medicine.

He completed his residency in ophthalmology at the Medical College of Virginia, and clinical and research fellowships in glaucoma at the Howe Laboratory of Ophthalmology, part of Harvard Medical School’s Massachusetts Eye and Ear Infirmary.

Dr. Schuman and colleagues were honored in 2012 with the Champalimaud Vision Award for invention and validation of a revolutionary imaging system that reveals vivid details of eye anatomy, and Dr. Schuman also was given the Carnegie Life Sciences Award. He received the New York Academy of Medicine’s Lewis Rudin Glaucoma Prize in 2002.

In 2013, he received the American Academy of Ophthalmology Life Achievement Honor Award, and he was named a Gold Fellow of the Association for Research in Vision and Ophthalmology Fellows Class of 2014. He has published more than 300 peer-reviewed scientific journal articles, authored or edited eight books, and contributed more than 50 book chapters.
80% of patients achieved 20/20 uncorrected visual acuity (UCVA), and 98% had 20/40 or better UCVA. Several patients (6.8%) lost two more lines of best-corrected visual acuity.

Despite the initial LASIK fanfare, some complications were associated with it, and that is likely what led to the establishment of LASIK complication websites and foundations that continue today, Dr. Donnenfeld said.

“Their goals are noble and should be embraced,” he said. “Yet, it’s unfortunate that the activists and ophthalmologists have not gotten together to work constructively to improve outcomes.”

Some complications revealed earlier on via the peer-review literature included flap-related problems, ectasia, dry eye, and infections. One common infectious issue, atypical mycobacteria, has nearly been eliminated because of antibiotics and the realization that tap water is a contaminant, Dr. Donnenfeld said.

Studies related to dry eye and LASIK have found that although there is a significant loss of corneal sensation with LASIK, it improves after 3 to 6 months.

An FDA hearing took place in 2008 to review LASIK concerns, said Dr. Donnenfeld, who both spoke on behalf of LASIK at the hearing and listened to many of the patients giving testimonies with stories about depression, suicide, and other mental issues tied to previous LASIK.

“Overwhelmingly, the most common concern I heard patients felt is abandonment by their surgeon,” he said. “I promised myself that would never happen at my practice.”

After the hearing, the only action the FDA took was updating some of the LASIK-related information on its website, according to Dr. Donnenfeld.

More recently, results released last year from the FDA’s PROWL 1 and 2 studies showed that 99% and 96% of subjects achieved 20/20 bilateral UCVA, with no enhancements needed. The study also demonstrated LASIK’s safety. Dr. Donnenfeld was surprised to learn from the research that most subjects with glare and halo before LASIK actually had a reduction in these symptoms after LASIK. He had always presumed that these patients were not good candidates for the procedure.

Continues on page 22: LASIK

Dr. Donnenfeld reviewed the clinical history of LASIK and discussed myths and misconceptions associated with the procedure.

The procedure has undergone numerous refinements in efficacy, safety, and patient selection, so it still is a viable option for many patients, said Dr. Donnenfeld, founding partner of Ophthalmic Consultants of Long Island and Connecticut, Rockville Centre, NY, and clinical professor of ophthalmology, New York University Medical Center, New York.

Interest in LASIK has declined for several years—is the procedure worth saving?

The answer is an unequivocal “yes,” according to Eric D. Donnenfeld, MD. The procedure has undergone numerous refinements in efficacy, safety, and patient selection, so it still is a viable option for many patients, said Dr. Donnenfeld, founding partner of Ophthalmic Consultants of Long Island and Connecticut, Rockville Centre, NY, and clinical professor of ophthalmology, New York University Medical Center, New York.

Dr. Donnenfeld reviewed the clinical history of LASIK and discussed myths and misconceptions associated with the procedure.

The “red-letter day” for LASIK in the United States was Oct. 20, 1995, when the Summit excimer laser was first improved in the FDA, he noted. At that time, one FDA trial showed that
ADD SIMBRINZA® Suspension to a PGA for Even Lower IOP1*

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

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

IMPORTANT SAFETY INFORMATION

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

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

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

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

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

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

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

Prescribe SIMBRINZA® Suspension as adjunctive therapy to a PGA for appropriate patients
SIMBRINZA® Suspension should be taken at least five (5) minutes apart from other topical ophthalmic drugs.

Up to 7.1 mm Hg additional IOP lowering observed from baseline when added to a PGA1

5.6 mm Hg additional mean diurnal IOP lowering observed from baseline when added to a PGA1

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


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Although the FDA studies did show that 30% of patients got new dry eye after LASIK, that was evaluated at 3 months. Dr. Donnenfeld believes the results would have been lower had they waited until research. However, they found that patients on suspension that has been evaluated at 3 months. Dr. Donnenfeld believes the latest patient satisfaction rate of any procedure done on an elective basis today, with 91% of patients satisfied in various studies, Dr. Donnenfeld reported. Researchers also have busted the myth that ophthalmologists do not get LASIK done on their own eyes—they are actually four times more likely to have laser vision correction compared with the general population.2

Looking Forward

Recent technological improvements have strengthened LASIK’s potential, including pupil tracking, hazing management, customized and optimized ablation, and better-trained equipment, Dr. Donnenfeld said. However, there are further refinements that will take place.

References

“Have we an unmet need with dry eye, but now we know that preparative testing to elucidate dry eye before surgery can make a difference,” he said. “We have thinner and smaller flaps, topical cyclosporine, and a new of new medications for dry eye that will come for free.”

- Eric D. Donnenfeld, MD
Matrix therapy may promote faster corneal healing after epi-off CXL
Ongoing study of novel treatment may collect longer-term results, evaluate haze

By Michelle Dalton, ELS; Reviewed by Koray Gumus, MD

KAYSERI, TURKEY ::

A NEW MATRIX THERAPY AGENT (CACICOL20) may provide faster corneal healing after epithelial-off crosslinking with ultraviolet A and riboflavin, said Koray Gumus, MD.

Corneal crosslinking (CXL) has become a gold standard for slowing progression of keratoconus, but the debate continues about which technique—epithelial-on or epithelial-off (epi-on and epi-off, respectively)—is better, as there are advantages and disadvantages to both. Recent studies have shown that even the epi-on technique can cause epithelial damage, and result in ocular discomfort.

“Some complications might be related to the corneal wound healing,” said Dr. Gumus, Erzurum University School of Medicine, Kayseri, Turkey. “We need to promote better healing in these patients.”

Topical treatment with the regenerating agent (RGTA) is promising, said Dr. Gumus, noting it is an engineered biopolymer, mimicking heparin sulfate in the process to take place.

According to Dr. Gumus, RGTA replaces endogenous glycosaminoglycans (GAGs) that have been degraded by the glycogenolysis. Their binding to matrix proteins, collagen, elastin, and fibronectin results in a mechanical protection against proteolytic degradation. Restoration of extracellular matrix scaffolding properties is then induced and so is the communication between cells.

These effects allow the re-creation of a suitable microenvironment for cells to respond properly to the cascade of signals needed for the normal tissue regeneration process to take place.

Previous case series and animal model studies found RGTA “potentially useful in alternative noninvasive therapeutic approach in challenging cases, especially for the resistant and the neurotrophic corneal ulcers,” Dr. Gumus said.

His group investigated whether RGTA would speed up the corneal healing and reduce ocular symptoms after epi-off accelerated CXL.

The prospective, randomized, single-masked clinical study enrolled 60 eyes—all of which underwent epi-off accelerated CXL by one surgeon (KG). At the end of the procedure, eyes were randomly assigned to receive the topical RGTA eye drop just prior to contact lens fitting or to the control group, which received just a control medication therapy and were monitored up to 5% so we did not need to use any hypertonic riboflavin solution, which has a very unique composition, helping to maintain the cornea up to 5% so we did not need to use any hypertonic riboflavin solution,” he added.

All patients received the same postoperative medication therapy and were monitored three consecutive days. The contact lens was not removed on day 1, and if there was incomplete healing by day 2 or day 3, the size of the corneal epithelial defect was measured at the slit lamp, he said.

During the CXL procedure, “I kept the lid speculum throughout the procedure,” Dr. Gumus said. “I marked the cornea with the same size trephine to standardize the area and I touched the corneal surface with the tip of a triangle sponge soaked in 20% of ethanol.

“I used the same isotonic riboflavin solution, which has a very unique composition, helping to maintain the cornea even slightly swell the cornea up to 5% so we did not need to use any hypertonic riboflavin solution,” he added.

All patients received the same postoperative medication therapy and were monitored for three consecutive days. The contact lens was not removed on day 1, and if there was incomplete healing by day 2 or day 3, the size of the corneal epithelial defect was measured at the slit lamp, he said.

Continues on page 24 : Healing
Advances for refractive laser surgery aim to boost predictability, precision

Improvements to treatment planning could enhance efficacy, safety for certain groups

By Vanessa Caceres; Reviewed by Michael Mrochen, PhD

ZURICH ::

**REFRACTIVE LASER PLATFORMS**

provide outstanding results, have reliable technology with excellent predictability and outcomes, and provide a broad range of applications. Better diagnostic imaging is possible with optical coherence tomography and Scheimpflug technology, and the advances of femtosecond lasers are moving into cataract surgery, said Michael Mrochen, PhD.

“An element connecting all these components is treatment planning,” said Dr. Mrochen, founder of IROC Science, Zurich, Switzerland. “We are seeing improvement in software and customized treatment modalities.”

However, there still is room for improvement, Dr. Mrochen said.

For instance, efficacy and predictability could be improved for high myopia or myopic astigmatism, hyperopia and hyperopic astigmatism, presbyopia correction, and irregular cornea and higher-order aberration correction.

Although refractive lasers are very safe and effective, they could still be made safer to avoid dry eye issues, flap-related complications, epithelium and biomechanical considerations, and the ability to reverse treatments (such as in patients with presbyopia), according to Dr. Mrochen.

There are even improvements that could be made in the realm of convenience, such as the consideration of a patient’s fear about surgery or the ability for the surgeon to make easy treatment decisions and planning.

Some technology under way is already aiming toward improvements in these areas, Dr. Mrochen said.

For example, the introduction of ray-tracing ablation profiles that consider individual eye models will help boost refractive predictability.

“There’s a huge potential with treatment planning in this area,” he said.

Another improvement that could come soon is better precision with the introduction of ultraviolet (UV) femtosecond lasers instead of infrared lasers for small-incision lenticule extraction (SMILE). Although SMILE effectively helps highly myopic patients, Dr. Mrochen said, the procedure’s use of infrared lasers causes some limitations in accuracy. In fact, the accuracy compared with UV lasers is notably lower. By experimenting with ways to use less energy, surgeons can switch to UV light application, he noted.

“This will use lower energies and get a more precise cutting element for SMILE,” Dr. Mrochen said.

In corneal collagen crosslinking for keratoconus, there are efforts under way to use non-cutting treatments to correct low refractive errors, especially after cataract lens implantation.

The use of laser shaped lenticule onlays and an inlay from donor eyes for patients with hyperopia is an approach that is currently under examination, Dr. Mrochen said.

Yet, one more advance under assessment is the use of infrared lasers to modify the sclera and increase the ability of the lens to restore accommodation.

Though there is no one advancement outlined above to address all of the efficacy, safety, or convenience concerns that Dr. Mrochen outlined, they all might play a part in improving refractive surgery in future, he said.

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This article was adapted from a presentation by Dr. Mrochen during Refractive Surgery Subspecialty Day at the 2015 meeting of the American Academy of Ophthalmology. Dr. Mrochen is founder of IROC Science, Zurich, Switzerland.

HEALING

(Continued from page 23)

At baseline, the mean age, gender, and corneal epithelial defect size were comparable between groups. While 25 eyes (83.3%) with RGTA revealed complete healing on day 2, only 4 eyes (13.3%) revealed complete healing in the control group.

“The conjunctival hyperemia scores were also significantly lower in the RGTA group on day 1 and 2,” he said. “When we look at the ocular pain scores on days 0, 1 and 2, ocular pain scores were significantly lower in RGTA group. Similarly, the other symptoms also particularly were low on day 2 in the RGTA group.”

At the time of his presentation, there was only one other paper published on the same topic with RGTA in the literature, but some substantial methodological differences between the two were noted, he said.

For one, Kymionis et al. randomly assigned 36 eyes (18 patients) to RGTA or artificial tears.

“While we used RGTA only once before fitting the contact lens, that group used 1 drop RGTA daily till complete re-epithelization,” Dr. Gumus said. Similarly, Kymionis et al. concluded RGTA instillation seems to result in faster corneal re-epithelialization after CXL.

Differently, “our results showed complete healing one day earlier, on day 2,” he said. “Frequent use of RGTA might have decreased its effect on wound healing.”

Additionally, the authors did not find any significant effect in subject pain or discomfort, Dr. Gumus said.

In that study, it may have been difficult for patients to discern ocular symptoms between their eyes since both were enrolled, he said.

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This article was adapted from a presentation by Dr. Mrochen during Refractive Surgery Subspecialty Day at the 2015 meeting of the American Academy of Ophthalmology. Dr. Mrochen is founder of IROC Science, Zurich, Switzerland.

Reference


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This article was adapted from Dr. Gumus’ presentation at the 2015 meeting of the American Academy of Ophthalmology. Dr. Gumus has no financial interests to disclose.
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Enhanced corneal smoothness: Shorter recovery time of visual acuity
Technology also yields higher levels of postop visual quality, less re-epithelialization time

By Lynda Charters; Reviewed by David T.C. Lin, MD, FRCSC

VANCOUVER, BRITISH COLUMBIA ::

**EXTENDED PERIODS** of healing—and therefore, delayed visual recovery—after surface ablations may be a thing of the past with the advent of technology that was seen to enhance corneal smoothness in a multicenter evaluation.

Investigators reported shorter recovery time of visual acuity, higher levels of postoperative visual quality, and shorter time to re-epithelialization using SmartPulse Technology (SPT) (SCHWIND AMARIS).

SPT was evaluated retrospectively in eight clinical centers worldwide.

“The starting point of this innovation was the recognition that a smoother cornea has a positive effect on vision, particularly during the first few days after treatment,” according to David T.C. Lin, MD, FRCSC, lead author of the multicenter evaluation.

The developers of SPT redefined the ablation profile in geometric structure and pulse definition and distribution, explained Dr. Lin, clinical associate professor of ophthalmology, University of British Columbia, Vancouver, and medical director, Pacific Laser Eye Centre, Vancouver.

SPT uses a geometric model of the cornea that is based on a three-dimensional fullerene structure that realistically portrays the corneal curvature, which allows the pulses to be positioned more closely than previously, especially in the corneal periphery.

Pulse definition changed from second-order super-gaussian to truncated quasi-gaussian, whereas the pulse distribution changed from random to a global optimization strategy.

All of this results in a very smooth corneal surface.

**HOW IT WORKS**

This treatment can be used for both stromal and surface procedures, but the effect is more marked in surface procedures.

SPT is used for all ablations (and cannot be enabled/disabled per procedure) irrespective of the technique (LASIK, PRK, or transPRK), type (PTK, refractive treatments, presbyopic treatments or keratoconic treatments) or level of customization (aspheric, corneal, or ocular wavefront-guided).

SPT positively/synergistically combines with other features of the AMARIS, such as dual fluence (using a high fluence level for some 80% of the treatment to speed up ablation, and a low fluence level to smooth out), or small spot size of just 0.54 mm (enabling fine structures to be effectively ablated, while keeping pulse energy low even for the high fluence level).

The low fluence level is not an additional polishing procedure but the final step of the ablation using a lower energy/fluence to fill up the remaining (not completely ablated) gaps. Using SPT, the two levels of fluence move from coarse/line to fine/finer.

**RETROSPECTIVE STUDY**

A total of 1,159 eyes were treated underwent TransPRK. This procedure was chosen for evaluation because of the increased roughness of the corneal surface compared with other surface procedures. The retrospective chart review made among the eight centers on healthy eyes and initial treatments revealed preoperative manifest refractions ranging from -12.25 to +3.25 D, with astigmatism up to 8 D.

Sixty-six percent (765 eyes) of eyes were evaluated immediately after surgery (day 0), 60% (695 eyes) on day 1 postoperatively, 59% (679 eyes) on week 1, 41% (471 eyes) on week 2, and 46% (538 eyes) on month 1.

Investigators reported that the mean visual acuity was 20/40 (range centers, 20/25-20/96) immediately after surgery. The early outcomes are especially noteworthy because they were obtained with transPRK, a surface treatment, which is characterized by longer visual recovery compared with LASIK in the early postoperative stage, according to surgeons.

“”These results confirm excellent visual performance in the early postoperative stage compared with the reported visual recovery after surface treatments,” Dr. Lin said. “We are at the front edge of a paradigm shift in refractive surgery. Most patients comment that shortly after surgery, they are seeing almost as well as previously with their glasses. SPT has brought the ‘wow’ effect to transPRK.”

By month 1 postoperatively, UDVA was comparable to preoperative corrected distance visual acuity (CDVA).

Importantly, SPT exhibited a high safety profile. At the 1-month evaluation 75% of eyes had not lost any lines of Snellen CDVA; and 27% of eyes had gained one or more lines of Snellen CDVA, according to Dr. Lin.

In addition to the safety profile, the predictability of the target refraction was also very good. At the 1-month time point, the mean spherical equivalent was +0.13 ± 0.42 D. The great majority of eyes (81%) were within ±0.5 D of the target refraction.

The study investigators concluded: “SPT provides excellent results, particularly in the early postoperative stage after surgery. The contributing surgeons reported shorter recovery time of visual acuity, higher levels of postoperative visual quality, and shorter re-epithelialization time using SPT. Most patients commented that immediately after surgery they were seeing almost as well as previously with their glasses.”

The early outcomes are especially noteworthy because they were obtained with transPRK, a surface treatment, which is characterized by longer visual recovery compared with LASIK in the early postoperative stage, according to investigators.
PERTH, AUSTRALIA ::

GENETIC STUDIES WILL LIKELY play an important role in the course of myopia research, as twin studies have been invaluable in bringing investigators to the point they have reached today, said David A. Mackey, MD.

Interestingly, in a meta-analysis of data derived from 50 years of twin studies, ophthalmology traits were found to have the highest heritability of any group of traits measured. “This is probably related to our ability to accurately phenotype and define disease and our high precision at measuring ocular structures,” said Dr. Mackey, managing director and chairman, Centre for Ophthalmology and Visual Science, University of Western Australia, Perth.

In a twin study of the central corneal thickness, Dr. Mackey demonstrated the tight correlation of corneal thicknesses when one identical twin was compared with his or her sibling.

In contrast, in non-identical twins, there also was a correlation between the central corneal thicknesses but it was nowhere near as tight as that seen in the identical twins.

“This difference between the two types of twins indicates that there is a strong genetic component,” he said.

Myopia and refractive error were shown to have very high heritability scores in the twin studies. However, axial length and corneal curvature had even higher scores, suggesting that they are more genetically driven, according to Dr. Mackey.

A strong message in twin studies was that genes and environment did not act independently of each other and that the combination of the two factors was a driving force.

“It is by working out how the two work together that we should be able to understand the etiology of myopia,” he said.

When investigators determine the distribution of myopia in a population, the distribution appears to be normal.

However, Dr. Mackey explained that a larger number of individuals are grouped around zero than may be expected. This finding suggested that there are subtle feedback mechanisms pushing people who are either slightly hypermetropic or slightly myopic toward emmetropia. When there is a large refractive error, therefore, the feedback mechanism has been overcome.

Syndromic myopia—where myopia is associated with retinitis pigmentosa, congenital stationary night blindness, Marfan syndrome, or Stickler syndrome—is responsible for only a small percentage of myopia in the general population, according to Dr. Mackey.

In contrast, a recent meta-analysis of multi-ancestral cohorts—with 31 patient cohorts of more than 50,000 patients conducted by the International Consortium for Refractive Error and Myopia (CREAM)—found that more than 20 genes were associated with myopia (Verhoeven VJ et al. Nature Genetics 2013;45:314-318).

“This provided a whole new insight into the molecular mechanisms involved in myopia,” he said.

Another genome-wide analysis (Kiefer AK et al. PLoS Genetics (2013;9:e1003299) also identified a number of genes similar to that in the Nature Genetics report, 12 of which overlapped with those found by the consortium.

Dr. Mackey explained that investigators can “pool the genes into pathways and show where we may be able to look at future interventions” by which myopia can be stopped or treated.

Dr. Mackey takes-home

With myopia on the rise, greater understanding of genetic and environmental factors is key to refine interventions that may reduce disease progression.

Perth, Australia ::

Genetic, environmental twin studies provide clues to myopia research

Combination of factors a driving force for understanding etiology of disease

By Lynda Charters; Reviewed by David A. Mackey, MD

(FIGURE 1) Conjunctival UV autofluorescence (CUVAF) photograph showing the area of CUVAF outlined.

(FIGURE 2) Comparison of central corneal thickness measurement of twin 1 with twin 2 for monozygotic (MZ) twin pairs on the left compared with twin 1 with twin 2 for dizygotic (DZ) twin pairs on the right. The large difference between the two groups of twins suggests a high heritability. (Images courtesy of David A. Mackey, MD)
MYOPIA

Continued from page 27

When data from these two large studies were combined, more than 100 genes involved in myopia were found.

ENVIRONMENTAL IMPACT

The prevalence of myopia is high in Asian individuals and has been seen to be booming, perhaps in association with increased levels of education and study. This was also recognized in younger European cohorts compared with older Europeans.

“This was particularly correlated with the increasing amount of higher education in the European population in more recent generations,” Dr. Mackey said.

Using a genetic risk score from the CREAM study data, there was a strong interaction of genetically at-risk individuals with education levels.

On the other side of the coin, participation in outdoor activities has been recognized as providing protection against myopia.

“People with myopia spend less time outside,” Dr. Mackey said. “This [association] is being found consistently in different countries with different levels of outdoor behavior and climate.”

AUSTRALIAN FINDINGS

A large number of myopia studies have been—and still are—under way on the continent and have provided substantial data that have contributed to the understanding of the effect of environment and other genetic factors. These studies include the Blue Mountains Eye Study, the Melbourne Visual Impairment Project, Tasmanian and Queensland twins studies, the Norfolk Islands Eye Study, the Western Australian Raine Eye Health Study, and the Busselton Healthy Aging Study.

In an evaluation of European Australian individuals in the Blue Mountains Eye Study and the Melbourne Visual Impairment Project who matched the age of those in the Busselton Healthy Aging Study, remarkably, Dr. Mackey reported: “There is no evidence of a major increase in the myopia rates in Australia comparing people born before 1940 to baby boomers born between 1946 and 1964. Further, evaluation of 20-year-old patients in the Raine Eye Health Study also showed no large increase in myopia in European Australians.”

Another comparison of older cohorts of patients in Australia with North American and European cohorts, the patients in the Blue Mountains Eye Study in Melbourne had lower myopia compared with the Baltimore, Beaver Dam, and Rotterdam studies, Dr. Mackey noted.

THE SUN FACTOR

Considering these findings, investigators are speculating whether the higher number of sunny days that encourage outdoor activities in Australia may be responsible for lower myopia rates—although this very factor is related to substantially higher rates of skin cancer, with Australia having the highest rates in the world.

In light of this, Dr. Mackey and colleagues are evaluating (in addition to melanoma rates) other markers of outdoor activity, such as skin mole counts, skin wrinkling, vitamin D levels, bone density, the results of ultraviolet (UV) monitors, the incidence of pterygium, and conjunctival UV autofluorescence.

Findings related to conjunctival UV autofluorescence showed that autofluorescence was present in the area in which pterygia would normally develop. Investigators measured the areas of autofluorescence as a biomarker of ocular sun exposure. When this concept was applied in 800 inhabitants who participated in the Norfolk Island Eye Study conducted between Australia and New Zealand, there was a significant correlation between pterygia and a large amount of autofluorescence and an inverse association with myopia.

“The individuals with myopia were more likely to be in the lowest quartiles of conjunctival autofluorescence, while those who were emmetropic and hyperopic had more evidence of sun damage to the eye,” Dr. Mackey said.

These results were borne out in a comparison of identical and non-identical Australian twins, in which the correlation of conjunctival UV autofluorescence was similar in the two groups.

“The similarity of the correlations suggests that the genetics is not the main component and is a common environment that the two twins share,” he explained.

When investigators compared the twins from subtropical Brisbane with those from temperate Tasmania—the former of which live at a more tropical latitude—the degree of autofluorescence in the Brisbane group was significantly larger.

When investigators evaluated the vitamin D levels in twins from Western Australia with those with northern European ancestry, the high vitamin D level was associated with lower myopia. In children with East Asian ancestry, there was a much stronger correlation between the vitamin D level and high myopia.

Regarding the presence of skin cancer, in the Busselton Healthy Aging Study that included patients aged 45 to 64 years, 7.7% of the patients had already undergone a surgery for skin cancer.

“Dramatically, only 11.6% of these patients had myopia,” Dr. Markey said.

The consistent message is that markers of outdoor activity are associated with myopia protection, he added.

MANAGING MYOPIA

The fear in this area concerns pathological myopia that will accompany the myopia boom, particularly in Asia, Dr. Mackey noted. Complications include retinal detachment, myopic maculopathy, cataract, and glaucoma.

“Myopic maculopathy is now the second-leading cause of blindness in working-age adults in China,” he said.
Of the options to treat myopia, ortho-k seems the most effective for preventing progression of the disease, he noted. In three meta-analyses that contain 10 studies of ortho-k, they found a difference in axial length of about 0.27 mm over 2 years and 45% less progression of myopia—with greater effects seen in Asian than in European patients, and more noticeable in higher levels of myopia, Dr. Mackey explained.

Investigators are also exploring atropine as a treatment avenue for myopia.

Again, the impact with Asian children appears greater than in Caucasian European children. The Singapore ATOMI+2 studies reported that the lowest (0.01%) dose of atropine is associated with the lowest rebound compared with the 0.5% and 0.1% doses. A concern with this treatment is the impact of even a slightly dilated pupil on the desire for outdoor activity.

A 2015 study from Guangzhou, China, found that increasing outdoor activity by only 40 minutes at the end of the day had a small effect on reducing myopia. Spreading 80 minutes of activity over the course of the day in a study of Taiwanese children also showed a small effect in reducing myopia progression.

With both strategies, atropine had the greater effect, but increasing outdoor activity markedly is associated with a higher risk of skin cancer, Dr. Mackey cautioned.

“To shift someone by 4 D, the risk of skin cancer is probably doubled,” he said.

**INDICATIONS AND USAGE**

TRAVATAN Z® (travoprost ophthalmic solution) 0.004% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

**Dosage and Administration**

The recommended dosage is 1 drop in the affected eye(s) once daily in the evening. TRAVATAN Z® Solution should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the IOP-lowering effect.

TRAVATAN Z® Solution may be used concomitantly with other topical ophthalmic drug products to lower IOP. If more than 1 topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes apart.

**IMPORTANT SAFETY INFORMATION**

**Warnings and Precautions**

Pigmentation—TRAVATAN Z® solution has been reported to increase the pigmentation of the iris, perilental tissue (eyelids), and eyelashes. Pigmentation is expected to increase as long as travoprost is administered. After discontinuation of travoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the perilental tissue and eyelash changes have been reported to be reversible in some patients. The long-term effects of increased pigmentation are not known. With treatment with TRAVATAN Z® Solution can be continued in patients who develop noticeably increased pigmentation, three patients should be examined regularly.

**CHALLENGING PERSPECTIVES IN REFRACTIVE SURGERY**

Finally, Dr. Mackey presented some challenges for the future.

Economic considerations are whether society can afford to treat 90% of the population and then make global societal changes to prevent myopia, such as increasing outdoor time and decreasing classroom time.
Corneal biomechanics may pave way for personalized refractive surgery

Computer simulation-based medicine an important part of treatment

By Vanessa Caceres

ADVANCES IN CORNEAL biomechanics will continue to lead to better and more personalized results in refractive surgery, said William J. Djupe Jr., MD, PhD.

“The corneal biomechanical link between the structure and functional data of the cornea is exquisite,” said Djupe, staff, ophthalmology, biomedical engineering and transplant, Cole Eye Institute, Cleveland Clinic, Cleveland, and founder, OptoQuest Inc.

“Small changes in elevation or curvature make an enormous difference in optical properties,” he added.

The relationship between corneal biomechanics and the practice of refractive surgery continues to evolve, said Djupe, noting that more recently, computer-based biomechanical models are helping leverage the potential of existing tools to transform diagnosis and surgery.

Although refractive surgeons have a number of precise tools for corneal measurement and treatment delivery at their fingertips, tools for leveraging this precision in treatment planning have not kept pace.

For example, nomograms incorporate very little patient-specific information from the preoperative exam and are lacking altogether for newer, off-label, or combined refractive treatments.

Corneal biomechanics may eventually help fill that gap.

“Current paradigms are more retrospective, probabilistic, and population-based,” Dr. Dups said. “In the future, they will be more prospective, deterministic, and more personalized. The way to get there is through simulation-based medicine.”

In refractive surgery, simulation can help surgeons and researchers test treatment hypotheses, simulate treatments in a pre-clinical setting without putting patients at risk, and evaluate novel treatment designs and personalized optimizations.

“I can predict refractive outcomes more precisely in a virtual domain, this can help us to select right procedure for a patient or opti-
**Topical drop therapy shows promise as treatment for presbyopia**

Agent allowed a ‘dynamic’ pupil and was without significant adverse effects

By Cheryl Guttman Krader; Reviewed by Luis Felipe Vejarano, MD

The study enrolled 20 patients, of whom 9 were natural emmetropes and 11 had a history of LASIK (6 using the Vejarano Method for Presbyopia). The patients ranged in age from 41 to 57 years with a mean of about 50 years.

Assessments for efficacy and safety were performed prior to instillation of a single drop in each eye and after 0.5, 1, 2, 3, 4, and 5 hours, 7 and 30 days.

“Although this study was designed to assess the efficacy and safety after using a single drop in each eye, the topical formulation is intended to be used twice daily, once in the morning and once in the afternoon,” Dr. Vejarano said.

The results showed near uncorrected visual acuity (UCVA) improved by about 2 to 3 lines in each eye and binocularly from a baseline mean of about J3.5 to about J1.5. Mean UCVA at far was 20/25 at baseline, and except for a slight decrease after 1 hour, was improved by an average of about 1 line in each eye at all follow-up measurements. Binocularly, UCVA at far increased by 1 line on average, and no patient had a loss in binocular UCVA at far.

“Whereas other presbyopia drops improve near vision by causing an extreme miosis or a myopic shift that can reduce far vision, refractive measurements in this study showed there was a maximum myopic shift of just 0.5 D that occurred only at 1 hour post-treatment,” he said.

Measurement of objective scatter index (HD Analyzer, Simovision) prior to drop instillation and after 2 hours showed no change in optical quality of the eye but an increase in the accommodative amplitude by 0.75 D. Defocus curve measurements showed a 1.25 to 1.75 D in the accommodative range at near, increase of 0.75 D also in the accommodative amplitude and 20/25 or better in all of the patients for intermediate vision, Dr. Vejarano said.

“The improvement in accommodative range was also proven using ray tracing aberrometry [iTrace, Tracey Technologies] with the same result,” he said.

Pupil diameter was also measured and found to be mildly affected by the topical treatment (“dynamic miosis”).

**RESULTS OF A PROSPECTIVE study** show that treatment with a proprietary topical ophthalmic formulation (PresbV Tears) safely and effectively increases physiological accommodation to improve uncorrected near and intermediate vision without compromising distance vision in presbyopic emmetropes, said its inventor, Luis Felipe Vejarano, MD.

“This topical agent represents a noninvasive solution for addressing presbyopia that I believe meets all of the criteria for an ideal treatment,” said Dr. Vejarano, associate professor of ophthalmology, University of Cauca, Popayán, Colombia. “It is binocular, truly accommodative, improves near, intermediate, and far vision or at least doesn’t alter it, and allows a dynamic pupil in different light conditions (‘dynamic pseudoaccommodation’) that could also diminish glare and avoid decrease in contrast sensitivity.”

The agent is non–toxic, causing no adverse effects on the lacrimal film, corneal epithelium or endothelial cells, macula, or trabecular meshwork, he noted.

The study enrolled 20 patients, of whom 9 were natural emmetropes and 11 had a history of LASIK (6 using the Vejarano Method for Presbyopia). The patients ranged in age from 41 to 57 years with a mean of about 50 years.

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“The improvement in accommodative range was also proven using ray tracing aberrometry [iTrace, Tracey Technologies] with the same result,” he said.

Pupil diameter was also measured and found to be mildly affected by the topical treatment (“dynamic miosis”).

**take-home**

- In a prospective study including 20 presbyopic emmetropes, treatment with a proprietary topical ophthalmic formulation (PresbV Tears) demonstrated benefit for improving near, intermediate, and far uncorrected visual acuity.

**BIOMECHANICS**

(Continued from page 30)

mimize it appropriately,” he said. “For screening, it provides feedback on the likely structural response and may help reduce ectasia risk. It will also be a new tool for designing and refining the next generation of corneal refractive treatments.”

Examples of applications include evaluating how a refractive surgery candidate might fare from a structural risk standpoint with LASIK, PRK or SMILE, or assessing how a patient with a particular keratoconus geometry might respond to various crosslinking patterns.

To drive the predictive simulations, surgeons will be able to capture patient-specific information from devices they are already using, such as Scheimpflug tomography or optical coherence tomography, and then eventually include information from emerging corneal biomechanical characterization tools.

The goal of developing a software interface that can combine this information, simulate the outcome of a procedure, and produce a report for the surgeon is becoming a reality with the help of National Institutes of Health support and a commercialization grant from the State of Ohio, Dr. Dupps said.

**WILLIAM J. DUPPS JR., MD, PHD**

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This article was adapted from Dr. Dupps’ keynote presentation at Refractive Surgery Subspecialty Day at the 2015 meeting of the American Academy of Ophthalmology. Dr. Dupps is founder of OptoQuest Inc. and has intellectual property through Cleveland Clinic Innovations related to computational modeling and biomechanical measurement in ophthalmology.
New custom ablation treatment raises bar in laser vision correction outcomes

Topography-guided procedure improved visual acuity, symptoms at 12-month visit

By Cheryl Guttman Krader; Reviewed by Karl G. Stonecipher, MD

CHAPEL HILL, NC ::

A UNIQUE TREATMENT THAT personalizes the ablation to the cornea—topography-guided LASIK (Contoura Vision, Alcon Laboratories)—is delivering unsurpassed visual quality and quantity outcomes, said Karl G. Stonecipher, MD.

The treatment is the first topography-guided LASIK to receive FDA approval. It is performed using the WaveLight Topolyzer Vario Diagnostic Device, proprietary treatment planning software, and either the Allegra Wave Eye-Q or WaveLight EX500 Excimer Laser systems (all Alcon products).

It is indicated for use in patients ages 18 years and older for the reduction of up to −9 D of spherical equivalent (SE) myopia or myopia with astigmatism, with up to −8 D of spherical component and up to −3 D of astigmatic component in the spectacle plane. Treated eyes should have a normal cornea (e.g., normal thickness and only minor variations in topography, such as an asymmetric bowtie pattern) and stable refraction.

“Contoura Vision represents an additional option for improving our outcomes with laser vision correction,” said Dr. Stonecipher, who was an investigator in the study and is clinical associate professor of ophthalmology, University of North Carolina, Chapel Hill. “It normalizes the cornea, optimizing the optics, and in the U.S.-based multicenter clinical trial, it was associated with amazing results for improving objective visual acuity measurements and, most remarkably, for improving visual symptoms.”

249 EYES TREATED

A total of 249 eyes were treated in the trial, of which 230 were evaluated at 12 months. Visual acuity measurements at 12 months showed uncorrected visual acuity (UCVA) was 20/20 or better in 92.7% of eyes, 20/16 or better in 68.9%, and 20/12.5 or better in 31.6%.

“Compared with the preoperative best spectacle-corrected visual acuity (BSCVA), postoperative UCVA was better by 1 or more lines in 29.6% of eyes and equal to or better in 60.3%,” Dr. Stonecipher said.

In addition, the refractive outcomes were accurate and stable. Mean postoperative MRSE at 12 months was 0.06 D and the mean achieved surgical correction was nearly the same as the intended surgical correction, 1.23 D MRSE versus 1.27 D MRSE.

Contrast sensitivity was also measured, and the results showed improvements under mesopic and photopic conditions across all spatial frequencies.

Furthermore, many patients benefited with improvement of existing visual and/or ocular symptoms. Compared with preoperatively, reports of marked-to-severe problems with light sensitivity, difficulty driving at night, reading difficulty, fluctuation in vision, glare, halos, starbursts, dryness and pain were all reduced after the topography-guided procedure.

The difference between the proportions of patients with marked to severe problems preoperatively versus postoperatively was statistically significant for light sensitivity, difficulty driving at night, reading difficulty, and glare.

“This is the first LASIK clinical trial in which we have ever seen statistically significant improvements in these visual symptoms,” said Dr. Stonecipher, who is also medical director, TLC Greensboro, NC.

Safety was excellent. BSCVA was 20/40 or better in all eyes. Eye dryness was the most commonly reported issue in the first 3 months after surgery. “Compared with baseline, however, there was a 1.6% decrease at 3 months in the incidence of moderate to severe eye dryness,” he said.

Dr. Stonecipher said his results with the topography-guided LASIK procedure match or surpass those achieved in the clinical trial, even as he is still working to refine his nomogram.

“All of my patients are seeing 20/20 or better uncorrected on postop day 1, almost three-fourths are achieving 20/16 or better UCVA, and around 10% are 20/10,” he said.

Dr. Stonecipher said he is now performing a topography-guided procedure in about 30% of his LASIK population, and he is finding that querying patients about existing visual symptoms can be a guide to identifying good candidates.

REMOVES VISUAL SYMPTOMS

“The topography-guided LASIK procedure has opened the door for us in terms of reducing visual symptoms that can be induced with other LASIK approaches,” he said. “I have begun to be more proactive in asking patients whether they have problems with glare, halos, starburst, or difficulty driving at night as that can be a clue to some subtle topographic abnormality.”

Obtaining good preoperative topography is requisite to achieving good results.

“As with conventional or wavefront-guided LASIK, noise-in equals noise-out, and with the topography-guided LASIK procedure, the planning software will not work without reliable topography,” Dr. Stonecipher said.

Candidates should be carefully evaluated and treated for ocular surface disease preoperatively.

“About one-third of my refractive surgery population comes in with some type of ocular surface disease,” he said. “When performing topography-guided LASIK, we want to be sure that the topography reflects real abnormalities in the corneal surface and not an irregularity related to ocular surface disease and a poor tear film.”
3-D OCT option to improve refractive outcomes after cataract surgery

Intraocular morphology assessment proposed as paradigm for pELP prediction algorithm

By Cheryl Guttman Krader; Reviewed by Joseph J.K. Ma, MD

TORONTO ::
AN ALGORITHM USING three-dimensional (3-D) intraocular morphology shows promise for improving postoperative effective lens position (pELP) predictability, and therefore the accuracy of refractive outcomes after cataract surgery, said Joseph J.K. Ma, MD.

“pELP is the most significant source of error in modern IOL power calculations,” said Dr. Ma, assistant professor of ophthalmology, University of Toronto, Ontario. “Our current paradigm for refining these formulas relies on postoperative manual refraction, which can result in a pELP error, that can range anywhere from 280 to 400 μm, depending on the consistency of the refraction and power of the IOL that is implanted.

“In our study, we used a 3-D morphology-based algorithm that utilized the direct measurement of the true lens position in patients who underwent femtosecond laser assisted cataract surgery (FLACS),” Dr. Ma added. “We believe that we can achieve a mean pELP error in the range of 52 μm using direct morphology based measurements.”

In addition, both the correlation coefficient and the 95% limits of agreement between the predicted and measured mean pELP were significantly better using the 3-D algorithm than with theoretically calculated multivariate estimates of pELP. The next step is to conduct additional analyses to validate these findings, including in patients not undergoing FLACS, he noted.

Dr. Ma’s study was a retrospective analysis including data from 143 consecutive eyes evaluated intraoperatively with the integrated OCT from a femtosecond laser platform and with Scheimpflug imaging and swept-source OCT at an average of more than 5 months after surgery.

Results for pELP predictability were compared with those obtained using the Haigis formula, which uses axial length for pELP prediction, and the Olsen formula, which combines axial length with measurements of anterior chamber depth and crystalline lens thickness.

Scatter plots mapping the true lens position against the algorithm predictions showed a much tighter spread of the data using the 3-D algorithm than with either of the theoretical formulas. The correlation coefficient for the agreement between the measured and predicted pELP was significantly higher using the 3-D algorithm than with the Haigis and Olsen formulas (0.86 versus 0.58 and 0.73, respectively).

FORMULA SUPERIORITY

“Of note, the correlation coefficients for the two theoretical formulas are much higher than those published previously,” Dr. Ma said. “The discrepancy may be explained by use of the femtosecond laser for capsulorhexis creation in the eyes included in our study.”

The data were also analyzed using Bland Altman plots that showed superiority of the 3-D algorithm compared with the Haigis and Olsen formulas for tightening the 95% limits of agreement between predicted and actual pELPs (-0.66 versus -1.96 and -1.08, respectively).

Because the ability to perform topography-guided LASIK and its outcome depends on the quality of the diagnostic information, it involves some extra work preoperatively on the part of the technician and the surgeon. The technician has to obtain high quality topographic images with a reproducible map over at least 70% of the cornea, and the surgeon has to review the images against the treatment plan to confirm the ablation will achieve the refraction goal.

Although the indication for the topography-guided LASIK procedure allows treatment of up to –9 D SE, Dr. Stonecipher said refractive surgeons would do best to limit their selection of patients initially to “easier cases” that he described as eyes with up to –4 D of myopia and up to –2 D astigmatism.

START LOW AND SLOW

“My advice is to start low and slow because there is a challenge and some art to topography-guided LASIK planning,” Dr. Stoneciper said. “Assuming one might have 10% error in refractive accuracy initially, it will be much less of an issue treating an eye with a lower than a higher SE. That is why any surgeon starting with a new laser or new software should start low and work up.”

He also cautioned that while refractive surgeons outside of the United States, where topography-guided LASIK has been available, are addressing “20/unhappy patients” with aberrated corneas associated with previous refractive surgery or keratoconus, the platform is not approved for such use in the United States. This application requires further development, Dr. Stonecipher said.

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This article was adapted from a presentation by Dr. Ma during Refractive Surgery Subspecialty Day at the 2015 meeting of the American Academy of Ophthalmology. Dr. Ma is a consultant and lecturer for Alcon Laboratories and Abbott Medical Optics and a consultant to Bausch + Lomb.
A novel method has been developed that visualizes three-dimensional IOL formulas. Referred to as the “super formula,” the Ladas Super Formula is comprised of the ideal segments taken from five of the existing IOL formulas currently used and uses the ideal IOL formula for individual eyes, said John G. Ladas, MD, PhD.

The investigators who developed this method hope that it will fulfill three goals: “broaden the conceptual understanding of IOL calculations, improve clinical outcomes for patients, and stimulate further progress in IOL formula research.”

Surgeons can attest to the fact that calculating the appropriate IOL power for individual patients can be difficult.

However, undertaking the task is important to obtain the best vision possible postoperatively, said Dr. Ladas, assistant professor of ophthalmology, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore.

As Dr. Ladas and colleagues pointed out, in general, all of the existing IOL formulas are highly accurate in predicting which IOL should be used for certain refractions.

“However,” they noted, “certain formulas have been found to be more accurate under specific conditions related to the input variables that are used, such as axial length and corneal power, which is likely related to the different ways the formulas use these data to determine the theoretical effective lens position based on the input data.”

However, the rub is that no one formula performs perfectly in all situations, surgeons must then make an educated guess about which formula to use.

Working with Albert Jun, MD, PhD, Aazim Siddiqui, MD, and Uday Devgan, MD, they developed a method to represent IOL calculations in three dimensions. This methodology uses the most accurate and current information on IOL formulas, adjustments, and lens design to create one “super surface” leading to the development of an IOL super formula.

The existing formulas that were included in their initial study were the Hoffer Q, Holladay I, Holladay I with Koch adjustment, Haigis, and SRK/T. The investigators then determined at what point the IOL powers calculated using those formulas differed by more than 0.5 D, 1.0 D, and 1.5 D from each of the other formulas. A super surface was created that included the ideal portions from four of the five formulas to generate the super formula.

The IOL powers from 100 consecutive eyes of 100 patients then were calculated using the five formulas and the super formula. The
main outcomes measures were the IOL powers and the degree of disagreement between a currently used IOL formula and the new super formula. The authors published their findings in *JAMA Ophthalmol.* doi:10.1001/jamaophthalmol.2015.3832.

**LITERATURE REVIEW**

Based on a literature review, the authors used the Hoffer Q formula for eyes with an axial length of 21.49 mm or shorter, the Holladay I formula with the Koch adjustment for those with an axial length exceeding 25 mm, the Haigis formula when a negatively powered IOL was needed, and, the Holladay I formula for all others.

“Although the existing formulas gave similar results over a range of input parameters, they also diverged significantly at specified ranges of input parameters,” the authors said. “This divergence results in clinical dilemmas for surgeons and potential suboptimal results for patients.”

The authors found that all formulas differed from at least one of the other four formulas by more than 0.5 D over the range of parameters.

“When the tolerance for divergence between formulas is increased to 1.0 D in predicted IOL power (a clinically undesirable level), there are areas of correspondence between all formulas tested, which increase further when tolerance is raised to 1.5 D,” the study reported. “Thus, resolving these areas of discrepancy is of high clinical relevance.”

When they included the most accurate output portions of each IOL formula in a combined super formula, they found stepwise development and evolution of a singular multifaceted surface, including the most accurate portions of multiple individual formulas based on specified ranges of input variables.

At this point, they tested the super formula in the 100 study eyes and reported that “the super formula localized to the correct portion of the super surface 100% of the time and thus chose the most appropriate IOL power value.”

**POWER RESULTS**

The individual formulas deviated from the optimal super formula IOL power values by more than 0.5 D 30% of the time in Hoffer Q, 16% in Holladay I, 22% in Holladay I with Koch adjustment, 48% in Haigis, and 24% in SRK/T. The individual formulas deviated from the optimal super formula IOL power values by more than 1.0 D 12% of the time in Hoffer Q, 5% in Holladay I, 2% in Holladay I with Koch adjustment, 8% in Haigis, and 1% in SRK/T.

Dr. Ladas and colleagues emphasized that the results show how often there is clinical disparity in the IOL powers determined by the currently used IOL formulas. The hope is that their method can broaden the conceptual understanding of IOL calculations, improve clinical outcomes for patients, and stimulate further progress in IOL formula research.

More information on this methodology can be found at www.iolcalc.com.

**JOHN G. LADAS, MD, PHD**

The authors have an ownership interest in the Ladas Super Formula and Ladas Super Surface and associated methodologies and processes.

Dr. William Rich focuses on advocacy as 2016 president of AAO

SAN FRANCISCO ::

**AS HIS TERM** begins as the 119th president of the American Academy of Ophthalmology (AAO), William L. Rich III, MD, FACS, plans to focus on strengthening the profession of ophthalmology’s engagement with government and policymakers by demonstrating how their actions directly affect patient care.

“To ensure that our patients can get the best possible care, ophthalmologists must play a more active role in the academy’s government advocacy initiatives,” said Dr. Rich, who practices general ophthalmology as the senior partner at Northern Virginia Ophthalmology Associates, Falls Church.

“Lawmakers need to hear directly from ophthalmologists about how their policies have deep, long-lasting impacts on our patients,” Dr. Rich said. “During my term as president, I hope to help mobilize more of our members and raise their voices so that government can more clearly understand the key issues that impact patient care and physicians’ ability to deliver it in a sustainable manner.”

Dr. Rich brings more than 20 years of experience in health policy, health-care financing, and clinical quality metrics to his role in leading the academy in 2016. He has served the academy and the profession of ophthalmology in a number of capacities, including medical director of Health Policy.

He is also chairman of the academy’s IRIS Registry committee, guiding the implementation of the largest clinical data registry within any medical specialty. Dr. Rich will continue to continue to serve the academy in these capacities during his term as president.

His experience extends throughout the medical profession. He is a former chairman of the American Medical Association’s Resource-Based Relative Values Scale Update Committee.

He has also consulted with the Robert Wood Johnson Foundation, the National Health Policy Forum and the Institute of Medicine. Dr. Rich remains actively involved in patient care.
Congress closes some Social Security loopholes

New law eliminates small number of claiming benefits that resulted in higher benefits

Money Matters By Traudy Grande, CFP; John J. Grande, CFP; and John S. Grande, CFP

A financial question that surfaces frequently, usually from physicians ages 55 years and older, is: “When and how should my spouse and I take our Social Security benefits?” Unfortunately, these types of questions recently got complicated.

Because of the legislation passed by the U.S. Congress in November 2015, the clock is now ticking—which is expected to shut some doors for many individuals. This topic will be addressed in more detail later in the year. However, this column will attempt to simplify a complex topic. Just remember to explore the options thoroughly.

The first point is that individuals age 70 or older—or those who will be 70 in 2016—will not be impacted by this legislation. Anyone 66 years or over and not yet 70 should re-evaluate their current strategies for claiming Social Security benefits before April 30, 2016.

Congress outlined these changes to Social Security as “closing unintended loopholes” in order to protect the solvency of the Social Security System. The new law will eliminate a small number of claiming strategies that could have resulted in cumulatively higher benefits for some people under the old law.

Under the old law, individuals can’t restrict their application to the benefit they want. Instead, individuals must take the highest available benefit. The new rules apply to individuals who are not age 62 by the end of 2015. Individuals age 62 and over are “grandfathered” and they can still apply the old rules when they reach full retirement age.

FILE AND SUSPEND

Americans can still file for benefits, suspend taking them, and earn delayed retirement credits for a higher benefit later. But under the new law, a spouse will not be able to collect benefits based on one’s earnings record while suspending their own benefit.

There is a short window of opportunity here. If an individual has reached full retirement age, or will reach it by April 30, 2016, then he/she can still take advantage of the “old” rules by filing and suspending benefits—but she/she must take advantage of the rule by April 3, 2016.

LUMP-SUM REINSTATEMENT

Under the “old” rules, individuals who chose to file and suspend could later change their mind and retroactively recover the unpaid amounts during suspension. This is no longer possible under the new rules. Individuals can’t restrict their ability to retroactively recover benefits, but they must reach full retirement age, file for benefits, and suspend them by April 30, 2016.

If individuals filed a restricted application, or chose to file and suspend, before the new law was enacted, they can continue to enjoy the benefits of the claiming strategies under the “old” rules. Even if you are already receiving benefits, individuals have an opportunity to re-evaluate whether suspension could be a benefit.

The recent budget compromise may have shut the door on some popular claiming strategies, but many other planning opportunities still exist. Knowing one’s options and correctly claiming benefits could result in tens of thousands of additional dollars over a lifetime.

The Social Security Administration is a stickler for punctuality. Therefore, if it is applicable to an individual’s situation, he/she may want to avoid being locked out, as it could have significant implications to one’s retirement lifestyle.

As part of the partnership with Ophthalmology Times, it is a pleasure to offer, at no cost, a robust software analysis that can help one analyze many of the Social Security benefit scenarios available.

It is prudent for spouses to discuss possible retirement dates and to begin planning ahead just when and how to take their Social Security benefits to maximize their future income.

JOHN J., JOHN S., AND TRAUDY F. GRANDE, CFPs, are the editors of the Money Matters column. They are owners and principals of Grande Financial Services Inc. and registered principals of Wells Fargo & Co., member of SIPC. The Grandes advise physicians across the country on a diverse range of investment and financial matters. Readers may submit their financial questions to them at 800/722-1258, online at www.grandefs.com or by e-mail at john.s.grande@wafinet.com.

Ophthalmology Times and the Grande Financial Services Inc. have collaborated to launch the Money Matters Resource Center. If you are looking for financial educational information, please visit the resource center at http://bit.ly/205fomw

TAKE-HOME

Financial question that surfaces frequently, usually from physicians ages 55 years and older, is: “When and how should my spouse and I take our Social Security benefits?”

These types of questions recently got complicated with the recent passage of new legislation by the U.S. Congress.
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Silicon Valley’s vision for healthcare: Better care, outcomes; lower costs

Google, Apple, IBM, and others seek to revolutionize how healthcare is delivered

By Shelly K. Schwartz

IT WASN’T ONLY the aging demographic that prompted high-tech firms to throw their hats in the healthcare ring. Nor was it the market opportunities created by the Affordable Care Act (ACA), or investor enthusiasm for software solutions that may solve some of the healthcare industry’s most pressing problems. It was all three.

Over the past 5 years, tech titans including Google, Intel, IBM, and Apple have set their sights on the roughly $40 billion healthcare IT market, joining a proliferation of Silicon Valley startups that are developing new products to help achieve the “Triple Aim” of better care, improved outcomes, and lower costs.

“Since passage of the ACA [in 2010], these trends have combined and we’ve now got more than $10 billion of new venture capital dollars flowing into the healthcare IT industry, and more than 500 new companies created,” said Bob Kocher, MD, an internist and partner with venture capital firm Venrock in Palo Alto, CA, which invests primarily in healthcare IT, and technology.

An additional 17 million Americans, he noted, have gained health insurance coverage under the ACA, at a time when retiring Baby Boomers are already fueling a spike in demand for healthcare services. “We’re adding 10,000 Medicare beneficiaries every day and older people spend more on healthcare, so from a purely economic standpoint, the opportunity in the healthcare market is enormous, interesting, and growing,” said Kocher.

“Most of the ‘hot’ stories in healthcare IT today are related to patient care/outcomes,” said Spencer Nam, a senior research fellow for the Clayton Christensen Institute for Disruptive Innovation, who was interviewed by e-mail. “Even if the solution itself is more related to operational improvements, they are still being positioned and marketed as ‘patient outcome’-related solutions,” said Nam.

Partly because of the ACA’s mandate for electronic health records (EHRs), telemedicine, and computerized provider order entry systems, is expected to top $105 billion by 2020, up from $41 billion in 2013, according to market research firm Grand View Research in San Francisco. To a large degree, that growth is being powered by the cloud, clinical- and claims-based analytics, and mobile technologies.

HEALTHCARE AS ‘AN INFORMATION BUSINESS’

Sam Glick, a partner with New York-based management consulting firm Oliver Wyman, said IT innovators are uniquely positioned to uncover new sources of value as payers and providers digitize patient records and researchers aggregate mountains of medical data.

“They’re foray into healthcare, he noted, follows a more pervasive corporate trend. “There is a move across all industries, from hospitality to financial services to retail, to empower consumers and find new ways to engage them,” said Glick. “Companies are using big data to make for a better, more convenient, more targeted consumer experience.” It’s a move toward mass personalization, he said, in which service providers have the power to customize for the individual—and healthcare is no exception.

Analytics, simulation models, and optimization programs are already giving early adopters the insight to deliver more personalized, proactive care. A 2014 Price Waterhouse Coopers survey found that 63% of healthcare executives say they’ve changed the way they make important decisions as a result of “big data,” such as whether they should change their delivery model, collaborate with competitors, commit to a major business investment, or encourage the use of mobile health technologies.

The survey found that some 40% rely primarily on data and analytic inputs, 29% draw on their own experience and intuition, and 31% look first to the relevant experience of others. Many of the larger medical groups who responded also said they had recently created a dedicated data insights team to inform strategic decisions.

“Healthcare IT includes an array of technologies to store, share, and analyze health information. For patients, it enables better access to care via telemedicine and patient portals. For researchers, it allows for more granular analysis of health data for the development of new therapies, and for providers it helps identify opportunities to improve efficiency and outcomes.

Many of the latest innovations are aimed at personal health treatment for patients—particularly those suffering from chronic illness, which consumes 86% of the nation’s healthcare costs, the Centers for Disease Control and Prevention reports.

PRODUCTIVE PARTNERSHIPS

“Most of the ‘hot’ stories in healthcare IT today are related to patient care/outcomes,” said Spencer Nam, a senior research fellow for healthcare at the San Mateo, California-based Clayton Christensen Institute for Disruptive Innovation, who was interviewed by e-mail.

“Even if the solution itself is more related to operational improvements, they are still being positioned and marketed as ‘patient outcome’-related solutions,” said Nam.

In part, that’s because administrative functions are largely tied to—and limited by—EHRs, for which the Affordable Care Act mandated systematic adoption. “So, from the EHR space, the model is trying to develop new applications...
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that could interface with existing EHR solutions to deliver greater efficiency,” said Nam. “While there are a ton of companies working on these solutions, they have to deal with the restrictions imposed by the EHR players, so it is a bit more difficult to make a business case.”

It is far easier to develop more universal solutions that improve patient care and outcomes, including physician concierge services, data mining services, and scheduling apps that attract more investors and public attention, he said.

IBM’s Watson Health Cloud is an example. Launched in 2015, the open technology platform is designed specifically to enhance the quality and effectiveness of personal healthcare using language processing and machine learning. It is intended to help doctors, researchers, and others in the healthcare field to automate and improve patient outreach, boost patient engagement, and reduce costly hospital readmissions.

Google Genomics and Amazon Web Services also are jockeying for position in the high-stakes race to store DNA data. Both companies are marketing their cloud databases to drug makers and research institutions, which are themselves rushing to sequence hundreds of thousands of human genomes for medical research and development.

Tech firms bring a unique skill set to the market, said Glick. “They bring expertise in technology, but also in consumer engagement,” he said. “People love Google and Apple and Amazon for the user experience they provide. They are much more beloved by the average consumer than most hospitals or health plans.”

— Sam Glick, partner, Oliver Wyman

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Recently, the most substantial commitments to healthcare IT have been partnerships between tech firms and medical researchers, which lend not only scientific credibility to their discoveries, but multidisciplinary expertise. “Pharmacists, nurses, and doctors are among the most trusted professionals in the U.S. so these partnerships are really important right now,” said Glick, who adds that that may change as delivery channels evolve.

“Today, most patients go into their doctor’s office to receive care, but I could envision a world 10 years from now where instead of going to a clinic or urgent care center, they might click on Google and find a link across the top of the page next to ‘news’ that said ‘medical visit’ where they could be seen using telehealth technology.”

Collaborations between IT firms and medical organizations also enable access to health data, which tech firms need to develop new products and service platforms. Due to regulatory and legal constraints, they would otherwise be forced to gather such data on their own, which would be time consuming and costly, but potentially better for the industry, said Nam. “Partnering with healthcare enterprises expedites time to access and obviates the need for ‘reinventing the wheels’ of gathering data,” he said.

But there’s always a risk of tech companies being exposed to the existing bias of their partners. “To some extent, I wish tech companies were bolder and more innovative by running their own trials, gathering data themselves (with help of in-house experts, of course), and presenting them to the medical community,” said Nam, noting that’s the likely next step in their evolution. “But, for now, these newly built relationships allow the tech companies to speed up on their healthcare domain knowledge as well as gain hard-to-access patient data.”

Wearable tech and cognitive computing may sound futuristic, but they’re also good examples of disruptive innovation. The Carnegie Mellon University Disruptive Health Technology Institute defines disruptive technology as the process by which a product or service takes root initially in simple applications at the bottom of a market and then relentlessly moves up-market, eventually displacing established competitors to yield an unexpected benefit to consumers.

Aided by new diagnostic and therapeutic tools, non-physician providers (nurse practitioners, for example) now can treat conditions that once required the expertise of a physician at clinics in CVS, Walgreens, and Wal-Mart stores. That same evolution is enabling physicians to perform tests and procedures in the exam room that once required a high-priced specialist or hospital admission.

By all accounts, innovation is the cure to fix the ailing healthcare system. New gadgets and gizmos, however, are just the beginning. As big data redefines the way doctors deliver care, medical schools, payers and providers will need to keep pace, said Glick.

“Right now we have a lot of experiments between Apple and the Mayo Clinic, for example, but if we get to the point where big data tells us that we should be treating patients differently, that this population of patients needs more care and these need less, we’re going to have to adjust our entire healthcare system,” Glick said.

Doctors may no longer need a stethoscope, but learn instead to wield a smartphone app that defines more precisely what each patient needs. “Training may have to focus more on information skills,” said Glick. “We may need a whole new category of professionals who are able to interpret genetic test results, or coaches who help people change behaviors and stay healthy.”

At the same time, payers will need to alter their reimbursement structure so providers at all levels get paid fairly for the work they do. “It’s an exciting time and I’m very optimistic, but if we succeed, and I think we will, we’re going to have to think about how the rest of the system needs to evolve.”

Kocher agrees. By bringing their resources to bear and soliciting input from healthcare decision makers, he said, Silicon Valley can help doctors deliver more cost-effective, patient-centered care.

Their foray into the field is already paying dividends. “There’s no question that the interest of these tech companies is a good thing because it draws more attention, creativity and resources to healthcare,” said Kocher. “When you have (Google co-founder) Larry Page talking about healthcare to investors on a Google call, that’s a whole lot of people who wouldn’t have thought about glucose monitoring.”

Editor’s Note: A version of this article originally appeared in the Jan. 10, 2016 issue of sister publication, Medical Economics.
THE AVERAGE FIRST Pass Resolution Rate (FPRR), otherwise known as the “clean claims rate,” for an efficient, well-run physician practice should be more than 90%. The FPRR tells a practice what percentage of the time its claim is paid the first time it is submitted to an insurance company for review and payment.

On average, however, most physician practices fall in the range of 70% to 80% FPRR, which means that such a practice could have as many as 30% of its claims denied or contested on the first submission. If these claims are ultimately paid (some will not be), the delay in payment, coupled with the time and effort necessary to resolve the cause of the denial or contest, can cause serious financial strain for a practice.

While no strategy is foolproof, there are a few simple but effective methods that you can implement to increase your FPRR and increase your likelihood of success should legal action be required to collect.

1/ KNOW YOUR PROVIDER CONTRACTS
The easiest, but most frequently overlooked, way to improve insurance reimbursement rates is to familiarize yourself with the provider contract. While the payment process is almost entirely automated, that process begins with an individual at the insurance carrier “loading” the contracted rate for reimbursement into the system that processes and pays your claims. Simple human error in the loading process could cost your practice thousands of dollars or more before being noticed, if noticed at all.

Implementing semi-annual claims payment reviews to verify you are receiving your contracted rate is an effective way to avoid this problem. Such a practice is important if your contract contains any provisions for an increase in reimbursement rates associated with annual milestones or panel membership.

The provider contract also will include provisions relating to the appeals process for contesting a denied or partially denied claim. While the appeals process may seem like a hassle, if used properly it can be the most cost-efficient way to remedy the denial and provide a learning opportunity to prevent future denials.

Regardless, many of these provisions mandate that you exhaust the appeals process before pursuing any legal action against the insurance carrier for reimbursement. Those provisions also may impose deadlines for contesting and appealing a denial of a claim. Failure to contest the denial within these deadlines may result in waiver of your claim. In some instances, the provider contract will also mandate “alternative dispute resolution” processes such as mediation or arbitration that can limit legal remedies.

2/ KNOW YOUR PATIENT’S CONTRACTS
When treating a patient who is insured by a carrier with whom you do not have a contract, obtain as much information as possible about the patient’s insurance plan.

As is standard practice, most providers secure an assignment of insurance benefits from the patient that, in essence, places the provider “in the shoes” of the insured patient and bestows upon the provider all the rights and obligations of the patient’s insurance plan.

In an emergency setting it can be difficult, and sometimes impossible, to get complete information relating to the patient’s insurance plan.

In that case, it should be standard business practice to follow up with the patient to obtain necessary information. Establishing a general practice of gathering such information can be critical to obtaining reimbursement.

In order to obtain a “binding” pre-authorization you must be clear that you are seeking exactly that and detail the services that you anticipate providing. Typically, the average insurance representative answering the “coverage call” has no authority to provide a pre-authorization for services so, in a non-emergency situation, you may have to request a pre-authorization in writing, a process that may take a few days.

The value of a pre-authorization is significant because most courts find a pre-authorization to be a binding promise between the provider and the carrier for payment that is not subject to the federal preemption defenses discussed above.

3/ KNOW THE LAW
Most states have “prompt pay” statutes which, as the name implies, mandate that insurance carriers promptly pay claims. Because these statutes vary from state to state, you should consult with a local attorney area for a complete explanation of the law in your state.

Generally, these statutes set out the obligations of the provider and carrier in terms of submitting and paying “clean claims.” A “clean claim” is defined as a claim with no defect or impropriety, including lack of required substantiating documentation. Some states have avoided defining in detail a “clean claim,” but even those states require the claim be complete and include proper coding and documentation remains.

4/ KNOW YOUR BILLING CODES
One of the most frequent causes of claim denial is improper documentation and coding resulting from poorly trained staff. With the 10th revision to the Clinical Modification (ICD-10), proper documentation and coding have become more critical. At the same time, coding has become more difficult due to the increase in the number of codes available from about 4,000 procedure codes and 14,000 diagnosis codes under ICD-9-CM to 72,000 and 70,000, respectively, under ICD-10 CM/PCS.

Under many prompt pay statutes, the provider has a limited window within which to provide any additional information needed to rectify a denied or contested claim. As a consequence, practices should consider providing proper and additional training to staff relating to the new billing codes and procedures.

As an alternative, a practice might consider outsourcing claims coding to minimize the impact of the ICD-10 change. No matter the decision, serious consideration must be given to employing a dedicated team to address denied or contested claims in a timely fashion or risk not being paid at all.

Editor’s Note: A version of this article originally appeared in the Jan. 10, 2016 issue of sister publication, Medical Economics.
Putting It In View By Dianna E. Graves, COMT, BS Ed

Putting It In View

WHEN PEERS ASK if I ever tire of traveling, I enthusiastically reply: “No way. Traveling often has the reverse effect on me that it does on others. I go to new places, talk with folks who want to learn and at the same time, I have the opportunity to learn as well.”

To me, it is a win-win situation.

What do I learn? I learn what it is your staff and mine (by default) are thinking about.

It’s called “peripheral hearing” and I acquired this talent when I worked at the hospital. Most managers have this ability if they work in a large clinic or hospital setting.

Some say it is a form of inattentiveness—being able to have a conversation with someone while listening to other conversations around you. I call it survival.

In the clinic, you have to be able to focus on multiple scenarios at once. Almost an auditory triage process so to speak.

What patient appears ill in the waiting room? Who’s getting a little too vocal regarding their wait? Who’s holding it together by a thread and is ready to let it fly at any moment?

thing in the class prompts them to ask questions, or vent, or they seek out instructors to ask for opinions on issues in their clinic lives.

At the annual meeting of the American Academy of Ophthalmology (AAO) last fall in Las Vegas, there was much discussion regarding certification, Meaningful Use, micromanaging physicians, and lastly, office politics. Office politics is a continual discussion.

WHAT’S ON YOUR STAFF’S MIND?

CERTIFICATION IS A BIG TOPIC OF CONFUSION.

In most cases, there are two categories: those who are already certified because their office either required it or supported it as a condition of hiring, or those who have worked in your office for years and are now being made to become certified.

The second group is terrified of having to take the exam because they may have been told that if they don’t pass it, they will lose their jobs. Or, if they were not required sends a mixed message that they interpret as: “You are looking for a way to fire me.” I have had managers report that staff refuse to do certification and want help in scripting the message that they need to do this.

Educate them, encourage them, and help then get the materials they need. They can do the COA—they just haven’t taken a test in 10 years and are afraid.

TAKE-HOME

▷ Pay attention to what staff members are thinking. Failure to do so may mean others will inadvertently hear about the issue at hand.

‘Discuss and educate staff on what their involvement is—and what Meaningful Use and their involvement—means to your practice.’

— Dianna E. Graves, COMT, BS Ed

If you can achieve this talent, you often go home at the end of the day mentally fried. Unfortunately, this skill never shuts down with me. It’s always at full radar. Not only does it work in the clinic, it really kicks in at meetings and the airport.

Meetings and classes are an excellent time to talk with your staff. Either some-told this, they perceive that would be the outcome.

There is still a great deal of confusion on who needs to be certified.

Whether you are in ophthalmology or optometry, if you are entering lab orders/results, ultrasound testing (not IOLMaster) but definitely A and B Scans, as well as some forms of pachymetry and ocular coherence tomography, you must be “certified something” in order to comply for Meaningful Use.

This rule boggles my mind as the emphasis is on certification of the staff entering the information into the CPOE portion of the chart versus focusing the certification on the person performing the test.

Staff blames you for making them become certified. You need to educate them to Meaningful Use and ensure that they are aware of the continual changes and updates. Decreasing the need to be certified after years of telling them it wasn’t required is a good start.

2. “MEANINGFUL USE MEANS NOTHING TO ME.”

Most of your staff is aware of Meaningful Use and know it is in the office, but they have no real idea of their role in it. Discuss and educate them on what their involvement is—and what Meaningful Use and their involvement—means to your practice.

In most cases, staff understands that the practice needs to be successful and compliant. While they may be aware of Meaningful Use, ICD-10 is more prevalent on their radar. They are sticklers for coding and making sure they have enough documentation to code a given code, yet they look at Meaningful Use as something that the physician must comply with and do not realize the impact they also have.

While ICD-10 and Meaningful Use in-
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Duties will include providing clinical care to ophthalmology patients, teaching the principles of ophthalmology to medical students and undergraduate students in Allied Health programs, developing basic and/or clinical research, and performing additional departmental and/or sectional administrative duties as assigned by the Chair of the Department of Surgery.

The University is especially interested in candidates who can contribute to the diversity and excellence of the academic community through their research, teaching, and/or service. Applicants are requested to include in their cover letter information about how they will further this goal. The University of Vermont is an Affirmative Action/Equal Opportunity Employer. Applications from women, veterans and people of diverse racial, ethnic and cultural backgrounds are encouraged. Applications will be accepted until the positions are filled.

Interested individuals should electronically submit their curriculum vitae with a cover letter and contact information for four references electronically to Brian Kim, MD at Brian.Kim@uvmhealth.org or apply on-line at https://www.uvmjobs.com
tertwine in many ways, they need to be equally aware of both.

3. THEY FOLLOW YOUR LEAD.
I often do a question-and-answer session with attending staff after classes and will ask: “Who calls in the doctor medication orders?” I define it as handing an Rx to a patient, calling it in, E-Scribing, etc.

When I ask if they are “certified something,” their answer is: “No. The doctor says he’s overseeing everything in the office and he doesn’t care that I am certified!”

‘My biggest bit of advice it to listen to what the staff is not saying.’
— Dianna E. Graves, COMT, BS Ed

I even had one attendee report: “We’re from North Carolina and that doesn’t pertain to us.”

Final answer is: Yes, it does.

4. OFFICE POLITICS.
Probably what I hear the most is:

a. “My doctor doesn’t like me because I am not his favorite technician.”

b. “My manager doesn’t make the doctor’s favorite technician follow the rules because she is afraid of the doctor—but runs the rest of us with an iron fist.”

c. “They promised me I would learn new skills so I joined. Now I realize I am on the bottom of the pile with no chance to move up unless someone dies!”

Staff is very loyal and often it takes a lot for them to talk with a stranger regarding office politics. When they feel they have no other option, they will talk. What becomes concerning to the health of your technician pool is when the talk becomes negative and derisive. If they are willing to share the office dirty laundry when they are out of town, what are they doing when they are back home and local?

5. “OUR DOCTOR MICROMANAGES EVERYTHING—IT MAKES US A WRECK.”
That one is easy. I advise the staff to listen to what is making the physician feel the need to micromanage, and stop doing it immediately. In most cases, physicians do not like to be involved in the everyday grind of triviality that most managers get to live. However, they will become involved if they perceive that their clinic world is spiraling to a place they do not want to see it going to.

Remove the issues that have them concerned, and they will return to their world of seeing patients and running their practices.

LISTEN TO WHAT STAFF IS NOT SAYING
Quite honestly, I learn more from my “eavesdropping” and discussion time at meetings than I do from the classes.

Then, when I return back to my world, I try to ensure that I have the bases covered in these areas of concern. Since I am a manager, just like the rest of you, I need to be a little more covert about my listening.

My biggest bit of advice it to listen to what the staff is not saying. Listen to the types of questions they are asking and try and assuage their concerns. And head off the concerns as you “hear” them.

If you don’t listen—someone with great “peripheral hearing” will certainly hear it all.
IRIS Registry may create opportunity beyond improved patient outcomes

May play role in move toward using registries to conduct trials more quickly, at lower cost

By Nancy Groves; Reviewed by Michael F. Chiang, MD

By Nancy Groves; Reviewed by Michael F. Chiang, MD

FEW PHYSICIANS WOULD argue with the goal of improving patient outcomes, but it is easy to lose sight of this ideal amid the pressures of daily medical practice, according to Michael F. Chiang, MD.

However, the American Academy of Ophthalmology (AAO) IRIS Registry (Intelligent Research in Sight)—a national clinical data registry to improve eye care that was launched in 2014—is designed to help physicians get the information they need to make adjustments in patient care, Dr. Chiang noted.

The IRIS Registry is both a data registry and reporting tool, generating benchmark reports from a dataset of electronic health records and patient information.

“What we’re seeing is a convergence of technology, policymaking, big data, analytics, and patient care. There’s going to be an evolution of the healthcare delivery process, and I think the IRIS Registry is a huge step in all of this,” said Dr. Chiang, Knowles Professor of Ophthalmology and Medical Informatics and Clinical Epidemiology at the Oregon Health and Science University Casey Eye Institute. He is also a member of the AAO’s IRIS Registry Executive Committee and chairman of the Academy Task Force on IRIS Registry Analytics and Research.

MEASURE OF SUCCESS
A “clinical dashboard” is the means by which physicians can visualize their performance on specific measures within the IRIS Registry—for example, achieving good visual acuity within 90 days following cataract surgery.

“When we, as doctors, see what measures we’re doing well on as well as what measures we’re not doing well on, that’s how we can identify gaps in care and where we can improve,” Dr. Chiang said.

Results from the first year of the IRIS Registry already show some improvement in performance, he added.

For instance, complication rates after cataract surgery improved from 2% to 1%, and counseling patients with age-related macular degeneration about antioxidant supplements improved from 46% to 54%.

The IRIS Registry also taps advances in technology to obtain “big data.” By interfacing with electronic health records, the registry (as of Nov. 1, 2015) included information on 61 million patient visits and 17.6 million unique patients, while data sets from a few decades ago relied on either sampling or time-consuming manual data entry, and even the largest often had far less information than is available via the IRIS Registry.

So far, more than 10,000 ophthalmologists have submitted to the IRIS Registry.

“This will create unprecedented opportunities that extend beyond quality improvement and into areas such as monitoring of outcomes from medical and surgical procedures, natural history of disease, post-market surveillance of new devices, and clinical research,” Dr. Chiang said.

The registry also may prove to be an asset if a new model of clinical research is validated. Carrying out clinical trials within the framework of existing high-quality registries may make them less expensive and more efficient, according to Dr. Chiang.

In an often-cited example of this model, the TASTE trial (Thrombus Aspiration during ST-Elevation Myocardial Infarction) had an incremental cost of $300,000, or $50 for each participant who underwent randomization. This was possible since the investigators built their study on clinical information that was already being gathered for a large registry on coronary angiography and angioplasty and other pre-existing databases.

In a 2013 editorial on the TASTE trial and the potentially “disruptive” new model, Lauer and D’Agostino cited the potential of the randomized registry trial but added that questions about the quality of the underlying data sets would need to be addressed.

Dr. Chiang echoed the commentary’s point that randomized trials costing hundreds of millions of dollars are no longer affordable and that registries and other digital platforms may enable investigators to design and conduct mega-trials with bigger data and smaller budgets.

While the idea of using analytics for quality control may unnerve some in the medical community, it is highly likely they have already come into contact with it outside of the office, Dr. Chiang said, explaining that amazon.com uses it to make product recommendations to shoppers, sports franchises analyze data to select players and plays, and Facebook targets advertising to users based on their posts and search history.

“Applying these methods toward clinical research will create enormous opportunities for the future of ophthalmic care, research, and quality improvement,” Dr. Chiang added.

References

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This article was adapted from Dr. Chiang’s presentation at the 2015 meeting of the American Academy of Ophthalmology. Dr. Chiang is an unpaid board member for Clarity Medical Systems and has received funding from the National Eye Institute.
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