

#### **Disclosures**

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



#### **Definitions**

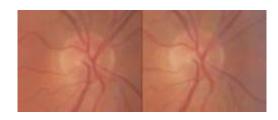
- "Ocular tissue damage at least partially related to intraocular pressure"
- A chronic, bilateral, often asymmetrical disease in adults, featuring acquired loss of optic nerve fibers and abnormality of visual field with an open anterior chamber angle.

#### 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

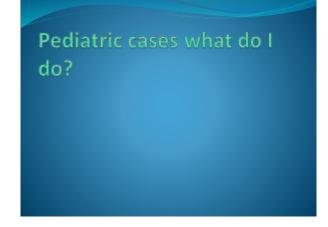
#### Gold standard

- Simultaneous stereo photography!
  - Problems?



#### Glaucoma evaluation

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

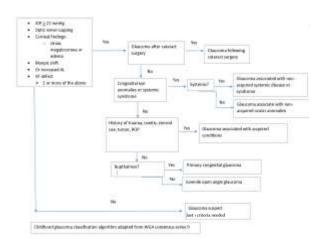


## Definitions of glaucoma- two or more required

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

### 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 dimeter or axial length in normal IOP



#### 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	

\* Person S. Da Prizzo S. Persoutt A. Tetranou e presson in chidnes. J. Fedior Contralnol Stratomor 1992;29:79



# Early detection fields • Magno cellular testing- Like pulsar testing

#### 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-onwhite perimetry

#### Learning curve in visual fields

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

Patient has cataract what do I do with Visual fields?

# Effect of Cataract Opacity Type and Glaucoma Severity on Visual Field Index Her Jin Charge, Jeong Hoon Charl, Young-Chun Loe<sup>2</sup>, and Su-Young Kim<sup>3</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

construction and also was 40, 40 to 5, 57 years constructed as a value statement Consider to 6 on an absolute figures p

#### Cataract in glaucoma patient

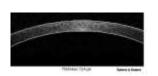
- Dilate as much as possible
- Depend on PSD plot more than total deviation
- Use imaging modalities more.

#### Sources of error

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

#### Anterior segment OCT







## Difference between optical and ultrasound pachymetry measurments

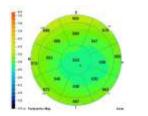
Author	Difference in OCT and ultrasound values
Kim et al AJO 2008	26 microns
Wang et al J Refract Surg 2008	38 microns
Gunvant & Darner Medical Imaging 2011	13 microns

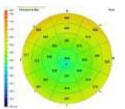
Kim, H.Y., Budenz, D.L., Lee P.S, et al., "Comparison of central corneal thickness using anterior segment optical coherence tonography viultrasonic pachymetry, Am J Ophthalmol., 145:228-232 (2008).

Wang, J.C., Bunce, C., and Lee, H.M., Thraoperative corneal thickness measurement using optical coherence pachymetry and corneo-gai plus ultrasound pachymetry. J Refract Surg. 24(6):610-4 (2008)

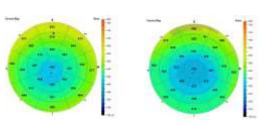
P Gunvant, R Darmer: Evaluation of corneal thickness measurements obtained using optical coherence tomography and ultrasound technique and determination of specificity in keratoconus screening Medical Imaging: 70661 B1-B8

#### **Corneal Thickness Maps**





#### Stromal thickness



#### Glaucoma Symptom Scale



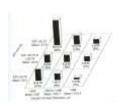
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Spenerachiedness	15 (50)	13 (33)	.01
Sunningsone bright inging	17/55	34 (00)	38
leating of committing the year	73 (44)	3.000	20
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fact to our or stylight	7573485	TOW.	31

Lee B et al. Arch Ophthalmol 1998

## 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 ??

## How to use CCT data in glaucoma management?



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

## 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 o.oo to o.8

#### Gonioscopy



Iris insertion

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

C = Scleral spur Iris root at the level of scleral spur D = Deep anterior ciliary body seen.

seen. E = extremely deep

Guidelines recommend once a year procedure



Angle approach

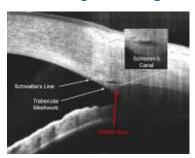


Curvature of periheral iris

## Angle Measurement with Quantification



#### **Anterior segment Angle Analysis**



#### 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

#### 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 2 -weeks to a month.

### 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

#### Maximal tolerated medical therapy

- ## Blackers

  Timolol
  Betaxolol
  Levobunolol
  Levobunolol
  Metipranolol
  Systemic
  Systemic
  Forical:
  Dornolamide
  Brincolamide
  Brincolamide
  Brincolamide
  Adrenorgie Agonists
  Norweweiff:
- Conventional/Trabecular
  Cholinergic agonists (parasymphathomimetics):
  Pilocarpine
  Echothisphate iolide
  Carbachol
  Prostaglandin derivatives:
- Nonspecific adrenergic agonists:
  Dipivefrin (epinephrine)
- Nonconventional/Uveosclera Prostoglandin derivatives: • Latanoprost
- Latanoprost
   Bimatoprost
   Travoprost
- scific: pivefrin (epinephrine) – also increases conventional title
- Brimonidine also increases uveoscleral outflow
   Approchaiding also increases uveoscleral outflow

### 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
- treated differently
- Complete angle closure
- Adherence, compliance, persistence issues
- Effect of medications and future outcomes of surgery

#### 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

#### 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

#### Medications

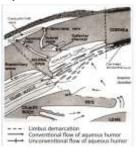
- First line drugs- prostaglandin analogs, prostonoid
- Second line: Beta blockers, Alpha 2 agonist, Carbonic anhydrase inhibitor, rock inhibitor
- Combination Rocklatan (PGA+ rock inhibitor)
- Third: Combination with prostaglandin
  - Eg: PGA (Travatan z) and CAI+ Beta blocker (COSOPT)
  - PGA + brinzolamide/brimonidine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

#### New drugs

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

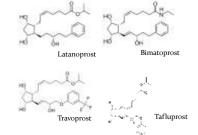
 Latanoprostene bunod (LBN, BOL-303259-X) is a nitric oxide (NO)-donating prostanoid FP receptor agonist Prostaglandin analog group

#### Aqueous humor dynamics



#### 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)

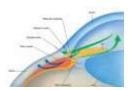


#### Prostaglandin analogs (PGs)

- 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

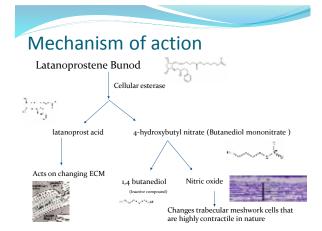
#### Mechanism of action

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



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

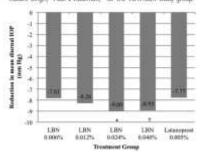
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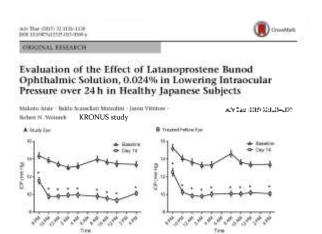


## Latanoprostene Bunod FDA and international trials

A randomised, componed 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> Jasun L Vittitow, <sup>2</sup> Kuldini Singh, <sup>3</sup> Paul 1 Kaufman, <sup>a</sup> for the VOYAGER study group





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

The APOLLO Study

Robert N. Weinels, MD, Baldo Scassolian Storador, PhD, Laon Vintou, PhD, Leftrey Liebeners, MD

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

# Week 2 Street 4 Months 2 Month

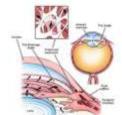
#### Summary findings of Latanoprostene Bunod (LBN)

- 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



# Mechanism of action • Changes to trabecular meshwork-cytoskeletal modulating drugs

## Tomas Comments of the Comments



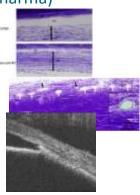
#### Ripasudil (K-115

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

#### Netarsudil (AERI pharma)

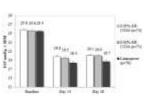
#### Rhopressa™

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



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

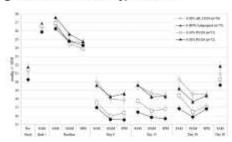
Jaux Burluruck, MD.; Harney B. Dobner, MD.; Brian Lens, OD, MS, \*Cates C. Kotegoulii, PhD.; Gary D. Nimack, PhD.; Far die AR-13324-CS202 Study Group\*



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

Ophthalmology 2015;122:302-307

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



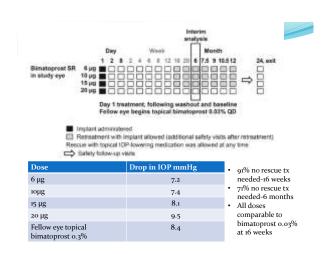
Lewis SA, et al. St / Quodratical 2016; 100 339-341.

#### **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



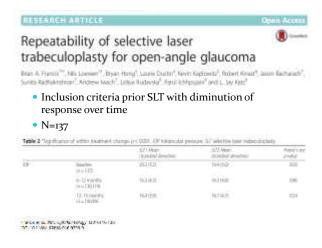




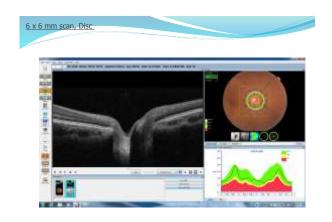


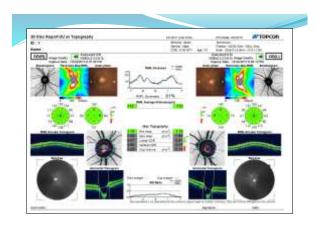
#### SLT and glaucoma

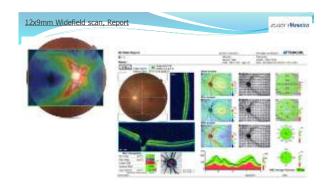
- Great first or second line option.
- Non-compliant individuals
- Individuals that fluctuation of IOP is a concern
- In theory can be repeated to lower IOP.
- Is the IOP lowering the same second attempt?

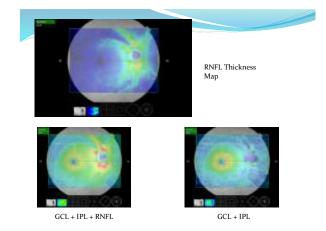


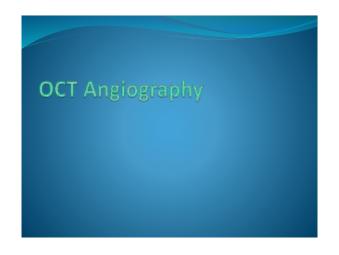




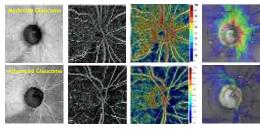




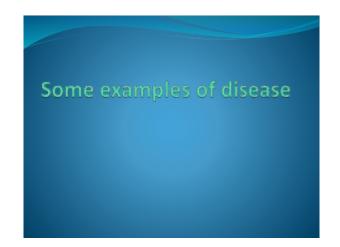


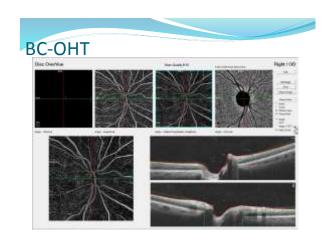


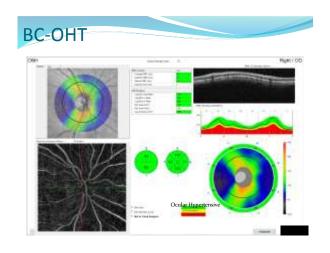
#### Disc Overview Report Brings New Information to Glaucoma Management

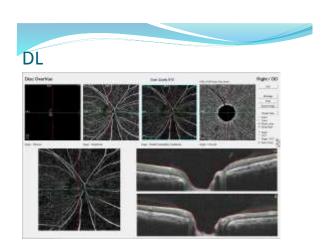


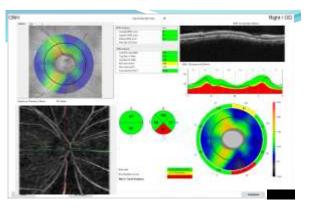


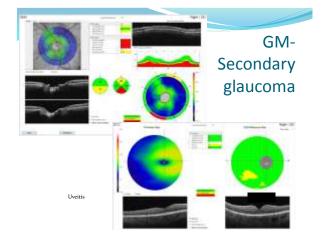




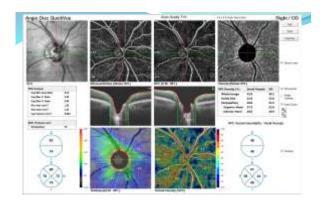


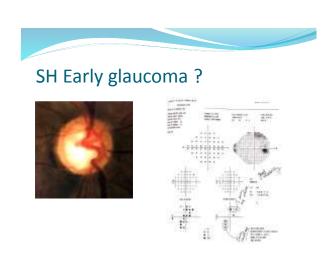


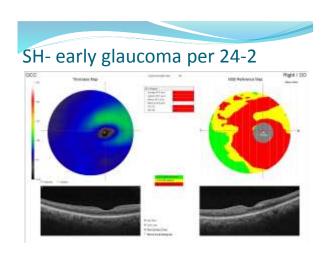


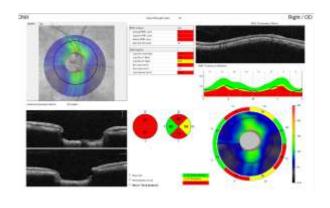


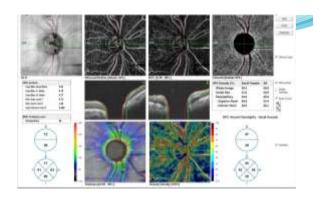












Does vessel density reduction occur first, or does it follow other damage?

#### Cause or effect?

• Not sure ... evidence building up in favor of

Conclusions: Peripapillary and parafoveal vascular changes precede functional decline. The extent of VD reduction and RNFL thinning varies in different peripapillary sectors and longitudinal studies are required to better understand the temporal relationship of vascular and RNFL loss.

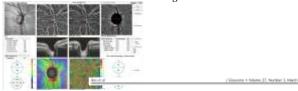
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Souranc + Holone 27, Humber 6, June 20

Structure and Function correlation

#### What does RPC correlate best with?

- Visual fields?
- Retinal Nerve fiber layer?
- Inferior RPC probably the best correlation
- Correlation not strong
- Take home- We are looking at a new Biomarker



Changes with intraocular pressure

#### IOP can alter blood flow but...

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(1881) Marines MET per Moles II, 46 (4-1) 1984 I Casserra "Moles III, Harrior S. April 1998

E-10 (FE) (FE) (FE) (FE)

/ Channel - Polices St. Plantier S, January 2017

Valsalva Maneuver and Peripapillary OCT Angiography Vessel Density

) Chancers • Palama D. Phanton P. John D. H.

- Small IOP fluctuations no effect
- Holding your breath during measurements no effect
- Large IOP reductions
  - · Treatment efficacy
  - Neuroprotection?

Early glaucoma changes

#### RPC bed and early glaucoma

- The density of RPC bed is declined in early glaucoma
- The RNFL and GCC may also show changes in early glaucoma.
- Questions remains if one may actually be always earlier than other...?
  - Possibly not given glaucoma is such a heterogenous disease!

So how and what do I use from OCT angiography data?

#### Lots of information

- OCT angiography provides a wealth of structure and function information
  - Radial Peripapillary Capillaries
  - Macular region capillaries network
  - Montage
  - GCC, RNFL, ONH, SLO image, Vitreous and choroid
  - Progression

Narrow angles, angle closure and elevated pressure

#### 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



#### Elevated pressure

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

#### 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

#### **Oral medications**

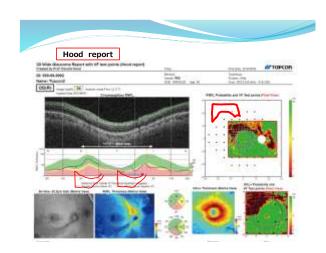
- Oral Carbonic anhydrase inhibitor
- Two tablets of 250 mg acetozolamide (Caution sulpha allergies contraindication)
- Works good when patient can retain medication -Vomiting common with angle closure glaucoma

- 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

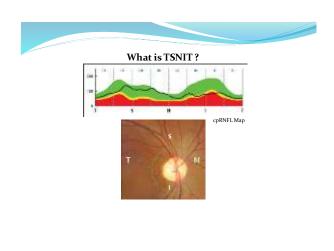
#### Take home medication

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

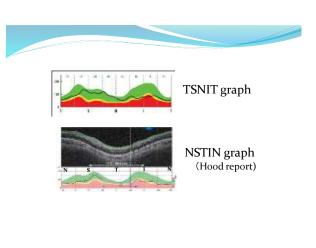


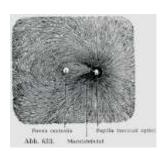






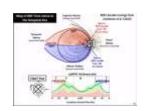
Why change from TSNIT to NSTIN ?

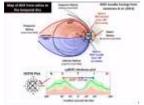




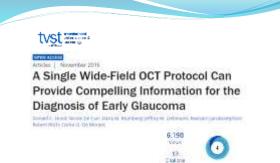
Rauber Konsch Banda, Abb-633

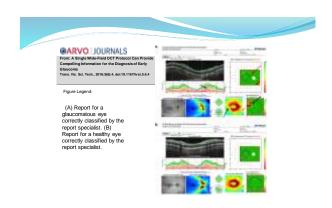
#### **TSNIT Versus NSTIN**





Slide from Dr. Hood AAO 2016 booth seminar

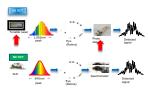




What is Swept Source OCT?



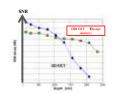


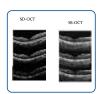


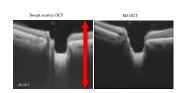




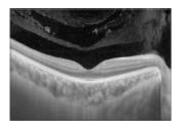
Signal to noise roll-off characteristics in tissue



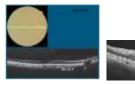


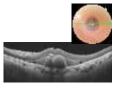


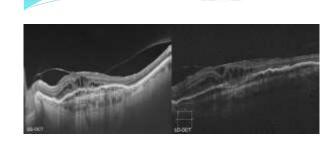


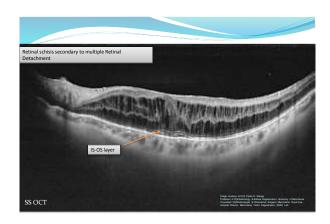












#### **Summary**

- 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

#### **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

#### **Summary**

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