New Developments in Glaucoma
Colorado Optometric Association
Denver, Colorado
July 17, 2017

Disclosure
- Speakers Bureau for Alcon, Allergan, Biotissue, Centervue, Oculus, Optovue, Synemed

What's New With Tonometry?
Can We Calculate a Corrected IOP based Upon CCT?
Icare® ic100

- New design
- Enhanced Ergonomics
- Clinically robust
- Easy to use
- Accurate
- Precise

Icare® AMS: Automatic Measurement Sequence

Select between two modes:

Series mode: Press the measurement button for a sustained period of time (more than 2 seconds) and the tonometer will take six samples in rapid succession.

Single mode: In this mode, the measurement button must be pressed each time to initiate measurement (six samples – a complete measurement cycle).
Rebound Technology

- Easy-to-use
- Quick, effective routine barely noticeable by the patient
- Revolutionizes early glaucoma detection and control
- No topical anaesthetics or disinfection needed
- Disposable probe touches the cornea very lightly
- Suitable also for non-compliant patients and children
- Proven accurate by several independent studies
- Truly portable

Measurement Basics

- The probe touches the cornea very gently
- Measurement takes place in 0.1 seconds
- Corneal reflex after 0.2 seconds
- Measurement of motion parameters
- To be repeated 6 times in order to minimize deviation and to produce a calculated measurement value
- Whole procedure (6x both eyes) takes about one minute

Rebound Tonometry is Accurate

- Bench testing
- Repeatability (coefficient of variation): <8%

<table>
<thead>
<tr>
<th>Range of IOP</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>≤ 20 mmHg</td>
<td>± 1.2 mmHg</td>
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<tr>
<td>&gt; 20 mmHg</td>
<td>± 2.2 mmHg</td>
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Clinical Studies

**REPRODUCIBILITY AND TOLERABILITY OF THE ICARE REBOUND TONOMETER IN SCHOOL CHILDREN**

*Measurement of intraocular pressure (IOP) with the rebound tonometer (RBT) is a highly reproducible method in schoolchildren showing high intraobserver and interobserver correlation and it seems to be very comfortable when performing IOP measurements in schoolchildren without an anesthetic.*

Sahin A, Basmak H, Niyaz L, Yildirim N. J Glaucoma. 2007 Mar;16(2):185–8

**AGREEMENT OF REBOUND TONOMETER IN MEASURING INTRAOCULAR PRESSURE WITH THREE TYPES OF APPLANATION TONOMETERS**

"iCare agrees well with applanation tonometers"

Nakamura M, Darhad U, Tatsumi Y, Fujoka M, Kusuhara A, Magda H, Negi A


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**Icare HOME: Comparison With Goldmann**

- 130 patients
- Compared IOP measured using Icare HOME by patient to IOP measured by Icare HOME unit and GAT by an OMD
- 98%, (128/130) were able to correctly conduct self-measurement
- Mean IOP
  - GAT: \(12.2 \pm 2.8\) mm Hg
  - HOME patient: \(12.8 \pm 3.7\) mm Hg
  - HOME OMD: \(13.1 \pm 3.8\) mm Hg

Takagi, D; Sawada, A et al. Glaucoma: July 2017; 26(7): 613–618

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**Results (cont.); Conclusion**

- The IOP difference between the HOMEp and GAT measurements was >3 mm Hg in 9.4% of cases (12/128), and >5 mm Hg in 2.3% of cases (3/128).
- Difference between HOMEp and GAT values was significantly increased with increasing CCT \((P=0.024)\), indicating that a 10% increase in CCT predicted a 1.2% increase in the difference.
- Conclusion: The Icare HOME tonometer is feasible for use in self–monitoring of IOP. Icare HOME tonometry measurements tend to overestimate IOP relative to GAT measurements.
Annette

- 69yoWF referred with large cups
- IOP
  - R 16, 11, 14 mmHg
  - L 18, 13, 16 mmHg
  - (three separate exams)
- ORA IOP R 15.3  L 17.5  CH R 9.8  L 9.9
- CCT R 599  L 603
Should we do 10–2 Visual fields?

Prevalence and Nature of Early Glaucomatous VF Defects on 10–2

- 100 glaucomatous eyes with 24–2 MD < 6dB
  - Tested with 10–2
- As many abnormal 10–2 hemifields (53%) as abnormal 24–2 hemifields (59%).
- Of the eyes with normal 24–2 hemifields, 16% were classified as abnormal with the 10–2 test
- Of the abnormal 10–2 hemifields, 68%, 8%, and 25% were arcuatelike, widespread, and other, respectively
- Superior VF defects were deeper and closer to fixation than those in the inferior VF

Conclusion

- The 10–2 VF was abnormal in nearly as many hemifields as was the 24–2 VF, including some with normal 24–2 VF, suggesting that the 24–2 test is not optimal for detecting early damage of the macula.
- The pattern of the defects was in agreement with a recent model of macular damage.

10–2 vs. 24–2 VF Progression Analysis in Glaucoma

- Compare the efficacy of 10–2 vs. 24–2 VFs in detecting progression of initial parafoveal scotoma (IPFS) in glaucomatous eye
- 50 eyes followed for 5.7 years
- Ave. of 7.7 VF’s obtained

Results

- Mean global progression rate was significantly greater in 10–2 analysis (−0.40±0.51 dB/yr) than in 24–2 analysis (−0.23 ± 0.28 dB/yr) (P=0.01).
- Within the central 10 degrees of VF, 10–2 analysis detected significantly more progressing eyes than 24–2 analysis (24 vs. 7 eyes; P<0.001).
- Within the central 10 degrees, mean localized progression rate (−1.3 vs. −0.4 dB/yr) and mean number of progressing points (2.5 vs. 0.5) were significantly greater in 10–2 than in 24–2 analyses (10–2 vs. 24–2; all P<0.001).
Conclusion

- In glaucoma patients with an IPFS, the 10–2 VF detects more progressing eyes than the 24–2 VF, suggesting that closer surveillance of the central VF using 10–2 VF is warranted in these eyes.

Comparing Glaucoma Progression on 24–2 and 10–2 Visual Field’s

- Compared mean deviation change on 10–2 and 24–2 VF’s
- 167 eyes with glaucoma
- Mean of 9 VF’s obtained over 9 years FU
- Compared the rates of MD change in eyes with different severities of VF loss (early [MD better than –6 dB], moderate [–6 dB to –12 dB], advanced [–12 to –20 dB] and severe [MD worse than –20 dB]) at baseline (based on the MD on 24–2 VF)
- Median rate of MD change was comparable in mild (–0.45 dB/year vs. –0.40 dB/year, P = 0.42) and moderate (–0.32 dB/year vs. –0.40 dB/year, P = 0.26) VF loss categories
- Significantly greater on 10–2 VFs in advanced (–0.28 dB/year vs. –0.21 dB/year, P = 0.04) and severe (–0.18 dB/year vs. –0.06 dB/year, P<0.001) VF loss categories

Does blood flow to the optic nerve matter in glaucoma?
The Evidence Against Blood Supply as a Risk Factor for Development of Glaucoma

Factors NOT Predictive

- Ocular Hypertension Treatment Study
  - Migraine
  - Cerebral vascular accident
  - High OR low blood pressure
  - Use of oral Beta blockers, Calcium channel blockers
  - Diabetes
- Early Manifest Glaucoma Trial
  - High blood pressure
  - Cardiovascular disease
  - Migraine or Raynaud’s Disease
  - Smoker (current or prior)

What About Normal Tension Glaucoma??
Collaborative NTG Study
No added risk

- Blood pressure
- Pulse rate
- Cardiac arrhythmia
- Major cardiovascular crisis
  - Hypotension
  - Shock
  - Blood transfusion
  - Major surgery

Risk factors for progression of VF abnormalities in NTG AJOP: 2011; 131:699-708

Risk Factors That Did Not Affect Risk of Progression

- Cardiovascular disease
  - HTN
  - Angina
  - Myocardial infarction
- Diabetes mellitus
- Peripheral vascular disease
- Raynaud phenomenon
- Anemia
- Tendency for low blood pressure
- Family history of DM and stroke

World Glaucoma Association

1. Glaucoma Diagnosis 2004
2. Glaucoma Surgery
3. Angle Closure
4. IOP
5. Glaucoma Screening
7. Medical Treatment
8. Progression
9. Childhood Glaucoma
10. Diagnosis of POAG 2013
WGA Consensus on Blood Flow

- Ft. Lauderdale on May 2, 2009
- Goals:
  - To obtain consensus on the relationship between ocular blood flow and glaucoma
  - To establish a foundation for OBF research of glaucoma and the best practice for its testing in clinical practice.
- Consensus statements and comments based on published literature and expert opinion


Consensus Points

- Blood Pressure is positively correlated with IOP.
- It is unclear whether the level of BP is a risk factor for having or progressing OAG in an individual patient.
- Lower OPP is a risk factor for primary OAG.
- OBF parameters measured with various methods are impaired in OAG, especially in NTG.
- Vascular dysregulation may contribute to the pathogenesis of glaucoma, more likely in people with lower IOP.


Conclusion

- “The relationship among BP, IOP and development of OAG is complex and requires further investigation.”

Ocular Perfusion Pressure and Glaucoma

Ocular Perfusion Pressure: Terminology
- OPP – Ocular Perfusion Pressure
- SPP – Systolic Perfusion Pressure
- DPP – Diastolic Perfusion Pressure
- MPP – Mean Perfusion Pressure

\[
\text{SPP} = \text{SBP} - \text{IOP} \\
\text{DPP} = \text{DBP} - \text{IOP} \\
\text{MPP} = \frac{2}{3} \text{mean arterial pressure} - \text{IOP} \\
\text{Arterial Pressure} = \text{DBP} + \frac{1}{3}(\text{SBP} - \text{DBP})
\]
OPP and Glaucoma: Population Studies

Baltimore Eye Survey
- AA and Caucasian

Egna–Numarkt Study
- Caucasian

Barbados Eye Study
- African–Caribbean

Proyecto Ver
- Hispanic

OPP: Proyecto VER

Lavon 2/11

- 36yo WF referred as glaucoma suspect
- MH: no illnesses; no migraines
- VA 20/15 OU
- Ta: R 26 L 25
- CCT: R 595 L 608
- DCT: R 28 L 23
Lavon 3/11

- Ta: R 27 L 27
- BP: 109/66
- DOPP: 66 – 27 = 39

Plan:
- Advised of ORB of Rx vs. no Rx, asymptomatic nature of early glaucoma and need for careful FU
- Will follow without Rx for now

Low ocular perfusion pressure (OPP) (the difference between systemic blood pressure and intraocular pressure) is associated with increased prevalence of open-angle glaucoma in cross-sectional studies.

Comments: The value of OPP monitoring in daily clinical practice is not established. Due to the intrinsic relationship between OPP and IOP, it is difficult to establish an independent contribution of OPP as a risk factor for the development of glaucoma.


Lower IOP improves OPP

Higher systemic BP improves OPP but don’t necessarily want to raise BP
- Stroke #3 cause of death in US behind CVD and CA!
- Avoid drugs that lower systemic BP beyond patient’s desired systemic control
- Avoid nocturnal hypotension
Nocturnal Hypotension and OPP

- Low BP at night, coupled with high IOP in supine position, compromise OPP
- Using systemic BP meds in the AM to minimize nocturnal hypotension makes sense
- Using IOP lowering drugs that lower IOP while sleeping makes sense
- Avoiding IOP meds that LOWER systemic BP at night (beta blockers, alpha agonists) makes sense

Graham, Drance, Surv Ophthalmol. 1999;43(suppl 1):S10-16

Diurnal v. Nocturnal Effect of Medications

IOP is Higher at Night

PURPOSE: To characterize the 24 hr pattern of IOP in untreated patients

METHODS:
- 24 untreated patients with newly diagnosed glaucomatous optic discs and/or abnormal visual fields
- 24 hr IOP values obtained with a pneumotonometer at 2 hr intervals, in the sitting and supine position during the diurnal/wake period and in the supine position during the nocturnal/sleep period

IOP is Higher at Night

Travoprost Diurnal/Nocturnal

Nocturnal and Diurnal Habitual IOP
Comparing Diurnal and Nocturnal Effects of Brinzolamide and Timolol on IOP in Patients Receiving Latanoprost Monotherapy

**Results:**

- **Diurnal period,** the mean IOP under brinzolamide or timolol add-on treatment was significantly lower than the baseline IOP in both the sitting and supine positions. There was no statistical difference between the 2 add-on treatments.
- **Nocturnal period,** the supine IOP under brinzolamide add-on treatment was significantly lower than both the baseline and the timolol add-on treatment.
- There was no difference in nocturnal IOP between the timolol add-on treatment and the baseline.


44 eyes in 22 NTG patients

IOP measured at 10AM, 1PM, 4PM, 10PM, 1AM, 3AM

Goldmann in sitting position

Latanoprost as primary, Brinzolamide as adjunct

**Diurnal mean IOP reduction:**
- latanoprost and brinzolamide=19.8%, latanoprost=14.1%, P<0.001
- **Nocturnal mean IOP reduction:**
  - latanoprost and brinzolamide=13.4%, latanoprost=10.0%, P<0.05

Diurnal and Nocturnal Effects of Brimonidine Monotherapy on Intraocular Pressure

John H. E. Liu, PhD, Felipe A. Maloney, MD, PhD, J. Rhyg Slat, MD, Robert N. Williams, MD

- 0.1% brimonidine TID for 4 weeks
- Results: The diurnal IOP mean was significantly lower than the baseline IOP in both the sitting and supine positions.
- No statistically significant change in IOP under the brimonidine treatment from the baseline during the nocturnal period.

Liu JH et al AJO 2010

Brimonidine Habitual Position

- Cross over study of effect of different classes of IOP lowering meds on DPP
  - PGA and CAI significantly increased DPP at all time points
  - Beta-blocker significantly increased DPP from 4AM to 4PM but had no effect at other times
  - Alpha agonist significantly reduced DPP at multiple time points, primarily due to significant decrease in systemic BP

Effects of Bimatoprost and Timolol on Circadian IOP, BP and OPP

- OHTN or OAG patients treated with bimatoprost 0.01% QD or timolol 0.5% bid
- Measured IOP, BP, HR, OPP after 8 weeks
- Mean 24h IOP was significantly lower after 8 weeks of treatment with bimatoprost 0.01% than timolol 0.5% bid (15.7 vs 16.8 mmHg, p = 0.0003).
- Mean IOP during the day was significantly reduced from baseline by both drugs while mean IOP during the night was reduced by -2.3 mmHg (p = 0.0002) by bimatoprost and by -1.1 mmHg by timolol 0.5% bid (p = 0.06).
- Timolol 0.5% significantly reduced the mean 24h systolic BP from baseline, the diastolic BP during the day hours, the HR during the night hours, and the mean 24h systolic OPP.


Conclusion

- Both Bimatoprost 0.01% and Timolol 0.5% are effective in reducing the mean 24h IOP from an untreated baseline but Bimatoprost 0.01% is more effective than timolol 0.5% throughout the 24h.
- Timolol 0.5% effect on IOP is reduced during the night hours and is associated with reduced BP, HR and ocular perfusion pressure.


Beta Blockers

- Patients using topical beta blockers had:
  - Lower minimum nocturnal heart rate
  - Lower minimum nocturnal DBP
  - Greater percentage drop in nocturnal DBP1
- Timolol:
  - Controversial
  - Most studies report no significant or rather unfavorable results.2
- Betaxolol:
  - Reports vary: beneficial or not significant
  - More favorable than Timolol

PGA’s, CAI’s

- Prostaglandin Analogues: Latanoprost, Bimatoprost and Travoprost
  - Generally show beneficial effects on retrobulbar hemodynamics
- Carbonic Anhydrase Inhibitors (CAI’s)
- Dorzolamide, Brinzolamide:
  - Reports mixed but more showed positive effects on OBF
  - Others showed no significant effect

Consensus Point

- Certain drugs, even when formulated in an eye drop, may have an impact on ocular blood flow and its regulation.
  - Comment: The impact of eye drop related changes in OBF on the development and progress of glaucoma is unknown.
  - Some data support increased blood flow and the enhancement of OBF regulation with CAI’s. These appear to exceed what one would expect from their ocular hypotensive effect alone.

Efficacy of Latanoprostene Bunod 0.024% Compared With Timolol 0.5% in Lowering Intraocular Pressure Over 24 Hours

- Compared the diurnal and nocturnal effects of latanoprostene bunod with timolol maleate 0.5% solution on IOP and ocular perfusion pressure (OPP)
- 25 patients with OHTN or early OAG
- Baseline IOP and blood pressure were measured in a sleep lab Q2H in the sitting and supine positions during the 16-hour diurnal/wake period and in the supine position during the 8-hour nocturnal/sleep period
- Subjects were randomly assigned to bilateral treatments of latanoprostene at 8 PM or timolol at 8 AM and 8 PM.
- The second laboratory recording occurred after the 4-week treatment. Subjects were crossed over to the comparator treatment for 4 weeks before the third laboratory recording.
- Mean IOP and calculated ocular perfusion pressure were compared for the diurnal and nocturnal periods.

There was a significant IOP reduction with the latanoprostene bunod treatment during the diurnal/wake period and during the nocturnal/sleep period compared to baseline. The nocturnal IOP-lowering effect of latanoprostene bunod appeared less than the effect during the diurnal period. Posture was not a factor for the relatively smaller nocturnal IOP-lowering effect, since both the 24-hour supine IOP profile and the 24-hour habitual IOP profile showed comparable diurnal vs nocturnal IOP reductions from the baselines.

Latanoprostene bunod

- There was a significant IOP reduction with the latanoprostene bunod treatment during the diurnal/wake period and during the nocturnal/sleep period compared to baseline. The nocturnal IOP-lowering effect of latanoprostene bunod appeared less than the effect during the diurnal period. Posture was not a factor for the relatively smaller nocturnal IOP-lowering effect, since both the 24-hour supine IOP profile and the 24-hour habitual IOP profile showed comparable diurnal vs nocturnal IOP reductions from the baselines.
Discussion

- Low OPP has been proposed as a risk factor for glaucomatous damages. Alteration of OPP pressure can occur by changes in BP and/or IOP. Although the mean arterial blood pressure did not change significantly under either test agent of latanoprostene bunod or timolol over the 24-hour period, the latanoprostene treatment increased the diurnal OPP over the baseline owing to a significant IOP reduction during the diurnal period. Treatment with timolol showed no significant effect on diurnal OPP, probably because of a relatively smaller IOP reduction. Results also showed a greater nocturnal OPP under the latanoprostene treatment compared to the timolol treatment, reflecting the smaller effect of timolol on IOP lowering combined with some reduction in MAP. The latanoprostene treatment is expected to be more beneficial than the timolol treatment if one considers the difference in ocular perfusion pressure during the day and at night.

Summary

- Treatment with latanoprostene bunod 0.024% once daily resulted in IOP lowering during the diurnal/wake period as well as during the nocturnal/sleep period. Treatment with latanoprostene bunod showed a greater nocturnal IOP-lowering efficacy compared to treatment with timolol 0.5% solution twice daily. Latanoprostene bunod treatment significantly increased diurnal ocular perfusion pressure from the baseline. Ocular perfusion pressure during the nocturnal period was higher under latanoprostene bunod treatment than under timolol treatment.
Minimally Invasive Glaucoma Surgery (MIGS)

- Bypass trabecular meshwork or use suprachoroidal approach
- Usually performed in conjunction with cataract surgery
- More effective in lowering IOP than Phaco alone
- Easier for surgeon and patient than trabeculectomy though less effective
- May reduce or eliminate dependence on meds

MIGS Procedures Being Investigated

- Suprachoroidal Approach
  - CyPass Micro-Stent (Transcend Medical, Inc)
- Trabecular Bypass
  - Trabectome (NeoMedix Corporation)
  - iStent Trabecular Micro-Bypass Stent (Glaukos)
  - iStent Supra (Glaukos Corporation)
  - Hydrus Microstent (Ivantis, Inc.)
  - AqueSys Implant (AqueSys, Inc.)

Nguyen, QH Combined Cataract Surgery and MIGS: Which Procedures will be a Match Made in Heaven? Glaucoma Today; March-April 2013

iStent® (Glaukos)
Indication For Use

The iStent Trabecular Micro-Bypass Stent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication.
Specifications

iStent is the smallest medical device known to be implanted in the human body and weighs just 60 µg

- Dimensions are customized for a natural fit within the 270 µm canal space
- Made of surgical-grade nonferromagnetic titanium
- Heparin-coated to promote self-priming

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Specifications

<table>
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<th>iStent Specifications</th>
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<tr>
<td>Length: 1 mm</td>
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<td>Height: 0.3 mm</td>
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<td>Snorled: 120 µm (inner diameter)</td>
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- Surgical-grade, nonferromagnetic titanium
- Heparin-coated to promote self-priming
Therapeutic Objectives

Designed to be used in conjunction with cataract surgery to safely and effectively reduce IOP while facilitating the eye’s natural outflow in mild to moderate OAG patients.

- Lowers IOP while helping to reduce medication burden
- Decrease risk of IOP fluctuations associated with non-adherence to prescription medication regimens
- Avoid serious complications associated with end-stage filtration and shunt procedures
- Spare the conjunctiva and safely preserve future treatment options
- Minimizes risks of hypotony and bleb related complications

*ab interno* trabecular micro-bypass stent for the treatment of glaucoma:

- Placed in inferonasal locations with high presence of collector channel congregations
- Designed to improve continuous, physiological outflow in the lower nasal quadrants

Injector System
Snorkel in TM

- Rails are seated against scleral wall of Schlemm's canal
- Snorkel sits parallel to the iris plane

Surgical Procedure
Surgical Procedure

- Rails are seated against scleral wall of Schlemm's canal
- Snorkel sits parallel to the iris plane
One Day Postop

Single iStent + Cataract Surgery Achieves IOP < 15 mm Hg Through 3 Years

- Consecutive series of 62 eyes: decision to implant based on patient desire to reduce topical meds and intent to offer surgical treatment with favorable safety profile
- In consistent cohort of 39 eyes followed through 36 months, mean IOP was 14.9 mm Hg, a 36% reduction
- Over same period, mean number of topical meds declined from 1.8 to 0.3 or 86%


Long-Term Data Through 5 Years

- Prospective, non-comparative, uncontrolled, non-randomized, interventional case series
- 19 patients with uncontrolled mild to moderate OAG using 1 or more topical glaucoma medications
- Results after mean follow-up of 54 months
- 42% of all patients were medication free, with mean IOP reduction to 16.1 mm Hg
- Mean IOP declined to 16.1 mm Hg versus preoperative medications IOP of 19.4 mm Hg
- Number of topical medications used declined from 1.3 to 0.8

Which is better? 1 or 2? Or 3?

- 1, 2 or 3 iStents in OAG subjects on drops
  - 1 stent: 38; 2 stents 41; 3 stents 40
  - 12 month IOP reduction unmedicated IOP ≤ 15 mmHg
    - 1 stent: 64.9%
    - 2 stents: 85.4%
    - 3 stents: 92.1%
  - 18 months, mean unmedicated IOP
    - 1 stent: 15.9 ± 0.9 mmHg
    - 2 stents: 14.1 ± 1.0 mmHg
    - 3 stents: 12.2 ± 1.1 mmHg
  - Month 18 IOP reduction was significantly greater (P<0.001) with implantation of each additional stent, with mean of 1.84 mmHg for three-stent vs two-stent groups and 1.73 mmHg for two-stent vs one-stent groups.

Katz LJ Clinical Oph 11 December 2015
More to come

Cypass Shunt

Approved for use in conjunction with cataract surgery

Supra–ciliary Space

Cypass Aqueous Flow

Cypass in position Aqueous Flow
XEN® Gel Stent

**Innovative approach**
- Requires a small corneal incision\(^1\)
- The first ab-interno approach to create a new pathway for aqueous flow from the anterior chamber to the subconjunctival space in refractory glaucoma patients\(^1\)
- XEN® is the first procedure that creates a low-lying, ab-interno bleb in refractory glaucoma\(^2\)

**Gel stent design**
- 6-mm length, 45-micron lumen diameter\(^1\) — about the length of an eyelash\(^2\)
- Gelatin, cross-linked with glutaraldehyde\(^1\)
- Hydrates and minimally swells, softens, and becomes flexible after implantation\(^1\)
- Preloaded, disposable injector\(^1\) with a 27-gauge, double-beveled needle\(^2,4,5\)

Innovative approach
- Requires a small corneal incision\(^1\)
- The first ab-interno approach to create a new pathway for aqueous flow from the anterior chamber to the subconjunctival space in refractory glaucoma patients\(^1\)
- XEN® is the first procedure that creates a low-lying, ab-interno bleb in refractory glaucoma\(^2\)

Minimally Invasive
- Inserted using the XEN® injector via an ab-interno approach, through a small corneal incision.\(^1\)

In the clinical investigation, standard ophthalmic surgery techniques, viscoelastic, and mitomycin C (0.2 mg/mL) were used before injection.\(^1\)

Ab-Interno Bleb Low-lying diffuse
- Controlled flow through lumen restriction
- Tenon capsule adhesions intact
- Undisturbed, low-lying drainage space
CLINICAL TRIAL CRITERIA

Established in a phase 3, prospective, multicenter, single-arm, open-label, 13-month, US clinical trial.

Study population:
- 65 patients with refractory glaucoma
- Mean age: 70.0 years
- Prior cataract surgery: 45 (69.2%)
- Prior incisional glaucoma procedure: 41 (63.1%) (e.g., trabeculectomy, tube shunt, canaloplasty, trabeculotomy, AquaFlow)
- No prior glaucoma procedure and unresponsive to maximally tolerated medical therapy: 10 (15.4%)
- Mean cup-to-disc ratio: 0.8
- Mean visual field mean deviation (MD) score: -15 dB
- Mean medicated IOP at baseline: 25.1 (±3.7) mm Hg
- Mean IOP-lowering medications at baseline: 3.5 (±1.0)

Primary effectiveness measures:
- Proportion of subjects at 12 months achieving ≥ 20% IOP reduction from baseline on the same or fewer number of medications than at baseline
- Mean decrease in IOP from baseline to 12 months

Primary safety measures:
- Procedure-related complications
- Biomicroscopic slit lamp and ophthalmoscopy findings
- Ocular adverse events

Established in a phase 3, prospective, multicenter, single-arm, open-label, 12-month, US clinical trial.

XEN® reduced mean IOP by ≥ 25% in 80.8% of eyes. 6

15.4% (n = 10/65) of patients had no prior glaucoma procedures. 1
- Refractory patients unresponsive to maximally tolerated medical therapy

ESTABLISHED EFFECTIVENESS

Reduced IOP and medication use at month 12

Mean IOP reduced to 15.9 mm Hg (N = 52) from 25.1 mm Hg at medicated baseline. 1,6
Mean IOP-lowering medications reduced to 1.7 (N = 52) from 3.5 at medicated baseline. 1,6

Results of a prospective, multicenter, single-arm, open-label, US clinical trial to evaluate the safety and effectiveness of the XEN® Gel Stent in refractory glaucoma subjects (N = 65) where previous filtering or cilioablative procedures failed, or IOP was unresponsive to maximally tolerated medication. Medication washout was not performed; all IOP lowering medications were discontinued on the day of surgery. 1

Primary Effectiveness Analyses 1,6

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<td>Proportion of Subjects with 12-Month Mean Diurnal IOP Reduction of ≥ 20% from Baseline on Same or Fewer Medications (N=65)</td>
<td>76.3% (65.8%, 86.8%)</td>
<td>-6.4 ± 1.1 mmHg (-8.7, -4.2)</td>
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1*Baseline 25.1 (±3.7) mm Hg; 12-month 15.9 (±3.0) mm Hg.

2Baseline 3.5 (±1.0); 12-month average 1.7 (±1.3) medications.

*Results of prospective, randomized, single-arm, open-label, US clinical trial to evaluate the safety and effectiveness of the XEN® Gel Stent in refractory glaucoma subjects.

6-30 subjects per arm. Truncating the glaucoma procedures failed, or IOP was unresponsive to maximally tolerated medication. Medication washout was not performed; all IOP lowering medications were discontinued on the day of surgery. 1

*Baseline 25.1 (±3.7) mm Hg; 12-month 15.9 (±3.0) mm Hg.

7Baseline 3.5 (±1.0); 12-month average 1.7 (±1.3) medications.

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<td>Proportion of Subjects with 12-Month Mean Diurnal IOP Reduction of ≥ 20% from Baseline on Same or Fewer Medications (N=65)</td>
<td>76.3% (65.8%, 86.8%)</td>
<td>-6.4 ± 1.1 mmHg (-8.7, -4.2)</td>
</tr>
</tbody>
</table>

1*Study eyes undergoing glaucoma-related secondary surgical intervention and/or removal of XEN® 45 Gel Stent prior to the 12-month evaluation were considered to be nonresponders. Seven subjects in the study underwent needling procedures with mitomycin C; 4 of these subjects were considered responders.

2Primary effectiveness analysis using observed data and failure for subjects with glaucoma-related secondary surgical intervention and multiple imputations for missing data. Groups effectiveness analysis using observed data & worst within eye IOP for subjects with glaucoma-related secondary surgical intervention and multiple imputations for missing data.

3Exact confidence limits per Clopper-Pearson method.

4Based on t-distribution.
DEMONSTRATED SAFETY

In the Pivotal Clinical Trial
• 0 of 65 subjects experienced intraoperative complications\(^1\)
  • 0% surgical complications
  • 0% hyphema
  • 0% conjunctival perforation
  • 0% iris/lens damage
• 0 of 65 subjects experienced persistent hypotony (IOP < 6 mm Hg at 2 visits > 30 days apart)\(^1,2\)
  • Hypotony (IOP < 6 mm Hg at any time): 24.6% (16/65)\(^1\)

*No clinically significant consequences were associated with hypotony, such as choroidal effusions, suprachoroidal hemorrhage, or hypotony maculopathy. IOP < 6 mm Hg was defined as an adverse event, regardless of whether there were any associated complications or sequelae related to the low pressure. Thirteen cases occurred at the 1-day visit. There were no cases of persistent hypotony, and no surgical intervention was required for the onset of hypotony.\(^1\)

Carl 10-3-12
• 72yo WM treated for COAG Travatan-Z OU
• Ran out of Travatan while on vacation in June
• Never refilled Rx
• IOP R 23 L 18
• S/P ½ SLT OS
• VA R 20/20 L 20/50
• Contrast Sensitivity/Glare 20/100 OU
9 Days post phaco/IOL/iStent OS
VA sc L 20/25
IOP L 18
Still on Travatan-Z OU
Some meds work 24hrs. Some do not!
- Prostaglandins, CAI’s DO
- Timolol, alpha agonists DO NOT

The role of blood supply as a risk factor in glaucoma is poorly understood and remains controversial

Be aware of vascular health issues in our glaucoma patients
- Low Blood pressure
- Vascular dysregulation eg Migraines

Measure BP and calculate OPP
Take Home Points

- Lower IOP improves OPP
- Higher systemic BP improves OPP but don’t necessarily want to raise BP
  - Stroke #1 cause of death in US behind CVD and CA!
- Avoid drugs that lower systemic BP beyond patient’s desired systemic control
- Avoid nocturnal hypotension
  - Use HTN meds in the AM in consultation with the patient’s PCP/internist
- Encourage good lifestyle habits
  - Diet
    - Exercise
    - Stop smoking
    - Avoid headstands with yoga
- Refer for appropriate evaluation and management of possible risk factors
  - Sleep apnea
  - Vasospasm