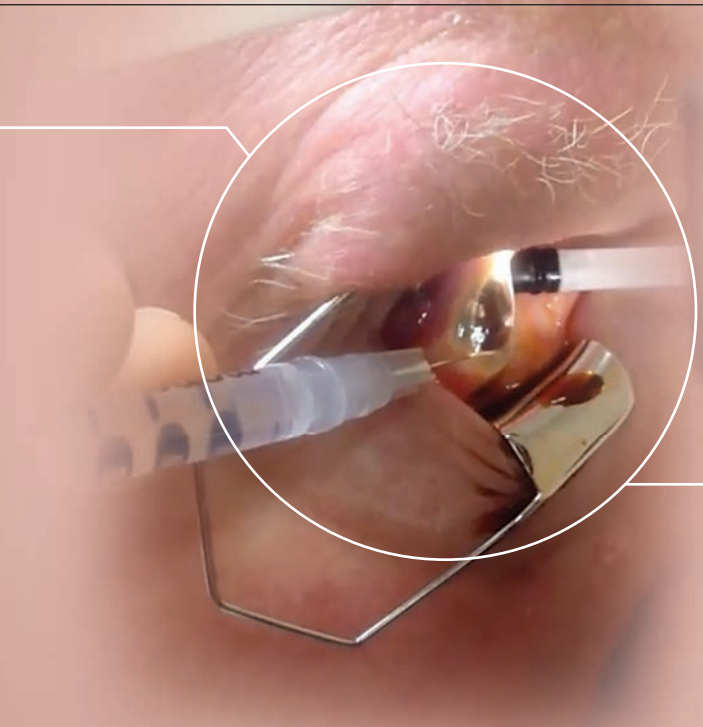
A PUBLICATION BY REVIEW of Ophthalmology

RETINA SPECIALIST

NOVEMBER 2015



PEARLS FOR PERFORMING PNEUMATIC RETINOPEXY

Online Video

A less-costly alternative well-suited to repair small superior retinal breaks.

PAGE 18

Online Video

Drainage Retinotomy Sans Laser

PAGE 22

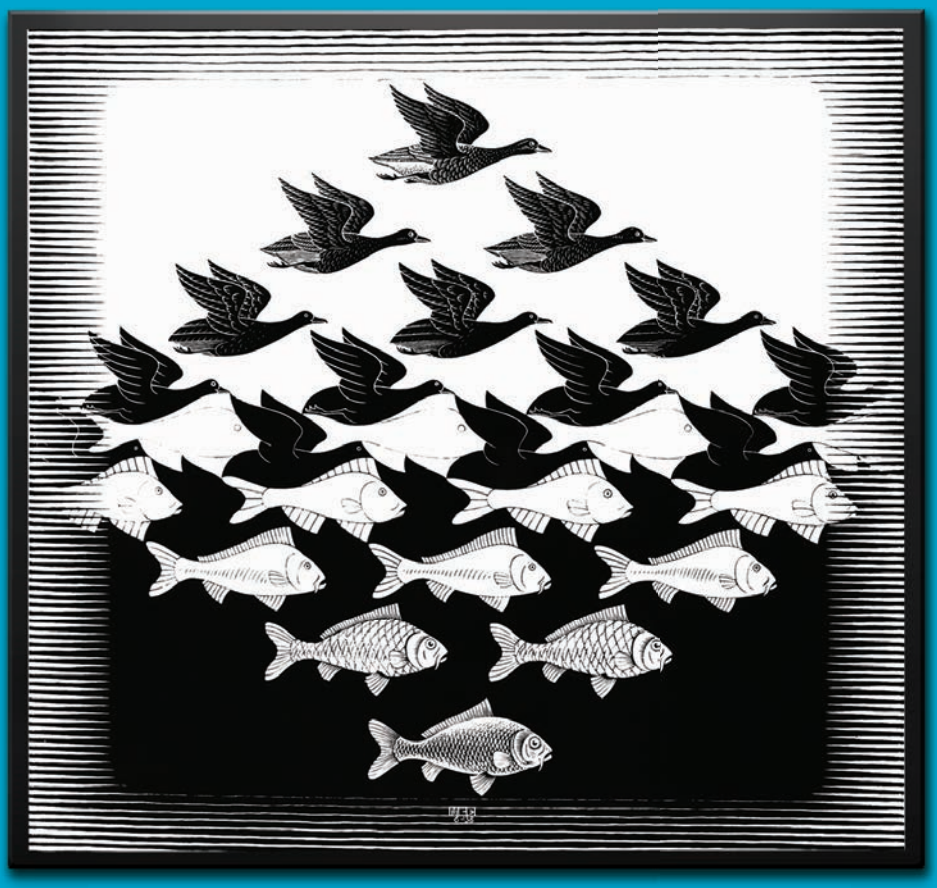
Computer-Navigated Laser For DME: How We Got Here

PAGE 26

NEW: Surgical Pearl Video: Reflux Chromovitrectomy

PAGE 16

A different perspective can have the power to change your approach



Indication and Usage
Diabetic Macular Edema
OZURDEX® (dexamethasone intravitreal implant) is a corticosteroid indicated for the treatment of diabetic macular edema.

Dosage and Administration
FOR OPHTHALMIC INTRAVITREAL INJECTION.
The intravitreal injection procedure should be carried out under controlled aseptic conditions. Following the intravitreal injection, patients should be monitored for elevation in intraocular pressure and for endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis without delay.

IMPORTANT SAFETY INFORMATION
Contraindications
Ocular or Periocular Infections: OZURDEX® (dexamethasone intravitreal implant) is contraindicated in patients with active or suspected ocular or periocular infections including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.

Glaucoma: OZURDEX® is contraindicated in patients with glaucoma, who have cup to disc ratios of greater than 0.8.

Torn or Ruptured Posterior Lens Capsule: OZURDEX® is contraindicated in patients whose posterior lens capsule is torn or ruptured because of the risk of migration into the anterior chamber. Laser posterior capsulotomy in pseudophakic patients is not a contraindication for OZURDEX® use.

Hypersensitivity: OZURDEX® is contraindicated in patients with known hypersensitivity to any components of this product.

Warnings and Precautions
Intravitreal Injection-related Effects: Intravitreal injections, including those with OZURDEX®, have been associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments. Patients should be monitored regularly following the injection.

Steroid-related Effects: Use of corticosteroids including OZURDEX® may produce posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses.

Corticosteroids should be used cautiously in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

Adverse Reactions
Ocular adverse reactions reported by greater than or equal to 1% of patients in the two combined 3-year clinical trials following injection of OZURDEX® for diabetic macular edema include: cataract (68%), conjunctival hemorrhage (23%), visual acuity reduced (9%), conjunctivitis (6%), vitreous floaters (5%), conjunctival edema (5%), dry eye (5%), vitreous

SEE DME Differently.

- **The pathophysiology**
  — An **inflammatory cascade** plays a key role[1-5]
- **The therapeutic targets**
  — Suppress multiple **inflammatory cytokines**[6]
- **The clinical results**
  — Achieve clinically significant **3-line gains** in BCVA[6,*]

The #1 steroid in U.S. market share for DME[7,†]

IMPORTANT SAFETY INFORMATION (continued)
Adverse Reactions (continued)
detachment (4%), vitreous opacities (3%), retinal aneurysm (3%), foreign body sensation (2%), corneal erosion (2%), keratitis (2%), anterior chamber inflammation (2%), retinal tear (2%), eyelid ptosis (2%). Non-ocular adverse reactions reported by greater than or equal to 5% of patients include: hypertension (13%) and bronchitis (5%).

Increased Intraocular Pressure: IOP elevation greater than or equal to 10 mm Hg from baseline at any visit was seen in 28% of OZURDEX® (dexamethasone intravitreal implant) patients versus 4% of sham patients. 42% of the patients who received OZURDEX® (dexamethasone intravitreal implant) were subsequently treated with IOP-lowering medications during the study versus 10% of sham patients.

The increase in mean IOP was seen with each treatment cycle, and the mean IOP generally returned to baseline between treatment cycles (at the end of the 6-month period).

Cataracts and Cataract Surgery: The incidence of cataract development in patients who had a phakic study eye was higher in the OZURDEX® group (68%) compared with Sham (21%). The median time of cataract being reported as an adverse event was approximately 15 months in the OZURDEX® (dexamethasone intravitreal implant) group and 12 months in the Sham group. Among these patients, 61% of OZURDEX® subjects versus 8% of sham-controlled subjects underwent cataract surgery, generally between Month 18 and Month 39 (Median Month 21 for OZURDEX® group and 20 for Sham) of the studies.

Please see Brief Summary of full Prescribing Information on next page.

*Best-corrected visual acuity.
†Based on U.S. market share of DME patients treated with intravitreal steroids: December 2014.[7]

Ozurdex®
(dexamethasone intravitreal implant) 0.7 mg

1. Jain A, Varshney N, Smith C. The evolving treatment options for diabetic macular edema. *Int J Inflam.* 2013;2013:689276. **2.** Bhagat N, Grigorian RA, Tutela A, Zarbin MA. Diabetic macular edema: pathogenesis and treatment. *Surv Ophthalmol.* 2009;54(1):1-32. **3.** Ehrlich R, Harris A, Ciulla TA, Kheradiya N, Winston DM, Wirostko B. Diabetic macular oedema: physical, physiological and molecular factors contribute to this pathological process. *Acta Ophthalmol.* 2010;88(3):279-291. **4.** Scholl S, Kirchhof J, Augustin AJ. Pathophysiology of macular edema. *Ophthalmologica.* 2010;224(suppl 1):8-15. **5.** Zhang W, Liu H, Al-Shabrawey M, Caldwell RW, Caldwell RB. Inflammation and diabetic retinal microvascular complications. *J Cardiovasc Dis Res.* 2011;2(2):96-103. **6.** OZURDEX® Prescribing Information. **7.** IMS Health Dx data through December 2014.

OZURDEX®

(dexamethasone intravitreal implant) 0.7 mg

Brief Summary—Please see the OZURDEX® package insert for full Prescribing Information.

INDICATIONS AND USAGE

Retinal Vein Occlusion: OZURDEX® (dexamethasone intravitreal implant) is a corticosteroid indicated for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

Posterior Segment Uveitis: OZURDEX® is indicated for the treatment of non-infectious uveitis affecting the posterior segment of the eye.

Diabetic Macular Edema

OZURDEX® is indicated for the treatment of diabetic macular edema.

CONTRAINDICATIONS

Ocular or Periocular Infections: OZURDEX® (dexamethasone intravitreal implant) is contraindicated in patients with active or suspected ocular or periocular infections including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.

Glaucoma: OZURDEX® is contraindicated in patients with glaucoma, who have cup to disc ratios of greater than 0.8.

Torn or Ruptured Posterior Lens Capsule: OZURDEX® is contraindicated in patients whose posterior lens capsule is torn or ruptured because of the risk of migration into the anterior chamber. Laser posterior capsulotomy in pseudophakic patients is not a contraindication for OZURDEX® use.

Hypersensitivity: OZURDEX® is contraindicated in patients with known hypersensitivity to any components of this product *[see Adverse Reactions]*.

WARNINGS AND PRECAUTIONS

Intravitreal Injection-related Effects: Intravitreal injections, including those with OZURDEX®, have been associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments.

Patients should be monitored regularly following the injection *[see Patient Counseling Information]*.

Steroid-related Effects: Use of corticosteroids including OZURDEX® may produce posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses *[see Adverse Reactions]*.

Corticosteroids should be used cautiously in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

ADVERSE REACTIONS

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

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

Retinal Vein Occlusion and Posterior Segment Uveitis

The following information is based on the combined clinical trial results from 3 initial, randomized, 6-month, sham-controlled studies (2 for retinal vein occlusion and 1 for posterior segment uveitis):

Adverse Reactions Reported by Greater than 2% of Patients

MedDRA Term	OZURDEX® N=497 (%)	Sham N=498 (%)
Intraocular pressure increased	125 (25%)	10 (2%)
Conjunctival hemorrhage	108 (22%)	79 (16%)
Eye pain	40 (8%)	26 (5%)
Conjunctival hyperemia	33 (7%)	27 (5%)
Ocular hypertension	23 (5%)	3 (1%)
Cataract	24 (5%)	10 (2%)
Vitreous detachment	12 (2%)	8 (2%)
Headache	19 (4%)	12 (2%)

Increased IOP with OZURDEX® peaked at approximately week 8. During the initial treatment period, 1% (3/421) of the patients who received OZURDEX® required surgical procedures for management of elevated IOP.

Following a second injection of OZURDEX® (dexamethasone intravitreal implant) in cases where a second injection was indicated, the overall incidence of cataracts was higher after 1 year.

Diabetic Macular Edema

The following information is based on the combined clinical trial results from 2 randomized, 3-year, sham-controlled studies in patients with diabetic macular edema. Discontinuation rates due to the adverse reactions listed in the table below were 3% in the OZURDEX® group and 1% in the Sham group. The most common ocular (study eye) and non-ocular adverse reactions are as follows:

Ocular Adverse Reactions Reported by ≥ 1% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients

MedDRA Term	OZURDEX® N=324 (%)	Sham N=328 (%)
Ocular		
Cataract[1]	166/243[2] (68%)	49/230 (21%)
Conjunctival hemorrhage	73 (23%)	44 (13%)
Visual acuity reduced	28 (9%)	13 (4%)
Conjunctivitis	19 (6%)	8 (2%)
Vitreous floaters	16 (5%)	6 (2%)
Conjunctival edema	15 (5%)	4 (1%)
Dry eye	15 (5%)	7 (2%)
Vitreous detachment	14 (4%)	8 (2%)
Vitreous opacities	11 (3%)	3 (1%)
Retinal aneurysm	10 (3%)	5 (2%)
Foreign body sensation	7 (2%)	4 (1%)
Corneal erosion	7 (2%)	3 (1%)
Keratitis	6 (2%)	3 (1%)
Anterior Chamber Inflammation	6 (2%)	0 (0%)
Retinal tear	5 (2%)	2 (1%)
Eyelid ptosis	5 (2%)	2 (1%)
Non-ocular		
Hypertension	41 (13%)	21 (6%)
Bronchitis	15 (5%)	8 (2%)

[1] Includes cataract, cataract nuclear, cataract subcapsular, lenticular opacities in patients who were phakic at baseline. Among these patients, 61% of OZURDEX® subjects vs. 8% of sham-controlled subjects underwent cataract surgery.

[2] 243 of the 324 OZURDEX® subjects were phakic at baseline; 230 of 328 sham-controlled subjects were phakic at baseline.

Increased Intraocular Pressure

Summary of Elevated IOP Related Adverse Reactions

	Treatment: N (%)	
IOP	**OZURDEX®** N=324	**Sham** N=328
IOP elevation ≥10 mm Hg from Baseline at any visit	91 (28%)	13 (4%)
≥30 mm Hg IOP at any visit	50 (15%)	5 (2%)
Any IOP lowering medication	136 (42%)	32 (10%)
Any surgical intervention for elevated IOP*	4 (1.2%)	1 (0.3%)

* OZURDEX®: 1 surgical trabeculectomy for steroid-induced IOP increase, 1 surgical trabeculectomy for iris neovascularization,1 laser iridotomy, 1 surgical iridectomy
Sham: 1 laser iridotomy

Cataracts and Cataract Surgery

At baseline, 243 of the 324 OZURDEX® subjects were phakic; 230 of 328 sham-controlled subjects were phakic. The incidence of cataract development in patients who had a phakic study eye was higher in the OZURDEX® group (68%) compared with Sham (21%). The median time of cataract being reported as an adverse event was approximately 15 months in the OZURDEX® group and 12 months in the Sham group. Among these patients, 61% of OZURDEX® subjects vs. 8% of sham-controlled subjects underwent cataract surgery, generally between Month 18 and Month 39 (Median Month 21 for OZURDEX® group and 20 for Sham) of the studies.

The increase in mean IOP was seen with each treatment cycle, and the mean IOP generally returned to baseline between treatment cycles (at the end of the 6 month period).

USE IN SPECIFIC POPULATIONS

Pregnancy Category C

Risk Summary

There are no adequate and well-controlled studies with OZURDEX® in pregnant women. Animal reproduction studies using topical ocular administration of dexamethasone were conducted in mice and rabbits. Cleft palate and embryofetal death in mice and malformations of the intestines and kidneys in rabbits were observed. OZURDEX® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

Topical ocular administration of 0.15% dexamethasone (0.375 mg/kg/day) on gestational days 10 to 13 produced embryofetal lethality and a high incidence of cleft palate in mice. A dose of 0.375 mg/kg/day in the mouse is approximately 3 times an OZURDEX® injection in humans (0.7 mg dexamethasone) on a mg/m2 basis. In rabbits, topical ocular administration of 0.1% dexamethasone throughout organogenesis (0.13 mg/kg/day, on gestational day 6 followed by 0.20 mg/kg/day on gestational days 7-18) produced intestinal anomalies, intestinal aplasia, gastroschisis and hypoplastic kidneys. A dose of 0.13 mg/kg/day in the rabbit is approximately 4 times an OZURDEX® injection in humans (0.7 mg dexamethasone) on a mg/m2 basis.

Nursing Mothers: Systemically administered corticosteroids are present in human milk and can suppress growth and interfere with endogenous corticosteroid production. The systemic concentration of dexamethasone following intravitreal treatment with OZURDEX® is low. It is not known whether intravitreal treatment with OZURDEX® could result in sufficient systemic absorption to produce detectable quantities in human milk. Exercise caution when OZURDEX® is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of OZURDEX® in pediatric patients have not been established.

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

No adequate studies in animals have been conducted to determine whether OZURDEX® (dexamethasone intravitreal implant) has the potential for carcinogenesis.

Although no adequate studies have been conducted to determine the mutagenic potential of OZURDEX®, dexamethasone has been shown to have no mutagenic effects in bacterial and mammalian cells *in vitro* or in the *in vivo* mouse micronucleus test. Adequate fertility studies have not been conducted in animals.

PATIENT COUNSELING INFORMATION

Steroid-related Effects

Advise patients that a cataract may occur after repeated treatment with OZURDEX®. If this occurs, advise patients that their vision will decrease, and they will need an operation to remove the cataract and restore their vision.

Advise patients that they may develop increased intraocular pressure with OZURDEX® treatment, and the increased IOP will need to be managed with eye drops, and, rarely, with surgery.

Intravitreal Injection-related Effects

Advise patients that in the days following intravitreal injection of OZURDEX®, patients are at risk for potential complications including in particular, but not limited to, the development of endophthalmitis or elevated intraocular pressure.

When to Seek Physician Advice

Advise patients that if the eye becomes red, sensitive to light, painful, or develops a change in vision, they should seek immediate care from an ophthalmologist.

Driving and Using Machines

Inform patients that they may experience temporary visual blurring after receiving an intravitreal injection. Advise patients not to drive or use machines until this has been resolved.

A PUBLICATION BY REVIEW OF OPHTHALMOLOGY
RETINA SPECIALIST

11 Campus Blvd., Suite 100
Newtown Square, PA 19073
Telephone (610) 492-1000
Fax (610) 492-1039

Editorial inquiries (610) 492-1000
Advertising inquiries (610) 492-1011
E-mail retinaspecialist@jobson.com

Jobson Medical Information LLC

EDITOR'S PAGE

By Charles C. Wykoff, MD, PhD

Reptilian Trauma And ICD-10

So how is it going using ICD-10?

In the 1860s in London, Florence Nightingale, who is credited with establishing modern nursing, may have been the first to propose systematic collection of medical data. As sentiment coalesced around the need for uniform documentation of diseases, ICD-1 was implemented by 1900 to classify causes of death in the United States.

Here we are a century later, grappling with the latest version containing more than 64,000 codes. Despite popular belief, our government did not create the International Classification of Diseases (ICD) to frustrate practitioners and interfere with doctor-patient relationships, although it might do both exceedingly well.

Rather, since 1948 ICD has been updated and disseminated by a distinctly non-U.S.-based organization, the World Health Organization, and more than 100 countries use it. Maybe there are areas outside your neighborhood where it is important to distinguish between being "struck" vs. "crushed" vs. "bitten" by an alligator (Crushed: W58.03XA) vs. by a crocodile (Crushed: W58.13XA). Maybe such variety of reptilian trauma was identified by accidents reported to Bascom Palmer from the nearby Florida Everglades?

In time, payers may use the increased specificity of ICD-10 codes as leverage to dictate medical necessity and deny claims deemed unnecessary in the name of cost-savings.

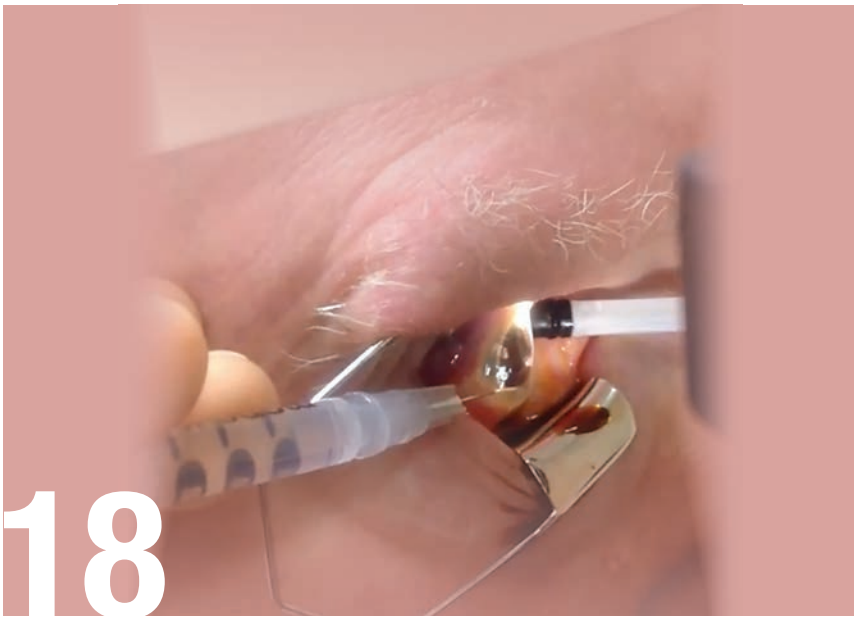
Despite the ridiculous granularity of some pathologies in ICD-10, there are remarkable deficiencies in others. A single code, H35.31, describes "Nonexudative AMD," a disease that ophthalmologists have known for decades can range from asymptomatic drusen to debilitating, severe geographic atrophy. Similarly, a single code, H43.82, describes vitreous-macular interface findings ranging from simple vitreomacular adhesion to severe vitreomacular traction.

There is hope that more specific coding will translate into improved patient outcomes. ICD-10 reduces the need for codes such as "unspecified" or "not elsewhere classified." More specific data may bring about a deeper understanding of diseases and inform clinical practice—more promises of Big Data that collaborative endeavors such as the American Academy of Ophthalmology IRIS Registry may fulfill.

Not yet comfortable with ICD-10? Don't worry. You have at least two years to figure it out before the WHO presents the ICD-11 code set, currently slated for 2018.

A PUBLICATION BY REVIEW

RETINA SPECIALIST



18

NOVEMBER 2015

FEATURES

DEPARTMENTS

IN BRIEF

• The **National Multiple Sclerosis Society** presented its **2015 Barancik Prize for Innovation in MS** to a trio of research ophthalmologists from New York University Langone Medical Center, Johns Hopkins School of Medicine and University of Texas Southwestern Medical Center. The organization honored Laura Balcer, MD, MSCE, of NYU, Peter Calabresi, MD, of Johns Hopkins and Elliott Frohman, MD, PHD, of UT Southwestern for "novel, groundbreaking and impactful research" of the retina and other ocular structures in people with multiple sclerosis (MS). "Thanks in large part to this team's efforts, [optical coherence tomography] has transitioned from a tool for ophthalmologists who treat glaucoma patients to a mainstream tool used to study disease mechanisms underlying MS in particular, but new evolving research suggests that such observations may apply to neurodegenerative disorders in general," the society said in announcing the prize.

• Patients with **diabetic macular edema** who had one to three years of monthly ranibizumab (Lucentis, Genentech) therapy maintained their vision gains with a notable reduction in treatment frequency, according to an open-label extension phase of the Phase III RIDE and RISE trials. In results published online in ***Ophthalmology***, subjects had an average of 4.5 injections over a follow-up of 14.1 months. Approximately 25 percent of subjects did not require further treatment, and mean best-corrected visual acuity was sustained or improved through the end of follow-up.

Is Retina Poised To Lead the Precision Medicine Movement?

Now that a national framework has been put forward to advance precision medicine, developers of genetic therapies for retinal and macular disorders may be poised to be in the vanguard of the movement, according to a prominent investigator of genetics in retinal disease.

"Ophthalmology is a promising specialty for implementing precision medicine because of the eye's amenability to intervention and the significant human and economic burdens it incurs," says Stephen H. Tsang, MD, PhD, an associate professor in ophthalmology, pathology and cell biology at Columbia University in New York. Dr. Tsang's clinic has genotyped more than 800 patients with retinitis pigmentosa and juvenile macular degeneration.

The National Institutes of Health (NIH) advisory committee in September released a framework for building a cohort of 1 million or more Americans that researchers can draw on for data and specimens. The Precision Medicine Initiative stands to receive $215 million in government funding fiscal year 2016. NIH will lead efforts in cancer genomics, as well as the development of the participant cohort.

The Precision Medicine Working Group developed the framework to form and manage the large research cohort. Among the goals of the framework are to help investigators discover biological markers that signal disease risk and create platforms for trials.

"Ophthalmic precision medicine is facilitated by the eye's relative immune privilege and accessibility, and the effects of treatment can be precisely monitored non-invasively at the resolution of a single cell with adaptive optics imaging," Dr. Tsang said. Because the eye is a "pair organ," it provides ideal treatment-control conditions and carries a low risk of rejection of gene and stem cell therapies.

"In fact, therapies involving embryonic stem cell transplants for macular degenerations are the only FDA-approved regenerative medicine trials currently," Dr. Tsang said. Ocata Therapeutics is conducting the Phase II clinical trial of its proprietary RPE cells in patients with dry age-related macular degeneration.

Dr. Tsang also noted that Spark Therapeutics, a late-stage gene therapy company, received both breakthrough therapy and orphan product designation from the U.S. Food and Drug Administration last year for its lead product candidate, SPK-RPE65, for the treatment of genetic retinal disorders. SPK-RPE65 is now in a fully enrolled, pivotal Phase III clinical trial, and Spark has said it plans to file for FDA biologics license application in 2016. (*More on page 38.*)

"Supporting vision research will be essential to making therapies based on precision medicine at

Columbia a reality," Dr. Tsang said. "An office to liaise with the FDA on approving gene therapy and autologous stem cell transplantations provides just one example of the additional resources that will be needed."

He is hopeful that the NIH framework for precision medicine is a step in that direction.

With Synergetics Acquisition, Valeant to Integrate Two Vitrectomy Platforms

Now that Valeant Pharmaceuticals International has completed its acquisition of Synergetics USA, Valeant's Bausch + Lomb unit is positioning itself to be a bigger player in vitreoretinal surgery, Andrew Chang, general manager and vice president of B+L's U.S. Surgical business said.

Valeant completed the Synergetics acquisition in October. The acquisition brings two vitrectomy platforms, B+L's Stellaris and Synergetics VersaVIT, under one corporate structure. Synergetics also has other products for ophthalmology and neurosurgery.

Mr. Chang hinted that Stellaris and VersaVIT would be integrated into a single product.

"We are particularly excited to pair the extensive breadth of accessories featured in the Synergetics platform with our Stellaris PC microsurgical system to increase the procedural opportunities for our customers," he said. "We also look forward to integrating the VersaVit and Stellaris PC portfolios to provide one unified product offering very soon."

Synergetics has been "fully integrated" with B+L, Mr. Chang said. The combination more than doubles B+L's vitreoretinal sales force.

"As a result, we've combined the Synergetics and Bausch + Lomb research and development teams to leverage their efforts in identifying and developing new retina-focused advancements and improvements to help address the ever evolving needs of the eye-care community," he said.

Synergetics, based in the St. Louis suburb of O'Fallon, Mo., expects its operations to remain there, David M. Hable, Synergetics president and CEO, previously told the *St. Louis Post-Dispatch*.

Quotable

"We are particularly excited to pair the extensive breadth of accessories in the Synergetics platform with our Stellaris PC microsurgical system to increase procedural opportunities for our customers."

- Andrew Chang, general manager and vice president, B+L US Surgical

RETINA SPECIALIST

BUSINESS OFFICES
11 CAMPUS BOULEVARD, SUITE 100
NEWTOWN SQUARE, PA 19073
SUBSCRIPTION INQUIRIES (877) 529-1746
(USA ONLY); OUTSIDE USA, CALL (847) 763-9630

BUSINESS STAFF
PUBLISHER
JAMES HENNE
(610) 492-1017 JHENNE@JOBSON.COM

REGIONAL SALES MANAGER
MICHELE BARRETT
(610) 492-1014 MBARRETT@JOBSON.COM

REGIONAL SALES MANAGER
MICHAEL HOSTER
(610) 492-1028 MHOSTER@JOBSON.COM

CLASSIFIED ADVERTISING
(888)-498-1460

VICE PRESIDENT OF OPERATIONS
CASEY FOSTER
(610) 492-1007 CFOSTER@JOBSON.COM

PRODUCTION MANAGER
SCOTT TOBIN
(610) 492-1011 STOBIN@JOBSON.COM

SUBSCRIPTIONS
US ONE YEAR: $63.00
CANADIAN ONE YEAR: $99.00
FOREIGN ONE YEAR: $158.00
SUBSCRIPTIONS E-MAIL:
RETINASPECIALIST@CAMBEYWEST.COM

CIRCULATION
RETINA SPECIALIST
PO BOX 397
CONGERS, NY 10920-0397
CIRCULATION CUSTOMER SERVICE
PHONE: (877) 529-1746 (U.S)
OR(845) 267-3065 (OUTSIDE U.S)

SENIOR CIRCULATION MANAGER
HAMILTON MAHER
(212) 219-7870 hmaher@jhihealth.com

CEO, INFORMATION GROUP SERVICES
MARC FERRARA

SENIOR VICE PRESIDENT, OPERATIONS
JEFF LEVITZ

SENIOR VICE PRESIDENT, HUMAN RESOURCES
LORRAINE ORLANDO

VICE PRESIDENT, CREATIVE SERVICES & PRODUCTION
MONICA TETTAMANZI

VICE PRESIDENT, CIRCULATION
EMELDA BAREA

jmi
100 Avenue of the Americas
New York, NY 10013

ILUVIEN®
(fluocinolone acetonide intravitreal implant) 0.19mg

FACT OR FICTION? You Decide.
An Interactive Reception

Join your peers for a unique ILUVIEN fact-or-fiction reception at the AAO!

You will also have the opportunity to visit multiple interactive stations where your peers will share real-world ILUVIEN experiences.

Cocktails and hors d'oeuvres will be served.

DATE & TIME: Saturday, November 14, 2015
5:45 - 6:00PM - Registration
6:00 - 7:30PM - Interactive Reception

LOCATION: TAO Opium Room
(Located in the Venetian Hotel)
3377 S. Las Vegas Boulevard
Las Vegas, Nevada 89109

TAO®

HOSTS: MC: Nancy Holekamp, MD
Victor Gonzalez, MD
Fahd Quhill, MD
Nathan Radcliffe, MD
Christopher Riemann, MD

This event is non-CME. This program is not affiliated with the official program of the AAO. Please, no guests or spouses.

REGISTER NOW!

Online: www.revophth.com/iluvien2015

Email: reviewmeetings@jobson.com

Phone: 877-451-6511

Go to the registration website for this event by scanning the code below.

Sponsored by Alimera Sciences. Administered by Review of Ophthalmology®.

By Zuhair H. Peracha, MD, and Philip J. Rosenfeld, MD, PhD

Managing DME During Pregnancy

Intravitreal steroids may be considered in cases refractory to blood glucose control and laser.

Pregnant women with diabetes are at high risk for the development and progression of retinopathy, as multiple studies, most notably the Diabetes Control and Complications Trial (DCCT) and the Diabetes in Early Pregnancy study (DIEP), have reported.[1-5] A Danish study found that 16 percent of type I diabetics had macular edema at their baseline exam in early pregnancy, with another 10 percent developing macular edema as the pregnancy progressed.[4]

So what are the treatment options for these patients with diabetic macular edema (DME)? For the past 30 years, the recommended treatment of DME in pregnancy has remained essentially unchanged despite great progress in the management of DME. In addition to the standard laser option, newer treatment options include subthreshold laser, such as the MicroPulse (Iridex) or Endpoint Management (Topcon Medical Systems) lasers, intravitreal corticosteroids and even intravitreal inhibitors of vascular endothelial growth factor therapies (VEGF).

Observation and Laser

If a pregnant patient presents initially with mild to moderate DME, then it's reasonable to recommend close observation with an emphasis on blood glucose control. In a report from Copenhagen University Hospital,[5] two diabetic patients early in their pregnancies presented with macular edema between 500 and 1,500 µm from the fovea. With good blood glucose control, both had improvement and required no further intervention.

Although observation is a reasonable option, it is important to monitor these patients more closely than one would a normal adult because pregnancy can accelerate the severity of the retinopathy and edema.

If DME does not improve after a period of observation, the first treatment option should be laser. As reported in the Early Treatment Diabetic Retinopathy Study (ETDRS), grid or focal laser for clinically significant macular edema is effective in preventing future vision loss.[6,7] In another study out of Copenhagen,[4] two pregnant patients with type 1 diabetes and macular edema received focal laser and required no further treatment for the term of their pregnancies.

When foveal involvement precludes the safe use of conventional laser, subthreshold MicroPulse or Endpoint Management could be considered. Investigators at the University of Genoa, Italy,[8] demonstrated significant short-term improvement in DME and vision after treatment with the MicroPulse laser.

However, not all patients with macular edema are good candidates for laser. In a case report by Elisabet Agardh, MD, in Sweden, a pregnant woman with type 1 diabetes developed bilateral macular edema and high-risk nonproliferative diabetic retinopathy (NPDR) at week 19 of gestation.[9] As the pregnancy progressed, the persistent macular edema involved the fovea and Dr. Agardh determined it was too extensive for conventional laser. She observed the patient instead.

Ultimately, the patient received macular grid laser therapy in the right eye during the postpartum period and observation in the left eye. Final visual acuities were 20/40 and 20/50 in the right and left eyes, respectively, vs. 20/20 in both eyes at baseline. What other options were available even if this patient had been refractory to conventional laser during her pregnancy?

When Laser Won't Work

For DME refractory to laser, intravitreal steroids are thought to be a safe option during pregnancy. The Diabetic Retinopathy Clinical Research Network (DRCR.net), which found laser to be superior to intravitreal triamcinolone for treatment of DME at three years, actually found steroids to be more efficacious than laser after four months in terms of visual acuity and retinal thickening.[10,11]

Although long-term outcomes are generally the primary focus of any treatment, in pregnancy, which spans a finite period of time, short-term outcomes are equally, if not more, important.

A 2011 case report described a 23-year-old woman with type 1 diabetes who had injections of 0.05 ml triamcinolone acetonide.[12] She presented with NPDR and bilateral fovea-involving DME with central macular thicknesses of 578 µm and 667 µm in the right and left eyes, respectively, and 20/40 vision in both eyes. After consultation with the obstetrician, the patient had the injections in each eye one week apart.

Six weeks later, the retinal thickness measurements were 159 µm and 202 µm and Snellen visual acuities were 20/20 and 20/25 in the right and left eyes, respectively. The patient had no related complications such as glaucoma or cataract, and she delivered a healthy baby.

It is noteworthy that some studies

have associated first trimester systemic corticosteroid use with oral clefts[13] and topical corticosteroids with low birth weight.[14] However, the systemic absorption of intravitreal triamcinolone has been shown to be minimal.[15]

On the other hand, intravitreal steroids have been shown to cause increased intraocular pressure and the development of cataracts.[16] Although this is the only reported case of intravitreal triamcinolone administered during pregnancy, it is an effective option that should be considered safe in patients with refractory DME.

Role of Anti-VEGF Therapy

In the modern practice of medical retina, no discussion is complete without the mention of anti-VEGF therapy. In a patient with foveal involving DME with a contraindication to steroids, anti-VEGF could be considered. As the DRCR.net study demonstrated comparing anti-VEGF plus laser vs. laser alone, anti-VEGF therapies are very effective in the treatment of DME.[17]

Although there are no reports of anti-VEGF use in pregnancy for DME, there have been reports of its use in pregnancy for other indications. To date, there have been 21 reported intravitreal injections of anti-VEGF drugs into the eyes of pregnant women.[18] Overall, 20 unique patients have been treated, with one patient having received treatment during two separate pregnancies.

Within this group, three pregnancies resulted in fetal demise during the first month of gestation and one had a complicated birth at 29 weeks in the setting of preeclampsia.[18] Although the three cases of fetal demise are concerning, it's important to keep in mind that the rate of spontaneous miscarriage is between 15 and 20 percent. As a result, it's difficult to know if anti-VEGF therapy played a role.[19]

Regarding the complicated birth in the setting of preeclampsia, the mother had a significant medical history that included diabetes, hypertension and a prior emergent Cesarean section for fetal distress. Although anti-VEGF therapy has not been proven to be unsafe in pregnancy, much more investigation is needed before this can become a routine treatment option.

Conclusion

First-line treatments for DME in pregnancy are and should remain blood glucose control and laser. In severe instances of DME that are refractory to those approaches, intravitreal steroids can be considered. Treatment should be offered only in the second or third trimesters and the risks of intraocular pressure elevation and cataract development, and the remote risk of fetal harm, should be fully discussed with the patient.

Finally, only consider anti-VEGF therapy as a last resort due to the lack of long-term safety data in pregnancy and preferably within the third trimester of pregnancy. Caring for a pregnant mother and her fetus presents a great responsibility and, as a result, we as physicians appropriately act with great caution. However, it is our duty to inform patients of all available treatment options and allow them to fully participate in the decision-making process.

REFERENCES

1. Diabetes Control and Complications Trial Research Group. Effect of pregnancy on microvascular complications in the diabetes control and complications trial. Diabetes Care. 2000;23:1084-1091.
2. Chew EY, Mills JL, Metzger BE. Metabolic control and progression of retinopathy. The Diabetes in Early Pregnancy Study. National Institute of Child Health and Human Development Diabetes in Early Pregnancy Study. Diabetes Care. 1995;18;631-637.
3. Klein B E, Moss S E, Klein R. Effect of pregnancy on progression of diabetic retinopathy. Diabetes Care. 1990;13:34-40.
4. Vestgaard M, Ringholm L, Laugesen CS, Rasmussen KL, Damm P, Mathiesen ER. Pregnancy-induced sight-threatening diabetic retinopathy in women with Type 1 diabetes. Diabet Med. 2010;27:431-435.
5. Rasmussen KL, Laugesen CS, Ringholm L, Vestagaard M, Damm P, Mathiesen ER. Progression of diabetic retinopathy during pregnancy in women with type 2 diabetes. Diabetologia. 2010;53:1076-1083.
6. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Early Treatment Diabetic Retinopathy Study research group. Archives of ophthalmology 103, 1796-1806 (1985).
7. Dedania V S, Bakri S J. Novel pharmacotherapies in diabetic retinopathy. Mid E African J Ophthalmol. 2015;22:164-173.
8.Nicolo M, Musetti D, Traverso CE. Yellow micropulse laser in diabetic macular edema: a short-term pilot study. Euro J Ophthalmol. 2014; 24:885-889, doi:10.5301/ejo.5000495 (2014).
9. Agardh E. A case of progression of diabetic retinopathy during pregnancy. Acta ophthalmologica Scandinavica 80, 524-530 (2002).
10. Diabetic Retinopathy Clinical Research Network. A randomized trial comparing intravitreal triamcinolone acetonide and focal/grid photocoagulation for diabetic macular edema. Ophthalmology. 2008;115:1447-1449.
11. Diabetic Retinopathy Clinical Research Network. Three-year follow-up of a randomized trial comparing focal/grid photocoagulation and intravitreal triamcinolone for diabetic macular edema. Arch Ophthalmol. 2009;127:245-251.
12. Fazelat A, Lashkari K. Off-label use of intravitreal triamcinolone acetonide for diabetic macular edema in a pregnant patient. Clin Ophthalmol. 2011;5:439-441.
13. Oren D, Nulman I, Makhija M, Ito S, Koren G. Using corticosteroids during pregnancy. Are topical, inhaled, or systemic agents associated with risk? Can Fam Phys. 2004;50:1083-1085.
14. Chi CC, Wang SH, Kirtschig G, Wojnarowska F. Systematic review of the safety of topical corticosteroids in pregnancy. J Am Acad Dermatol. 2010;62:694-705.
15. Degenring R F, Jonas JB. Serum levels of triamcinolone acetonide after intravitreal injection. Am J Ophthalmol. 2004;137:1142-1143.
16. Scott IU, Ip MS, VanVeldhuisen PC, et al. A randomized trial comparing the efficacy and safety of intravitreal triamcinolone with standard care to treat vision loss associated with macular edema secondary to branch retinal vein occlusion: the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) study report 6. Arch Ophthalmol. 2009;127:1115-1128.
17. Diabetic Retinopathy Clinical Research Network. Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. Ophthalmology. 2010;117:1064-1077.
18. Polizzi S, Mahajan VB. Intravitreal anti-VEGF injections in pregnancy: Case series and review of literature. J Ocul Pharmacol Ther. 2015 Aug 24. Epub ahead of print.
19. Robinson GE. Pregnancy loss. Best Prac Res Clin Obstet Gynaecol. 2014;28: 169-178.

Bascom Palmer Eye Institute
UNIVERSITY OF MIAMI HEALTH SYSTEM

Dr. Rosenfeld is a professor at Bascom Palmer Eye Institute, University of Miami Miller School of Medicine. He has been the principal investigator and study chair for several clinical trials. Dr. Peracha is a medical retina fellow at Bascom Palmer.

KEEP UP WITH EVERYTHING RETINA BY KEEPING UP WITH RETINA SPECIALIST

THREE WAYS TO DO IT:

1
Go to our website @ www.retina-specialist.com

2
Follow us on Twitter @ RetinaSpecialst (drop the last "i")

3
Like us on Facebook @ RetinaSpecialistMag

Which White Dot Syndrome Is It?

Vitritis and characteristic cream-colored lesions in both eyes provided valuable clues.

By Stavros N. Moysidis, MD and Meena S. George, MD, PhD

A 47-year-old Caucasian woman was referred to the Retina Service of the University of Southern California Eye Institute with a chief complaint of gradually decreasing vision in both eyes over the past year, accelerating over the past six months.

She reported difficulty seeing in the dark and against dark backgrounds. She said she was concerned that she could not locate small items at work when they fall to the floor, which is dark in color. "I am looking for answers," she said.

Medical History and Exam

The patient has a history of cervical cancer, resected four years previously without recurrence. Otherwise, ocular and medical histories were unremarkable. She takes the antidepressant citalopram 20 mg PO daily for generalized anxiety disorder. She has a 10-plus pack-year history of smoking but she denied abuse of alcohol or other drugs.

Best-corrected visual acuity was 20/30-1 and 20/30+1, with intraocular pressures of 12 and 13 mmHg OD and OS, respectively. Pupils were normal without afferent pupillary defect. Extraocular movements and confrontation visual fields were full OU.

The anterior segment exam was normal OU. We noted 1+ anterior vitreous cell and many round, cream-colored lesions deep to the retinal vessels extending from the optic disc and the vascular arcades out to the equator in both eyes. These lesions appeared less round and more ovoid as they extended peripherally (*Figures 1A and B*).

Diagnosis and Workup

Given the vitritis and the characteristic, symmetric, cream-colored lesions in both eyes, the differential diagnosis centered on the primary inflammatory choriocapillaropathies, also known as the white spot (or dot) syndromes. These include bird-shot chorioretinopathy, acute zonal occult outer retinopathy, multiple evanescent white dot syndrome and multifocal choroiditis and panuveitis.[1]

We also considered infectious etiologies such as tuberculosis, syphilis and presumed ocular histoplasmosis. Although these etiologies are less likely, their management greatly differs from the white spot syndromes.

Other noninfectious etiologies we considered were sarcoidosis and intraocular lymphoma. Chest X-ray and blood tests for syphilis (rapid plasma reagin [RPR] and fluorescent treponemal antibody absorption [FTA-ABS]) were negative.

Fundus autofluorescence (FAF) revealed speckled hyperautofluorescence surrounding the disc OU. Optical coherence tomography (OCT) of the macula revealed fine vitreous opacities, small, cystic intraretinal fluid and an epiretinal membrane in both eyes (*Figure 1C*). Indocyanine green angiography (ICGA) revealed many hypofluorescent patches corresponding to the cream-colored lesions OU (*Figures 2A-C*).

Fluorescein angiography (FA) revealed a few areas of arteriolar narrowing and some mild pruning with a few mildly hyperfluorescent terminal vascular bulbs, likely representing microaneurysms. During early venous filling, a small peripapillary rim of hyperfluorescence began to form, which became a densely hyperfluorescent peripapillary ring on later phases.

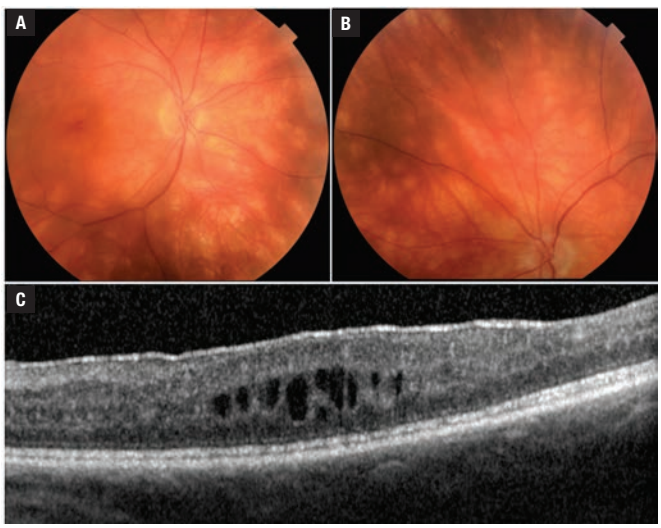


Figure 1. Fundus photo of the right eye (A) revealed round, cream-colored lesions about 1/4 disc diameter in size. Some of the more peripheral lesions are ovoid in appearance. In the left eye (B), round and ovoid cream-colored lesions deep to the retinal vessels were visible. Spectral domain optical coherence tomography of the macula OD (C) revealed cystic intraretinal fluid, most of which localized to the inner nuclear layer, although all layers from the inner plexiform to the outer nuclear layer were involved. The ellipsoid zone band and retinal pigment epithelium were intact and no subretinal fluid was present.

There were also many small, round hyperfluorescent foci surrounding the fovea, which increased in intensity but not diameter, in the later phases of FA (*Figures 2D-F*).

Treatment Plan

We determined that the patient's clinical presentation was consistent with bird-shot chorioretinopathy with cystoid macular edema (CME) OU. We started her on cyclosporine 100 mg PO daily and prednisone 5 mg PO daily. We placed the dexamethasone intravitreal implant (Ozurdex, Allergan) in each eye, one week apart, to achieve local control of the inflammation and CME.

We counseled the patient to stop smoking because smokers have an increased risk of developing noninfectious uveitis and uveitis with CME. However, she explained that she is not ready to quit.[2-4] We also ordered further testing, including complete metabolic profile (CMP), complete blood count (CBC) and human leukocyte antigen (HLA) A29 to confirm the diagnosis.

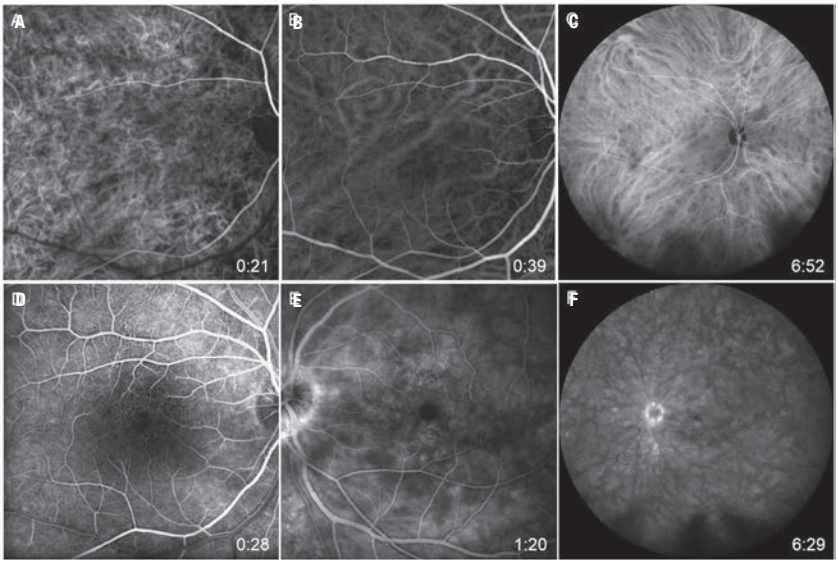


Figure 2. Indocyanine green angiography revealed the following findings in the right eye: at 21 seconds (A), a somewhat patchy appearance to the choroid with mild hyperfluorescence and some fuzziness to the choroidal vessels, especially in the superior macula, with a few round hypofluorescent lesions; at 39 seconds (B), a more normal appearance, but again with a mild fuzzy quality to some of the choroidal vessels; and at 6:52 (C), many round and ovoid hypofluorescent lesions. Fluorescein angiography (FA) of the right eye, at 28 seconds (D), revealed a few areas of arteriolar narrowing and some mild pruning, with a few mildly hyperfluorescent terminal vascular bulbs, likely representing microaneurysms. In the left eye, FA, at 1:20 (E), revealed a small peripapillary rim of hyperfluorescence with patchy, background hyperfluorescence and many small hyperfluorescent foci throughout the macula; and at 6:29 (F), conveyed a dense hyperfluorescent, peripapillary ring. The background conveyed patchy and mild hyperfluorescence. Multiple, small hyperfluorescent foci near the vessels inferior to the disc were visible, as were many small, faint, hyperfluorescent foci in the macula.

Discussion

Bird-shot chorioretinopathy, previously termed vitiliginous chorioretinopathy, is a bilateral, chronic uveitis that may present with vitritis, retinal vasculitis and cystoid macular edema.[1] The term bird-shot chorioretinopathy was coined by Stephen J. Ryan, MD, and A. Edward Maumenee, MD, in 1980, to describe the manner in which the lesions scatter away from the optic disc and toward the equator, giving a "shotgun" appearance.[5]

Bird-shot chorioretinopathy has the strongest link to HLA class I antigen of any disease in medicine, with a positive antigen HLA-A29 conferring a relative risk of 49.9.[6] It is a rare disease, accounting for 6 to 7.9 percent of patients with posterior uveitis. Slightly more than half of patients are women, and all but two reported cases have been in Caucasian patients.[7]

The presentation is classically described as involving oval or round, cream-colored lesions, about 1/2 to 1/4 disc diameter in size that are deep to the retina, cluster near the nerve, and are more predominant inferior and nasal to the disc.[1,8] As the lesions track further toward the equator, they may become more ovoid in appearance; vitritis may be present, but anterior chamber cell is typically absent or mild.[1,5]

These bird-shot lesions are not usually seen on FA, but appear on ICGA as hypofluorescent lesions during the early stages of the disease, and may represent blockage from inflammatory infiltrates or, less likely, choroidal ischemia.[9]

Consensus diagnostic criteria for this disease include bilateral disease, three or more peripapillary lesions inferior or nasal to the optic nerve in one eye, and low-grade vitreous and anterior chamber inflammation. Factors supporting the diagnosis are a positive

(Continued on page 17)

By Paul Hahn, MD, PhD »

Reflux Chromovitrectomy

This technique avoids the awkward one-handed balance of the syringe and cannula.

Operating by yourself has unique challenges. I remember when I finished fellowship and started operating solo, I found it cumbersome to self-inject chromovitrectomy agents I commonly use—triamcinolone and indocyanine green (ICG). I would hold the syringe and cannula in one hand and self-inject in a uni-manual approach that I found awkward, unsteady and even unsafe.

Vitreous Cutter as Injector

To address this challenge, I have developed a technique that I have called "reflux chromovitrectomy."[1] Rather than using a syringe with cannula to inject the chromovitrectomy agent, I now use a standard vitreous cutter.

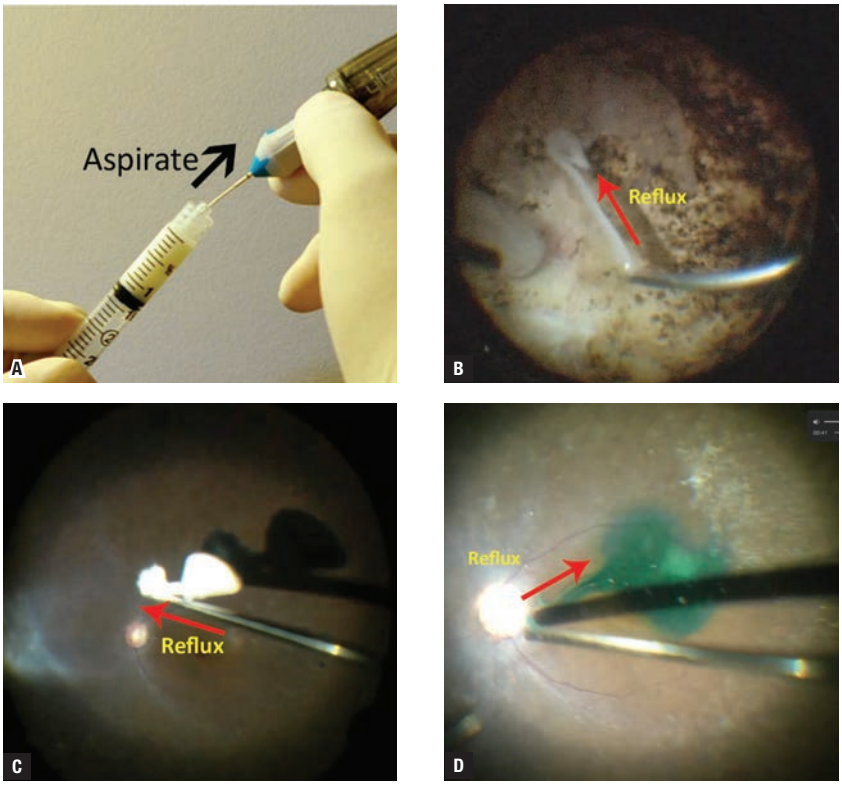
To do this, I ask the nurse to draw up the agent in a syringe in standard fashion. Next, I insert the cutter into the syringe to aspirate a small volume of agent. Then, I insert the cutter into the eye and use the vitrectomy foot pedal to directly reflux the agent into the vitreous cavity (*Figure*). Immediately, without instrument exchange, I can use the vitreous cutter already in the eye to proceed with the vitrectomy, hyaloid elevation, removal of excess agent or whatever the next step may be.

Taking Precautions

I recommend these three precautionary steps when attempting this maneuver:

Watch the Video

A video in which Dr. Hahn describes the technique is available at www.retina-specialist.com



Reflux chromovitrectomy starts with aspirating the agent into the vitreous cutter (A). Views of reflux Triesence (Alcon) with the hyaloid separated (B) and hyaloid attached (C), and reflux indocyanine green (D). Online video available at http://goo.gl/vVfcPQ

- To avoid air bubbles, I recommend aspiration of the agent rather than cut/aspiration, and I reflux a small amount first outside the eye.
- Undiluted kenalog does not reflux very smoothly. Diluting kenalog or using undiluted (or diluted) Triesence (Alcon) may be preferable.
- Because of the sideways-facing port of the vitreous cutter, application of dyes on the retinal surface requires turning the port down or allowing additional time for the dye to settle and stain. I dilute my ICG (25 mg) in 20 ml of 5% dextrose in water, and not the diluent included with the product. This facilitates settling. I usually allow it to sit for approximately 15 seconds before I remove it.

With these precautions in mind, I have found this technique to be universally accessible, effective, efficient, easy and surgeon-controlled. It spares the use and cost of additional injection cannulas.

Visualizing Triamcinolone Flow

Visualization of the flow of triamcinolone reflux provides feedback on the vitreous morphology. A stream suggests the hyaloid is syneretic or elevated, while a slow, clumping reflux suggests a formed,

usually attached, vitreous (*Figure*). The sideways-facing port is directional, which allows peripheral application even in phakic patients, minimizes flow directly at the surface of the retina, and can be rotated to direct toxic dyes away from a macular hole or other retinal break

In today's environment, with increasing pressures toward greater efficiency and lower cost, maximizing multi-functional capabilities is paramount. Current small-gauge vitreous cutters have emerged as the retina specialist's "Swiss Army Knife," often replacing the need for secondary instruments.

Reflux is a powerful extension of this multi-functionality, and its capabilities extend beyond refluxing inadvertently engaged retina or dispersing settled heme. "Reflux hydrodissection" can help separate planes in traction retinal detachments.[2]

I find reflux very useful for diagnostic vitrectomies to cut/aspirate undiluted vitreous samples and reflux them directly into a collection tube, bypassing the need for assistant-controlled (or what I consider to be uncontrolled) aspiration of a connected syringe. For me, using reflux and other multi-functional capabilities is an important step to becoming a better, safer and more efficient surgeon.

Dr. Hahn is an assistant professor of ophthalmology at Duke University Eye Center, Durham, N.C.
Disclosures: *Dr. Hahn serves as a consultant for Second Sight Medical Products and Bausch + Lomb.*

REFERENCES

1. Hahn P. Simple surgeon-controlled method of safe, cost-effective, and efficient application of chromovitrectomy agents through reflux. Retina. 2015;3:371-373.
2. Dugel P. Proportional reflux hydrodissection. Retina. 2012;32:629-630.

Which White Dot Syndrome Is It?

(**Retina Rounds**, *continued from page 15*)

HLA-A29 test, retinal vasculitis and cystic macular edema (CME). Severe inflammation leading to synechiae or keratic precipitates may be suggestive of a different diagnosis.[10]

The pathophysiology remains only partially elucidated with pathologic specimens revealing accumulation of primarily CD8+ T-lymphocytes within choroidal vessels.[11]

The most common cause of vision loss in these patients is secondary to CME, while choroidal neovascularization (CNV) develops in only 5 percent of eyes but results in more severe vision loss. CNV in cases of bird-shot chorioretinopathy is thought to occur secondary to a uveitic rather than an ischemic mechanism.[1,12]

Little consensus exists on management of bird-shot chorioretinopathy. Oral corticosteroids have long been the mainstay of treatment, and many physicians include a second immunosuppressive medication as well. Low-dose cyclosporine 100 mg PO daily has been shown to be efficacious with concurrent lower-dose oral corticosteroid.[13]

The patient must be monitored for nephrotoxicity and hypertension while on cyclosporine. Recently, intravitreal injections of sustained-release fluocinolone acetonide and dexamethasone have been delivered to allow for higher potency and localized drug delivery. However, an increased risk of cataract and glaucoma with these modalities has been reported.[14,15]

Smoking confers 2.96 times greater odds of developing noninfectious uveitis and 3.9 to eight times greater odds of uveitis with CME. Thus, physicians should discuss tobacco cessation with these patients.[2-4] The treatment plan should be optimized for each individual patient.

REFERENCES

1. Mirza RG, Jampol LM. White Spot Syndromes and Related Diseases. Retina 5th ed. 2012;2:1337-1380.
2. Lin P, Loh AR, Margolis TP, Acharya NR. Cigarette smoking as a risk factor for uveitis. Ophthalmology. 2010;117:585-590.
3. Thorne JE, Daniel E, Jabs DA, Kedhar SR, Peters GB, Dunn JP. Smoking as a risk factor for cystoid macular edema complicating intermediate uveitis. Am J Ophthalmol. 2008;145:841-846.
4. Yuen BG, Tham VM, Browne EN, et al. Association between Smoking and Uveitis: Results from the Pacific Ocular Inflammation Study. Ophthalmology. 2015;122:1257-1261.
5. Ryan SJ, Maumenee AE. Bird-shot retinochoroidopathy. Am J Ophthalmol. 1980;89:31-45.
6. Nussenblatt RB, Mittal KK, Ryan S, Green WR, Maumenee AE. Bird-shot retinochoroidopathy associated with HLA-A29 antigen and immune responsiveness to retinal S-antigen. Am J Ophthalmol. 1982;94:147-158.
7. Shah KH, Levinson RD, Yu F, et al. Bird-shot chorioretinopathy. Surv Ophthalmol. 2005;50:519-541.
8. Gasch AT, Smith JA, Whitcup SM. Bird-shot retinochoroidopathy. Br J Ophthalmol.1999;83:241-249.
9. Fardeau C, Herbort CP, Kullmann N, Quentel G, LeHoang P. Indocyanine green angiography in bird-shot chorioretinopathy. Ophthalmology. 1999;106:1928-1934.
10. Levinson RD, Brezin A, Rothova A, Accorinti M, Holland GN. Research criteria for the diagnosis of bird-shot chorioretinopathy: results of an international consensus conference. Am J Ophthalmol. 2006;141:185-187.
11. Gaudio PA, Kaye DB, Crawford JB. Histopathology of bird-shot retinochoroidopathy. Br J Ophthalmol. 2002;86:1439-1441.
12. Brucker AJ, Deglin EA, Bene C, Hoffman ME. Subretinal choroidal neovascularization in bird-shot retinochoroidopathy. Am J Ophthalmol. 1985;99:40-44.
13. Vitale AT, Rodriguez A, Foster CS. Low-dose cyclosporine therapy in the treatment of bird-shot retinochoroidopathy. Ophthalmology. 1994;101:822-831.
14. Yap YC, Papathomas T, Kamal A. Results of intravitreal dexamethasone implant 0.7 mg (Ozurdex(R)) in non-infectious posterior uveitis. Int J Ophthalmol. 2015;8:835-838.
15. Rush RB, Goldstein DA, Callanan DG, Meghpara B, Feuer WJ, Davis JL. Outcomes of bird-shot chorioretinopathy treated with an intravitreal sustained-release fluocinolone acetonide-containing device. Am J Ophthalmol. 2011;151:630-636.

USC Eye Institute

Dr. Olmos de Koo is an assistant professor of ophthalmology at the University of Southern California Eye Institute and director of the vitreoretinal fellowship at the Keck School of Medicine of USC in Los Angeles.

Dr. Moysidis is an ophthalmology resident at the USC Eye Institute/Los Angeles County + USC program. Dr. George is a senior surgical vitreoretinal fellow at USC Eye Institute.

PEARLS FOR PERFORMING PNEUMATIC RETINOPEXY

This in-office procedure is a less-costly alternative and is well-suited to repair small superior retinal breaks.

By Efrem D. Mandelcorn, MD, FRCSC, Joshua S. Manusow, MD, FRCSC, and Mark S. Mandelcorn, MD, FRCSC

Pneumatic retinopexy (PR) is the least invasive method to successfully reattach a detached retina with a good final visual outcome. PR works best for small superior retinal breaks. Discomfort is minimal, diplopia does not occur at any stage and cataract formation is not a common complication.[1] PR is an in-office procedure and requires no operating room resources. This article reviews our technique for performing PR.

Indications and Patient Selection

Classically, PR was indicated in the following types of retinal detachments (RD): a single break no larger than one clock hour located in the superior eight clock hours of the ocular fundus; or a group of small breaks within one clock hour without grade C or D proliferative vitreoretinopathy, glaucoma, retinal breaks in the inferior four clock hours or in a patient unable to comply with head positioning.[2,3]

Many retinal surgeons have attempted to expand the use of PR beyond these classic 1986 indications to treat recurrent detachments following scleral buckle (SB) or pars plana vitrectomy (PPV) to include inferior retinal breaks, giant retinal tears and dialyses.[4-9]

Another not yet reported indication is to use pneumatic retinopexy to keep the macula attached in a macula-on RD so that vitrectomy or scleral buckling surgery can be delayed to a more appropriate time when the proper surgical team and resources are in place. By injecting the gas bubble and positioning the patient face down, the macula will remain attached until a more definitive procedure can take place.

Anecdotally, we have done this procedure with great success when, for various reasons, we cannot get a patient into the operating room

View the Video
Watch the video at
www.retina-specialist.com

ABOUT THE AUTHORS

Dr. Efrem Mandelcorn is an attending vitreoretinal surgeon at the Toronto Western Hospital of the University of Toronto University Health Network. He was fellowship-trained at the University of Toronto and the Bascom Palmer Eye Institute, University of Miami.

Dr. Mark Mandelcorn is a retina specialist practicing surgical and medical retina at Toronto Western Hospital of the University of Toronto, where he has been involved in clinical teaching, research and administration.

Dr. Manusow is a vitreoretinal surgery fellow at the University of Toronto, where he also completed his ophthalmology residency and served as chief resident.

DISCLOSURES: The authors have no relevant disclosures.

as fast as we would like or if the patient needs to delay the procedure.

Our Current Technique

Before performing a PR, the surgeon must note anterior segment findings such as lens status and chamber depth. A detailed fundus drawing noting the number, size and location of all retinal breaks, subretinal fluid accumulation and the presence of retinal breaks or lattice degeneration in the areas of attached retina is essential.[10,11]

These are the key steps and considerations involved in our approach to performing pneumatic retinopexy:[12]

• ***Laser retinopexy.*** Before the procedure, we barricade with laser any retinal breaks or lesions predisposing to retinal breaks, such as lattice degeneration in the flat retina.

• ***Anesthesia and asepsis.*** We begin with anesthetic eye drops followed with either xylocaine gel or subconjunctival lidocaine injection. Then we insert an eyelid speculum and instill a drop of povidone 5% into the conjunctival sac, especially over the area of the intended injection site.

• ***Anterior chamber paracentesis.*** With the patient seated at the slit lamp, we perform an anterior chamber paracentesis with a 30- or 27-gauge needle. We introduce the needle horizontally at the inferotemporal limbus, creating a beveled entry that is self-sealing (*Figure*). Exerting pressure on the nasal-scleral side of the entry site encourages drainage of anterior chamber fluid. We aim for a 0.3-cc tap. (*Online video*)

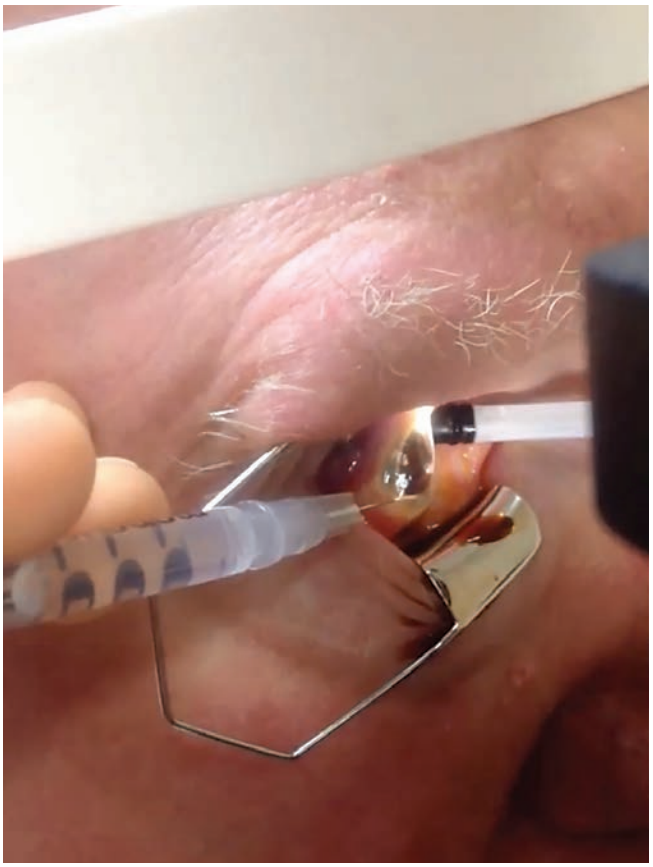


Figure. To perform the anterior chamber paracentesis, we introduce the 30- or 27-gauge needle horizontally at the inferotemporal limbus, creating a beveled entry that is self-sealing. Applying pressure on the nasal-scleral side of the entry site facilitates drainage of fluid from the anterior chamber. Online video available at http://goo.gl/6BfBoc

• ***Intraocular gas injection.*** The needle should enter at the highest point of the eye. Some prefer injecting the gas at the 12 o'clock position while others inject in the superonasal or superotemporal quadrant away from the most bullous area of detachment. We inject 4 mm from the limbus in phakic patients and 3.5 mm from the limbus in pseudophakic patients.

We lean the patient back in the examining chair and ask him to look down. We make the injection using a slow continuous movement on the syringe plunger so that a gas bubble develops at the tip of the needle in the vitreous cavity and the needle remains in the bubble as it expands with more gas. The needle and syringe are removed in a quick movement to allow the external puncture opening to self-seal. Some surgeons use a sterile cotton-tipped applicator to immediately massage the puncture site and avoid gas leakage.

• ***Choice and volume of injected gas.*** We use SF6 or C3F8 gas, injecting 0.6 ml of the former or 0.3 ml of the latter. The bubble will slowly expand over days to a volume of 1.2 ml allowing for slow equilibration of intraocular pressure.[13]

• ***Control of intraocular pressure after gas injection***. If the optic nerve is not perfused immediately following the gas injection, we make another paracentesis with the 27- or 30-gauge needle through the orig-

Take-home Point

Pneumatic retinopexy is an in-office procedure that, in our hands, works well to reattach a majority of retinal detachments. It is minimally invasive with few complications, with little downside to employing it as an initial procedure. The key to success is experience, patient selection, patience and communication.

inal paracentesis site. Perfusion of the nerve must be verified before the patient leaves.

• ***Assessing the size and adequacy of the gas bubble.*** Using the indirect ophthalmolscope, we assess the size and number of the gas bubble(s). The procedure is finished.

Care After the Injection

Care of the patient following the injection involves the following steps:

• ***Post-injection positioning.*** The goal of positioning is to allow the gas bubble to tamponade the retinal break. Some retinal surgeons carry out a "steamroller" maneuver to try to keep subretinal fluid from tracking into the macula. The patient is instructed to begin positioning immediately.

• ***Laser retinopexy 24 to 48 hours later.*** If the retina around the retinal breaks is now attached, it is possible to administer laser photocoagulation around the retinal breaks within two days after the injection. The laser indirect ophthalmoscope, in our hands, is the best method of doing this. The patient continues positioning for another several days to ensure that a firm chorioretinal adhesion forms in the laser-treated area.[14]

Troubleshooting

Even with the best-planned procedures, problems and complications can occur. Here is how we avoid the most common postoperative issues and manage them if they do occur.

• ***"Fish eggs."*** Multiple small bubbles called "fish eggs"[1] are a nuisance because they can potentially gain access to the subretinal space through a large break, or make visualization extremely difficult. A few small bubbles are sometimes unavoidable and usually will coalesce over one to two days. If not, the eye can be gently tapped or flicked to encourage this.

To avoid fish eggs, we recommend you ensure the needle is at the highest point of the globe when injecting. We generally push the needle one-third of the way in, and then withdraw it until the tip is just in the vitreous cavity. Making the injection with steady pressure and the needle stationary will help keep the tip within the expanding bubble and prevent fish eggs.

If you encounter fish eggs, simply position the patient in a way as to move them out of view by adjusting the angle of the chair or putting the patient on his side during the laser retinopexy in order to achieve better visualization. Fish eggs can still tamponade a retinal break, and we have seen many retinas successfully reattached despite multiple small bubbles.

• ***Sub-retinal fluid despite a flat break.*** Not all retinal pigment epithelium is created equal. A not-uncommon scenario we see is that the patient returns 48 hours after gas injection with a flat retinal break but persistent subretinal fluid elsewhere. In such a case, it is important to thoroughly reexamine the eye to ensure no open breaks exist. If there are none, we laser barricade the flat break and observe patiently.

Some patients have a weak RPE pump that prolongs the time it can take for the retina to flatten. We have waited days to weeks for some retinas to fully flatten. The goal of PR is to flatten the area of retinal break so that it can be barricaded. It is helpful to be patient with persistent subretinal fluid as long as no open retinal breaks are present.

• ***A perfect candidate but failed procedure.*** Occasionally, we perform PR on the perfect candidate with a phakic superior RD and one small break, but the retina does not flatten around the break. If examination of the fundus does not reveal a missed open break, the problem may be poor patient positioning.

Better physician communication can remedy this. We often write down specific positioning instructions or place an arrow on the patient's forehead to clearly indicate the correct position to maintain. Sometimes, we also have the patient position in the office before he leaves to ensure he has it right. This allows us to ensure that the bubble is tamponading the break with direct visualization.

It is sometimes helpful to have the patient position on one side or the other and not face down because side positioning often covers at least four or five clock hours of temporal or nasal retina.

• ***Difficulty with laser retinopexy.*** Skill with indirect laser retinopexy is essential to performing PR well. This is by far the most technically challenging part of the procedure and requires practice. To avoid difficulty with visualization secondary to the refractive change at the edge of the bubble, position the patient to either laser through the center of the bubble or turn the patient's head while the he is supine so that the bubble moves completely out of view.

Once the retina flattens, it can sometimes be difficult to identify small holes that were easier to see in the detached retina. Careful fundus drawing, especially noting adjacent landmarks such as blood vessels and pigmentary changes that could aid in finding the break later, also help.

Marking the location of the break in an area of adjacent attached retina prior to injection of the gas bubble is also helpful. We do this by placing a laser burn either in the adjacent flat retina or the pars plana. Cryotherapy prior to gas injection can also help to eliminate the need to find and treat the break again after gas injection. However, we prefer to perform laser because it less inflammatory.

Finally, if you cannot identify the break definitively, you can apply diffuse peripheral laser in the sus-pected area.

• ***Inferior retinal breaks.*** We have performed many PR procedures for patients with inferior retinal breaks for various reasons, including patient preference, patient age and lens status. Although it's not as successful as it has been in patients with more classic indications, we have had good results.

In our experience, positioning the patient directly on his side can usually achieve tamponade of inferior retinal breaks, which allows the gas bubble to cover the inferotemporal or inferonasal retina.

In cases of 6 o'clock breaks, a second gas bubble injection 24-48 hours after the first provides tamponade to the additional inferior clock hours to 6 o'clock when the patient is positioned on his side.

Serial pneumatic retinopexy, or a "double bubble," can be performed in the same way as a single procedure, 24 to 48 hours later. This involves performing an AC tap to make room for the second bubble. This second bubble is then injected into the first fully expanded gas bubble to achieve a single larger bubble.

Outcomes and Results

We typically quote our patients a success rate of 70 to 80 percent with PR depending on their clinical features. The original randomized clinical trial reported a single operation success rate of 73 percent—but it defined a single operation strictly as retinal reattachment at six months after one surgical intervention or injection of gas with one laser and/or cryotherapy performed immediately or within 72 hours.[3]

In reality, success with PR requires much more manipulation of gas bubble positioning and sometimes supplementation with sequential gas bubble injections as well as more than one laser treatment. Other studies have reported retinal reattachment rates of 60 to 91 percent.[2,8,11,15-18]

Inexpensive Yet Unpopular

Economic analyses have shown that PR is more than 50 percent less expensive than scleral buckling or pars plana vitrectomy, and has the most utility when dollars/quality-of-life-year saved is studied.[19-20] Despite this, recent surveys found only 25 percent of retina specialists would use PR for a retinal detachment with a single superior break, which is a decline from previous data.[21]

Overall, only 15 percent of retinal detachments are treated with PR in the United States, and studies have estimated that Medicare would save $6 million to $30 million if this rate increased to just 20 to 35 percent.[19,22]

Conclusion

We have found little downside to employing pneumatic retinopexy as an initial procedure and we would choose to undergo it before vitrectomy or scleral buckle were our own retinas to become detached. We recommend retina specialists make it a part of their practice.

REFERENCES

1. Feng H, Adelman RA. Cataract formation following vitreoretinal procedures. Clin Ophthalmol. 2014;8:1957-1965.
2. Tornambe PE, Hilton GF. Pneumatic retinopexy. A multicenter randomized controlled clinical trial comparing pneumatic retinopexy with scleral buckling. The Retinal Detachment Study Group. Ophthalmology. 1989;96:772-784.
3. Hilton GF, Das T, Majji AB, Jalali S. Pneumatic retinopexy: principles and practice. Indian J Ophthalmol. 1996;44:131-143.
4. Hilton GF, Grizzard WS. Pneumatic retinopexy. A two-step outpatient operation without conjunctival incision. Ophthalmology. 1986;93:626-641.
5. Friberg TR, Eller AW. Laser pneumatic retinopexy for repair of recurrent retinal detachment after failed scleral buckle--ten years experience. Ophthalmic Surg Lasers. 2001;32:13-18.
6. Modi YS, Townsend J, Epstein AE, et al. Pneumatic retinopexy for retinal detachment occurring after prior scleral buckle or pars plana vitrectomy. Ophthalmic Surg Lasers Imaging Retina. 2014;45:409-413.
7. Chang TS, Pelzek CD, Nguyen RL, et al. Inverted pneumatic retinopexy: A method of treating retinal detachments associated with inferior retinal breaks. Ophthalmology. 2003;110:589-594.
8. Tornambe PE, Hilton GF, Kelly NF, et al. Expanded indications for pneumatic retinopexy. Ophthalmology. 1988;95:597-600.
9. Melgen SE, Michels M. Pneumatic retinopexy for the treatment of giant retinal dialyses. Am J Ophthalmol. 1994;118:762-765.
10. Tornambe PE. Pneumatic retinopexy: The evolution of case selection and surgical technique. A twelve-year study of 302 eyes. Trans Am Ophthalmol Soc. 1997;95: 551-578.
11.Rootman DB, Luu S, M Conti S, et al. Predictors of treatment failure for pneumatic retinopexy. Can J Ophthalmol. 2013;48:549-552.
12. Mandelcorn E, Mandelcorn M, Manusow JS. Update on pneumatic retinopexy. Curr Opinion Ophthalmol. 2015;26:194-199.
13. Lincoff H, Kreissig I, Brodie S, Wilcox L. Expanding gas bubbles for the repair of tears in the posterior pole. Graefes Arch Clin Exp Ophthalmol. 1982;219:193-197.
14. Poliner LS, Tornambe PE. Failed retinal detachment repair after intravitreal air injection. Arch Ophthalmol. 1989;107:487-488.
15. Hilton GF, Kelly NE, Salzano TC, Tornambe PE, Wells JW, Wendel RT. Pneumatic retinopexy. A collaborative report of the first 100 cases. Ophthalmology. 1987;94: 307-314.
16. Tornambe PE, Hilton GF, Brinton DA, et al. Pneumatic retinopexy. A two-year follow-up study of the multicenter clinical trial comparing pneumatic retinopexy with scleral buckling. Ophthalmology. 1991;98:1115-1123.
17. Fabian ID, Kinori M, Efrati M, et al. Pneumatic retinopexy for the repair of primary rhegmatogenous retinal detachment: A 10-year retrospective analysis. JAMA Ophthalmol. 2013;131:166-171.
18. Gilca M, Duval R, Goodyear E, et al. Factors associated with outcomes of pneumatic retinopexy for rhegmatogenous retinal detachments: A retrospective review of 422 cases. Retina. 2014;34:693-699.
19. Goldman DR, Shah CP, Heier JS. Expanded criteria for pneumatic retinopexy and potential cost savings. Ophthalmology. 2014;121:318-326.
20. Chang JS, Smiddy WE. Cost-effectiveness of retinal detachment repair. Ophthalmology 2014;121:946-951.
21. Williams PD, Hariprasad SM. Evolving trends in primary retinal detachment repair: Microincisional vitrectomy and the role of OCT. Ophthalmic Surg Lasers Imaging Retina. 2014;45:268-272.
22. Hwang JC. Regional practice patterns for retinal detachment repair in the United States. Am J Ophthalmol. 2012;153:1125-1128.

DRAINAGE RETINOTOMY SANS LASER

An alternative approach can leave retinotomies unlasered in most routine cases.

By Ryan Isom, MD

Rhegmatogenous retinal detachments occur when the neurosensory retina separates from the retinal pigment epithelium due to subretinal fluid from one or more breaks. They affect about one person in 10,000 a year and, if left untreated, can lead to significant and permanent vision loss.

Surgical interventions began in the 1930s with the introduction of the scleral buckle, followed by pneumatic retinopexy and, more recently, vitrectomy with or without a scleral buckle. This article will discuss various methods of subretinal fluid drainage with case presentations of non-lasered drainage retinotomies.

Methods of Subretinal Fluid Drainage

Various techniques exist for draining subretinal fluid during vitrectomy for repair of rhegmatogenous retinal detachments. Three common techniques include:

- Drainage from a preexisting retinal break.
- Perfluorocarbon liquids.
- Draining retinotomies.

Each technique has its benefits and possible complications. The surgical approach often depends on surgeon preference, surgical setting, available equipment and economic factors.

View the Video
Watch the video at www.retina-specialist.com.

Ideally fluid is drained from an already present retinal break during a fluid-air exchange with complete flattening of the retina. This technique avoids the need to create additional retinal holes and the cost and possible complications of perfluorocarbon liquids.

Draining through a peripheral break can be challenging due to residual vitreous around the break, difficulty of access in phakic eyes and residual subretinal fluid. Significant amounts of residual subretinal fluid can lead to retinal folds, which have been reported in up to 3 percent of cases postoperatively in one series.[1]

Intraoperative head tilt can minimize residual, posterior subretinal fluid. This makes the area of the break the most dependent to pool the fluid closer to the hole. Although the head tilt may compromise the view, a greater amount of fluid may be removed to decrease the risk of postoperative retinal folds.

Role of Liquid Fluorocarbons

Stanley Chang, MD, first introduced low-viscosity liquid fluorocarbons, such as perfluorocarbon, in the late 1980s.[2] Their use made sig-

ABOUT THE AUTHOR

Dr. Isom is in private practice in Salt Lake City, Utah and participates as adjunct faculty at the Moran Eye Center.

DISCLOSURES: Dr. Isom has no relevant conflicts to disclose.

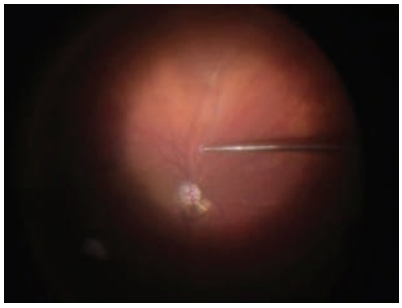


Figure 1. Screen capture from a video of inferior non-lasered drainage retinotomy of a macula-off retinal detachment. Video available at http://goo.gl/7xdexW

nificant improvements in the repair of complex retinal detachments. The initial benefits of liquid fluorocarbons in complicated cases of giant retinal tears and proliferative vitreoretinopathy (PVR) retinal detachments have led to their use in less-complicated retinal detachments.

Some surgeons prefer to use liquid fluorocarbons routinely to avoid the need for posterior drainage retinotomies. Although perfluorocarbons have been a useful addition to the repair of retinal detachments, they remain expensive and carry the risk of retention in the subretinal space.

One study found the rate of subretinal perfluorocarbon to be just over 11 percent.[3] However, all of the cases of retained subretinal perfluorocarbon involved retinectomies of over 120°. Valved cannulas and a greater familiarity with these liquids can decrease the risk of subretinal retention.

However, as surgeons' outcomes are being more closely scrutinized for their cost-effectiveness, the cost of items such as perfluorocarbons may begin to affect their use in routine cases.

Drainage Retinotomies

Steve Charles, MD, first popularized drainage retinotomies to aid in the transretinal subretinal fluid drainage during a gas exchange. A more complete drainage of subretinal fluid is usually achieved because the surgeon can drain from the "bottom of the bowl" as opposed to draining from a peripheral retinal break. A more complete drainage of subretinal fluid decreases the risk of postoperative retinal folds.

The complications of posterior drainage retinotomies include visual field scotomas, risk of subsequent epiretinal membrane and proliferative vitreoretinopathy, as well as subretinal choroidal neovascular membrane formation.

Traditionally, drainage retinotomies are surrounded by barricade laser after a complete gas exchange. We have found that creating smaller and non-lasered drainage retinotomies may minimize some complications associated with this technique (*Figure 1 and online video*).

(Continued on page 24)

Take-home Point

The techniques employed to repair retinal detachments continue to vary and improve over time. Drainage of subretinal fluid from a primary break is ideal, but in cases of persistent posterior fluid, a drainage retinotomy may decrease the risk of postoperative retinal folds and decrease the cost of surgery. These retinotomies may be left unlasered in most routine cases. Further evaluation in a larger series is necessary to evaluate any increase in epiretinal membranes, size of induced visual field scotoma and effect on redetachment rate.

Figure 2. Postoperative optical coherence tomography shows no associated subretinal fluid or redetachment from the retinotomy.

Non-lasered Retinotomies

The rationale to laser a drainage retinotomy is to prevent redetachment from the retinotomy site. However, a hole in the retina does not lead to a detachment unless another force is acting upon it. The retina "wants" to stay attached through a variety of systems: the negative pressure gradient between the vitreous and the choroid; the pumping mechanism of retinal pigment epithelium; and subcellular "glue" components of the retinal pigment epithelium. This is evidenced by macular holes that are rarely the cause of rhegmatogenous retinal detachments, aside from in very myopic eyes.

The easiest way to create a drainage retinotomy is with diathermy. We have found that cauterizing the retina briefly with diathermy to create a non-perforated white spot, followed by perforation with the sharp tip of the diathermy, can create a very small opening through which subretinal fluid may be removed during a gas exchange. Prior removal of all viscous subretinal fluid through a peripheral break will further reduce the expansion of a retinotomy during a fluid-gas exchange.

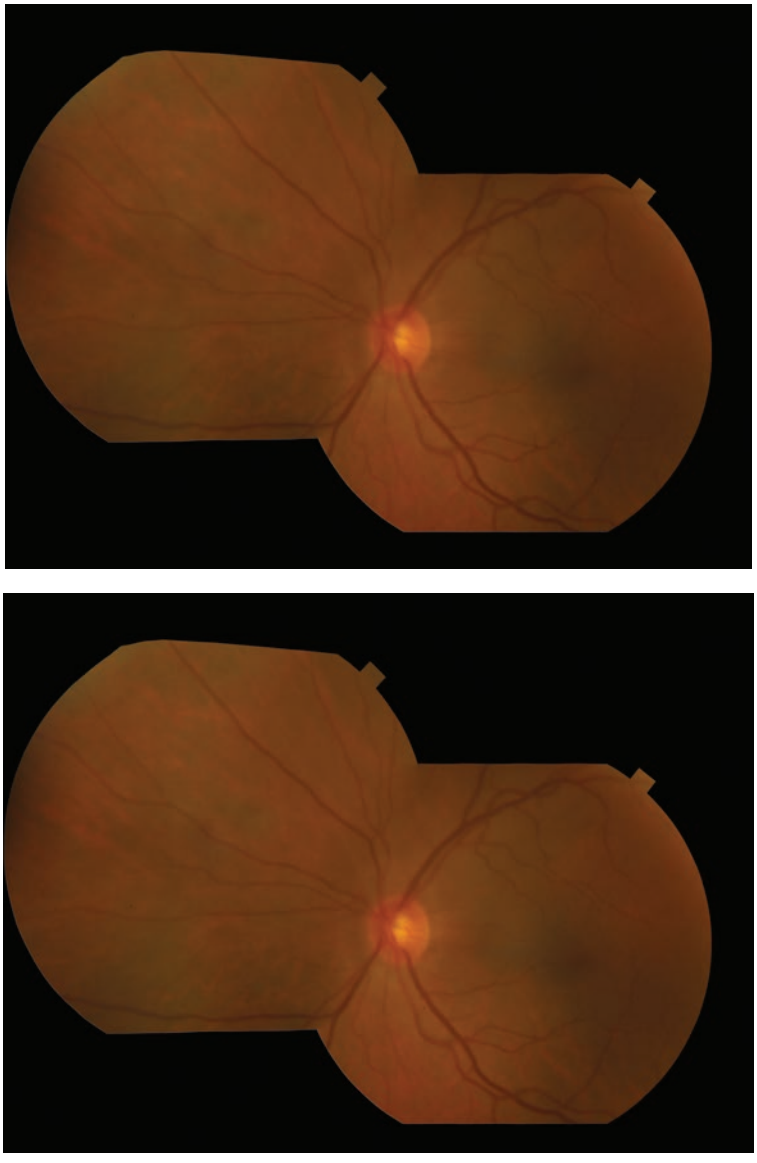


Figure 3. Fundus photographs show an almost normal posterior pole in the area of the retinotomy.

In uncomplicated rhegmatogenous retinal detachment cases, these drainage retinotomies may be left unlasered to decrease the size of the scotoma. It is our experience that patients do not appreciate any scotoma from these small retinotomies, although we have not performed extensive postoperative visual field testing.

Several different surgeons have used this technique of non-lasered retinotomy with excellent results. The figures here show results from two patients with excellent postoperative outcomes. We are in the process of compiling a more extensive series of patients. Postoperative optical coherence tomography (*Figure 2, page 23*) shows no associated subretinal fluid or redetachment from the retinotomy. Color fundus photography (*Figure 3*) can also show an almost normal posterior pole appearance in the area of the retinotomy.

Surgeons should use caution in using drainage retinotomies in young patients or in cases of inflammation or trauma due to concern for promoting PVR. If there is intraoperative or postoperative concern for PVR, drainage retinotomies should be lasered to prevent redetachment from the site.

REFERENCES

1. Van Meurs JC, Humalda D, Mertens DA, Peperkamp E: Retinal folds through the macula. Doc Ophthalmol. 1991;78:335–340.
2. Chang S. Low viscosity liquid fluorochemicals in vitreous surgery. Am J Ophthalmol. 1987;103:38-43.
3. Garcia-Valenzuela E, Ito Y, Abrams GW. Risk factors for retention of subretinal perfluorocarbon liquid in vitreoretinal surgery. Retina. 2004;24:746-752.
4. Richards SC, Maberley AL. Complications of retinotomies for subretinal fluid drainage. Can J Ophthalmol. 1993;28:24-27.

Reimbursement Update Course for Ophthalmology and Optometry

TOPICS THAT WILL BE COVERED:

- Coding Eye Exams With Corcoran's Office Visit Matrix: Better & Faster
- Resolving ICD-10 Problems After Inauguration
- Responding To A Payer's Chart Audit and Criticism
- What's New in the Medicare Program?
- Getting Modifiers Right: Fast-paced Interactive Challenge
- Update On Medicare's Incentive Programs (PQRS, VBPM, MU)
- Utilization Benchmarking: Identifying Underused And Overused Services

REGISTER TODAY!

Space is limited

KEVIN J. CORCORAN
COE, CPC, CPMA, FNAO
President
Over 39 years Ophthalmic experience

MARY PAT JOHNSON
COMT, COE, CPC, CPMA
Senior Consultant
Over 30 years Ophthalmic experience

TRICIA L. KOLB
COT, CPC, OSC
Associate Consultant
Over 20 years Ophthalmic experience

PAUL M. LARSON
MMSC, MBA, COMT, COE, CPC, CPMA
Senior Consultant
Over 39 years Ophthalmic experience

KIRK A. MACK
COMT, COE, CPC, CPMA
Senior Consultant
Over 25 years Ophthalmic experience

DONNA M. MCCUNE
CCS-P, COE, CPMA
Vice President
Over 29 years Ophthalmic experience

Course approved for 8.0 Continuing Education Credits for **AAPC, COPE, NBCOE and JCAHPO**

Corcoran Consulting Group

www.corcoranccg.com **1.800.399.6565**

COMPUTER-NAVIGATED LASER FOR DME: HOW WE GOT HERE

The latest development in macular laser has been shown to be accurate, safe and effective, but more study is needed. **By John F. Payne, MD, and W. Lloyd Clark, MD**

In the evolution of lasers, argon laser photocoagulation had been the gold standard for treatment of diabetic macular edema (DME) until relatively recently, when anti-vascular endothelial growth factor (VEGF) medications were found to be more efficacious. Yet, retina specialists continue to employ focal laser treatment adjunctively with anti-VEGF and/or intravitreal corticosteroid therapy for center-involving DME and as primary therapy for noncentral DME.

Recently, a computer-guided laser photocoagulation system that utilizes real-time imaging and tracking has emerged to enhance the safety and accuracy of focal laser treatment and improve visual outcomes. This article describes the evolution of computer-guided focal laser therapy for the treatment of DME and explores the clinical experience with this approach to date.

Tracking Avoids Near Misses

Focal/grid laser therapy has been traditionally performed with a slit-lamp delivery system, and requires the treating physician to localize and treat all microaneurysms in the areas of edema. This treatment can sometimes be problematic due to inadequate visualization of all leaking microaneurysms and an inability to accurately target the lesions on a living, moving fundus. Near misses of laser treatments can cause collateral damage, which can lead to macular scarring and scotomas. Additionally, physician variability makes it difficult to analyze data that utilize traditional focal/grid laser therapy in clinical trials.

Advances in computer-assisted tracking systems have enabled the development of a computer-guided, laser-targeting device. The navigated laser photocoagulator, also known as the Navilas laser system (OD-OS GmbH), utilizes a retinal eye-tracking laser delivery system with integrated digital fundus imaging (*Figure 1*). Registered image overlays allow the physician to map and target microaneurysms and provide laser stabilization through real-time fundus tracking.

The instrument is the first to use real-time retinal tracking and takes approximately 25 images per second in order to maintain registration during planning and treatment.[1] The Navilas photocoagulator was designed to improve the accuracy of laser photocoagulation and provide the ability to localize all microaneurysms and other lesions that require accurate treatment while overcoming the difficulties of slit-lamp based delivery. An additional benefit is that the operator can follow laser protocols in a

ABOUT THE AUTHORS

Drs. Payne (top) and Clark are vitreoretinal specialists at Palmetto Retina Center and are associate clinical professors at the University of South Carolina School of Medicine, Columbia.

DISCLOSURES: Dr. Payne has received grants from OD-OS, Genentech and Regeneron. He is the principal investigator of the TREX-DME trial.

Dr. Clark has received grants from Genentech, OD-OS, Regeneron, Allergan and Santen, and is a consultant to Bayer, Genentech, Regeneron and Santen.

more precise and standardized way.

The standard Navilas system uses a diode-pumped, solid-state laser (532 nm) for single-spot, grid and panretinal photocoagulation. Unlike conventional and semi-automated delivery systems, the Navilas laser is fundus-camera based. This allows for reflex-free visualization of larger areas of the retina during treatment, and the infrared light used during treatment is more comfortable for the patient. Figures 2A and B demonstrate a typical laser session in which microaneurysms are targeted on the digital display. Figure 2C displays the treatment effect immediately following treatment.

A newer model of the Navilas, which received Food and Drug Administration approval in February 2015, uses a 577-nm wavelength yellow laser to minimize laser scatter and maximize tissue absorption. Targeted, computer-guided laser therapy should allow for less energy to be delivered and less uptake from macular pigments, leading to less collateral damage to the photoreceptors. This latest version of the Navilas laser system also allows for a navigated microsecond pulsing option for subthreshold delivery. The digital display enables the physician to apply evenly spaced confluent grids of laser and document exactly where treatments are applied. This function is invaluable when giving subthreshold treatment because the laser burns are not visible clinically.

Take-home Point

Computer-navigated laser, the latest development in the 50-year history of focal laser therapy, has been shown to be accurate, safe and effective at reducing the treatment burden for patients. While further clinical research is needed, this technology is advancing our understanding of diabetic macular edema treatment.

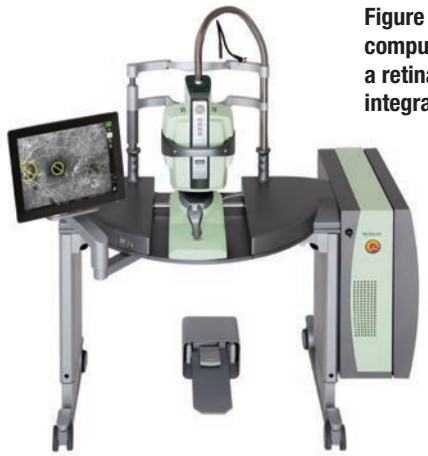


Figure 1. The Navilas laser photocoagulator is a computer-navigated laser system, which utilizes a retinal eye-tracking laser delivery system with integrated digital fundus imaging.

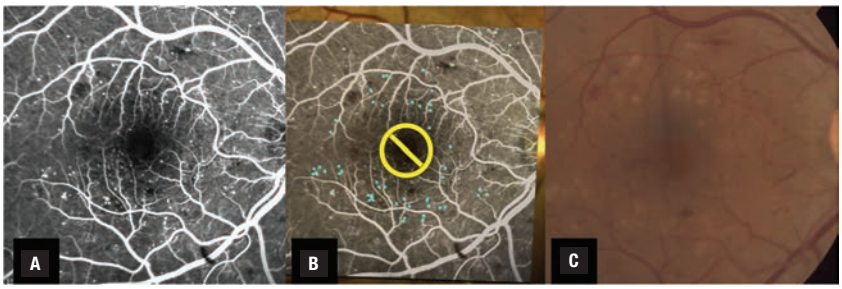


Figure 2. Clinical example of a Navilas focal laser session for diabetic macular edema, where microaneurysms are targeted on the fluorescein-angiogram image (A and B), and treatment effect is immediately visible with faint gray laser burns (C).

Clinical Trial Results

The Navilas laser has been shown to have greater accuracy than conventional focal/grid laser treatment. In 2011, Igor Kozak, MD, and colleagues assessed the accuracy of 400 random focal spots from the Navilas system performed on 86 patients and found that the laser achieved a 92-percent microaneurysm hit rate. This was statistically significant when compared to the 72-percent accuracy rate of conventional focal/grid laser treatment in the control group (p <0.01).[2]

Shortly after that, Aljoscha S. Neubauer, MD, and colleagues at Ludwig-Maximilians University in Munich compared results of patients who had undergone Navilas treatment and a control group of 28 matched patients who received conventional laser at their institution.[3] Three months after treatment, the Navilas group had improved visual acuity by a mean of 2.9 letters, whereas the control group had lost a mean of 4.0 letters (p=0.03). At six months, the Navilas group had maintained an improvement of 3.3 letters while the control group had improved 1.9 letters from baseline. Furthermore, the investigators observed lower retreatment rates with the navigated laser system.

In 2014, another group at Ludwig-Maximilians University prospectively compared the efficacy of combination therapy of navigated laser and intravitreal ranibizumab (Lucentis, Genentech) to ranibizumab monotherapy for treatment of DME.[4] They reported that both groups showed similar improvements in visual acuity at 12 months (+8.4 letters vs. +6.3 letters), and those in the combination therapy group required an average of three fewer injections at one year. Additionally, 65 percent of eyes in the

The Evolution of Computer Navigation for Lasers

Physicians have used light energy to treat retinal diseases since Gerd Meyer-Schwickerath, MD, began using sunlight and xenon arc coagulation in the 1950s.[6,7] Laser pioneers such as Charles Campbell, MD, and H. Christian Zweng, MD,[8,9] experimented with the ruby laser for the treatment of retinal conditions. Soon, Francis L'Esperance Jr., MD, and Arnall Patz, MD, worked on a more precise way to deliver light energy to the retina with the argon laser.[10,11]

While physicians were still establishing the pathogenic mechanisms of diabetic retinal disease, many began realizing that direct treatment of microaneurysms with laser photocoagulation often had a beneficial effect. We still do not completely understand the exact mechanisms of action for laser photocoagulation, but one theory holds that decreased edema may result from direct closure of leaking microaneurysms.[12]

Investigators have suggested that photocoagulation decreases edema because it reduces retinal tissue, leading to decreased retinal blood flow because of alterations in autoregulation.[13,14] Others have hypothesized that reduced retinal blood flow and edema is due to improved oxygenation after laser treatment.[4] Studies have shown that photocoagulation alters the retina pigment epithelial cells that produce proangiogenic cytokines like vascular endothelial growth factor.[15,16]

ETDRS Shows the Way Forward

In 1985, the Early Treatment Diabetic Retinopathy Study (ETDRS) established a clear beneficial effect of focal/grid laser photocoagulation for diabetic macular edema (DME).[17] Focal/grid laser involved two strategies within areas of retinal thickening:

- Direct treatment to microaneurysms within two disc diameters of the center of the macula.
- Scatter or grid treatment approximately two burn widths apart to areas of diffuse thickening to reduce the risk of moderate vision loss in DME and mild to moderate nonproliferative diabetic retinopathy (NPDR) regardless of baseline visual acuity by approximately 50 percent at three years.[18]

Additionally, 17 percent of those treated with focal laser had a three-line improvement in vision at five years vs. 5 percent of those not treated with laser.[19] Patients with the greatest visual benefit after treatment had clinically significant macular edema at baseline.[17–19]

Retina specialists adopted a modified laser approach utilizing less-intense burns, with results similar to the original ETDRS protocol.[12] Investigators later compared grid laser photocoagulation, termed mild macular grid technique, with the modified ETDRS treatment consisting of both focal closure of microaneurysms and application of light grid photocoagulation. They reported that grid treatment alone was not as effective as the modified ETDRS treatment.[20] Also, eyes in the modified ETDRS group experienced a slightly greater reduction in retinal thickening and a trend toward a slightly better visual acuity outcome.[20]

But as lasers evolved, so too did the realization that macular laser treatment can cause retinal scarring, which can enlarge over time and cause scotomas. This finding was a motivating factor for the development of computer-assisted retinal-tracking systems.

Laser Therapy vs. Intravitreal Therapy

Focal/grid laser therapy continued to serve as the standard of care for primary treatment of DME until the arrival of intravitreal therapies. Before anti-VEGF medications, preservative-free intravitreal triamcinolone acetonide (IVTA) was used to decrease macular edema by inhibiting VEGF expression and other pro-inflammatory cytokines that cause vascular permeability.

In 2008, the Diabetic Retinopathy Clinical Research Network (DRCR.net) compared laser photocoagulation with two doses of IVTA.[21] Despite early results favoring 4 mg IVTA at four months, the DRCR.net found that IVTA was not superior to focal/grid photocoagulation in terms of visual acuity improvement or optical coherence tomography findings at two years. Additionally, rates of intraocular pressure elevation and cataract formation were higher in the IVTA groups than in the laser groups.[21]

Growing evidence has shown that anti-VEGF treatments are more efficacious and safer than focal laser alone for DME. In early 2015, the DRCR.net researchers published five-year data that concluded that focal/grid laser treatment at the initiation of ranibizumab (Lucentis, Genentech) therapy is no better than deferring laser treatment for at least six months in eyes with center-involving DME. Additionally, they reported that while approximately half of the eyes in the deferred laser treatment group avoided laser for at least five years, these eyes often required more injections. The eyes assigned to the prompt laser group needed fewer injections (median difference of four, or approximately 25 percent fewer injections) than the deferred laser group.[21] This finding suggested that focal/grid treatment may decrease treatment burden over a long period of time.

combination therapy group remained injection-free at month 12 (after the initial loading phase) compared to only 16 percent of patients in the monotherapy group.

TREX DME Trial

The investigator-sponsored treat-and-extend (TREX) DME trial (NCT01934556) utilizing the Navilas as adjunct treatment for DME is underway. This multicenter, prospective trial utilizing ranibizumab compares a treat-and-extend algorithm with and without angiography-guided macular laser to monthly dosing for center-involving DME. To date, 150 eyes have been enrolled into three well-balanced groups—monthly cohort, treat-and-extend (TREX cohort) and treat-and-extend with angiography-guided laser photocoagulation (GILA cohort).[5]

At six months, mean visual acuity improved by 7.8 letters and mean retinal thickness improved 89.7 µm on optical coherence tomography (OCT) in the monthly group. This can be compared to an improvement of 9.2 letters and 130.4 µm in the TREX

cohort and 8.3 letters and 140.8 µm in the GILA group. The primary endpoint is the change in best-corrected visual acuity at two years, and the one-year outcomes will be available in 2016.

Figure 3 depicts a clinical example of a patient in the TREX DME trial with bilateral center-involving DME who had both eyes enrolled into the study. The left eye was randomized into the TREX cohort, in which eyes receive four monthly injections of ranibizumab and then begin a TREX regimen of intravitreal ranibizumab based on disease activity. The right eye was randomized into the GILA cohort, where subjects follow the same ranibizumab treatment scheme but have fluorescein angiography-guided macular laser at month one and then again every three months if leaking microaneuryms are present.

At baseline, both eyes had severe nonproliferative diabetic retinopathy and diffuse DME. The screening visual acuity was 20/50 in both eyes and central foveal thickness measurements on spectral-domain OCT were 516 µm in the right eye and 548 µm in the left eye. At one year, the eye receiving guided laser therapy showed greater improvement in vision (+23 letters vs. +10 letters) and a more significant decrease in foveal thickness (-275 µm vs. -148 µm). Additionally, the eye that received guided laser treatment required five fewer injections at one year. While not every patient responds to laser treatment as dramatically, this case illustrates that guided-laser therapy for DME can improve visual and anatomical outcomes and decrease treatment burden.

Further clinical research, such as the TREX DME trial, will determine how effective computer-navigated laser therapy can be. This technology pushes the boundary of our understanding of DME treatment and provides alternative strategies for management of this disease. RS

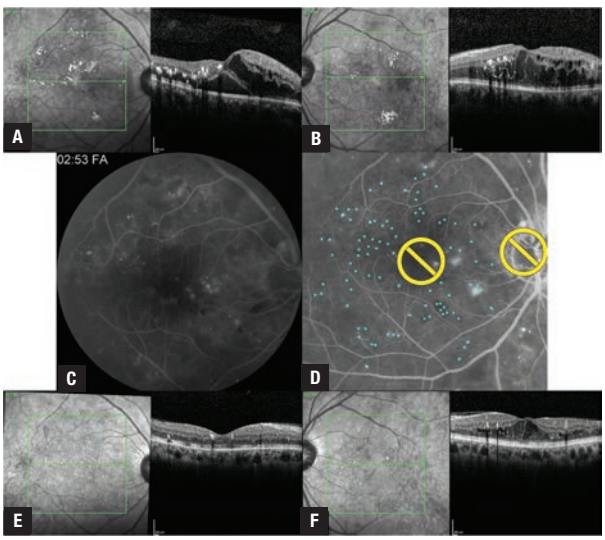


Figure 3. Imaging of a subject enrolled into the TREX-DME trial. Both eyes received four monthly injections of intravitreal ranibizumab and then underwent a treat-and-extend regimen of ranibizumab based on disease activity. The right eye also received navigated laser therapy at month one and again at every three months if leaking microaneurysms were present. Figures A and B (screening) demonstrate diffuse center-involving diabetic macular edema in both eyes. Fluorescein angiography shows numerous areas of leakage on fluorescein angiography in the right eye (C) that were targeted for treatment (D). At one year (E and F), the retinal anatomy showed dramatic improvement, particularly in the right eye that received navigated laser therapy.

REFERENCES

1. Kernt M, Cheuteu R, Vounotrypidis E, et al. Focal and panretinal photocoagulation with a navigated laser (NAVILAS). Acta Ophthalmol. 2011;89:e662-664.
2. Kozak I, Oster SF, Cortes MA, et al. Clinical evaluation and treatment accuracy in diabetic macular edema using navigated laser photocoagulator NAVILAS. Ophthalmology. 2011;118:1119-1124.
3. Neubauer A, Langer J, Leigl R, et al. Navigated macular laser decreases retreatment rate for diabetic macular edema: a comparison with conventional macular laser. Clin Ophthalmol. 2013;7:121-128.
4. Liegl R, Langer J, Seidensticker F, et al. Comparative evaluation of combined navigated laser photocoagulation and intravitreal ranibizumab in the treatment of diabetic macular edema. PLoS One. 2014;9:e113981.
5. ClinicalTrials.gov. A safety and efficacy trial of a treat and extend protocol using ranibizumab with and without laser photocoagulation for diabetic macular edema (TREX-DME). Available at: https://www.clinicaltrials.gov/ct2/show/NCT01934556?term=TREX&rank=3. Accessed October 14, 2015.
6. Meyer-Schwickerath G. Light coagulation: a method for treatment and prevention of the retinal detachment. Albrecht Von Graefes Arch Ophthalmol. 1954;156:2-34.
7. Wolfensberger TJ, Hamilton AM. Diabetic retinopathy—an historical review. Semin Ophthalmol. 2001;16:2-7.
8. Campbell CJ, Rittler MC, Koester CJ. The optical maser as a retinal coagulator: an evaluation. Trans Am Acad Ophthalmol Otolaryngol. 1963;67:58-67.
9. Zweng HC, Flocks M, Kapany NS. Experimental laser photocoagulation. Am J Ophthalmol. 1964;58:353-362.
10. L'Esperance FA. An ophthalmic argon laser photocoagulation system: design, construction, and laboratory investigations. Trans Am Ophthalmol Soc. 1968;66:827-904.
11. Patz A, Maumenee AE, Ryan SJ. Argon laser photocoagulation: advantages and limitations. Trans Am Acad Ophthalmol Otolaryngol. 1971;75:569-579.
12. Shah AM, Bressler NM, Jampol LM. Does laser still have a role in the management of retinal vascular and neovascular diseases. Am J Ophthalmol. 2011;152:332-339.
13. Wilson DJ, Finkelstein D, Quigley HA, Green WR. Macular grid photocoagulation: an experimental study on the primate retina. Arch Ophthalmol. 1988;106:100-105.
14. Arnarsson A, Stefansson E. Laser treatment and the mechanism of edema reduction in branch retinal vein occlusion. Invest Ophthalmol Vis Sci. 2000;41:877-879.
15. Ogata N, Ando A, Uyama M, Matsumura M. Expression of cytokines and transcription factors in photocoagulated human retinal pigment epithelial cells. Graefes Arch Clin Exp Ophthalmol. 2001;239:87-95.
16. Ogata N, Tombran-Tink J, Jo N, Mrazek D, Matsumura M. Upregulation of pigment epithelium-derived growth factor after laser photocoagulation. Am J Ophthalmol. 2001;132:427-429.
17. Early Treatment Diabetic Retinopathy Study Research Group. Photocoagulation for diabetic macular edema: Early Treatment Diabetic Retinopathy Study report number 1. Arch Ophthalmol. 1985;103:1796-1806.
18. Early Treatment Diabetic Retinopathy Study Research Group. Photocoagulation for diabetic macular edema: Early Treatment Diabetic Retinopathy Study report no. 4. Int Ophthalmol Clin. 1987;27:265-72.
19. Early Treatment Diabetic Retinopathy Study Research Group. Early photocoagulation for diabetic retinopathy. ETDRS report no. 9. Ophthalmology. 1991;98(suppl):767-785.
20. Writing Committee for the Diabetic Retinopathy Clinical Research Network. Comparison of the modified Early Treatment Diabetic Retinopathy Study and mild macular grid laser photocoagulation strategies for diabetic macular edema. Arch Ophthalmol. 2007;125:469-480.
21. Diabetic Retinopathy Clinical Research Network. A randomized trial comparing intravitreal triamcinolone acetonide and focal/grid photocoagulation for diabetic macular edema. Ophthalmology. 2008;115:1447-1459.

WIDEFIELD IMAGING FINDS ITS PLACE IN THE PRACTICE

Expanding the utility of photography and angiography in pediatric retina, oncology and more.

By Ankoor R. Shah, MD

Digital imaging technologies are changing rapidly and offer ophthalmologists novel and improved ways of imaging the retina. Development of swept source optical coherence tomography (OCT), intraoperative OCT and enhancements in widefield (WF) imaging with fluorescein angiography (FA) are just a few of such novel imaging modalities.

While some of these technologies remain in the early experimental phase, use of WF photography and FA have already led to significant changes in the ability to monitor and evaluate the peripheral retina. Here we review the current literature and highlight the uses of WF imaging.

Widefield Imaging Systems

Widefield imaging systems generally fall into two categories: either portable or office-based. The RetCam (Clarity Medical Systems) is a commonly used portable system. Such portable systems are valuable for screening in neonatal intensive care units for retinopathy of prematurity (ROP) and can be used to examine the peripheral retina in pediatric patients under anesthesia.

Office-based systems can include those that use optional contact/non-contact widefield lenses to modify standard fundus photography, such as the Spectralis system (Heidelberg Engineering). However, some imaging systems are exclusively designed for widefield use, such as the 200Tx and Daytona systems by Optos. These cameras can produce a 200° view compared to the 75° view when using overlapping seven standard stereoscopic fields based on the Early Treatment for Diabetic Retinopathy Study (ETDRS) protocols.[1,2]

WF Imaging in Pediatric Retina

The greatest impact of WF imaging has been in pediatric retina. ROP surveillance with RetCam has proved so effective that many centers utilize nurse practitioners to capture images, which the screening ophthalmologist then reviews (*Figure 1*). This approach had been validated as early as 2001 and has since been replicated.[3]

Diseases such as familial exudative vitreoretinopathy (FEVR), which frequently have subtle vascular changes during the early stages, have also benefited from WF FA. Not only does it aid in staging patients whose retinal periphery appears normal on clinical exam, but it also aids as a screening tool to evaluate asymptomatic family members of patients with FEVR.[4]

Finally, WF imaging has been useful to obtain fundus photography when the patient is too young to co-

ABOUT THE AUTHOR

Dr. Shah practices with Retina Consultants of Houston and is with the Department of Ophthalmology, Blanton Eye Institute, The Methodist Hospital, Houston.

DISCLOSURES: Dr. Shah has no relationships to disclose.

operate fully and/or diseases such as persistent fetal vasculature syndrome, Norrie disease and Coats' disease require evaluating peripheral pathology.

Applications in Uveitis

WF imaging has been helpful to identify and monitor the extent of disease in uveitic patients, particularly those with peripheral lesions or retinal vasculitis, has been helpful. In multiple evanescent white dot syndrome, multi-modality imaging makes the extent of peripheral pathology more evident (*Figure 2*).

A small, consecutive case series of four patients with retinal vasculitis that compared conventional FA based on ETDRS protocols to WF FA found that conventional FA could not visualize the full extent of vasculitis and capillary occlusion in any fields.[5] While the diagnosis of retinal vasculitis was established, the underlying etiology was not determined in all but one patient diagnosed with Vogt-Koyanagi-Harada disease. Notably, the study found conventional FA would not have detected the posterior extent of vasculitis in two cases.

More recent work has evaluated uveitic patients using widefield FA to describe novel methods for quantifying peripheral vascular pathology to identify visually significant parameters.[6] Variables such as peripheral ischemia, peripheral non-perfusion and peripheral leakage, which previously could not be quantified, can now be studied to look for diagnostic and prognostic implications.[6]

Uses in Ocular Oncology

Retina specialists frequently use WF photography to monitor choroidal nevi and choroidal melanoma for growth, as well as to evaluate edges of plaque-treated choroidal melanomas for recurrence. Multiple modality imaging can be particularly effective in ocular oncology. For instance, WF autofluorescence contrasted against fundus photos can often be used to identify subtle development of orange pigment in choroidal nevi.

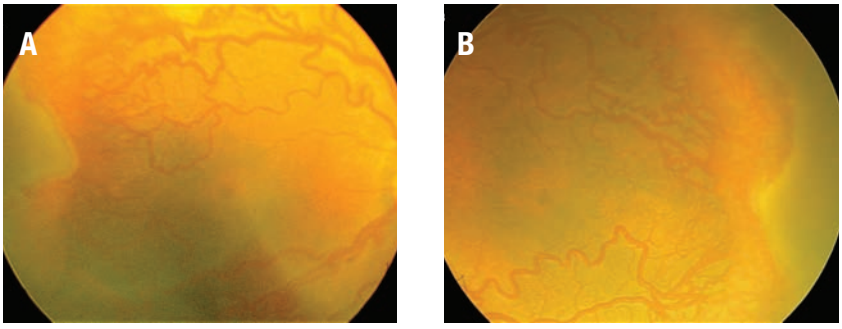


Figure 1. RetCam images of a premature infant screened for retinopathy of prematurity (ROP) show stage 3 ROP in zone 1 (A) and more peripheral stage 3 ROP in zone 2 (B).

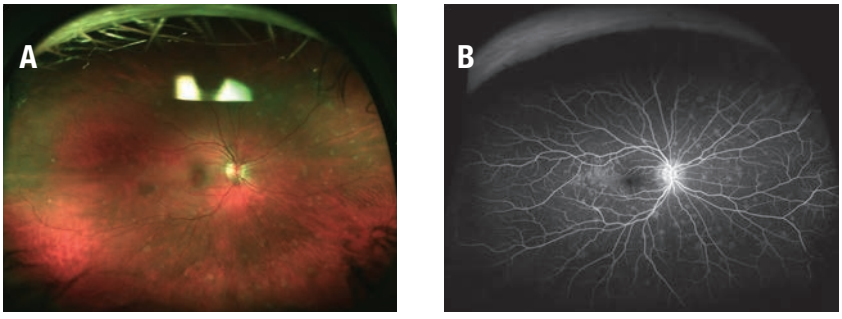


Figure 2. Optos widefield images of a patient with multiple evanescent white dot syndrome. The color fundus photo demonstrates multiple focal gray/white lesions in the posterior pole and, more extensively, in the periphery (A). Similar findings are more apparent on fluorescein angiography with notable late-phase staining (B).

Other applications of WF photography in ocular oncology under investigation include monitoring mimicking diagnoses such as peripheral exudative hemorrhagic choroidopathy[7] and retinal pigment epithelium adenomas.[8]

WF Imaging and AMD

Retinal specialists have seen significant impact where WF FA has been broadly applied in the study of age-related macular degeneration (AMD),[9] central serous chorioretinopathy (CSR)[10] and pathologic myopia.[11] In AMD specifically, use of other WF modalities such as autofluorescence has detected significant changes in the periphery that are more common in neovascular AMD compared to non-neovascular AMD or normal patients.[9] Clinically, WF FA has also been useful to identify the extent of vascular compromise in arterial and venous occlusive diseases.

(Continued on page 32)

Take-home Point

Portable and office-based systems have made widefield imaging with fluorescein angiography and retinal photography widely available. This has improved the ability of retina specialists to more accurately evaluate pathology, especially in the peripheral retina, in a variety of diseases, including retinopathy of prematurity, uveitis, ocular cancer and age-related macular degeneration.

Clinicians have increasingly used this imaging modality in diabetic retinopathy because ETDRS protocol fundus photography can miss the true extent of peripheral non-perfusion and neovascularization (*Figure 3*).[12,13] More recent research has focused on evaluating the role of ischemia in the periphery and its implications and relationship with diabetic retinopathy and ischemia within the macula.[14] Research targeting these relationships remains ongoing.

More Studies Are Needed

Much has been written about peripheral retinal findings in various diseases, yet what still remains lacking is an understanding of the "normal" retinal periphery. Studies of normal retinal peripheral pathology are largely lacking because such studies would unnecessarily expose healthy patients to the known risks of FA.[15]

A recent study evaluating the retinal periphery in eyes with epiretinal membranes and choroidal nevi, used as surrogates for "normal" retinal periphery, revealed a high prevalence of peripheral vascular anatomic variations. These included vessels crossing the horizontal raphe, right-angle vessels, terminal networks, absence of capillary details, ground glass hyperfluorescence, peripheral drusen and microaneurysms.[16] Anton Orlin, MD, and colleagues nicely described a set of 33 control eyes in a study of white without pressure, but some of those controls had conditions (uveitis, vein occlusions and myopia) that have been associated with peripheral changes.[17]

The literature on normal retinal peripheral vascular anatomy will likely continue to grow and serve as a reference base for future studies examining the pathologic angiographic features of the peripheral retina.

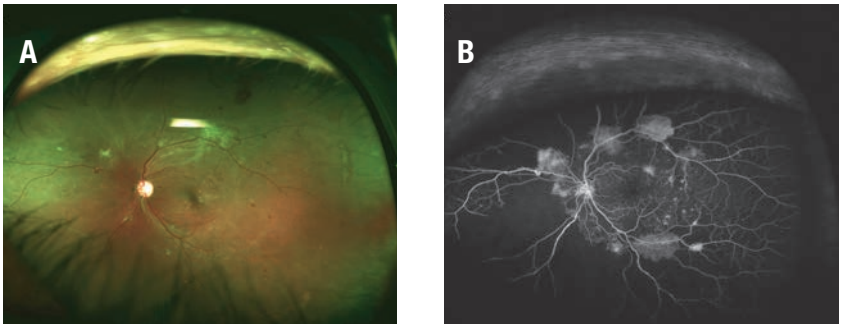


Figure 3. Optos color photos demonstrating extensive neovascularization consistent with proliferative diabetic retinopathy (A). The true extent of the capillary non-perfusion seen on widefield fluorescein angiography would have been missed with standard seven-field montage images (B).

Conclusion

As experience with WF imaging grows, so does awareness of peripheral findings in a broad range of retinal pathologies. Only recently have we begun to analyze the retinal periphery in normal patients to establish a meaningful baseline for comparison to the numerous pathologic states currently under study.

The future comparison of normal and pathologic populations will be invaluable, particularly as multiple imaging modalities such as color photography, autofluorescence, fluorescein angiography and indocyanine green angiography have recently become available. We remain at the forefront of an imaging revolution within ophthalmology that ultimately should enable better diagnostic testing and monitoring, leading to more effective patient care.

REFERENCES

1. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. Early Treatment Diabetic Retinopathy Study Research Group. Ophthalmology. 1991;98(5 Suppl):823-833.
2. Silva PS, Cavallerano JD, Sun JK, et al. Nonmydriatic ultrawide field retinal imaging compared with dilated standard 7-field 35-mm photography and retinal specialist examination for evaluation of diabetic retinopathy. Am J Ophthalmol 2012;154:549-559 e2.
3. Photographic Screening for Retinopathy of Prematurity (Photo-ROP) Cooperative Group. The photographic screening for retinopathy of prematurity study (photo-ROP). Primary outcomes. Retina. 2008;28(3 Suppl):S47-54.
4. Kashani AH, Learned D, Nudleman E, et al. High prevalence of peripheral retinal vascular anomalies in family members of patients with familial exudative vitreoretinopathy. Ophthalmology. 2014;121:262-268.
5. Hong BK, Nazari Khanamiri H, Rao NA. Role of ultra-widefield fluorescein angiography in the management of uveitis. Can J Ophthalmol. 2013;48:489-493.
6. Karampelas M, Sim DA, Chu C, et al. Quantitative analysis of peripheral vasculitis, ischemia, and vascular leakage in uveitis using ultra-widefield fluorescein angiography. Am J Ophthalmol. 2015;159:1161-1168 e1.
7. Tsui I, Jain A, Shah S, et al. Ultra-widefield imaging of peripheral exudative hemorrhagic chorioretinopathy. Semin Ophthalmol. 2009;24:25-28.
8. Shah SP, Jain A, Coffee RE, McCannel TA. Optos Panoramic 200MA ultrawide-field imaging of peripheral RPE adenoma. Semin Ophthalmol. 2009;24:37-39.
9. Tan CS, Heussen F, Sadda SR. Peripheral autofluorescence and clinical findings in neovascular and non-neovascular age-related macular degeneration. Ophthalmology. 2013;120:1271-1277.
10. Pang CE, Shah VP, Sarraf D, Freund KB. Ultra-widefield imaging with autofluorescence and indocyanine green angiography in central serous chorioretinopathy. Am J Ophthalmol. 2014;158:362-371 e2.
11. Kaneko Y, Moriyama M, Hirahara S, et al. Areas of nonperfusion in peripheral retina of eyes with pathologic myopia detected by ultra-widefield fluorescein angiography. Invest Ophthalmol Vis Sci. 2014;55:1432-1439.
12. Kernt M, Pinter F, Hadi I, et al. [Diabetic retinopathy: comparison of the diagnostic features of ultra-widefield scanning laser ophthalmoscopy Optomap with ETDRS 7-field fundus photography]. Ophthalmologe 2011;108:117-123.
13. Patel RD, Messner LV, Teitelbaum B, et al. Characterization of ischemic index using ultra-widefield fluorescein angiography in patients with focal and diffuse recalcitrant diabetic macular edema. Am J Ophthalmol. 2013;155:1038-4194 e2.
14. Sim DA, Keane PA, Rajendram R, et al. Patterns of peripheral retinal and central macula ischemia in diabetic retinopathy as evaluated by ultra-widefield fluorescein angiography. Am J Ophthalmol. 2014;158:144-153 e1.
15. Yannuzzi LA, Rohrer KT, Tindel LJ, et al. Fluorescein angiography complication survey. Ophthalmology. 1986;93:611-617.
16. Shah AR, Abbey AM, Yonekawa Y, et al. Widefield fluorescein angiography in patients without peripheral disease: A study of normal peripheral findings. Retina. 2015. [In-Press]
17. Orlin A, Fatoo A, Ehrlich J, et al. Ultra-widefield fluorescein angiography of white without pressure. Clin Ophthalmol. 2013;7:959-964.

By Warren Laurita »

The Case for a Drug Inventory System

A robust system should do more than count supplies. It should monitor storage and set reorder levels, too. ***By Warren Laurita***

Over the past decade the U.S. Food and Drug Administration has approved numerous new drugs for the treatment of diseases of the retina. This cornucopia of new, and often expensive, drugs has underscored the vital need for efficiency and accuracy in managing drug inventories. An inventory management system must be able to account for each drug vial from the time it's ordered to when it's administered to a patient.

A successful inventory system tracks the ordering, receiving, supply and usage of all medications. It can be managed at the practice or individual office level.

What the Job Involves

The practice should determine if it can handle its current volume of drugs using a manual system (typically on Excel spreadsheets) or if it needs an automated system that uses barcodes or radio frequency identification devices. It's advisable to have one employee in the practice responsible for ordering all drugs. If the practice has multiple locations open all week, having a responsible person at each office may be a good idea.

The practice should establish reorder points for each drug. To accomplish this, review the utilization of each drug in each office over a six-month period, and calculate the average use per week per drug. Reorder points can then be set for weekly ordering at the average weekly utilization rate plus a percentage to allow for fluctuations. Consider the reorder point a guide that can be modified if necessary to allow for physician time out of the office. The same person should order and receive drug shipments to ensure each order is correct and properly entered into the inventory system.

Upon receipt of an order, the inventory manager should check a few things: make sure the order is not damaged; that it was delivered at the appropriate temperature; the quantity is correct; the lot numbers on the invoice and the individual vials match; and that the expiration date has appropriate dating. Drugs that will expire in a relatively short time frame should not be accepted.

Each refrigerator or freezer containing drugs should have medical thermometers with alarms and they should be monitored daily. Some of the newer inventory systems automate this process by creating a cloud-based log-in and portal as well as alarms that can trigger a text message or e-mail to a specific person.

Tracking Supply

Besides a count of how much of each drug is in inventory, the system should record drugs dispensed, cost, lot number, expiration date and the patient's name who received the drug. Ideally, it will also match the reimbursement for each dose.

An actual physical count of the drugs should be done on a regular basis to ensure the system numbers are accurate or corrected as needed.

The true difficulty is in selecting the right type of drug. That is, picking between a purchased drug, a sample or a patient-specific drug from a specialty pharmacy. The system should maintain and store each of these types of drugs separately.

A best practice is a drug "timeout" immediately before the injection. This involves the doctor, technician and patient all pausing to agree on the eye being injected and the drug being used.

An automated drug inventory system that uses barcode technology can reduce the risk of lost drugs. (Courtesy Physician Office Drug Inventory System)

A drug may become contaminated if it's dropped, if the syringe is touched or in other ways. When this happens, the inventory system must report it. In most cases, the manufacturers of FDA-approved drugs have replacement polices for contaminated or spoiled drugs. Any contaminated or spoiled drug must be removed from inventory. When the replacement drug arrives, it should be entered into the system to account for the one removed.

A complete inventory system can save staff time, reduce the risk of lost drugs and improve the drug injection process as well as the work environment in the practice. RS

Mr. Laurita is chief operating officer at Retina Associates of Cleveland Inc. in Ohio.

By Kirk A. Mack, COMT, COE, CPC, CPMA »

What VBPM Can Mean to Your Practice

A deep dive into how CMS defines and uses Value Based Payment Modifier. Part 2 of 2.

In the last article, we discussed the double-dipping process the Centers for Medicare & Medicaid Services (CMS) uses for the Physician Quality Reporting System (PQRS) and the Value Based Payment Modifier (VBPM). Clients ask us, "What is the VBPM and how will it impact the practice?" Here is how CMS defines the VBPM:

> *The Value Modifier provides for differential payment to a physician or group of physicians under the Medicare Physician Fee Schedule (PFS) based upon the quality of care furnished compared to the cost of care during a performance period. In the future, the Value Modifier will be used to adjust Medicare PFS payments to non-physician eligible professionals (EPs), in addition to physicians. The Value Modifier is an adjustment made on a per claim basis to Medicare payments for items and services under the Medicare PFS. It is applied at the Taxpayer Identification Number (TIN) level to physicians (and beginning in 2018, to non-physician EPs) billing under the TIN.*[1]

The Two Parts of VBPM

Groups of 10 or more providers were initiated into the process in 2014, while smaller groups started in 2015. Within the VBPM, there are essentially two parts: quality and cost. The quality aspect aligns with PQRS reporting. Failure to successfully report PQRS in 2015 results in a PQRS penalty of 2 percent for all providers in 2017. In addition, for groups of 10 or more, the VBPM quality aspect adds an additional 4 percent penalty, resulting in a 6 percent cumulative hit in 2017. Groups of fewer than 10 providers receive an additional 2 percent VBPM penalty for a 4 percent cumulative in 2017.[1]

Table 1: Groups With Fewer Than 10 Eligible Professionals

Cost / Quality	Low Quality	Average Quality	High Quality
Low Cost	+0.0%	+1.0x	+2.0x
Average Cost	+0.0%	+0.0%	+1.0x
High Cost	+0.0%	+0.0%	+0.0%

The second part, the cost analysis, is more complex and uses two different costs. First, CMS considers the total per-capita costs for all attributed beneficiaries and, second, the total per capita costs for beneficiaries with specific conditions: diabetes; coronary artery disease; chronic obstructive pulmonary disease; and heart failure.

CMS uses a two-step attribution process for assigning patients to providers. In step one, beneficiaries are assigned to the taxpayer identification number (TIN) of a primary-care practice (e.g., family medicine, internal medicine, etc.). Patients not assigned to a primary-care TIN are assigned, in the next step, to a TIN whose providers accounted for the majority of primary-care services.

Step two includes specialists, ophthalmologists among them, who provide primary-care services. The primary-care service codes do not include eye codes (920xx) but do include outpatient Evaluation and Management (E/M) codes for new and established visits (992xx). Therefore, the attribution process could assign patients to an ophthalmologist's TIN.[2] For any patients attributed to your TIN, their total per-capita costs are also attributed to your TIN.

Tying in Quality Measures

The *2014 Annual Quality and Resource Use Reports* (QRURs) use the data from the patients attributed to each TIN to show how groups and solo practitioners performed in 2014 on the quality-and-cost measures used to calculate the 2016 Value Modifier.[3] Every practice should review its QRURs to see how they compare to the established benchmarks and preview the future application of the VBPM. The 2013 and 2014 QRUR reports are available. Follow the *Guide for Accessing the 2014 Annual QRURs* to acquire the information for your practice.[4]

After the cost-and-quality analysis, the TIN receives quality and cost scores (low, average and high). Combining the quality and cost scores determines the potential positive or

Table 2: Groups of 10 Eligible Professionals or More

Cost / Quality	Low Quality	Average Quality	High Quality
Low Cost	+0.0%	+2.0x	+4.0x
Average Cost	-2.0%	+0.0%	+2.0x
High Cost	-4.0%	-2.0%	+0.0%

negative adjustments. Tables 1 and 2 reflect the 2017 potential adjustments based on 2015 information. Once the performance period (2015) ends, and the aggregate downward amounts are determined, CMS will apply an adjustment factor ("x") to determine upward payments.

For those practices in year one of VBPM, there is no cost penalty in 2017 (*Table 1*). However, for those practices in the second year of VBPM (*Table 2*), there are potential up and down adjustments for both cost and quality in 2017. According to CMS, Part B drug payments are not subject to VBPM adjustment; however the administration (i.e., injection) is subject to the adjustment.[5]

Fee-for-Service Is Changing

The fee-for-service reimbursement methodology we are familiar with is undergoing significant changes. Successfully reporting PQRS avoids the automatic negative quality adjustments. Practices have control over the success of PQRS, but hold limited influence on the VBPM cost analysis due to its complexity.

Remember the "benchmarks" for cost analysis are not determined until the performance period is completed. However, acquiring your past QRUR reports will provide an indication of your standing, including general information on patients attributed to your TIN. Use the CMS detailed guide *Understanding Your QRUR* when reviewing the QRUR.[6] VBPM represents the beginnings of considerable change to future reimbursements. RS

Mr. Mack is a senior consultant with Corcoran Consulting Group. He can be reached at 1 (800) 399-6565 or at www.corcoranccg.com.

REFERENCES

1. CMS.gov Centers for Medicare & Medicaid Services. Medicare FFS Feedback Program/Value Based Payment Modifier. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeedbackProgram/valuebasedpaymentmodifier.html. Accessed October 29, 2015.
2. Centers for Medicare & Medicaid Services Fact Sheet. Two-step attribution for measures included in the Value Modifier. August 2015. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeedbackProgram/Downloads/Attribution-Fact-Sheet.pdf. Accessed October 29, 2015.
3. CMS.gov Centers for Medicare & Medicaid Services. Medicare FFS Physician Feedback Program/Value Based Modifier. 2014 Annual Quality and Resource Use Reports. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeedbackProgram/2014-QRUR.html#2014-annual-qrur. Accessed October 29, 2015.
4. Centers for Medicare & Medicaid Services. Guide for Accessing the 2014 Annual QRURs and Supplementary Exhibits. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeedbackProgram/Downloads/Guide-for-accessing-2014-Annual-QRURs.pdf Accessed October 29, 2015.
5. CMS.gov Centers for Medicare & Medicaid Services. CMS Frequently Asked Questions. Available at: https://questions.cms.gov/faq.php?id=5005&faqId=11892. Accessed October 29, 2015.
6. Centers for Medicare & Medicaid Services. Understanding your QRUR. September 2015. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeedbackProgram/Downloads/2014-UnderstandingYourQRUR.pdf. Accessed October 29, 2015.

By Richard Mark Kirkner »

A Widefield Platform on a Tabletop

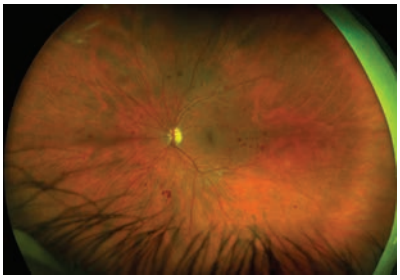
Combining up to eight imaging functions into one device.

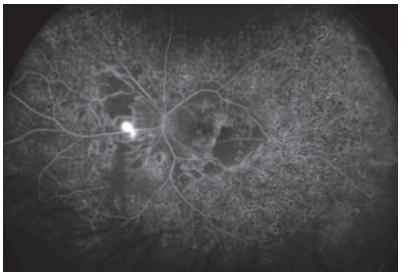
When he got one of the first of the new generation California ultra-widefield imaging devices from Optos in his Houston retina practice, David Brown, MD, FACS, looked forward to having a host of imaging modalities contained in one unit, but he admits he was somewhat skeptical of its ability to deliver high-quality indocyanine green (ICG) angiography images.

Then he saw the images. "They were actually very good," says Dr. Brown, whose Retina Consultants of Houston has 14 offices in southeastern Texas.

The newest offering in Optos' line of imaging systems is capable of capturing images in eight modalities, including fundus photography, autofluorescence and fluorescein angiography, along with ICG angiography. The California is a step up from the Optos 200TX, which offers all the same imaging functions except for ICG angiography.

Other features of the California that appeal to Dr. Brown are its small footprint and ease of access for patients. Its compact size—the California fits on a tabletop—is a significant improvement over the original Optos platforms that required a space half the size of an exam lane. "If you had a different fluorescein camera, the California will fit in the same space if not smaller," Dr. Brown says. "They also did some better ergonomics so it's easier to get patients in and out."

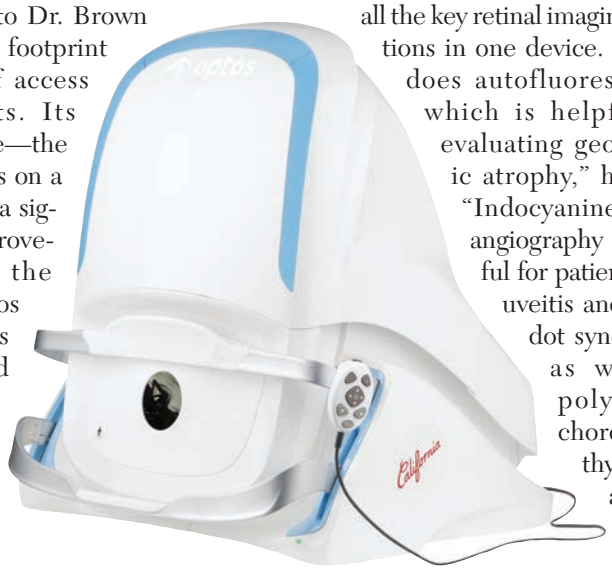




Examples of color Optomap image (left) and fluorescein angiography (right) of diabetic retinopathy from the Optos California, which fits on a tabletop.

The device also delivers high-quality imaging out to 200° of the retinal periphery, Dr. Brown says. Changes in the software and placement of image-capturing lasers from the Optos 200TX model translate into better imaging in the superior and anterior areas. "The de-warping mechanisms also makes images more spherical as opposed to more of a warped image with other systems," he says.

Dr. Brown finds it helpful to have all the key retinal imaging functions in one device. "It also does autofluorescence, which is helpful for evaluating geographic atrophy," he says. "Indocyanine green angiography is helpful for patients with uveitis and white dot syndromes as well as polypoidal choroidopathy, a variant of macular degeneration."



Optos California also uses browser-based software for viewing images. "While it's always counterintuitive to use a new software program, it is much faster to go through images with the new software once you get the hang of it," Dr. Brown says.

At first, Optos offered one version of California that included all eight imaging modalities, but it is introducing three different models within the California line at the American Academy of Ophthalmology: one with color photography and autofluorescence; another that adds fluorescein angiography; and a third that includes color photography, autofluorescence, fluorescein and ICG angiography.

"I think it's imperative to have widefield angiography for practices that have a high percentage of patients with diabetic retinopathy or that see a lot of patients with retinal vascular disease," Dr. Brown says.

While standard field views can capture most of the pathology in macular degeneration, "for global disease like diabetic retinopathy and retinal vascular disease, I would feel incredibly handicapped without having a widefield angiogram," Dr. Brown says. RS

Edited by Emmett T. Cunningham, MD, PhD»

SPK-RPE65 Gene 'Augmentation'

This biological agent targets mutations in genes that mediate visual transduction.

When Spark Therapeutics announced positive topline results from the Phase III pivotal trial of its lead gene candidate, SPK-RPE65, last month, investigators and investors alike paid close attention because this is the first randomized, controlled Phase III trial of a gene therapy for genetic disease.

SPK-RPE65 targets the RPE65 gene, mutations in which have been linked to subtypes of Leber's congenital amaurosis and retinitis pigmentosa. RPE65 is an enzyme that helps enable the conversion of light into electrical signals that the brain recognizes as vision. When this enzyme isn't present or doesn't work correctly, the inputs for vision get disrupted.

Besides meeting its primary endpoint demonstrating improvement of functional vision, the trial also showed SPK-RPE65 recipients performed better than controls across two secondary endpoints: full-field light sensitivity threshold testing and in completing an obstacle course with the worse eye.

Principal investigator (PI) Stephen R. Russell, MD, clinical director of the Stephen A. Wynn Institute for Vision Research at the University of Iowa, presented Phase III data along with data on the three-year durability of results from an earlier Phase I trial at the 48th Retina Society Scientific Meeting in Paris. Dr. Russell and co-PI Albert M. Maguire, MD, of the University of Pennsylvania, are scheduled to present more data at the American Academy of Ophthalmology 2015 meeting. Dr. Maguire, along with Jean Bennett, MD, PhD, of the University of Pennsylvania, have worked with Children's Hospital of Philadelphia in their research.

A rendering of the effect retinitis pigmentosa has on vision. Courtesy National Eye Institute.

Here, Dr. Russell provides insight into the SPK-RPE65 trials.

The mechanism of action in his words:

RPE65 is the rhodopsin kinase, the enzyme that converts vitamin A from its inactive form, which is the all-trans form, into the active high-energy form, which is the 11-cis retinal form of vitamin A. Even in patients who have mutations of the RPE65 gene, they may have some residual function, so we've actually called this RPE65 augmentation gene therapy.

Essentially what we're trying to do is to instill the genes with the enzymes to create active copies of the RPE65 with as much excess as possible to drive this reaction, to create the activated vitamin A for visual transduction.

The analogy I use is that vitamin A is kind of like a mousetrap. In its extended form, it has a lot of energy built up in the molecule, and when it gets hit with the photons, like a mousetrap gets hit by a pingpong ball, that starts the cascade of visual transduction.

A comment on the topline Phase III results:

The mobility course results were unequivocally positive and they matched nicely the light sensitivity increases that these patients experienced of approximately two orders of magnitude: the FST (white light), the mean difference was 2.1 log10 units, which is a little more than a 100-fold difference in light sensitivity between those that received SPK-RPE65 and those that did not; and, although the mobility test course is not precisely correlated in a geometric scale, unfortunately, it approximates that, so it was basically a 1.6 light level difference between those that received SPK-RPE65 and those that did not.

Results of the secondary endpoints:

The FST, the full field light sensitivity, was one of those endpoints, and it was confirmatory of the primary endpoint. The p values of the obstacle course result of a 1.6 light

level gain (p=0.004) and for light sensitivity (p=0.001) were outstanding for a small study with a very small number of patients.

As for the other secondary endpoints, one was the obstacle course for the first treated eye. The Food and Drug Administration was concerned with trying to differentiate whether the bilateral obstacle course results were driven by only the better-seeing eye; they wanted to see what the poorest-seeing eye contributed. In general we treated the poorer eye first and then the better-seeing eye to try to minimize any effect of amblyopia because we were recruiting subjects down to age 4. That result also was highly statistically positive.

The other secondary endpoint that got a lot of attention was visual acuity. This topline result did not show a statistically significant difference—an eight-letter difference between those that received SPK-RPE65 and those that did not—but there may have been many explanations for why there was not a statistically significant result. But, that was not one of the goals of the surgery.

The other important result of the trial:

We did not find any severe adverse events associated with either the surgery or the agent in first year. There were some minor mild to moderate adverse events, but they mostly consisted of what one might expect in the postoperative period: irritation; redness; some mild inflammation; and so on. There was no persistent inflammation, which was a concern based on the results of one of the other RPE65 trials.

How these results can help inform other trials of gene therapy:

The first thing people have been waiting on in gene therapy was to see one sort of "dart on the board" to be an example you could point to that would meet the satisfaction of the scientific community and, hopefully, the FDA (although that's still to be determined). At least to the scientific community, we agree this appears to be efficacious, safe and of reasonable duration (although we don't know how long term it is going to be).

The study met that criteria, and I think that's what a lot of people have been waiting for. At this point, this is the largest success so far with gene therapy, period—not just the eye. I think that's sort of the green light for a lot of investors, interested parties and for other investigators both within ophthalmology and outside of it. RS

RETINA CALENDAR

NOVEMBER

22 – 25
XXXVII INTER-AMERICAN COURSE IN CLINICAL OPHTHALMOLOGY
InterContinental Hotel, Miami
No CME offered.
Contact: curso@med.miami.edu
http://bascompalmer.org/cme/inter-american-course-in-clinical-ophthalmology

DECEMBER

5
WINTER OPHTHALMIC SYMPOSIUM
New York Hilton, New York
CME is available.
Contact: dholmes@postgradhealthed.com
www.revophth.com/WinterOS2015

5
OPHTHALMIC IMAGING 2016 OPTICAL COHERENCE TOMOGRAPHY (OCT) APPLICATIONS AND FUTURE TECHNOLOGY
The Breakers, Palm Beach, Fla.
CME Credits: 6.5 AMA Cat. 1
Contact: bpeicme@med.miami.edu
http://bascompalmer.org/cme/ophthalmic-imaging.

11 – 12
THIRD INTERNATIONAL CONGRESS ON EN FACE OCT
Hotel NH Vittorio Veneto, Rome
No CME credit offered.
Contact: anna.porro@apmeetings.com
www.apmeetings.com/singolo_evento.php?id=28

JANUARY 2016

8
ATLANTIC COAST RETINAL CLUB AND MACULA 2016
The LuEsther T. Mertz Retinal Research Center, New York
CME is available.
Contact: mtitherington@retinal-research.org
www.eventbrite.com/e/atlantic-coast-retinal-club-and-macula-2016-tickets-17448119796?aff=eac2

16 – 22
HAWAIIAN EYE AND RETINA
Hilton Waikoloa Village, Waikoloa Village, Hawaii
Contact: registration@contactAMS.com
www.healio.com/meeting/hawaiianeyemeeting/home

23
SIXTH EURETINA WINTER MEETING
University Medical Center, Rotterdam, The Netherlands
Contact: euretina@euretina.org
www.euretina.org/meeting-calendar.asp

FEBRUARY 2016

4 – 7
2016 TAHOE RETINA SYMPOSIUM
The Ritz-Carlton, Lake Tahoe, Truckee, Calif.
Contact: Laura Wendel squawvalleyretina@comcast.net
www.squawvalleyretina.com.

5 – 9
WORLD OPHTHALMOLOGY CONGRESS OF THE INTERNATIONAL COUNCIL OF OPHTHALMOLOGY
Guadalajara, Mexico
Contact: woc2016@servimed.com.mx
https://woc2016.org

A High Performance Ophthalmic Platform

DORC's history in innovation is changing the surgical landscape.

- VTi fluidics
  - Linear Displacement Pump provides surgeons with flexibility & enhanced control
  - Vacuum or Flow options
- TDC (Two Dimensional Cutting)
  - Up to 16,000 cpm
  - Port open design enhances surgeon control & efficiency
- LED illumination
  - 10,000 hours of consistent light output
- Dual capabilities
  - Phaco – MICS 1.8 capable
  - Vitrectomy – 20g, 23g, 25g & 27g options

DUTCH OPHTHALMIC USA

#evabydorc www.dorc.eu

inspired by you created by DORC

Less Pain, More Gain

MAXIMIZING OUTCOMES OF TREATMENT FOR RETINAL VASCULAR DISEASE.

"When I use Endpoint Management with my PASCAL laser, treatments are quick and patients don't feel any pain or discomfort."

Dr. Daniel Lavinsky
Porto Alegre, Brazil

PASCAL® Synthesis™
Pattern Scanning Laser Photocoagulator

EpM endpoint MANAGEMENT™

Experience the PASCAL advantage – The PASCAL Synthesis lets you treat your patients faster, more effectively and with greater comfort. Using optional Endpoint Management, physicians can treat macular disorders using non-damaging* retinal laser therapy. **Learn more at AAO Booth #3732.**

PASCAL | The Most Trusted Pattern Scanning Laser Technology

TOPCON MEDICAL LASER SYSTEMS, INC.
Toll Free (USA only): 1.888.760.8657 Website: topconmedical.com

*Treatment is non-damaging based on set parameters of Endpoint Management

PERFORMANCE
YOU CAN COUNT ON

TOPCON