Innovations in Glaucoma
Next Generation Technology, Medications, and Delivery
Vance Thompson Vision, Sioux Falls, South Dakota
Optometric Externship Director

Financial Disclosure – Justin Schweitzer, OD, FAAO
- Aerie
- Alcon
- Allergan
- Bausch + Lomb
- Ocular Therapeutix
- EyePoint
- Sight Sciences
- Dompe
- Modern Optometry – Co-Chief Medical Editor

Today’s Optometrists
“To be on the cutting edge of optometry, you need to be on the cutting edge of science and technology.”

Influences on IOP Measurement
- CCT
- Post-Refractive
- Time of Day
- Medications
- Physical Activity and Posture

Poll Question

How are you currently measuring intraocular pressure in your glaucoma patients?

A. Rebound Tonometry (iCare or TonoPen)
B. GAT
C. Ocular Response Analyzer
D. NCT
E. Other

The Correcting Applanation Tonometer Surface (CATS)


IOP “corneal-compensated” (IOPcc)

213 Eyes of 125 glaucomatous patients followed for 2.4 years

- GAT: 11.1% (.11)
- ORA: 24.5% (.24)
- RBT: 5.8% (.05)
Home IOP Monitoring

A device is intended as an adjunct for monitoring IOP of adult patients (self-use). The HOME tonometer is designed for use at home or on the go.

Continuous IOP Sensors

What is Triggerfish?

Smart Contact Lens - A soft, disposable silicone contact lens with an embedded micro-sensor that captures circumferential changes near the corneoscleral junction. Triggerfish is measuring ocular volume change over a 24-hour period. Ocular volume change is associated with the eye's ability to handle increases in pressure as they are related to tissue elasticity.

Implandata Eyemate

- Sulcus based IOP sensor
- 8 pressure-sensitive capacitors
- Diameter: 11.2 mm
- Thickness: 0.9 mm

ARGOS Study: 1 year results

- 6 Patients
- 4/6 developed post-op AC inflammation
- 6/6 pupil distortion, PDS, narrowing of angle
ARGOS-02 Trial: 1 year results

- 22 Patients
- Major Design Changes:
  - 0.9 to 0.5mm thickness with 0.1mm rounded tapering
  - 4 haptics to prevent ciliary sulcus rotation
- IOP Concordance:
  - D30:
    - Eyemate: 22.2 ± 9.2 mmHg
    - GAT: 19.5 ± 6.8 mmHg
  - D360:
    - Eyemate: 15.7 ± 3.8 mmHg
    - GAT: 14.1 ± 2.2 mmHg

Sensors on the horizon...

- AcuMEMS (Menlo Park, CA)
  - Sense System: implantable sensor
- Glaukos (San Clemente, CA)
  - DOSE Medical IOP Sensor
- Implantdata Ophthalmic Products GmbH
  - Suprachoroidal IOP sensor
- Injectsense Inc (Emeryville, CA)
  - Configurable on-demand sensor
- LaunchPoint Technologies (Goleta, CA)
  - Sensor attached to IOL or injected into vitreous
- Solx (Waltham, MA)
  - Wireless intraocular sensor

Corneal Hysteresis, IOP, CCT

- Corneal Hysteresis reflects the ability of the corneal tissue to dissipate energy
- Function of viscoelastic damping

Two predictive functions
1. Which glaucomatous eyes are most susceptible to visual field loss progression and risk of rate of progression?
2. Which eyes are susceptible to glaucoma?
Average CH in Normal Subjects

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<tr>
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<th>460 eyes of 334 glaucoma patients Follow-up – 4.3 years Well controlled if IOP &lt; 18 mm HG</th>
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147 eyes of 96 glaucoma patients Follow-up – 3.5 years

Choroidal thickness

Lower IOP change

Low Corneal hysteresis

Each 1 mmHg lower CH = 0.66 microns of posterior ALCS displacement


Resulting SITA Faster 24-2C Pattern on HFA3

Objective Visual Field Testing

FDA 510(k) Cleared

Tests OU simultaneously in 7 minutes

Measures the response of the pupils to a stimulus
OCT-Angiography

Images retinal and peripapillary microvasculature without dye injection

Displays structure and function from a single imaging system

Trend Analysis

Poll Question

I currently utilize telemedicine to manage __% of my glaucoma patients:

A. 100%
B. 75%
C. 50%
D. 25%
E. 0%
Evaluation of an AI system for the automated detection of glaucoma from stereoscopic optic disc photographs: the European Optic Disc Assessment Study

- Objectives - To evaluate the performance of a deep learning based Artificial Intelligence (AI) software for detection of glaucoma from stereoscopic optic disc photographs, and to compare this performance to the performance of a large cohort of ophthalmologists and optometrists.
- Results
  - Pegasus was able to detect glaucomatous optic neuropathy with an accuracy of 83.4% (95% CI: 77.6–89.2)
  - This is comparable to an average ophthalmologist / optometrist accuracy of 80.5% / 80% respectively (95% CI: 67.2–93.8) / (95% CI: 67–88) on the same images.
  - There was no statistically significant difference between the performance of the deep learning system and ophthalmologists or optometrists.

Rogers, TW, Jaccard, N., Carbonara, F. et al. Eye 2019. DOI:10.1038/s41433-019-09519-0

Nitric Oxide
Endogenous in the human body
Causes alterations in the cytoskeletal network
Reduced NO in TM, Schlemm’s canal, and ciliary muscle


Nocturnal IOP Lowering


latanoprostene bunod 0.024% (Vyzulta)

latanoprost ophthalmic emulsion 0.005% (Xelpros)

BAK-free latanoprost ophthalmic emulsion

Swollen Micelle Microemulsion (SMM) Technology

Reduces IOP up to a mean of 6 mmHg to 8 mmHg in randomized clinical trials
netarsudil 0.02% (Rhopressa)

- ROCK inhibitors
- Prostaglandin analogs
- Alpha agonists
- Beta blockers
- Alpha agonists

MDA
- aqueous humor production
- trabecular outflow
- episcleral venous pressure

Schlemm’s canal
- trabecular meshwork
- Unopened outflow

PUBL-0121
- netarsudil 0.02% (Rhopressa)

- Prostaglandin analogs
- Alpha agonists
- Beta blockers
- Alpha agonists
- CAIs
- ROCK inhibitors

Increased from 0.27 ± 0.10 ul/min/mmHg to 0.33 ± 0.11 ul/min/mmHg

Diurnal EVP decreased from 7.9 ± 7.9 mmHg to 7.2 ± 1.8 mmHg

- RHO protein kinase (destabilizes actin in TM)
- Rock inhibitor (lowers EVP)
- Latanoprost (uveoscleral outflow)
- NET Inhibition (decrease aqueous production)

PATIENTS, %

IOP REDUCTION FROM BASELINE, %

Mean IOP reduction at 3 months

Ocular AEs

Conjunctival Hyperemia

51.0%

Cornea Verticillata

51.0%

Conjunctival Hemorrhage

85.2%


- Diurnal Outflow Facility

- The Effects of Netarsudil Ophthalmic Solution on Aqueous Humor Dynamics in a Randomized Study to Increase Diurnal Outflow Facility

- Mean ± SD: In treated eyes from baseline change in Diurnal Outflow Facility from 0.27 ± 0.10 ul/min/mmHg to 0.33 ± 0.11 ul/min/mmHg, a change of 0.06 ± 0.20 ul/min/mmHg (95% confidence interval: 0.01, 0.11). In placebo eyes, no change in Diurnal Outflow Facility from baseline change of 0.30 ± 0.11 ul/min/mmHg to 0.30 ± 0.11 ul/min/mmHg, a change of 0.00 ± 0.12 ul/min/mmHg (95% confidence interval: -0.03, 0.03). The change in Diurnal Outflow Facility between treatment and placebo groups was 0.06 ± 0.20 ul/min/mmHg (95% confidence interval: 0.02, 0.11), indicating treatment efficacy. In treated eyes, 94.4% of subjects maintained their baseline change in Diurnal Outflow Facility compared to 80.7% of subjects in the placebo group. The change in IOP at 3 months was 0.0 ± 0.0 mmHg in treated eyes and 0.0 ± 0.0 mmHg in placebo eyes, indicating no change from baseline in treated and placebo eyes. The sum of the changes in IOP at 3 months in treated eyes compared to placebo was 0.0 ± 0.0 mmHg (95% confidence interval: -0.03, 0.03), indicating no difference in IOP change between groups.

- IOP REDUCTION FROM BASELINE, %

- PATIENTS, %

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- Mean IOP reduction at 3 months


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- PATIENTS, %

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Poll Question

I have recommended, referred, or comanaged a patient with a glaucoma drug delivery device:

A. Yes
B. No

More than 90% of patients are nonadherent to their ocular medication dosing regimens, and nearly 50% discontinue taking their medications before 6 months.

Poll Question

What would be the minimal length of efficacy of a glaucoma drug delivery or procedure for you to recommend it to your glaucoma patient?

A. 3 months  
B. 6 months  
C. 12 months  
D. Greater than 12 months

Patients Attitudes Towards Drug Delivery

Triple Combination Eye Drop – 85%  
Microdose Eye Spray – 54%  
Drug-eluting Contact Lens – 31%  
Drug-eluting Periocular Ring Insert – 43%  
Injectable Subconjunctival Drug Insert – 32%  
Injectable Anterior Chamber Implant – 30%


Microdose latanoprost  
(Eveliova)

Delivers microdoses of latanoprost with Optejet delivery  
Advantages: 75% less drug and preservative  
Achieved 29% IOP lowering from baseline in Phase 2 study


Bimatoprost Ring  
(Allergan)

\[ \text{Baseline} = 23.9 \text{ mmHg} \]
\[ \text{1 mo} = 18.7 \text{ mmHg} \]
\[ \text{6 mo} = 18.8 \text{ mmHg} \]

Retention Rate – 89%
Conjunctival Hyperemia – 14.1%


Retention Rate – 89%
Conjunctival Hyperemia – 14.1%

Punctal Plug Delivery System
(Mati Therapeutics)

Latanoprost and Travoprost designs

U.S. Phase II Multi-center Trials (Lower Puncta)
Glau 12 (n=92) – 96% retention rate
Glau 13 (n=87) – 92% retention rate

Phase II Clinical Study
L-Enkate – 5.5 mmHg IOP lowering over 12 weeks study

Travoprost Intracanalicular Insert
(Ocular Therapeutix)

Bioreabsorbable sustained-release intracanalicular insert
Designed for continuous steady-release of travoprost to the ocular surface for up to 90 days

Preservative free
Allows visualization

Low Ocular Adverse Events:
Globe reactions – 0.2%
Lacrimal structure disorder – 0.6%
### Travoprost Intracanalicular Insert
(Ocular Therapeutix)

Phase III randomized, double-blind, placebo-controlled clinical trial

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<th>2 Week</th>
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Diurnal Time Points

#### Bimatoprost SR (Allergan)

- Biodegradable bimatoprost sustained-release implant
- FDA-approved and indicated to reduce IOP in patients with open angle glaucoma or OHT
- Single intracameral administration
- Phase I/II/III Studies

**Bimatoprost SR (Allergan)**

(10-microgram bimatoprost sustained-release implant)

**24 Month Phase I/II Clinical Trial**

- **bimatoprost pellet** (6, 10, 15, or 20 micrograms)
- **topical bimatoprost 0.03%**

75 subjects

24 Month Phase I/II Clinical Trial

Bimatoprost pellet

(6, 10, 15, or 20 micrograms)

Topical bimatoprost 0.03%

24 months – IOP reduction
7.5, 7.3, 7.3, 8.9 mm Hg

24 months – IOP reduction of 8.2 mm Hg

No Rescue or Retreatment

68% - 6 mos.
40% – 12 mos.
28% – 24 mos.

Conclusion: Noninferior to timolol administered as an eye drop twice a day.

2 x 20 Month Phase III (ARTEMIS)

- The device as implanted intracameral at 4-month intervals for 1 year (Office-based procedure)
- 1,112 subjects
- Durysta vs 2 x topical timolol
- 30% IOP reduction from baseline over 12 week primary efficacy period

Phase III (ARTEMIS 3)

- The device as implanted intracameral at 4-month intervals for 1 year (Office-based procedure)
- 742 subjects
- Durysta vs 2 x topical timolol
- Baseline IOP 24 mm Hg
- At 1 Year IOP maintained at 16-17 mm Hg

*80% - additional 12 months without retreatment

Travoprost Intracameral Implant

(Ocular Therapeutix)

Biodegradable sustained-release implant injected into the AC

Goal: Steady release of travoprost with target duration from 4 to 6 months

**Phase 1, prospective, multi-center, open label**

- **Cohort 1** (n=5)
  - (15 micrograms)
  - Cohort 1: 6.7 - 7.5 mm Hg (n=5)
  - *Mo. 6 – 7.5 mm Hg (n=5)

- **Cohort 2** (n=4)
  - (26 micrograms)
  - Day 28: 8.0 mm Hg (n=4)
  - Mo. 4 – 4.0 mm Hg (n=4)
  - *Mo. 4 – 4.0 mm Hg (n=4)

- **Cohort 3** (n=4)
  - (15 micrograms, Fast Degrading)
  - Day 28: 8.0 mm Hg (n=4)
  - Mo. 4 – 4.0 mm Hg (n=4)
  - *Mo. 4 – 4.0 mm Hg (n=4)

- **Cohort 4** (n=3)
  - (15 micrograms)
  - Day 28: 8.0 mm Hg (n=3)
  - Mo. 4 – 4.0 mm Hg (n=3)
  - *Mo. 4 – 4.0 mm Hg (n=3)

Travoprost Intracameral Implant

(Ocular Therapeutix)

Phase I, prospective, multi-center, open label

- **Cohort 1** (n=5)
  - (15 micrograms)
  - Day 28: 8.0 mm Hg (n=5)
  - Mo. 4 – 4.0 mm Hg (n=4)
  - *Mo. 4 – 4.0 mm Hg (n=4)

- **Cohort 2** (n=4)
  - (26 micrograms)
  - Day 28: 8.0 mm Hg (n=4)
  - Mo. 4 – 4.0 mm Hg (n=4)
  - *Mo. 4 – 4.0 mm Hg (n=4)

- **Cohort 3** (n=4)
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- **Cohort 4** (n=3)
  - (15 micrograms)
  - Day 28: 8.0 mm Hg (n=3)
  - Mo. 4 – 4.0 mm Hg (n=3)
  - *Mo. 4 – 4.0 mm Hg (n=3)
Travoprost intraocular implant

(Alcon)

Resides in AC angle, anchored behind TM

- Length: 1.8 mm
- Diameter: 0.5 mm
- Titanium
- Non-ferrous

24-Month Update

Average IOP reductions from baseline = 7.9 mm Hg and 7.4 mm Hg in the fast and slow release arms.

Favorable safety profile with no SIC loss, no corneal adverse events, no adverse events of conjunctival hyperemia

Iontophoresis

Electrical field generated by a low-level current to enhance the mobility of charged particles. Applicator placed on the conjunctiva at the limbus and a generator connected to an electrode attached to the patient’s forehead. The generator creates an electric field inside the applicator and an opposite charge on the electrode.

Nanoparticles with ocular hypotensive agents delivered in a sustained-release strategy into the conjunctival tissue to produce once-monthly treatment for glaucoma

Refractive Capsule

(Reveral)

- Drug delivery
- Biometric sensors
- Lens technology
Common Belief:
Glaucoma is a 1 Pressure Disease

Likely Truth
Glaucoma is a 2 Pressure Disease


ICP changes with age

CSF pressure

BERDAHL REN OHT Control POAG NTG
We are Pressurized

Treatment in glaucoma

Technological is nothing.
What's important is that you have a faith in people, that they're basically good and smart, and if you give them tools, they'll do wonderful things with them.