CALIFORNIA STATE BOARD OF OPTOMETRY

Continuing Education Course
Approval Checklist

Title: East Bay Center Multispecialty CME

Provider Name: East Bay Eye Center c/o Dr. Todd Severin, MD

☑Completed Application
Open to all Optometrists? ☐Yes ☑No
Maintain Record Agreement? ☑Yes ☐No

☑Correct Application Fee

☐Detailed Course Summary

☑Detailed Course Outline

☑PowerPoint and/or other Presentation Materials

☐Advertising (optional)

☑CV for EACH Course Instructor

☑License Verification for Each Course Instructor
Disciplinary History? ☐Yes ☑No

**EAST BAY EYE CENTER**

*Excellence in Eye Care*

**Todd D. Severin, M.D.**
Diplomate American Board
of Ophthalmology
Glaucoma, Anterior Segment Surgery

**Sanford L. Severin, M.D., F.I.C.S.**
Diplomate American Board
of Ophthalmology
Medical Ophthalmology

**Viet H. Ho, M.D.**
Diplomate American Board
of Ophthalmology
Oculoplastic, Orbital and
Reconstructive Surgery

**Aimée R. P. Edell, M.D.**
Diplomate American Board
of Ophthalmology
Corneal Surgery and Disorders of
the Anterior Segment

**Elliot B. Werner, M.D.**
Diplomate American Board
of Ophthalmology
Glaucoma and Medical Ophthalmology

**Vahid Feiz, M.D.**
Diplomate American Board
Of Ophthalmology
Cornea and Refractive Surgery

**Edward A. Laubach, O.D.**
Contact Lens Services

**Nahid Abdali, O.D.**
Glaucoma Certified

**5801 Norris Canyon Road**
**Suite 200**
**San Ramon, CA 94583-5406**
**T: 925 830-8823 F: 925 866-6610**
**www.severinmd.com**
**eastbayeye@severinmd.com**

May 1, 2017

State Board of Optometry
2450 Del Paso Road
Suite 105
Sacramento, CA 95834

Attention: Continuing Education Course Approval:

Please find attached an application for our "East Bay Eye Center Multispecialty CME" course scheduled for the 25th. I have included separate applications for each instructor, but it is one course with multiple speakers, as we have done in the past.

This is a two hour course and I am aware of the required 45 days in order for your processing, but I had difficulty rounding up all the doctors for outlines and signatures. I hope it will be alright to indicate credit is "Pending", and we will mail out their certificates of attendance once the course number is received.

If there is anything else you need from me, please contact me.

Regards,

Deborah Valentine
Practice Administrator

EAST BAY EYE CENTER

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May 17, 2017

State Board of Optometry
2450 Del Paso Road
Suite 105
Sacramento, CA 95834

Kristina,

I have emailed Dr. Todd Severin's CV, Power Point Presentation, copy of the check for an additional lecturer, Dr. Aimée Edell, (even though they are tag-teaming this 2 hour lecture)....(these will be the only doctors giving the lecture now), and the application that I have adjusted to allow all OD's, if seating available.

I sent Dr. Edell's separately as I had tried previously and it did not go through together with Dr. Severin's (I believe you have received this email).

Please notify me if you do not receive the email with Dr. Severin's power point presentation, etc.

If you need any further clarification, please let me know.

Regards,

Deborah Valentine, COT, OSA, OSC
Practice Administrator

DV:nsp


5801 Norris Canyon Road
Suite 200
San Ramon, CA 94583-5406

## Please join us for an evening of discussion with 2 hours of CE

Topics: Glaucoma
Cornea, Cataract and External Diseases
Oculoplastic Surgery

Featuring: Todd Severin, M.D.
Glaucoma & Anterior Segment Surgery
Aimée Edell, M.D.
Cornea, Cataract & External Diseases
Viet Ho, M.D.
Oculoplastic, Orbital & Reconstructive Surgery
Elliott B. Werner, M.D.
Professor Emeritus, Drexel/Hahnemann Medical College
Glaucoma & Medical Ophthalmology

Introducing: Vahid Feiz, M.D.
Cornea and Refractive Surgery

Hosted by: Todd Severin, M.D. & Sanford Severin, M.D.

Date: Thursday, May 25, 2017 6:30 - 9:00 PM

Location: EBEC Office in San Ramon

RSVP: Deborah Valentine at deborah@severinmd.com by May 18
Phone: (925) 830-8823 ext. 21

*Food and Beverages will be served*

CALIFORNIA STATE BOARD OF OPTOMETRY

**STATE BOARD OF OPTOMETRY**
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P (916) 575-7170 F (916) 575-7292 www.optometry.ca.gov

# CONTINUING EDUCATION COURSE APPROVAL APPLICATION

**$50 Mandatory Fee**

$100 PAID

Pursuant to California Code of Regulations (CCR) § 1536, the Board will approve continuing education (CE) courses after receiving the applicable fee, the requested information below and it has been determined that the course meets criteria specified in CCR § 1536(g).

In addition to the information requested below, please attach a copy of the course schedule, a detailed course outline and presentation materials (e.g., PowerPoint presentation). Applications must be submitted 45 days prior to the course presentation date.

**Please type or print clearly.**

| **Course Title** | **Course Presentation Date** |
|---|---|
| East Bay Eye Center Multispeciality CME | 05/25/2017 |

**Course Provider Contact Information**

**Provider Name**

| Todd | Severin | D |
|---|---|---|
| (First) | (Last) | (Middle) |

**Provider Mailing Address**

**Street** 5801 Norris Canyon R **City** San Ramon **State** CA **Zip** 94583

**Provider Email Address** eastbayeye@severinmd.com

| | |
|---|---|
| **Will the proposed course be open to all California licensed optometrists?** | ☑ YES ☐ NO |
| **Do you agree to maintain and furnish to the Board and/or attending licensee such records of course content and attendance as the Board requires, for a period of at least three years from the date of course presentation?** | ☑ YES ☐ NO |

**Course Instructor Information**

Please provide the information below and attach the curriculum vitae for each instructor or lecturer involved in the course. If there are more instructors in the course, please provide the requested information on a separate sheet of paper.

**Instructor Name**

| Aimée | Edell | R |
|---|---|---|
| (First) | (Last) | (Middle) |

| | |
|---|---|
| **License Number** A136631 | **License Type** Medical - Ophthalmology |
| **Phone Number** (925) 830-8823 | **Email Address** eastbayeye@severinmd.com |

***I declare under penalty of perjury under the laws of the State of California that all the information submitted on this form and on any accompanying attachments submitted is true and correct.***

Aimée Edell — 4/20/2017

***Signature of Course Provider*** ***Date***

# Ocular Surface Disease: Approach to Diagnosis and Management

May 25, 2017

Aimée Edell, M.D.
Cornea, Cataract, and External Diseases
East Bay Eye Center, San Ramon, CA

1. The ocular surface
   - A. Definition
   - B. Prevalence of disease, Clinical significance

2. Clinical evaluation
   - A. Tears
     - a. Clinical exam tips
     - b. Advanced diagnostics
   - B. Blink
     - a. Clinical exam tips
     - b. Special considerations: post-trauma, malignancy
   - C. Sensation
     - a. Clinical exam signs
     - b. Special considerations: malignancy, herpetic disease
   - D. Stem cells
     - a. Clinical exam tips
     - b. Review of causes

3. Management
   - A. Step-wise approach conservative → → surgical
   - B. Special considerations
     - a. Autologous serum tears
       - i. Indications
       - ii. Availability
     - b. Amniotic membrane
       - i. Indications
       - ii. Available therapeutic options
     - c. PROSE device
       - i. Indications
       - ii. Access
       - iii. Laser and transplant therapies

4. Instructive cases

# Corneal Collagen Cross-linking

Aimée Edell, MD
Cornea, Cataract, and External Disease
East Bay Eye Center

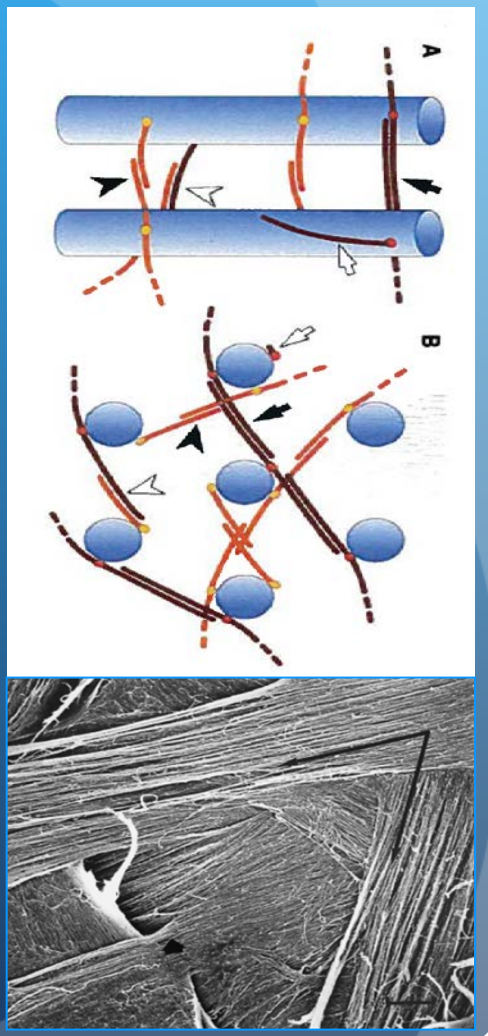
Optometric Clinic Education August 25, 2016

# Surgical Therapy for Corneal Ectasia

- First studied at the University of Dresden in the late 1990's
- Uses UV light and a photosensitizer to strengthen chemical bonds in the cornea
- Goal of therapy (currently in the US) is to halt progressive ectatic changes in the cornea, most commonly as seen in keratoconus
- After a long wait, corneal collagen cross-linking (CXL) using riboflavin (Vitamin B2) and UVA light was approved in the US for treatment of progressive keratoconus on April 18, 2016

# What is cross-linking?

- Riboflavin 5'-phosphate sodium (Vitamin B2) is a precursor to two coenzymes: flavin adenosine dinucleotide and flavin mononucleotide
- Under Dresden protocol conditions, riboflavin works with UVA irradiation to create oxygen free radicals that promote cross-links in corneal collagen
- Results in shortening and thickening of collagen fibrils and leads to stiffening of the cornea



# The only FDA approved product: Avedro KXL System


- Photrexa Viscous (riboflavin 5’-phosphate in 20% dextran ophthalmic solution) 0.146%
- Photrexa (riboflavin 5’-phosphate ophthalmic solution) 0.146%. Hypotonic.

avedro

# KXL System

## INDICATION AND USAGE

- Photrexa Viscous and Photrexa are photoenhancers indicated for use with the KXL System in corneal collagen cross-linking for the treatment of progressive keratoconus.

## CONTRAINDICATIONS

- None

## WARNINGS AND PRECAUTIONS

- Ulcerative keratitis can occur, so monitor for resolution of epithelial defects.  Post op treat like PRK.

## ADVERSE REACTIONS

- The most common ocular adverse reactions in any CXL-treated eye were corneal opacity (haze), punctate keratitis, corneal striae, corneal epithelium defect, eye pain, reduced visual acuity, and blurred vision.

# Procedure – Dresden protocol

- 9 mm epithelium removal
- Photrexa Viscous: 1 drop topically every 2 min for 30 min
- Check for riboflavin flare in anterior chamber
  - If yellow flare not detected, add 1 drop of Photrexa Viscous every 2 minutes for an addl 2 to 3 drops. Recheck for flare.
  - Repeat as necessary.
- Ultrasound pachymetry:
  - If <400 µm, 2 drops Photrexa every 5-10 sec until ≥400 µm.
  - Irradiation should not be performed unless 400 µm is met
- 30 minutes UV exposure with KXL System
  - 365 nm UV, 3mW/cm$^2$
  - Continue Photrexa Viscous every 2 min

# (other protocols – under investigation)

Phase III clinical trials

- KXL-001: A multi-Center, Randomized, Placebo-controlled Evaluation of the Safety and Efficacy of the KXL System with VibeX for Corneal Collagen Cross-Linking in Eyes with Keratoconus. **30mW/cm^2 x 4 minutes.**
- KXL-005: A multi-Center, Randomized, Placebo-controlled Evaluation of the Safety and Efficacy of the KXL System with VibeX for Corneal Collagen Cross-Linking in Eyes with Keratoconus. **30mW/cm^2 for 8 minutes with on/off cycle of 1 second UVA on/1 second UVA off. Allows for oxygenation of tissue.**

# US Clinical Studies

- Avedro's NDA submission encompassed data from three prospective, randomized, parallel-group, open-label, placebo-controlled, 12-month trials conducted in the United States to evaluate the safety and effectiveness of riboflavin ophthalmic solution/UVA irradiation for performing corneal collagen cross-linking.

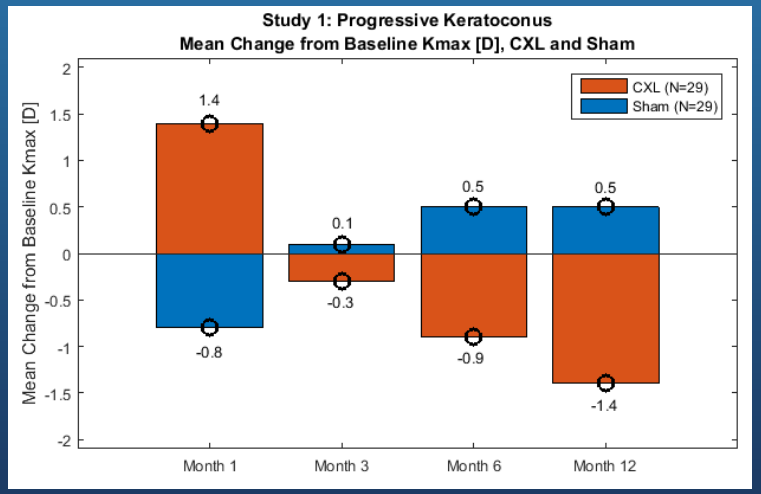
- The trials included:
  - Study 1: 58 patients with progressive keratoconus.
  - Study 2: 147 patients with progressive keratoconus.
  - Raiskup F et al. J Cataract Refract Surg. 2015;41(1):41-46. 10 year results of CXL. Kmax avg 53.2D → 49.5D. Astig 5.7D → 4.0D. VA improved 0.14logMAR (about 20/50 → 20/30).

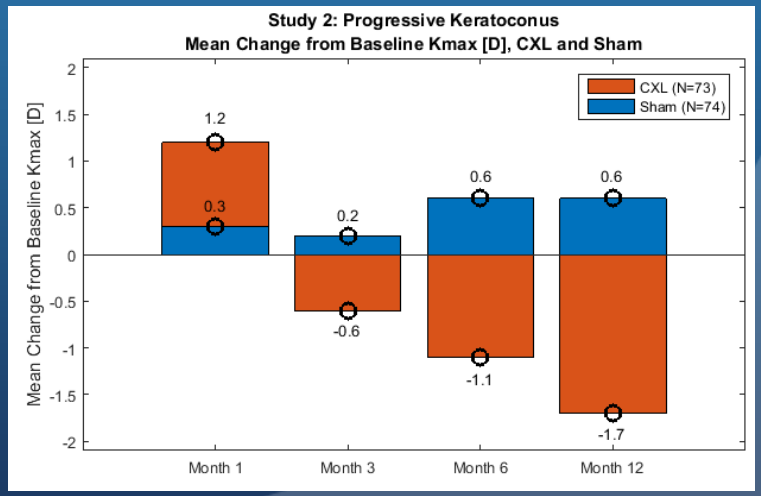
- Schedule of Assessments:
  - Screening/baseline, Day 0 (randomization/treatment day), 1 day, 1 week, and 1, 3, 6 and 12 months after treatment.

- Primary Endpoint was $K_{max}$, as measured by keratometry

# Efficacy: Mean change from baseline Kmax, CXL vs. sham

- In the studies, treated eyes showed improvement in $K_{max}$ at 12 months, while in untreated eyes Kmax continued to worsen.
- At Month 12, CXL treated eyes had an average $K_{max}$ reduction of 1.4 and 1.7 diopter in Study 1 and Study 2, respectively while the sham eyes had an average increase of 0.5 and 0.6 diopter in Study 1 and Study 2, respectively.
- Patients should be monitored for resolution of epithelial defects as ulcerative keratitis can occur.



# Adverse events

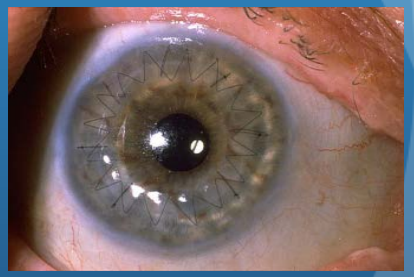
- The most common ocular adverse reactions in CXL-treated eyes were corneal opacity (haze), punctate keratitis, corneal striae, corneal epithelium defect, eye pain, reduced visual acuity, and blurred vision
- The majority of adverse events reported resolved during the first month
- Corneal epithelium defect, corneal striae, punctate keratitis, photophobia, dry eye and eye pain, and decreased visual acuity took up to 6 months to resolve
- Corneal opacity or haze took up to 12 months to resolve
- In 1-2% of patients, corneal epithelium defect, corneal edema, corneal opacity and corneal scar continued to be observed at 12 months

# Patient population

Keratoconus is a bilateral, progressive corneal ectasia resulting in irregular astigmatism and loss of visual function, with onset in teenage years[1]

Affects 1 in 2000 people[2]

- CXL for the treatment of keratoconus granted orphan designation in the US by FDA due to rare nature.



Alternative Treatment options include:

- Rigid or Specialty Contact Lens
- Intra-corneal ring segments
- Corneal Transplant

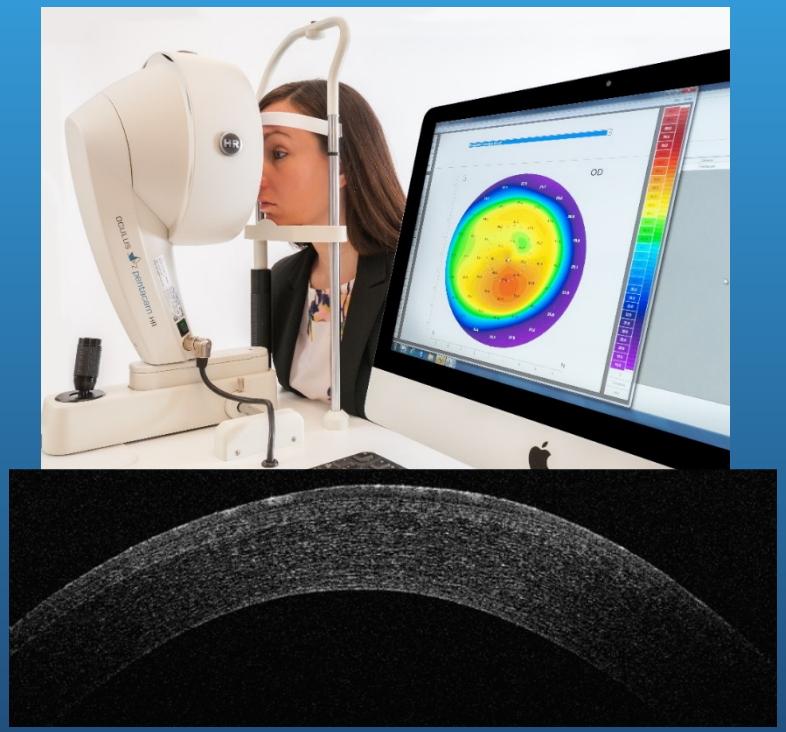
Predicted 73% of grafts fail within 20 years; 98% at 30 years[3]

- Potential for multiple transplants

Eye Bank Association of America noted >6,900 transplants/year in patients with keratoconus (16% total penetrating keratoplasty in U.S.)[4]

[1] Olivares JL, Guerrero JC, Bermudez FR. Keratoconus: age of onset and natural history. Optom Vis Sci 1997;74:147 151.
[2] National Eye Institute, National Institutes of Health. http://www.nei.nih.gov/health/cornealdisease/#h.
[3] Borderie VM, Boelle PY, Touzeau O, et al. Predicted long term Outcome of corneal transplantation. Ophthalmology 2009;2354 2360
[4] Eye Bank Association of America Statistical Report, 2014

# Patient selection/treatment criteria



- Screening exams for early diagnosis to identify patients and monitor for progression* of keratoconus
- Pediatric Use
  - 14 years of age and older
- Geriatric Use
  - No subjects enrolled in the clinical studies were 65 years of age or older

* "progression" = no standard but generally >1D steepening Kmax in 6-12 month period

# Pre-op patient counseling

- Set the expectation that cross-linking is not refractive surgery
  - Contact lenses and/or spectacles still required
- Educate patients regarding the time course of the post-operative healing process.
  - On average, steepening of Kmax is observed at 1 month postoperatively, followed by flattening through 12 months.
  - In 1-2% of patients, corneal epithelium defect, corneal edema, corneal opacity and corneal scar continued to be observed at 12 months

# Post-op patient counseling

- Patients should be advised **not to rub their eyes** for the first five days after their procedure.
- Patients may be **sensitive to light and have a foreign body sensation**. Patients should be advised that there may be discomfort in the treated eye and that sunglasses may help with light sensitivity.
- If patients experience severe pain in the eye or any sudden decrease in their vision, they should be advised to contact their physician immediately.
- If the **bandage contact lens** that was placed on the patient's eye on the day of treatment falls out or becomes dislodged, the patient should be advised not to replace it and to contact their physician immediately.

East Bay Eye Center is now accepting referrals for patients with progressive ectasia.

Thank you!

Aimée Edell, MD
aimeeedell@gmail.com

**Aimée Peck Edell, M.D.**

**EDUCATION:**

| | |
|---|---|
| 7/2014 – 7/2015 | Fellow, Cornea and External Diseases, Ophthalmic Consultants of Boston & Tufts University Medical Center, Boston, MA |
| 7/2011 – 6/2014 | Residency, NYU-Langone Medical Center, New York, NY, Department of Ophthalmology, (Chief Resident, May 2013 to June 2014) |
| 7/2010 – 6/2011 | Internship, NYU-Langone Medical Center, New York, NY, Department of Medicine |
| 8/2006 – 6/2010 | Medical School, Dartmouth Medical School, Hanover, NH |
| 8/2002 – 6/2006 | Bachelor of Arts, Magna cum Laude, Barnard College, New York, NY |

**AWARDS / HONORS:**

| | |
|---|---|
| 4/2009 – Present | Alpha Omega Alpha Honor Medical Society |
| 2/2013 | New York State Ophthalmologic Society Resident Grand Rounds Contest, Finalist, $1000.00 prize to attend the American Academy of Ophthalmology Mid-year Forum and Congressional Advocacy Day 2013 |
| 8/2009 | International Film Festival South Africa, Award Nominee 2009, 37 Million and Counting documentary film |
| 8/2009 | Accolade Film Awards, Winner, 37 Million and Counting documentary film |
| 7/2007 | Dartmouth International Health Group Summer Fellowship, $2000 for 37 Million and Counting, a documentary film about onchocerciasis filmed on location in Tanzania |
| 7/2007 | Medical Scholars Program Fellowship, Infectious Diseases Society of America, $2000 For 37 Million and Counting documentary film |

**PUBLICATIONS:**

Edell A, Teng C. High-resolution imaging before and after successful treatment of a large traumatic cyclodialysis cleft with argon laser photocoagulation. *In preparation*.

Edell A, Mitry M, Biser S. Clinical response to dehydroepiandrosterone-supplemented artificial tears in androgen-deficient patients with dry eye who have failed conventional therapy. *In submission.*

Edell A, Cohen E. Herpetic eye disease: Presentation and management at a city hospital for the under-served in the United States. Eye & Contact Lens. 2013:39(4):311-4.

Jung J, Elkin Z, Li X, Goldberg J, Edell A, Cohen M, Chen K, Perskin M, Park L, Cohen E. Increasing use of the vaccine against zoster through recommendation and administration by ophthalmologists at a city hospital. Am J Ophthalmol. 2013:155(5):787-95.

Edell A, Jung J, Solomon J. Palu R. Distracted pedestrian sustains orbital fracture while on cell phone. Clinical Ophthalmology. 2013:7;671-673.

Edell A. "Primecuts – This Week in the Journals," Clinical Correlations online medical blog, July 26, 2010. Available at http://www.clinicalcorrelations.org/?p=2921.

Peck A. "37 Million and Counting." The Lancet Student. Online issue published October 26, 2010. Available at: Http://www.thelancestudent.com/legacy/2007/10/26/37-million-abd-counting/.

Shinnar AE, Allen A, Peck A, Tal L, Goldstein R, Roberts L. squalamine family of aminosterol antibiotics from various shark species. FASEB J. 2007:21;791.4.

PRESENTATIONS:

Edell A, Kanellopoulos J. Evaluation of corneal topometric parameters and visual rehabilitation in clear corneal cataract surgery. Original abstract presentation. ASCRS Meeting, San Francisco, California, April 22, 2013.

Edell A, Cohen E. Herpetic eye disease: Presentation and management at a city hospital for the under-served. Poster presentation. Association for Research and Vision in Ophthalmology, Fort Lauderdale, Florida, May 10, 2012.

Edell A, Chen G, Park L. The effect of cataract surgery on intraocular pressure in patients with diabetes. Poster presentation. 115 annual meeting of the American Academy of Ophthalmology, Orlando, Florida, October 2011.

Kurland ES, Peck A, McMahon DJ, Bilezikian JP. A novel relationship between estrogen and leptin levels in men with idiopathic osteoporosis. 27$^{th}$ annual meeting of the ASBMR, Nashville, Tennessee, September 2005/

CALIFORNIA STATE BOARD OF OPTOMETRY

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P (916) 575-7170 F (916) 575-7292 www.optometry.ca.gov

# CONTINUING EDUCATION COURSE APPROVAL APPLICATION

**$50 Mandatory Fee**

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In addition to the information requested below, please attach a copy of the course schedule, a detailed course outline and presentation materials (e.g., PowerPoint presentation). Applications must be submitted 45 days prior to the course presentation date.

**Please type or print clearly.**

| **Course Title** | **Course Presentation Date** |
|---|---|
| East Bay Eye Center Multispeciality CME | 05/25/2017 |

**Course Provider Contact Information**

**Provider Name**

Todd (First) Severin (Last) D (Middle)

**Provider Mailing Address**

**Street** 5801 Norris Canyon R **City** San Ramon **State** CA **Zip** 94583

**Provider Email Address** eastbayeye@severinmd.com

| | |
|---|---|
| **Will the proposed course be open to all California licensed optometrists?** | ☑ YES ☐ NO |
| **Do you agree to maintain and furnish to the Board and/or attending licensee such records of course content and attendance as the Board requires, for a period of at least three years from the date of course presentation?** | ☑ YES ☐ NO |

**Course Instructor Information**

Please provide the information below and attach the curriculum vitae for each instructor or lecturer involved in the course. If there are more instructors in the course, please provide the requested information on a separate sheet of paper.

**Instructor Name**

Todd (First) Severin (Last) D (Middle)

| | |
|---|---|
| **License Number** G71183 | **License Type** Medical - Ophthalmology |
| **Phone Number** (925) 830-8823 | **Email Address** eastbayeye@severinmd.com |

***I declare under penalty of perjury under the laws of the State of California that all the information submitted on this form and on any accompanying attachments submitted is true and correct.***

*Signature of Course Provider* — *Date* 4/20/2017

Form CE-01, Rev. 5/16

# Updates in Glaucoma and Glaucoma Treatments

May 25, 2017

Todd D. Severin, M.D.
Director of Glaucoma Services
East Bay Eye Center, San Ramon, CA

Glaucoma is a disease where the optic nerve dies. We are not sure why or how this happens (there are many mechanical, vascular, and biochemical theories) but high intraocular pressure certainly seems to be associated, if not entirely the cause, of optic nerve death. Glaucoma is one of the leading causes of preventable blindness in the U.S., and patients with acute glaucoma can develop irreversible vision loss within a few hours, so it is important that you understand how this disease works and recognize it in your patients.

## The Aqueous Pathway

Before continuing we should review the pathway of aqueous humor flow. Aqueous is the fluid that fills the front part of the eye, and it is important for maintaining the shape of the eye and providing nourishment for the avascular lens and cornea. Aqueous humor is first produced by the ciliary body within the posterior chamber. After filling the posterior chamber, aqueous moves forward around the lens and flows through the pupil into the anterior chamber. As the anterior chamber fills, the aqueous spreads outwards into the angle formed by the iris and cornea. Within this irido-corneal angle the aqueous exits the eye by filtering through the trabecular meshwork into the Canal of Schlemm, where it returns back into the blood circulation. The pressure within the eye is maintained by this steady state of aqueous production and egress, and it is an imbalance in this equilibrium that causes the increase pressure associated with glaucoma.

## Open vs. Closed-Angle Glaucoma

There are two categories of glaucoma and they have very different mechanisms. Open-angle glaucoma is the most common type in our country. It occurs from decreased aqueous drainage caused by an unidentified dysfunction or microscopic clogging of the trabecular meshwork. This leads to chronically elevated eye pressure, and over many years, gradual vision loss.

This differs from closed-angle glaucoma, also called "acute glaucoma," which occurs when the angle between the cornea and iris closes abruptly. With this closure, aqueous fluid can't access the drainage pathway entirely, causing ocular pressure to increase rapidly. This is an ophthalmological emergency and patients can lose all vision in their eye within hours.
Let's examine each of these types of glaucoma in more detail.

## Open-Angle Glaucoma

The majority of glaucoma patients (about 80% ) have chronic open angle glaucoma. Most patients are over the age of 40. This condition is more common in African Americans, and has a strong familial inheritance. The major risk factors are family history, age, race, high eye pressure, and large vertical nerve cupping. More recently, thin-corneas have been found to be a major risk factor, though this mechanism is not well understood.

The underlying mechanism for open-angle glaucoma involves degeneration of the trabecular meshwork filter, usually by unknown causes, that leads to aqueous backup and chronically elevated eye pressure. With prolonged high pressure, the ganglion nerves in the retina (the same nerves that form the optic nerve) atrophy. The exact mechanism for this nerve damage is poorly understood and proposed mechanisms include stretching, vascular compromise, and glutamate transmitter pathways. As the ganglion nerves are progressively destroyed, vision is gradually lost.

Open-angle glaucoma has the reputation of being the "sneaky thief of sight" because the visual loss occurs so slowly that many patients don't realize they have the disease until it is far advanced.

Because the disease is otherwise asymptomatic, detecting open-angle glaucoma requires early pressure screening. Free screening clinics also use different types of automated visual-field testing to detect subtle peripheral vision loss.

## Presentation

Open-angle glaucoma patients usually present with three exam findings: elevated eye pressures, optic disk changes, and repeatable visual field loss patterns.

1. Pressure: The most accurate way to measure eye pressure is with the Goldman applanation tonometer. This is a device mounted on the slit-lamp that measures the force required to flatten a fixed area of the cornea. Normal pressures range from 10 to 22 mm Hg, while glaucoma patients can measure over 22 mm Hg. Keep in mind that eye pressure can fluctuate throughout the day (typically highest in the morning) so the pressure should be checked with each visit and the time of measurement should be noted. Also, some glaucomatous eyes have a "normal" pressure. In other words, a "good pressure" doesn't rule out glaucoma, nor does a high pressure necessarily indicate glaucoma.

You can also measure pressure with a device called a "Tono-Pen." This expensive little device is handy for bed-bound patients and down in the emergency room, though it's inaccurate in the wrong hands!

Corneal Thickness can affect your pressure measurement:
When we measure the pressure in the eye, we are actually measuring how much resistance we get when pressing on the cornea. This is analogous to kicking a car-tire with your foot or pressing your hand against a bicycle tire to estimate how much air pressure is inside. We do the same thing with the Goldman applanation tonometer mounted on the slit-lamp – we measure how much force it takes to flatten a 3mm diameter area of corneal surface.

The pressure measurements on the Goldman were calibrated using an average corneal thickness of approximately 540nm. However, some patients have very thin or thick corneas. I like to describe these as "thin bicycle" or "thick truck-tire" corneas. When you press on a thick cornea (a truck-tire cornea) the pressure will seem higher than it really is! This makes sense … if you kick a flat truck-tire, it will still hurt your foot because that rubber is so darn thick. The opposite is true for thin corneas – they feel squishy no matter how much air pressure.

This thickness variability is important in glaucoma clinic so we can calibrate the accuracy of our pressure readings. This is why we always check corneal thickness with an ultrasonic pachymeter on the first visit.

2. Fundus Exam: The optic disk looks striking in advanced glaucoma. In normal patients, the optic disk has a physiological indentation or "cup" that is less than one-third the disk diameter. With glaucoma, the ganglion nerve layer slowly dies away, and, as fewer ganglion nerves course through the optic disk, the amount of cupping increases. A cup to disk ratio greater than 0.5 or an asymmetry between the eyes suggests ganglion atrophy caused by glaucoma.

The ISNT Rule
When you look at your patient's optic nerve, you'll notice that the cup doesn't sit directly in the middle of the disk. The cup is slightly off-center – this makes sense as the optic nerve enters the back of the eyeball at an angle.

The space between the inner cup and surrounding disk is called the neural rim and is comprised of the actual retinal ganglion nerves. In a normal eye, this rim follows the ISNT rule of decreasing thickness … meaning that the Inferior rim is thickest while the Temporal rim is the skinniest.

With glaucoma, you often see vertical thinning and notching of the inferior and superior rims. This deviation from the ISNT rule is another clue that glaucoma might be killing off the nerve. You can also see undermining of the rim (like in the right drawing) where the blood vessels dive out of view under the rim edge.

3. Visual Loss: The vision loss from chronic glaucoma occurs in characteristic patterns that can be followed by automated perimetry (machines that map out the peripheral vision). The central vision is typically spared – in fact, late stage patients may have 20/20 central vision, but be otherwise legally blind because of peripheral blindness.

FUN FACT!

The giant squid has the largest eyeball in the world. This enormous deep-sea predator can weigh up to 2.5 tons and 55 feet in length. Its eye can be a more than a foot in diameter! Wow!

Treatment:
Since IOP is the only risk factor we can treat, the primary treatment of glaucoma focuses on decreasing eye pressure to less than 20 mm Hg or even lower depending upon the severity of disease. Treatment may be either medical or surgical.

Medical Treatment
Topical beta-blockers are the traditional therapy for these patients and have been around for decades. Beta-blockers work by decreasing aqueous humor production at the ciliary body. Unfortunately, systemic side effects can occur from nasal absorption, making it especially important to ask your patients about history of asthma, COPD, and cardiac problems.

These days, many physicians are using newer drugs like topical CAIs, alpha-agonists, and prostaglandin analogues for first-line therapy, as they have fewer systemic side effects.

Prostaglandin analogues like latanoprost (Xalatan™) are the newest of these glaucoma drugs, and they are very popular as a first-line agent. They work by increasing aqueous humor outflow. They do have some side effects, though. They can make eyelashes grow longer (many patients actually like this), and in a few patients may darken the iris color, turning green and blue eyes brown.

Surgical Treatment for Chronic Glaucoma
gl-trabeculectomy.jpgIf eyedrops aren't working, there are several surgical techniques available to relieve eye pressure. One common surgery is the trabeculectomy, where an alternate drainage pathway is surgically created. A small hole is cut through the superior limbus, creating a drainage tract from the anterior chamber to a space under the conjunctiva. This can be very effective in decreasing pressure, but if the patient is a rapid healer the shunt can scar down and close, so anti-metabolites like mitomycin-C are often applied to the site. If this surgery doesn't work, a plastic tube-shunt can be inserted into the anterior chamber that drains to a plate fixed under the conjunctiva further back.

Several laser procedures can also help. Argon laser trabeculoplasty (ALT) can be used to burn portions of the trabecular meshwork itself. The resulting scarring opens up the meshwork and increases outflow. A laser can also be used to burn the ciliary body to decrease aqueous production at its source.

Acute Glaucoma
Acute glaucoma is a medical emergency. The most common mechanism is pupillary block. This occurs when the lens plasters up against the back of the iris, blocking aqueous flow through the pupil. This resistance produces a pressure gradient (this is a good buzz word to memorize) across the iris that forces the iris and lens to move anteriorly. When the iris moves forward, the irido-corneal angle closes, blocking the trabecular meshwork. Without an exit pathway, aqueous fluid builds up, eye pressure increases rapidly, and the retina is damaged from stretching and decreased blood supply.

The outflow angle can close for many reasons, and people with naturally shallow anterior chambers such as hyperopes (far-sighted people with small eyes) and Asians are predisposed to developing angle closure. One inciting condition that is typical in acute glaucoma is pupil dilation — many patients describe onset of their symptoms occurring while in the dark or during stressful situations. When the iris dilates, the iris muscle gets thicker and the irido-corneal angle becomes smaller, making it more likely to spontaneously close. Along those lines, medications that dilate the eye, such as over-the-counter antihistamines and cold medications, also predispose angle closure.

Presentation
These patients will present with an extremely red and painful eye, often complaining of nausea and vomiting. On exam, you'll find their pupil sluggish and mid-dilated. Pressures in the affected eye can be very high, often 60 mm Hg or higher. The eye will feel rock hard, and you can actually palpate the difference between the eyes with your fingers. One classic sign that patients often describe is seeing halos around lights. This occurs because the cornea swells as water is pushed under high pressure through the endothelium into the corneal stroma. This corneal swelling also makes it hard for you to see into the eye, further complicating diagnosis and treatment.

Acute Glaucoma Exam Techniques:
Ophthalmologic examination for acute glaucoma involves measuring the eye pressure, accessing the anterior chamber angle, and a fundus exam.

gl-flashlight.jpgOne trick to determine whether an angle is shallow is to shine a simple penlight across the eyes. If the iris is pushed forward, it will cast a shadow. Additionally, an ophthalmologist can visualize the angle directly through gonioscopy. Here's how it works:

Gonioscopy:
Normally, the inside angle cannot be seen with a microscope because the cornea-air interface creates "total internal reflection." However, we can use a goniolens, which is a special glass lens with mirrors on its sides, to look directly at the angle. When the glass lens is placed directly onto the cornea, the cornea-air interface reflection is broken and light from the angle can escape and be seen through the mirrors.

We can see the concept of "total internal reflection" in nature. For example, if you've ever gone snorkeling in water, you may notice that the water's surface above you looks like a mirror. The flying fish uses this phenomenon to escape from predators. When attacked, the flying fish leaps from the water and glides above the surface so the shark can't see them – effectively disappearing. This is also how fiber optic cables work, with light bouncing off the walls of the cable.

Acute Glaucoma Treatment
In cases of acute glaucoma, you want to decrease the pressure in the eye as quickly as possible. A "kitchen sink" approach is often used, throwing many treatments on at once. You can decrease aqueous production using a topical beta-blocker like Timolol and a carbonic anhydrase inhibitor like Diamox. Also, osmotic agents such as oral glycerin or IV mannitol (even ethanol, in a bind) can be given systemically to draw fluid out of the eye and back into the bloodstream. Finally, a miotic such as pilocarpine may be helpful in certain cases to constrict the pupil and thus open up the outflow angle. You can also use topical glycerin to transiently dehydrate/clear the cornea to aid with examination.

Ultimately, these patients need surgical treatment to avoid recurrence of their angle closure. A high intensity laser can burn a hole through the iris and create a communication between the posterior and anterior chambers, relieving the pressure gradient (buzzword!!) across the iris, and allowing it to move back into a normal position. This opens up the trabecular meshwork and allows aqueous fluid to flow freely out of the eye. This procedure is typically performed on both eyes because these patients are predisposed to having attacks in the other eye as well.

Other types of glaucoma

1. Neovascular Glaucoma:
This can occur in diabetic patients or those with a retinal vein occlusion. VEGF production from areas of ischemic retina can float forward through the pupil and promote neovascularization of the iris. In the early stages, a fibrous membrane forms on the iris-cornea angle that blocks outflow and forms an open-angle

glaucoma. At later stages of neovascularization, the new vessels actually pull the iris forward and cause a closed angle glaucoma that is essentially irreversible. You treat this by lasering the peripheral retina to decrease the angiogenic VEGF production and decrease the rate of neovascularization. Neovascular glaucoma is very hard to treat and most of these patients end up needing a surgical intervention like a tube-shunt.

2. Pigment Dispersion Syndrome (PDS):
Occurs when the pigmented back-surface of the iris rubs against the radial zonules supporting the lens. Little flecks of pigment are shed into the aqueous and end up clogging the trabecular meshwork drain. This process usually occurs in young white males with myopic eyes. They suffer from attacks of high pressure after exercise when pigment gets rubbed off the iris. You can see this pigment in the trabecular meshwork on gonioscopy, and even find trans-illumination defects of the iris at the slit-lamp.

Some of the pigment will stick to the inner-corneal surface, and because of convection currents in the aqueous, form a vertical line of pigment on the inner corneal surface called a Krukenberg spindle.

3. Pseudoexfoliation Syndrome (PXF)
In this systemic condition, basement membrane-like material is deposited throughout the body. This material adheres to the anterior lens capsule, creating a rough surface. As the overlying iris dilates and contracts with daily activity, pigment is rubbed off and clogs the trabecular drain. These patients also suffer from zonular instability, making cataract operations difficult.

Summary
That is glaucoma in a nutshell. Chronic, open-angle glaucoma is very common (in this country) and leads to gradual visual loss, while acute closed-angle glaucoma is infrequent but an emergency that needs urgent treatment to avoid blindness.

PIMP QUESTIONS

1. What is glaucoma? What actually causes damage to the neurons and optic nerve with glaucoma?
Nobody is sure exactly "what glaucoma is" but at its most basic, glaucoma is gradual death of the optic nerve. If an attending asks you this question, say "knowbody knows" or "death of the optic nerve." If you say "high pressure" you'll be laughed at (glaucoma specialists are odd ducks). The optic nerve damage arises from pressure, stretching, sheer forces, vascular compromise, or some kind of hormone regulator – we're not sure of the mechanism.

2. What is the flow-pathway for aqueous fluid? Where is it made, and where does it leave the eye?
Aqueous is first produced by the ciliary body. It then flows forward through the pupil into the anterior chamber. Finally, aqueous drains through the trabecular meshwork and back into the venous system via the canal of Schlemm.

3. What's the difference between open-angle and closed-angle glaucoma? How about chronic versus acute glaucoma?
Open angle is a common, chronic condition where aqueous drainage is impaired. Closed-angle glaucoma is caused by acute closure of the irido-corneal angle leading to blockage of ALL aqueous drainage – an ophthalmologic emergency that can quickly lead to blindness.

4. What are the risk factors for developing primary open-angle glaucoma?

This is an important list and since I glossed over them in the chapter, here they are again:
High intraocular pressure (obviously)
Age
Family history

Race (African American and Hispanics)
Suspicious optic nerve appearance (large vertical cupping)
Thin central corneal thickness (** remember this one!)

There are other possible risk factors, but I'd focus on those above. These risk factors explain why we always ask our patients about familial history and why we check pachymetry (corneal thickness by ultrasound) on the first glaucoma visit.

5. What do we measure to monitor and follow progression in glaucoma patients?
We generally check three things: pressure, disk changes by 3D photograph, and visual fields. Good stereo slides are difficult to obtain, so many use other imaging modalities like HRT or OCT.

6. What does corneal thickness have to do with glaucoma (as far as risk for developing glaucoma)?
The OHTS trial showed that people with thin corneas are at higher risk for glaucoma, independent of other risk factors. We're not sure why, but it's believed that people with thin corneas are anatomically predisposed to optic nerve damage. We measure corneal thickness with a small ultrasound probe (this is called pachymetry) with all new glaucoma patients.

7. What's a normal eye pressure? Does a patient with pressure of 14 have glaucoma?
About 10 to 22. While glaucoma is classically associated with high pressure, there is a significant minority of patients with glaucoma with normal pressure. Also, pressure fluctuates throughout the day and we typically write down the time in the notes. Some studies have noted higher rates of glaucoma in people with large diurnal shifts in eye-pressure. This observation could be compared to diabetic suspects with large diurnal shifts in random-glucose measurements.

8. A glaucoma suspect is found on first visit to have a pressure of 19. Her corneal thickness, however, measures only 450nm. Do you think her actual eye pressure is HIGHER or LOWER than 19?
Definitely higher. This patient has thin "bicycle-tire corneas" that "feel soft" when measured by the Goldman applanation. This woman's actual pressure is probably well over 22, increasing her risk for glaucomatous damage progression.

9. What kind of vision loss occurs with glaucoma?
Typically loss of eyesight occurs in the periphery first where the loss is less noticeable. Scotomas (visual field loss areas) in glaucoma tend to follow certain patterns that start in the mid-periphery. Many patients don't notice visual symptoms until the disease is far progressed. Generally, the central vision is spared until very late stages of glaucoma.

10. Why can't you see the trabecular meshwork with the slit-lamp microscope?
Because the trabecular drain is behind the limbus (around the corner) and we can't see this area directly because of "total internal reflection" at the cornea-air interface. Gonioscopy allows direct visualization of the trabecular meshwork by interrupting the cornea-air interface with a glass lens.

11. What mechanisms do the glaucoma drops use to decrease pressure?
Drops either decrease the amount of aqueous produced at the ciliary body or increase the aqueous outflow from the eye (generally via the uveal-scleral pathway or by direct trabecular meshwork outflow).

12. What retina findings do you see with glaucoma?
You see increased cupping of the optic disk, usually in a vertical pattern that goes against the ISNT rule. You can sometimes see hemorrhages at the disk and undermining of the blood vessels as they exit the disk.

13. How can diabetes cause acute glaucoma?
Retinal ischemia can produce VEFG. As this molecule floats forward it can cause neovascularization of the iris, forming vascular membranes that cover the trabecular meshwork and clog the drainage angle. This leads to a severe neovascular glaucoma that is hard to manage.

14. You have a patient who appears to have a shallow anterior chambers and occludable angles. Would you use pilocarpine?

In most cases, yes. Pilocarpine will constrict the pupils — by flattening the iris you potentially open up the drainage angle next to the trabecular meshwork. Pilocarpine will also decrease pressure in the eye by affecting aqueous production and egress. You probably wouldn't use it long term in patients with occludable angles though, as pilo has a lot of side effects such as headache and blurry vision. Ultimately, anyone with occludable angles needs a laser peripheral iridotomy to equalize the pressure between anterior and posterior chambers.

# Lowering IOP in the Real World

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# Let's Get Real World

1. **Today**, for my glaucoma patient, how can I understand their **risk** for **progression**?

2. What can I do to help **reduce** their **risk** of progression today?

# Program Overview

1. **Glaucoma is a progressive optic neuropathy**
2. **IOP is the only modifiable risk factor**
3. **Clinical trials suggest reduction of IOP decreases, but does not eliminate, the risk of progression**
4. **Medical management of glaucoma**
   - IOP fluctuation
   - Peak IOP
   - Disruption of therapy
5. **Monitoring for progression**
6. **Risk vs reward**
   - Individualized therapy
   - Considerations for an aging population

# How Often Does Glaucoma Progress?

| Study | N | Follow-up | % Progression | |
|---|---|---|---|---|
| | | | Tx | No Tx |
| **Clinic-based** | | | | |
| OHTS1 | 1636 patients | 5 years | 4.4% | 9.5% |
| EGPS2 | 1081 patients | 5 years | 13.4% | 14.1% |
| DIGS3 | 126 patients | 7 years | N/A | 25% |
| EMGT4 | 255 patients | 6 years | 45% | 62% |
| CNTGS5 | 140 eyes | 7 years | 12% | 35% |
| CIGTS6 | 607 patients | 5 years | 10.7%-13.5% | N/A |
| AGIS7 | 747 eyes | 8-13 years | 28.1%-32.5% | N/A |
| **Population-based** | | | | |
| St. Lucia8 | 205 patients | 10 years | N/A | 52%-73% |

# 68-Year-Old White Female: Initial Visit, Year 0

- Referred from colleague
- History of high IOP in left eye at times
- Past history of LASIK, OU
  - Pachymetry was 460 microns, OU
- Vision 20/20 OU
  - IOP by Goldmann (GAT)
  - 16 mm Hg OD
  - 18 mm Hg OS
  - Cup-to-disc ratio (C/D): 0.3/0.35 with the same size discs
- Gonioscopy: open angles
- Referring doctor's visual field (VF) interpreted as "NL"
- Recommended observation

# Case Study:
# 68-Year-Old White Female: Initial Visit, Year 0

How did we make the decision this was ocular hypertension (OHT) and decide to observe?

- Individual patient determination based upon:
  - Risk of progression to glaucoma
  - Patient's decision
- Options:
  - Observe
  - Treat
    - Target 20% decrease in IOP based on OHTS

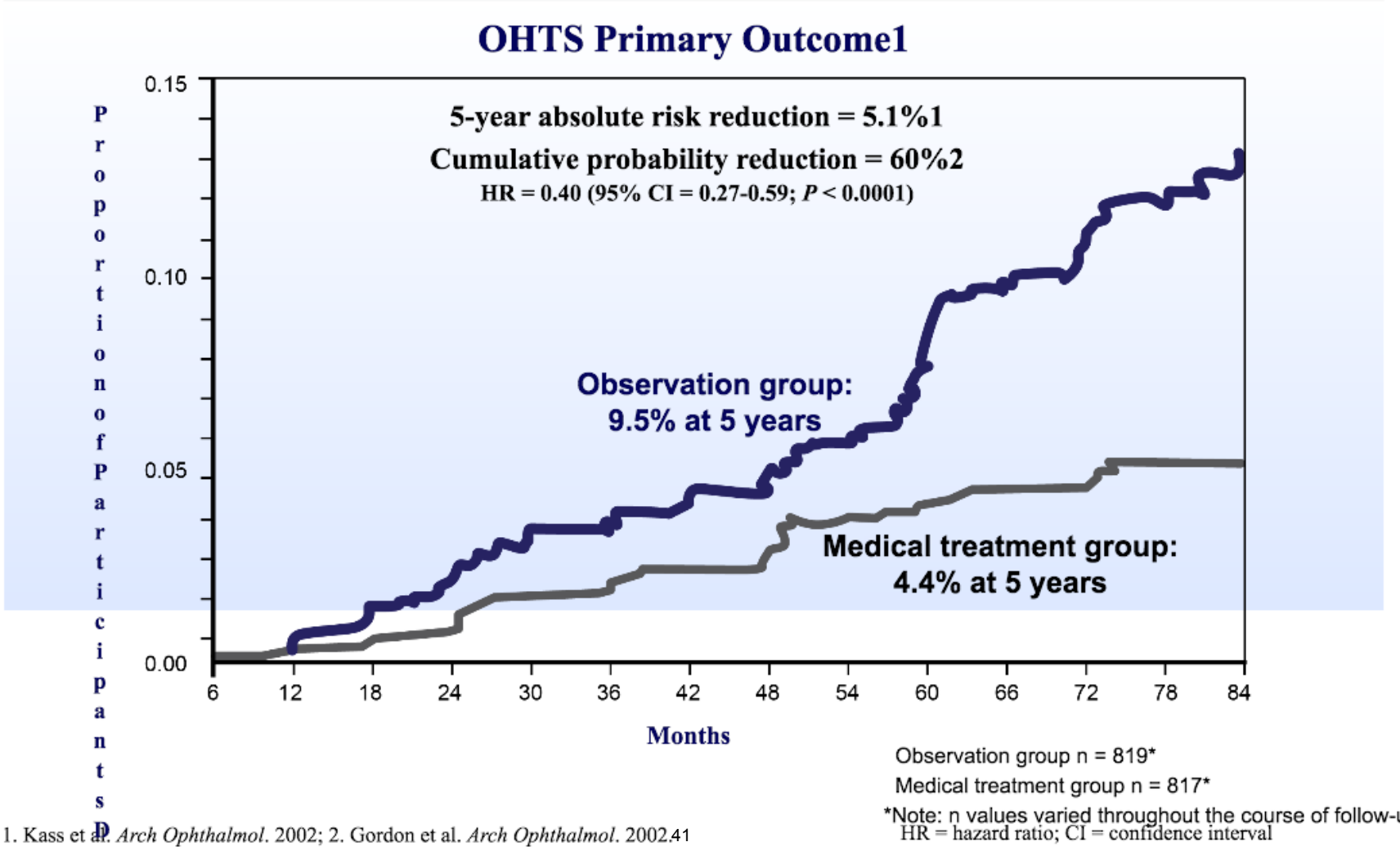
# **Today,** for my patient, how can I estimate their risk for **progression**?

| OHTS Multivariate Hazard Ratios (95% CI) for Development of POAG1 | |
|---|---|
| Corneal thickness (per 40 m thinner) | 1.71 (1.40-2.09) |
| Vertical C/D ratio (per 0.1 larger) | 1.32 (1.19-1.47) |
| Horizontal C/D ratio (per 0.1 larger) | 1.27 (1.14-1.40) |
| PSD (per 0.2 dB greater) | 1.27 (1.06-1.52) |
| Age (per decade) | 1.22 (1.01-1.49) |
| IOP (per mm Hg) | 1.10 (1.04-1.17) |

CI = confidence interval; PSD = pattern standard deviation

- **Predicting risk** of **development** of glaucoma
  - **ohts.wustl.edu/risk/**
  - 5-year risk of individual with OHT developing POAG
  - Based on OHTS and EGPS
- **Predicting risk** of **progression** of glaucoma
  - Need to build this calculator for individual patients

# Does Treatment of OHT Make Primary Open-Angle Glaucoma (POAG) Development Less Likely?

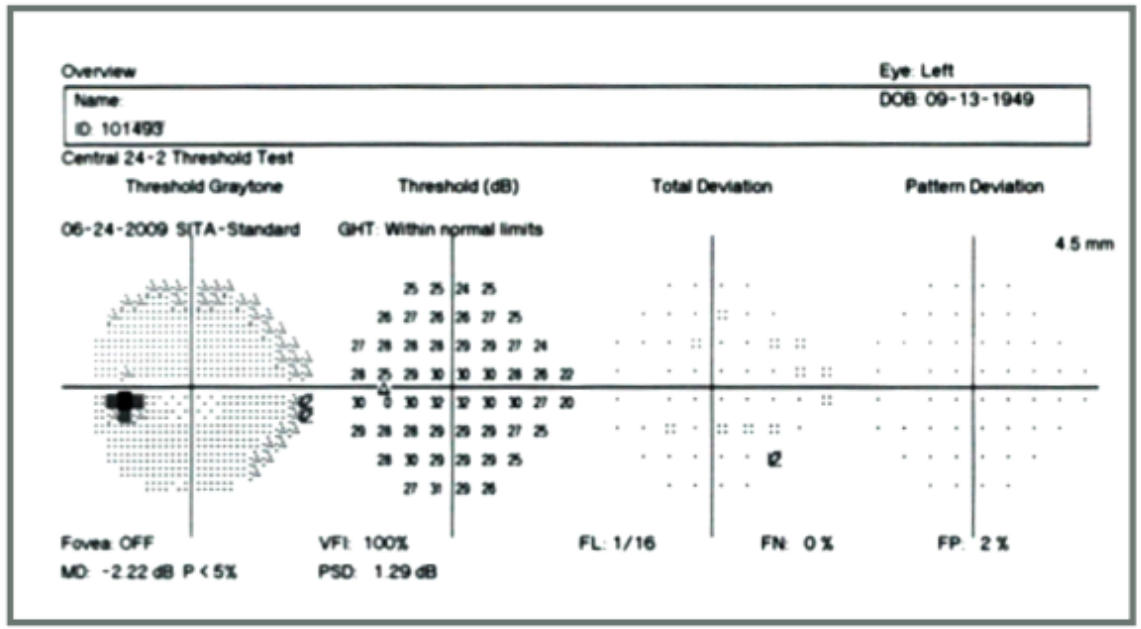





1. Kass et al. *Arch Ophthalmol*. 2002; 2. Gordon et al. *Arch Ophthalmol*. 2002.41

# Case Study: Follow-up at Year 1

- Visual acuity (V/A): 20/20 OU
- IOP:
  - 16 OD, 22 OS
- C/D: 0.3/0.4
- Visual field (SITA)
  - Slight decreased sensitivity
  - Reliable



# Independent Risk Factors for Progression

| | AGIS1, 2 | CIGTS3 | CNTGS4 | EMGT5,6 | EGPS7,8 | OHTS9-11 |
|---|---|---|---|---|---|---|
| **Age** | X | X | | X | X | X |
| **Elevated IOP** | X | | | X | X | X |
| **Central corneal thickness (thinner)** | | | | X | X | X |
| **Disc hemorrhage** | | | X | X | | X |
| Visual field (higher PSD) | | | | | X | X |
| Cup-to-disc ratio (greater) | | | | | X | X |
| Visual field (greater MD) | | | | X | | |
| Pseudoexfoliation | | | | X | | |
| Low ocular perfusion pressure | | | | X | | |
| Abnormal baseline HRT | | | | | | X |
| Race (nonwhite) | | X | | | | |

MD = mean deviation; HRT = Heidelberg retina tomograph

# Risk Factors Our Patient

- Age
- **IOP: asymmetric**
- **Central corneal thickness (CCT): thin, but post LASIK?**
- Disc hemorrhage
- **Worse visual field: possible**
- **More disc cupping: probable**
- Exfoliation
- Race

# Risk Factors

| Risk Factor | Modifiable? |
|---|---|
| IOP | Yes |
| Disc hemorrhage | No Control |
| Worse VF | No Control |
| More disc cupping | No Control |
| Age | No Control |
| CCT | No Control |
| Race | No Control |
| Exfoliation | No Control |

# Case Study: Year 1: Impression and Plan

- Glaucoma suspect vs likely early glaucoma
- OHTS, risk factors
  - Increased cup asymmetry (new)
  - Mean deviation (MD): -2.2 OS
  - Thin pachymetry post LASIK confounds ability to use risk calculators or IOP by Goldmann
- Reviewed treatment options
- Choice:
  - Medical therapy with a prostaglandin analog (PGA), OS
- Sent back to see referring doctor in 1 month
  - 1-year follow-up here

# Lowering IOP Reduces the Risk of Disease Progression

| Study | IOP | Progression (Tx/No Tx) |
|---|---|---|
| OHTS1 | 20% reduction | 4.4%/9.5%a (5 years) |
| EMGT2* | 25% reductionb | 45%/62%c (6 years) |
| CNTGS3 | 30% reduction | 12%/35%d (7 years) |
| CIGTS4 (medicine) | ≈ 35% reductionb | No progressionb,e (5 years) |
| CIGTS4 (surgery) | ≈ 48% reductionb | No progressionb,e (5 years) |
| AGIS5 | < 18 mm Hg | No progressionb,f (6 years) |
| AGIS5 | > 18 mm Hg | 1.93 unitsb,g (7 years) |

aProbability of developing POAG; bAverage; cPatients (%) meeting computer-generated perimetric progression criteria based on VF and optic disc (OD) outcomes; dPatients (%) developing glaucomatous OD progression or VF loss; eProgression measured as loss of VF in either medicine or surgery group; fProgression measured as increase in units of VF defect score in eyes with 100% of visits showing IOP 18 mm Hg; gProgression measured in eyes with < 50% of visits showing IOP < 18 mm Hg.

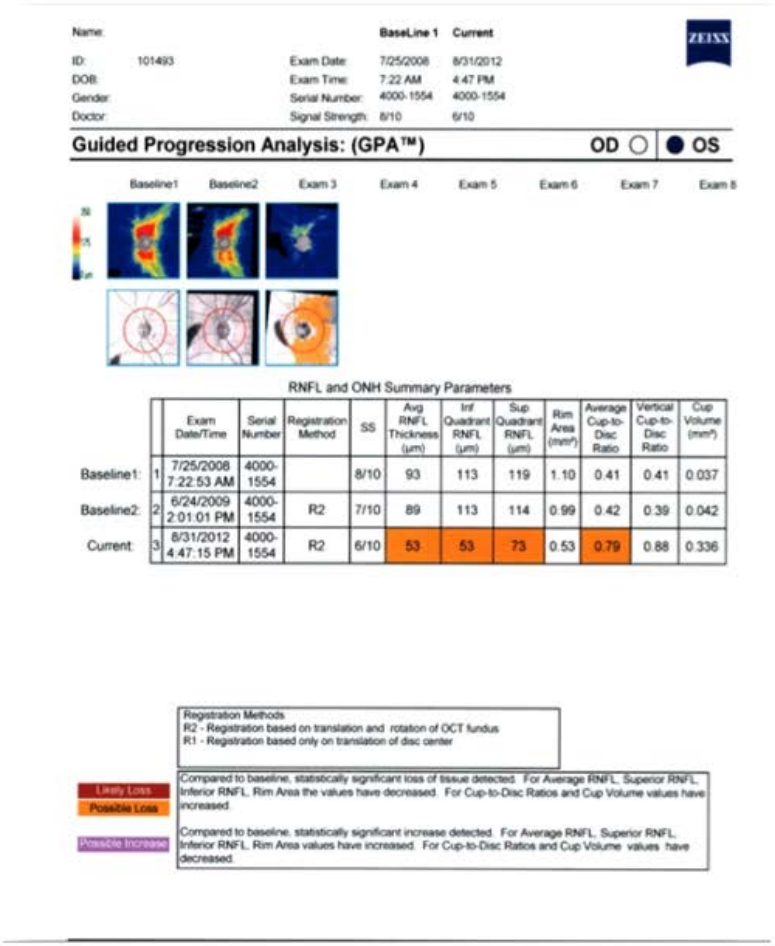
*EMGT study showed 10% reduction in risk with every 1 mm Hg of IOP lowering2

1. Kass et al. *Arch Ophthalmol*. 2002; 2. Heijl et al. *Arch Ophthalmol.* 2002; 3. CNTG Study Group. *Am J Ophthalmol.* 1998; 4. Lichter et al. *Ophthalmology*. 2001; 5. AGIS Investigators. *Am J Ophthalmol*. 2000.

# Case Study: Year 2

- No-show
- Follow-up reminder sent and called referring doctor

# Case Study: Year 3: OCT and VF GPAs



Name:

ID: 101493

DOB:

Gender:

Doctor:

| | BaseLine 1 | Current |
|---|---|---|
| Exam Date: | 7/25/2008 | 8/31/2012 |
| Exam Time: | 7:22 AM | 4:47 PM |
| Serial Number: | 4000-1554 | 4000-1554 |
| Signal Strength: | 8/10 | 6/10 |

**Guided Progression Analysis: (GPA™)** OD ○ ● OS

Baseline1 Baseline2 Exam 3 Exam 4 Exam 5 Exam 6 Exam 7 Exam 8

RNFL and ONH Summary Parameters

| | | Exam Date/Time | Serial Number | Registration Method | SS | Avg RNFL Thickness (µm) | Inf Quadrant RNFL (µm) | Sup Quadrant RNFL (µm) | Rim Area (mm²) | Average Cup-to-Disc Ratio | Vertical Cup-to-Disc Ratio | Cup Volume (mm³) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Baseline1: | 1 | 7/25/2008 7:22:53 AM | 4000-1554 | | 8/10 | 93 | 113 | 119 | 1.10 | 0.41 | 0.41 | 0.037 |
| Baseline2: | 2 | 6/24/2009 2:01:01 PM | 4000-1554 | R2 | 7/10 | 89 | 113 | 114 | 0.99 | 0.42 | 0.39 | 0.042 |
| Current: | 3 | 8/31/2012 4:47:15 PM | 4000-1554 | R2 | 6/10 | 53 | 53 | 73 | 0.53 | 0.79 | 0.88 | 0.336 |

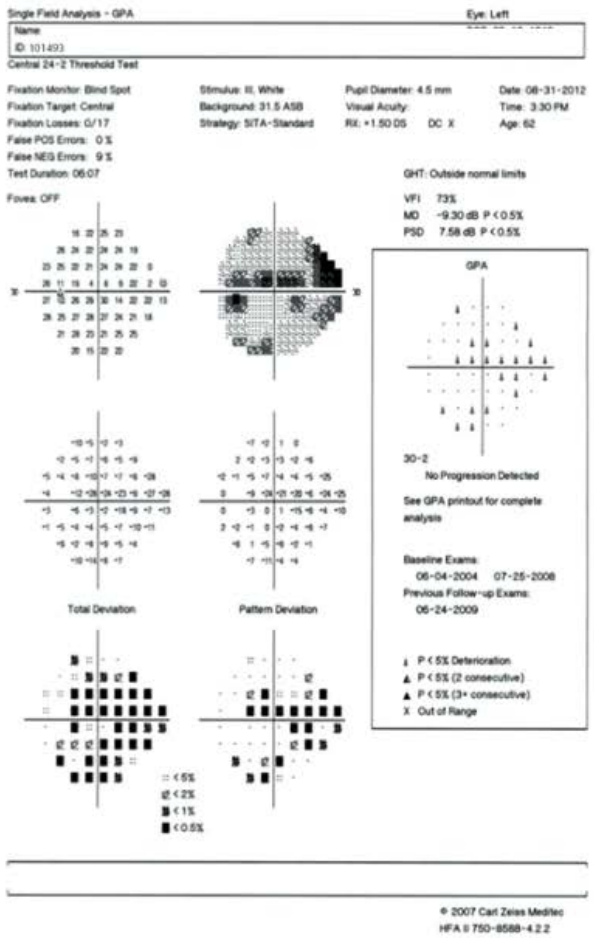
Registration Methods:
R2 - Registration based on translation and rotation of OCT fundus
R1 - Registration based only on translation of disc center

Likely Loss
Possible Loss

Compared to baseline, statistically significant loss of tissue detected. For Average RNFL, Superior RNFL, Inferior RNFL, Rim Area the values have decreased. For Cup-to-Disc Ratios and Cup Volume values have increased.

Possible Increase

Compared to baseline, statistically significant increase detected. For Average RNFL, Superior RNFL, Inferior RNFL, Rim Area values have increased. For Cup-to-Disc Ratios and Cup Volume values have decreased.



Single Field Analysis - GPA

Eye: Left

Name:

ID: 101493

Central 24-2 Threshold Test

Fixation Monitor: Blind Spot
Fixation Target: Central
Fixation Losses: 0/17
False POS Errors: 0 %
False NEG Errors: 9 %
Test Duration: 06:07

Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard

Pupil Diameter: 4.5 mm
Visual Acuity:
RX: +1.50 DS DC X

Date: 08-31-2012
Time: 3:30 PM
Age: 62

GHT: Outside normal limits
VFI 73%
MD -9.30 dB P < 0.5%
PSD 7.58 dB P < 0.5%

Fovea: OFF

GPA

30-2

No Progression Detected

See GPA printout for complete analysis

Baseline Exams:
06-04-2004 07-25-2008
Previous Follow-up Exams:
06-24-2009

P < 5% Deterioration
P < 5% (2 consecutive)
P < 5% (3+ consecutive)
X Out of Range

Total Deviation

Pattern Deviation

< 5%
< 2%
< 1%
< 0.5%

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HFA II 750-8588-4.2.2

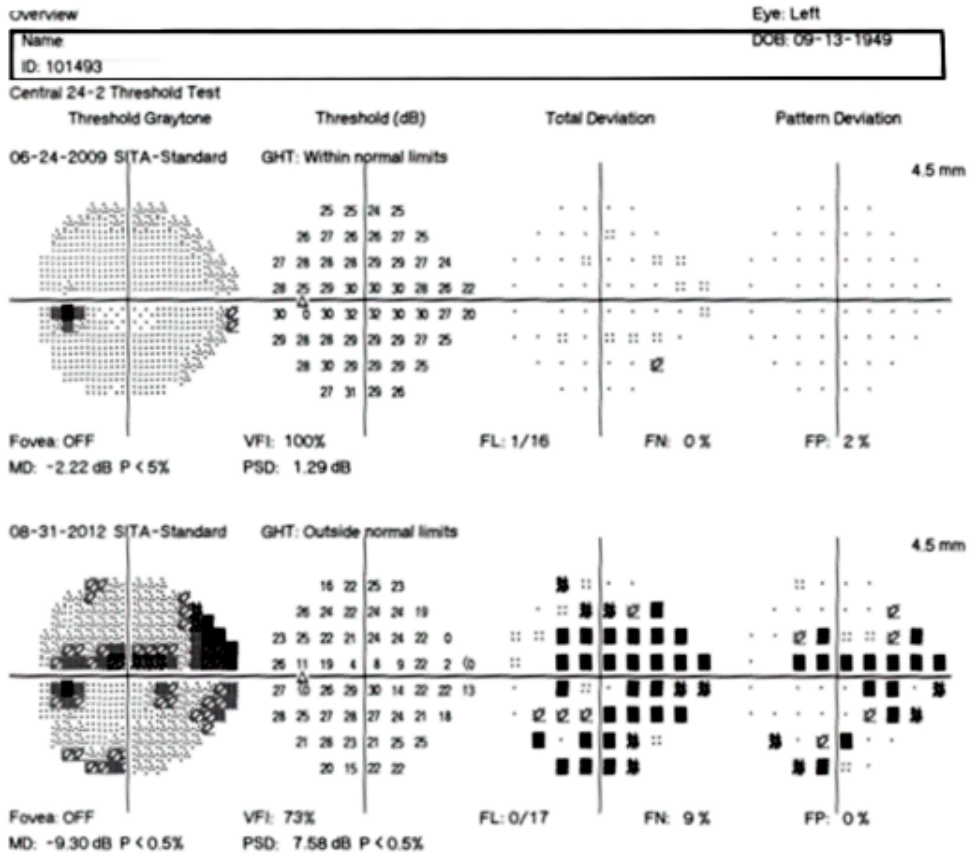
# Case Study: Year 3: Impression

## Severe:

Vision impaired
by glaucoma

## Possible explanations:

- Target inadequate
- IOP fluctuation
- Non-adherent



# Real-World IOP

What can I do to lower IOP to help **reduce** the **risk** of progression today?

- Incisional surgery
- Laser trabeculoplasty
- Modify current medication regimen if additional IOP lowering is required

# What can I do to lower IOP to help **reduce** the **risk** of progression today?

- Incisional surgery

  Indications for surgery include:

  Continued progression despite medical and/or laser treatment1-3

  Target pressure required to prevent progression cannot be reached with topical or laser treatments2,3

  Advanced disease2-4

  Other therapies unsuitable due to side effects or difficulties using therapy appropriately2,3

  Adequate benefit of microinvasive glaucoma surgery (MIGS)

1. *AAO Preferred Practice Pattern*® Guidelines. 2010; 2. European Glaucoma Society Terminology and Guidelines for Glaucoma. 2008; 3. Pepple and Allingham. In: *The Essentials of Glaucoma Surgery*. 2012; 4. Musch et al. *Ophthalmology*. 2009; 5. Saheb and Ahmed. *Curr Opin Ophthalmol*. 2012; 6. Brandão and Grieshaber. *J*

# What can I do to lower IOP to help **reduce** the **risk** of progression today?

- Laser trabeculoplasty
  - Expectations
    - 75% to 85% initial success[1,2]
    - 1- to 5-year duration[3]
    - Up to 20% to 30% drop in IOP[3,4]
    - Continue current medications[3,5]

1. *AAO Preferred Practice Pattern*® Guidelines. 2010; 2. European Glaucoma Society Terminology and Guidelines for Glaucoma. 2008; 3. Juzych et al. *Ophthalmology*. 2004; 4. Nagar et al. *Br J Ophthalmol*. 2005; 5. Damji et al. *Br J Ophthalmol.* 2006; 6. Hong et al. *J Glaucoma*. 2009.

# What can I do to lower IOP to help **reduce** the **risk** of progression today?

- Efficient decision making when changing medical therapy
  - Inadequate benefit from current therapy
  - Additional efficacy desired
  - Maximize IOP lowering, minimize negative impact
    - Side effects
    - Treatment disruptions
    - Visits
    - Calls

# Maximize IOP lowering, minimize negative impact

**Efficacy considerations when changing therapy**

- **When adding a new medication**
  - Single agent vs fixed combination
  - Mechanism of action
  - Expands the probability of specific adverse events
- **When making a change in therapy within class**
  - Generic vs branded
  - Differences among PGAs
  - Adverse events

# IOP Fluctuation Related to VF Progression at Lower IOPs and in More Advanced Disease


- More aggressive IOP reduction
- More advanced disease


- More modest IOP reduction
- Earlier stage disease

1. Caprioli and Coleman. *Ophthalmology*. 2008; 2. Nouri-Mahdavi et al. *Ophthalmology*. 2004; 3. Musch et al. *Ophthalmology*. 2009;
4. Hong et al. *Arch Ophthalmol*. 2007; 5. Lee et al. *Am J Ophthalmol*. 2007; 6. Bengtsson et al. *Ophthalmology*. 2007; 7. Medeiros et al. *Ophthalmology*.

# Multiple IOP Parameters Associated with VF Progression in Treated Glaucoma

- Cohort of the New York Glaucoma Progression Study1
- 587 eyes of 587 patients with repeatable VF loss (minimum 8 HVF)1
- Progression determined by pointwise linear regression1

**Univariate Models of Relationship Between IOP Parameters and Progression Endpoint**[1]

| Parameter | OR (95% CI) | *P* Value |
|---|---|---|
| Mean IOP, per mm Hg higher | 1.10 (1.04-1.17) | < 0.01 |
| Peak IOP, per mm Hg higher | 1.10 (1.06-1.15) | < 0.01 |
| SD IOP, per 0.1 mm Hg higher | 1.03 (1.01-1.04) | < 0.01 |
| Covariance IOP, per mm Hg higher | 1.02 (1.01-1.03) | 0.01 |

**Increased risk of progression is associated with higher mean or peak IOP**

OR = odds ratio; CI = confidence interval; SD = standard deviation

‹#› 1. De Moraes et al. *Arch Ophthalmol.* 2011; 2. Ahrlich et al. *Invest Ophthalmol Vis Sci.* 2010.

# Clinical Insight: Peak IOP May Be an Important IOP-Related Risk Factor for VF Progression

- In the multivariate model, both IOP-dependent and IOP-independent risk factors were associated with progression of treated glaucoma1
  - Peak IOP (OR = 1.13 per 1 mm Hg, $P < 0.01$)
  - CCT (OR = 1.45 per 40 µm thinner, $P < 0.01$)
  - Disc hemorrhage (OR = 2.59, $P < 0.01$)
  - Beta-zone peripapillary atrophy (OR = 2.38, $P < 0.01$)
- Peak IOP (measured during clinic hours) was a strong predictor of progression1

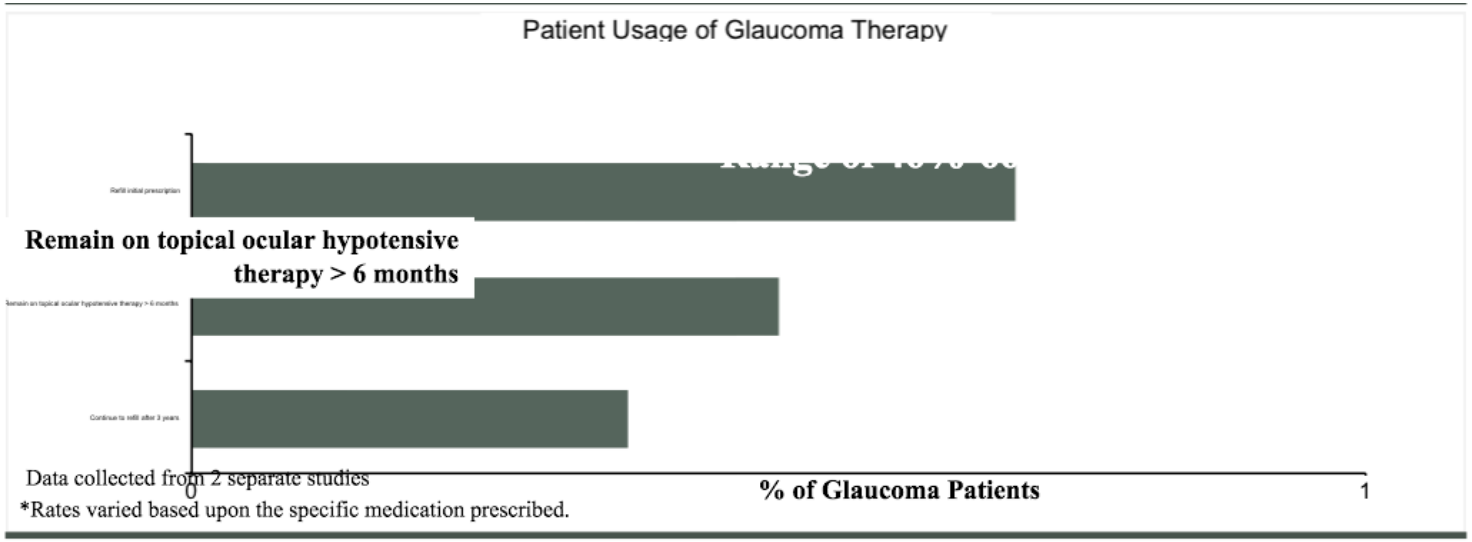
OR = odds ratio

# Real-World IOP: Challenges With Medication

## Medication Challenges

- Simplify regimen when possible
- Maintain easy access to correct medication
  - Tier status
  - Pharmacy location and hours
  - Adequate refills

# Patient Usage of Glaucoma Therapy




- Between 34% and 54% of glaucoma patients did not refill their initial prescription1
- Nearly 50% of glaucoma patients stopped using their topical ocular hypotensive therapy within 6 months2
- At 3 years after first dispensing, 63% did not refill the initially prescribed medication within 60 to 120 days2

# Disruptions in Medical Therapy

**Disruptions in Glaucoma Prescription Regimens1**


- Up to 80% of patients may stop initial therapy after 36 months1
- Nearly 50% of patients may not continue with treatment at 6 months1

**The majority of glaucoma patients have trouble staying *committed* to their prescription regimens**



1. Nordstrom et al. *Am J Ophthalmol.* 2005.

# Common Reasons Patients Stop Therapy

- Patient use of medication may be affected by:
  - Number of agents a patient is taking and the complexity of dosing[1-4]
  - Patient understanding of glaucoma and its treatment[4,5]
  - Patient forgetfulness[2,5]
  - Cost of medication[2]

# Real-World IOP: Monitoring Medication

**At each patient visit**

- Assess efficacy/side effects of current medication
  - Re-evaluate therapy as needed
- Confirm regimen
  - Pharmacy/plan switches
  - If they understand it, they are more likely to follow it!

# Real-World IOP: Managing Patient Calls

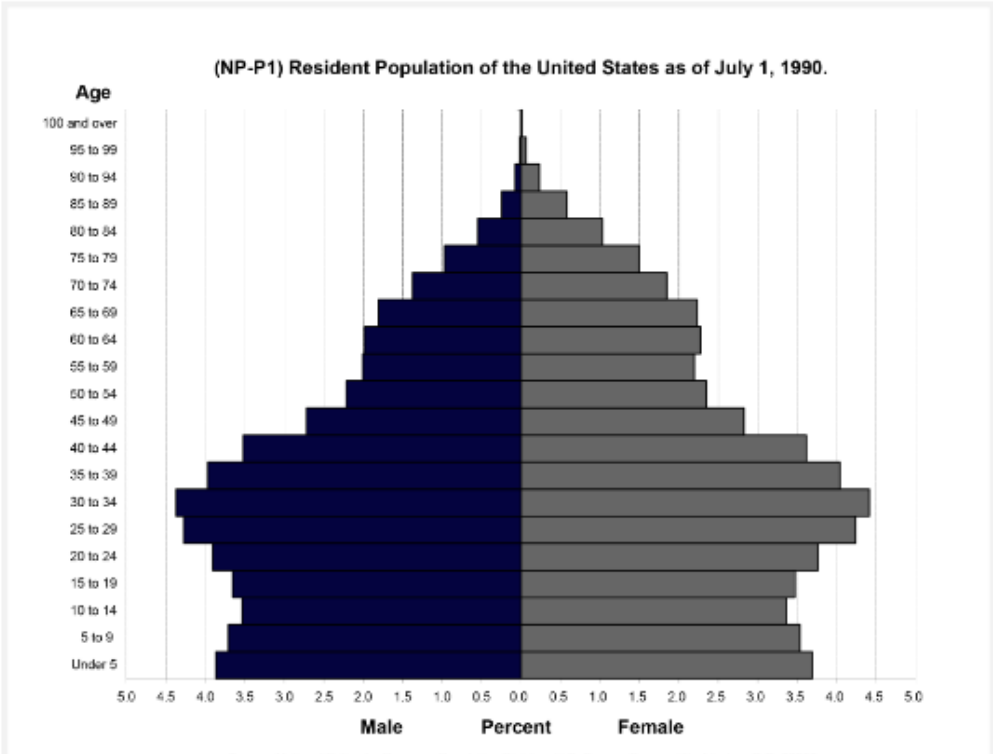

- Minimize unnecessary calls
- Educate the patient
  - Treatment options
  - Involve the patient in decision-making process
- Determine the answers to FAQs
  - Patients
  - Pharmacists
  - Plans

# Clinical Trials Do Not Always Reflect the Real World

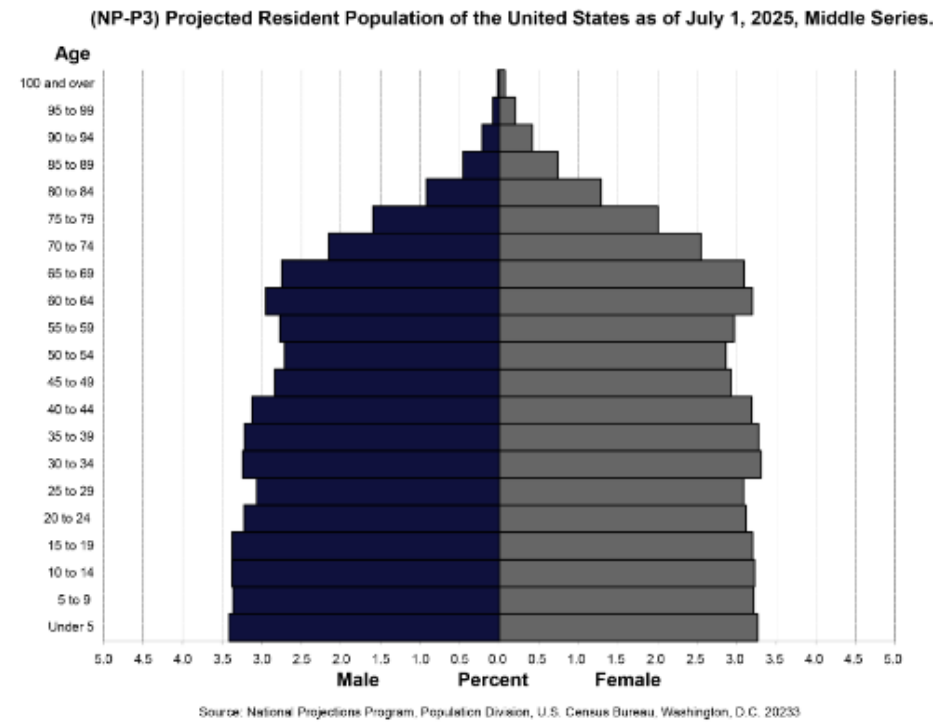
- Patients who enroll in clinical trials meet specific criteria
- Care (and transportation) is often provided at no cost
- Study coordinators provide invaluable encouragement to patients, potentially improving adherence with study protocol and follow-up visits

# United States Population Pyramids: 1990-2025

## Resident Population of the US–1990

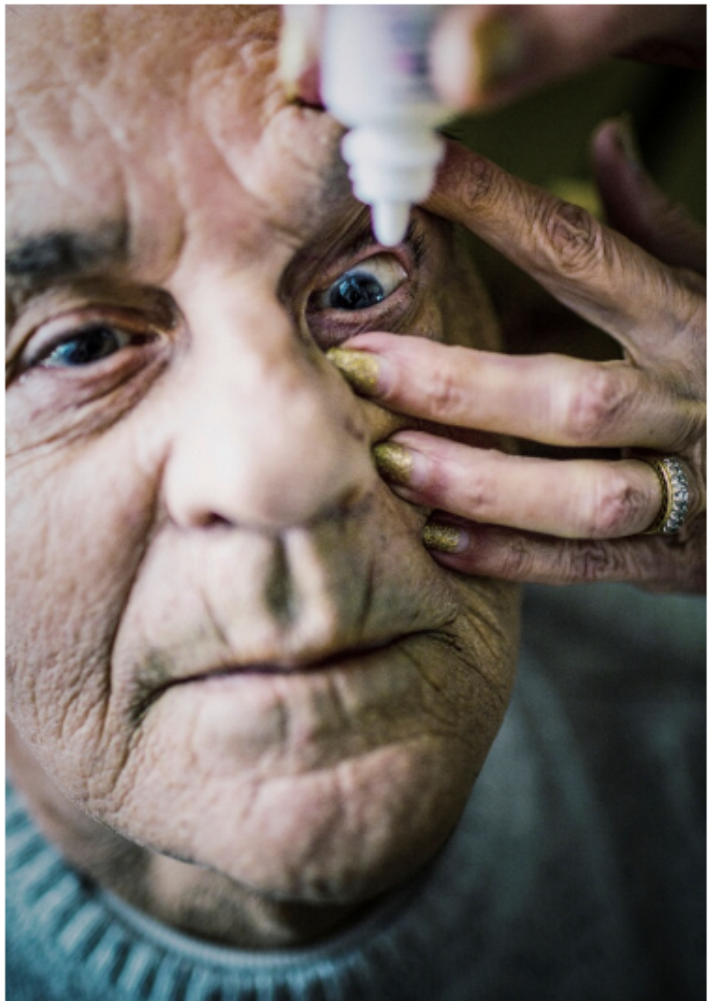



## Resident Population of the US–2025

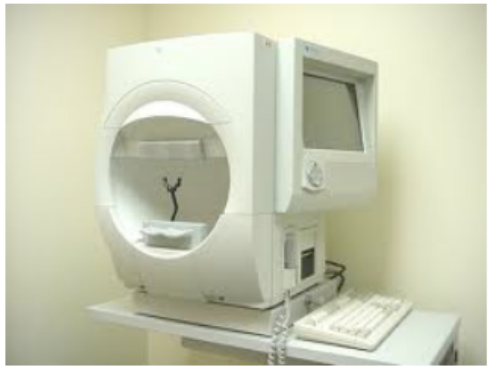


# Challenges of the Very Elderly Patient With Glaucoma

- Medications and the elderly
- Special considerations
  - Technique of instillation
  - Cost
  - Disruptions to therapy
  - Adverse effects
  - Drug interactions
- Topical ocular medications overlooked in medication reviews by primary care doctors
- Implications of systemic effects



# Optic Nerve Imaging and Aging



- Visual field reliability
- IOP-independent factors
  - Blood pressure
  - Ocular perfusion
- Optic nerve imaging and aging
- Cross-sectional studies across wide age range1-3
  - Prior longitudinal studies of disc photos—no significant changes of C/D over time (9-16 years)1,2
  - Challenge of obtaining longitudinal data with changing technologies
  - Computerized planimetry/scanning laser ophthalmoscopy—decrease of neuroretinal rim, increased C/D3

# Optic Nerve Imaging and Aging (cont)

**Budenz DL et al. *Ophthalmol.* 2007.**

- 328 normal subjects (18-85 years old)
- Measured by Stratus OCT
- Primary outcome measures included linear regression analysis of age, ethnicity, axial length, optic disc size on peripheral RNFL thickness
- RNFL thickness decreased by 2.0 μm for every decade of increased age
- Age-related change in RNFL thickness should be taken into account when interpreting the lower limits of the normal range for diagnosis

**Feuer WJ et al. *J Glaucoma.* 2011.**

- 425 normal subjects (18-85 years old)
- Age-related progressive loss of RNFL thickness per decade of age most prominent in superior (-4.3 μm) vs inferior quadrant (-1.5 μm)
- Glaucomatous loss = decline of average thickness more rapidly than fastest rate of age-related decline at the 95% confidence limit

‹#› 1. Budenz et al. *Ophthalmology*. 2007; 2. Feuer et al. *J Glaucoma*. 2011.

# Estimating Risk of Progression

- Statistical computation of lifespan
- Risk of progression
- Projection of progression rates
- Success/failure of interventions

# Real-World IOP

## Maximize IOP lowering, minimize negative impact

- Adequate IOP lowering is critical in managing glaucoma
- Medical therapy and procedures can help lower IOP, when appropriate and adequate
- Use structural and functional assessments to diagnose and monitor patients
- Barriers exist to our current intended therapies
  - A knowledge of the issues at play is essential to successful treatment
  - We cannot accurately measure patient use of medical therapy
- Simplify the medical regimen to give the best chance
- If a patient is getting worse, aim to lower the IOP even more

# Thank You

# CURRICULUM VITAE

## PERSONAL DATA

Name: Todd Dana Severin
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San Ramon, CA 94583
Telephone: (925) 830-8823
Email: tseverin@aol.com
Fax: (925) 866-6610

## EDUCATION

| | |
|---|---|
| Clinical Fellowship: | Baylor College of Medicine<br>Cullen Institute of Ophthalmology<br>Glaucoma Service<br>Ronald L. Gross, M.D., Director<br>Houston, Texas<br>July 1993 - July 1994 |
| Residency: | University of California, San Diego<br>Department of Ophthalmology<br>UCSD Medical Center, San Diego, California<br>July, 1990 - June 1993<br>Chief Resident 1992-1993 |
| Post-graduate Internship: | Kaiser Permanente Medical Center<br>Stanford Medical Center Affiliate Hospital<br>Department of Internal Medicine<br>Santa Clara, California<br>June, 1989 - July, 1990 |
| Medical: | University of California, San Diego<br>School of Medicine<br>San Diego, California<br>Doctor of Medicine with honors<br>1985-1989 |
| Undergraduate: | Pomona College<br>Claremont, California<br>Bachelor of Arts: Behavioral Biology<br>1981- 1985 cum laude |

## PROFESSIONAL APPOINTMENTS

Assistant Clinical Professor, Ophthalmology, University of California, Berkeley

Director Glaucoma Services, East Bay Eye Centers, San Ramon, California

Advisory Panel, University of California, Berkeley Clinical Research Center

Medical Director University of California Glaucoma Certification Program

International Speakers Bureau, Allergan Pharmaceuticals, Alcon Pharmaceuticals, Ista Pharmaceuticals

National Speakers Bureau, Merck Pharmaceuticals, Pfizer Pharmaceuticals, Humphrey Instruments

Assistant Clinical Instructor, Baylor College of Medicine Department of Ophthalmology, Cullen Eye Center, Houston, Texas

Assistant Surgical Director, Flying Samaritans Eye Clinic, Tecate, Mexico

Lecturer, Meiji College of Oriental Medicine, San Francisco, California

JCAHPO Skills Test Examiner, Cullen Eye Center, Houston, Texas

## INTERNATIONAL MEDICAL MISSIONS

Flying Samaritans Ophthalmology Clinic, Tecate Mexico

Opalvision Hong Kong Vision Quest

## ACADEMIC HONORS AND AWARDS

Editorial Science Review Board, *Ophthalmology* 2012

Editorial Science Review Board, *Ophthalmology* 2011

Editorial Science Review Board, *Ophthalmology* 2010

29th Annual Telly Award Winner for Best Health-Related Television Programming, 2009

Editorial Science Review Board, *Ophthalmology* 2009

Gift of Appreciation, Turkish Ophthalmology Society 2008

Editorial Science Review Board, *Ophthalmology* 2008

Editorial Science Review Board, *Ophthalmology* 2007

Editorial Science Review Board, *Ophthalmology* 2006

Moderator, Ocular Symposium, San Francisco 2005

Gift of Appreciation, Hong Kong Ophthalmology Society, Hong Kong, 2005

Gift of Appreciation, Taiwanese Ophthalmologic Society, Taiwan 2005

Maintenance of Certificate, American Board of Ophthalmology 2004

Diplomate National Board of Ophthalmology 2004

Editorial Science Review Board, *Ophthalmology* 2004

Gift of Appreciation, Royal College of Ophthalmic Surgeons, Thailand 2004

Certificate of Appreciation, Singapore Society of Ophthalmology 2004

Dean′s Teaching Recognition, University of California 2004

National Faculty, Clinical Signs of Glaucoma, 2003

Editorial Science Review Board, *Ophthalmology* 2002

National Faculty, Three Targets for Glaucoma Therapy, 2002

Certificate of Recognition, National College of Naturopathic Medicine 2001

National Faculty, Neuroprotection: Bringing Clinical Science to Practice, 2001

Moderator Ocular Symposium 2001

Editorial Science Review Board, *Ophthalmology* 2001

National Faculty, Glaucoma 2000, 2000

Moderator Ocular Symposium, 2000

Outstanding Service Award East Bay Ophthalmologic Society 2000

Annenberg Center for Health Sciences Distinguished Speaker Award 2000

President East Bay Ophthalmologic Society 1999-2000

Certificate of Appreciation, Minneapolis Ophthalmology Society 1998

Vice President East Bay Ophthalmologic Society 1998-1999

Dean's Teaching Recognition, University of California, Berkeley 1998

Dean's Teaching Recognition, University of California, Berkeley 1997

Fellow American Academy of Ophthalmology 1995

Diplomate American Board of Ophthalmology 1994

Chief Resident Department of Ophthalmology, UC San Diego 1992-1993

Diplomate National Board of Medical Examiners 1992

Subintern Moorfield's Eye Hospital, London England 1989

Academic Honors Internal Medicine 1988

Academic Honors Neurology 1988

Lange Medical Publications Award 1987

Cum Laude, Pomona College 1985

Pomona College Dean’s List 1981-1985

Pomona College Scholar for Academic Excellence 1981-1985

Pomona College Honors at Entrance 1981

Bank of America Achievement Award in Science and Mathematics 1981

PUBLICATIONS AND ABSTRACTS (Peer and non-peer reviewed)

Quinones, R., Severin TD., Mundorf T., Efficacy of Bimatorprost 0.03% In Untreated Glaucoma and Ocular Hypertension Patients: Results From a Large Community-Based Clinical Trial, *J Ocul Pharmacol Ther*., 20 (2): 115-22, April 2004

Severin, TD, The Safety and Efficacy of Bimatoprost 0.03% (Lumigan) In a Worldwide Large-Scale Open-Label Clinical Trial. (ARVO Abstract) *Invest Ophthal and Vis Sci*, 45:4 May 2004

Coleman AL, Baerveldt G, Severin TD, et al: Development of Evidence-Based Treatment Recommendations for the Medical Management of Glaucoma. Initial Findings: Definitions of Disease States and Goals of Therapy, (ARVO Abstract*) Investigative Ophthalmology and Visual Science* 44; 4, May 2003

Severin T: Use of Brimonidine Purite in Patients with Previous Allergy to Brimonidine (ARVO Abstract*) Investigative Ophthalmology and Visual Science* 44; 4, May 2003

Bournias T, Noecker R, Severin T, Simmons S: Implementing Three Targets for Glaucoma Therapy, *Supplement to Ocular Surgery News*, Sept 15, 2002

Searle J, Cantor L, Gross R, Severin T, et. al.: Best Practice Treatment Algorithm for Primary Open-Angle Glaucoma: Implications for U.S. Ophthalmology Practice, *Managed Care Interface* 15 (7) 37-48, July 2002

Severin T: How Should I Assess IOP After Myopic Lasik? Ophthalmic Practice, 19(7) 294-296, October 2001

Samuelson T, Cohen J, Kent A, Mundorf T, Severin T, Simmons S, Whitson J: Therapeutic Considerations in Glaucoma Management: Focus on Neuroprotection: *Supplement to Ocular Surgery News*, Nov 1, 2001

Severin T, Monotherapy and Replacement Therapy*, Proceedings of the Ocular Drug and Surgical Therapy Update Meetin*g, July 15, 2001

Samuelson TW, Abelson MB, Cantor LB, DuBiner HB, Noecker RJ, Severin TD, Simmons ST: New Paradigm for the Clinical Management of Glaucoma, *Supplement to Ocular Surgery News*, Sept 15, 2000

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Oram O, Gross RL, Orengo-Nania S, Severin TD: Picosecond Neodymium Lithium Fluoride (Nd:YLF) Laser Peripheral Iridotomy. *American Journal of Ophthalmology* 119(4) 408-414 Apr 1995.

Gross RL, Oram O, Severin TD, Orengo-Nania S, Feldman RM: Gonioscopic Ab Interno Picosecond Nd:YLF Laser Sclerostomy in Human Cadaver Eyes. *Ophthalmic Surgery* 26(2) 136-138 March/April 1995

Oram O, Gross RL, Severin TD, Orengo-Nania S, Feldman RM: Gonioscopic Sclerostomy with the Picosecond Nd:YLF Laser. *Journal of the Turkish Ophthalmic Society, 26th Annual Meeting Supplement* October 1994

Oram O, Gross RL, Feldman RM, Severin TD, Tam C, Orengo-Nania S: Risk Factors for Trabeculectomy Failure at One Year. *Ophthalmology* Supplement 130, October 1994

Oram O, Gross RL, Severin TD, Orengo-Nania S, Feldman RM: Opening of an Occluded Molteno Tube with the Picosecond ND:YLF Laser. *Archives of Ophthalmology* 112:1203 August 1994

Oram O, Gross RL, Severin TD, Orengo-Nania S: A Cadaver Eye Model For Anterior and Posterior Segment Laser Applications. *Ophthalmic Surgery* 25(7) 449-451 July 1994

Severin TD, Oram O, Gross RL, Orengo-Nania S, Font R: A Histopathologic Comparison of Peripheral Iridotomies Performed with the Nd:YLF and Nd:YAG Lasers (ARVO Abstract) *Investigative Ophthalmology and Visual Science* 35:4, March 1994

Gross RL, Oram O, Severin TD, Orengo-Nania S: Gonioscopic Ab Interno Nd: YLF laser Sclerostory in Human Cadaver Eyes (ARVO Abstract) *Investigative Opthalmology and Visual Science* 35:4, March 1994

Oram O, Gross RL, Orengo-Nania S, Severin TD: Picosecond Nd:YLF Laser Peripheral Iridotomy in Human Cadaver Eyes (ARVO Abstract) *Investigative Ophthalmology and Visual Science* 35:4 March 1994

Orengo-Nania S, Severin TD, Oram O, Gross RL: Effect of Atropine on Central and Peripheral Anterior Chamber Depth and Anterior Chamber Angle After Trabeculectomy with and without Atropine (ARVO Abstract) *Investigative Ophthalmology and Visual Science* 35:4 March 1994

Severin TD and Severin SL: Pseudophakic Cystoid Macular Edema: A Revised Comparison of the Incidence with Intracapsular and Extracapsular Cataract Extraction. *Ophthalmic Surgery* 19:2, 1988

Severin TD and Severin SL: A Clinical Evaluation of the Potential Acuity Meter in 210 Cases. *Annals of Ophthalmology*. 20:10, 1988

Munroe R, Munroe R, Brasher A, Severin T, Schweickart D, Moore R: Sex Differences in East African Dreams. *Journal of Social Psychology,* 125:3, 1985

<u>CLINICAL INVESTIGATIONS: FDA PHASE III AND IV</u>

Comparison of CIRRUS Photo Measurements of Ganglion Cell Analysis (GCA) to the Cirrus HD-OCT In Subjects with Glaucoma. Protocol Cirrus photo-GCA-2012-1

Repeatability and Reproducibility of RNFL Thickness and Macular Thickness Measurements of the Cirrus photo and Cirrus Model 4000 in Subjects with Glaucoma and Retinal Disease. Protocol #Cirrus-photo-2011-3

A Study to Evaluate the Clinical and Microbial Efficacy of 0.6% ISV-403 Compared to Vigamox in the Treatment of Bacterial Conjuctivitis. Protocol ISV-403

Patient Dosing with Travatan Using the Travatan Dosing Aid. Alcon Protocol C-05-13

Three Month Clinical Study Comparing the Efficacy and Tolerability of Alphagan and Xalatan as First-line Treatment in Subjects with Chronic Open Angle Glaucoma or Chronic Ocular Hypertension. Allergan #98068

A Four Week Therapy Study of the Efficacy of Travatan 0.004% in Patients Whose IOP is not Adequately Controlled or Who Are Intolerant to Other IOP Lowering Medications. Alcon #CM-01-06

Success of Therapy of Switching to Latanoprost from Previously Failed Monotherapy: Axis Assessing Xalatan in Switched Patients. Pharmacia 912 optt 0091-145

Three Month Multi-center Double-masked Study of the Efficacy of Travoprost 0.004% Timolol 0.5% Ophthalmic Solution Compared to Travatan and Timolol 0.5.% in Subjects with Open Angle Glaucoma or Ocular Hypertension. Alcon C-01-69

A Three Month Multi-center, Double-masked Study of the Safety and Efficacy of Travoprost 0.004% Timolol 0.5% Dosed Comcomitantly in Subjects with Open-Angle Glaucoma or Ocular Hypertension. Alcon C-01-70

IOP Lowering Efficacy of Bimatoprost and Latanoprost as Adjunctive Agents in Subjects Presently Using Brimonidine. Allergan 1875.

A Multicenter, Ranodmized, Double-Masked Comparison of the Efficacy of Lumigan versus Travatan in African Americans with Glaucoma or Ocular Hypertension. Allergan Pharmaceuticals.

A Three Month Study Comparing the Efficacy and Tolerability of Brimonidine and Latanoprost as First Line Treatment for Chronic Open Angle Glaucoma: Allergan Pharmaceuticals. WIRB approval #980868

A Three Month Clinical Study Comparing the Efficacy and Tolerability of Alphagan and Xalatan in Subjects with Chronic Open Angle Glaucoma or Chronic Ocular Hypertension Already on Beta Blockers: Allergan Pharmaceuticals. WIRB approval #961199

A Twelve-Month, Triple-Masked, Parallel Group, Primary Therapy Study of the Safety and Efficacy of AL-6221 0.005% and AL-6221 0.004% Compared to Timoptic 0.5% and Xalatan 0.005% in Patients with Open-Angle Glaucoma or Ocular Hypertension. Alcon Laboratories Protocol C-97-71.

An Ascending, Multiple-Dose, Double-Masked, Parallel Placedbo-Controlled (4 Week) Tolerabilllity Study Of Pirenzepine Ophthalmic Gel With An

Extension Providing One Year Of Treatment In Myopic Children. Valley Forge Pharmaceuticals Protocol No. Pir-201.

A Three-Month Assesment of Alphagan in Elderly Patients Stabilized on Chronic Beta Blocker Therapy: University of Arizona #1012197.

Johns Hopkins Glaucoma Surgical Outcomes Study (GSOS). Multicenter Clinical Investigation.

Tolerability of Brimonidine-P 0.15% in Patients with Prior Allergic Response to Brimonidine 0.2%. Allergan #1805

A Four-Week, Primary Therapy Study to Compare IOP-Lowering Efficacy of Travatan 0.004% in African-American Patients in Open-Angle Glaucoma or Ocular Hypertension Treated with Latanoprost 0.005%. Alcon #CM-01-02 IRB 1764 Pharmaceuticals.

A Four Week Therapy Study of the Efficacy of Travatan T.M. 0.004% in Patients Whose IOP Is Not Adequately Controlled or Who Are Intolerant to Other IOP Lowering Medications. Alcon Clinical Protocol #CM-01-06

Success of Therapy of Switching to Latanoprost from Previously Failed Monotherapy Axis Assessing Xalatan in Switched Pateints. Pharmacia 912 Optt 0091-145 (PRN 00-035)

## SCIENTIFIC POSTER PRESENTATIONS

Severin, TD, The Safety and Efficacy of Bimatoprost 0.03% (Lumigan) In a Worldwide Large-Scale Open-Label Clinical Trial. Presented at the Annual Meeting of the Association of Research In Vision and Ophthalmology, Fort Lauderdale Fl, May 2004

Severin T: Use of Brimonidine Purite in Patients with Previous Allergy to Brimonidine. Presented at Annual Meeting of the Association of Research in Vision and Ophthalmology, Fort Lauderdale FL, May 2003

Coleman AL, Baerveldt G, Severin TD, et al: Development of Evidence-Based Treatment Recommendations for the Medical Management of Glaucoma. Initial Findings: Definitions of Disease States and Goals of Therapy.

Presented at Annual Meeting of the Association of Research in Vision and Ophthalmology, Fort Lauderdale FL, May 2003

Severin T, Severin S, Hecker M: Effect of Lasik on the Retinal NFL. Paper presented at Annual Meeting of the Association of Cataract and Refractive Surgery. Philadelphia PA, June 2002

Lee D, Gross R, Mundorf T, Severin T for the Lumigan Early Experience Study: Efficacy and Safety of Bimatoprost 0.03% (Lumigan) in a Large-scale, Open-label Clinical Trial. Paper presented at: Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale FL, May 2002

Noecker R, Cantor L, Katz J, Katzman B, Kent A, LeBlanc R, Severin T: An Evaluation of Brimondine Use in Elderly Patients Previously on Chronic, Nonselective Beta-Blocker Therapy for Glaucoma. American Academy of Ophthalmology Meeting, New Orleans LA, November 2001

Myers J, Severin TD, Feldman RM: Visual Improvement Following Trabeculectomy. American Academy of Ophthalmology Meeting, New Orleans LA, October 1998

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Rad CN, Boren RA, Fortune B, Schneck ME, Severin TD: Selective S-cone System Loss in Glaucoma and Glaucoma Suspects Measured with Isoluminant VEP's. ARVO Annual Meeting, Ft. Lauderdale, Fl April 1997

Oram O, Gross RL, Feldman RM, Severin TD, Tam C, Orengo-Nania S: Risk Factors for Trabeculectomy Failure at One Year. American Academy of Ophthalmology Meeting, San Francisco CA, October 1994

Severin TD, Oram O, Gross RL, Orengo-Nania S, Font R: A Histopathologic Comparison of Peripheral Iridotomies Performed with the Nd:YLF and Nd:YAG Lasers. ARVO Annual Meeting, Sarasota FL March 1994

Gross RL, Oram O, Severin TD, Orengo-Nania S: Gonioscopic Ab Interno ND: YLF laser Sclerostory in Human Cadaver Eyes. ARVO Annual Meeting, Sarasota FL March 1994

Oram O, Gross RL, Orengo-Nania S, Severin TD: Picosecond Nd:YLF Laser Peripheral Iridotomy in Human Cadaver Eyes. ARVO Annual Meeting, Sarasota Fl, March 1994

Orengo-Nania S, Severin TD, Oram O, Gross RL: Effect of Atropine on Central and Peripheral Anterior Chamber Depth and Anterior Chamber Angle After Trabeculectomy with and without Atropine. ARVO Annual Meeting, Sarasota Fl, March 1994

TEXTS

"Combination Drug Therapy for Glaucoma," *The Glaucoma Book*, Editors Paul Schaknow and John Samples, Springer Science and Business Media, 2010

"Post-operative Complications "*Introduction to Cataract Surgery: Pre-operative, Intraoperative and Post-operative considerations.* Quality Eye Care Alliance. Editor: Mark Richard Mandel, 1995

INVITED LECTURE PRESENTATIONS (2000 to present: full list available)

Medical Management in Glaucoma: Presented at the Cleveland Glaucoma Update, Cleveland, April 26, 2012

Medical Management in Glaucoma: Presented at the Pittsburgh Glaucoma Update, Pittsburgh, April 25, 2012

Medical Management in Glaucoma: Presented at the Kansas City Glaucoma Update, Kansas City, April 24, 2012

Lumigan 0.1% - Lowering IOP Therapy. ASCRS booth presentation, ASCRS Meeting Chicago , April 21, 2012

Medical Management in Glaucoma: Presented at the Southern California Glaucoma Conference, Hollywood, Jan 21, 2012

Therapeutic Update in Glaucoma: Presented at the Fresno Glaucoma Update, Fresno, Dec 14 2011

Therapeutic Update in Glaucoma: Presented at the Minnesota Glaucoma Update, Nov 12, 2011

Medical Management in Glaucoma: Presented at the Harrisburg Glaucoma Update, Minneapolis, Nov 11, 2011

Glaucoma and Low Tension Glaucoma: Presented at the Pittsburg Glaucoma Meeting, Pittsburgh, Nov 1, 2011

Therapeutic Update in Glaucoma: Presented at the Central Valley Glaucoma Update, Modesto, Feb 28, 2011

Medical Management in Glaucoma: Presented at the Southern California Glaucoma Conference, Hollywood, Feb 21, 2011

Therapeutic Update in Glaucoma: Presented at the Minnesota Glaucoma Update, Nov 27, 2010

Medical Management in Glaucoma: Presented at the Minneapolis Glaucoma Update, Minneapolis, Nov 26, 2010

Glaucoma and Low Tension Glaucoma: Presented at the Pittsburg Glaucoma Meeting, Pittsburgh, Nov 1, 2010

Medical Management in Glaucoma: Presented at the Canadian Glaucoma Update Meeting, Montreal, Canada, Oct 12, 2010

Medical Management in Glaucoma: Presented at the Canadian Glaucoma Update Meeting, Hamilton, Canada, Oct 11, 2010

Medical Management in Glaucoma: Presented at the Canadian Glaucoma Update Meeting, Quebec, Canada, Oct 10, 2010

Low Tension Glaucoma, Presented at the Houston Area Glaucoma Update, Houston TX, Oct 3, 2010

Commonly Asked Questions in Glaucoma, Allergan Glaucoma update, Los Angeles Ca, May 25, 2010

Commonly Asked Questions in Glaucoma, Allergan Glaucoma update, Long Beach Ca, May 16, 2010

Commonly Asked Questions in Glaucoma, Allergan Glaucoma update, Los Gatos Ca, May 5, 2010

Medical Management in Glaucoma: Presented at the Canadian Glaucoma Update Meeting, Winnipeg, Canada, April 7, 2010

Medical Management in Glaucoma: Presented at the Canadian Glaucoma Update Meeting, Vancouver, Canada, April 6, 2010

Medical Management in Glaucoma: Presented at the Canadian Glaucoma Update Meeting, Toronto, Canada, April 5, 2010

Updates In Glaucoma, Presented at the Houston Area Glaucoma Update, Houston TX, March 13, 2010

Low Tension Glaucoma, Presented at the Central Coast Glaucoma Update, Santa Maria, Feb 3, 2010

Medical Management in Glaucoma: Presented at the PrimeTime Ocular Meeting, Wailea, HI, Dec 6, 2009

Management of Ocular Trauma: Presented at the PrimeTime Ocular Meeting, Wailea, HI, Dec 6, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Minneapolis Glaucoma Meeting, November 19, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the South Houston Glaucoma Meeting, Oct 1, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Houston Glaucoma Meeting, Sept 30, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Victoria Glaucoma Meeting, Sept 30, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Vancouver Glaucoma Meeting, Sept 28, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Winnipeg Glaucoma Meeting, Sept 27, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Quebec Glaucoma Meeting, Sept 26, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Pittsburgh Glaucoma Dinner, May 27, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Toronto Ophthalmologic Society Meeting, May 26, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Ontario Society Meeting, May 25, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Montreal Glaucoma Meeting, May 24, 2009

Commonly Asked Questions about Modern Glaucoma Therapy: Presented at the Santa Barbara Ophthalmologic Society Meeting, May 20, 2009

Update on Glaucoma Therapy: Presented at the Allergan Glaucoma Update: Cleveland, OH, Apr 4, 2009

Update on Glaucoma Therapy: Presented at the Allergan Glaucoma Update: Phoenix, Az, Mar 24, 2009

Glaucoma in Refractive Surgery; Presented at the Canadian National Glaucoma Young Guns Meeting, Miami, Florida, Dec 8, 2008

New Insights into Neuroprotection: Presented at the Turkish National Ophthalmologic Meeting, Antalya, Turkey, Nov 18, 2008

Updates on Glaucoma; Presented at the Houston Glaucoma Symposium, Sept 20, 2008

Prostaglandin Therapy in Glaucoma, Presented at the Southern Californian Glaucoma Symposium; Newport Beach, July 28, 2008

New Strategies for Monitoring and Treating Glaucoma: Presented at the National Glaucoma Society Meeting, Las Vegas, NV, Feb 17, 2008

Controversies in Glaucoma: Presented at the National Glaucoma Society Meeting, Las Vegas, NV Feb 17, 2008

New Adjunctive Therapy for Glaucoma: Presented at the El Paso Eye Society Meeting, El Paso TX, Feb 15, 2008

New Approach towards Intraocular Pressure: Presented at the Houston Glaucoma Dinner, Houston TX, Jan 13, 2008

New Strategies in Glaucoma: Presented at the Austin Glaucoma Meeting, Austin TX, Nov 15 2007

New Strategies in Glaucoma: Presented at the Western Regional Consultants Meeting, San Diego CA, May 20, 2007

Update on Glaucoma: Presented at the Oregon Optometric Annual Meeting, Bend Oregon, May 18, 2007

Surgical Therapies in Glaucoma: Presented at the National Glaucoma Symposium West, Newport Beach CA, July 2006

Controversies in Glaucoma: Presented at the National Glaucoma Symposium West, Newport Beach CA, July 2006

New Diagnostic Modalities for Glaucoma: Presented at the Ocular Symposium, San Francisco CA, June 2006

Importance of IOP in Glaucoma: Presented at the Southwest Glaucoma Meeting, Phoenix AZ, March 2006

The Art of Pain Management: Presented at OptoWest COA Annual Meeting, Long Beach CA, March 2006

Optic Disc Evaluation in Glaucoma: Presented at OptoWest COA Annual Meeting, Long Beach CA, March 2006

Advances in Glaucoma Diagnostics: Presented at SECO Meeting, Atlanta GA, Feb 2006

Developments in Medical Therapy for Glaucoma: Presented at the West Coast Regional Consultants Meeting, Las Vegas, NV, Feb 2006

Optic Nerve Evaluation in Glaucoma: Presented at the Las Vegas Ophthalmology Society Meeting, Nov 2005

Digital Imaging in Glaucoma: Presented at the UC Berkeley Primetime Meeting, Kona, Hawaii Nov 2005

FORGE and REAL Efficacy: Presented at the East Coast Regional Consultants Meeting, Washington DC Oct 2005

FORGE and REAL Efficacy: Presented at the West Coast Regional Consultants Meeting, Newport CA, June 2005

Advances in Medical Treatment of Glaucoma: Presented at the Ocular Symposium, San Francisco CA, June 2005

New Developments in Glaucoma: Presented at the Hong Kong Ophthalmologic Society Meeting, Hong Kong, June 2005

FORGE and REAL Efficacy: Presented at the East Coast Regional Consultants Meeting, Atlantic City NJ, May 2005

Reframing Glaucoma Diagnosis: Presented at the Taiwan Ophthalmologic Society, Taipei, Taiwan, Nov 2004

Refractive Surgery Complications: Presented at the PrimeTime Annual Ocular Disease Conference, Waikailoa, HI, Nov 2004

Concerns with Pain Management: Presented at the PrimeTime Annual Ocular Disease Conference, Waikailoa, HI, Nov 2004

Evaluation of the Optic Disc in Glaucoma: Presented at the PrimeTime Annual Ocular Disease Conference, Waikailoa, HI, Nov 2004

Diagnosing Progression In Glaucoma: Presented at the California Optometric Association Annual Meeting, Monterey Ca, Nov 2004

Glaucoma Concerns In the Refractive Surgery Patient: Presented at the California Optometric Association Annual Meeting, Monterey Ca, Nov 2004

Reframing Glaucoma Diagnosis: Presented at the Northern California Glaucoma Advisory Board, Sonoma CA, Oct 2004

Halting Glaucoma Progression: Presented at the Save Sight Symposia, Phuket, Thailand, July 2004

Luminary Ideas for Halting Glaucoma Progression; Keynote Lecture Address, Presented at the 13th Meeting of the Royal College of Ophthalmic Surgeons, Thailand, Bangkok, Thailand, July 2004

New Glaucoma Medications, Presented at the Singapore/Malaysia Joint Ophthalmology Conference, Singapore, May 2004

How to Diagnosis and When and How to Treat Glaucoma, Presented at the Singapore/Malaysaia Joint Ophthalmology Conference, Singapore, May 2004

Weight of the Evidence: Need for IOP Lowering in Glaucoma Treatment, Presented at the Western Regional Glaucoma Conference, Newport Beach, Ca April 2004

Glaucoma Concerns with Refractive Surgery, Presented at the Southern Oregon Optometric Society Meeting, Redmond OR, March 2004

Update on Glaucoma Diagnosis and Management, Presented at the Western Australia Ophthalmology Society, Perth Australia, March 2004

Update on Glaucoma Diagnosis and Management, Presented at the Southern Australia Ophthalmology Society, Adelaide Australia, March 2004

Update on Glaucoma Diagnosis and Management, Presented at the Tasmanian Ophthalmology Society, Hobart Australia, March 2004

Evaluation of the Optic Nerve, Presented at the Keynote Address, Allergan Glaucoma Symposium, American Academy of Ophthalmology, Anaheim Ca, October 2003

Dimensions in Diagnosis and Treatment of Glaucoma, Presented at the Western Regional Glaucoma Symposium, San Diego Ca, May 2003

Neuroprotection in Glaucoma: Presented at the California Optometric Association Annual Meeting, Anaheim Ca, April 2003

The Science Behind Vitamin and Herbal Supplementation for Ocular Disease: Presented at the California Optometric Association Annual Meeting, Anaheim Ca, April 2003

New Paradigms in Glaucoma Management: Presented at the San Joaquin Valley Eye Society Annual Meeting, Stockton Ca, Feb 2002

Surgical Therapy for Glaucoma: Presented at the University of California, Berkeley Practicum, Berkeley Ca, Nov 2002

Mono Versus Dual Therapy for Glaucoma: Presented at the American Academy of Ophthalmology Annual Meeting, Orlando Fl, October 2002

Neuroprotection: The Third Target for Glaucoma Therapy: Presented at the Three Targets Meeting, Seattle Wa, Oct 2002

OHTS and AGIS: Impact on Clinical Practice: Presented at the San Diego Ophthalmologic Society Meeting, San Diego Ca, Sept 2002

Neuroprotection: The Third Target for Glaucoma Therapy: Presented at the Three Targets Meeting, St. Louis Mo, Sept 2002

Advances in Glaucoma Therapy: Presented at the Ocular Symposium, San Francisco CA. June 2, 2002

Three Targets for Glaucoma Therapy: Presented at the EBOS Regional Meeting. Berkeley CA, May 28 2002

Medical Concerns of Lasik in the Glaucoma Patient: Presented at the Sarver Lecture Series. Berkeley CA, April 20, 2002

New Thoughts in Glaucoma: Presented at OptoWest, Sacramento CA, April 5, 2002

Herbal and Vitamin Therapy for Ocular Disease: Presented at OptoWest, Sacramento Ca, April 5, 2002

Interaction of Lasik and Glaucoma: Presented at the VisionQuest Symposium, Chicago IL, August 12 2001

Neuroprotection: Connecting Research to Practice. Presented at the Slack National Neuroprotection Conference. Boston, May 24, 2001

Evaluation of Mono vs Dual Therapy for Glaucoma, Presented at the Ocular Drug and Surgical Therapy Update, Laguna Nigel, CA, February 10, 2001

New Concepts in Neuroprotection, Presented at the Southwest Regional Glaucoma Symposium, Tucson, AZ, January 26, 2001

Neuroprotection: Presented at the Los Angeles Regional Glaucoma Symposium, Los Angeles, CA, November 4, 2000

Glaucoma 2000: Presented at the Annenberg Center for Health Sciences Seminar, Seattle WA, November 2, 2000

Relationship of Lasik and NFL: Presented at the American Academy of Ophthalmology Annual Meeting, Dallas TX, October 20, 2000

New Paradigm in Glaucoma Management: Presented at the American Academy of Ophthalmology Annual Meeting, Dallas TX, October 21, 2000

How Do I Assess IOP After Lasik? Presented at the American Academy of Ophthalmology Annual Meeting, Dallas TX, October 20, 2000

New Paradigm in Glaucoma Medical Management: Presented at the Hawaiian Ophthalmology Society, Honolulu HI, Oct 8, 2000

Glaucoma 2000: Presented at the North Carolina Regional Glaucoma Symposium. Charlotte, NC, Sept 21, 2000

PROFESSIONAL SOCIETIES

American Academy of Ophthalmology
American Glaucoma Society

West Coast Glaucoma Society
Association for Research in Vision and Ophthalmology
American Society of Cataract and Refractive Surgeons
California Ophthalmology Association
Contra Costa/Alameda Medical Association
East Bay Ophthalmologic Society

MEDICAL SERVICE INFORMATION

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| Specialty: | Clinical Practice specialized in the medical and surgical treatment of glaucoma, cataract surgery and intraocular lens. |
| Hospital Affiliations: | San Ramon Regional Medical Center<br>Alta Bates Medical Center, Berkeley<br>John Muir Hospital, Walnut Creek |
| Office Locations: | 5801 Norris Canyon Road #200<br>San Ramon, CA 94583<br>(925) 830-8823<br><br>University of California, Berkeley<br>Ophthalmology Clinic<br>Berkeley, CA 94720<br>(510) 642-0996 |