

## Glaucoma: how to manage

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Professor



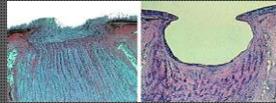
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## Disclosures

- **Speakers bureau** Optovue, Bausch and Lomb, Haag Streit
- **Consultant** Haag-Striet, ZeaVision, VectorVision, Optovue
- **Research** ZeaVision, Optovue, VectorVision

2

## Glaucoma



3

## Definitions

- “Ocular tissue damage at least partially related to intraocular pressure”
- A chronic, bilateral, often asymmetrical disease in adults, featuring acquired loss of optic nerve fibers and abnormality of visual field with an open anterior chamber angle.

4

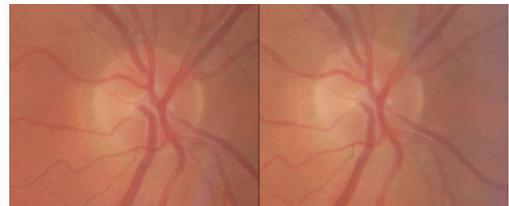
## Goals

- Document status of optic nerve structure and function
- Target pressure- so damage is unlikely to happen
- Maintain IOP below target pressure
- Monitor status of the optic nerve and reset target pressure if deterioration occurs.
- Minimize side effects of management and impact on vision and general health and quality of life.
- Educate and engage the patient in management

5

## Gold standard

- Simultaneous stereo photography!
  - Problems?



6

## Glaucoma evaluation

- Anterior chamber evaluation
  - Angle evaluation
  - Corneal thickness
- Macula evaluation
- Retinal Nerve fiber layer
- Optic disc photography

7

## Pediatric cases what do I do?

8

## Definitions of glaucoma- two or more required

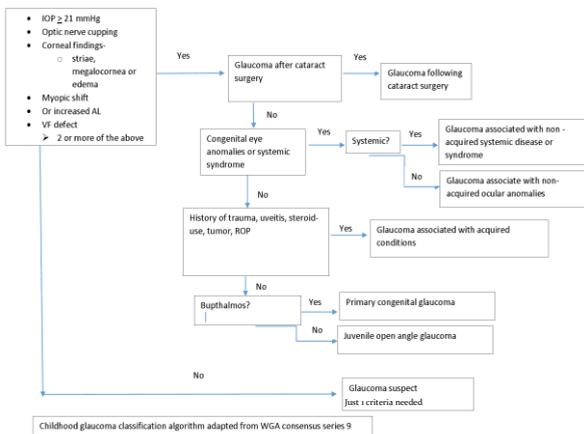
- IOP >21 mmHg
- Optic disc cupping: neuro retinal rim narrowing, progressive increase in CDR, CD asymmetry  $\geq 0.2$  when optic disc are similar in size
- Corneal findings of Haab striae, corneal edema
  - corneal diameter
    - $\geq 11$  mm in new born
    - $\geq 12$  mm in child <1 year of age
    - > 13 any age
- Progressive myopia or myopic shift
- Reproducible visual field defect consistent with glaucoma

9

## Glaucoma Suspect at least 1 required

- IOP > 21 mmHg on two separate occasions
- Suspicious disc appearance of glaucoma ie. Increased CDR
- Suspicious visual fields
- Increased corneal diameter or axial length in normal IOP

10



11

## Intraocular pressure

- Normal neonates IOP lower than adults
- Increases to adult levels by teenage years

Age in years	IOP in mmHg*
Birth	9-6
0-1	10.6
1-2	12.0
2-3	12.6
3-5	13.6
5-7	14.2
7-9	14.2
9-12	14.3
12-16	14.5

\* Pensiero S, Da Pozzo S, Perissutti P. Intraocular pressure in children. J Pediatr Ophthalmol Strabismus 1992;29:79.

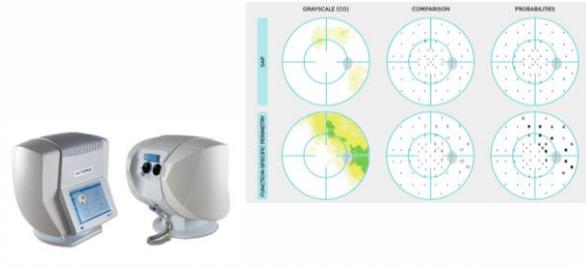
12

## Visual fields

13

## Early detection fields

- Magno cellular testing- Like pulsar testing



14

## Special features of Pulsar

- Patient can use their own glasses
- More resistant to blur
- Early detection of defects
- Progression analysis is also present
- Remember its most suitable for early glaucoma when a patient has advanced glaucoma switch to white-on-white perimetry

15

## Learning curve in visual fields

- Learning curve can be substantial
- At least two visual fields are needed to establish baseline

16

## Patient has cataract what do I do with Visual fields?

17

### ORIGINAL ARTICLE

## Effect of Cataract Opacity Type and Glaucoma Severity on Visual Field Index

Hye Jin Chung\*, Jeong Hoon Choi<sup>†</sup>, Young-Chun Lee<sup>‡</sup>,  
and Su-Young Kim<sup>‡</sup>

- Visual field parameters improved after cataract surgery
- MD, PSD and VFI- less influenced in nuclear sclerosis
- MD, PSD and VFI – greater effect in cortical cataract, particularly for early glaucoma

1540-5488/16/0936-3575\$0 VOL. 93, NO. 6, PP. 575-578  
OPTOMETRY AND VISION SCIENCE  
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18

## Cataract in glaucoma patient

- Dilate as much as possible
- Depend on PSD plot more than total deviation
- Use imaging modalities more.

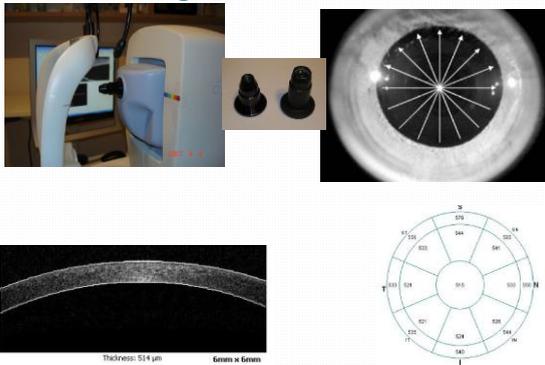
19

## Sources of error

- Miosis: decreases threshold peripherally, increases variability centrally
- Lens opacities
- Uncorrected refractive error –decrease in contrast sensitivity
- Spectacles
- Ptosis

20

## Anterior segment OCT



21

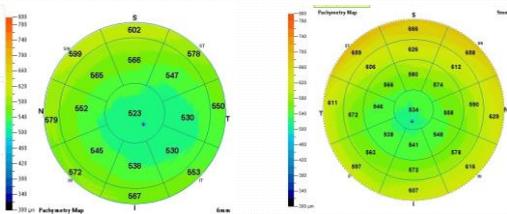
## Difference between optical and ultrasound pachymetry measurements

Author	Difference in OCT and ultrasound values
Kim et al <i>AJO</i> 2008	26 microns
Wang et al <i>J Refract Surg</i> 2008	38 microns
Gunvant & Darner <i>Medical Imaging</i> 2011	13 microns

Kim, H.Y., Rudenz, D.L., Lee P.S, et al. " Comparison of central corneal thickness using anterior segment optical coherence tomography vs ultrasonic pachymetry, *Am J Ophthalmol*, 145:228-234 (2008).  
 Wang, J.C., Bunce, C., and Lee, H.M. " Intraoperative corneal thickness measurement using optical coherence pachymetry and corneo-gage plus ultrasound pachymetry *J Refract Surg*, 24(6):600-4 (2008).  
 P.Gunvant, R.Darner: Evaluation of corneal thickness measurements obtained using optical coherence tomography and ultrasound technique and determination of specificity in keratoconus screening *Medical Imaging*: 7966: B1-B8

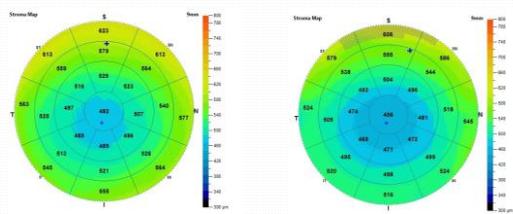
22

## Corneal Thickness Maps



23

## Stromal thickness



24

## Glaucoma Symptom Scale

Have you experienced any of the following problems in the last 4 weeks?  
(Please respond for both the left and right eyes.)

a. Burning, Smarting, Stinging

Left Eye → How bothersome has it been?  
 Yes → Very  
 Somewhat  
 A Little  
 Not at All  
 No

Right Eye → How bothersome has it been?  
 Yes → Very  
 Somewhat  
 A Little  
 Not at All  
 No

b. Tearing  
c. Dryness  
d. Itching  
e. Soreness, Tiredness  
f. Blurry/Dim Vision  
g. Feeling of Something in Your Eye  
h. Hard to See in Daylight  
i. Hard to See in Dark Places  
j. Halos Around Lights

Table 2. Item Level Responses\*

Symptom	No. (%) Reporting Presence of Symptoms		P
	Glaucoma Group	Reference Group	
Tearing	75 (51)	17 (39)	.15
Soreness/Itchedness	73 (50)	14 (32)	.04
Burning/Smarting/Itching	73 (49)	9 (20)	.01
Feeling of something in eye	66 (45)	17 (39)	.48
Itching	48 (33)	14 (32)	.92
Dryness	120 (82)	14 (32)	.01
Hard to see in darkness	100 (70)	10 (41)	.01
Blurry/dim vision	58 (39)	6 (14)	.01
Hard to see in daylight	67 (45)	7 (16)	.01

\*χ<sup>2</sup> Tests were used to compare the distribution of positive values.

Lee B et al. Arch Ophthalmol 1998

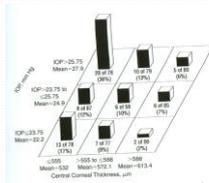
25

## Evaluate the cornea and conjunctiva

- Look at Epithelium
- Pay attention to dry eye and glaucoma –particularly if multiple meds
- Even when patient does not complain they may have sub-clinical dry eyes.
- Extreme dryness changes in stromal thickness
  - Erroneous estimates of risk ??

26

## How to use CCT data in glaucoma management?



- Error in IOP measurements
- Ocular hypertensive patients
  - Thinner cornea at greater risk of developing glaucoma

27

## The Scoring Tool for Assessing Risk (S.T.A.R. II) calculator



**Probability of conversion in 5- years**  
**<5% observe and monitor**  
**5 to 15% consider treatment**  
**>15% treat**

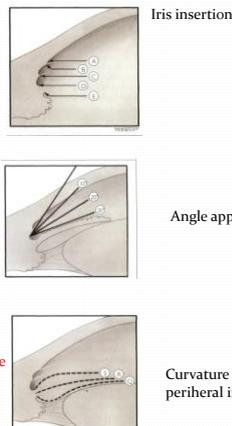
- OHTs and EGPS data
- Intended for use only in untreated OHT patients
- Age (30-80)
- IOP 20-32 mmHg
- CCT 475 to 650 microns
- PSD 0.50 to 3.00 dB
- C/D ratio vertical 0.00 to 0.8

28

## Gonioscopy

A = Above Schwalbe line, totally occluded angle.  
 B = Behind the Schwalbe line, peripheral iris is in contact with TM.  
 C = Scleral spur Iris root at the level of scleral spur  
 D = Deep anterior ciliary body seen.  
 E = extremely deep

Guidelines recommend once a year procedure



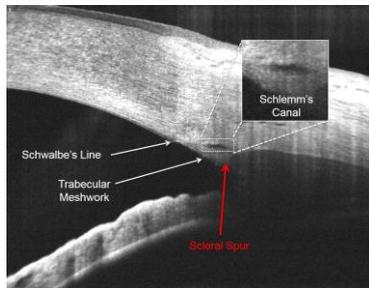
29

## Angle Measurement with Quantification



30

## Anterior segment Angle Analysis



31

## When do I see my patient back?

- Depends multiple visits while diagnosing glaucoma
- Once treatment started depending on treatment
  - PGA 1 month follow-up, Beta Blockers Alpha 2 agonists 2 -weeks to a month.

33

## Maximal tolerated medical therapy

- $\beta$ -Blockers
  - Timolol
  - Betaxolol
  - Levobunolol
  - Carteolol
  - Metipranolol
- Carbonic Anhydrase Inhibitors (CAIs)
  - Systemic:
    - Acetazolamide
    - Methazolamide
  - Topical:
    - Dorzolamide
    - Brinzolamide
- Adrenergic Agonists
  - Nonspecific:
    - Dipivefrin (epinephrine) - also increases conventional outflow
  - $\alpha_2$ -Agonists:
    - Brimonidine - also increases uveoscleral outflow
    - Apraclonidine - also increases uveoscleral outflow
- Conventional/Trabecular
  - Cholinergic agonists (parasympathomimetics):
    - Pilocarpine
    - Echothiophate iodide
    - Carbachol
  - Prostaglandin derivatives:
    - Bimatoprost
    - Latanoprost
  - Nonspecific adrenergic agonists:
    - Dipivefrin (epinephrine)
- Nonconventional/Uveoscleral
  - Prostaglandin derivatives:
    - Latanoprost
    - Bimatoprost
    - Travoprost
  - $\alpha_2$ -Agonists:
    - Brimonidine

35

## Current practice patterns

- Unacceptable high pressures will inevitably destroy optic nerve tissue
- Safe levels of IOP by any means warranted
  - If these don't work or not sufficient
    - drugs like - prostaglandins
    - reduction in inflow - beta blockers
- Maximal medical therapy
- Consider surgery

32

## Once established when do I see my patient?

- Once established need regular follow-up
- IOP check 4 times a year
- Two visual fields twice a year
- OCT twice a year
- Fundus photos twice a year
- Gonioscopy once a year
- Pattern ERG twice a year

34

## Do we really have the luxury to use them all?

- Stage of disease
  - Visual field status
- Stage of nerve damage
  - Rim tissue remaining
- Type of glaucoma
  - POAG - medical first makes sense
  - Secondary glaucoma
  - Congenital glaucoma
  - Complete angle closure

} treated differently
- Adherence, compliance, persistence issues
- Effect of medications and future outcomes of surgery

36

## Target pressure

- A theoretical value below which visual field and ONH appear stable (not deteriorating).
- Calculated from highest recorded IOP.
- Conventionally 20-30% decrease in IOP.
- 40% or more if severe glaucoma

37

## Where should the IOP be?

- No real number
- Start with 30% drop
- Monitor for progression
- Advanced glaucoma you want IOP to be less than 12
- Pressure should not fluctuate much

38

## Medications

- First line drugs- prostaglandin analogs, prostonoid
- Second line: Beta blockers, Alpha 2 agonist, Carbonic anhydrase inhibitor, rock inhibitor
- Combination Rocklatan (PGA+ rock inhibitor)
- Third: Combination with prostaglandin
  - Eg: PGA (Travatan z) and CAI+ Beta blocker (COSOPT)
  - PGA + brinzolamide/brimonidine (Simbrinza)

39

## New drugs

40

## Latanoprostene Bunod- Bausch and Lomb (Vyzulta™)

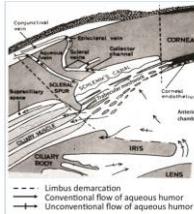
- Latanoprostene bunod (LBN, BOL-303259-X) is a nitric oxide (NO)-donating prostanoid FP receptor agonist

41

## Prostaglandin analog group

42

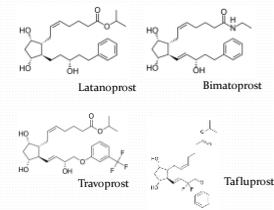
## Aqueous humor dynamics



43

## Various prostaglandin analogs

- Latanoprost (formerly XALATAN 0.005%, Pfizer, New York, NY)
- Travoprost (TRAVATAN Z 0.004%, Alcon, Fort Worth, Tex.)
- Bimatoprost (LUMIGAN 0.03%, Allergan, Irvine, Calif.)
- Tafluprost (ZIOPTAN, Akorn Illinois)



44

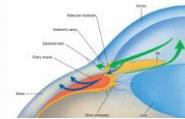
## Prostaglandin analogs (PGs)

- All PGs have similar structure
- They are prodrugs of Prostaglandin  $F_{2\alpha}$
- Converted by corneal enzymes into its active form
- Activates the  $F_{2\alpha}$  prostaglandin receptors on ciliary body

45

## Mechanism of action

- Increases outflow through uveoscleral pathway.
- Small percentage increase in conventional outflow.
- Does not reduce aqueous production



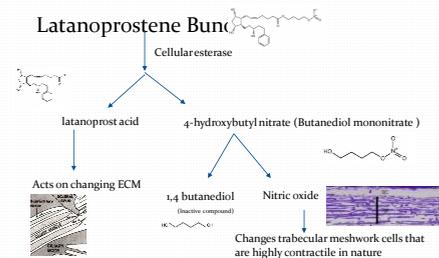
46

## Latanoprostene Bunod- Bausch and Lomb (Vyzulta™)

- Latanoprostene bunod (LBN, BOL-303259-X) is a nitric oxide (NO)-donating prostanoid FP receptor agonist

47

## Mechanism of action



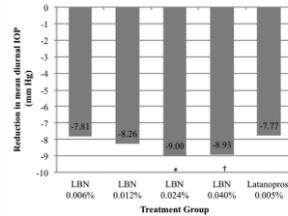
48

# Latanoprostene Bunod FDA and international trials

49

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,<sup>1</sup> Tuyen Ong,<sup>2</sup> Baldo Scassellati Sforzolini,<sup>2</sup> Jason L Vittitow,<sup>2</sup> Kuldev Singh,<sup>3</sup> Paul L Kaufman,<sup>4</sup> for the VOYAGER study group

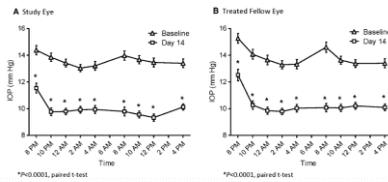


50

Adv Ther (2015) 32:1128–1139  
DOI 10.1007/s12325-015-0260-y  
ORIGINAL RESEARCH

## Evaluation of the Effect of Latanoprostene Bunod Ophthalmic Solution, 0.024% in Lowering Intraocular Pressure over 24 h in Healthy Japanese Subjects

Makoto Araki · Baldo Scassellati Sforzolini · Jason Vittitow · Robert N. Weinreb  
KRONUS study



51

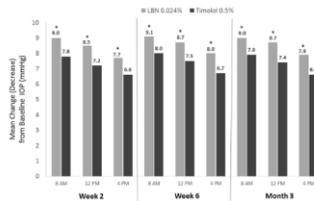
## Latanoprostene Bunod 0.024% versus Timolol Maleate 0.5% in Subjects with Open-Angle Glaucoma or Ocular Hypertension

The APOLLO Study

Robert N. Weinreb, MD,<sup>1</sup> Baldo Scassellati Sforzolini, PhD,<sup>2</sup> Jason Vittitow, PhD,<sup>2</sup> Jeffrey Liebmann, MD<sup>3</sup>

Sample size 420 (387 completed)  
Timolol Maleate 0.5% or Latanoprostene Bunod 0.024%  
IOP measured at 8 AM, 12 noon and 4 PM at week 2, 6, and 3 months

52



53

## Summary findings of Latanoprostene Bunod (LBN)

- LBN Statistically superior IOP lowering vs. Latanoprost (> 1 mmHg) in a Phase II study
- LBN Statistically superior IOP lowering vs. Timolol in 17/18 time points in two Phase III studies
- LBN marked and sustained (24h) IOP lowering in healthy normotensive subjects
- LBN No significant AEs (average 5-7% hyperemia rates across all studies)
- LBN Nocturnal IOP significantly lower than baseline and significantly lower than timolol maleate

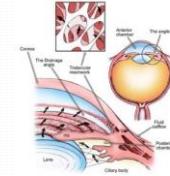
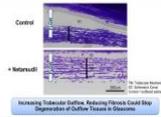
54

# Rhokinase inhibitors

55

## Mechanism of action

- Changes to trabecular meshwork-cytoskeletal modulating drugs



56

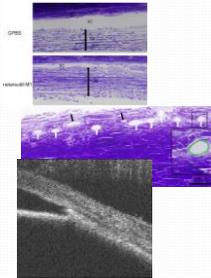
## Ripasudil (K-115)

- Approved in Japan-2014
- Works on TM
- IOP lowering via changes TM
- Not approved in USA – studies far away.

57

## Netarsudil (AERI pharma) Rhopressa™

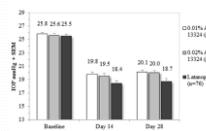
- Another class of ROCK-inhibitor Small-molecule
- Alter TM cells
- Alters norepinephrine transporter (NET)-
  - NET inhibitor to lower aqueous production
- Changes episcleral venous pressure



58

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

Jason Bachrach, MD,<sup>1</sup> Harvey B. Dubsler, MD,<sup>2</sup> Brian Levy, OD, MS,<sup>2</sup> Casey C. Kocopoulos, PhD,<sup>2</sup> Gary D. Novack, PhD,<sup>2</sup> for the AR-13324-CSJ02 Study Group\*

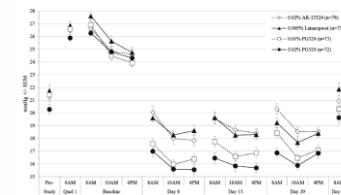


Ophthalmology 2015;122:302-307

- Diff-IOP approx. 1 mmHg
- Conjunctival hyperemia- 52-57%
- Increased lacrimation 5-7%
- Conjunctival hemorrhages 5-6%

59

### Fixed-dose combination of AR-13324 and latanoprost: a double-masked, 28-day, randomised, controlled study in patients with open-angle glaucoma or ocular hypertension



Lewis RA, et al. Br J Ophthalmol 2016;100:339-344.

60

## Summary

- Rhokinase inhibitors are a new class of drug .
- Rhopressa- shows promise as second line drug to PGA
- Roclatan- Shows IOP lowering effect better than Latanoprost and Rhopressa.
- Side effects conjunctival hyperemia
- Cornea issues- Erosions, changes in endothelium and cornea verticillata

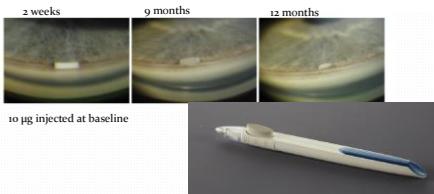
61

## Sustained release

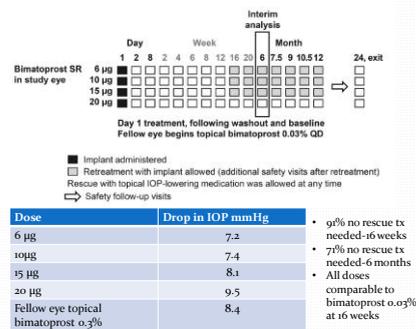
62

### Bimatoprost Sustained-Release Implants for Glaucoma Therapy: 6-Month Results From a Phase I/II Clinical Trial

RICHARD A. LEWIS, WILLIAM C. CHRISTIE, DOUGLAS G. DAY, E. RANDY CRAVEN, THOMAS WALTERS, MARINA BEJANIAN, SUSAN S. LEE, MARGOT L. GOODKIN, JANE ZHANG, SCOTT M. WHITCUP, AND MICHAEL R. ROBINSON, FOR THE BIMATOPROST SR STUDY GROUP



63



64

## Selective laser trabeculopalsty

## SLT and glaucoma

- Great first or second line option.
- Non-compliant individuals
- Individuals that fluctuation of IOP is a concern
- In theory can be repeated to lower IOP.
- Is the IOP lowering the same second attempt?

65

66

## RESEARCH ARTICLE

Open Access

## Repeatability of selective laser trabeculoplasty for open-angle glaucoma

Brian A. Francis<sup>1</sup>\*, Nils Loewen<sup>2</sup>, Bryan Hong<sup>3</sup>, Laurie Dustin<sup>4</sup>, Kevin Kaplowitz<sup>5</sup>, Robert Kinard<sup>6</sup>, Jason Bacharach<sup>7</sup>, Sunita Radhakrishnan<sup>1</sup>, Andrew Iwach<sup>7</sup>, Lidvke Rudavski<sup>8</sup>, Panul Kichipuni<sup>9</sup> and L. Jay Katz<sup>9</sup>

- Inclusion criteria prior SLT with diminution of response over time
- N=137

Table 2 \*Significance of within treatment change,  $p < 0.001$ . IOP, intraocular pressure; SLT, selective laser trabeculoplasty

	SLT Mean (standard deviation)	SLT Mean (standard deviation)	Significance $p$ -value
IOP			
Baseline (n=137)	20.3 (5.2)	19.4 (5.0)	0.03
6-12 months (n=135/119)	16.3 (4.3)	16.3 (4.8)	0.86
13-15 months (n=102/99)	16.4 (3.9)	16.7 (4.7)	0.24

Francis et al. BMC Ophthalmology (2015) 15:128  
DOI 10.1186/s12886-015-0299-9

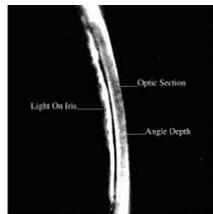
67

## Narrow angles, angle closure and elevated pressure

68

## Narrow angles

- Grade 1 Van Herrick
- 1: <1/4 – Angle closure likely, VH grade 1
- 180 degrees no structure visible
- Perform indentation gonioscopy
- Laser PI



69

## Elevated pressure

- Angle closure or
- No angle closure but marked elevated pressure

70

## In office Treatment of elevated IOP

- Alpha -2 agonist- Brimonidine
- Beta blocker- Timolol (caution in asthmatics ) or Betaxolol
- Carbonic anhydrase inhibitor – Dorzolamide (Caution sulpha allergy contraindication)
- Each medication given every 15 minutes
- Perform 3 times

71

## Oral medications

- Oral Carbonic anhydrase inhibitor
- Two tablets of 250 mg acetazolamide (Caution sulpha allergies contraindication)
- Works good when patient can retain medication – Vomiting common with angle closure glaucoma

72

- Check intraocular pressure after 1 hour if lower than 40
- If angle closure Add Pilocarpine every 15 minutes for 45 minutes and repeat procedure ABC procedure
- If not no pilo. Just repeat ABC
- Seek ophthalmologist opinion-refer patient

73

## Summary

- OCT is a must in clinics that would like to manage any chronic diseases
- Particularly when monitoring change overtime
- Good quality data is a must in getting the best clinical outcome

75

## Summary

- Early detection is getting within reach.
- Functional measures and structural measures are improving rapidly.
- Next step....reverse glaucomatous damage

77

## Take home medication

- Prednisolone acetate 1% q1-6 hours (approx every 3 hours)
- Acetazolamide 500 mg sequel BID
- Alpha agonist or beta blocker BID
- Pilocarpine 2% QID

74

## Summary

- We are living in exciting times
- OCT is aiding in overall basic understanding of disease
- New drugs with new MOA
- Combination drugs that lower IOP 8-9 mmHg
- Sustained release, Lasers and Stents make IOP dynamics more stable with less fluctuations

76