Advances in Glaucoma Technology

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Ganglion Cell Analysis

The analysis contains:
• Data for both eyes (OU)
• Thickness Map - shows thickness measurements of the GCL + IPL in the 6mm by 6mm cube and contains an elliptical annulus centered about the fovea.
• Deviation Maps - shows a comparison of GCL + IPL thickness to normative data.
• Thickness table - shows average and minimum thickness within the elliptical annulus.
• Sector maps - divides the elliptical annulus of the Thickness Map into 6 regions: 3 equally sized sectors in the superior region and 3 equally sized sectors in the inferior region. Values are compared to normative data.
• Horizontal and Vertical B-scans.

Ganglion Cell Analysis: How Accurate Is It?

• DIAGNOSTIC ACCURACY AND REPRODUCIBILITY
  Tan et al
  Across-sectional study, the researchers employed existing data from patients enrolled in the Advanced Imaging for Glaucoma Study. Participants were categorized into three groups: normal (65 eyes), perimetric glaucoma (78 eyes), and preperimetric glaucoma (52 eyes).
  With regard to reproducibility, the GCC parameters outperformed (smaller coefficients of variation) RNFL parameters in normal ($P = .0002$) and perimetric glaucomatous ($P > .001$) eyes but not preperimetric glaucomatous ($P = .11$) eyes.
10/13/2015

Ganglion Cell Anatomy

- Macular pathology
  - AMD
  - ERM
  - VMT
  - VMA
- Peripheral Pathology
  - Early VF loss outside of macular region

Ganglion Cell VF Pathology

- Analysis of VF in RGC loss in Glaucoma
  - 24-2 protocol has 6 degrees separation allowing for thinning the RGC to be missed due to point placement
  - Drazdo et al: Vision Research 2007
  - 10-2 testing substantially improves correlation with RGC analysis
    - Hood and Raza: Vis Science 2011
    - Stampa (1984) identified the relationship between NTG and macular damage with typically near fixation visual field loss
  - Heijl & Ljungqvist 1984
    - 45 patients followed from normal to abnormal VFs using test points at 5, 10, 15, and 20 degrees from fixation
    - Largest number at 15 degrees but a surprising number at 5 degrees

Ganglion Cell Analysis

10

Carl Zeiss Meditec, Inc Cirrus 6.0 Speaker Slide Set CIR.3992 Rev B 01/2012

Ganglion Cell Analysis: Neurodegenerative Disease

Visual dysfunction in multiple sclerosis correlates better with optical coherence tomography derived estimates of macular ganglion cell layer thickness than peripapillary retinal nerve fiber layer thickness.

Saidha S1, Syc SB, Durbin MK, Eckstein C, Oakley JD, Meyer SA, Conger A, Frohman TC, Newsome S, Ratchford JN, Frohman EM, Calabresi PA.

Author information


BACKGROUND:
Post-mortem analyses of multiple sclerosis (MS) eyes demonstrate prominent retinal neuronal ganglion cell layer (GCL) loss, in addition to related peripapillary nerve fiber layer (NFL) loss. Despite this, clinical correlations of retinal neuronal layers remain largely unexplored in MS.

RESULTS:
GCL+inner plexiform layer (GCIP) was thinner in relapsing-remitting MS (RRMS; n = 96, 71.6 µm), secondary progressive MS (SPMS; n = 20, 66.4 µm) and primary progressive MS (PPMS; n = 16, 74.1 µm) than in healthy controls (81.8 µm; p < 0.001 for all). GCIP thickness was most decreased in SPMS, and although GCIP thickness correlated significantly with disease duration, after adjusting for this, GCIP thickness remained significantly lower in SPMS than RRMS. GCIP thickness correlated significantly, and better than NFL thickness, with EDSS, high-contrast, 2.5% low-contrast and 1.25% low-contrast letter acuity in MS. 13.6% of patients also demonstrated inner or outer nuclear layer thinning.

CONCLUSIONS:
OCT segmentation demonstrates in vivo GCIP thinning in all MS subtypes. GCIP thickness demonstrates better structure-function correlations with vision and disability in MS than NFL thickness. In addition to commonly observed NFL/GCIP thinning, retinal inner and outer nuclear layer thinning occurs in MS.

Ganglion Cell in Neuro Degenerative Disease

Optic nerve degeneration in Alzheimer’s disease — Huntley et al

Alzheimer’s disease is a devastating disorder. A unique cause of which is degeneration of the optic nerve. Using post-mortem studies, we identified widespread diffuse degeneration in the optic nerves of 10 patients with Alzheimer’s disease. The retinas of 10 patients with Alzheimer’s disease and 10 healthy controls were also examined histopathically. Finally, these histological changes were also noted in vivo by optical coherence tomography (OCT). The findings in all cases were consistent with degeneration that occurs in Alzheimer’s disease. These findings may help in understanding the disease process and may be useful in developing new treatments.
Updated Guided Progression Analysis (GPA™)

- Optic Nerve Head information now included
- Average Cup-to-Disc information plotted on graph with rate of change information.
- RNFL/ONH Summary includes item “Average Cup-to-Disc Progression”.
- Printout includes an optional second page with table of values, including Rim Area, Disc Area, Average & Vertical Cup-to-Disc Ratio and Cup Volume. Each cell of the table can be color coded if change is detected.
- Miscellaneous updates to the report design.

Tracking the Elusive Diurnal!

- Sensimed: Swiss medical device company. Jean Marc Wismer CEO
- Device is called Triggerfish
- Tracks fluid pressure in the eye and beams data to palm size recorder.
- Uses a circular antenna taped around the eye and connected to a battery powered portable recorder.
- This transmits radio frequency energy to an ultra thin gold ring in the CL. This powers a chip embedded in the lens.
- Additionally on the lens in an ultra thin platinum ring that stretches in response to pressure.
- Available in Europe. Primary trial at University Hospitals of Geneva

Sensimed “Triggerfish”

- Based on assumption that IOP and corneal curvature radius are related
- Measurements are taken every 5 minutes for 30 sec seconds
- Results are presented as an arbitrary unit not mmHg
**Imaging Glaucoma**

- Argyropoulou, M; British Journal of Radiology: May 2009
- 26 patients with elevated pressure cOAG
- 26 age matched controls
- cMRI imaging
- 261 WMH’s (white matter hyperintensities) in COAG vs: 127 in controls
- Suggests that hypoperfusion d/t microangiopathy may play a pathogenetic role

**ICP & Glaucoma**

- Berdahl, J et al: Ophth 2008
- The impact of ICP on Glaucoma progression
- 66,000 LP patients / 66 Glaucoma/27 OHTN
- ICP Control: 11.8 mmHg
- ICP OHTN: 12.6 mmHg
- ICP Glaucoma: 8.6 mmHg

**Autofluorescence**

- Some materials contain naturally autofluorescent components of a molecule that can be visualized if illuminated by a specific excitation wavelength.

**Normal FAF distribution**

- Optic nerve head: absence of autofluorescent material
- Retinal blood vessels: absorption phenomena by blood contents
- Foveal area: absorption from luteal pigment
- Parafoveal area: mildly decreased intensity maybe caused by increased melanin deposition and lower density of LF granules in central RPE cells

**ONH Drusen**
Parapapillary Autofluorescence
Important tool for early diagnosis?

- Advanced Glaucoma
  - Histological LF accumulation parapapillary region
- POAG, PSXG, NTG, OHT
  - ↑FAF signal in parapapillary atrophic zone
    - Increased latency in blue on yellow VEP pattern (OHT)
    - LF correlated w. stage of progression.


Glaucoma and Lipofuscin

Pseudo-Ex: The New Low Tension

- J Glaucoma: 2009
- 178 patients /178 eyes with PXE no Tx
  Two groups:
  - Those with Glaucomatous Sx
  - Those without Glaucoma Sx
- 27 eyes (24%) were Dx with NTG
- No multivariate differences by sex, age, etc
- Increased Diurnal IOP with NTG/PXE

Two Halves are worse than One!

- Arch Ophthalmol; 2009
- 205 eyes of 205 patients with glaucomatous optic neuropathy
- Minimum 10 QVF’s over 5 years < 6dB
- 3 groups;
  - 79 with initial superior defect
  - 61 with initial inferior defect
  - 65 with both hemifields
- Mean follow up was 6.5 years
- Group C had most rapid progression

Trabeculectomy with Express Minishunt

- No difference
  - postoperative IOP
  - proportional decrease in IOP
- Ex-PRESS group
  - Significantly less medication to control IOP at 3 months
  - No difference at 6 months or 1 year (P≥0.28)
  - More Ex-PRESS patients had good IOP control without meds at 3 (P=0.057) and 6 months (P=0.076)
  - No difference was found in the rates of sight-threatening complications (P≥0.22)

Resident Surgery with Ex-PRESS

- Seider MI. Resident-performed Ex-PRESS Shunt Implantation Versus Trabeculectomy. J Glaucoma 2011 Apr 25. [Epub ahead of print]
Retrospective Case Series

- Final percent IOP lowering was similar
- Moorefields Bleb Grading System
  - Less vascularity and height but more diffuse area associated with the Ex-PRESS blebs
- Fewer cases of early postoperative hypotony and hyphema
- Quicker visual recovery
  - The Ex-PRESS group required fewer postoperative visits compared with the trabeculectomy group (P < .000).


**SIMBRINZA** (Brinzolamide/brimonidine)

IOP Control at All Time Points at Month 3 (Study 1, Study 2)

Across studies, SIMBRINZA™ Suspension provides 21%–35% IOP reduction1,2


**GLAUCOMA DRUGS ON THE HORIZON**
Novel Drugs in Development

<table>
<thead>
<tr>
<th>Target</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosine receptor agonist</td>
<td>Santen, Brobeck, Alcon/Otsuka</td>
</tr>
<tr>
<td>Cannabinoid receptor agonist</td>
<td>Inotek, Acucela/Otsuka</td>
</tr>
<tr>
<td>Corticosteroid isozyme inhibitor</td>
<td>Novartis</td>
</tr>
<tr>
<td>Rho kinase inhibitor</td>
<td>Aerie, Kowa, Seru/Novartis</td>
</tr>
<tr>
<td>Nitric oxide-donating prostaglandin</td>
<td>Bausch &amp; Lomb</td>
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ROCK/NET Inhibitors

Inhibitors of Rho Kinase (ROCK) and Norepinephrine Transporter (NET)

Pathways to Lower IOP

Outflow
- $\alpha_2$-agonists
- Cholinergics
- Prostaglandins

Inflow
- $\alpha_2$-agonists
- $\beta$-blockers
- ONS

SNJ-1656 Dose-Response Curve


SNJ-1656 0.1%-Induced Conjunctival Hyperemia


Aerie Pharmaceuticals

- ROCK (Rho associated coiled coil-forming protein kinase)
- Lower IOP by acting on actin cytoskeleton and cellular motility in the TM, SC and ciliary muscle
- Possible relaxation of trabecular meshwork
Aerie Pharmaceuticals
ROCK/NET Inhibitor Pipeline

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Development Phase</th>
</tr>
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<tbody>
<tr>
<td>Rhopressa™</td>
<td>Phase 3 trials began July 2014</td>
</tr>
<tr>
<td>Roclatan™</td>
<td>Phase 2b trial completed June 2014</td>
</tr>
<tr>
<td>AR-23533</td>
<td>Preclinical</td>
</tr>
</tbody>
</table>

Rhopressa™ – ROCK/NET inhibitor
Roclatan™ – combination of Rhopressa and latanoprost
AR-23533 – second-generation ROCK/NET inhibitor

Latanoprostene Bunod (Vesneo)

Nitric Oxide and Glaucoma

- Patients with primary open-angle glaucoma (POAG) have lower levels of NO synthase activity in the trabecular meshwork (TM), Schlemm’s canal, and ciliary muscle.
- NO donors lower IOP in normal and POAG eyes.
- A major site of action for NO donors is the TM.
  - NO relaxes the TM and ciliary muscle.
  - NO donors increase outflow facility in anterior segments, mediated by a decrease in TM cell volume.
  - Endothelial NO synthase (eNOS) overexpression increases conventional outflow and lowers IOP in a mouse eye model.

BOL-303259-X (Latanoprostene Bunod)

- Nitric Oxide (NO)-donating prostaglandin F2α agonist that is rapidly metabolized in situ to latanoprost acid and BDMN, a NO-donating moiety.
- Exhibited potent and effective intraocular pressure (IOP)-lowering activity in 3 ocular hypertensive glaucoma animal models.

Efficacy Results: Primary Endpoint

TRABODENOSEN (INO-8875)

- Inotek
  - Adenosine-1 receptor agonist (action is on trabecular meshwork)
  - Preclinical Trial demonstrated ganglion cell preservation
  - 2014 ARVO presentation
  - Primary phase in 2012 (IOP reduction of 7 mmHg at 28 days)
  - March 10, 2014 Phase II trial in conjunction with latanoprost
  - 120 patients with OHTN/POAG
Singapore Nanyang Technology University
• 2/11/2015
• Injectable glaucoma medication
• Extended release Nanotechnology
• Six patient initial trial 2013
• Anticipated submission to US clinical trials 2016

Punctal Plugs with Latanoprost
MATI Therapeutics
• 44-g Latanoprost Punctal Plug Delivery System
• Phase II
• Data:
  - Mean change from baseline -3.5 mmHg
  - 36% showed reduction of >/= 5mmHg
  - Overall goal of 90% retention/ Initial 75%
  - Second generation plug 90%
  - Goal of therapy 90 days of Tx

Mati Therapeutics
• AUSTIN, Texas, Oct. 28, 2013 (GLOBE NEWSWIRE) -- Mati Therapeutics Inc. (“Mati”) today announced the initiation of a Phase II trial of its L-PPDS drug delivery system in patients with ocular hypertension or primary open angle glaucoma. The study will be a U.S. based, randomized, multi-center trial of approximately 100 patients treated with L-PPDS or timolol eye drops for up to 14 weeks. The primary end point for the comparative treatments will be change from baseline in intraocular pressure (IOP). A number of secondary endpoints will also be evaluated.
• This trial is the first trial to compare L-PPDS to timolol eye drop therapy. Results from this trial are expected by the third quarter of 2014 and will be used to determine the appropriate study design for a potential Phase III pivotal trial of L-PPDS. To date, more than 570 subjects have been treated in various L-PPDS dose-ranging Phase II studies. The Phase II study will evaluate a 95ug formulation of latanoprost

Ocular Therpeutix
• Phase II trial of OTX-TP2
• Hydrogel plugs that deliver travoprost
• Umhlanga Medical Center & Netcare Alberito Hospital, South Africa
• 20 patients (up to 40 eyes) with OHTN or Glaucoma
• 88% retention at one month

Contact Lens Embedded IOP Lowering Drug
• Dean Ho, UCLA Dentistry School Research Team
• Nanogel that is embedded in CL’s
• IOP lowering capacity
• Uses nanotechnolgy with small diamonds that timolol until tear enzymes (lysozyme) activate it
• The octohedron structure of the nanodiamonds has a unique charge that binds drugs to its surface
Drug Eluting Contacts
- Harvard Medical Center Researchers
- Recipients of MIT innovators in Life Sciences competition
- Daniel Kohane, MD, PhD (anesthesiology)
- Coating Polyactic co-glycolic acid (PLGA) is coated with films containing Polyhydroxy-methacrylate by UV polymerization
- Research is being funded by:
  - National Institute of Medical Studies
  - National Eye Institute
  - Boston KPro foundation
- Duration can be as long as 300 days
- Limitation will be the duration of CL wear

Envisia Therapeutics
- ARVO 2014
- ENV515 Intracameral Implant with a polymer implant that has an extended release formulation of travoprost
- 30% IOP lowering in beagles at 24 weeks
- CEO Ben Yerxa
- Utilizes PRINT (Particle Replication In Non-Wetting Templates) technology
- Anticipated NDA 4Q 2015

SLT: Only Child or Twins?
- Pasquale, J et al: ARVO Annual Meeting 2010
- Determined the predictive affect of first eye response in SLT
- 178 eyes treated. Average time seperation 13 months
- Success 3mmHg drop without meds
- 75% showed same results regardless of outcome
  - SLT successful first eye 27%/ 87.5 % successful on second eye
  - SLT failure first eye 73%/ 71% failure on second eye
- Found correlation with increased energy use on second eye and increased rate of success in failed first eyes

ORA Signal Analysis
The ORA optical system records 400 data samples of reflected IR light intensity during the rapid (30 ms) in/out corneal deformation.
The optical signal (red curve) is a “dynamic map” of the cornea during the rapid in/out deformation.
The signal provides additional information about corneal biomechanical properties, revealing “signature” characteristics of the eye being measured.

IOPcc: IOP compensated for corneal effects, including corneal hysteresis, a measure of viscoelasticity of the cornea (elasticity)
IOPg: Goldmann equivalent IOP
Corneal Hysteresis

Identified by David Luce, Ph.D., Corneal Hysteresis is the difference in the inward and outward pressure values obtained during the dynamic bi-directional applanation process employed in the Ocular Response Analyzer, as a result of viscous damping in the cornea.

CH: P1 - P2

Corneal Resistance Factor

An indicator of the overall "resistance" of the cornea, including both the viscous and elastic properties. It is significantly correlated with Central Corneal Thickness (CCT) and GAT, as one might expect, but not with IOPCC.

CRF = P1-(0.7*P2)

Corneal-Compensated IOP (IOPcc)

- An Intraocular Pressure measurement that is less affected by corneal properties than other methods of tonometry, such as Goldmann (GAT). IOPcc has essentially zero correlation with CCT in normal eyes and stays relatively constant post-LASIK.

IOPcc = P2 - (0.43*P1)

CH predicts Laterality in Asymmetric Glaucoma

CH had a higher odds ratio of predicting asymmetric glaucoma damage than GAT, CCT, or Myopia and the best sensitivity and specificity.

Lower Corneal Hysteresis is Associated With More Rapid Glaucomatous Visual Field Progression

- 153 glaucomatous eyes, with >8 visual fields, followed for > 5 years
- Progressing eyes (n=25) had lower CCT (525 μ vs 542 μ, P=0.04) and lower CH (7.5 mmHg vs 9.0 mmHg), P<0.01) compared with nonprogressing eyes.
- By multivariate analysis, peak intraocular pressure (OR=1.13, P<0.01), age (OR=1.57, P=0.03), and CH (OR=1.55, P<0.01) were significant predictors of progression.
Surgical Continuous IOP Monitoring Device

- Nature Medicine 2014
  - Yossi Mandel, Bar-Ilan/ Stephen Quake, Stanford
  - Utilizes a variable float tube in the IOL
  - Smart Phone app allows acquisition of data
  - Anticipated in 2-3 years

Technologies in the Diagnosis and Management of Glaucoma

Pupillometry Visual Field


Pattern Electroretinogram / Visual Evoked Potential


Technologies in the Diagnosis and Management of Glaucoma

PERG VEP


Technologies in the Diagnosis and Management of Glaucoma

Asymptomatic

Healthy

Glucoma


Technologies in the Diagnosis and Management of Glaucoma

Acular

Healthy

DCT

Glucoma

Non documented structural damage

Documented structural damage

Healthy VF

Glaucoma

Documented structural damage

Non documented structural damage

OCT

PERG/VEP

Non documented functional damage

Documented functional damage


Technologies in the Diagnosis and Management of Glaucoma

ECP

ECP Advantages

- Quick procedure, especially in cataract setting
- Titratable
- Can be done with outflow procedures
- Hypotony unlikely

OHT

Glaucoma

Normal IOP

Technologies in the Diagnosis and Management of Glaucoma

Technologies in the Diagnosis and Management of Glaucoma
ECP Disadvantages

- Some learning curve to avoid complications
- Inflammation possible
- IOP does not decrease rapidly
- Difficult to do in some eyes

Canaloplasty: Enhancing Circumferential Outflow using a Flexible Microcatheter in Schlemm’s Canal in POAG

Gonioscopy

Differentiates:
- Open Angle
- Closed Angle
- Recessed Angle

Now

CB
SS
TM

40°
PAS
Pig.

Review: Angle Anatomy

- Cannot be viewed directly through intact cornea (‘total internal reflection’)
- Gonio lenses eliminate total internal reflection, allow indirect views of structures
- Replaces air-cornea interface with material composed of greater index of refraction than cornea, tear film

Trabeculum

- Average width ~ 600um
- Anterior portion
  - whitish coloration
  - non-functioning
  - non-pigmented
- Posterior portion
  - greyish-blue / translucent
  - functional
  - pigmented
- Site of glaucoma laser Tx...

Indentation Gonioscopy

Benefits of 4-mirror gonioscopy lens vs. “traditional” 3-mirror lens...
Peripheral Anterior Synechiae (PAS)

Classification of Glaucoma

- Open Angle Glaucoma
  - 1º OAG
  - NTG
  - JOAG
  - 2º OAG
    - PGx
    - P3G
    - Steroid-induced

- Angle Closure Glaucoma
  - 1º ACG w/ relative pupil block
  - Acute Angle Closure
  - Sub-acute/Intermittent Angle Closure
  - Chronic ACG
  - 2º ACG w/ pupil block
  - 2º ACG w/o pupil block
  - Anterior pulling mechanisms
    - Posterior pushing mechanism
    - Plateau Iris Syndrome

- Childhood Glaucoma
  - 1º Congenital/Infantile Glaucoma
  - Assoc. w/ Congenital Anomalies
    - Ocular disorders
    - Systemic disorders
  - 2º Glaucoma in infants/children

MIGS – Micro-Invasive Glaucoma Surgery

- Ab-interno approach
  - Clear corneal micro-incision (<2.0mm)
  - Conjunctival sparing
- Minimally traumatic
  - Negligible disruption of normal anatomy/physiology
  - Excellent biocompatibility
- Efficacious
- Extremely high safety profile
- Rapid recovery

Filtering Surgery – Trabeculectomy

- "Gold standard" for glaucoma surgery – creates a "bleb" (artificial outflow pathway)
- 47% cumulative probability of failure after 5 years
- Re-operations carry high failure rates
- High complication rate
  - Over-filtration, hypotony, 1-2% annual risk of endophthalmitis
- 78% increase in risk of cataracts
  - Hyphema, anterior chamber shallowing, choroidal suprachoroidal hemorrhages

Complications of Filtering Surgery

- Tube shunt erosion
- Vitreous hemorrhage
- Retinal detachment
- Uveitis
- Diplopia
- Hyphema, anterior chamber shallowing, choroidal suprachoroidal hemorrhages

iStent (Glaukos)

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Zhou et al introduced a hypothesis that evaluated the effect of a theoretical channel created through the TM (a trabecular bypass) on the facility of outflow and IOP.

- The authors established equations that govern the pressure and circumferential flow in Schlemm's canal.
- Two types of bypasses permitting either unidirectional or bidirectional flow were incorporated to derive the facility of outflow and the reduced IOP.

Results:
- In normal healthy eyes, the facility of outflow increased by 13% and 26% in the presence of a unidirectional and bidirectional bypass, respectively.
- Circumferential flow was significant only in the immediate quadrant to the bypass.
- In either case, the higher the baseline IOP, the greater the reduction.

Stent / Efficacy:
- Schlemm's canal is part of the aqueous outflow pathway.
- iStent® restores aqueous outflow chain by bypassing only the blockage that occurs with glaucoma in the trabecular meshwork.
- IOP reductions to mid teens.

Surgical Procedure / Safety:
- No filtering bleb or conjunctival scaring.
- Decreased chance of hypotony because of episcleral venous pressure.
- Small clear corneal incision incorporates with existing surgeries.
- Preserves all other surgical and medical options.

iStent® Implantation and Actions:
- Delivered ab interno via 1-1.5mm clear corneal incision.
- Designed to perforate TM and reside within Schlemm's canal.
- Base stents open Schlemm's canal.
- iStent permanently stents open trabecular meshwork.
- Restores outflow path from AC to Schlemm's canal.

iStent Stability?
Dye Flow Test

Trypan blue dye delineates aqueous outflow field from iStent location

Clinical Evidence

- **Purpose:** To evaluate the safety and efficacy of the iStent Trabecular Micro-bypass Stent in patients undergoing concurrent cataract and glaucoma surgery
- **Methods:**
  - Prospective, 24-month multicenter, multi-country study of 58 patients with uncontrolled POAG and cataract.
  - Patients underwent clear cornea phaco followed by ab-interno gonioscopically guided implantation of the iStent through the same temporal incision used to extract the cataract. Primary outcome was proportion of patients with an IOP ≤ 18 mm Hg with or without medication(s).

Glaukos Efficacy

- **Mean IOP (mm Hg):**
  - Study Visit Day 1, Day 7, Month 1, Month 2, Month 3, Month 6, Month 12
  - Mean IOP at different study visits:
    - Baseline: 4.1, 5.7
    - Month 1: 4.4, 5.3
    - Month 2: 4.0, 4.0
    - Month 3: 3.4, 3.4
    - Month 6: 2.5, 3.0
    - Month 12: 2.0, 2.0

- **Mean Number of Medications:**
  - At baseline, the mean number of medications was 1.6 ± 0.8 (n=42).
  - Postop, the mean number of medications in the PP group ranged between 0.3 and 0.5 MEDS.
  - Reduction in medication use at 12 months postop ranged from 1.0 to 1.3, with a mean decrease of 1.2 ± 0.7 (P<0.001).

Glaukos Disadvantages

- Very low IOPs not likely
- Need open angle
- Placement of earlier device is sometimes difficult

Conclusions

- The Glaukos iStent is an effective treatment option for open-angle glaucoma. This is supported by three types of data:
  - Theoretical
  - In vitro
  - Clinical
- Re-establishing physiologic outflow by creating a patent bypass channel into Schlemm’s canal can provide substantial reductions in IOP and drug burden in OAG patients.
- Trabecular bypass into Schlemm’s canal is a promising treatment for glaucoma. Additional research into fully exploiting circumferential flow within Schlemm’s canal is ongoing.