CONTINUING EDUCATION CERTIFICATE

Glaucoma Symposium
Saturday, January 06, 2018
EVENT # 114779

PACIFIC UNIVERSITY COLLEGE OF OPTOMETRY **2043 COLLEGE WAY** **FOREST GROVE, OR 97116** **503-352-2207 503-352-2929 FAX**	**WILLOWS LODGE** **15480 NE 145TH STREET** **WOODINVILLE, WA 98072**

Name: _____ OE Tracker # _____

Address: _____ City, State, Zip: _____

Signature: _____ License # _____ State: _____

Upon completion of each course, you must present this form to the monitor who will validate your attendance.

COPE ID	Course Title/Instructor	Duration	Validation
55903-GL	**NEW CONCEPTS RELATED TO GLAUCOMA DIAGNOSIS AND MANAGEMENT** OCT Angiography and glaucoma — Howard Barnebey, MD What is Glaucoma — Murray Fingeret, OD Assessing the Angle – How often and why? — Howard Barnebey, MD Glaucoma Test Results: To Believe or Not to Believe — Murray Fingeret, OD	2.0 hrs	
59904-GL	**NEW CONCEPTS RELATED TO GLAUCOMA THERAPY** Glaucoma Therapy Update - Medications — Murray Fingeret, OD Glaucoma Therapy Update - Surgery — Howard Barnebey, MD Glaucoma – New Technology Update — Murray Fingeret, OD Glaucoma – Selecting the best Glaucoma Strategy — Howard Barnebey, MD	2.0 hrs	
55905-GL	**NEW IDEAS IN GLAUCOMA** Journal Club 2018 — Murray Fingeret, OD and Howard Barnebey, MD New Methods to monitor IOP — Murray Fingeret, OD	2.0 hrs	
55901-GL	**GLAUCOMA GRAND ROUNDS** Murray Fingeret, OD and Howard Barnebey, MD	1.0 hr	
	GLAUCOMA SYMPOSIUM 2018 **Total Hours Attended:**		*Total Hours Offered: 7*

Retain a copy of this certificate as your validated record of attendance. Please be advised that your individual state boards will make the final determination of applicable hours.

to our Glaucoma Symposium Supporters:

NOVARTIS

aerie Pharmaceuticals, Inc.

BAUSCH + LOMB

Allergan

Alcon
a Novartis company

ZEISS CARL ZEISS MEDITEC

HEIDELBERG ENGINEERING

OPTOVUE

MEDS IN MOTION PHARMACY

centervue
Engineering Italian Creativity

GLAUCOMA SYMPOSIUM
JANUARY 6, 2018

6:30 REGISTRATION & CONTINENTAL BREAKFAST
7:20 WELCOME INTRODUCTION

7:30 – 9:30: NEW CONCEPTS RELATED TO GLAUCOMA DIAGNOSIS AND MANAGEMENT

OCT ANGIOGRAPHY AND GLAUCOMA — **COURSEBOOK PAGES 1-15**
HOWARD BARNEBEY, MD

WHAT IS GLAUCOMA? — **COURSEBOOK PAGES 16-21**
MURRAY FINGERET, OD

ASSESSING THE ANGLE – HOW OFTEN AND WHY? — **COURSEBOOK PAGES 22-53**
HOWARD BARNEBEY, MD

GLAUCOMA TEST RESULTS: TO BELIEVE OR NOT TO BELIEVE — **COURSEBOOK PAGES 54-59**
MURRAY FINGERET, OD

9:30 BREAK

10:00 – 12:00: NEW CONCEPTS RELATED TO GLAUCOMA THERAPY

UPDATE ON GLAUCOMA THERAPY MEDICATIONS — **COURSEBOOK PAGES 60-72**
MURRAY FINGERET, OD

NEW GLAUCOMA SURGICAL UPDATE — **COURSEBOOK PAGES 73-104**
HOWARD BARNEBEY, MD

GLAUCOMA – DRUG DELIVERY DEVICES — **COURSEBOOK PAGES 105-116**
MURRAY FINGERET, OD

SELECTING THE BEST TREATMENT STRATEGY — **COURSEBOOK PAGES 117-126**
HOWARD BARNEBEY, MD

12:00 LUNCH

1:00 – 3:00: NEW IDEAS IN GLAUCOMA & JOURNAL CLUB

JOURNAL CLUB — **COURSEBOOK PAGES 127-136**
MURRAY FINGERET, OD AND HOWARD BARNEBEY, MD

NEW TECHNOLOGY UPDATE — **COURSEBOOK PAGES 137-146**
MURRAY FINGERET, OD

BRANDED VERSUS GENERIC MEDICATIONS — **COURSEBOOK PAGES 147-160**
HOWARD BARNEBEY, MD

3:00 BREAK

3:30 – 4:30: GLAUCOMA GRAND ROUNDS

GLAUCOMA GRAND ROUNDS — **COURSEBOOK PAGES 161-184**
HOWARD BARNEBEY, MD & MURRAY FINGERET, OD

OCT ANGIOGRAPHY

HOWARD BARNEBEY, MD

POAG: PATHOGENESIS

- Multifactorial optic neuropathy of unknown cause.
  - Structural injury often precedes detectable visual field (VF) loss
  - Glaucomatous VF damage confined to a single hemifield both the retinal nerve fiber layer (RNFL) and the macular ganglion cell complex thickness are reduced even in the retinal hemispheres corresponding to the perimetrically intact hemifields.[12, 13, 14]
  - Limited information if microvasculature is reduced in eyes with localized glaucomatous functional loss
  - Possible contribution to the natural course of the disease.[15]
- Ocular vasculature in glaucoma limitations in the imaging modalities
  - contribution of ocular vasculature in the pathogenesis of glaucoma unclear
- Optical coherence tomography angiography (OCT-A)[16] is a noninvasive imaging technique that provides reproducible quantitative assessment of the vasculature in the optic nerve, peripapillary retina, and macula.

OPTIC NERVE BLOOD SUPPLY

- Central Retinal Artery
  - superficial layers of the optic nerve head
    - nerve fiber layer
- Posterior Ciliary Artery
  - deeper layers
    - prelaminar, lamina cribrosa & retrolaminar regions
- Primary site of ONH lesion in glaucoma is nourished by the microcirculation of PCA[1]

[1]S. S. Hayreh. IOVS 45(3), 749–757, 748 (2004).

OCT A: WHY?

- Earlier diagnosis
- More sensitive to detect change
- More sensitive in advanced glaucoma where RNFL and VF loss is severe
- Isolated subsets of glaucoma where vascular issues maybe significant
  - low tension glaucoma
  - ischemic optic neuropathy
  - retinal vascular abnormalities
  - NFL hemorrhage

OCT

- Doppler OCT
  - measuring total human retinal blood flow (TRBF) around the ONH
  - large vessels around the ONH can be quantified
  - microcirculation of the ONH cannot be resolved
    - velocities in the small vessels are too low to be accurately measured from Doppler shift
- OCT: coherence detection technique
  - Capable of detecting Doppler frequency shift of the backscattered light
    - information on blood flow
- split-spectrum amplitude-decorrelation angiography (SSADA) algorithm
  - SSADA is based on the variation of reflectance amplitude
    - sensitive to motion and flow in all directions
    - detect perfusion in a way that is independent of beam incidence angle

GLAUCOMA AND BLOOD FLOW: DOPPLER

PURPOSE:: To detect and quantify changes in optic nerve head (ONH) and peripapillary retinal blood flow by scanning laser Doppler flowmetry (SLDF) intraocular pressure (IOP) reduction.

DESIGN: Prospective, nonrandomized, self-controlled trial.

PARTICIPANTS: Twenty patients (OAG) and 20 patients (OHT)

INTERVENTION: IOP reductions more than 20% and a minimum of 4 weeks follow-up.

MAIN OUTCOME MEASURES: Blood flow measurements using Heidelberg Retina Flowmeter images.

RESULTS:

OAG had a mean IOP reduction of 37% after treatment.	OHT patients had a mean IOP reduction of 33% after treatment
Mean rim blood flow increased by 67%.	Mean rim blood flow 7.5% increase P = 0.41 NS
Mean temporal peripapillary retinal flow decreased by 7.4%	Mean temporal (P = 0.35) 0.88) peripapillary
Mean nasal peripapillary retinal flow increased by 0.3%	Mean nasal (P = 0.88) NS+/- 140 arbitrary units, P = 0.41) nor the.

CONCLUSIONS: OAG patients had a statistically significant improvement of blood flow in the neuroretinal rim of the ONH vs OHT
Peripapillary retinal blood flow expected to be affected less in glaucoma, remained stable in both groups.
Suggest that ONH autoregulation may be defective in OAG while intact in OHT

Changes in optic nerve head blood flow after therapeutic intraocular pressure reduction in glaucoma patients and ocular hypertensives. Hafez ET AL Ophthalmol 2003 110:201-10.

GLAUCOMA ANGIOGRAPHY: PILOT STUDY

Purpose: Investigate blood flow changes in retinal and optic nerve diseases with Doppler Fourier domain optical coherence tomography (OCT).

Methods: Sixty-two participants were divided into five groups: normal, glaucoma, nonarteritic ischemic optic neuropathy (NAION), treated proliferative diabetic retinopathy (PDR), and branch retinal vein occlusion (BRVO). Doppler OCT was used to scan concentric circles of 3.4- and 3.75-mm diameters around the optic nerve head. Flow in retinal veins was calculated from the OCT velocity profiles. Arterial and venous diameters were measured from OCT Doppler and reflectance images.

Results: Total retinal blood flow in normal subjects averaged 47.6 μL/min. The coefficient of variation 11% in normal eyes and 14% in diseased eyes. Eyes with glaucoma, NAION, treated PDR, and BRVO had significantly decreased retinal blood flow compared with normal eyes ($P < 0.001$). In glaucoma patients, the decrease in blood flow was highly correlated with the severity of visual field loss ($P = 0.003$). In NAION and BRVO patients, the hemisphere with more severe disease also had lower blood flow.

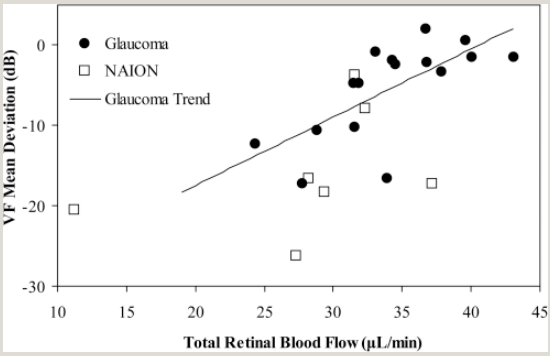
Conclusions Doppler OCT retinal blood flow measurements showed good repeatability and excellent correlation with visual field and clinical presentations.

Pilot Study of Optical Coherence Tomography Measurement of Retinal Blood Flow in Retinal and Optic Nerve Diseases, Wang et al. IOVS 2011 Feb; 52(2): 840–845

GLAUCOMA ANGIOGRAPHY

VF MD & total retinal blood flow in the glaucoma significant correlation ($P = 0.003$)

Flow deficit correlated well with visual field loss



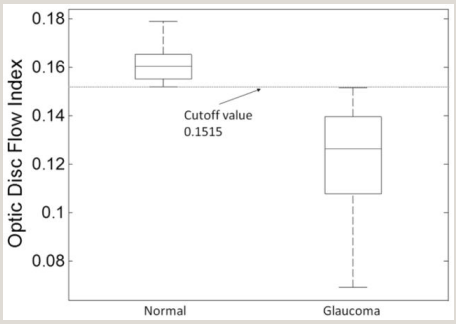
Pilot Study of OCT Measurement of Retinal Blood Flow in Retinal and Optic Nerve Diseases, Wang et al. IOVS 2011 Feb; 52(2): 840–845

OCTA

- **Purpose**To compare optic disc perfusion between normal and glaucoma subjects using optical coherence tomography (OCT) angiography
- **Design:** Observational, cross-sectional study.
- **Participants:** Twenty-four normal subjects and 11 glaucoma patients were included.
- **Methods:** One eye of each subject was scanned by a high-speed 1050 nm wavelength swept-source OCT instrument. The split-spectrum amplitude-decorrelation angiography algorithm (SSADA) was used to compute three-dimensional optic disc angiography. A disc flow index was computed from four registered scans. Confocal scanning laser ophthalmoscopy (cSLO) was used to measure disc rim area, and stereo photography was used to evaluate cup/disc ratios. Wide field OCT scans over the discs were used to measure retinal nerve fiber layer (NFL) thickness.
- **Results:** In normal discs, a dense microvascular network was visible on OCT angiography. This network was visibly attenuated in glaucoma subjects. The disc flow index was reduced by 25% in the glaucoma group ($p = 0.003$). Sensitivity and specificity were both 100% using an optimized cutoff. flow index was highly correlated with VF pattern standard deviation ($R^2 = 0.752$, $p = 0.001$). These correlations were significant even after accounting for age, cup/disc area ratio, NFL, and rim area.
- **Conclusions:** OCT angiography, generated by the new SSADA algorithm, repeatably measures optic disc perfusion. OCT angiography could be useful in the evaluation of glaucoma and glaucoma progression

Optical Coherence Tomography Angiography of Optic Disc Perfusion in Glaucoma, Yali et al. Ophthalmol 2014; 121(7): 1322

OCTA



Optical Coherence Tomography Angiography of Optic Disc Perfusion in Glaucoma, Yali et al. Ophthalmol 2014; 121(7): 1322

POAG: PATHOGENESIS

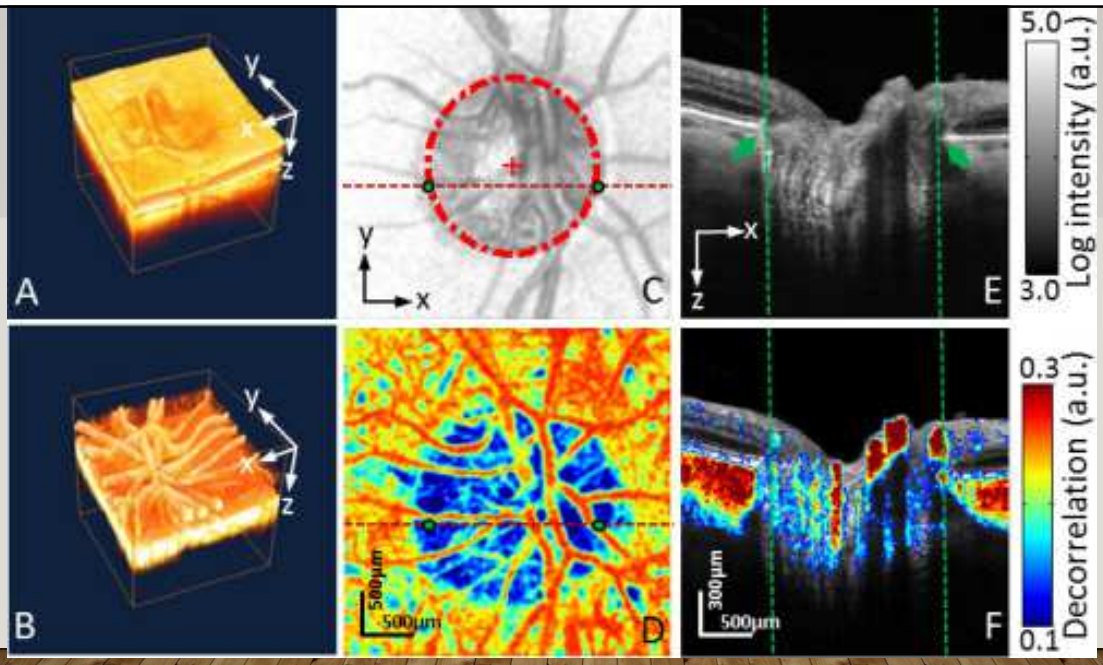
- pathogenesis unclear
- Structural Changes
- Ocular blood flow

  OCT-angiography (OCT-A) allows visualization of retinal microvasculature
  high level of precision
  reproducible quantitative measurement of the vascular networks

OCT-A in glaucoma have demonstrated that vessel density measurements in the optic disc, peripapillary retina, macula, and choroidal structures are associated with the severity of glaucomatous VF damage.[29, 30, 31, 32, 33, 34] Most recently, it has been shown that OCT-A is capable of detecting microvascular attenuation of the peripapillary and macular regions even in perimetrically intact hemiretinae of eyes with single-hemifield VF defects.[35]

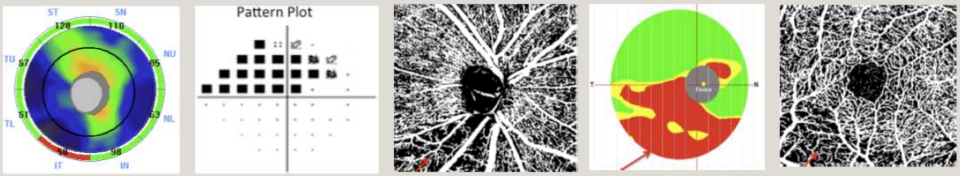
SSADA

- Key step: splitting the raw full spectrum into multiple spectrums (narrow bandwidths)
  Narrower bandwidths lower the OCT axial resolution
  Reduce the pulsatory bulk motion noise along the axial direction
  Optimize flow detection along the transverse direction
- Fourier-transformed low resolution OCT amplitude frames used to calculate decorrelation
- Inter-B-scan decorrelation determined at each of the narrower spectral bands separately and then averaged
- Recombining the decorrelation images from the multiple narrow spectral bands



OCT ANGIOGRAPHY: GLAUCOMA

- Glaucoma VF loss severity associated with vessel density measurements in the optic disc, peripapillary retina, macula, and choroidal structures [1]
- OCT-A can detect microvascular attenuation of the peripapillary and macular regions in perimetrically intact hemiretinae of eyes with single-hemifield VF defects.[2]



[1]Yarmohammadi, A., Zangwill, L.M., Diniz-Filho, A. et al. *Ophthalmology*. 2016; 123: 2498–2508
[2]Yarmohammadi, A., Zangwill, L.M., Diniz-Filho, A. et al. *Ophthalmology*. 2017; 124: 709–719

PERIPAPILLARY AND MACULAR VESSEL DENSITY IN PATIENTS WITH POAG & UNILATERAL VISUAL FIELD LOSS

YARMOHAMMADI, ZANGWILL,MANALASTAS, FULLER,DINIZ FILHO,SAUNDERS,SUH,HASENSTAB, WEINREB

- Purpose: To characterize OCT angiography (OCT-A) vessel density of patients with primary open-angle glaucoma (POAG) with unilateral visual field (VF) loss.
- Design: Cross-sectional study (N=33 patients with POAG with a VF defect in 1 eye); healthy controls
- Main Outcome Measures: Difference in OCT-A vessel density and SD OCT structural parameters between unaffected eyes of patients with POAG with the fellow affected eyes and healthy controls.

DOI: http://dx.doi.org/10.1016/j.ophtha.2017.10.029

PERIPAPILLARY AND MACULAR VESSEL DENSITY IN PATIENTS WITH POAG & UNILATERAL VISUAL FIELD LOSS

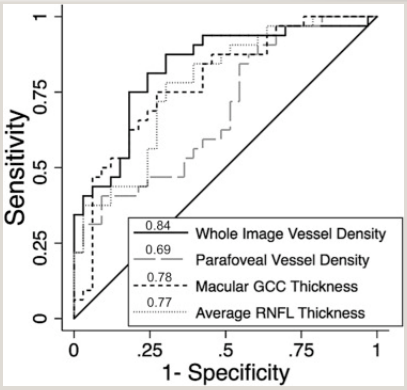
YARMOHAMMADI, ZANGWILL,MANALASTAS, FULLER,DINIZ FILHO,SAUNDERS,SUH,HASENSTAB, WEINREB

- Results:
  1. Mean whole image vessel density in unaffected eyes of patients with POAG (52.0%) was higher than in their fellow affected eyes (48.8%) but lower than in healthy eyes (55.9%; $P < 0.001$)
  2. Mean circumpapillary RNFL (cpRNFL) thickness, mGCC thickness, and rim area measurement in unaffected eyes of patients with POAG were higher than those measurements in their fellow and lower than in healthy eyes The AUROCs for differentiating unaffected eyes of patients with POAG from healthy eyes were highest for wiVD (0.84), followed by mGCC (0.78), cpRNFL (0.77), and pfVD (0.69).
- Conclusion: OCT-A measures detect changes in retinal microvasculature before VF damage is detectable in patients with POAG

DOI: http://dx.doi.org/10.1016/j.ophtha.2017.10.029

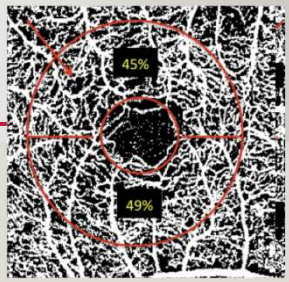
PERIPAPILLARY AND MACULAR VESSEL DENSITY IN PATIENTS WITH POAG & UNILATERAL VISUAL FIELD LOSS
YARMOHAMMADI, ZANGWILL,MANALASTAS, FULLER,DINIZ FILHO,SAUNDERS,SUH,HASENSTAB, WEINREB

- AUROCs for differentiating unaffected eyes highest:
  Whole Image vessel density (VD) (0.84)
  Macular GCC thickness (0.78)
  Parapapillary RNFL VD (0.77)
  Parafoveal VD (0.69).



DOI: http://dx.doi.org/10.1016/j.ophtha.2017.10.029

OCT ANGIOGRAPHY



- Avanti SD OCT (AnvioVue)
  Optovue, Inc: Commercially available
- Noninvasive method of characterizing the vascular structures of the retina at the capillary level
- Details [25]
  - split-spectrum amplitude-decorrelation angiography algorithm (SSAAA)
    - captures dynamic motion of moving particles, such as red blood cells
    - provides a high-resolution 3-dimensional angiogram of perfused retinal vasculature
  - AngioVue software
    - characterizes vascular information at various user-defined retinal layers
    - qualitatively: vessel density map and color-coded vessel area density
    - quantitatively: vessel density (%) measurements calculated
      - percentage of measured area occupied by flowing blood vessels
      - blood vessels defined as pixels having SSAAA values above the threshold level.

Jia, Y. et al. Split-spectrum amplitude-decorrelation angiography with OCT *Opt Express.* 2012; 20: 4710–4725

OCT ANGIOGRAPHY OF THE SUPERFICIAL MICROVASCULATURE IN THE MACULAR AND PERIPAPILLARY AREAS IN GLAUCOMATOUS AND HEALTHY EYES

CHEN HS, LIU CH, WU WC, TSENG HJ, LEE YS.

- Whole image vessel density in glaucomatous eyes was lower than in healthy eyes
  macular area: 38.5% ± 2.2% vs. 43.2% ± 2.3%, P < 0.001
  peripapillary areas: 43.8% ± 5.7% vs. 53.3% ± 3.0% P < 0.001
- Circumpapillary vessel density (cpVD) was lower in glaucomatous eyes (53.3% ± 7.0% vs. 61.5% ± 3.2%, P < 0.001)
- AUROCs discriminating between glaucomatous and healthy eyes:
  Highest for cpRNFL (0.95) and GCC (0.95)
  Macular VD (0.94)
  Peripapillary wiVD (0.93)
  CP VD (0.89)
- SAP correlations severity strongest:
  Peripapillary wiVD (R2 = 0.58)> cpVD (R2 = 0.55) > GCC (R2 = 0.51) > cpRNFL (R2 = 0.42) > macular wiVD (R2 = 0.36)

IOVS 2017 Jul 1;58(9):3637-3645.

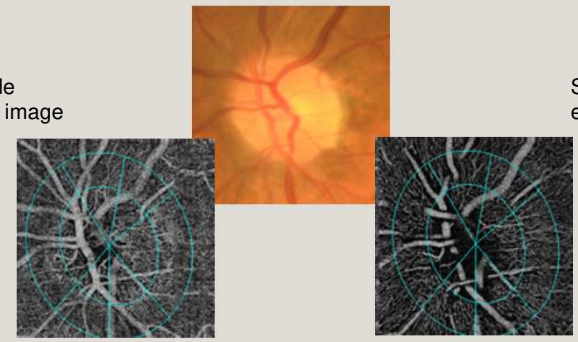
OCT ANGIOGRAPHY OF THE SUPERFICIAL MICROVASCULATURE IN GLAUCOMATOUS AND HEALTHY EYES

CHEN HS ET AL

Conclusions:

- 1. Medically managed glaucomatous eyes show sparser superficial microvasculature in the macular area than do healthy eyes
- 2. Measurement of the macular superficial vessel density had similar diagnostic accuracy to peripapillary RNFL and macular GCC thickness for differentiating between glaucomatous and healthy eyes.

Whole-signal-mode
en face projection image

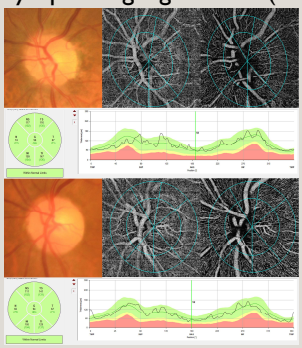


Surface-mode
en face projection image

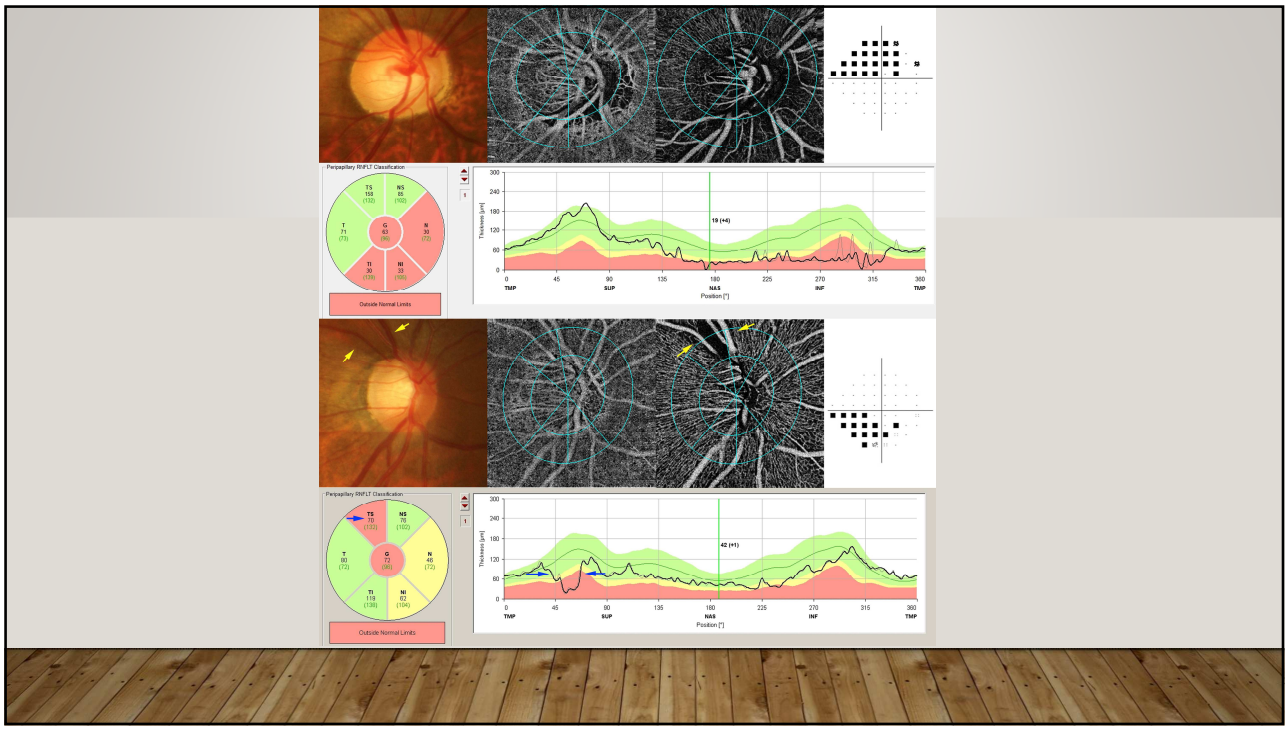
OCT ANGIOGRAPHY: MICROVASCULAR DENSITY IN GLAUCOMATOUS EYES WITH HEMIFIELD VISUAL FIELD DEFECTS

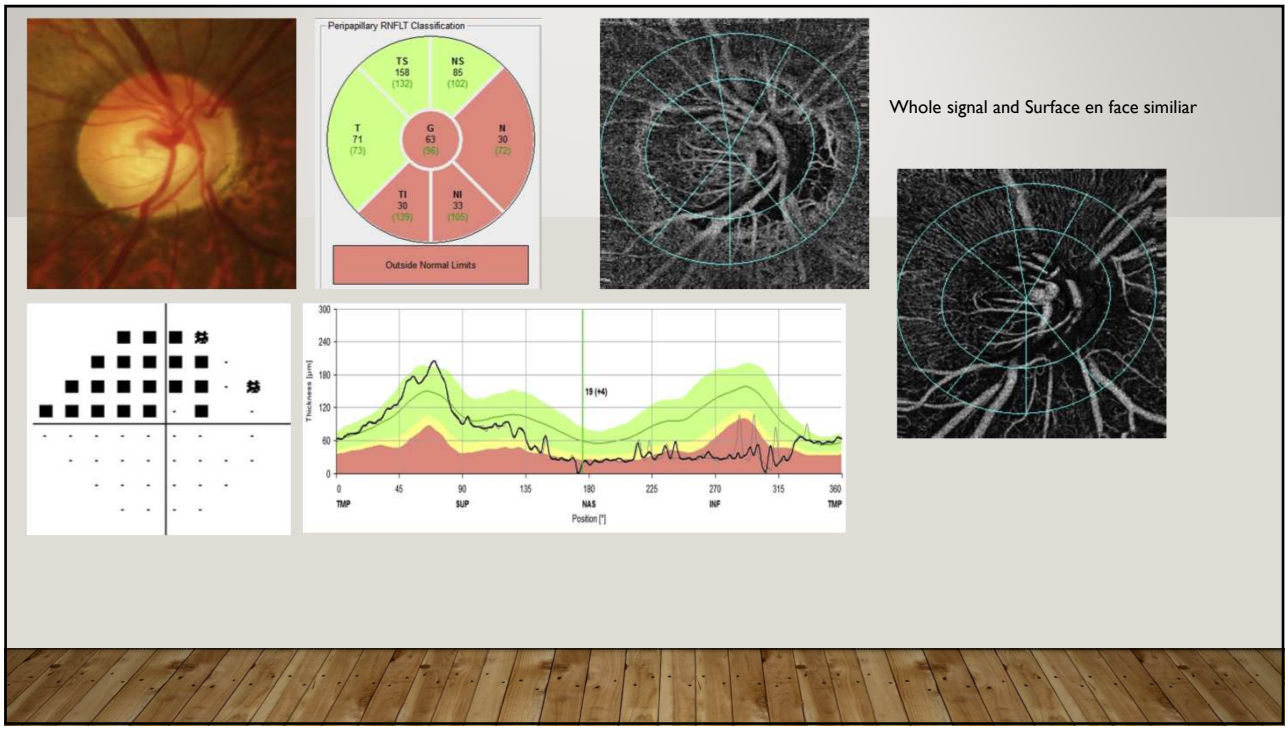
AKAGI T, IIDA Y, NAKANISHI H, TERADA N, MOROOKA S, YAMADA H, HASEGAWA T, YOKOTA S, YOSHIKAWA M, YOSHIMURA N.

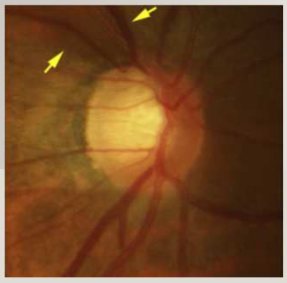
- PURPOSE: To investigate microcirculation of peripapillary retina and optic disc in eyes with primary open-angle glaucoma (POAG) and hemifield visual field (VF) defects

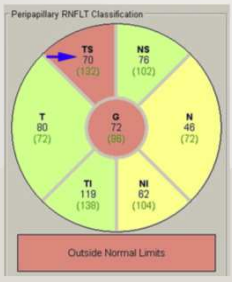


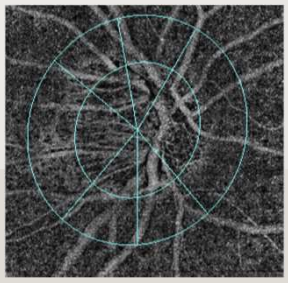
AJO 2016 Aug;168:237-49. Epub 2016 Jun 11.


Peripapillary RNFLT Classification
TS 158 (132)
NS 85 (102)
T 71 (73)
G 63 (86)
N 30 (72)
TI 30 (139)
NI 33 (105)
Outside Normal Limits
Thickness [µm]
19 (+4)
0 45 90 135 180 225 270 315 360
TMP SUP NAS INF TMP
Position [°]
Peripapillary RNFLT Classification
TS 70 (102)
NS 78 (102)
T 80 (73)
G 72 (86)
N 46 (72)
TI 118 (139)
NI 82 (104)
Outside Normal Limits
Thickness [µm]
42 (+1)
0 45 90 135 180 225 270 315 360
TMP SUP NAS INF TMP
Position [°]

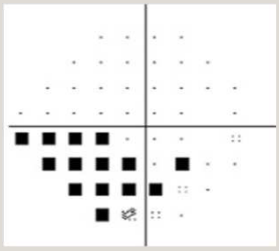

Peripapillary RNFLT Classification
TS 158 (132)
NS 85 (102)
T 71 (73)
G 63 (86)
N 30 (72)
TI 30 (139)
NI 33 (105)
Outside Normal Limits
Thickness [µm]
19 (+4)
0 45 90 135 180 225 270 315 360
TMP SUP NAS INF TMP
Position [°]
Whole signal and Surface en face similiar

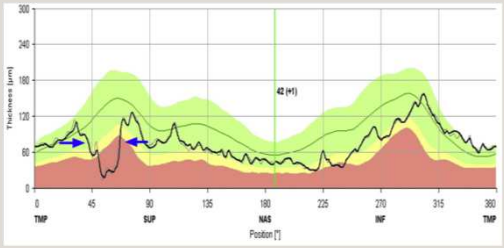


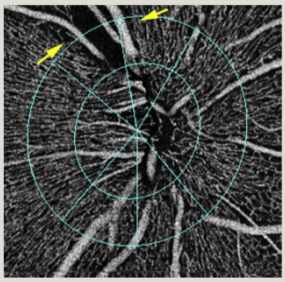




Whole-signal-mode en face projection







Surface-mode en face projection focal pericapillary dropout

OCT ANGIOGRAPHY: MICROVASCULAR DENSITY IN GLAUCOMATOUS EYES WITH HEMIFIELD VISUAL FIELD DEFECTS

AKAGI T, IIDA Y, NAKANISHI H, TERADA N, MOROOKA S, YAMADA H, HASEGAWA T, YOKOTA S, YOSHIKAWA M, YOSHIMURA N.

- PURPOSE: To investigate microcirculation of peripapillary retina and optic disc in eyes with primary open-angle glaucoma (POAG) and hemifield visual field (VF) defects
- RESULTS: Peripapillary vessel densities significantly reduced at VF corresponding location non-highly myopic ($P < .001$, $P = .006$) & highly myopic glaucomatous eyes ($P < .001$, $P = .005$

Vessel densities of the optic discs significantly reduced at locations corresponding to the VF defects in eyes without high myopia but only with inferior hemifield VF defects ($P = .006$)

Vessel densities in the peripapillary retina were significantly associated with visual field total deviation values at their corresponding sides

Choroidal microvascular reduction in the peripapillary area extended to the α-peripapillary atrophy (PPA) as well as β-PPA zones.

AJO 2016 Aug;168:237-49. Epub 2016 Jun 11.

MICROVASCULAR DENSITY IN GLAUCOMATOUS EYES WITH HEMIFIELD VISUAL FIELD DEFECTS

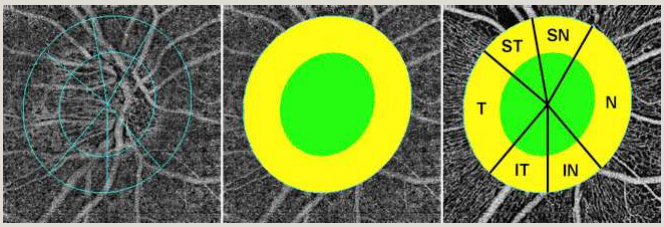
AKAGI T ET AL

- CONCLUSIONS:

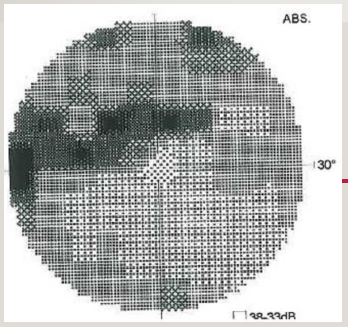
  Microvascular reduction was associated with VF defects in a region-specific manner:

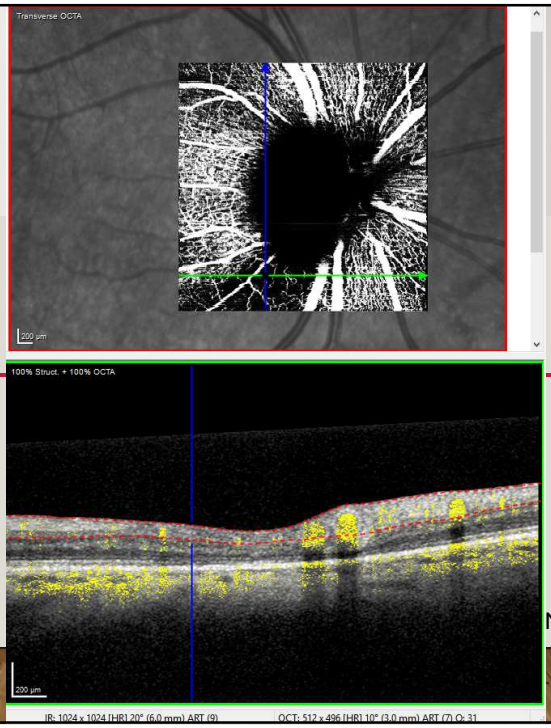
  significantly in the peripapillary retina

  partially significantly in the optic disc



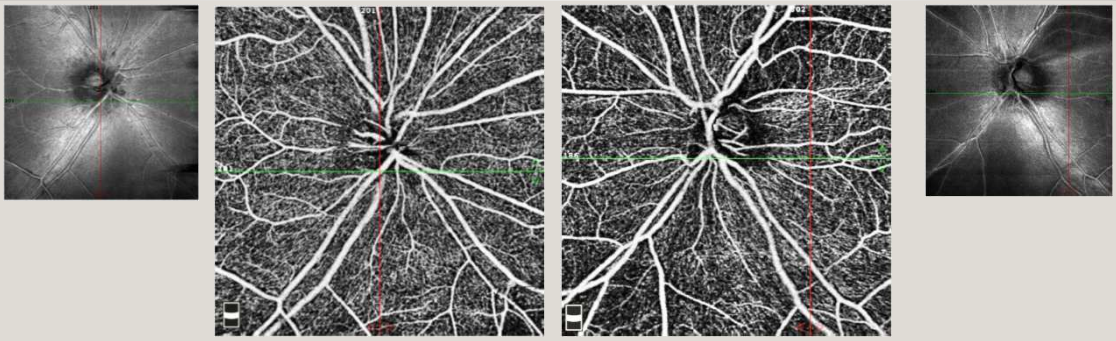
87 yo male patient





Not FDA cleared

CASE PRESENTATION



What is Glaucoma?

Murray Fingeret, OD

What is Glaucoma?

Studies of glaucoma employ a variety of structural and functional measures when defining glaucoma. Earlier this year, Dr. Harry Quigley invited glaucoma specialists across the globe to join a group to ". . . consider a formal definition of glaucoma's optic neuropathy using a combination of findings from OCT imaging and visual field testing." The objective was to develop ". . . a consensus definition for clinical research, to allow comparison across studies." The response was overwhelmingly positive and illustrated the need for such a definition. Based upon initial email discussions, a framework for possible definitions of GON for use in clinical research was developed; it is reproduced in Table 1.

Table 1. DEFINITION OF GLAUCOMATOUS OPTIC NEUROPATHY (GON)- modified from XXXX.

A. Definite GON requires that all of the four criteria below are satisfied

1) An OCT structural defect is present.
2) A 24-2 visual field defect is present.
3) The OCT and visual field defects should be in the matching hemi-retina/ hemi-field.
4) A clinical examination eliminates other visible causes of the findings and is at least compatible with GON

In addition, persons are defined as definite glaucoma if they qualify as possible GON in at least one eye AND have defined, documented progressive worsening in either OCT or visual field in the same eye

B. Possible GON is defined by any of the following 4 situations

1) OCT abnormal but visual field normal, and IOP is abnormal or a disc hemorrhage was observed
2) Field abnormal, but OCT normal, and IOP is abnormal or a disc hemorrhage was observed
3) OCT and field abnormal, but clinical exam is not definitely compatible with GON (e.g. severely myopic eyes)
4) OCT and field abnormal, but not in matching hemi-fields

What is Glaucoma

- "*Actually glaucoma diagnosis is essentially clinical. Indeed, so far there is no a marker to make the diagnosis for glaucoma, like blood glucose for diabetes*."
  - Look at the formal criteria for diseases like diabetes, hypertension, Alzheimers, etc. attempted by their expert panels
  - Glaucoma is in much better shape for describing in objective means the "disorder" or "disease" of glaucoma, one key aspect of which is its glaucomatous optic neuropathy (GON)
  - Elevated blood glucose or high blood pressure doesn't make the diagnosis of diabetes or hypertension, if by diagnosis one means the abnormal effect of the disease on the body or quality of life of the person affected
    - Elevated blood glucose or high blood pressure are closer to IOP than markers of disease.
  - The CNS community would love to have an OCT and field equivalent to measure Alzheimers in life
  - The diabetes definition(s) are multiple phrases of "either/or" and in some cases very subjective parameters

An Update to the Diagnosis of Glaucoma

- *Compare metrics [e.g. GHT, PSD, MD etc. for 24-2 visual fields and global pRNFL thickness, quadrant analysis etc, for OCT) to qualitative visual inspection of a one-page report based upon OCT scans of both the macula and disc. Based upon this work, as well as previous work consider the following:*
  - *Need for macular cube scan and RGC analysis*
    - *Routine testing should include OCT cube scans that include the macular region (±8°) as well as the disc*
    - *Either two separate scans or a wide scan that includes both will do*
    - *Macular damage can be missed if you rely on peripapillary OCT analysis w/o a macular cube scan and a RGC analysis*

An Update to the Diagnosis of Glaucoma

- Need for 10-2 visual field – central points
  - Damage to the macula is common in early glaucoma and the 24-2 test can miss and/or underestimate this damage
  - While OCT cube scans of the macula will usually detect this damage, functional damage should be confirmed using a pattern with a higher density of points in the macula
    - e.g. 10-2 pattern or 24-2 pattern with more central points added

The Central Field in Glaucoma

- Does the 24-2 detect functional vision loss in the central 10^0 in all cases?
  - Points in test grid are 6^0 apart in a grid pattern
- Is there a role for a complementary test such as the 10-2 in which 55 points are placed in a 10^0 area that are 2^0 apart?
  - Will this detect small scotomas that fall between the cracks?
- Is glaucoma a disease that involves the macula region early in the condition?

Progress in Retinal and Eye Research 32 (2013) 1–21

Contents lists available at SciVerse ScienceDirect

Progress in Retinal and Eye Research

journal homepage: www.elsevier.com/locate/prer

Glaucomatous damage of the macula

Donald C. Hood [a,b,*,1], Ali S. Raza [a,c,1], Carlos Gustavo V. de Moraes [d,e,1], Jeffrey M. Liebmann [d,e,1], Robert Ritch [d,f,1]

[a] Department of Psychology, Columbia University, New York, NY 10027-7004, USA
[b] Department of Ophthalmology, Columbia University, New York, NY 10027-7004, USA
[c] Department of Neurobiology and Behavior, Columbia University, New York, NY, USA
[d] Einhorn Clinical Research Center, New York Eye and Ear Infirmary, New York, NY, USA
[e] Department of Ophthalmology, New York University, New York, NY, USA
[f] Department of Ophthalmology and Visual Science, New York Medical College, Valhalla, NY, USA

ARTICLE INFO

Article history:
Available online 17 September 2012

Keywords:
Glaucoma
OCT
Macula
Retinal ganglion cell
Visual field

ABSTRACT

There is a growing body of evidence that early glaucomatous damage involves the macula. The anatomical basis of this damage can be studied using frequency domain optical coherence tomography (fdOCT), by which the local thickness of the retinal nerve fiber layer (RNFL) and local retinal ganglion cell plus inner plexiform (RGC+) layer can be measured. Based upon averaged fdOCT results from healthy controls and patients, we show that: 1. For healthy controls, the average RGC+ layer thickness closely matches human histological data; 2. For glaucoma patients and suspects, the average RGC+ layer shows greater glaucomatous thinning in the inferior retina (superior visual field (VF)); and 3. The central test points of the 6° VF grid (24-2 test pattern) miss the region of greatest RGC+ thinning. Based upon fdOCT results from individual patients, we have learned that: 1. Local RGC+ loss is associated with local VF sensitivity loss as long as the displacement of RGCs from the foveal center is taken into consideration; and 2. Macular damage is typically arcuate in nature and often associated with local RNFL thinning in a narrow region of the disc, which we call the macular vulnerability zone (MVZ). According to our schematic model of macular damage, most of the inferior region of the macula projects to the MVZ, which is located largely in the inferior quadrant of the disc, a region that is particularly susceptible to glaucomatous damage. A small (cecocentral) region of the inferior macula, and all of the superior macula (inferior VF), project to the temporal quadrant, a region that is less susceptible to damage. The overall message is clear; clinicians need to be aware that glaucomatous damage to the macula is common, can occur early in the disease, and can be missed and/or underestimated with standard VF tests that use a 6° grid, such as the 24-2 VF test.

Central Visual Fields and Glaucoma

- Recent papers have suggested that the 24-2 test pattern has limited ability to detect central field defects
  - 50% of retinal ganglion cells are found within 4.5mm of fovea
  - Macula region comprises only 10% of overall visual field area though it is responsible for 60% of area of visual cortex
  - Damage to central 10^0 associated with diminished contrast sensitivity, reduced reading ability

10-2 and 24-2

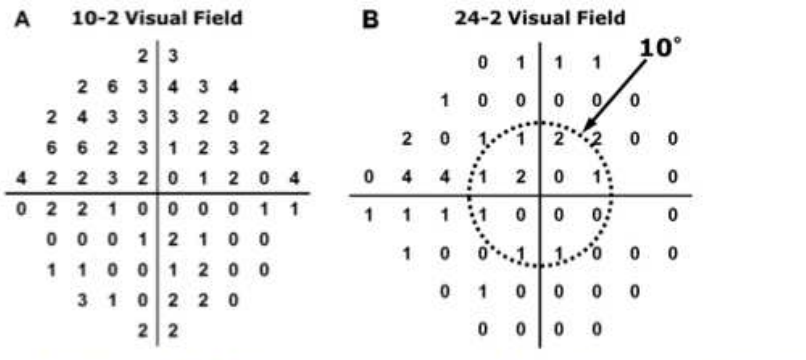


Figure 1. The number of progressing eyes (those having at least one significantly progressing test point) at each test point in (A) 10-2 and (B) 24-2 visual field analyses. Visual field data were mapped as right eyes. The central 10° of visual field on 24-2 testing is depicted by a dashed circle.

An Update to the Diagnosis of Glaucoma

- Need for qualitative assessment - look at the B scans
  - Typical metrics/measures of 24-2 (e.g. MD, PD, GHT, cluster criteria) can miss clear glaucomatous damage seen on OCT and have too many false positives as well
  - With relatively little training, one can do much better with a qualitative assessment of OCT RGC and RNFL thickness and probability plots
  - Many will argue that OCT and visual field evaluation MUST be objective and quantitative
  - We need to recover the reason for this widely held belief.
    - First it differs from what we typically do when combining fundus exam, history, IOP, visual fields and OCT to make judgments
    - Second, it differs from clinical research definitions for other disease entities such as ION and ON/MS, and largely AMD and diabetic retinopathy as well

An Update to the Diagnosis of Glaucoma

- *In the future, artificial intelligence algorithms (e.g. deep learning) may supply a single metric with high sensitivity and specificity*
- *In any case, when designing studies if we only use metrics, and do not include macular scans and 10-2 visual fields, we run the risk of ossifying further a flawed diagnostic approach to glaucoma, which relies on 24-2 visual fields and OCT disc scans*

GONIOSCOPY: HOW AND WHEN?

HOWARD BARNEBEY, MD

REFERALS: IS THIS GLAUCOMA?

- Top 3
  - 1. Suspicious optic nerve
  - 2. Narrow angle
  - 3. Abnormal visual field

GONIOSCOPY OUTLINE

- Cornerstone of Glaucoma Assessment
  - Angle
  - Anterior Chamber Depth
- Methodology
  - Slit Lamp
  - Gonioscopy
  - Anterior Segment OCT
- Advantages/Disadvantages

GONIOSCOPY OUTLINE

- Questions to Address
  - Is Angle Closure A Consideration
    - Today
    - Future: Dictates how often to repeat angle assessment
  - Is there "Something" in the Angle?
    - Pigment: PDS or PXF
    - Blood Vessels" : Rubeosis
    - Mass: Cyst vs Tumor
  - Surgical Devices
- Frequency of Angle Assessment
  - 6 mo or 2 years?
  - Where to look?

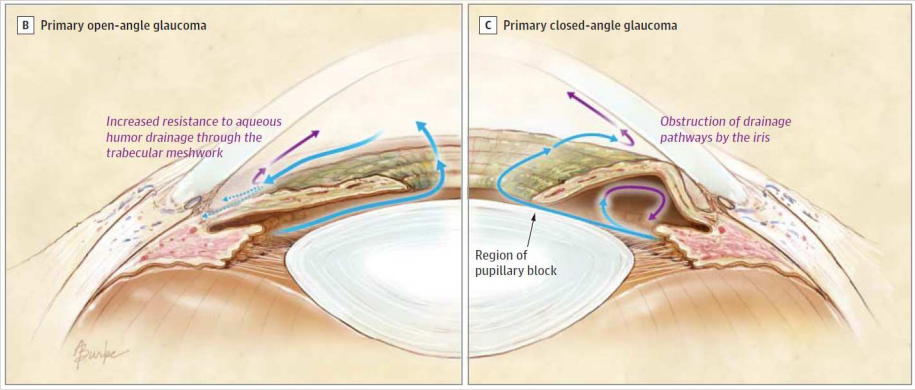
GONIOSCOPY: SUMMARY

- Glaucoma screening during routine exam
  - Demographic at risk
  - IOP elevation
  - Loss of vision
- Established glaucoma patients
  - Level of risk: 1-2 years

GONIOSCOPY: SUMMARY

- Focused Gonioscopy: Where?
  - Narrow angle: superior/temporal
  - Pigment dispersion: superior vs inferior
  - Secondary glaucoma: debris inferior angle
  - Neovascular: TM vascularization (vs blood reflux SC)

Aqueous Outflow - Glaucoma



Weinreb et al. JAMA 2014

EPIDEMIOLOGY

2010	Open Angle	Closed Angle	Total
Diagnose	44.7 M	15.7 M	60.5 M
Blind	4.5 M	3.9 M	8.4 M

EPIDEMIOLOGY

	2010	2020*
Diagnose	60.5 M	79.6 M
Blind	8.4 M	11.1 M

Equal numbers of people bilaterally blind from ACG & OAG (2020*)

Resnikoff et al. WHO 2004
Quigley and Broman. *Br J Ophthalmol* 2006

EPIDEMIOLOGY

2010	Open Angle	Closed Angle	Total	2020
Diagnose	44.7 M	15.7 M	60.5 M	79.6 M
Blind	4.5 M	3.9 M	8.4 M	11.1 M

Closed angle glaucoma: blindness ~3X as likely

Resnikoff et al. WHO 2004
Quigley and Broman. *Br J Ophthalmol* 2006

EPIDEMIOLOGY: WHO?

- Risk Factors

Demographic:	Family history of angle closure
	Advancing age
	Female gender
	Asian/Inuit descent
Anatomic:	Hyperopia
	Angle Area
	Iris volume
	Lens vault
	Choroid

EPIDEMIOLOGY: WHO?

- Risk Factors: Race Dependent

Asia: 86.5% of angle closure glaucoma (worldwide)
PACG in China:
- 56% of primary glaucomas
- 70% is chronic ACG
- 91% of glaucoma bilateral blindness
  - 3 M unilaterally blind
  - 1.5 M bilaterally blind

RISK FACTOR: RACE

Asia: 86.5% of angle closure glaucoma (worldwide)
PACG in China:
- 56% of primary glaucomas
- 70% is chronic ACG
- 91% of glaucoma bilateral blindness
  - 3 M unilaterally blind
  - 1.5 M bilaterally blind

RISK FACTOR: RACE

- US Relevance

Asian population grew 46% 2000 ⇨2010

Asian population expected 2010 ⇨2050

17.3 million (5.6%)

40.6 million (9.2%)

US Census Projections

US Census Projections

RISK FACTOR: AGE?

- Crystalline lens thickens with age
  - Lens thickness risk factor
- Aging of Americans
  - 40.2 million Americans > 65 years old
  - Next Decade:
    - White population: 581,000 with PACG, expected ↑18%
  - By 2050, Americans > 65 yo: expected 2x to 88.5 million

Day et al. *Br J Ophthalmol* 2012
US Census Projected

DEFINITION: ANGLE CLOSURE SUSPECT

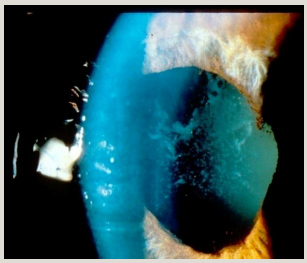
- What is primary narrow angle?
  - potentially occludable angle
  - no identifiable anatomic or syndrome-related causes
- Exam: appositional contact between peripheral iris & TM possible
  - not occurred yet

Cumba et al. *ISRN Ophthalmol* 2012

DEFINITION: PRIMARY ANGLE CLOSURE

- Includes at least one of following:

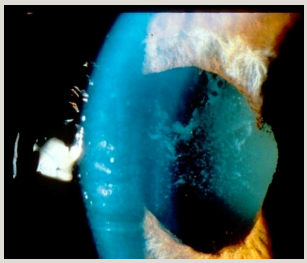
1. Gonioscopy
   - Evidence of angle closure
   - > 90-180^0 nonvisible posterior TM
   - PAS (superior)
   - Pigment deposition on surface of TM
2. Slit lamp evidence of previous acute angle closure:
   - Glaukomflecken
   - Sector Iris Atrophy
3. IOP $\geq$ 21 mm Hg
4. Using IOP-lowering medications



Cumba et al. *ISRN Ophthalmol* 2012

DEF: PRIMARY ANGLE CLOSURE GLAUCOMA

1^0 Angle Closure + damage
- RNFL/Optic nerve atrophy
- Visual field loss



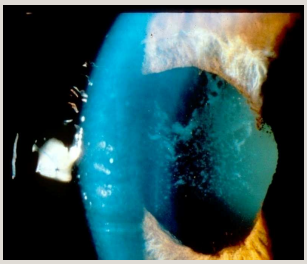
Cumba et al. *ISRN Ophthalmol* 2012

DEF: PRIMARY ANGLE CLOSURE SUBACUTE

History Driven:

Intermittent episodes of
- blurred vision
- +/- rainbow haloes around lights
- ocular discomfort or headaches
- More common at night

- May be relieved by light-induced or sleep-induced miosis
- Can result in permanent PAS and become asymptomatic but with persistent elevated IOP
- Maybe misdiagnosed as migraine

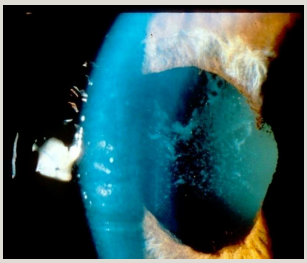


Cumba et al. *ISRN Ophthalmol* 2012

DEF: CHRONIC PRIMARY ANGLE CLOSURE

- Most common type of angle closure
  Often asymptomatic

- Appositional angle closure with or without permanent PAS may result in elevated IOP
- Can develop in eyes with previously open angles
- Diagnosis depends on careful gonioscopy
  PAS tend to begin superiorly
  indentation can help distinguish
  appositional closure
  synechial closure

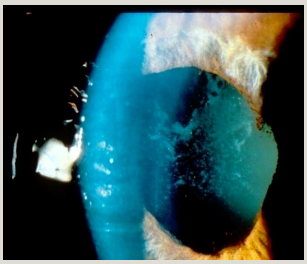


Cumba et al. *ISRN Ophthalmol* 2012

DEFINITION: ANGLE CLOSURE RISK

Predisposed eye:

- Not all equally narrow angles develop angle closure
- Factors:
  - Lens size
  - Angle width
  - Iris thickness
  - Iris dilator insertion position?
  - Choroidal thickness



Cumba et al. *ISRN Ophthalmol* 2012

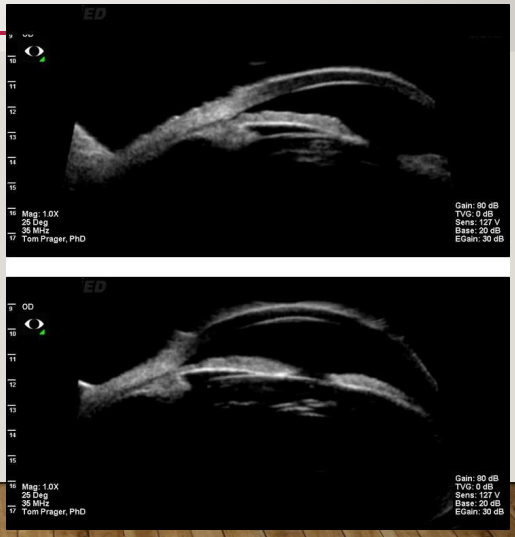
ANGLE CLOSURE: DYNAMIC PROCESS

- Iris position with pupil size/accommodation
- Iris volume changes with pupil size/accommodation
- Choroidal volume changes
- Normal contact between iris and lens

  always a relative obstruction of aqueous flow from posterior to anterior chamber

ANGLE CLOSURE: DYNAMIC PROCESS

- Iris position with pupil size/accommodation
- Iris volume changes with pupil size/accommodation
- Light induced miosis



OFF

ON

PATHOPHYSIOLOGY: IRIS VOLUME / AREA

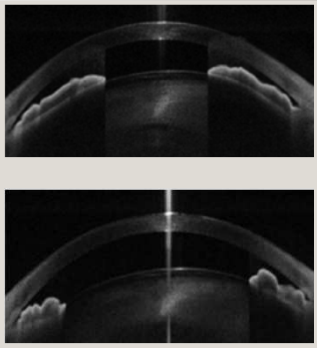
Zhang et al, *IOVS*, 2016 (retrospective)

- Population: Chinese
  31 PAC/PACG 31 PACS 31 normal eyes
- ASOCT changes in light to dark
- Statistically significant iris area decrease in all groups with dilation,
  smallest loss in PAC/PACG
  greatest loss in normal eyes (area loss per mm pupil dilation)

PATHOPHYSIOLOGY: IRIS VOLUME / AREA

Mak et al, *Ophthalmology*, 2013 (prospective)

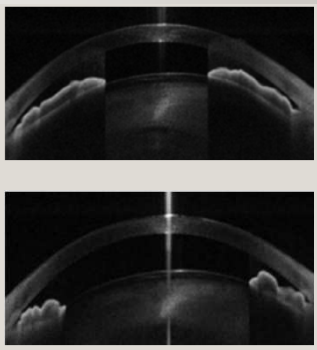
- Population: 86 eyes
  31 PAC/PACS 31 POAG 24 normal
- ASOCT imaging
- ↓ Mean iris volume after pupil dilation (both AC and OA eyes)
  Degree of reduction less:
  smaller anterior chamber
  older age

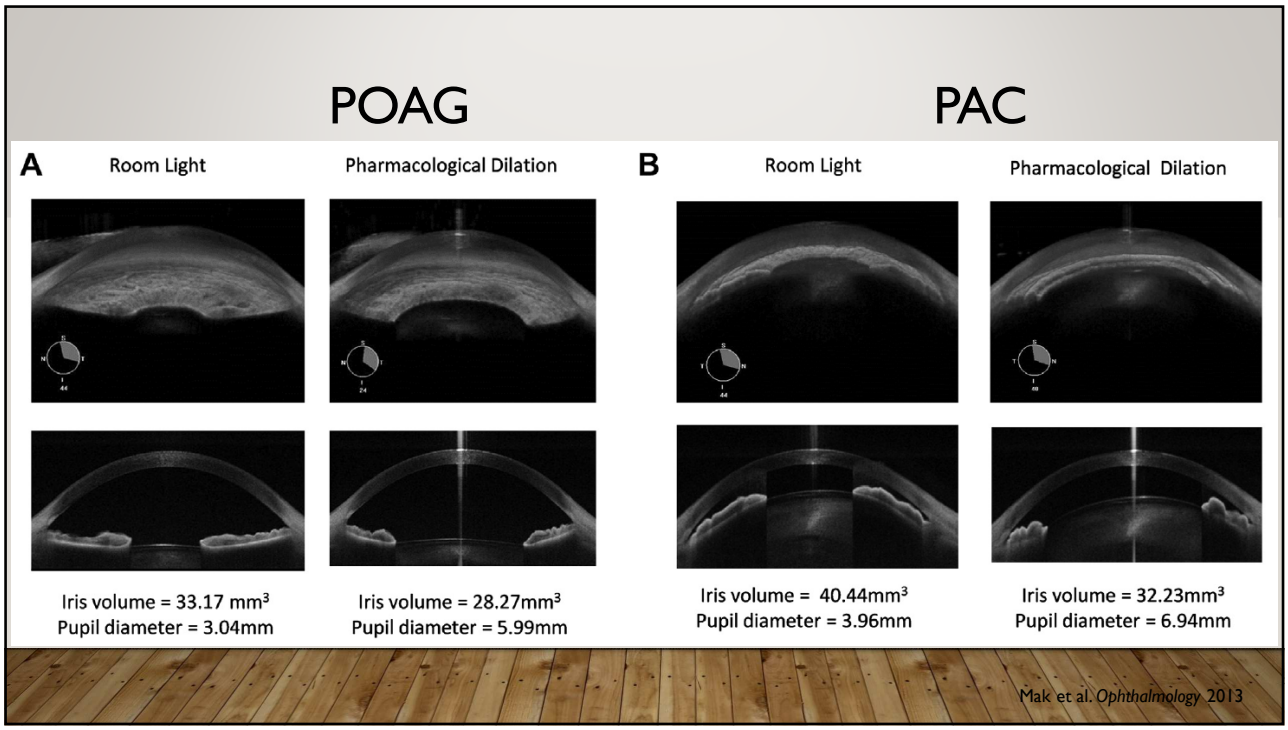


PATHOPHYSIOLOGY: IRIS VOLUME / AREA

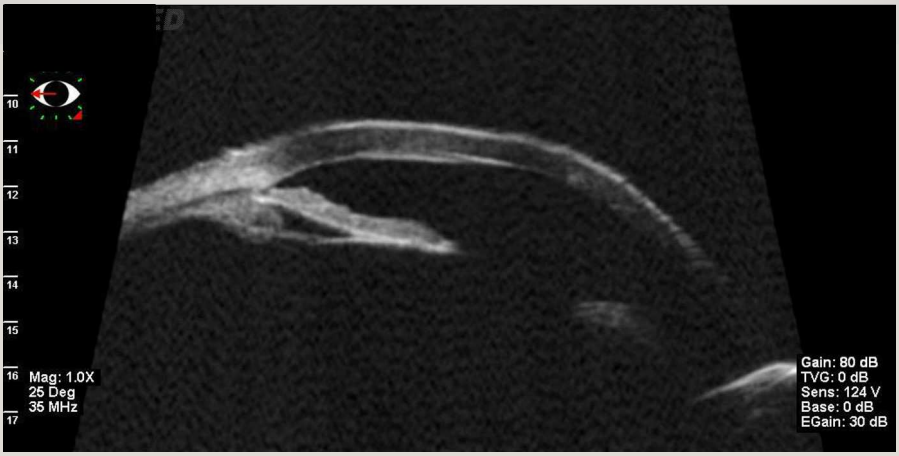
Mak et al, *Ophthalmology*, 2013 (prospective)

- Population: 86 eyes (31 PAC or PACS, 31 POAG, 24 normal), ASOCT imaging
- ↓ Mean iris volume after pupil dilation (both AC and OA eyes)
  Degree of reduction less with smaller anterior chamber and older age





CHOROIDAL VOLUME CHANGES



PATHOPHYSIOLOGY:CHOROIDAL CHANGES

Zhou et al

- Prospective study
  Population: 162 PAC spectrum eyes, 87 normal
- PAC eyes had greater macular choroidal thickness
- Higher choroidal thickness was associated with PAC after adjusting for other known biometric parameters

Acta Ophthalmologica, 2014

PATHOPHYSIOLOGY:CHOROIDAL CHANGES

- Li et al
- Population: Chinese 59 PACG 56 normal, age-matched
- OCT-EDI imaging compare macular thickness
- Choroidal thickness significantly increased in PACG eyes compared to normal
- Choroidal thickness not different between moderate and severe PACG

Acta Ophthalmologica, 2015

PATHOPHYSIOLOGY:CHOROIDAL CHANGES

Arora et al, *IOVS*, 2012

Population: 48 OAG/OAGS eyes 40 ACS/AC/ACG eye
70% White 30% non-White

Study: Drank 1 L of water and imaged with OCT after 30 minutes

Increase in choroidal thickness in AC group but not OA group

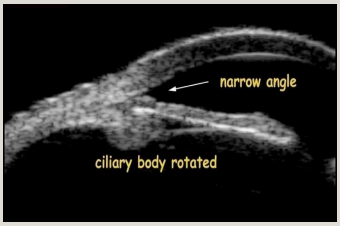
Iovs 2012

IMAGING MODALITIES

- UBM
- Scheimpflug
  - Pentacam (OCULUS): rotating Scheimpflug
  - Galilei (Ziemer): dual channel rotating Scheimpflug
- ASOCT

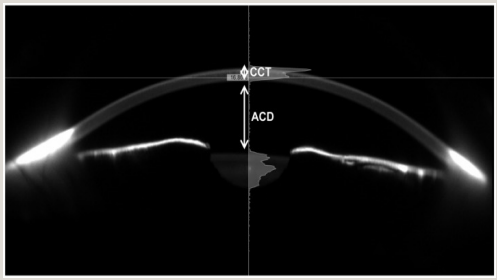
IMAGING MODALITIES: UBM

- Sound waves; can image posterior structures behind iris (i.e. ciliary body)
- Resolution: 50 µm lateral and 25 µm axial
- Limitations:
  operator-dependent
  contact technique
  may distort structures



IMAGING MODALITIES: SCHEIMPFLUG

- Uses light scattering Resolution: 4 µm lateral and 1 µm axial (Galilei)
- Limitations
  cannot directly visualize angle recess

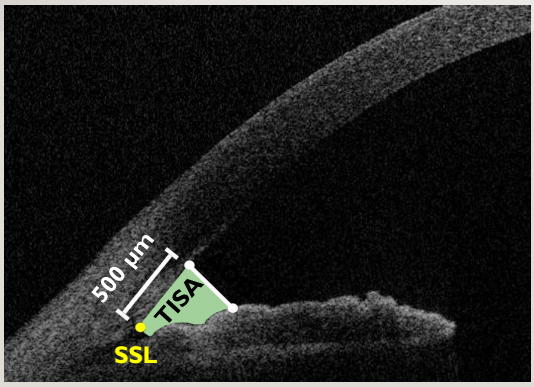


Courtesy Robert Feldman

IMAGING MODALITIES: ASOCT

- Uses 1310 nm light
  vs retinal OCT uses 840-870 nm
- Allows for better visualization of angle
  light penetrates further through tissues
  such as sclera and limbus that greatly scatter light
- Available devices:
  CASIA SS-1000 (Tomey)
  Visante (Carl Zeiss Meditec)

TISA AND DEFINITIONS

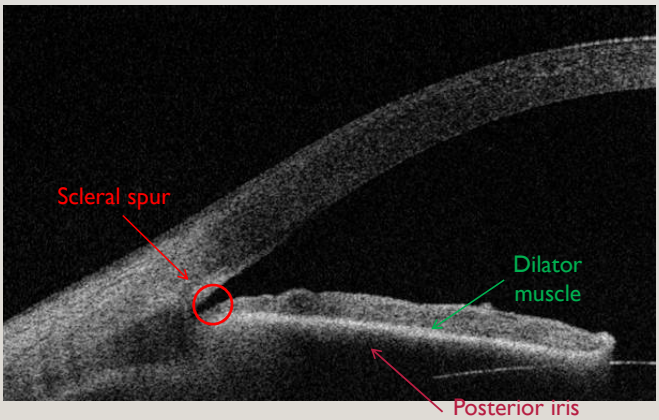


- TISA: trabecular iris surface area
- AOD: angle opening distance
- ARA: angle recess area
- TICV: trabecular iris circumference volume

- Iris volume
- Number following (i.e. 500, 750)

Cumba RJ et al. *J Ophthalmol.* 2012
Rigi et al. *J Ophthalmol.* 2014

ISSUES WITH DEFINITIONS



ANGLE ASSESSMENT: ASOCT V GONIOSCOPY

Kappa [95% CI]	Agree			Disagree n (%)
	Overall n (%)	Narrow n	Open n	
Visit 1 (N=86)				
0.66 [0.50, 0.83]	73 (85%)	22	51	13 (15%)
Visit 2 (N=71)				
0.69 [0.50, 0.89]	63 (89%)	13	50	8 (11%)

Gonioscopy "Pooled" Interobserver Agreement (Kappa (standard error) and [95% confidence interval])

kappa criteria: <0.2 poor 0.21 to 0.40 fair 0.41 – 0.60 moderate
0.61 to 0.80 good > 0.80 excellent.

Examiner	Kappa [95% CI]	N	Agree			Disagree n (%)
			Overall n (%)	Narrow n	Open n	
V	0.67 [0.10, 1.00]	6	5 (83%)	3	2	1 (17%)
W	0.72 [0.43, 1.00]	27	24 (89%)	6	18	3 (11%)
X	0.86 [0.68, 1.00]	32	30 (94%)	10	20	2 (6%)
Y	0.68 [0.43, 0.94]	36	31 (86%)	9	22	5 (14%)
Z	0.53 [0.07, 1.00]	41	38 (93%)	2	36	3 (7%)

Gonioscopic Intraobserver (intervisit) Agreement for Angle Classification by Examiner

Readers

Kappa [95% CI]	Agree			Disagree n (%)
	Overall n (%)	Narrow n	Open n	
Intraobserver - Visit 1 (N=85)				
0.73 [0.59, 0.88]	74 (87%)	30	44	11 (13%)
Intraobserver - Visit 2 (N=72)				
0.58 [0.39, 0.77]	58 (81%)	19	39	14 (19%)
Intraobserver (intervisit) agreement for Reader 1 (N=71)				
0.57 [0.37, 0.77]	57 (80%)	18	39	14 (20%)
Intraobserver (intervisit) agreement for Reader 2 (N=71)				
0.83 [0.69, 0.96]	65 (92%)	26	39	6 (8%)

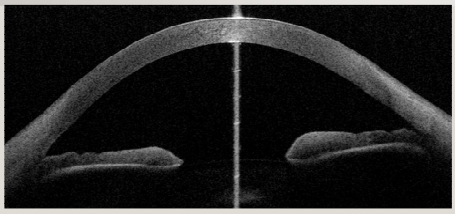
ASOCT Agreement

HOW TO USE CLINICALLY TODAY

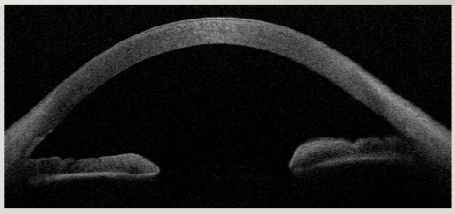
- OCT: image angle
- UBM: image ciliary body and sulcus
  - Allows us to avoid LPI in pure plateau
- Ruling out other etiology
  - Tumor
  - Choroidal hemorrhage or detachment
- Study endpoint

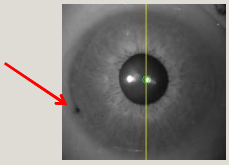
BEFORE AND AFTER LPI

Before



After





DOES LPI OPEN THE ANGLE?

- Retrospective review of patients who underwent iridotomy, have 20/40 or better vision, and at least one year of follow-up
- Population: 79 PAC spectrum eyes of 52 patients from 1995-2005; 42.3% White, 28.9% Black, 21.2% Hispanic, 7.7% Asian
- Exclusion criteria

  Previous:
  - Acute angle closure
  - Laser trabeculoplasty
  - Intraocular incisional surgery
  - Extraocular surgery
  - Intraocular injections

Cumba et al. *ISRN Ophthalmol* 2012

LPI EFFECT - GONIOSCOPY

- Overall
  - 67.2% (53 of 69 eyes) had angle deepening by at least 10 degrees
- PACS
  - 100% (25 eyes)

Cumba et al. *ISRN Ophthalmol* 2012

ASOCT: PRE- AND POST-LPI

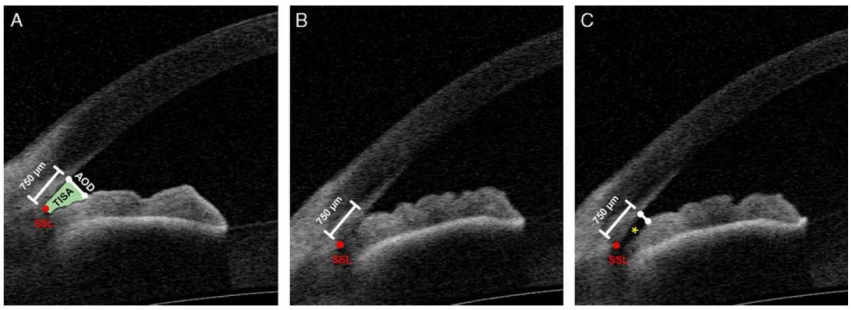


FIGURE 2. Comparison images of exhibiting TISA750 in a normal eye (A), before LPI in an eye with PAC spectrum disease (B), and after LPI in the same eye (TISA is indicated by yellow asterisk). TICV is TISA integrated over the peripheral angle. LPI indicates laser peripheral iridotomy; SSL, scleral spur landmark; TICV, trabecular iris circumference volume; TISA, trabecular-iris space area. full color online

Kansara et al. *J. Glaucoma* 2015

HOW LONG DOES LPI WORK?

Cumba et al, *ISRN Ophthalmol,* 2013 (retrospective)

- Mean f/u: 57.1 ± 29.0 months (13.8-150.6)
- 72% of PACS eyes (18 of 25) required meds by last follow-up
- 2 PACS eyes (of 25, 8%) progressed to glaucoma

How long does LPI work?

- Bansal et al, Am J Ophthalmol, 2015 (retrospective)
- Population: 1660 patients with bilateral LPIs in US managed care network, followed for 2 years

	Patients Taking Medication, N (%)[a]			Mean (SD) Number of Medication Classes for Those Receiving Glaucoma Medications[b]			
	Before First LPI	After Second LPI	*P* Value[c]	N	Before First LPI	After Second LPI	*P* Value[c]
Total	175 (10.5)	350 (21.1)	<.0001	145	1.48 (0.76)	1.80 (0.97)	<.0001
6 months	57 (3.4)	127 (7.7)	<.0001	24	1.21 (0.41)	1.33 (0.56)	.42
12 months	63 (3.8)	140 (8.4)	<.0001	26	1.23 (0.43)	1.42 (0.58)	.17
24 months	53 (3.2)	165 (9.9)	<.0001	36	1.11 (0.32)	1.25 (0.50)	.10

167 patients (10.1%) had $\geq$ 1 cataract surgery after 2nd LPI

79 patients (4.1%) had glaucoma surgery within 2 years of LPI

HOW LONG DOES LPI WORK?

Peng et al, *BJO,* 2011 (retrospective)

- Population: Vietnamese
- 17 of 239 PACS eyes (7.1%) required additional medication
- 9 of 239 (3.8%) PACS eyes progressed to glaucoma
- Mean follow-up time: 11.9 $\pm$ 1.5 years for PACS

HOW LONG DOES LPI WORK?

Blondeau et al, *Can J Ophthalmol*, 2011 (retrospective)

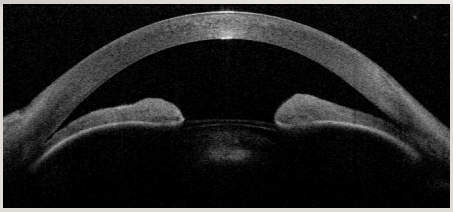
- Population: White PACS
- At 10 years, 38.7% (182 of 469 eyes) had increase in IOP
- Mean time to IOP > 21: 3.2 $\pm$ 3.6 years
- Mean time to treatment after LPI: 5.8 $\pm$ 4.8 years
- Mean follow-up time: 8.5 $\pm$ 5.53 years

CONCLUSION

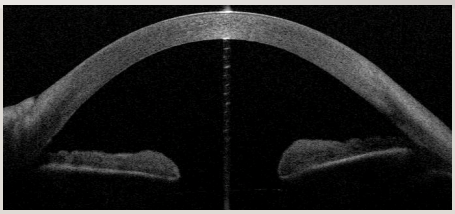
- LPI is reasonably effective, but further surgical intervention is likely in a patient's future.
- Is lens extraction better?

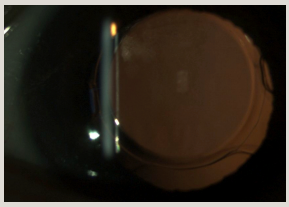
LENS REMOVAL

Before



After





Courtesy Robert Feldman

PHACO VS TRAB

Zhang et al, *J Glaucoma*, 2015 (prospective)

- 145 PACG eyes (87 acute, 58 chronic), Chinese, follow-up: 13.2 +/- 5.6 mo
- Randomized to phacoemulsification or trabeculectomy
- IOP lowered in both groups at 12 months
- AC significantly deeper in phaco group at 3 months
- Angle wider in phaco group at 12 months (UBM and gonio)
- No difference corneal endothelial density between groups before or after surgery

LE AND PAC

Shams et al, *J Glaucoma*, 2012 (retrospective)

- Population: UK, PAC/PACG with cataract; follow-up: 7.2 mo
- IOP, no. meds, PAS significantly reduced; increased angle width and AC depth; improved VA
- No difference in IOP reduction between eyes with prior LPI and eyes w/o LPI

LE AND PAC

Huang et al, *Arch Ophthalmol,* 2011 (prospective)

- Population: San Francisco, 26 narrow angle (NA) eyes, 37 OA eyes
- Follow-up: 6 mo
- Deeper AC, with NA group deepening more than OA group (about same depth after LE)
- ↓ IOP
  - Groups = after LE

LE AND PAC

Nonaka et al, *Ophthalmology*, 2006 (retrospective)

- Population: Japan, 31 eyes with PAC/PACG treated with cataract surgery alone
- UBM at 1 m and 3 m after LE
- 68% ↑ AC depth
- ↑ in angle opening (AOD500)
- Improved VA
- Ciliary processes shifted posteriorly

PRE- AND POST-LE

- 28 PAC spectrum eyes
- 15 females and 3 males; average age 64.8 (±6.4) years
- 8 White, 6 Black, 4 Hispanic

PRIMARY LE VS LPI

Hata et al, *J Med Invest*, 2008 (prospective)

- Population
  - Japanese
  - 50 eyes,
  - CACG or PAC,
  - Follow-up: 6 mo
- Mean postop IOP: ↓ in LE , = in LPI
- Meds: 0 in LE, ↓ in LPI

PHACO VS LPI

Dias-Santos et al, *Int Ophthalmol,* 2014 (prospective, randomized)

- Population: European, 30 eyes, cataract and PAC or PACG
  - Follow-up: 31.13 $\pm$ 4.97 mo

LPI VS PHACO

Lens Extraction	Laser Iridotomy
↓ IOP	No Change
↓ # meds	No Change
↑ AC angle degrees	No Change
↑ AC Volume	No Change

Dias-Santos et al, *Int Ophthalmol* 2014

SOME PATIENT CONSIDERATIONS

- Age (presbyopia)
- Refractive error
- Availability of treatment/cost
- Extensive PAS (over 270 degrees)

WHY ARE WE POISED TO GET AN ANSWER

- We can now reproducibly identify the scleral spur to within 80 microns (intra- and interobserver > 90% agreement) on ASOCT
- TICV, TISA
- We now have a reliable reproducible method to measure angles!

CLEAR LENS EXTRACTION

Dada et al, *JCRS*, 2015 (prospective)

- Indian population
- 44 PAC eyes with elevated IOP after LPI
- Mean IOP decreased from 27.1 ± 1.55 mm Hg preop to 13.2 ± 1.12 mm Hg 12 months postop (*P*<.001)
- AC angle widened
- Reduced need for IOP-lowering meds

CONCLUSION

- In 2010, it was estimated 15.7 million people have angle closure glaucoma worldwide.
- Almost 25%, almost 4 million people, are bilaterally blind.
- We can fix the angle and prevent blindness.

Acknowledge support from Robert Feldman

Glaucoma Test Results: To Believe or Not to Believe

Murray Fingeret, OD
Chief, Optometry Section, VA NYHHCS Brooklyn Campus
Clinical Professor, SUNY College of Optometry New York, NY

Disclosures

- Consultant
  - Aerie, Alcon, Allergan, Bausch & Lomb, Carl Zeiss Meditec, Heidelberg Engineering, Topcon

Glaucoma Test Results: To Believe or Not to Believe

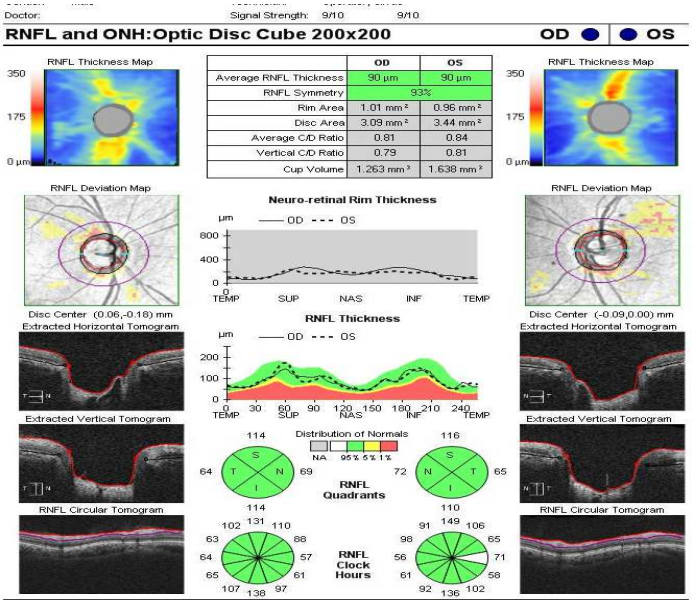
- Glaucoma test battery
  - Case history
    - Is it reliable?
    - Did the family member really have glaucoma? Or was it cataracts/
  - Intraocular pressure
    - Thick or thin cornea may lead to IOP being over or underestimated
  - Optic Nerve Assessment
    - Photos
    - Imaging
      - How is imaging impacted by false results?
      - Signal strength
      - Epiretinal membrane
  - Perimetry
    - Reliability important
    - Defects may appear or disappear depending upon patient performance

Central Corneal Thickness

- Thick cornea over estimates IOP and thin corneas underestimates pressure
- Not clear to what extent
- In OHTS, estimated that on basis of correction factors
  - 44% of NTG become POAG
  - 35% of OHT become normal

What Do You Look For When You Evaluate an OCT Scan

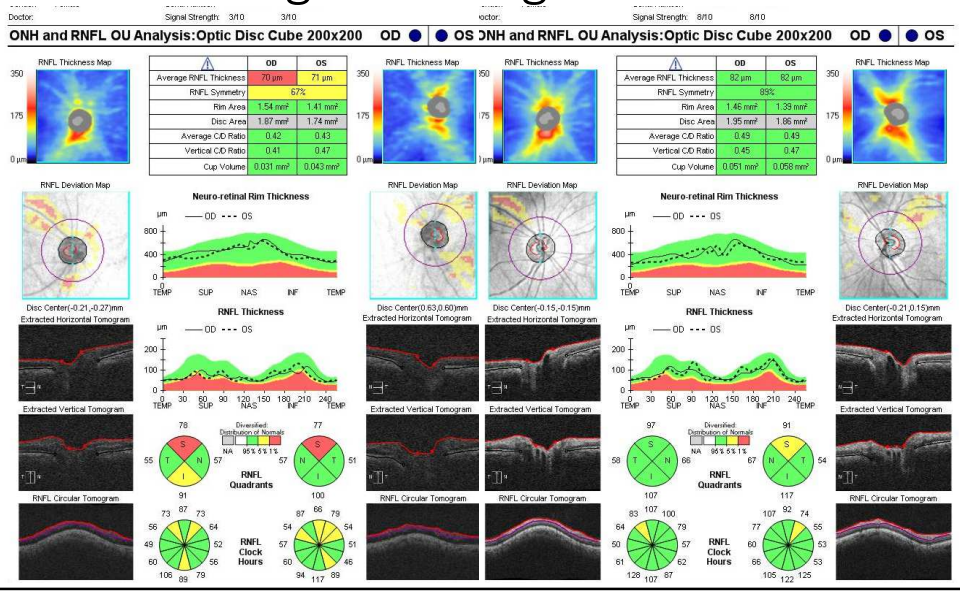
- Quality score
- Illumination
- Focus OK
- Image centered
- Any signs of eye moveme
- Segmentation accuracy
- B Scan Centration



Artifacts in Taking OCT Images Poor Quality Images

- Out of focus
- Reduced illumination
  - Not properly illuminated
- Reduced signal strength
  - Dry eye, cataracts, other media opacities or small pupils
  - There is a relationship between signal strength and RNFL thickness
  - Want signal strength to meet manufacturer's recommendations
  - Use any image in which quality scores are below recommendations with care
  - Even if Quality score is acceptable, there may still be problems with image

The Effect of Signal Strength



	OD	OS
Average RNFL Thickness	70 µm	71 µm
RNFL Symmetry	67%	
Rim Area	1.54 mm²	1.41 mm²
Disc Area	1.87 mm²	1.74 mm²
Average C/D Ratio	0.42	0.43
Vertical C/D Ratio	0.41	0.47
Cup Volume	0.031 mm³	0.043 mm³

	OD	OS
Average RNFL Thickness	82 µm	82 µm
RNFL Symmetry	89%	
Rim Area	1.46 mm²	1.39 mm²
Disc Area	1.95 mm²	1.86 mm²
Average C/D Ratio	0.49	0.49
Vertical C/D Ratio	0.45	0.47
Cup Volume	0.051 mm³	0.058 mm³

Image Artifacts that may make one think disease is present

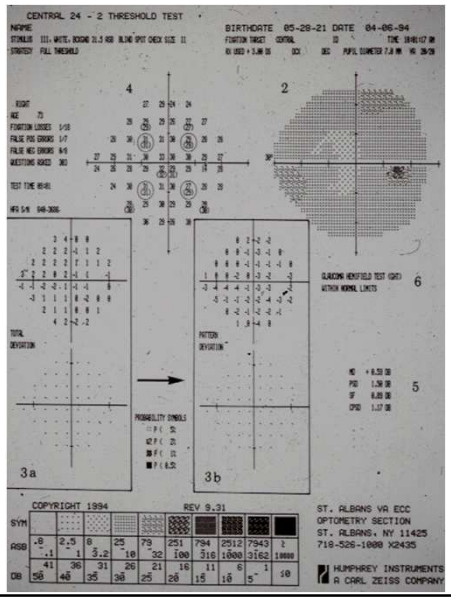
- Blink cutting off image
- Vitreous floaters obscuring tissue underneath
- Pathologies such as epiretinal membrane or chorioretinal scar

Artifacts in Taking OCT Images

- Algorithm failure
  - Epiretinal membrane
  - Segmentation errors
  - B scan segmentation inaccurate
  - Retinal assessment (RNFL, GCC, Retina thickness)
  - Disc margin error
    - Throws off disc size
  - Cup not properly outlined (material in cup throwing segmentation off)
    - Can not over ride this with Cirrus

6 Steps in Analyzing Visual Field

- Right Test
- Reliability
  - False positives
  - False negatives
  - Fixation errors
- Review Probability Plots
  - Global Indices and GHT
- RNFL pattern of loss
- Re-affirm the diagnosis



Visual Fields

- Important to assess reliability
  - False positives
  - False negative
  - Fixation errors
  - Gaze tracking
  - Blind spot plotted

Glaucoma Therapy Update- Medications

Murray Fingeret, OD
Chief, Optometry Section
Dept of Veterans Affairs NYHHCS Brooklyn, NY
Clinical Professor, SUNY Optometry

Disclosures

- Consultant
  - Alcon, Aerie Pharmaceuticals, Allergan, Bausch & Lomb, Carl Zeiss Meditec, Diopsys, Heidelberg Engineering, Reichert, Topcon

Glaucoma Therapy
An Overview

- Chronic disease that can be difficult to control
  - Person has the disease for the rest of their life
- Treatment often requires multiple medications and surgeries
- Treatment endpoints are poorly defined
- Treatment endpoints often difficult to achieve, even when defined
- Medication adherence challenges are common
  - Patients have difficulties taking medications for long periods of time
- Continuing need for new therapies and drug delivery techniques

What's New and What's Next in Glaucoma

- Therapy
  - Generics
  - Do glaucoma medications work around the clock
    - FDA does not require 24 hour testing
  - Fixed combination agents have moved up to 2nd line agents
  - New glaucoma surgical devices such as Xen implant, Cypass, iStent
    - MIGS type devices
  - New Medications
  - New drug delivery devices

Glaucoma Therapy Update

- In future, similar to cardiologists we may discuss with our patients smoking cessation, altering diet, weight loss, and increased physical activity as additional therapies for glaucoma
- Many of the new therapies will revolve around drug delivery directly into the eye via some form of injection (doctor) or insertion (patient)

Glaucoma Therapy Update

- There are currently 5 main classes of IOP-lowering medications
- Each works by altering 1 or more aspects of aqueous humor flow
- Beta-blockers and carbonic anhydrase inhibitors reduce the rate of aqueous production
- Prostaglandins increase outflow through the uveoscleral pathway
- Alpha-adrenergic agonists lower IOP by a dual mechanism
  - reducing aqueous production and increasing uveoscleral outflow
- None of these drugs works at the site of outflow impairment—the TM
- Miotic class of drugs do increase trabecular outflow, but only indirectly through actions on the ciliary muscle
  - not through any direct effects on the TM itself
  - generally poorly tolerated and not widely used in modern practice
- There has been an unmet need for an IOP-lowering medication that works at the TM
  - the main site of outflow obstruction in glaucomatous eyes

Glaucoma Therapy Update

- Trend in topical eyedrop therapeutics is combination compounds with multiple targets and mechanisms of action (MOA) with single daily dosing
- Targets will include trabecular meshwork and uveoscleral outflow, aqueous humor production and episcleral venous pressure (EVP)
- Stem cell and gene therapy are being developed but are years away from clinical use

What about quadruple therapy?

How Can This Medication be Prescribed?

- Does the medication(s) work?
  - Little data to support its efficacy
- Made by compounding pharmacy but needs a prescription
- Need to order the medication by calling the pharmacy
- They can send it to your office, or can call patient, get credit card info and mail direct to patient
- Need to pay for medication at time of order

Quadruple Therapy

- We don't know anything about the side effect profile of putting those 4 medications together in one bottle
- And what about effectiveness?
  - Is there an added benefit of having the 4 medications together compared to just 3 of them.... or even just two of them
  - We have seen that adding timolol to a prostaglandin in the same bottle really does not add any effectiveness to the prostaglandin alone
    - hence the lack of FDA approval of Xalcom, DuoTrav and Ganfort
- And how would you dose this?
  - There are two bid-tid medications, and two once a day medications in the same bottle
- Adherence should improve

GLAUCOMA THERAPY Up Until 11/2/2017

Table 1: Topical treatment options for glaucoma drug class

	Top-line properties	Drug	Average IOP reduction	Safety
Prostaglandin analogs (first-line drug)	Increase uveoscleral outflow. Once-daily dosing except for unoprostone, which requires twice-daily administration	Latanoprost Travoprost Tafluprost Unoprostone Bimatoprost	18–31% during day time and about 8.5–17% during night time	Mild conjunctival hyperemia, darkening of the irises, hypertrichosis, hyperpigmentation of the eye lashes and iris, periorbital fat atrophy, local irritation, cystoid macular edema, increased eyelash growth
β-adrenergic receptor antagonists* (first-line drug)	Reduce the production and secretion of aqueous humor, thereby reduce IOP. Twice-daily dosing	Timolol Levobunolol Carteolol Metipranolol Betaxolol	20–27% during day time	Stinging, blurring, local irritation, bronchospasm, headache, bradycardia, hypotension, dizziness, ocular pain, superficial punctuate keratitis, dryness, conjunctival hyperemia
α2-adrenergic receptor agonists (second-line treatments)	Decrease aqueous humor production; increased uveoscleral outflow. Thrice-daily dosing	Brimonidine tartrate Dipivefrin hydrochloride Apraclonidine Hydrochloride Epinephrine**	12.5–29%	Blepharoconjunctivitis, conjunctival hyperemia, blurry vision, irritation, dry mouth, drowsiness, ocular allergy, systemic hypotension, fatigue, headache, palpitations, high blood pressure, anxiety
Carbonic anhydrase inhibitors (second-line treatments)	Reduction of aqueous humor production via enzymatic inhibition. Twice- and thrice-daily dosing	Brinzolamide Dorzolamide Acetazolamide Methazolamide	13.2–22% Modest efficacy at night time	Ocular surface irritation, ocular allergy, transient blurred vision, stinging, itching, corneal edema, tearing, bitter, dry eyes, headache, paresthesia of fingertips and toes, fatigue, depression, kidney stones, thrombocytopenia, agranulocytosis, aplastic anemia
Cholinergic drugs (second-line treatments)	Increase trabecular aqueous humor outflow by contraction of ciliary muscle and scleral spur. Thrice-daily dosing except once daily dosing for echothiophate	Pilocarpine Carbachol Echothiophate	+	Pupillary constriction, ocular burning, brow ache, reduced night vision

New Drugs

- Latanoprost bunod
  - Approved November 2017
  - Nitric oxide donating Prostaglandin F2α
  - Vyzulta Bausch & Lomb
- Rho Kinase Inhibitors
  - 1st quarter 2018
  - Netarsudil 0.02%
  - Rhopressa
  - Aerie
- Rho Kinase Inhibitors and latanoprost
  - Roclatan
  - Aerie
  - 1st quarter 2019
- Lumigan SR
  - Sustained release bimatoprost implant
  - Phase III
- OTX-TP
  - Sustained release travoprost punctal plug
  - Ocular Therapeutix
- Xelpros (latanoprost BAK-free eye drops)
  - Sun Ophthalmics
  - 1st quarter 2018
  - Multi-dose PF bottle

GLAUCOMA DRUGS IN DEVELOPMENT

Table 1. US market status of topical medications for glaucoma

Medication	Sponsor	Mechanism of action	Current US market status
Netarsudil (AR-13324)	Aerie Pharmaceuticals	Rho kinase inhibitor + norepinephrine transporter inhibitor	Phase III trials completed
Netarsudil/latanoprost fixed-dose combination	Aerie Pharmaceuticals	Rho kinase inhibitor/ norepinephrine transporter inhibitor + prostaglandin analog	Phase III trials ongoing
Latanoprostene bunod	Bausch + Lomb	Nitric oxide donor + prostaglandin analog	New Drug Application pending with FDA[a]
Trabodenoson (INO-8875)	Inotek Pharmaceuticals Corporation	Adenosine receptor agonist	Phase III trials ongoing
DE-117	Santen Pharmaceuticals	Prostanoid receptor agonist	Phase II & III trials ongoing
ONO-9054	Ono Pharmaceuticals	Prostanoid receptor agonist	Phase II trials completed
Bamosiran (SYL040012)	Sylentis	Small interfering RNA	Phase II trials completed

Latanoprostone bunod (Vyzulta)

- 0.024% used once daily to reduced IOP
  - Bausch & Lomb
  - Waiting for FDA approval
- Metabolized to latanoprost acid plus butanediol mononitrate
- Butanediol mononitrate is a nitric-oxide donating moiety NO molecule attached to latanoprost backbone to provide dual action
- Works over 24 hour period with >35% IOP reduction
- One molecule leads to IOP reduction via the uveoscleral and trabecular meshwork pathways
- NO is a signaling molecule that regulates outflow facility via the TM
- Can dilate blood vessels
- Modulates TM contractility, cell adhesion and the cytoskeleton leading to reduced IOP
- Medication acts on both the
  - Uveoscleral outflow pathway by altering the extracellular matrix in the ciliary muscle and the sclera
  - Trabecular meshwork outflow by inhibiting actomyosin contractility in trabecular meshwork cells thereby relaxing the meshwork

Nitric Oxide (NO): An Emerging Target for the Treatment of Glaucoma

Megan E. Cavet,[1] Jason L. Vittitow,[2] Francesco Impagnatiello,[3] Ennio Ongini,[3] and Elena Bastia[3]

[1]Bausch & Lomb, Inc., Rochester, New York, United States
[2]Bausch & Lomb, Inc., Bridgewater, New Jersey, United States
[3]Nicox Research Institute, Bresso, Milan, Italy

Correspondence: Megan E. Cavet, Bausch & Lomb, Inc., 1400 North Goodman Street, Rochester, NY 14609, USA;
Megan.Cavet@bausch.com.

Submitted: April 3, 2014
Accepted: June 26, 2014

Citation: Cavet ME, Vittitow JL, Impagnatiello F, Ongini E, Bastia E. Nitric oxide (NO): an emerging target for the treatment of glaucoma. *Invest Ophthalmol Vis Sci.* 2014;55:5005–5015. DOI:10.1167/iovs.14-14515

The predominant risk factor for the progression of glaucoma is an increase in IOP, mediated via a reduction in aqueous outflow through the conventional (trabecular meshwork and Schlemm's canal) outflow pathway. Current IOP lowering pharmacological strategies target the uveoscleral (nonconventional) outflow pathway or aqueous humor production; however, to date no therapy that primarily targets the conventional pathway exists. Nitric oxide (NO) is an intracellular signaling molecule produced by endogenous NO synthases, well-known for its key role in vasodilation, through its action on smooth muscle cells. Under physiological conditions, NO mediates a multitude of diverse ocular effects, including maintenance of IOP. Nitric oxide donors have been shown to mediate IOP-lowering effects in both preclinical models and clinical studies, primarily through cell volume and contractility changes in the conventional outflow tissues. This review is focused on evaluating the current knowledge of the role and mechanism of action of endogenous NO and NO donors in IOP regulation. Data on key additional functions of NO in glaucoma pathology (i.e., ocular blood flow and effects on optic neuropathy) are also summarized. The potential for future therapeutic application of NO in the treatment of glaucoma is then discussed.

BJO

A randomised, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open angle glaucoma: the VOYAGER study

Robert N Weinreb, Tuyen Ong, Baldo Scassellati Sforzolini, Jason L Vittitow, Kuldev Singh and Paul L Kaufman

Br J Ophthalmol published online December 8, 2014

Phase II

ABSTRACT

Aim To assess the efficacy and safety of latanoprostene bunod (LBN) compared with latanoprost 0.005%, and to determine the optimum drug concentration(s) of LBN in reducing intraocular pressure (IOP) in subjects with open angle glaucoma or ocular hypertension.

Methods Randomised, investigator-masked, parallel-group, dose-ranging study. Subjects instilled one drop of study medication in the study eye once daily each evening for 28 days and completed five study visits. The primary efficacy endpoint was the reduction in mean diurnal IOP at Day 28.

Results Of the 413 subjects randomised (LBN 0.006%, n=82; LBN 0.012%, n=85; LBN 0.024%, n=83; LBN 0.040%, n=81; latanoprost, n=82), 396 subjects completed the study. Efficacy for LBN was dose-dependent reaching a plateau at 0.024%–0.040%. LBN 0.024% led to significantly greater reductions in diurnal IOP compared with latanoprost at the primary endpoint, Day 28 (p=0.005), as well as Days 7 (p=0.033) and 14 (p=0.015). The incidence of adverse events, mostly mild and transient, was numerically higher in the LBN treatment groups compared with the latanoprost group. Hyperaemia was similar across treatments.

Conclusions LBN 0.024% dosed once daily was the lower of the two most effective concentrations evaluated, with significantly greater IOP lowering and comparable side effects relative to latanoprost 0.005%. LBN dosed once daily for 28 days was well tolerated.

Clinical trial number NCT01223378.

In conclusion, LBN 0.024% dosed once daily was the lower of the two most effective LBN doses evaluated with significantly greater IOP lowering compared with latanoprost 0.005% solution. To the best of our knowledge, this is the first phase II study that demonstrates a drug that is more effective for IOP lowering, without increased ocular hyperaemia and with comparable overall side effects, than the commercially available latanoprost 0.005% solution.

AMERICAN ACADEMY™
OF OPHTHALMOLOGY

Latanoprostene Bunod 0.024% versus Timolol Maleate 0.5% in Subjects with Open-Angle Glaucoma or Ocular Hypertension

The APOLLO Study

Robert N. Weinreb, MD,[1] Baldo Scassellati Sforzolini, PhD,[2] Jason Vittitow, PhD,[2] Jeffrey Liebmann, MD[3]

Purpose: To compare the diurnal intraocular pressure (IOP)-lowering effect of latanoprostene bunod (LBN) ophthalmic solution 0.024% every evening (qPM) with timolol maleate 0.5% twice daily (BID) in subjects with open-angle glaucoma (OAG) or ocular hypertension (OHT).

Design: Phase 3, randomized, controlled, multicenter, double-masked, parallel-group clinical study.

Participants: Subjects aged ≥18 years with a diagnosis of OAG or OHT in 1 or both eyes.

Methods: Subjects were randomized (2:1) to a 3-month regimen of LBN 0.024% qPM or timolol 0.5% 1 drop BID. Intraocular pressure was measured at 8 AM, 12 PM, and 4 PM of each postrandomization visit (week 2, week 6, and month 3). Adverse events were recorded throughout the study.

Main Outcome Measures: The primary efficacy end point was IOP in the study eye measured at each of the 9 assessment time points. Secondary efficacy end points included the proportion of subjects with IOP ≤18 mmHg consistently at all 9 time points and the proportion of subjects with IOP reduction ≥25% consistently at all 9 time points.

Results: Of 420 subjects randomized, 387 completed the study (LBN 0.024%, n = 264; timolol 0.5%, n = 123). At all 9 time points, the mean IOP in the study eye was significantly lower in the LBN 0.024% group than in the timolol 0.5% group ($P \leq 0.002$). At all 9 time points, the percentage of subjects with mean IOP ≤18 mmHg and the percentage with IOP reduction ≥25% were significantly higher in the LBN 0.024% group versus the timolol 0.5% group (mean IOP ≤18 mmHg: 22.9% vs. 11.3%, $P = 0.005$; IOP reduction ≥25%: 34.9% vs. 19.5%, $P = 0.001$). Adverse events were similar in both treatment groups.

Conclusions: In this phase 3 study, LBN 0.024% qPM demonstrated significantly greater IOP lowering than timolol 0.5% BID throughout the day over 3 months of treatment. Latanoprostene bunod 0.024% was effective and safe in these adults with OAG or OHT. *Ophthalmology 2016;■:1–9 © 2016 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

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

JOHN H.K. LIU, JOHN R. SLIGHT, JASON L. VITTITOW, BALDO SCASSELLATI SFORZOLINI, AND ROBERT N. WEINREB

• PURPOSE: To compare the diurnal and nocturnal effects of latanoprostene bunod 0.024% solution with timolol maleate 0.5% solution on intraocular pressure (IOP) and ocular perfusion pressure.
• DESIGN: Prospective, open-label randomized crossover trial.
• METHODS: Twenty-five patients (aged 43–82 years) with ocular hypertension or early primary open-angle glaucoma were enrolled. Baseline IOP and blood pressure were measured in a sleep laboratory every 2 hours 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 bunod 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.
• RESULTS: Twenty-one subjects completed the study. Both treatments reduced diurnal sitting and supine IOP compared to baseline by 2.3–3.9 mm Hg (all $P <$ .001) with no statistically significant difference between the 2 treatments. Nocturnal IOP under latanoprostene bunod treatment was 2.5 ± 3.1 mm Hg (mean ± SD) less than baseline ($P = .002$) and 2.3 ± 3.0 mm Hg less than timolol treatment ($P = .004$). Latanoprostene bunod treatment resulted in greater diurnal sitting and supine ocular perfusion pressures compared with baseline ($P \leq .006$) and greater nocturnal ocular perfusion pressure compared with timolol treatment ($P = .010$).
• CONCLUSIONS: During the nocturnal period, latanoprostene bunod caused more IOP reduction and more increase of ocular perfusion pressure than timolol. (Am J Ophthalmol 2016;■:■–■. © 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).)

AJO.com Supplemental Material available at AJO.com.

Accepted for publication Apr 27, 2016.

From Hamilton Glaucoma Center, Department of Ophthalmology and Shiley Eye Institute, University of California, San Diego, La Jolla, California (J.H.K.L., J.R.S., R.N.W.), and Bausch & Lomb, Bridgewater, New Jersey (J.L.V., B.S.S.).
Baldo Scassellati Sforzolini is currently affiliated with Allergan, Jersey City, New Jersey.
Inquiries to John H.K. Liu, Department of Ophthalmology, University of California, San Diego, 9500 Gilman Dr, La Jolla, CA 92093-0946; e-mail: jolliu@ucsd.edu

LOWERING INTRAOCULAR PRESSURE (IOP) MAY DELAY the onset of glaucoma in ocular hypertensive patients and slow the disease progression in patients with existing glaucoma.[1] Whereas the highest IOP in patients with ocular hypertension and primary open-angle glaucoma frequently occur outside the diurnal/wake period,[2,3] currently available topical medications to treat these patients have shown variable IOP-lowering efficacies during the nocturnal/sleep period compared to their diurnal efficacies.[4–10] Prostaglandin analogues (including latanoprost, travoprost, and bimatoprost) applied once daily in the evening were shown to be effective in lowering IOP for 24 hours, but with less nocturnal efficacy than the diurnal efficacy.[5–7,10] Timolol, a β-adrenergic antagonist, applied in gel form once daily in the morning, had very limited IOP reduction during the nocturnal period compared to its diurnal efficacy.[5,8]

Latanoprostene bunod (Bausch & Lomb, Bridgewater, New Jersey, USA) is a new nitric oxide–donating prostaglandin $F_{2\alpha}$ analogue with unique biological properties. In situ, latanoprostene bunod is rapidly metabolized to latanoprost acid, a prostaglandin agonist, and butanediol mononitrate, a nitric oxide (NO)-donating moiety.[11] Latanoprost acid (as the active moiety of latanoprost 0.005% [Xalatan; Pfizer, New York, NY]) is reported to reduce IOP by primarily increasing uveoscleral outflow.[12,13] In contrast, NO released from the NO-donating moiety of latanoprostene bunod may lower IOP by increasing the trabecular meshwork outflow.[14–17] Nitric oxide is also a biological messenger for other physiological functions, including vasodilation and, on systemic administration, the reduction of blood pressure.[18]

A recent report showed that latanoprostene bunod was well tolerated and efficacious in lowering IOP in patients with primary open-angle glaucoma or ocular hypertension.[19] There was a dose-dependent reduction in diurnal IOP over 28 days at concentrations of 0.006% to 0.04%, reaching a maximum effect with the 0.024% and 0.04%

New Medication
Rho Kinase Inhibitors

- Rho kinase inhibitors
- Reduce cellular stiffness in trabecular meshwork
  - Target trabecular meshwork cells to enhance outflow
  - May offer neuroprotective as well as anti inflammatory effects
  - Aerie

New Glaucoma Medications

- Aerie Pharmaceuticals
  - Two compounds
    - Dual action Rho kinase (ROCK) + norepinephrine transport (NET) inhibitor (Netarsudil 0.02%) - Rhopressa
      - AR-13324 lowers IOP by enhance outflow through TM (ROCK) and inhibit aqueous production (NET)
      - Also believed to reduce episcleral venous pressure which may allow it to better reduce IOP when it is below 21 mm Hg
    - Triple action ROCK + NET + latanoprost (Roclatan)
      - PG324 fixed combination of AR-13324 and latanoprost
        - Additional IOP reduction through uveoscleral outflow
  - Both agents are once per day dosage
  - Hyperemia is most common side effect found in studies to date

Double-masked, Randomized, Dose–Response Study of AR-13324 versus Latanoprost in Patients with Elevated Intraocular Pressure

Jason Bacharach, MD,[1] Harvey B. Dubiner, MD,[2] Brian Levy, OD, MS,[3] Casey C. Kopczynski, PhD,[3] Gary D. Novack, PhD,[4] for the AR-13324-CS202 Study Group*

Objective: AR-13324 is a small-molecule inhibitor of Rho kinase and a norepinephrine transporter. The objective of this 28-day study was to evaluate the ocular hypotensive efficacy and safety of AR-13324 ophthalmic solution compared with a positive control, latanoprost ophthalmic solution, in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT).

Design: Double-masked, randomized study in 22 private practice ophthalmology clinics.

Participants: Participants were required to be adults with a diagnosis of OAG or OHT with unmedicated intraocular pressure (IOP) in the range of 22 to 36 mmHg.

Methods: Patients were randomized to receive AR-13324 ophthalmic solution 0.01%, daily (PM), AR-13324 ophthalmic solution 0.02% daily (PM), or latanoprost 0.005% daily (PM) for 28 days.

Main Outcome Measures: The primary efficacy endpoint was the mean diurnal IOP across subjects within the treatment group at day 28.

Results: Randomized and treated were 224 patients, 213 (95.1%) of whom completed the study. On day 28, mean diurnal IOP was 20.1, 20.0, and 18.7 mmHg in the AR-13324 0.01%, 0.02%, and latanoprost groups, respectively, representing a decrease from unmedicated baseline of 5.5, 5.7, and 6.8 mmHg ($P<0.001$). The 5.7-mmHg reduction in IOP by AR-13324 0.02% did not meet the criterion for noninferiority to latanoprost. The most frequently reported adverse event was conjunctival/ocular hyperemia, with a combined incidence of 52%, 57%, and 16%, respectively. On day 28 at 08:00 hours, the incidence of mild to moderate hyperemia by biomicroscopy was 18%, 24%, and 11%, respectively.

Conclusions: AR-13324 0.02% was less effective than latanoprost by approximately 1 mmHg in patients with unmedicated IOPs of 22 to 35 mmHg. The major safety finding was ocular hyperemia, which was more common for both concentrations of AR-13324 than for latanoprost. *Ophthalmology 2015;122:302-307 © 2015 by the American Academy of Ophthalmology.*

Roclatan

- Combination of Rhopressa with latanoprost
- Dosed once daily with significant IOP lowering
- Few systemic side effects
- Limited ocular side effects

Safety/Tolerability Overview of Roclatan™

- There were no drug-related serious adverse events (SAEs)
- The most common adverse event was conjunctival hyperemia with ~50% incidence*, the majority mild on biomicroscopy
- Other ocular AEs
  - AEs occurring in ~5-11% of subjects receiving Roclatan™ included: conjunctival hemorrhage, eye pruritus, lacrimation increased and cornea verticillata.

* Incidence of conjunctival hyperemia ~50% including baseline at ~20%

Roclatan™ Phase 3 Safety Profile

Adverse Events (≥5.0% in any group)	Roclatan™ n=238	Rhopressa™ n=244	Latanoprost n=236
Eye Disorders			
Conjunctival Hyperemia	126 (52.9%)	99 (40.6%)	33 (14.0%)
Conjunctival Hemorrhage	25 (10.5%)	34 (13.9%)	1 (0.4%)
Eye Pruritus	18 (7.6%)	17 (7.0%)	3 (1.3%)
Lacrimation Increased	14 (5.9%)	15 (6.1%)	1 (0.4%)
Cornea Verticillata	12 (5.0%)	9 (3.7%)	0 (0.0%)
Administration Site Conditions			
Instillation site pain	45 (18.9%)	51 (20.9%)	15 (6.4%)

Patients with known contraindications or hypersensitivity to latanoprost were excluded

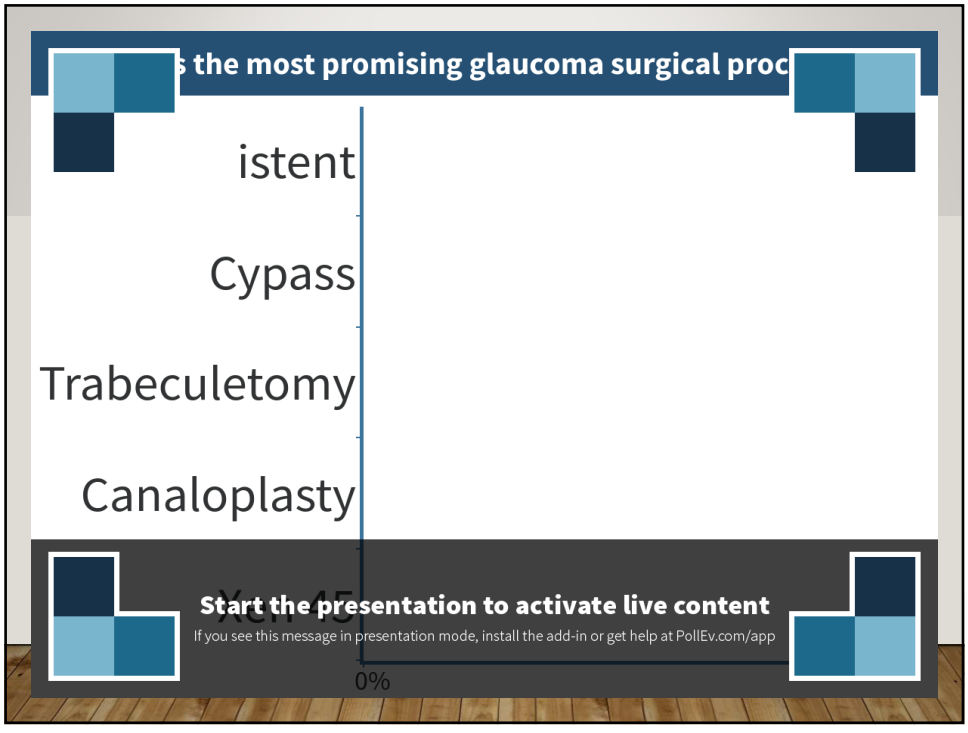
Roclatan™ Summary

- Demonstrated superiority over both latanoprost and Rhopressa™ for the primary efficacy analysis at all 9 time points ($p<0.0001$)
- IOP-lowering effect was greater (1-3 mmHg) than monotherapy with either latanoprost or Rhopressa™ throughout the duration of the study
- There were no drug-related serious adverse events
- The main adverse event was conjunctival hyperemia, ~50% of patients and was scored as mild for the large majority of these patients

25

NEW GLAUCOMA SURGICAL APPROACHES

HOWARD S. BARNEBEY, MD
SPECIALTY EYECARE CENTRE
SEATTLE



GLAUCOMA SURGERY

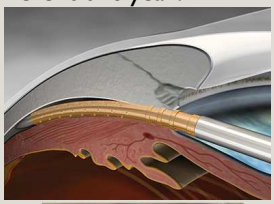
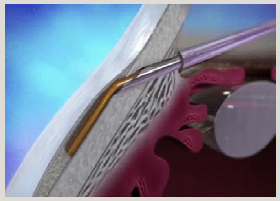
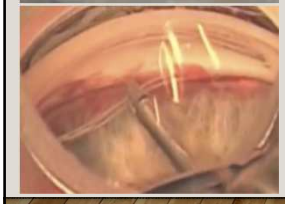
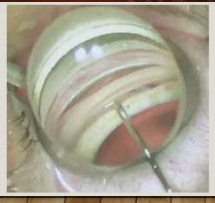
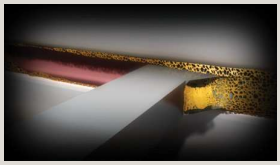
Relevant Disclosures

Consultant: Alcon Lab
Allergan

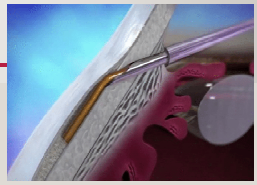
Research Support: Alcon Labs
Santen

GLAUCOMA SURGERY

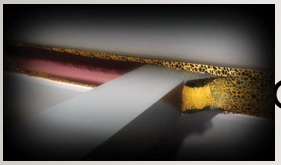
- What is different this year?

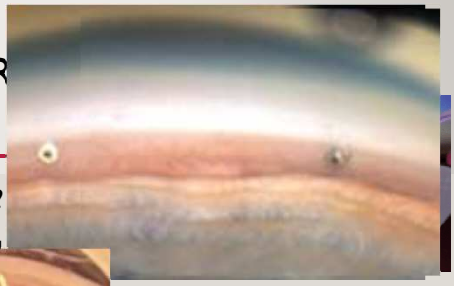
GLAUCOMA SURGERY



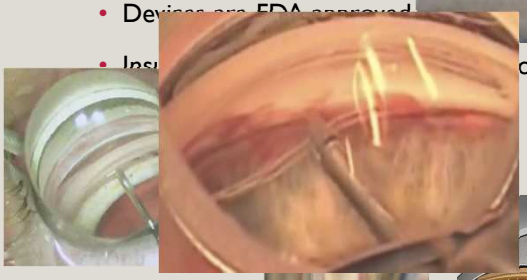
- What is different this year?
- Devices are FDA approved
- Insurance companies are covering procedures
  Inconsistently
- Collective experience is growing
- Magic bullet is still out there

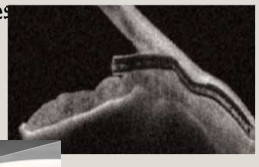


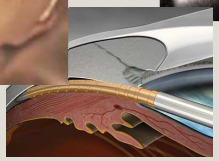
OMA SUR



- What is different this year?
- Dev
- Ins ocedures





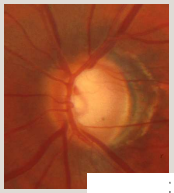


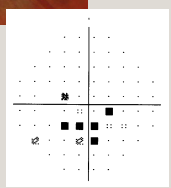
GLAUCOMA SURGICAL OBJECTIVES

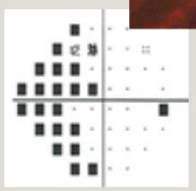
- Choice of surgical procedures for the glaucoma patient each with advantages and disadvantages.
- The procedure reflects:
  - type of glaucoma
  - status of the patient's glaucoma
  - experience of the glaucoma surgeon.

GLAUCOMA SURGICAL SELECTION

- Match the Procedure to the Glaucoma
  - Type of Glaucoma
  - Severity of Glaucoma
    - Status of VF
    - Status of ON/RNFL
    - Risk of progression (IOP)







QUESTION

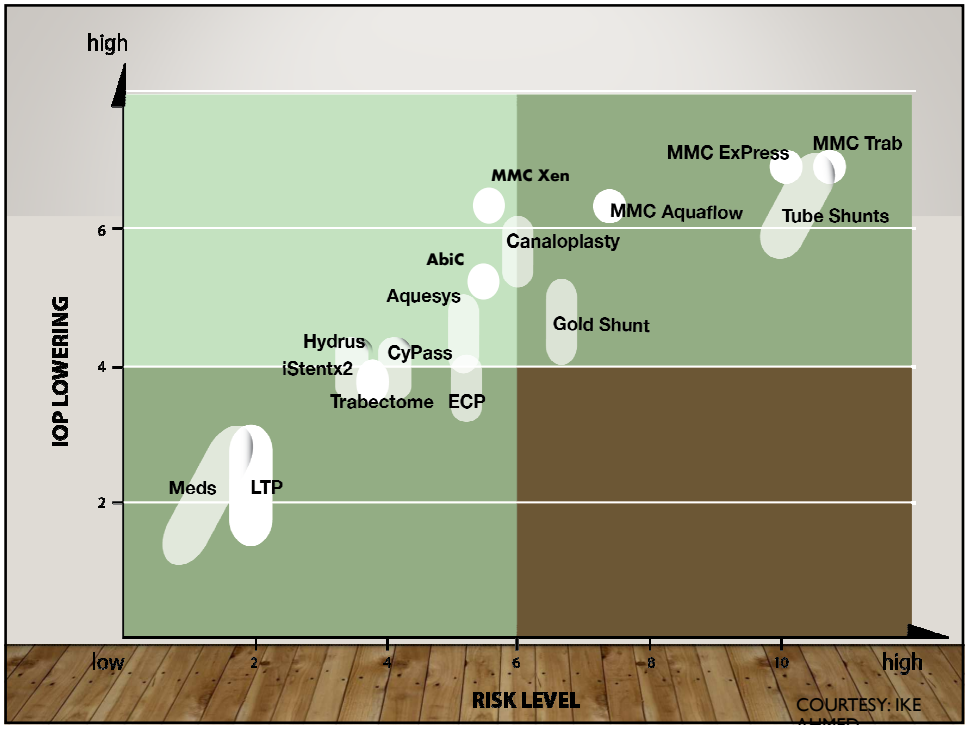
The following glaucoma procedures are considered minimally invasive and fulfill the MIG criteria:

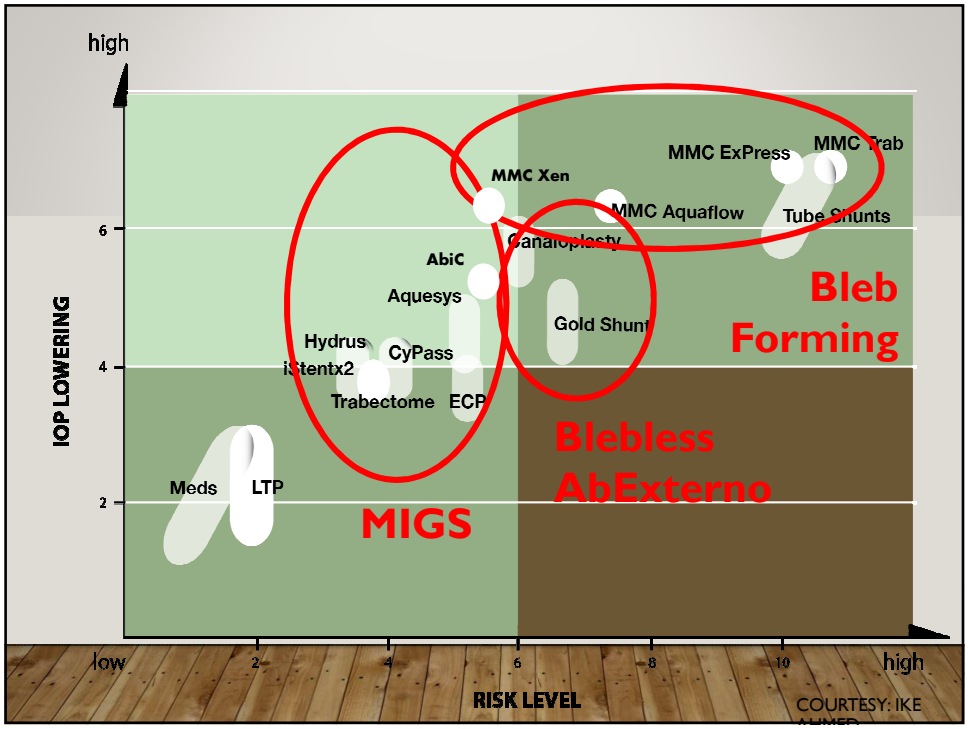
A. Trabeculectomy
B. Glaucoma Drainage Device
C. Canaloplasty
D. Express Shunt
E. iStent implant

QUESTION

- The major complaint of trabeculectomy has been:

A. Unpredictability
B. High incidence of post operative complications
C. High likelihood of bleb failure
D. All of the above
E. None of the above.


high
IOP LOWERING
6
4
2
MMC ExPress
MMC Trab
MMC Xen
MMC Aquaflow
Tube Shunts
Canaloplasty
AbiC
Aquesys
Gold Shunt
Hydrus
CyPass
iStentx2
Trabectome
ECP
Meds
LTP
low
2
4
6
8
10
high
RISK LEVEL
COURTESY: IKE


high
IOP LOWERING
6
4
2
MMC ExPress
MMC Xen
MMC Aquaflow
Tube Shunts
AbiC
Aquesys
Gold Shunt
Hydrus
CyPass
Trabectome
ECP
Meds
LTP
Bleb
Forming
Blebless
AbExterno
MIGS
low
2
4
6
8
10
high
RISK LEVEL
COURTESY: IKE

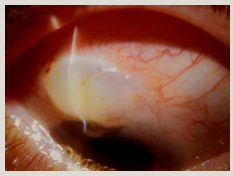
CATARACT SURGERY

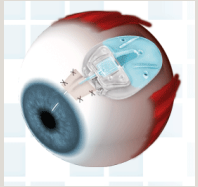
- Lowers IOP
- Variable response
- Ave: 4 mm Hg
- Mechanism unknown

GLAUCOMA SURGERY

What are your surgical choices?

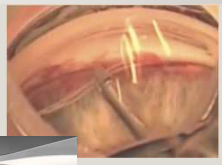
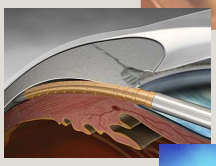
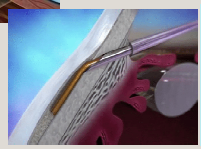
- Trabeculectomy
- Mini-shunt
- Tube
- Non-penetrating surgery
- Trabectome
- Cilio-destruction





SURGICAL OPTIONS

- Current Procedures
  - Newer Options
    - Express Shunt
    - Canaloplasty
    - Trabectome
    - i-stent
  - Current
    - Abicp
    - GATT
    - Kahook goniotomy
    - Visco 360
    - Cypass
    - Xen 45

MIGS

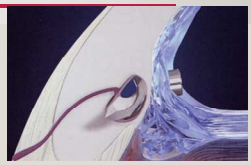
- Avoid a bleb (most)
- Lower risk profile
- Vision recovery
- Refractive changes minimal (Toric IOL)
- Less procedure time

MIGS

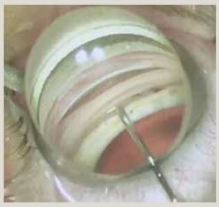
Mechanism of Action

- Improve conventional outflow via TM > SC
- Improve non-conventional outflow via suprachoroidal path
- Create new outflow path

ISTENT

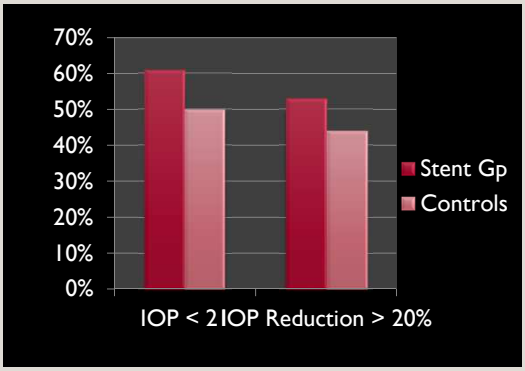


- *ab interno* micro-bypass implant
  Snorkel bore diameter of 120 µm
  Measures 0.5 mm/0.25 mm/1.0 mm
- Designed for optimal fit and retention within Schlemm's canal. The device is made of surgical grade nonferromagnetic titanium, weighs 60 µg
- Approved 2012



2 YEAR RESULTS

- Unmedicated

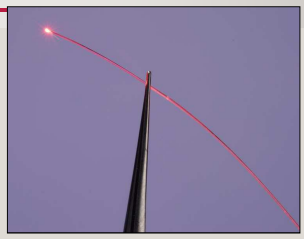


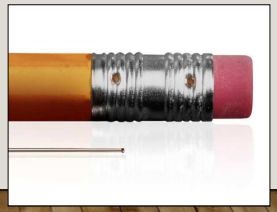
- MEAN IOP
- Baseline IOP (med washout)
  - 25.4 ± 3.6 mm Hg in the stent
    25.2 ± 3.6 mm Hg in the contro

Craven et al JCRS 2012; 38:1339–1345

CANALOPLASTY

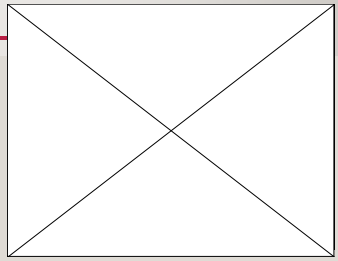
- Restoration of normal aqueous outflow pathway
- A flexible microcatheter with lighted beacon tip
- Injects viscoelastic to dilate the entire 360° of the canal and collector system
- Facilitates passage of tensioning suture to maintain patency of the



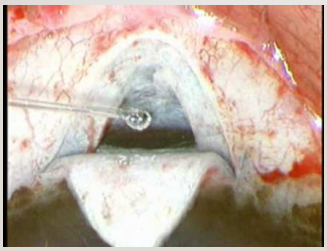


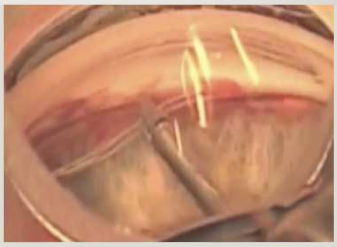
CANALOPLASTY

- Re-establish flow
  - physiologic control of IOP
  - Without requiring a bleb
- Non-penetrating
  - Trabeculo-descemetic window
  - 360° cannulation
    viscodilation Schlemm's canal
  - tensioning TM
    stent SC



EXTERNO VS INTERNO

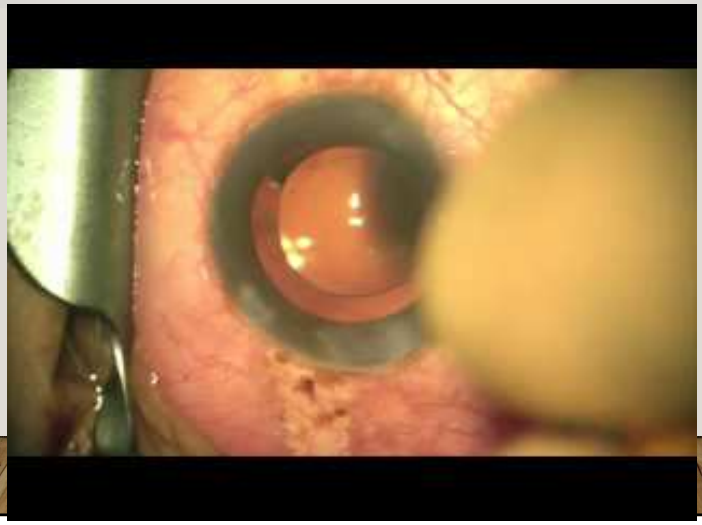


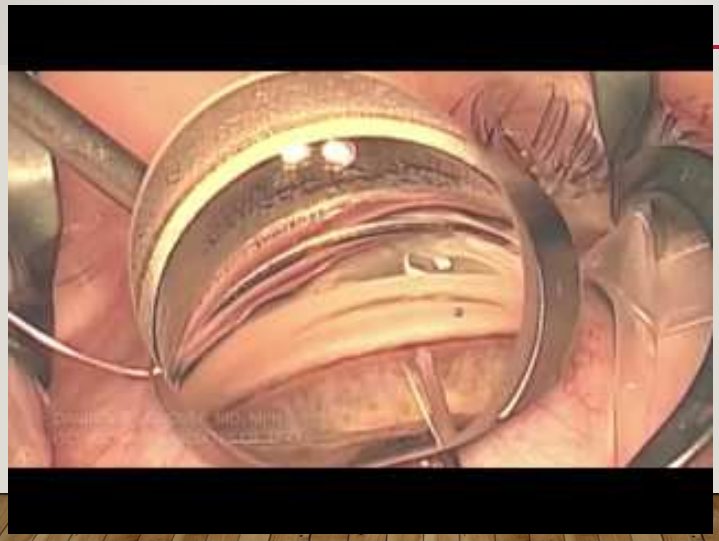


AB-INTERNO CANALOPLASTY, ABIC

- Ab-interno Canaloplasty is a new Minimally Invasive Glaucoma (MIGS) procedure, which achieves similar IOP-lowering effects to traditional (ab-externo) Canaloplasty in patients with mild-to moderate POAG without ever touching the sclera.
- Ab-interno Canaloplasty conserves the clinically proven benefits of 360° visco-dilation of Schlemm canal provided by traditional Canaloplasty via a clear corneal incision – and with the speed and ease of implementation of current MIGS procedures.

ABIC





ABIC CASE SERIES, COMBINED: ALL EYES

- Total reduction in mean IOP of 27.9% (at 6 months)
- 50% reduction in number of medications (at 6 months)

Exam	N	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	228	19.0 ± 6.5	2.0 ± 1.0
1 Month	215	15.7 ± 5.0	0.3 ± 0.7
3 Months	123	14.3 ± 3.8	1.0 ± 1.0
6 Months	52	13.7 ± 3.0	1.0 ± 1.0

ABIC CASE SERIES, COMBINED: WITH CATARACT SURGERY

- Total reduction in mean IOP of 23.52% (at 6 months)
- 100% reduction in number of medications (at 6 months)

Exam	N	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	127	17.0 ± 4.6	2.0 ± 1.0
1 Month	119	14.0 ± 3.9	0.2 ± 0.5
3 Months	76	13.4 ± 3.1	0.0 ± 1.0
6 Months	34	13.0 ± 2.9	0.0 ± 1.0

MIGS

- **Why Is This Developing?**
- **Advantages/disadvantages of "traditional" glaucoma surgery**

MIGS 2017

Advantages/Limitations

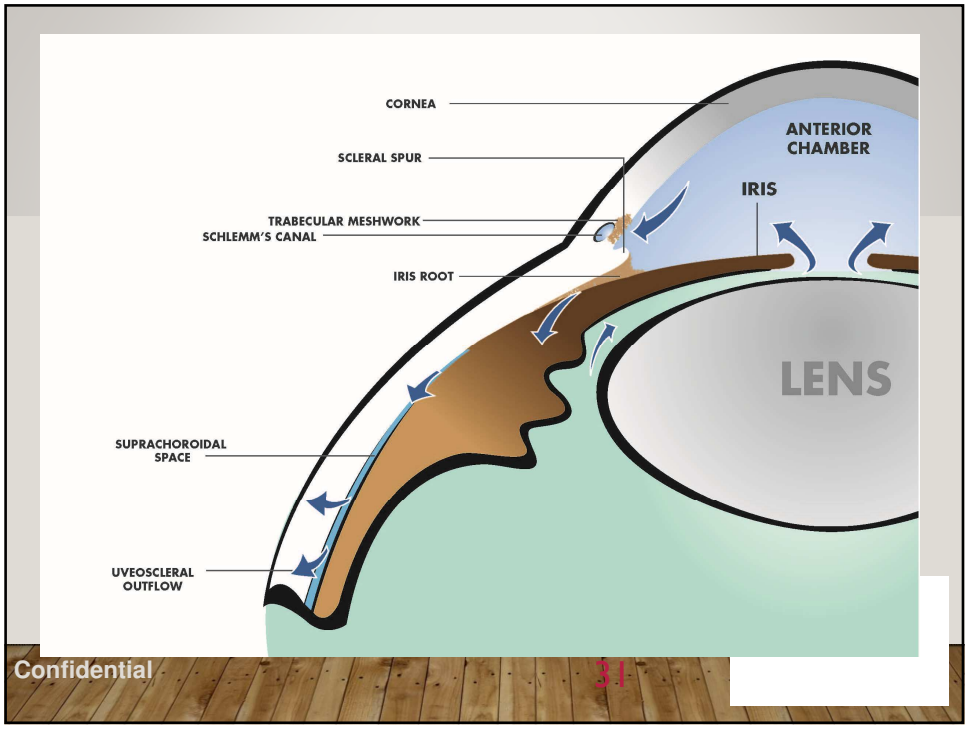
Cypass

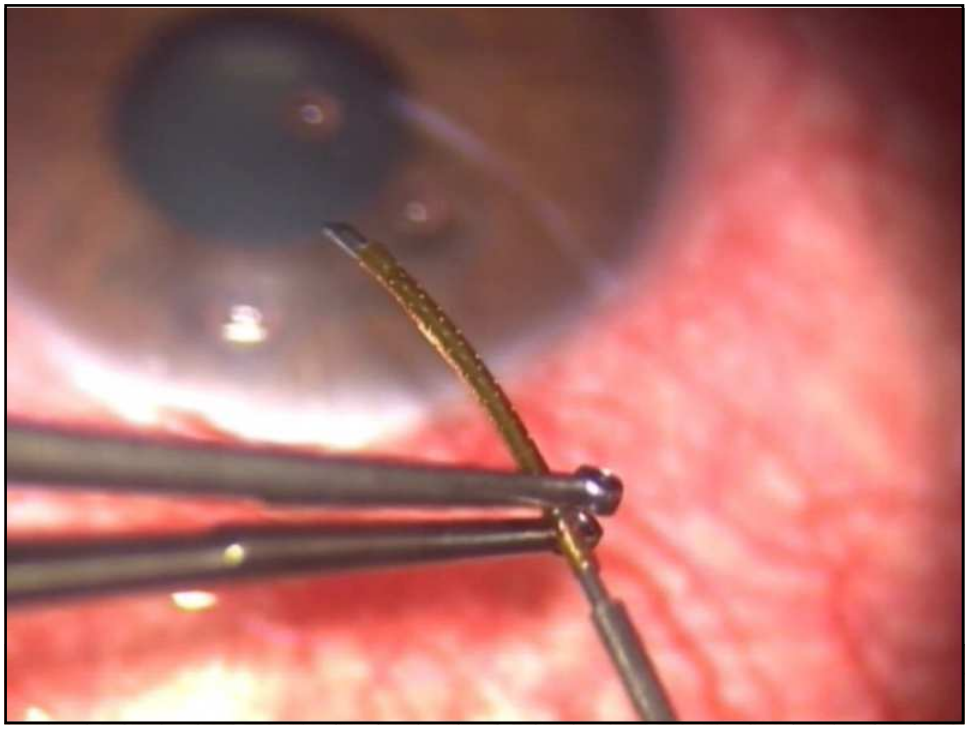
Xen 45

TRANSCEND CYPASS™ SYSTEM

CyPass FX Stent **CyPass Insertion Device**

Caution: Investigational device. Limited by Federal (USA) law to investigational use.


CORNEA
SCLERAL SPUR
TRABECULAR MESHWORK
SCHLEMM'S CANAL
IRIS ROOT
SUPRACHOROIDAL SPACE
UVEOSCLERAL OUTFLOW
ANTERIOR CHAMBER
IRIS
LENS
Confidential
31



EFFECTIVENESS RESULTS

CyPass System 241-S Instructions for Use 2016-08-09 LBL01039B

COMPASS: 2 YR

- Purpose: supraciliary microstenting mild-to-moderate primary open-angle glaucoma (POAG) in patients undergoing cataract surgery.
- Design Multicenter (24 US sites), interventional randomized clinical trial (RCT)
- POAG with mean diurnal unmedicated intraocular pressure (IOP) 21–33 mmHg and were undergoing phacoemulsification cataract surgery.
-

Two-Year COMPASS Trial Results: Steven Vold et al Ophthalmology 2016; 123:2103-2112

COMPASS: 2 YR

- Results: 131 control group(cataract) & 374 randomized microstent + cataract
  Baseline mean IOPs similar: 24.5±3.0 and 24.4±2.8 mmHg,
  mean medications were 1.3±1.0 and 1.4±0.9

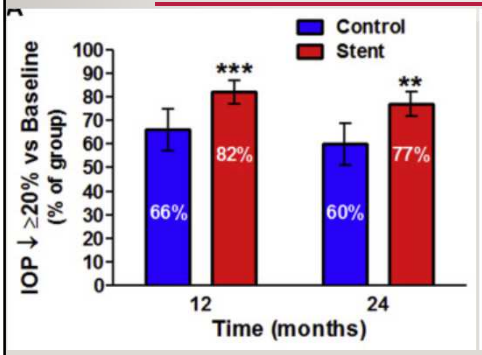
20% IOP reduction:	60% of controls	77% of microstent
Mean IOP reduction:	↓5.4 mmHg	↓7.4 mmHg
Med Use		
None:	59% of control	85% of microstent subjects
Needed:	0.6±0.8 drugs	0.2±0.6 drugs

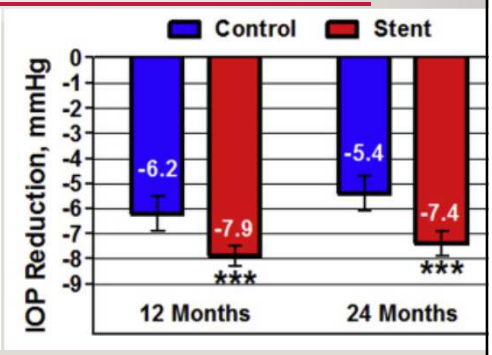
Two-Year COMPASS Trial Results: Steven Vold et al Ophthalmology 2016; 123:2103-2112

COMPASS

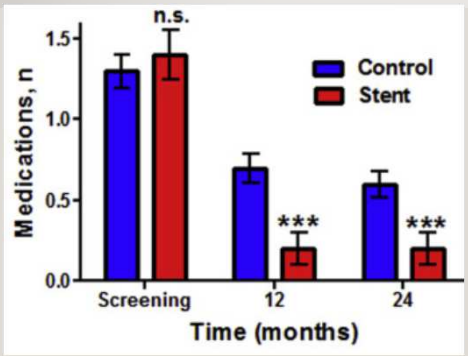
- Supraciliary microstenting offers concomitant intervention during cataract surgery
- low rate of complications
- ab interno, "bleb-less," conjunctiva-sparing technique

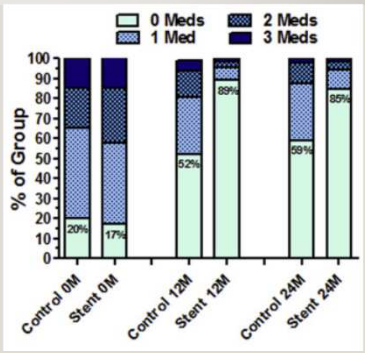
COMPASS CYPASS





COMPASS





OCULAR AE (2 YR)

AE	Stent (n = 374)	Control (n = 131)	P Value*
BCVA loss ≥10 letters	33 (8.8%)	20 (15.3%)	0.0466
Corneal abrasion	7 (1.9%)	2 (1.5%)	0.9999
Corneal edema	13 (3.5%)	2 (1.5%)	0.3741
Conjunctivitis	4 (1.0%)	3 (2.3%)	0.3828
Cyclodialysis cleft >2-mm circumference	7 (1.9%)	0 (0.0%)	0.1985
Hyphema, transient intraoperative	10 (2.7%)	0 (0.0%)	0.0706

OCULAR AE

Iritis	32 (8.6%)	5 (3.8%)	0.0809
Hypotony (IOP <6 mmHg)	11 (2.9%)	0 (0%)	0.0744
IOP ≥10 mmHg over baseline	16 (4.3%)	3 (2.3%)	0.4263
Maculopathy, cystoid edema	6 (1.3%)	1 (0.8%)	0.6829
Stent obstruction	8 (2.1%)	N/A	N/A
Subconjunctival hemorrhage	6 (1.6%)	1 (0.8%)	0.6829
Secondary ocular surgical intervention	20 (5.5%)	7 (5.3%)	0.9999
Visual field loss	25 (6.7%)	13 (9.9%)	0.2488

- Cypass Video

ONE YEAR STUDY RESULTS

- Xen 45

One-Year Results of an *Ab Interno* Gelatin Stent as a Standalone Procedure for the Treatment of Moderate Primary Open-Angle Glaucoma (APEX study)

Rohit Varma, MD, MPH[1]; Herbert A. Reitsamer, MD, PhD[2]

University of Southern California Roski Eye Institute, Los Angeles, CA, USA
[2]University of Salzburg, Salzburg, Austria

RV is a consultant to and/or has received research support from AqueSys

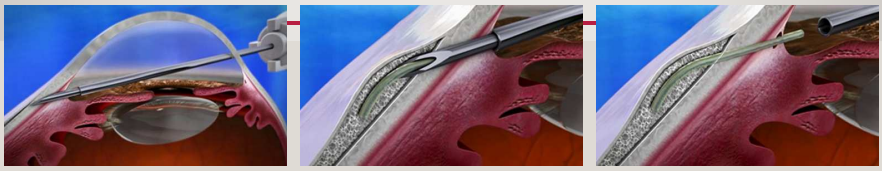
HAR is a consultant to and/or has received research support from Aliophtha; Allergan; AqueSys; Santen; and Transcend Medical

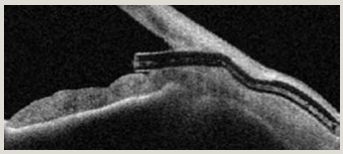
This study was sponsored by AqueSys Inc., Aliso Viejo, CA. USA,, now Allergan plc, Dublin, Ireland. Writing and editorial assistance was provided to the authors by Michele Jacob, PhD, of Envision Pharma Group, Philadelphia, PA, USA, and funded by Allergan plc, Dublin, Ireland. All authors met the ICMJE authorship criteria. Neither honoraria nor payments were made for authorship.

METHODS

- **Design**: Phase IV, non-randomized, prospective, 24-month, ongoing study
  - Subanalysis of patients who received the gelatin stent without cataract surgery
  - 22 sites in Europe, Venezuela
  - ClinicalTrials.gov registration number: NCT02006693
- **Population**: Moderate POAG (per the investigator's opinion)
- **Treatment**: Gelatin stent (stand-alone procedure)
  - Both eyes could be treated (≥30 days apart)
  - Use of an antimetabolite/antifibrotic agent prior to implantation was allowed at the investigator's discretion
- **1-year interim analysis of the following endpoints**
  - Mean IOP
  - Mean IOP change from baseline
  - Reduction in medications
  - Adverse events (AEs)

GELATIN STENT

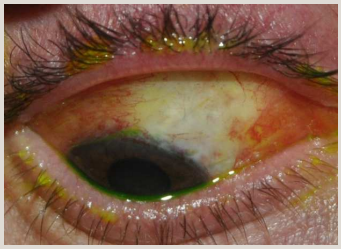


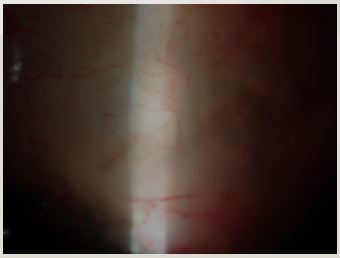


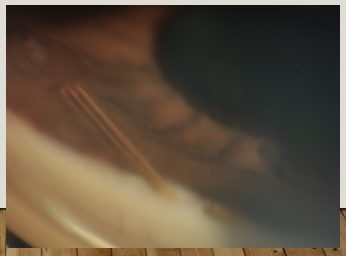
ASCRS Symposium 2016

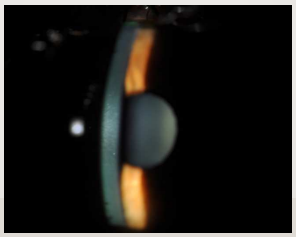
NEAR FUTURE: 2017

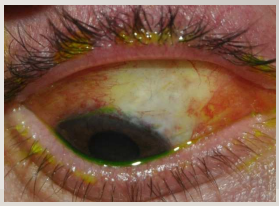
- AqueSys

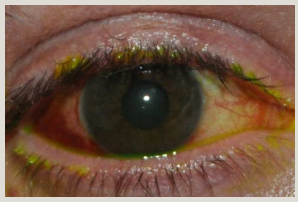


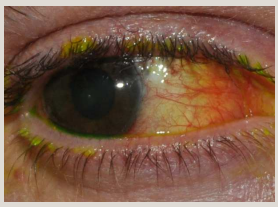




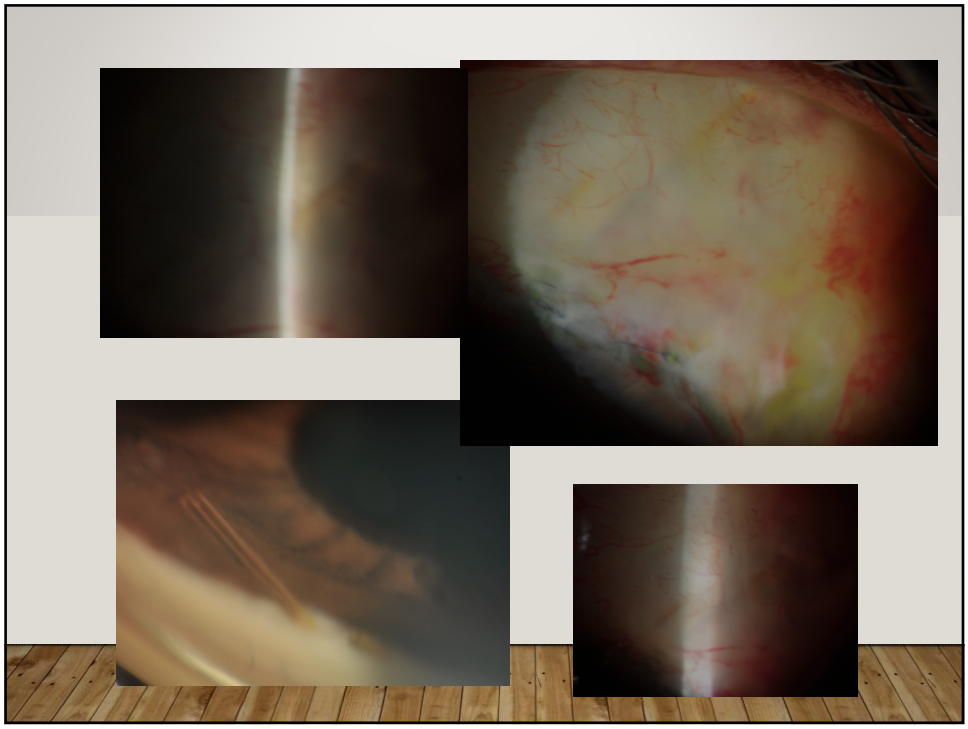








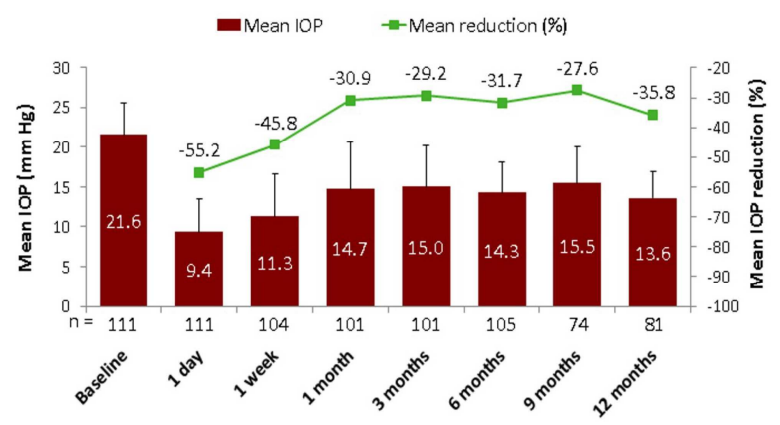
10 July 2014
Mike T AquaSys x 2



ONE YEAR STUDY RESULTS

Stand-alone gelatin stent	
Demographics and Baseline characteristics	**N=111**
Mean age (SD), years	68.1 (11.5)
Gender, n (%)	
Female	62 (55.9)
Male	49 (44.1)
Ethnicity, n (%)	
White	105 (94.6)
Black	3 (2.7)
Asian	2 (1.8)
Other	1 (0.9)
Surgery eye, n (%)	
OD	50 (45.0)
OS	61 (55.0)
Mean preoperative IOP (SD), mm Hg	21.6 (4.0)
Mean preoperative hypotensive medications, n (SD)	2.6 (1.1)

ONE YEAR STUDY



IOP Reduction 8 mm (SD ± 4.6)

MEDICATION USE

Visit	Eyes, n	Medications, n (SD)	Eyes on fewer medications post-surgery, %	Eyes without any medications, %
Preoperative	111	2.6 (1.1)	–	–
Day 1	111	0 (0.1)	98.2	99.1
Week 1	104	0 (0.1)	99.0	99.0
Month 1	101	0.2 (0.7)	93.1	88.1
Month 3	101	0.5 (1.0)	91.1	76.2
Month 6	105	0.6 (1.0)	85.7	66.7
Month 9	74	0.9 (1.1)	83.8	54.1
Month 12	**81**	**0.7 (0.9)**	**88.9**	**56.8**

IOP REDUCTION > 20%

Visit	Eyes, n	Eyes with 20% IOP reduction, %	Mean IOP (SD), mm Hg	Eyes with 20% IOP reduction and no hypotensive medications, %	Mean IOP (SD), mm Hg
Day 1	111	94.6	8.9 (3.6)	93.7	8.9 (3.6)
Week 1	104	85.6	9.9 (3.4)	85.6	9.9 (3.4)
Month 1	101	75.2	12.3 (3.6)	67.3	11.7 (3.0)
Month 3	101	72.3	12.7 (3.0)	63.4	12.5 (2.8)
Month 6	105	76.2	12.8 (2.5)	54.3	12.8 (2.7)
Month 9	74	71.6	13.5 (2.7)	47.3	12.9 (2.3)
Month 12	81	**86.4**	12.9 (3.0)	**55.6**	13.0 (3.0)

ADVERSE EVENTS

Operative AEs, n (%)	N=111
Conjunctival perforation	1 (0.9)
Postoperative ocular AEs, (%)	**N=111**
Secondary surgical procedure (related / unrelated to the stent)	7 (6.3) / 3 (2.7)
Hyphema (complaint if >30 days)	6 (5.4)
Conversion to trabeculectomy / EX-PRESS	5 (4.5)
Stent blockage	4 (3.6)
Shallow anterior chamber	2 (1.8)
Choroidal effusion (self-limiting, lasting <30 days)	2 (1.8)
Subconjunctival hemorrhage (occurring >30 days post-implantation)	2 (1.8)
Conjunctivitis (not involving stent or bleb)	2 (1.8)
Allergy to post-operative medication	2 (1.8)
Anterior chamber reformation	1 (0.9)
Intraocular lens subluxation	1 (0.9)
Large bleb associated with ocular surface symptoms	1 (0.9)
Stent exposure secondary to improper positioning	1 (0.9)
Spontaneous stent exposure	1 (0.9)
Stent fracture secondary to intervention (eg, needling)	1 (0.9)
Spontaneous stent fracture	1 (0.9)
Macular edema	1 (0.9)

BLEB NEEDLING

Needling, % of Eyes	N=111
Median	33.3
Range	0-80
First quartile	0
Third quartile	50.0

Pre-needle IOP: 20.4 ± 7.4 mm Hg
Post-needle IOP: 15.9 ± 6.1 mm Hg

SUMMARY: ONE YEAR

- Mean IOP ↓: 35.8%
- IOP 20% ↓: 86.4%
  55.6% Off Meds
- Fewer Rx: 88.9%
- No major AE reported

The Xen Procedure: 1-Year Results of an *Ab Interno* Gelatin Stent Along with Cataract Surgery for the Treatment of Glaucoma (APEX study)

Richard A. Lewis, MD[1]; Herbert A. Reitsamer, MD, PhD[2]

[1]Grutzmacher, Lewis & Sierra, Sacramento, CA, USA
[2]University of Salzburg, Salzburg, Austria

ASCRS Symposium 2016

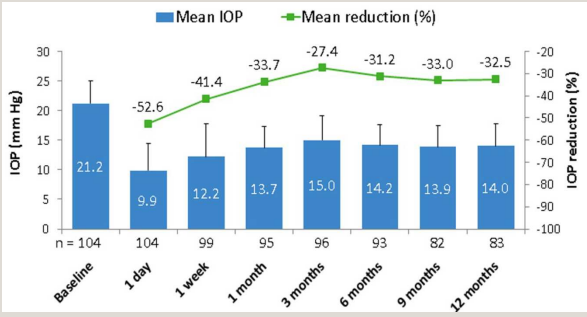
METHODS

- **Design**: Phase IV, prospective, non-randomized, 24-month, ongoing study
  - Subanalysis of combined gelatin stent placement and cataract removal
  - 22 sites in Europe, Venezuela
  - ClinicalTrials.gov registration number: NCT02006693
- **Population**: Moderate POAG with cataract
- **Treatment**: Gelatin stent + phacoemulsification
  - Both eyes could be treated (≥30 days apart)
  - Use of an antimetabolite/antifibrotic agent prior to implantation was allowed at the discretion of the investigator
- **1-year interim analysis of the following endpoints**
  - Mean IOP
  - Mean IOP change from baseline
  - Reduction in medications
  - Adverse events (AEs)

DEMOGRAPHICS

Demographics and Baseline characteristics	N=104
Mean age (SD), years	77.4 (6.2)
Gender, n (%)	
Female	54 (51.9)
Male	50 (48.1)
Ethnicity, n (%)	
White	100 (96.2)
Black	1 (1.0)
Asian	3 (2.9)
Surgery eye, n (%)	
OD	56 (53.8)
OS	48 (46.2)
Mean preoperative IOP (SD), mm Hg	21.2 (3.8)
Mean preoperative hypotensive medications, n (SD)	2.5 (1.1)

MEAN IOP REDUCTION FROM BASELINE



Mean IOP ↓ 7.2 (±5.0) mm Hg

XEN 45 + PHACO: MEDICATION USE

Visit	Eyes, n	Medications, n (SD)	Eyes on fewer medications post-surgery, %	Eyes without any medications, %
Preoperative	104	2.5 (1.1)	–	–
Day 1	104	0 (0.1)	100	99.0
Week 1	99	0.1 (0.4)	97.0	96.0
Month 1	95	0.3 (0.8)	93.7	82.1
Month 3	96	0.5 (1.0)	88.5	71.9
Month 6	93	0.6 (0.9)	87.1	66.7
Month 9	82	0.6 (0.9)	93.9	61.0
Month 12	**83**	**0.5 (0.7)**	**96.4**	**54.2**

IOP REDUCTION > 20%

Visit	Eyes, n	Eyes with 20% IOP reduction, %	Mean IOP (SD), mm Hg	Eyes with 20% IOP reduction and no hypotensive medications, %	Mean IOP (SD), mm Hg
Day 1	104	93.3	9.2 (3.6)	92.3	9.2 (3.6)
Week 1	99	81.8	10.2 (3.1)	80.8	10.3 (3.1)
Month 1	95	76.8	12.5 (2.8)	62.1	12.1 (2.6)
Month 3	96	74.0	13.3 (2.9)	54.2	13.1 (2.9)
Month 6	93	77.4	13.0 (2.5)	52.7	12.6 (2.4)
Month 9	82	79.3	12.8 (2.6)	52.4	12.6 (1.9)
Month 12	**83**	**79.5**	**12.7 (2.5)**	**47.0**	**12.4 (2.4)**

Phaco + Gelatin stent

ADVERSE EVENTS

Postoperative ocular AEs	n (%)
Secondary surgical procedure (unrelated to the stent)	6 (5.8)
Stent fracture secondary to intervention (eg, needling)	2 (1.9)
Hyphema (complaint if >30 days)	2 (1.9)
Corneal abrasion, defect	2 (1.9)
Secondary surgical procedure (related to the stent)	1 (1.0)
Stent exposure secondary to intervention (eg, needling)	1 (1.0)
Choroidal effusion (self-limiting, lasting <30 days)	1 (1.0)
Conjunctivitis (not involving stent or bleb)	1 (1.0)
Iritis	1 (1.0)
Large bleb associated with ocular surface symptoms	1 (1.0)
Explantation	1 (1.0)
Conversion to trabeculectomy / EX-PRESS	1 (1.0)
Reported vision loss (transient)	1 (1.0)
Retinal complications (>30 days post-surgery)	1 (1.0)
Chronic pain	1 (1.0)
Allergy to post-surgery medication	1 (1.0)

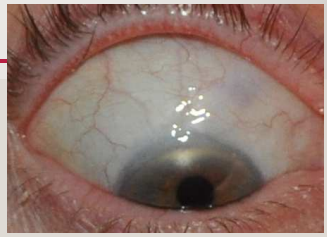
BLEB NEEDLING

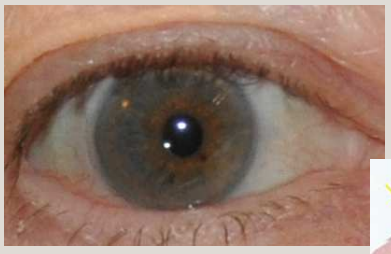
Needling, % of Eyes	N=104
Median	17.6
Range	0-100
First quartile	0
Third quartile	68.4

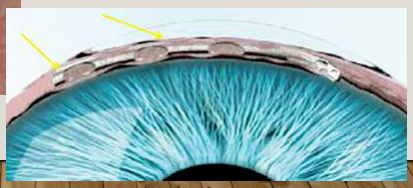
Phaco + Gelatin Stent
Pre-needle IOP: 22.2 ± 7.8 mm Hg
Post-needle IOP: 12.6 ± 5.8 mm Hg

MIGS 2020

Inn Focus
Hydrus







HYDRUS

- curved metal microstent that targets the Schlemm's canal
- 2015 RCT (N = 100)
  primary end point (2-yea) unmedicated IOP reduction by ≥20%
  46% of cataract surgery controls
  80% of stented subjects in the Hydrus study

  Medication-free rates (2 years)
  38% controls
  73% stented subjects

  IOP mean baseline medications numbered
  Baseline: control: 2 Stent: 2
  2 YR: control: 0.5 Stent: 1

Pfeiffer et al *Ophthalmology*. 2015; 122: 1283–1293

Glaucoma Therapy Update
Drug Delivery Devices

Murray Fingeret, OD

Drug Delivery

- Problem – poor adherence in patients taking their medications as directed
  - Common with chronic disease such as glaucoma
  - Estimated 40% or higher of medicines not taken
- Plan - develop therapeutic methods that are independent of patient and delivered by doctor
- Modalities include devices that reside on ocular surface, slow-release depots that are injected into the eye, and punctal plugs that deliver drugs directly into tear film

New Methods for Drug Delivery

- Patient's don't adhere well to instilling drops
- Eyedrops have drawbacks
  - Relatively inefficient in that large volume is placed in small space
  - Relies on patient's ability to comply and administer drops correctly
- Objectives of new drug delivery methods
  - Ensure drug delivered to the site of action in the eye
  - Reduce side effects of topical medications
  - Improve compliance
  - Improve clinical outcomes
  - Methods may be
    - patient centered and noninvasive or doctor centered and invasive

CrossMark

AMERICAN ACADEMY OF OPHTHALMOLOGY
The Eye M.D. Association

Patterns of Glaucoma Medication Adherence over Four Years of Follow-Up

Paula Anne Newman-Casey, MD, MS,[1,2] Taylor Blachley, MS,[1] Paul P. Lee, MD, JD,[1,2] Michele Heisler, MD, MPA,[2,3] Karen B. Farris, PhD,[4] Joshua D. Stein, MD, MS[1,2]

Purpose: To assess longer-term patterns of glaucoma medication adherence and identify whether patterns established during the first year of medication use persist during 3 subsequent years of follow-up.

Design: Retrospective, longitudinal cohort analysis.

Participants: Beneficiaries aged ≥40 years who were enrolled in a United States (US)-managed care plan for ≥7 years between 2001 and 2012 and newly diagnosed and treated for open-angle glaucoma.

Methods: For each enrollee, we quantified medication adherence using the medication possession ratio. Group-based trajectory modeling (GBTM) was applied to identify patterns of adherence for 1 and 4 years of follow-up. The percent of beneficiaries who remained in the same trajectory group in the 1- and 4-year models was tabulated to evaluate group stability. Factors impacting adherence at 1 and 4 years were identified using regression analyses.

Main Outcome Measures: Patterns of glaucoma medication adherence.

Results: Of the 1234 eligible beneficiaries, GBTM identified 5 distinct glaucoma medication adherence patterns in both the 1-year and 4-year follow-up periods. These groups were as follows: (1) *never adherent* after their index prescription fill (7.5% and 15.6% of persons in the 1- and 4-year models, respectively); (2) *persistently very poor adherence* (14.9% and 23.4% of persons in the 1- and 4-year models, respectively); (3) *declining adherence* (9.5% and 9.1% of persons in the 1- and 4-year models, respectively); (4) *persistently moderate adherence* (48.1% and 37.0% of persons in the 1- and 4-year models, respectively); and (5) *persistently good adherence* (20.0% and 15.0% of persons in the 1- and 4-year models, respectively). More than 90% of beneficiaries in the 4 groups with the worst and best adherence patterns (groups 1, 2, 3, 5) maintained their patterns from their first year throughout their 4 years of follow-up. Those with *persistently moderate adherence* (group 4), the largest group, were most likely to change groups from 1 to 4 years of follow-up. Persons with the best adherence over 4 years were more likely to be white, to be older, to earn >$60 000/year, and to have more eye care visits ($P < 0.05$ for all comparisons). Those with a higher initial copayment cost had lower adherence rates ($\beta = -0.06$/dollar, $P = 0.03$).

Conclusions: For most patients who were newly prescribed glaucoma medications, adherence patterns observed in the first year of treatment reflect adherence patterns over the subsequent 3 years. Investing resources in both identifying and helping patients with suboptimal adherence patterns over the first year may have a large impact on longer-term adherence. *Ophthalmology 2015;122:2010-2021 © 2015 by the American Academy of Ophthalmology.*

Drug Delivery

- An ideal sustained release drug delivery system should be able to encapsulate and deliver the necessary drug to the target tissues at a therapeutic level without any detriment to the drug
- Drug encapsulation should be as high as possible to minimize loss and unless it is specifically desired, the initial burst of drug release should be kept to a minimum
- By modifying various biomaterials, it is possible to achieve sustained drug delivery to both the anterior and posterior segments of the eye

- Ocular Surface
  - Contact lens
  - Punctal plug
- Sclera
- Anterior chamber
- Intravitreal
- Subconjunctival/subchoroidal

Ocular Drug Delivery Key Points

- Easy to place and easy to remove
- Tolerable
- Consistent efficacy
  - Works close to eye drop with improved compliance
  - Can it work better?
- Cosmetically invisible
- Stays in place
  - At least 90 days
- Use in multiple disease states

Drug Delivery Systems for Glaucoma

- Amorphex Therapeutics
  - A polymer, similar to a contact lens, that contains the drug and sits under the upper eyelid
  - Releases the drug over several months
- Envisa Therapeutics
  - Implantable extended-release device
- pSivida and SKS Ocular
  - Delivery devices
- Kala Pharmaceuticals
  - Drops that can get into the eye more easily
- Ocular Therapeutix
  - Tear duct plugs containing medication
- Foresight - Helios
- Mati Therapeutics Inc.
  - Punctal plug device
- Graybug
  - Sustained release

Platforms delivered outside the eye

- Helios (ForSight Vision 5) - Allergan
  - Bimatoprost-laden plymer-matrix insert embedded in compliant ring
- TODDD (Topical Ophthalmic Drug Delivery Device; Vista Scientific)
  - Nonerodible solid matrix under the eyelid embedded with a drug
  - Amoerphex Therapeutics
  - Most of the company's work has focused on timolol and prostaglandins.
- Punctal plugs:
  - Ocular Therapeutix (OTX-TP) is an intracanicular depot that dissolves over time
  - Mati Therapeutics (L-PPDS) is a latanoprost punctal plug delievery system
  - Kayla Pharmaceuticals
    - Drops that allow medication to get into the eye more effectively.
- Phenylboronic-Acid based polymeric micelles for mucoadhesive anterior segment ocular drug delivery

Platforms Delivered inside the eye

- Bimatoprost SR
  - Bimatoprost sustained-release implant (Allergan)
  - Currently in Phase 3 clinical trials.
- ENV515 -Envisia Therapeutics
  - Implantable biodegradable polymer drug delivery system using extended-release travoprost using engineered highly-precise microparticles and nanoparticles
- GrayBug microparticle
  - Polymer-based intraocular delivery technologies that would allow customizable sustained release of all therapeutic classes
- pSivida
  - Delivery devices or technology to allow a constant delivery of medication over months or years
- Ohr Pharmaceutical
  - Inject micro- or nanoparticles into the eye that would then release a glaucoma drug/drugs over an extended period of time
- ClearSide Biomedical, Inc.
  - Use of microneedles to inject medication into a specific spot for it to be most effective

Sustained Release Devices

- Questions to be considered:
  - Comfortability of device
  - Effectivity
    - Will it replace drops altogether or be replacement of one medication
    - Will OD's be granted rights to insert?
- What is taking so long?
  - Technicalities: Invention, investment, research
  - Modality and barriers within the eye itself
  - Comfortability/Usability for patients

Drug-Loaded Contact Lenses

- Approximately 35 million individuals in US wear contact lenses
- If a person requires glaucoma therapy and wear CLs, request individual to discontinue CL wear, at least while administering drug
  - This may impact on adherence of medication
- If CL is to contain medication, this combination must be as safe and effective as CL and drug is used singly
  - Cannot impact upon refractive properties of lens
  - Concern for preservatives concentrating in CL or concentrating in tear layer between CL and cornea

Drug-Loaded Contact Lenses
Simplistic Concept That Has Not Worked

- Soak CL in lens storage solution with drug
  - Hydrophilic matrix of soft CL absorbs drug and then releases it by simple diffusion
  - Limited by drug kinetics which leads to rapid diffusion
  - Diffusion varies drug to drug, often in under one hour
  - Medication with preservatives may cloud CL or effect oxygen permeability
- Issues with both forms
  - Want linear release which is difficult to achieve
- New Codes for 2016
  - 0365T Drug eluting contact lenses

Drug-Loaded Contact Lenses
Drug Loading Strategies

- Use colloidal nanoparticles or molecular imprinting
  - Sub-micron size particles either coated with or encapsulating drug
    - Liposomes
    - Colloidal gold or silver
    - Once CL is placed on eye, drug diffuses into tear layer
    - Packing of drug in colloidal allows for more sustained delivery
  - Drug imprinting
    - Modifies contact lens material to allow drug molecule to sit within hydrogel complex
    - Allows higher drug load than simple diffusion

Punctal Plug Drug Delivery Devices

- Insert slow-release medication depot into the punctum using a punctal plug
  - Plug may dissolved over time, be replenished or replaced
- Advantages
  - Track record of safety in using punctal plugs for dry eye
  - Minimally invasive and low-risk
  - Leverage existing medications used to treat glaucoma

Punctal Plug Drug Delivery Devices

- Disadvantages
  - Prone to fall out over time which is not acceptable for chronic condition where months occur b/w visits
    - Need to overcome this problem such as improving patient awareness that plug has fallen out
  - Drug delivery is passive depending upon tears to wash into the plug reservoir and transport active drug back into the tear film
    - In cases of severe dry eye or lid anatomy pathologies, plug may not deliver drug in predictable manner
  - Current medications may not be ideal for drug delivery
    - Plug may not hold enough
    - Pulsed dosing as seen with topical use versus constant delivery with depot may lead to different efficacy
      - Prostaglandin not as effective when used in constant manner
- Efficacy varies from slightly less than timolol to close to a PG

Punctal Plug Drug Delivery Devices

- Mati Therapeutics
  - Evolute
  - QLT started this work and has modified device to improve retention
  - Retention up to 95% depending if lower or upper punctum is used
  - Engaged in phase 2 trial with latanoprost
- Ocular Therapeutix
  - Using travoprost with 88% retention rate at 75 days
    - Phase 3 trial ongoing
  - Also working with allergy and steroid depot

Sustained-release Travoprost

- OTX-TP, Ocular Therapeutix
- Intracanalicular depot composed of polyethylene glycol hydrogel and drug-containing micro particles
- Sustained release prostaglandin analogs for the treatment of glaucoma and ocular hypertension
- Once drug placed in tear drainage system, the hydrogel expands to conform to surrounding tissue
- The plug resides within the canaliculus, delivering travoprost to the ocular surface for up to 90 days
- Reduce or eliminate the need for daily dosing.
- Reduces need of patient to take a medication
- Fluorescein is incorporated to serve as a visualization aid

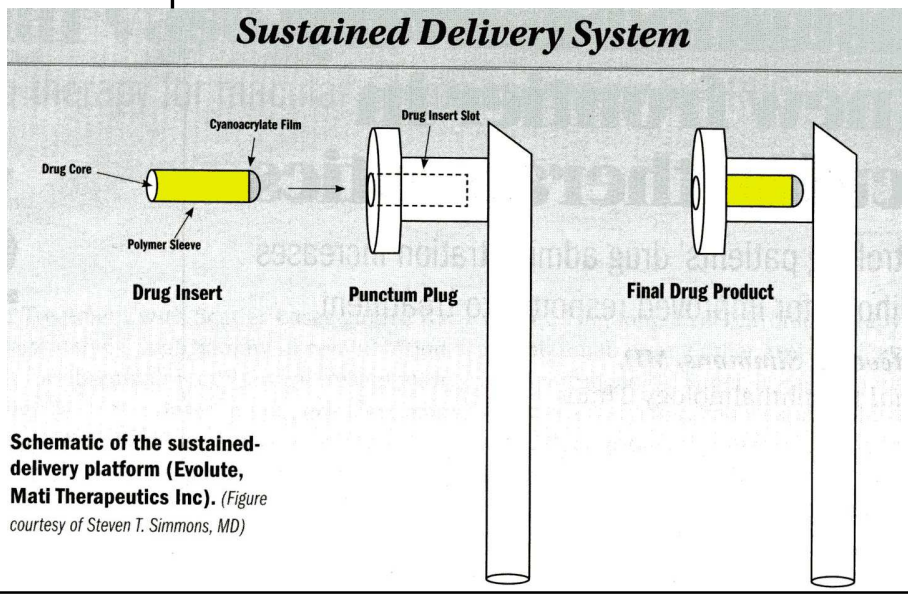
Sustained-release Travoprost Punctal Plug

- Sustained release prostaglandin analogs for the treatment of glaucoma and ocular hypertension.
- Inserted non-invasively through the punctum
- The plug resides within the canaliculus, delivering travoprost to the ocular surface for up to 90 days
- Reduce or eliminate the need for daily dosing
- Travoprost encapsulated in microparticles which are suspended in a dried polyethlene glycol resorbable hydrogel rod
- Hydrolysis of the microparticles mediates sustained release
- The product also contains a visualization aid (fluorescein) to monitor retention over the treatment period.
- After therapy is complete, the hydrogel resorbs and exits the nasolacrimal system, so there is no need for removal.
- Preservative - free

Mati Therapeutics

- "Evolute" Silicone Punctal Plug Device Used with Latanoprost w 5-6 mm Hg reduction
- Concern with plugs is retention, patient comfort and ease of insertion
  - 92-96% retention rate over 90 – 120 days
  - Easily removable if need be
- Long term efficacy also a concern
- Punctal opening – constant
- Elution in one direction into tear film due to valve
- Surface area exposed – constant
- Travoporst is the drug of choice for punctal plugs b/c of greater efficacy

Mati Therapeutics



Schematic of the sustained-delivery platform (Evolute, Mati Therapeutics Inc). *(Figure courtesy of Steven T. Simmons, MD)*

AMERICAN ACADEMY™ OF OPHTHALMOLOGY

CrossMark

Six-Month Intraocular Pressure Reduction with a Topical Bimatoprost Ocular Insert

Results of a Phase II Randomized Controlled Study

James D. Brandt, MD,[1] Kenneth Sall, MD,[2] Harvey DuBiner, MD,[3] Robert Benza, MD,[4] Yair Alster, MD,[5] Gary Walker, PhD,[5] Charles P. Semba, MD[5]

Purpose: Improving adherence to manage elevated intraocular pressure (IOP) remains an unmet need. A topical bimatoprost ocular insert was compared with twice-daily timolol eye drops in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT) treated for 6 months.

Design: Parallel-arm, multicenter, double-masked, randomized, controlled trial.

Participants: One hundred thirty adult OAG or OHT patients.

Methods: Eligible patients were randomized 1:1 to receive a bimatoprost insert plus artificial tears twice daily or a placebo insert plus timolol (0.5% solution) twice daily for 6 months after a screening washout period. Diurnal IOP measurements (at 0, 2, and 8 hours) were obtained at baseline; weeks 2, 6, and 12; and months 4, 5, and 6. Key eligibility included washout IOP of 23 mmHg or more at time 0, IOP of 20 mmHg or more at 2 and 8 hours, and IOP of 34 mmHg or less at all time points; no prior incisional surgery for OAG or OHT; and no known nonresponders to prostaglandins.

Main Outcome Measures: The primary efficacy end point examined the difference in mean change from baseline in diurnal IOPs (point estimate, 95% confidence interval) across 9 coprimary end points at weeks 2, 6, and 12 comparing the bimatoprost arm with the timolol arm using a noninferiority margin of 1.5 mmHg. Secondary end points were diurnal IOP measurements at months 4, 5, and 6 and adverse events (AEs).

Results: A mean reduction from baseline IOP of −3.2 to −6.4 mmHg was observed for the bimatoprost group compared with −4.2 to −6.4 mmHg for the timolol group over 6 months. The study met the noninferiority definition at 2 of 9 time points but was underpowered for the observed treatment effect. Adverse events were consistent with bimatoprost or timolol exposure; no unexpected ocular AEs were observed. Primary retention rate of the insert was 88.5% of patients at 6 months.

Conclusions: Clinically relevant reduction in mean IOP was observed over 6 months with a bimatoprost ocular insert and seems to be safe and well tolerated. The topically applied bimatoprost insert may provide an alternative to daily eye drops to improve adherence, consistency of delivery, and reduction of elevated IOP. *Ophthalmology 2016;123:1685-1694*

Bimatoprost SR

- Allergan
- Sustained release bioerodible implant that lasts 4-6 months with similar efficacy to eyedrops
- Small disolvable pellet is injected into the anterior chamber
  - Sits in/near the angle that resorbs over time
- Can be performed in the office
- Insert can be visualized in the inferior angle
- Ensures patient compliance
- Phase III trial underway comparing SR to timolol
- Will there ever be a need for removal?
- Could it cause cataracts?

Bimatoprost SR
Study Results

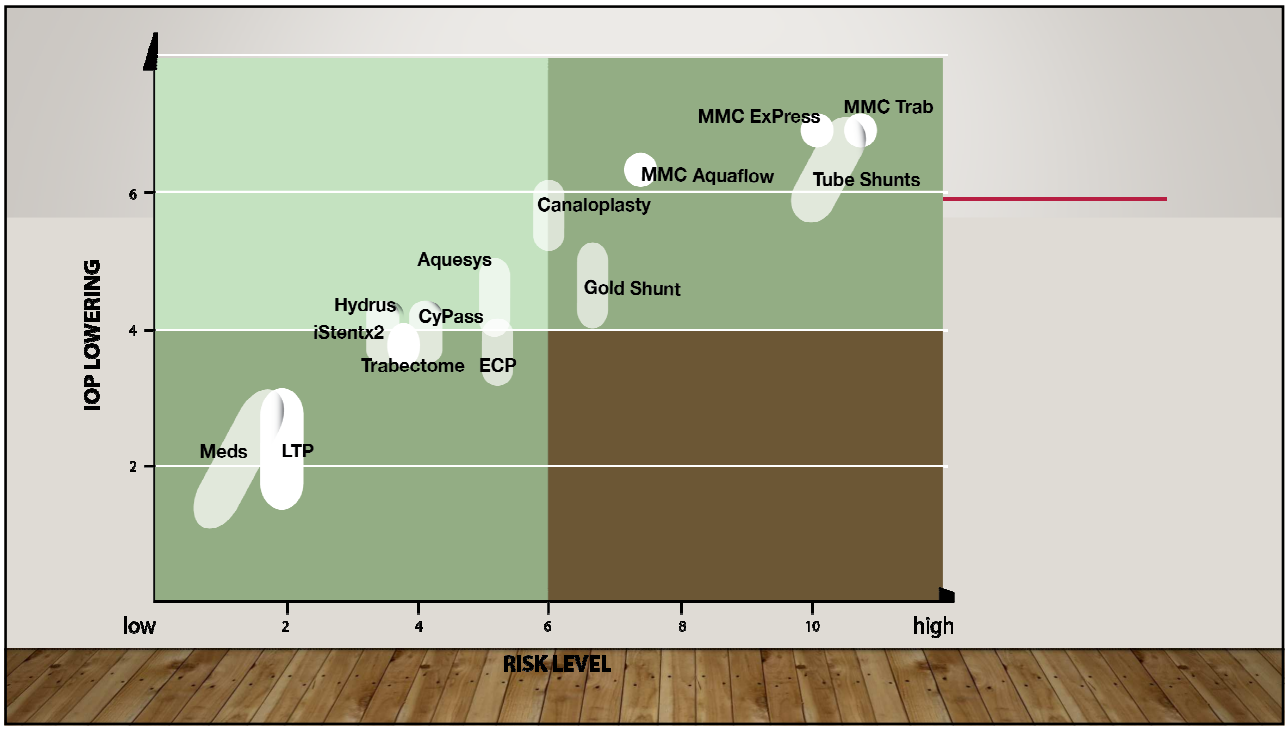
- Baseline IOP 25.2mm Hg
- Mean IOP reduction ranged from 7.2-9.5mm Hg at week 16
- Fellow eye IOP reduction 8.4 mm Hg with topical Bimatoprost eyedrops once daily
- Rescue therapy needed in 8% at week 16
- IOP reduction seen through 6 months
- At 6 moths, 71% did not require rescue therapy or a 2nd injection

BEST STRATEGY SELECTION

HOWARD BARNEBEY, MD

WHERE TO START

- Glaucoma patients vs Glaucoma suspect
- Note risk factors for progression: do risk factors translate?
  - CCT
  - Degree of damage: Structure and Function
  - IOP
  - Age
- Note risk factors for progression:
  - Slow progressors
  - Rapid progressors



TARGET IOP

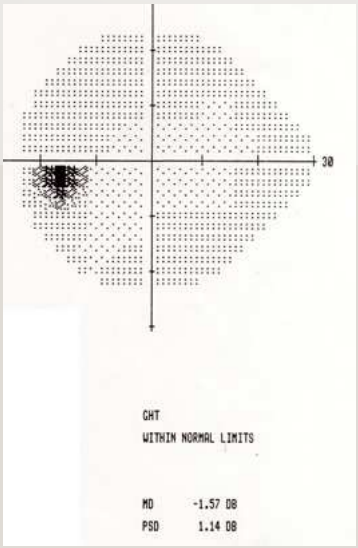
- Example

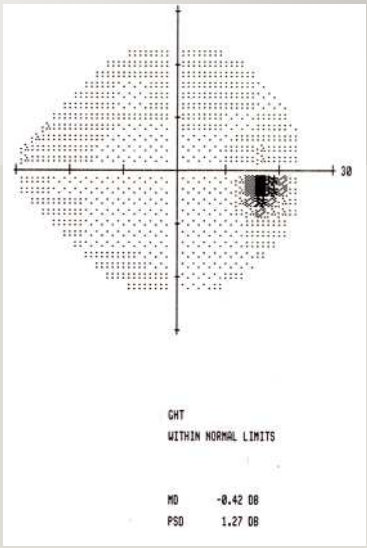
CASE PRESENTATION

43 yo Philipino female referred as glaucoma suspect

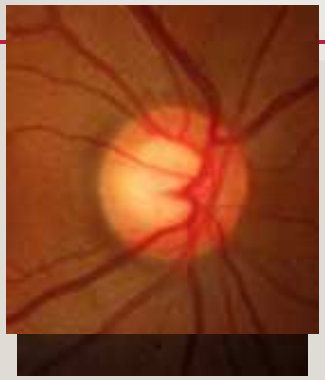
- IOP 18 mm Hg 14 mm Hg
- CCT 499 µ 500 µ

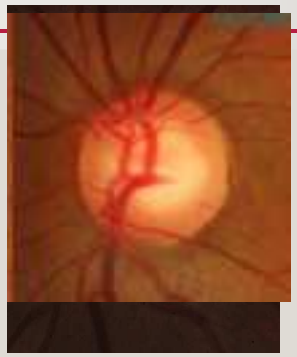
GLAUCOMA SUSPECT





2004 - 2008





OPTIONS

- Medication
- Laser
- Surgery

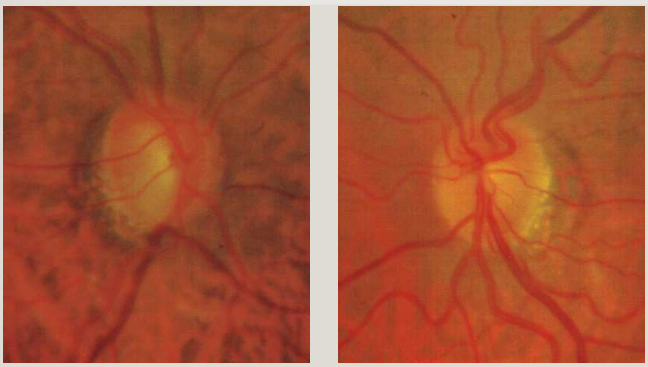
CASE PRESENTATION

CASE PRESENTATION

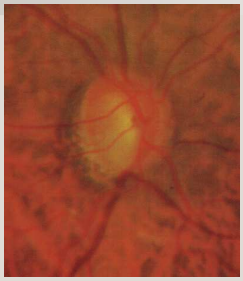
- 58 yo European male referred for glaucoma evaluation

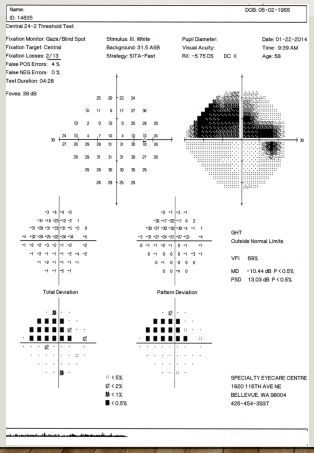
20/20 (-9.0)	20/20 (-6.00)
+1 NS	+1 NS
21 mm Hg	17 mm Hg (08:20)
549 μ	555 μ

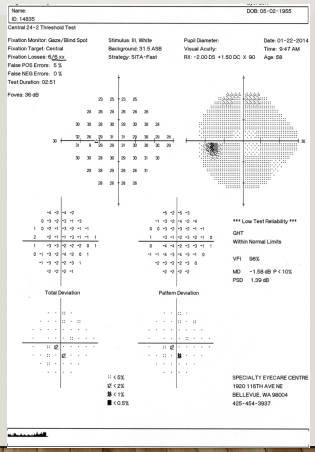
STRUCTURE

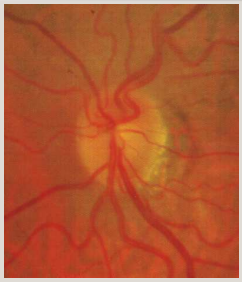


FUNCTION









MANAGEMENT

- Assessment: NTG (vs OAG)
- Treatment goal: ? Best Strategic Option
  - Pursue max medical treatment
  - Augment with laser
  - Surgery last step

SUMMARY

- Question: How aggressively do you pursue a "target" goal?
- Points of consideration:
  1. Young patient
  2. NTG
  3. Short follow up

MANAGEMENT

- Treatment goal: IOP < 14 mm Hg
- Medical Treatment:
  - Initiated PG (only OD): IOP 16/18
  - PG: Loss effect
  - Brimonidine: NR
  - Laser trabeculoplasty
  - Dorz-Tim FC: (current) IOP 18/18

MANAGEMENT

- Treatment goal: IOP < 14 mm Hg
- Currently: Medical Treatment + Laser
  IOP 18
- Structure-function: Stable (F/U 2 yr)
- Options:
  1.
  2.

MANAGEMENT

- Treatment goal: IOP < 14 mm Hg
- Currently: Medical Treatment + Laser
  IOP 18
- Structure-function: Stable (F/U 2 yr)
- Options:
  1. Observe on same Rx
  2. Consider surgery
     Cataract
     Glaucoma

OPTION CONSIDERATION

- Target Goal
- Adherence
- Cost of medication
- Side effects

SURGICAL OPTIONS

- Changed since introduction of MIGS
- Limitations
  - Cataract
  - Insurance coverage
  - IOP efficacy
  - Risk of surgery

Journal Club
Murray Fingeret, OD

JAMA Ophthalmology | Original Investigation

β-Zone Parapapillary Atrophy and Rates of Glaucomatous Visual Field Progression
African Descent and Glaucoma Evaluation Study

C. Gustavo De Moraes, MD, MPH; James T. Murphy, MD; Chad M. Kaplan, MD; Jeremy J. Reimann, MSPH; Alon Skaat, MD; Dana M. Blumberg, MD, MPH; Lama Al-Aswad, MD, MPH; George A. Cioffi, MD; Christopher A. Girkin, MD, MSPH; Felipe A. Medeiros, MD, PhD; Robert N. Weinreb, MD; Linda Zangwill, PhD; Jeffrey M. Liebmann, MD

JAMA Ophthalmol. 2017;135(6):617-623. doi:10.1001/jamaophthalmol.2017.1082
Published online May 11, 2017.

JAMA Ophthalmology | Original Investigation

β-Zone Parapapillary Atrophy and Rates of Glaucomatous Visual Field Progression
African Descent and Glaucoma Evaluation Study

C. Gustavo De Moraes, MD, MPH; James T. Murphy, MD; Chad M. Kaplan, MD; Jeremy J. Reimann, MSPH; Alon Skaat, MD; Dana M. Blumberg, MD, MPH; Lama Al-Aswad, MD, MPH; George A. Cioffi, MD; Christopher A. Girkin, MD, MSPH; Felipe A. Medeiros, MD, PhD; Robert N. Weinreb, MD; Linda Zangwill, PhD; Jeffrey M. Liebmann, MD

IMPORTANCE β-zone parapapillary atrophy (βPPA) has been reported as a risk factor for glaucoma onset and progression. Previous studies have shown that the prevalence of βPPA differs between individuals of African descent (AD) and European descent (ED).

OBJECTIVE To test whether the association between the presence and progression of βPPA vs visual field progression of glaucoma differs between these 2 ancestry groups.

DESIGN, SETTING, AND PARTICIPANTS In a prospective, multicenter, longitudinal cohort study, 634 individuals (1090 eyes) enrolled in the African Descent and Evaluation Study (ADAGES) with a diagnosis of glaucomatous optic neuropathy (GON) or ocular hypertension (OHT) and at least 2 disc stereophotographs were included. Two graders masked to clinical and ancestry data reviewed and graded the baseline and last disc stereophotographs for the presence of βPPA at baseline and βPPA progression (development or enlargement). Mixed-effects linear models were tested with visual field mean deviation as a dependent variable and time (alone and with interaction terms) as independent variables. ADAGES enrollment began in January 2003 and ended in July 2008; follow-up ended in 2016.

EXPOSURES Disc stereophotographs.

MAIN OUTCOMES AND MEASURES Progression of βPPA in AD and ED individuals.

RESULTS In 634 patients, a total of 814 eyes of AD (395 eyes) and ED (419) patients with GON and 276 eyes of AD (106) and ED (170) patients with OHT who were enrolled in ADAGES were analyzed. There were 336 (53.0%) women in the study; mean (SD) age was 61.9 (12.7) years. In the OHT group, the association between βPPA at baseline and visual field progression was not significantly different between AD and ED eyes (β = 0.071; 95% CI, −0.016 to 0.158; $P = .11$), nor was the association between βPPA progression and visual field progression (β = 0.020; 95% CI, −0.465 to 0.506; $P = .93$). In the GON group, ED eyes with baseline βPPA progressed faster than did AD eyes with baseline βPPA (β = −0.124; 95% CI, −0.241 to −0.007; $P = .04$), although the association between βPPA progression and visual field progression did not differ significantly between race groups (β = −0.101; 95% CI, −0.323 to 0.119; $P = .37$).

CONCLUSIONS AND RELEVANCE Race had a significant effect on the association between baseline βPPA and rates of visual field progression in eyes with GON. Progression of βPPA was not associated with faster visual field progression in either racial group.

JAMA Ophthalmol. 2017;135(6):617-623. doi:10.1001/jamaophthalmol.2017.1082
Published online May 11, 2017.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: C. Gustavo De Moraes, MD, MPH, Bernard and Shirlee Brown Glaucoma Research Laboratory, Edward S. Harkness Eye Institute, Department of Ophthalmology, Columbia University Medical Center, 635 W 165th St, PO Box 69, New York, NY 10032 (gustavo.demoraes@columbia.edu).

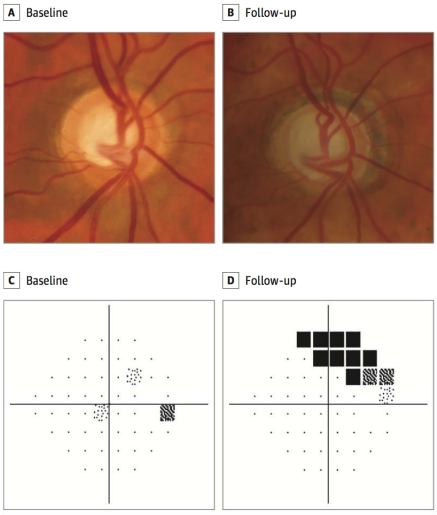
Key Points

Question Does race affect the association between β-zone parapapillary atrophy and the velocity of visual field progression?

Findings In a longitudinal cohort study of 634 patients (1090 eyes) with ocular hypertension or glaucoma followed up for a mean of 9 years, patients of European descent with glaucoma and β-zone parapapillary atrophy experienced faster visual field progression compared with those of African descent with β-zone parapapillary atrophy.

Meaning The results of this study suggest that the effect of β-zone parapapillary atrophy on the velocity of visual field progression depends on race and glaucoma status.

Figure. Example of β-Zone Parapapillary Atrophy (βPPA) Progression Accompanied by Visual Field Changes



A, Baseline disc stereophotograph. B, Follow-up disc stereophotograph (after 6 years) demonstrating βPPA progression. In addition, there was substantial neuroretinal rim thinning during the same period. Note that the βPPA location correlated spatially with the longest distance to the central retinal vessel trunk in the lamina cribrosa, as well as the most marked loss of rim in the disc. C, Baseline corresponding 24-2 Swedish Interactive Thresholding Algorithm standard automated perimetry visual fields of this patient. D, Follow-up visual fields (after 6 years). Note the progression of a superior arcuate defect.

Conclusions

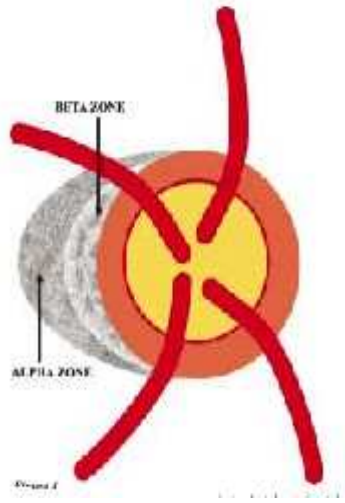
Whether βPPA is an epiphenomenon or causally connected with GON remains debatable. Nonetheless, our findings suggest that, when pondering the role of βPPA at baseline and its progression, clinicians should take into account where patients stand in the glaucoma continuum as well as their ancestry group. For the moment, clinicians should be aware that the presence of βPPA in individuals of ED increases the risk and rate of glaucomatous visual field progression. More research is needed to clarify the underlying microstructural characteristics of PPA and mechanisms that place some patients at greater risk of progression.

Zone Beta PPA and Glaucoma

- What is the cause of this change in the retinal structure?
- Is it a primary phenomenon?
  - parapapillary atrophy occurs first and leads to loss of neurons
- Is it a secondary phenomenon?
  - result of retinal ganglion cell death and/or other changes to optic nerve head
- Does it occur early as glaucoma develops or later on?
- Why was PPA more important as a diagnostic sign in ED?
- Primary tool to measure PPA has been with inspection of retinal photographs
  - Examining PPA has not been on our radar
- OCT with its new optic disc tools now capable of measure PPA

Parapapillary Atrophy and Glaucoma

- Parapapillary region consists of
  - optic disc margin
  - peripapillary scleral ring
  - beta zone
  - alpha zone
- PPA more common and greater in OAG
- Degree of PPA correlates with optic disk damage
- Location of PPA correlates with location of optic disk damage
- Location of PPA correlates with location of visual field defects
- Is PPA a biomarker for other change occuring?



Relationship Between Juxtapapillary Choroidal Volume and Beta-Zone Parapapillary Atrophy in Eyes With and Without Primary Open-Angle Glaucoma

MICHAEL SULLIVAN-MEE, NIMESH B. PATEL, DENISE PENSYL, AND CLIFFORD QUALLS

• PURPOSE: To evaluate whether quantity of choroidal tissue directly adjacent to the optic nerve differs between eyes with and without glaucoma and whether beta-zone parapapillary atrophy influences this relationship.
• DESIGN: Prospective cohort study.
• METHODS: Subjects were enrolled in a longitudinal, observational study at our institution. We studied 1 eye of 63 primary open-angle glaucoma (POAG), 30 ocular hypertension (OH), and 48 control subjects. Using optical coherence tomography enhanced depth imaging, we acquired 12 radial scans centered on the optic nerve head with 15 degrees of separation between scans. After images were enhanced, segmented, and corrected for ocular magnification, juxtapapillary choroidal volumetric parameters were calculated using raw thickness measurements and standard interpolation techniques. Juxtapapillary choroidal volume was then compared by diagnosis and by beta-zone parapapillary atrophy status.
• RESULTS: Total juxtapapillary choroidal volume was significantly reduced in POAG vs OH and control eyes (1.057 vs 1.228 vs 1.255 μL, $P = .04$) and it was reduced in eyes with vs without beta-zone parapapillary atrophy (1.076 μL, $n = 80$ vs 1.306 μL, $n = 61$, $P < .001$). Juxtapapillary choroidal volume did not differ between POAG, OH, and control eyes when beta-zone parapapillary atrophy was absent, but juxtapapillary choroidal volume was significantly reduced in POAG vs control eyes when beta-zone parapapillary atrophy was present (0.957 vs 1.196 μL, $P = .02$). Furthermore, POAG eyes with beta-zone parapapillary atrophy had substantially lower juxtapapillary choroidal volume compared to POAG eyes without beta-zone parapapillary atrophy (0.957 vs 1.356 μL, $P < .001$).
• CONCLUSIONS: The volume of choroid adjacent to the optic nerve was significantly reduced in POAG eyes when beta-zone parapapillary atrophy was present, suggesting that beta-zone parapapillary atrophy may be a biomarker for juxtapapillary choroidal atrophy and associated vascular compromise in POAG. (Am J Ophthalmol 2015;160(4):637–647. Published by Elsevier Inc.)

Accepted for publication Jun 24, 2015.
From the New Mexico Veterans Affairs Healthcare System, Albuquerque, New Mexico (M.S.-M., D.P., C.Q.); University of Houston, College of Optometry, Department of Vision Sciences, Houston, Texas (N.B.P.); and University of New Mexico, Department of Mathematics and Statistics, Albuquerque, New Mexico (C.Q.).
Inquiries to Michael Sullivan-Mee, New Mexico VA HCS, 1501 San Pedro SE, Albuquerque, NM 87108; e-mail: Michael.Sullivan-Mee@va.gov

A GROWING BODY OF EVIDENCE SUGGESTS vascular perfusion abnormality is a frequent contributor to glaucoma pathophysiology. Specifically, several large epidemiologic studies have identified reduced ocular perfusion as a risk factor for glaucoma prevalence,[1] incidence,[2] and progression.[3] Glaucoma is more common in patients with comorbid systemic vascular disorders[4,5] and several authors have shown, using a variety of techniques, that eyes with glaucoma commonly exhibit reduced blood flow compared to eyes without glaucoma.[6,7] Despite these reports, the specific underlying anatomic and physiologic factors that explicitly contribute to or result in vascular compromise and ultimately optic nerve damage remain unclear.

The primary blood supply for the prelaminar and, in some eyes, the laminar portions of the optic nerve is principally provided by vessels that arise in the region of the choroid that lies immediately adjacent to the optic nerve,[8] leading to hypotheses that disturbance of choroidal blood flow could contribute to glaucomatous optic neuropathy.[5,8,9] The development of spectral-domain optical coherence tomography (SD OCT) with enhanced depth imaging has facilitated greater resolution of deeper structures of the posterior segment,[10,11] leading to many recent studies of choroidal thickness in various ocular disease processes.[12–14] In studies using SD OCT to investigate choroidal thickness in glaucoma, results have been mixed, with some reports finding no difference in choroidal thickness between glaucomatous and normal eyes[14–21] and others reporting reduced choroidal thickness in glaucomatous eyes.[22–26] It is important to note, however, that none of these investigations systematically measured choroidal thickness in the region directly adjacent to the optic nerve. Rather, choroidal thickness was generally quantified either subfoveally or beneath the circular circumpapillary ring that is typically used for retinal nerve fiber layer (RNFL) measurement.

Journal Club

Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomized controlled trial

Prof Augusto Azuara-Blanco, PhD, Jennifer Burr, MD, Prof Craig Ramsay, PhD, David Cooper, PhD, Prof Paul J Foster, PhD, Prof David S Friedman, PhD, Graham Scotland, PhD, Mehdi Javanbakht, PhD, Claire Cochrane, MSc, Prof John Norrie, PhD

The Lancet
Volume 388, Issue 10052, Pages 1389-1397 (October 2016)
DOI: 10.1016/S0140-6736(16)30956-4

What is the best treatment for Angle Closure

- The standard of care for primary angle closure and primary angle-closure glaucoma is laser peripheral iridotomy
- Surgical lens extraction is an alternative approach for the management of primary angle-closure glaucoma. The efficacy and safety of this treatment in people with primary angle-closure glaucoma without cataract has not been fully assessed

EAGLE Study

- Hypothesis: initial clear-lens extraction would be associated with better quality of life, lower intraocular pressure, and less need for glaucoma surgery at 36 months than standard care.

EAGLE Study

- Methods: multicenter (N=30) , comparative effectiveness, randomized, controlled trial in in five countries: Australia, mainland China (one), Hong Kong, Malaysia, Singapore, and the UK
- Patient Enrollment Criteria: phakic; > 50 yo
  Primary Angle Closure IOP >30 mm Hg
  PAC defined as iridotrabecular contact, at least 180° on gonioscopy
  PACG glaucomatous VFD, glaucomatous optic neuropathy, or both
  IOP >21 mm Hg on at least one occasion.
- Exclusion:
  Symptomatic cataract, advanced glaucoma (VF MD > –15 dB or C/D ratio ≥0·9)
  Previous acute angle-closure attack
  Previous laser or ocular surgery

Outcome Questionnaires

- Health Status: European Quality of Life-5 Dimensions (EQ-5D)
  assesses five dimensions of health at 4 levels
  1. mobility
  2. self-care
  3. usual activity
  4. pain or discomfort
  5. anxiety or depression)
- National Eye Institute Visual Function Questionnaire-25
  assess the effects of vision problems on vision-targeted functioning and health-related QOL
- Glaucoma Utility Index
  descriptive profile in six dimensions
  1. central and near vision
  2. lighting and glare
  3. mobility
  4. activities of daily living
  5. eye discomfort
  6. other effects of glaucoma and its treatment

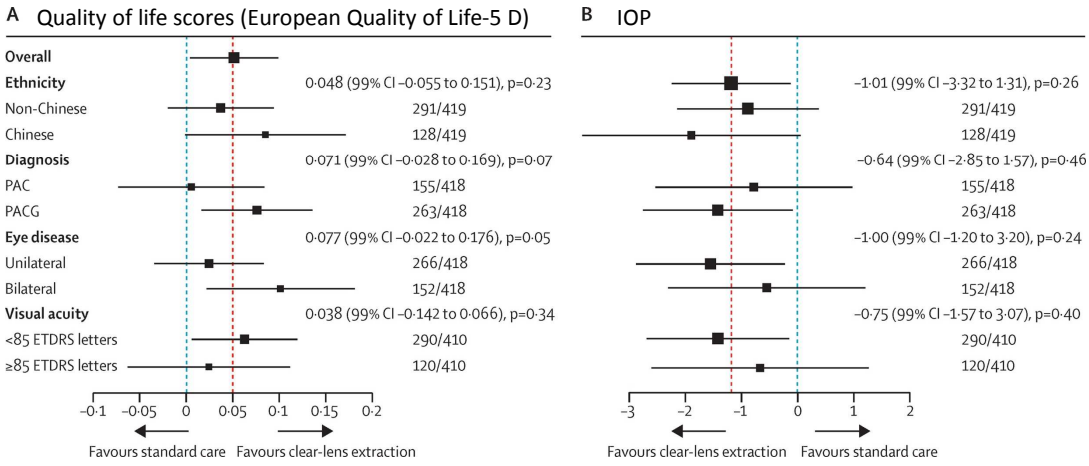
Glaucoma Metrics

- Best-corrected visual acuity (ETDRS)
- Gonioscopy: extension of angle closure
- Humphrey SITA 24-2 test

	Clear-lens extraction (n=208)	Laser peripheral iridotomy (n=211)	Missing data
Demographics			
Women	122 (59%)	121 (57%)	0
Chinese origin	62 (30%)	56 (31%)	0
Age (years)	67·0 (61·0–73·0)	67·0 (61·0–73·0)	0
Ocular characteristics and treatments			
Both eyes suitable for treatment	75 (37%)	76 (36%)	0
Study eye was right eye	110 (53%)	118 (56%)	0
Diagnosis in study eye			
PAC	80 (38%)	75 (36%)	0
PACG	127 (61%)	136 (64%)	0
Missing	1 (0%)		
Systemic warfarin use	11 (5%)	7 (3%)	1
Systemic α-agonist use	17 (8%)	25 (12%)	0
Glaucoma topical medication			
None	83 (40%)	79 (37%)	0
One	71 (34%)	79 (37%)	0
Two	35 (17%)	37 (18%)	0
Three	15 (7%)	10 (5%)	0
Four	2 (1%)	5 (2%)	0
Five	1 (0%)	1 (0%)	0
Glaucoma oral medication	0	2 (1%)	0
IOP (mmHg)	30·0 (24·0 to 34·0)	30·0 (26·0 to 33·0)	0
Axial length (mm)	22·5 (22·0 to 23·1)	22·7 (22·1 to 23·2)	7
Anterior chamber depth (mm)	2·5 (2·1 to 2·7)	2·5 (2·1 to 2·7)	17
Refractive error (dioptres)	1·6 (0·5 to 3·0)	1·1 (0·0 to 2·4)	39
Visual field mean deviation (dB)	−3·0 (−7·0 to −1·8)	−3·5 (−7·2 to −1·9)	42
Central corneal thickness (μm)	553·0 (528·0 to 576·0)	551·0 (522·0 to 582·0)	5
Gonioscopy (angle closure°)			
Closure without indentation	360·0 (270·0 to 360·0)	360·0 (270·0 to 360·0)	21
Synechial closure	90·0 (20·0 to 180·0)	90·0 (10·0 to 180·0)	247
BCVA, ETDRS (# letters)	80·0 (74·0 to 85·0)	79·0 (73·0 to 85·0)	7
Binocular BCVA, ETDRS	85·0 (79·0 to 88·0)	84·0 (79·0 to 88·0)	17
Patient-reported instrument scores			
NEI-VFQ-25	90·9 (83·6 to 95·5)	90·3 (83·3 to 95·9)	6
EQ-5D	1·000 (0·796 to 1·000)	1·000 (0·796 to 1·000)	11
Glaucoma Utility Index	0·897 (0·791 to 0·991)	0·921 (0·791 to 1·000)	17

	Clear-lens extraction (n=208)	Laser peripheral iridotomy (n=211)	Missing data
Patient-reported instrument scores			
NEI-VFQ-25	90·9 (83·6 to 95·5)	90·3 (83·3 to 95·9)	6
EQ-5D	1·000 (0·796 to 1·000)	1·000 (0·796 to 1·000)	11
Glaucoma Utility Index	0·897 (0·791 to 0·991)	0·921 (0·791 to 1·000)	17

Subgroup Results



Red dotted vertical line indicates overall differences

Conclusions

- Initial clear-lens extraction was superior to laser peripheral iridotomy plus topical medical treatment
- Overall health status, visual impairment and disability, and glaucoma-specific disability were all improved
- Multiple factors probably contributed:
  - reduced need for glaucoma medications and surgery
  - improvement of visual function
  - correction of refractive error

Conclusions

- IOP was better with clear-lens extraction
  - mean pressure 1 mm Hg lower
  - 21% of participants in the clear-lens extraction group received any further treatment for IOP
  - 61% who received at least one glaucoma drop (LPI group)
- Severe primary angle-close glaucoma patients were excluded
  - findings might not be applicable to patients

What is the best treatment for Angle Closure

- Cochrane analysis: no trials assessing early (clear) lens extraction as the primary treatment for chronic primary angle-closure glaucoma.
- This large multicentre randomized controlled trial provides evidence supporting the use of initial clear-lens extraction as a first-line intervention for primary angle-closure glaucoma and primary angle closure with high intraocular pressure.

New Technology in The Diagnosis and Management of Glaucoma

Murray Fingeret, OD

Chief, Optometry Section, VA NYHHCS, Brooklyn, nY

Clinical Professor, SUNY college of optometry, New York, NY

How Do We Monitor IOP Through the 24-Hour Day?

- How do we evaluate IOP if we only measure it briefly in office?
- Three approaches to measure IOP over 24 hour period
  - Self tonometry
  - Permanent continuous IOP monitoring
  - Temporary continuous IOP monitoring

Home IOP Monitoring

- Presents a challenge for patient but also provides a wealth of information
- One FDA approved device – Home iCare
  - Provides intermittent data
- One other FDA approved device – Triggerfish – not commercially available and does not provide IOP data
  - Provides progression risk data based upon corneal biomechanical properties
- Important to get more IOP data points
  - Provides insight into the true peak IOP and pattern of IOP fluctuation
- Minimize need for office visits that are scheduled for only IOP measurements
- Enable more timely adjustment of medications
- Promotes better patient adherence

Permanent Continuous Monitoring

- Provide daytime and nighttime IOP measurements through self-contained implant
- Accessed remotely with wireless technology
- Would not be measuring the surface but rather taking IOP measurements directly inside the eye
  - Subject to less noise
- Incorporate telemetric device with IOL or place inside eye at time of IOL surgery
- Digital signal would be sent form IOL to external device
- Alarm raised when elevated IOP is seen
- Long-term stability is unknown
- Not FDA approved
- In development

Home IOP Monitoring

- Implantable devices
  - Implandata (Eyemate)
    - Two devices
      - one placing a sensor in the sulcus during cataract surgery
      - other designed for subconjunctival or subscleral implantation
  - AcuMEMS (iSense)
    - Two versions
      - At time of cataract surgery, placed with IOL in capsular bag
      - Placed in anterior chamber as stand-alone procedure

Temporary Continuous Monitoring

- Non-invasive contact lens based system that measure IOP over 24-48 hour period
- Silicone contact lens which has strain gauge
  - must fit tight to reduce noise
- Corneal health issues with tight lens
- Problems with noise, discomfort
- Sensimed system in use in Europe that has contact lens, antennae system and recorder
- Recently FDA Approved but not yet available in the US
- Does not record IOP over time but instead measuring biomechanical changes associated with progression

Triggerfish Contact Lens IOP Device

- Consists of a clear, silicone contact lens ringed by a strain gauge and a microprocessor and antenna that transmits data to an external receiver
- The gauge continuously monitors the shape of the cornea, indicating greater or lesser intraocular pressure
- Information about volume changes is immediately transmitted via radio frequencies from the lens' microprocessor to a recording receiver
- The microprocessor is powered by an induction loop which uses a magnetic field around the eye to generate the tiny amounts of required electricity
  - Induction loops are also used to power hearing-aid implants

AMERICAN ACADEMY™
OF OPHTHALMOLOGY

Visual Field Change and 24-Hour IOP-Related Profile with a Contact Lens Sensor in Treated Glaucoma Patients

Carlos Gustavo De Moraes, MD, MPH,[1] Jessica V. Jasien, MEn,[2] Sonja Simon-Zoula, PhD,[3] Jeffrey M. Liebmann, MD,[1] Robert Ritch, MD[2]

Purpose: To test the hypothesis that a 24-hour recording of intraocular pressure (IOP)-related measurements derived from a contact lens sensor (CLS) correlates to the rate of visual field progression in treated glaucomatous eyes.

Design: Prospective, cross-sectional study.

Participants: Forty treated glaucomatous patients with 8 or more 24-2 visual field tests.

Methods: Twenty-four–hour recording with a CLS that provides IOP-related measurements.

Main Outcome Measures: Rates of visual field mean deviation (MD) change before and at the time of CLS recording and CLS parameters, namely number of large peaks, mean peak ratio, wake-to-sleep slope, amplitude and area under the cosine curve, and variability from the mean.

Results: When comparing the rate of MD change before and at the time of CLS recording of all patients, the average slope was −0.05 dB/year faster in the beginning compared with the end ($P = 0.087$), suggesting a deceleration of progression by the time of CLS recording. The number of long peaks and the mean peak ratio when patients were awake were the best predictors of faster progression. The combination of CLS parameters provided better measures of goodness of fit than Goldmann IOP parameters (mean, peak, and fluctuation) in the same period.

Conclusions: Intraocular pressure-related parameters obtained with 24-hour recording with a CLS were associated with the rate of visual field progression in treated glaucomatous eyes. This technology may be useful in detecting eyes at higher risk of glaucoma progression while receiving treatment. *Ophthalmology 2016;■ :1–10 © 2016 by the American Academy of Ophthalmology.*

Triggerfish - Summary

- A single 24-hour recording with the CLS provides a signature that correlates with the rates of VF progression 5 years prior to its recording
- That signature had better performance than the mean Goldmann IOP collected over years
- The results of studies testing its predictive value are pending

Self Tonometry

- Patients would monitor their IOP over 24-48 hour period
- Device would need to be easy to use and accurate
- Easiest approach in regards to continuous monitoring
- Adapt current device such as Noncontact tonometer or Rebound tonometer
- May be difficult for some patients to perform
- Not easy to obtain 24 hour IOP

New Technology in Glaucoma

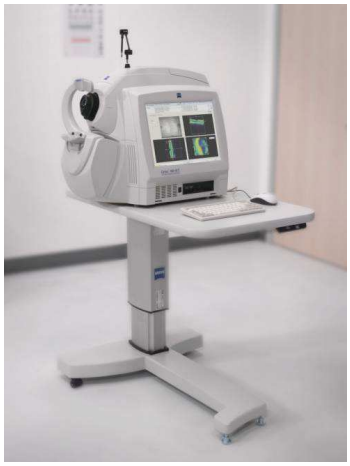
- Optic Nerve/RNFL/Posterior pole
  - What structure changes first as glaucoma develops?
  - Swept Source OCT
  - Confocal Laser Diode Scanner
    - improved form of retinal photography
  - Advances in Optical Coherence Tomography
  - Structure-function correlations
  - Flipping the TSNIT

Centervue Eidon Confocal Scanning LCD

- Scanning Laser Ophthalmoscopic systems are superior to conventional fundus cameras as they exploit confocal imaging principle
  - limits the effect of backscattered light from deeper layers and provides enhanced image quality
- Another advantage of SLO systems is that they operate with smaller pupils than conventional fundus cameras
- However, SLO systems do not provide color images, as they typically employ multiple, monochromatic, laser sources, resulting in black and white or pseudo-color images
- Different from existing SLO systems, EIDON uses WHITE light instead of monochromatic lasers
  - providing true color imaging

OCT: AN OVERVIEW

- Optical coherence tomography is an evolving biomedical imaging technology
- An important adjunct in the evaluation of the optic nerve/RNFL and macula for glaucoma
- Obtains high-resolution, cross-sectional images of biological microstructures
- Images are provided in real-time
- Non-invasive
- First generation – Time Domain
- Second generation – Spectral Domain
- Next generation – Swept Source



Swept Source OCT

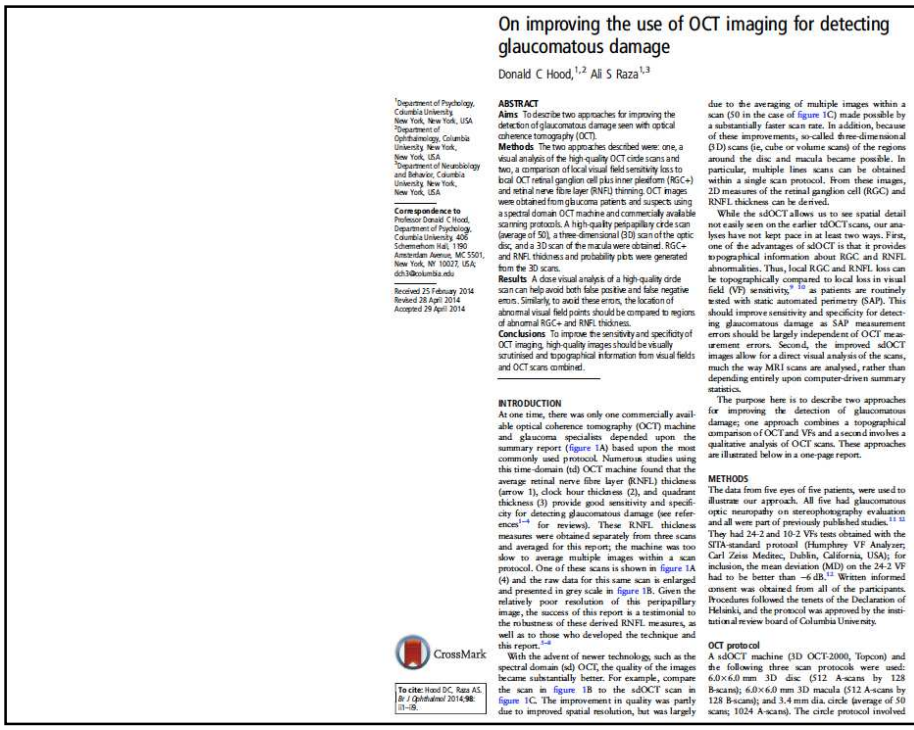
- Swept-source (SS) OCT is a next-generation Fourier domain OCT that demonstrates less signal decay over depth compared with the current SD OCT.
- Faster speed
- Probe light with a center wavelength of 1040 to 1060 nm, which allows high-penetration imaging deep retinal tissues such as Choroid and Sclera
- SS OCT improves visualization of the deep structures of the optic disc
- Compared with SD OCT, SS OCT is characterized by a higher speed scan rate and relatively lower sensitivity roll-off versus depth

Swept Source OCT

- 100,000 A scans per second w 1 micron wavelength lightsource (1050 nm)
- Deep Tissue Imaging
  - Penetrates deeper into retina for choroid and lamina assessment
- Images through cataracts
- Swept source OCT is faster because:
  - No spectrometer
  - No line-scan camera (for detector)
  - Utilizes tunable laser source
  - 'Sweeps' across spectrum rapidly
  - Photodiode detector (near instantaneous)

Advantages of Flipping the RNFL Curve with the OCT

- TSNIT was an arbitrary designation 25 years ago
- Temporal region is most important part of curve and with NITSN, region is not broken up and loss more obvious
- Easier to recognize structure-function correlation
  - RNFL loss correlates easily with field loss
- Center the visual field on the OCT
- Easier to understand if macula area may be involved and central field loss present
  - Is there a reduction in RNFL within the central 8^0



On improving the use of OCT imaging for detecting glaucomatous damage

Donald C Hood,[1,2] Ali S Raza[1,3]

[1]Department of Psychology, Columbia University, New York, New York, USA
[2]Department of Ophthalmology, Columbia University, New York, New York, USA
[3]Department of Neurobiology and Behavior, Columbia University, New York, New York, USA

Correspondence to
Professor Donald C Hood, Department of Psychology, Columbia University, 406 Schermerhorn Hall, 1190 Amsterdam Avenue, MC 5501, New York, NY 10027, USA; dch3@columbia.edu

Received 25 February 2014
Revised 28 April 2014
Accepted 29 April 2014

ABSTRACT

Aims To describe two approaches for improving the detection of glaucomatous damage seen with optical coherence tomography (OCT).

Methods The two approaches described were: one, a visual analysis of the high quality OCT circle scans and two, a comparison of local visual field sensitivity loss to local OCT retinal ganglion cell plus inner plexiform (RGC+) and retinal nerve fibre layer (RNFL) thinning. OCT images were obtained from glaucoma patients and suspects using a spectral domain OCT machine and commercially available scanning protocols. A high-quality peripapillary circle scan (average of 50), a three-dimensional (3D) scan of the optic disc, and a 3D scan of the macula were obtained. RGC+ and RNFL thickness and probability plots were generated from the 3D scans.

Results A close visual analysis of a high-quality circle scan can help avoid both false positive and false negative errors. Similarly, to avoid these errors, the location of abnormal visual field points should be compared to regions of abnormal RGC+ and RNFL thickness.

Conclusions To improve the sensitivity and specificity of OCT imaging, high-quality images should be visually scrutinised and topographical information from visual fields and OCT scans combined.

CrossMark

To cite: Hood DC, Raza AS. *Br J Ophthalmol* 2014;**98**:1–8.

INTRODUCTION

At one time, there was only one commercially available optical coherence tomography (OCT) machine and glaucoma specialists depended upon the summary report (figure 1A) based upon the most commonly used protocol. Numerous studies using this time-domain (td) OCT machine found that the average retinal nerve fibre layer (RNFL) thickness (arrow 1), clock hour thickness (2), and quadrant thickness (3) provide good sensitivity and specificity for detecting glaucomatous damage (see references[1–4] for reviews). These RNFL thickness measures were obtained separately from three scans and averaged for this report; the machine was too slow to average multiple images within a scan protocol. One of these scans is shown in figure 1A (4) and the raw data for this same scan is enlarged and presented in grey scale in figure 1B. Given the relatively poor resolution of this peripapillary image, the success of this report is a testimonial to the robustness of these derived RNFL measures, as well as to those who developed the technique and this report.[5–8]

With the advent of newer technology, such as the spectral domain (sd) OCT, the quality of the images became substantially better. For example, compare the scan in figure 1B to the sdOCT scan in figure 1C. The improvement in quality was partly due to improved spatial resolution, but was largely due to the averaging of multiple images within a scan (50 in the case of figure 1C) made possible by a substantially faster scan rate. In addition, because of these improvements, so-called three-dimensional (3D) scans (ie, cube or volume scans) of the regions around the disc and macula became possible. In particular, multiple lines scans can be obtained within a single scan protocol. From these images, 2D measures of the retinal ganglion cell (RGC) and RNFL thickness can be derived.

While the sdOCT allows us to see spatial detail not easily seen on the earlier tdOCT scans, our analyses have not kept pace in at least two ways. First, one of the advantages of sdOCT is that it provides topographical information about RGC and RNFL abnormalities. Thus, local RGC and RNFL loss can be topographically compared to local loss in visual field (VF) sensitivity,[9–10] as patients are routinely tested with static automated perimetry (SAP). This should improve sensitivity and specificity for detecting glaucomatous damage as SAP measurement errors should be largely independent of OCT measurement errors. Second, the improved sdOCT images allow for a direct visual analysis of the scans, much the way MRI scans are analysed, rather than depending entirely upon computer-driven summary statistics.

The purpose here is to describe two approaches for improving the detection of glaucomatous damage; one approach combines a topographical comparison of OCT and VFs and a second involves a qualitative analysis of OCT scans. These approaches are illustrated below in a one-page report.

METHODS

The data from five eyes of five patients, were used to illustrate our approach. All five had glaucomatous optic neuropathy on stereophotography evaluation and all were part of previously published studies.[11 12] They had 24-2 and 10-2 VFs tests obtained with the SITA-standard protocol (Humphrey VF Analyzer; Carl Zeiss Meditec, Dublin, California, USA); for inclusion, the mean deviation (MD) on the 24-2 VF had to be better than −6 dB.[12] Written informed consent was obtained from all of the participants. Procedures followed the tenets of the Declaration of Helsinki, and the protocol was approved by the institutional review board of Columbia University.

OCT protocol

A sdOCT machine (3D OCT-2000, Topcon) and the following three scan protocols were used: 6.0×6.0 mm 3D disc (512 A-scans by 128 B-scans); 6.0×6.0 mm 3D macula (512 A-scans by 128 B-scans); and 3.4 mm dia. circle (average of 50 scans; 1024 A-scans). The circle protocol involved

Compass – Centervue Fundus Automated Perimetry

- Confocal scanning laser LED camera
  - Focus on back of eye so no trial lens needed
  - No trial lens defect
- Has eye tracking so fixation no longer an issue
- Can tell if ptosis is a problem by watching monitor in real time
  - Shows back of eye and where targets are being presented
  - Uses ZEST algorithm
    - Longer than SITA

Fundus-Guided Perimetry

- Allows for assessment of visual function under direct observation of the fundus
- Visual function can be tested at specific structural loci
- May have role in glaucoma but requires an adequate understanding of structure-function mapping in order to accurately predict areas of interest to test
- An important difference between macular diseases and glaucoma is the degree of spatial congruence between the affected area of the retina and the associated location of dysfunction in visual function
- There is high congruence in retinal diseases
  - not the case for glaucoma
- Nevertheless, the fixation tracking technology associated with fundus-guided perimetry may prove useful for perimetric testing in glaucoma to minimize the effects of small eye movements on test-retest variability

New Technology in Glaucoma

- Present structural and functional information together
  - Hood presentation
  - Allows earlier damage to be recognized
- Role of central fields in diagnosing and monitoring glaucoma
  - Incorporating fields with imaging
- Combined Reports
  - OCT/Photographs with Visual Fields

DRUGS AND MONEY

HOWARD BARNEBEY, MD

WHAT IF PILOTS HAD TO DEAL WITH THE EQUIVALENT OF CHANGING FORMULARIES…

"Yes, I know you were scheduled to land in Chicago, but Chicago is no longer on our formulary. You will now have to land in St. Louis, even though Chicago always worked really well for people who wanted to actually go to Chicago.

You can appeal if you like and we'll have an answer for you in six weeks, if you want to stay in the air that long."

HEALTH INSURANCE & RX

- Health insurance is supposed to save you money on your Rx consumers are finding that isn't the case.
- In May, Patrik Swanljung handed his Medicare prescription card to the pharmacist at his local Anacortes Walgreens and was told that he owed $83.94 for a three-month supply.
- Mr. Swanljung went online and found Blink Health generic Crestor — for $45.89.
- He struck a better deal than UnitedHealthcare.

One Way to Slash Drug Prices: Leave Insurance Card at Home. NY Times Dec 10, 2017

HEALTH INSURANCE & RX

- Drug prices have ignited public outrage
- Insurers are requiring consumers to shoulder more costs
- People can sometimes get better deals than their own insurers.
- Drug companies, pharmacies, insurers and pharmacy benefit managers are taking a cut of the profits,
- Better deal on your own?
  10% of drug transactions involve such situations.
- The system is so complex that "there's no chance that a consumer can figure it out without help," Rx Savings Solutions

HEALTH INSURANCE & RX

- Pharmacy Benefit Managers (PBM)
  - deal with drug benefits on behalf of insurers
  - may negotiate better prices for consumers, esp for brand-name Rx
  - not necessarily true for some generic drugs
- Insurers' clients are employers overseeing large numbers of workers
  - focused on overall costs
  - insurers seek deals for generic drugs in batches
    - agreements for groups of different drugs vs. the lowest price on every drug.
- Complicated layers of negotiation are not made public
  - different insurers pay different prices for individual drugs
  - some insurers require a set co-payment for each prescription
    - even if the insurer reimburses the pharmacy at a lower rate

VALUE OF PBM: PATIENT OR INSURANCE

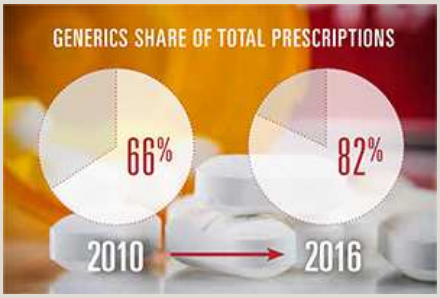


EXHIBIT 1: BRAND AND GENERIC SHARE OF PRESCRIPTIONS FILLED AND TOTAL SPENDING

	SHARE OF UTILIZATION		SHARE OF TOTAL SPENDING	
TYPE OF DRUG	2010	2016	2010	2016
GENERIC	66%	82%	23%	22%
BRAND	34%	18%	77%	78%

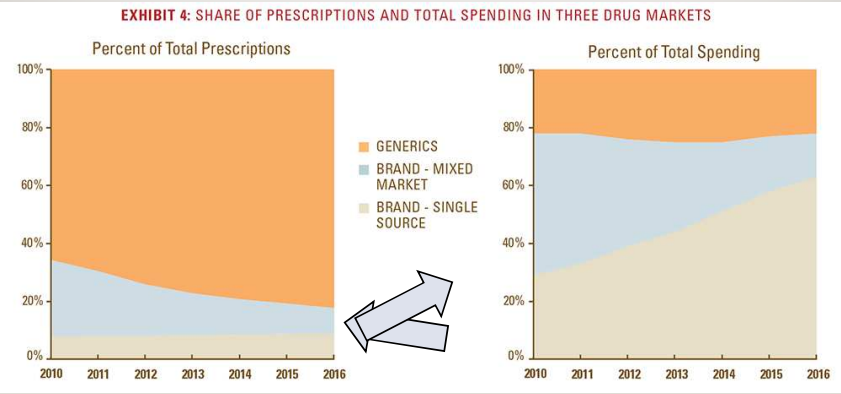
Blue Cross Blue Shield: The Health of America Report

DRUG MARKET SEGMENTATION

- mixed markets: brand drugs have a generic alternative
  Utilization: ↓12%
  Unit Price: ↑3%
  Total Annual Spending: ↓10%
- single-source markets: only patent-protected drugs exist
  49% of all brand prescriptions (2016)
  Total Annual Spending: ↑25%
-

Blue Cross Blue Shield: The Health of America Report

VALUE OF PBM: PATIENT OR INSURANCE



Blue Cross Blue Shield: The Health of America Report

CONSUMER R_X PRICING

- Several companies capitalize on consumer anger
  - Blink Health
  - Good Rx
  - Rx Savings Solutions
  - Express Scripts
  - Amazon ?

CONSUMER R_X PRICING

- Having insurance is clearly valuable,
- Consumers may face penalties if they don't use their insurance
  - Insurers won't let them apply those purchases to a deductible or out-of-pocket spending maximum.
- Still, many find that leaving their prescription card at home is worth it.

GLAUCOMA RX

- Monotherapy: 55-60%
- Multiple: 40-45%
- > 3 Rx: 5% to 10%

  Confusing
  constantly shifting paradigm as insurance companies switch manufacturers,
  over correct dosing and correct adherence regimen becomes ubiquitous
  Generic prices that have quadrupled during the past 10 years
  concerns with preservatives damaging the ocular surface.

DOES THIS HAPPEN TO YOU

- You write a prescription for a new glaucoma medication- it can be Travatan-Z or Lumigan or Vyzalta. Later on that day you receive a call from the patient that the medication is not available on their medical insurance plan. Can you write for another medication which is available?

OPTIONS

- 1. Same path and address on case-by-case basis
- 2. Change practice habits and directly Rx generics first
- 3. Create alternative pathway

OPTIONS

- 1. Same path and address on case-by-case basis
  - Time consuming
  - Ignoring major shift in market
  - Patient inconvenience
- 2. Change practice habits and directly Rx generics first
  - Assume all (most) generics comparable in efficacy
  - Ignore co-morbidity
  - Possible AE
- 3. Create alternative pathway

ALTERNATIVE PHARMACY PROGRAM

- Ease-

  From physician: only need the Rx and a way to call the patient.

  Pharmacy: obtain the patient demographic & insurance,

  activate and apply any coupons

  ship (free) directly to the patient

- Experience:

  know exactly how each drug coupon works

  how to get the maximum value for the patient > decreasing out of pocket costs.

  Full time call center

ALTERNATIVE PHARMACY PROGRAM

- Convenient:
  - Collaborative practice agreement with a therapeutic interchange

    allow changes in the event of a drug shortage, formulary change, or excessive drug cost

    no calls back to the office
  - Prior Authorizations:

    service available at no additional cost for Restasis.

    other medications are in the works.

GLAUCOMA MEDICATION ALGORITHM

- 1. Create a selection pathway
- 2. Find areas where there are deadends
- 3. Pathway includes PA
- 4. Find a pharmacy willing to participate in program
- 5. Create a document for the pharmacist to follow the medication sequencing

GLAUCOMA MEDICATION ALGORITHM: BARNEBEY

Prostaglandin

- Travatan-Z> Travaprost>Lumigan>bimatoprost>latanoprost
- Lumigan>Travatan-Z>bimatoprost>travoprost>latanoprost
- If BAK sensitive: Zioptan>Travatan-Z

GLAUCOMA MEDICATION ALGORITHM: BARNEBEY

β-blocker

- Timoptic GFS > timolol
- If BAK sensitive: Timolol PF <Deadstop>
- If asthma/COPD: Betoptic-0.25% S > Betaxolol 0.5% <Deadstop>

GLAUCOMA MEDICATION ALGORITHM: BARNEBEY

CAI

- Azopt>dorzolamide

Alpha-Agonist

- Alphagan-P>Brimonidine 0.15%>brimonidine 0.2%
- If BAK sensitive: Alphagan-P>Brimonidine 0.15%

GLAUCOMA MEDICATION ALGORITHM: BARNEBEY

- Alpha-Agonist
- Alphagan-P>Brimonidine 0.15%>brimonidine 0.2%
- If BAK sensitive: Alphagan-P>Brimonidine 0.15%
- Systemic CAI
- Diamox 500 mg sequel> Acetazolamide 500 mg sequel>Acetazolamide 250 mg tab

PT INFORMATION: EXPLAINING NEW OPTIONS

WHY?..... Dr. Barnebey and Golez want you to have the best drugs at the lower price to make your treatment affordable. This program is new and gives you choices based on available coupons and your drug insurance benefits by getting you the lowest prices.

To take advantage of this program, you need to set up an account with an online pharmacy, XXXX. This is a slightly different step than dealing with your regular pharmacy whether it be a brick and mortar store like Costco, Bartell's or Walgreen, for example, or an online pharmacy coordinated with your insurance benefit manager.

Your doctor's get nothing in return ***except the satisfaction*** that you are getting the best medicines for your eyes.

PHARMACIES PROVIDING

Meds In Motion	SenderraRx	US Bioservices
Avella	BioPlus	Diplomat
Infusiion Express	Solera	OptiMed
Apothecary by Design		Foundation Care

CONCERN FOR "MAIL" ORDER PHARMACIES

- I can get my Rx from a pharmacy out of the country
  Where the product was manufactured?
- Product and Quality

DRUG QUALITY AND SECURITY ACT: 2013

- 2012 outbreak of fungal meningitis killed at least 64 people
  - traced injectable drugs contaminated at the New England Compounding Center
  - unsanitary conditions, including fungus in steroid solutions
  - failed to sterilize products
  - Mats used to trap dust and dirt were dirty
  - sterile hoods were not properly cleaned
  - boiler was leaking next to a clean room,
- At the time, states responsible to regulate compounding pharmacies
  - but pharmacies selling large batches across state lines.
- Congress prompted to request the FDA in regulating this business.

DRUG QUALITY AND SECURITY ACT: 2013

Compounding pharmacies are divided into 2 types.

503A : Traditional compounding pharmacies facilities
- regulated primarily by individual states
- only compound drugs for individual
- cannot distribute across state lines more than 5% of their total prescription orders,

503B: Outsourcing facilities
- must comply with federal Current Good Manufacturing Practice (CGMP) regulations
- inspected by the FDA
- report to the FDA twice a year

Neither type of facility can compound copies of commercially available drugs that are not currently approved by the FDA,

NEW IDEAS: GENERIC FIXED COMBINATION

- timolol, bimonidine, and dorzolamide
- Latanoprost, timolol, bimonidine, and dorzolamide
- Dosing:
  triple combination drop twice per day
  triple drop in the morning and the quadruple drop at night (additional IOP)
- Simplies complex medical regimen
- drop in cost

GLAUCOMA PEARLS AND GRAND ROUNDS

Murray Fingeret, OD, FAAO
Howard Barnebey, MD

Glaucoma Grand Rounds

- Diagnosing and managing Ocular Hypertension and Glaucoma requires a series of decisions be made over the course of the lifetime of care
  - Is disease present?
    - What tests should be performed to aid in establishing diagnosis?
  - If disease is present, what type?
    - OHTN vs. Glaucoma
  - Is therapy required?
    - What therapy?
  - If glaucoma, what type?
    - Primary vs. secondary
    - Open vs. chronic angle closure
  - Grade severity of condition
  - Establish the target IOP
  - When should patient return?

Diagnosis of Glaucoma

- Tests
  - History
  - IOP
  - Gonioscopy
  - Pachymetry
  - Dilated optic nerve assessment- stereo
    - Imaging
      - HRT, GDx, OCT
  - Perimetry- Standard Automated Perimetry (SAP)
    - Selective perimetric tests
      - FDT, SITA SWAP

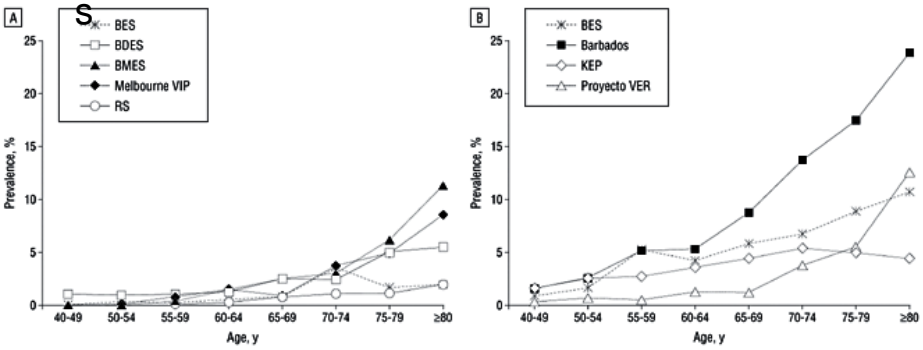
What are the Risks Associated with the Development of Glaucoma?

- Age
- Race
  - African descent
  - Hispanics
  - Asian for narrow angle
- Family history
- History cardiovascular disease & Reduced blood press
- Prior use of steroids
- Medications
  - Systemic beta blockers
  - Diuretics
- Perfusion pressure
  - Blood pressure minus IOP

Glaucoma Prevalence: Increasing with Age

Caucasians

African and Hispanic Descent



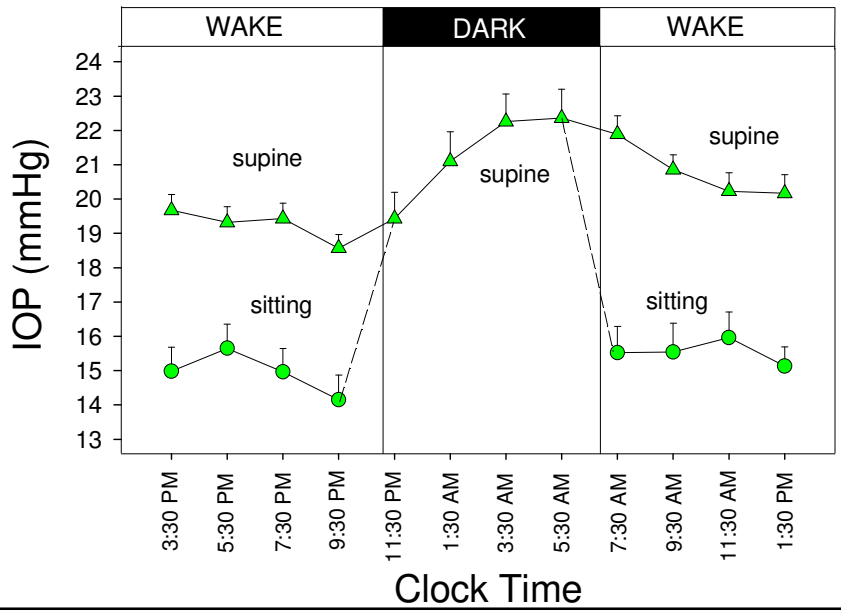
Goldmann Applanation Tonometry

- Goldmann applanation tonometry assumes central corneal thickness (CCT) of 500 um)
- GAT over- or under-estimates IOP by as much as 5 mmHg for every 70 um of CCT difference from ~520um

Central Corneal Thickness and the Diagnosis of Glaucoma

- Pachymetry is Part of the Ocular Examination Whenever Glaucoma is Suspected
- Re-classification on basis of correction factors
  - 44% of Normal Tension Glaucoma become POAG
  - 35% of Ocular Hypertension become normal

24-hour IOP pattern, young adults (18-25 years, N=21)



Key Factors for Gonioscopy

- Good anesthesia
- Dark room
- Start with 1mm, narrow beam of light
  - Keep beam away from pupil
- Patient's maintains primary gaze
- Minimize lens tilt
  - Only minor movements permitted to see over convexity of iris
  - Otherwise narrow open will appear open

Key Factors for Gonioscopy

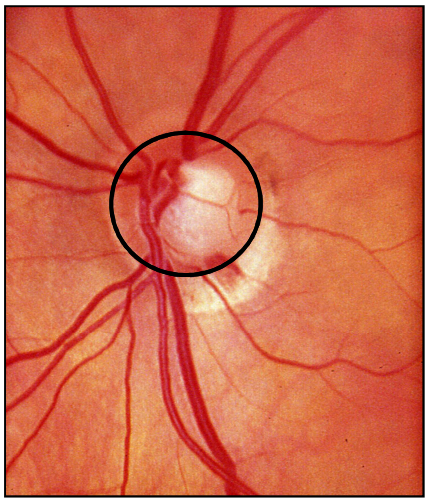
- Use high magnification
- Assess whether iris is in contact with TM
- If not, estimate geometric angle b/w TM and adjacent peripheral area of iris
- Describe level of most anterior point of contact b/w iris and cornea-scleral coat
- Once gonio is completed 360^0, repeat with increased illumination and indentation

Risk Assessment

- Age
- IOP
- Corneal Thickness
- Vertical Cup/Disc Ratio
  - Optic Nerve healthy
- PSD Visual Field
  - Global Indice
  - Field full
- Diabetes Status

Five Rules for Assessment of the Optic Disc in Glaucoma

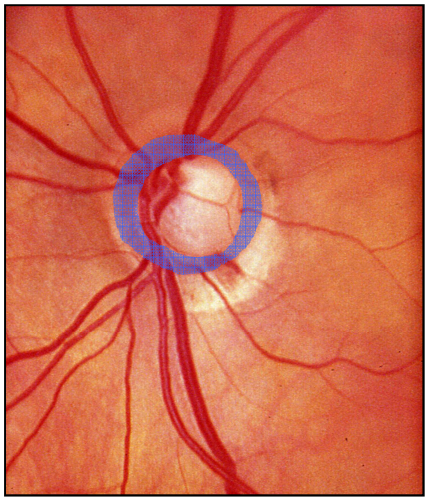
1 Observe the scleral Ring to identify the limits of the optic disc and its size



Five Rules for Assessment of the Optic Disc in Glaucoma

1 Observe the scleral Ring to identify the limits of the optic disc and its size

2 Identify the size of the Rim

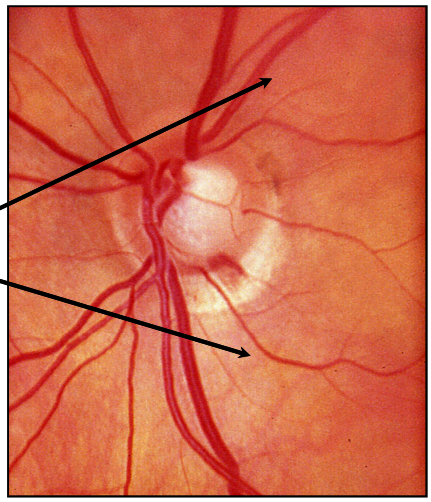


Five Rules for Assessment of the Optic Disc in Glaucoma

1 Observe the scleral Ring to identify the limits of the optic disc and its size

2 Identify the size of the Rim

3 Examine the Retinal nerve fiber layer



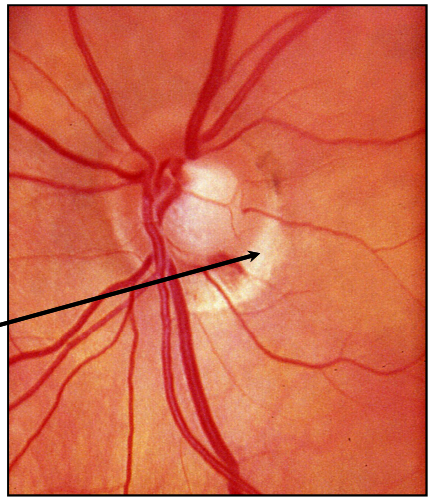
Five Rules for Assessment of the Optic Disc in Glaucoma

1 **Observe the scleral Ring to identify the limits of the optic disc and its size**

2 **Identify the size of the Rim**

3 **Examine the Retinal nerve fiber layer**

4 **Examine the Region of parapapillary atrophy**



Five Rules for Assessment of the Optic Disc in Glaucoma

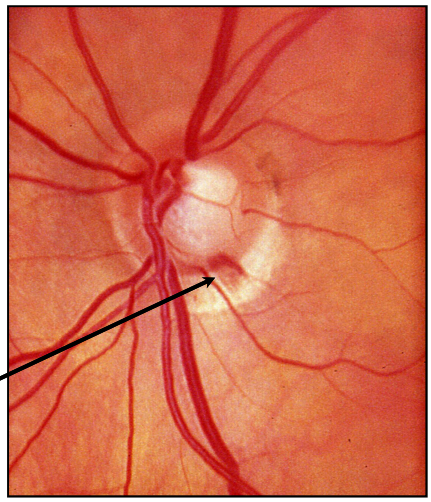
1 **Observe the scleral Ring to identify the limits of the optic disc and its size**

2 **Identify the size of the Rim**

3 **Examine the Retinal nerve fiber layer**

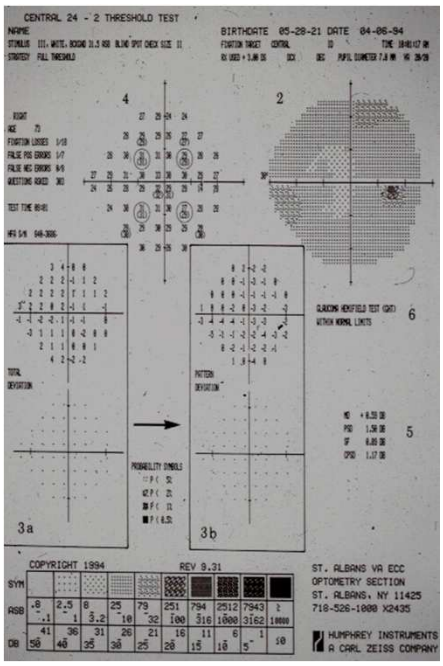
4 **Examine the Region of parapapillary atrophy**

5 **Look for Retinal and optic disc hemorrhages**



Six Steps in Analyzing the Single Field Printout

- Reliability Indices
- Gray Scale
- Raw Data
- Total/Pattern Deviation Printouts
  - Compare between the two
    - Explain any differences
- Global Indices
- Glaucoma Hemifield Test



False Positives may be the Most Important Reliability Indicator

Second Best is Whether the Blind Spot was Plotted

Is there a 0?

Unreliable Visual Field

- Excessive Fixation Losses
- High False Positives
- Borderline False Negatives
- White Scotomas
- GHT-Abnormally High Sensitivity

False Negatives are Not a Good Indicator of Unreliability

The Learning Curve is Real

Glaucomatous Visual Fields are Extremely Variable

Need to confirm change and confirm again

New Tools for Diagnosing Glaucoma

- Structure vs. Function
  - Structure – Imaging – OCT
  - Function – SAP, HEP, FDT
- Goal is to Detect Damage Very Early
- What do you do when imaging test is positive is everything else is negative
  - Should the imaging test drive the diagnosis?

Glaucoma Therapy An Overview

- Chronic disease that can be difficult to control
  - Person has the disease for the rest of their life
- Treatment often requires multiple medications and surgies
- Treatment endpoints are poorly defined
- Treatment endpoints are often difficult to achieve, even when defined
- Medication adherence challenges are common

Initial Medical Management of OAG

- Before starting therapy
  - obtain several IOP readings
    - either done on one day (diurnal curve) or over 2-3 days at different times
    - need detailed pretreatment information
      - medical and ocular
  - grade severity of glaucoma
    - based upon nerve appearance, fields and highest IOP

Describe and Understand Condition

- Open vs. Narrow Angle
  - Chronic angle closure glaucoma resembles open angle forms
    - detect with gonioscopy
    - Asians
- Primary vs. Secondary forms
  - detect with slit lamp evaluation
  - secondary glaucomas

Clinical Correlations in Glaucoma

- Compare the visual field and optic nerve appearance
- Does the disc and visual field correlate?
- Does the comparison between the right and left eyes fit?

Initial Medical Management of OAG

- Ask “How will optic nerve and visual field appear in twenty years”
  - not in 3 months
  - Hattenhauer
- Lower target IOPs
  - AGIS data
  - Sustained IOP reduction

Clinical Decisions in Glaucoma

- Target pressure
- Select therapy vs. No therapy
  - Medications
    - **Prostaglandins- most common first line agent**
    - Beta blockers
    - CAI
    - Adrenergic
  - Laser Trabeculoplasty
  - Filter Surgery

Topical Glaucoma Treatments

BRAND NAME/ MNFR	GENERIC NAME	CONCENTRATION/ BOTTLE SIZE
Beta Blockers Betagan/Allergan	levobunolol HCL	0.25% - 5mL, 10mL; 0.5% - 2mL, 5mL, 10mL, 15mL
Betimol/Vistakon	timolol hemihydrate	0.25% - 5mL; 0.5% - 5mL, 10mL, 15mL
Betoptic-S/Alcon	betaxaolol HCL	0.25% - 2.5mL, 5mL, 10mL, 15mL
Istalol/Ista	timolol maleate	0.5% - 5mL
Timoptic/Aton Pharma	timolol maleate	0.25% - 5mL, 10mL, 15mL; 0.5% - 5mL, 10mL, 15mL
Timoptic (preservative-free)/Aton Pharma	timolol maleate	0.25% - unit dose; 0.5% - unit dose
Timoptic-XE/Aton Pharma	timolol maleate	0.25% - 2.5mL, 5mL; 0.5% - 2.5mL, 5mL
Prostaglandin Analogs Lumigan/Allergan	bimatoprost	0.01% - 2.5mL, 5mL, 7.5mL
Rescula/Sucampo	unoprostone	0.15% - 2.5mL, 5mL
Travatan Z/Alcon	travoprost	0.004% - 2.5mL, 5mL
Generic	latanoprost	0.005% - 2.5mL
Zioptan/Merck	Tafluprost	2.5mL

30

Topical Glaucoma Treatments

BRAND NAME/ MNFR	GENERIC NAME	CONCENTRATION/ BOTTLE SIZE
Alpha Agonists Generic	brimonidine	0.1%, 0.15% - 5mL, 10mL, 15mL
Alphagan P/Allergan	brimonidine	0.1%, 0.15% - 5mL, 10mL, 15mL
Iopidine/Alcon	apraclonidine	0.5% - 5mL, 10mL; 1% - unit dose
Carbonic Anhydrase Inhibitors Azopt/Alcon	brinzolamide	1% - 5mL, 10mL, 15mL
Trusopt/Merck	dorzolamide	2% - 5mL, 10mL
Combination Glaucoma Medications Combigan/Allergan	brimonidine/timolol	0.2%/0.5% - 5mL, 10mL
Simbrinza/Alcon	Brinzolamide/brimonidine	1%/0.2% - 8 mL
Cosopt PF/Merck Generic	dorzolamide/timolol	2%/0.5% - 5mL, 10mL

31

Selecting the Primary Medication
Open Angle Glaucoma

- Base the decision on:
  - Stage of disease
    - driver for choosing initial therapy
  - Baseline IOPs
  - General health of patient
  - Insurance coverage
  - Systemic medications
    - consider Brimonidine or Latanoprost if on systemic β-blocker

Select Target Pressure

- Think in terms of Per Cent Reduction from highest IOP reading
- Greater the damage, lower the IOP needs to be

Setting Target Pressures

- Consider the following:
  - How bad is the glaucoma?
  - How long did it take to get that bad?
    - get from old records if possible
  - What is the life expectancy of the patient?
- Trend is for lower target IOPs
  - sustained reduction

Target Pressures

- Setting the target IOP, consider highest IOP
  - IOP in 40 with some cupping, asymmetry and early field loss
    - IOP in low 20s may work
  - Same amount of damage but presenting IOP of 20
    - need to be more aggressive

Modifying the Medical Regimen Lack of Control

- IOP too high
  - Reverse Monocular Trial
- IOP Variability
- Optic Nerve Progression
- Visual Field Loss
- Adding a medication
  - medications vs. laser vs. filter surgery
  - add medication vs. increase dosage or concentration

Risk Factors for the Progression of Glaucoma

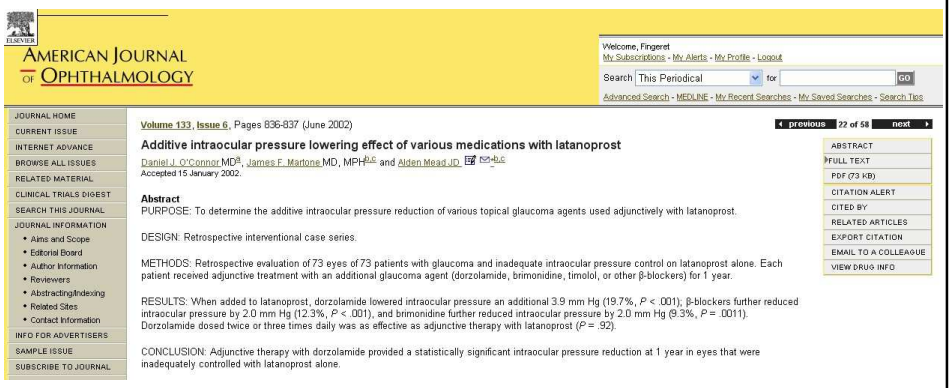
Risk Factors
Older age[1-3]
Higher IOP (baseline)[2]
Higher IOP (over follow-up)[2]
IOP fluctuation[4]
VF status at baseline[2]
Race (nonwhite)[3,5]
Disc hemorrhage[2,5]
Pseudoexfoliation[2]

When do you Add or Switch a Medication

- Beware of "Regression to Mean"
- Tendency is to do nothing or add medications
  - tolerance develops to some medications
    - Beta Blockers, Alpha Agonists
- Is the angle getting narrow?
  - Perform gonioscopy

Hypotensive Efficacy Adding to β–adrenergic Blockers

- Prostaglandins
- Miotics
- Carbonic anhydrase inhibitors (PO)
- α_2-adrenergic agonists
- Dorzolamide
- Dipivefrin=epinephrine



AMERICAN JOURNAL OF OPHTHALMOLOGY

Welcome, Fingeret
My Subscriptions - My Alerts - My Profile - Logout
Search This Periodical for GO
Advanced Search - MEDLINE - My Recent Searches - My Saved Searches - Search Tips

JOURNAL HOME
CURRENT ISSUE
INTERNET ADVANCE
BROWSE ALL ISSUES
RELATED MATERIAL
CLINICAL TRIALS DIGEST
SEARCH THIS JOURNAL
JOURNAL INFORMATION
• Aims and Scope
• Editorial Board
• Author Information
• Reviewers
• Abstracting/Indexing
• Related Sites
• Contact Information
INFO FOR ADVERTISERS
SAMPLE ISSUE
SUBSCRIBE TO JOURNAL

Volume 133, Issue 6, Pages 836-837 (June 2002)

previous 22 of 58 next

Additive intraocular pressure lowering effect of various medications with latanoprost

Daniel J. O'Connor MD[a], James F. Martone MD, MPH[b,c] and Alden Mead JD [b,c]
Accepted 15 January 2002.

ABSTRACT
FULL TEXT
PDF (73 KB)
CITATION ALERT
CITED BY
RELATED ARTICLES
EXPORT CITATION
EMAIL TO A COLLEAGUE
VIEW DRUG INFO

Abstract

PURPOSE: To determine the additive intraocular pressure reduction of various topical glaucoma agents used adjunctively with latanoprost.

DESIGN: Retrospective interventional case series.

METHODS: Retrospective evaluation of 73 eyes of 73 patients with glaucoma and inadequate intraocular pressure control on latanoprost alone. Each patient received adjunctive treatment with an additional glaucoma agent (dorzolamide, brimonidine, timolol, or other β-blockers) for 1 year.

RESULTS: When added to latanoprost, dorzolamide lowered intraocular pressure an additional 3.9 mm Hg (19.7%, $P < .001$); β-blockers further reduced intraocular pressure by 2.0 mm Hg (12.3%, $P < .001$), and brimonidine further reduced intraocular pressure by 2.0 mm Hg (9.3%, $P = .0011$). Dorzolamide dosed twice or three times daily was as effective as adjunctive therapy with latanoprost ($P = .92$).

CONCLUSION: Adjunctive therapy with dorzolamide provided a statistically significant intraocular pressure reduction at 1 year in eyes that were inadequately controlled with latanoprost alone.

Table 1. Intraocular Pressure Reduction at 1 Year by Various Agents Added to Latanoprost

Medication	Number of Eyes	Mean Baseline IOP (mm Hg)	Mean IOP at 1 Year (mm Hg)	Mean IOP Change (mm Hg [%])	*P* Value*
Dorzolamide ALL	25	19.8	16.0	−3.9 (19.7%)	*P* < .001
Dorzolamide BID	11	20.5	16.6	−3.9 (19.4%)	*P* < .001
Dorzolamide TID	14	19.4	15.5	−3.9 (19.9%)	*P* < .001
β-blockers	23	19.9	17.4	−2.5 (12.3%)	*P* < .001
Brimonidine	25	21.0	19.0	−2.0 (9.3%)	*P* = .0011

BID = twice a day; IOP = intraocular pressure; TID = three times a day.

[*] *P*-values are for change from latanoprost baseline.

Managing Glaucoma

- Initial medication Prostaglandin
- Second medication
  - Topical CAI or Beta Blocker
  - Or switch to different prostaglandin
- Third medication or Modality- Try to not exceed two bottles
  - Fixed Combination “CoSopt”
- Fourth medication or modality
  - Brimonidine or ALT/SLT
- Fifth modality- Surgery

When is surgery indicated?

- Poor control
  - progression noted in optic nerve or v. fields
  - account for variability on visual fields
    - repeat test to confirm change
- IOP above target pressure
  - exhausted several or all medical options
- Medication side effects
- Poor compliance

Surgical Options

- Placement of surgery within treatment regimen varies by clinician
  - Some will use SLT as primary therapy, others look at SLT as supplementary step if initial medical therapy is not successful or requires further IOP reduction
  - Filter surgery indicated as initial therapy when advanced glaucoma presents
  - Filter surgery for most glaucomas is indicated when condition needs significant IOP reduction/ medical therapy not fully effective

Surgical Options

- Laser trabeculoplasty
  - Argon, Selective
- Filter surgery (trabeculectomy)
  - With anti-fibroblastic agents
- Setons and valves
  - Molteno, Ahmed
- New surgical procedures
  - Canaloplasty, Express implant, Trabectome, iStent

UPCOMING EVENTS

Coeur d'Alene CE

April 27 & 28, 2018

10 hours of CE featuring: Bill Hefner, Kirk Halvorson, Aaron Bronner, Bill Prunty and Jennifer Prunty

$350

NW Residents Conference

June 8 & 9, 2018

10 hours of CE from the Residency capstone event

2018 Victoria Conference

July 12 – 15, 2018

Hotel Grand Pacific

10 hours of CE with Lee Carr, Anthony DeWilde, Beth Kinoshita, James Kundart, and Cathy Evans

$475

2019 Island Eyes Conference

January 20 – 26, 2019

Fairmont Orchid, Big Island

Up to 30 hours of CE

$700