# ManaMa

## Dec 3, 2022

2022 Master after Master Course organized by
Collegium Ophthalmologicum Belgica

# HANDBOOK
# Glaucoma

**December 3,2022 - 09:00 - 15:30**

*Uliège - Auditorium Roskam*
*Avenue de l'hôpital 1, 4000 Liège*

# Open angle glaucoma: IOP and non IOP related risk factors

Manama, Dec 3.2022

Dr Sophie Marchand, CITADELLE Liège

Citadelle Hopital

# Plan

Definition

IOP: definition and tonometry

Population based studies

IOP related risk factors: - HIGH IOP: - conversion, onset and progression (EMGT)
- conversion (OHTS)
- LOW IOP (CNTGS )
- corticoresponders

Non IOP related risk factors: - older age
- family history
- non white ethnicity
- disc haemorrhage
- myopia

# Definition

- POAG is a chronic, progressive, potentially blinding irreversible eye disease causing optic nerve rim and retinal nerve fibre layers ( RNFL) loss with related visuel field defects.
- Angle appearance is normal and **MAJOR RISKS FACTORS include the level of IOP and older age.**
- Visual disability is usually prevented by early diagnosis and treatment.

# IOP: definition

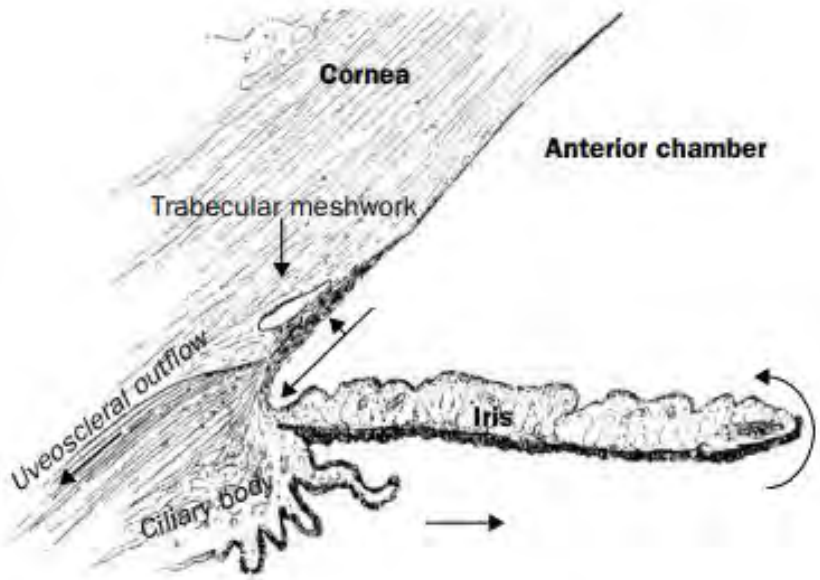
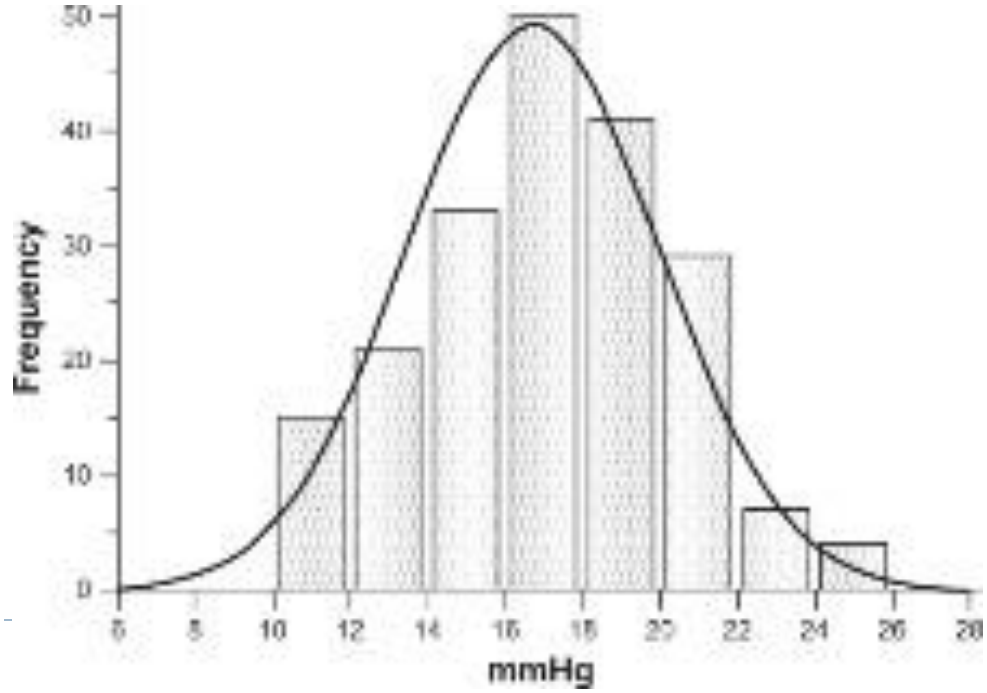
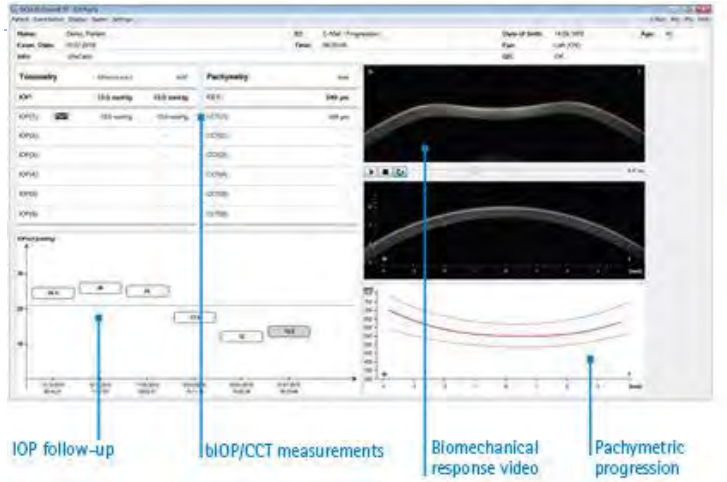


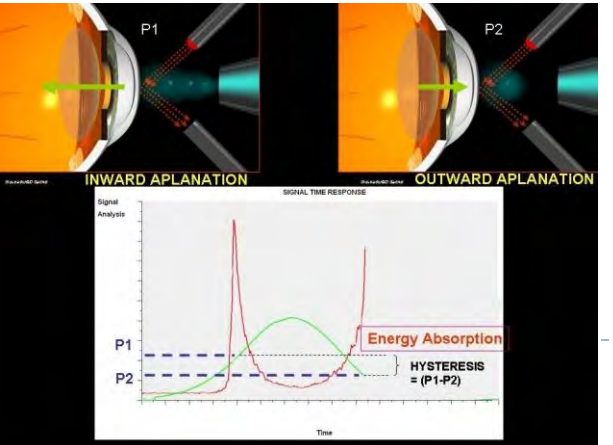

Figure 1: **Physiology of aqueous humour**
Intraocular pressure is determined by the balance between secretion and drainage of aqueous humour. Arrows show direction of flow; aqueous humour is secreted by the ciliary body into the posterior chamber, passes posterior to the iris and through the pupil into the anterior chamber, and exits through the trabecular meshwork or uveoscleral outflow pathways.

Primary Open-Angle Glaucoma, Weinreb, Khaw, LANCET 2004

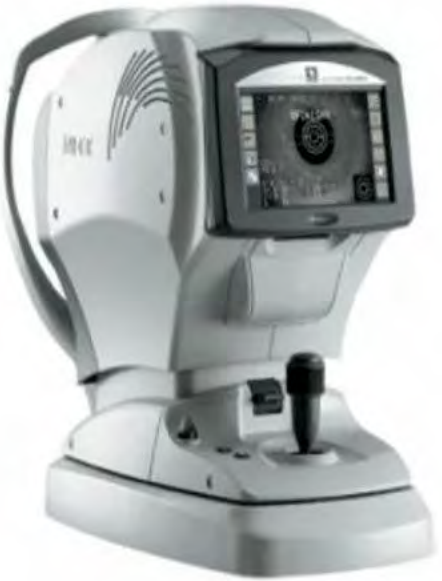


# IOP: tonometers






**1)** CCT-adjusted IOP algorithms.
IOP correction algorithms based on CCT are not validated and should be avoided.

**2)** Short-wavelength automated perimetry (SWAP) for glaucoma.
There is no evidence of better performance of swap and it has no role in current clinical practice.

**3)** Glaucoma diagnosis and progression based only on OCT.
OCT on its own does not provide a clinical diagnosis of glaucoma, just a statistical deviation from a reference database.
One should not rely on OCT only to diagnose progression.

**4)** Cup to disc ratio (CDR) for diagnosis of glaucoma or to detect progression.
Due to the large differences in size and shape of optic discs CDR cannot be used to diagnose glaucoma. In addition, the assessment of CDR, even by experts, has high variability and is not useful to detect progression.

**5)** Anterior chamber angle imaging to replace gonioscopy.
The accuracy of anterior segment imaging to diagnose angle closure is suboptimal.

**6)** Routine genetic testing and direct to consumer genetic genotyping.
Do not offer genotyping routinely to glaucoma patients.
Genetic information obtained with online home testing kits may be unreliable and should not be used to guide diagnosis or treatment.

# Population-based studies on glaucoma

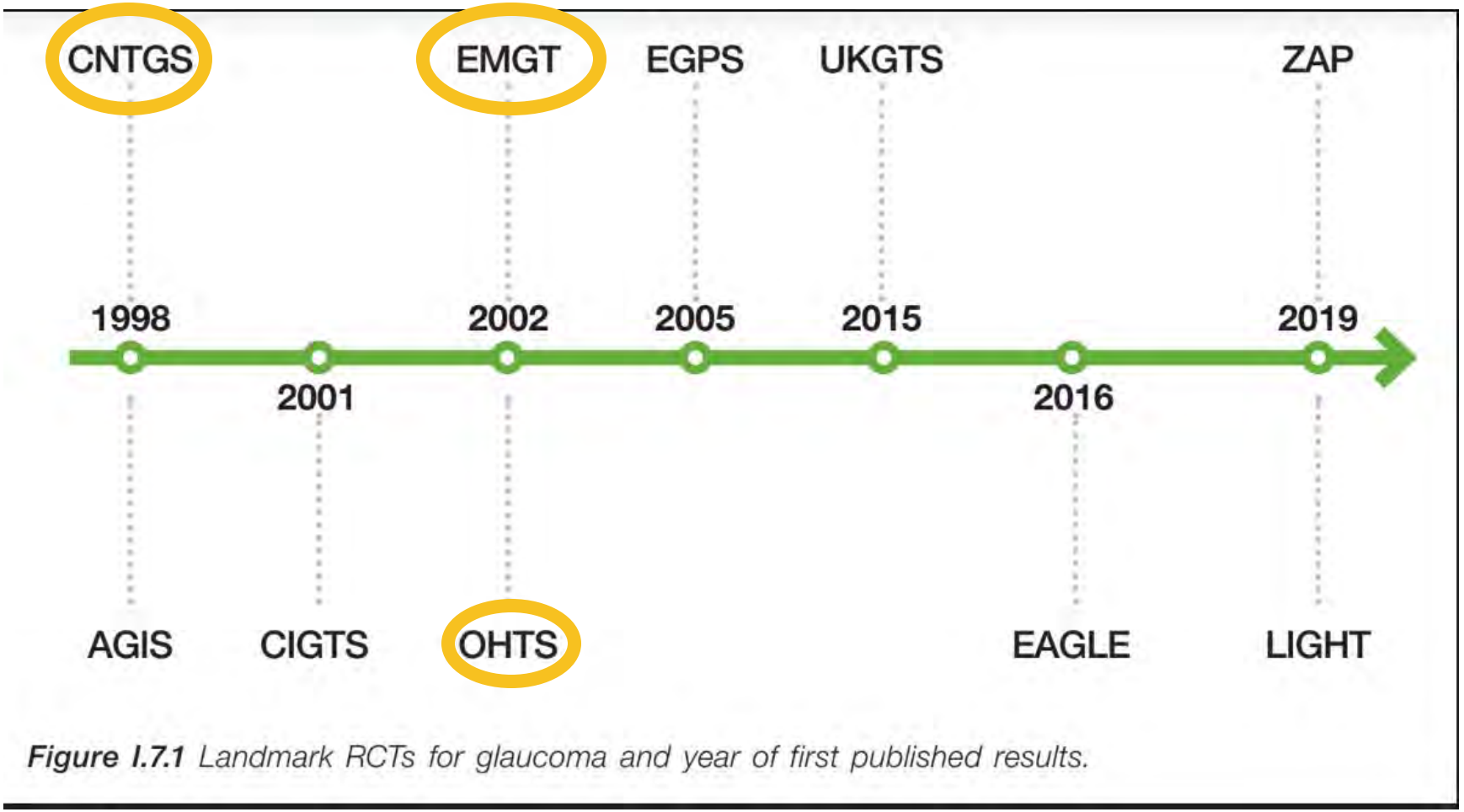



***Figure I.7.1*** *Landmark RCTs for glaucoma and year of first published results.*

# 3,5% OAG in 40-80 years old
# 76 millions in 2020
# 112 millions in 2040

**Global prevalence** of **glaucoma** and **projections** of **glaucoma** burden through 2040: a systematic review and meta-analysis.

Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY.

Ophthalmology. 2014 Nov;121(11):2081-90. doi: 10.1016/j.ophtha.2014.05.013. Epub 2014 Jun 26.

**Global data** on **visual impairment** in the year 2002.

Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, Mariotti SP.

Bull World Health Organ. 2004 Nov;82(11):844-51. Epub 2004 Dec 14.

## Brief Overview of Guidelines from Glaucoma Clinical Trials

### Ocular Hypertension Study: Risk factors for development of POAG

1. Older age
2. Higher IOP
3. Greater pattern standard deviation
4. Thinner central corneal thickness
5. Larger vertical cup-disc ratio

### Collaborative Normal Tension Glaucoma Study: Risk factors for progression

1. Female gender
2. Recurrent disc hemorrhages
3. History of migraines

### Early Manifest Glaucoma Treatment Trial: Risk factors for progression

1. Higher IOP
2. Exfoliation
3. Older age
4. Bilateral disease
5. Worse mean deviation on VF
6. Recurrent disc hemorrhages

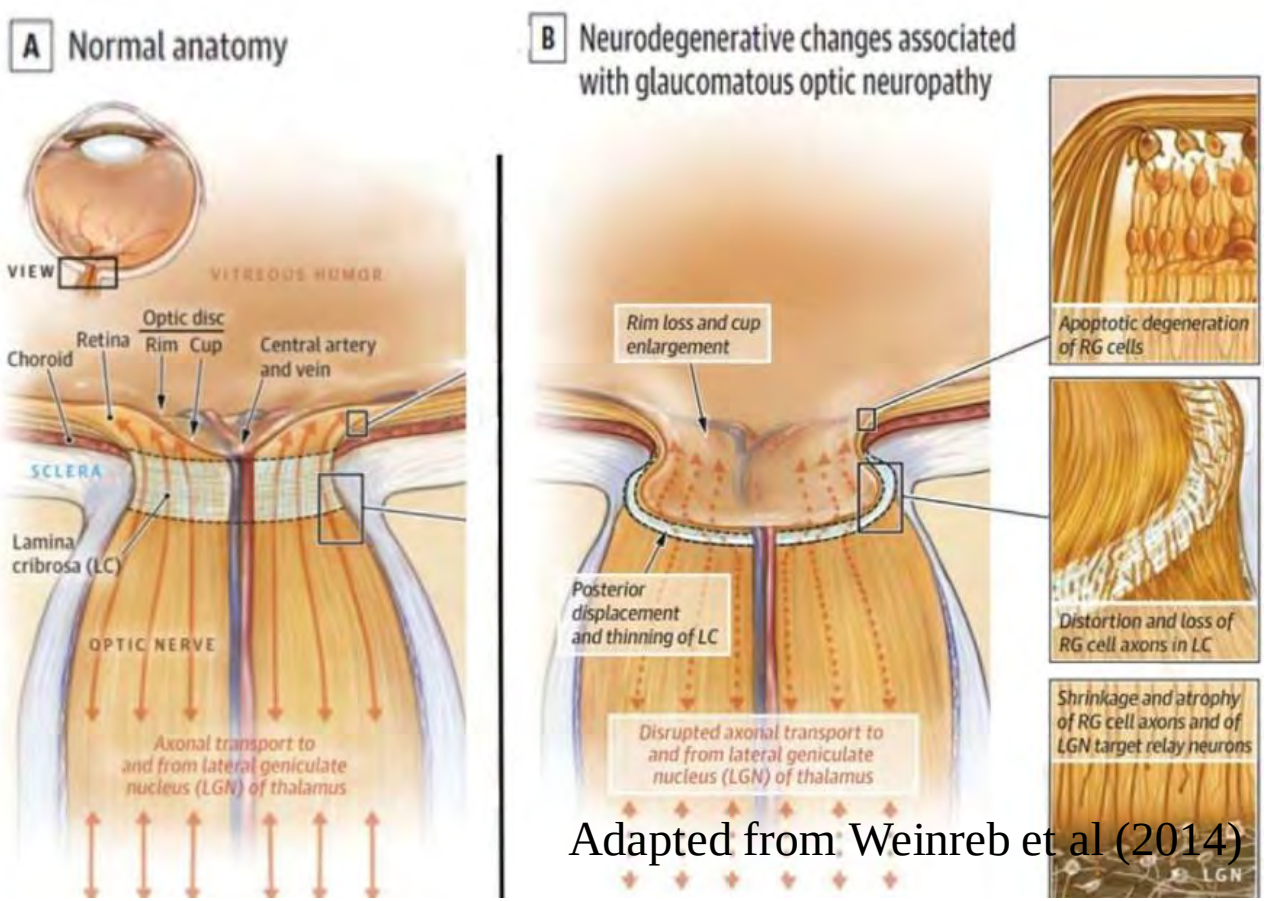
**IOP risk factors:**

- Higher level of IOP

**NON IOP risk factors:**

- Older age
- Myopia
- Family history of glaucoma
- Race
- Disc haemorrhages
- Thinner CCT
- PEX
- Genetic -

- HIGH LEVEL of IOP:
  CONVERSION, ONSET and PROGRESSION




Adapted from Weinreb et al (2014)

## IOP related risk factors

EMGT:

316 eyes from Sweden population early and previously untreated OAG

Treatment (SLT and Betaxolol) VS no treatment

Prospective 1993-97 until 2013

Primary outcome: progression of disease

# CONVERSION: OHT → OAG

- Thinner CCT
- Higher IOP
- Disc haemorrhages
- Older age
- Larger vertical and horizontal CDR
- Greater VF PSD

- *RISK CALCULATOR:*

*https://ohts.wustl.edu/risk/calculator.htm*

## IOP related risk factors

OHTS:

1636 patients

Treatment OR not

IOP <24mmHG (20% from baseline)

→ Development of primary open angle glaucoma

## POINT SYSTEM FOR ESTIMATING 5-YEAR RISK OF DEVELOPING POAG

**The estimated risk displayed below is a projection of the patient's likelihood of developing early glaucoma in at least one eye within 5 years, based on the information entered, and using the Point System developed by the OHTS-EGPS Collaboration and published in Ophthalmology: (in press).**

| FACTORS | Points for Factors | | | | |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| **Age (years)** | ☑ <45 | ☐ 45 to < 55 | ☐ 55 to <65 | ☐ 65 to <75 | ☐ ≥75 |
| **Intraocular Pressure (mm Hg) Mean** (3 measurements per eye and average of 2 eyes) | ☐ <22 | ☐ 22 to <24 | ☐ 24 to <26 | ☑ 26 to <28 | ☐ ≥28 |
| **Central Corneal Thickness (μ) Mean** (3 measurements per eye and average of 2 eyes) | ☐ ≥ 600 | ☐ 576-600 | ☑ 551-575 | ☐ 526-550 | ☐ ≤525 |
| **Vertical Cup/Disc Ratio by Contour Mean** (1 measurement per eye and average of 2 eyes) | ☐ <0.3 | ☐ 0.3 to <0.4 | ☐ 0.4 to <0.5 | ☑ 0.5 to <0.6 | ☐ ≥0.6 |
| **Visual Field: Humphrey Pattern Standard Deviation (dB) Mean** (2 measurements per eye and average of 2 eyes) | ☐ <1.8 | ☐ 1.8 to <2.0 | ☐ 2 to <2.4 | ☑ 2.4 to <2.8 | ☐ ≥2.8 |
| **- OR - Octopus Loss Variance Mean** (2 measurements per eye and average of 2 eyes) | ☐ < 3.24 | ☐ 3.24<4.0 | ☐ 4.0<5.76 | ☐ 5.78<7.84 | ☐ ≥7.84 |
| **Sum of Points and Estimated 5-Year Risk of Developing POAG** | | | | | |
| **Sum of Points** | 0-6 | 7-8 | 9-10 | 11-12 | >12 |
| **Estimated 5-Year Risk of Developing POAG** | ≤4.0% | 10% | 15% | 20% | ≥33% |

Total Points: 11 Estimated Risk: 20% The patient's estimated 5-year risk (%) of developing early glaucoma in at least one eye.

Print Reset

Interpretation:

| OHTS Score | 5 year risk of developing POAG | Risk - Recommendation |
|---|---|---|
| 0-6 | ≤4.0% | Low - Recommend observation every 6 months |
| 7-8 | 10% | Intermediate - Recommend counseling on risks/benefits of treatment versus close observation |
| 9-10 | 15% | |
| 11-12 | 20% | |
| >12 | ≥33% | High - Recommend initiating treatment |

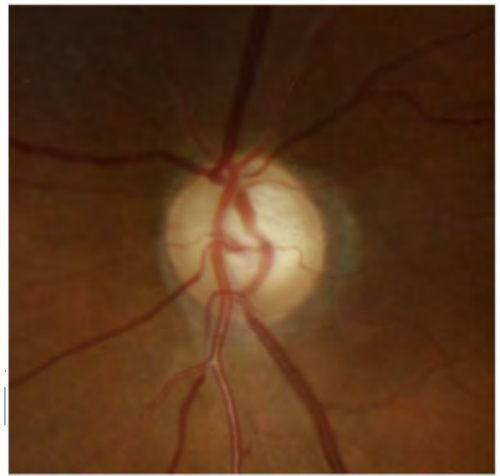
# And NTG?

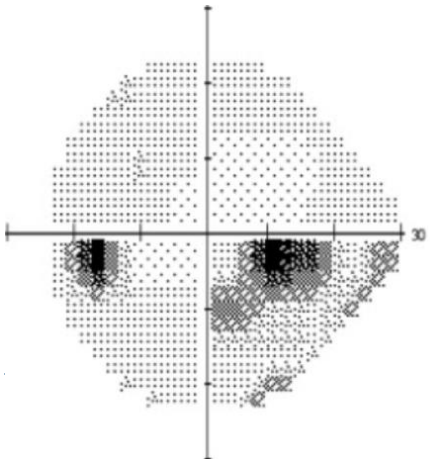
Rate of progression of untreated NTG highly variable (mean -0.41 dB/y)

Half did not progress on VF in 5 years

Factors associated with progression:

- female
- migraine
- disc haemorrhage on presentation





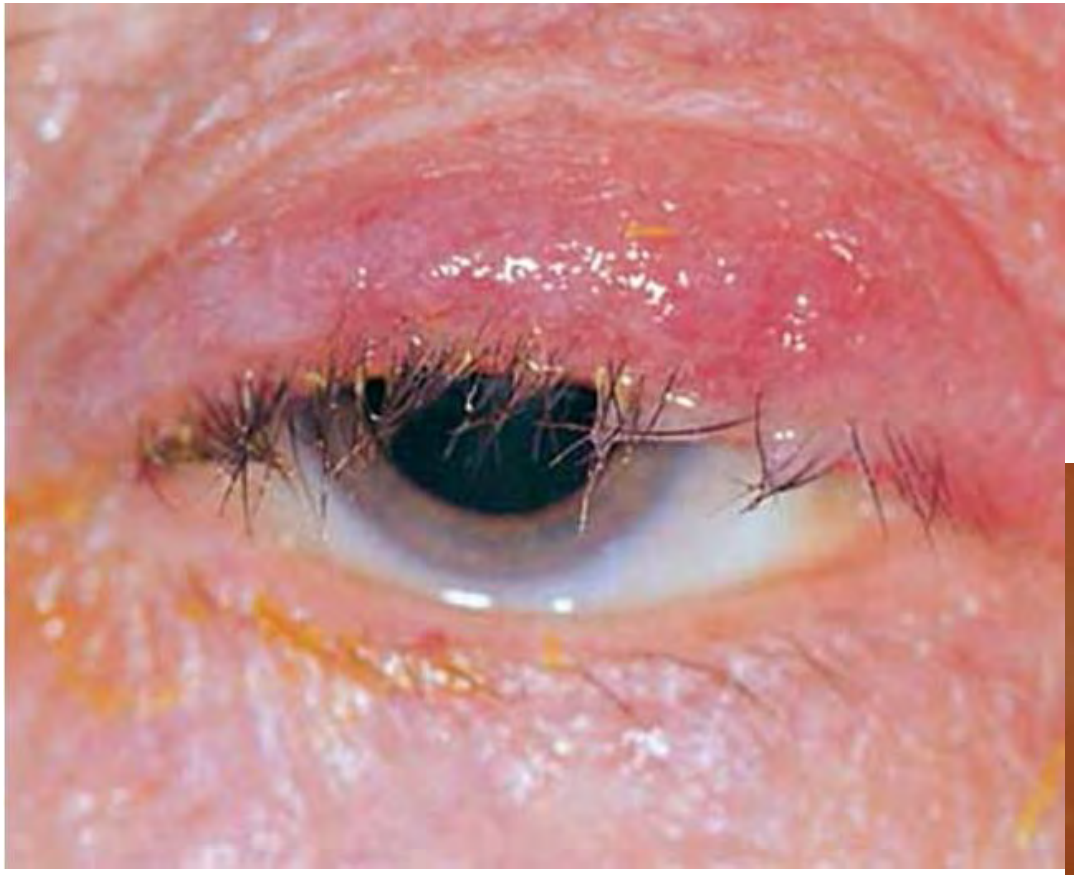
## IOP related risk factors

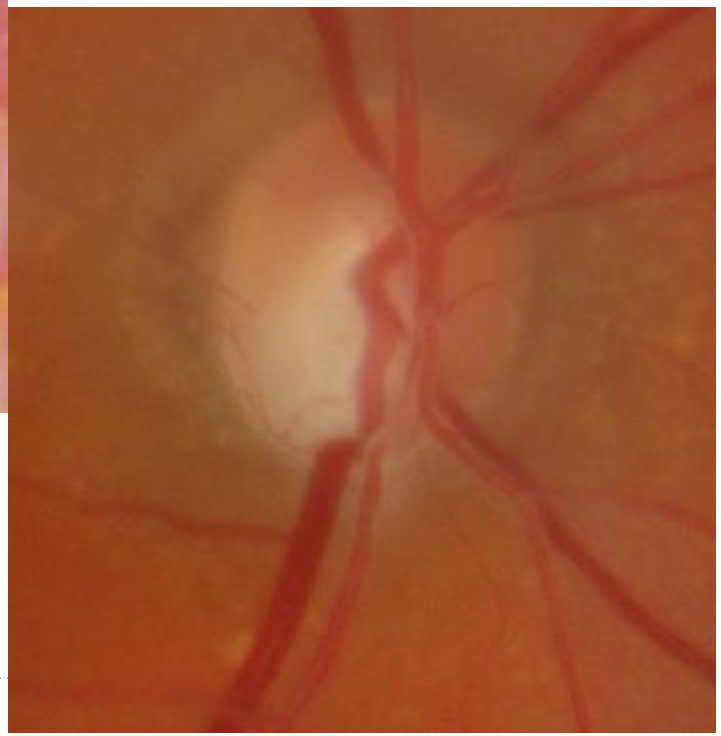
CNTGS:

- 230 patients with verified loss of visual field progression
- Treatment vs NO treatment
- 30% IOP reduction in 50%
- Progression in 12% treated and 35% not treated.

## IOP related risk factors

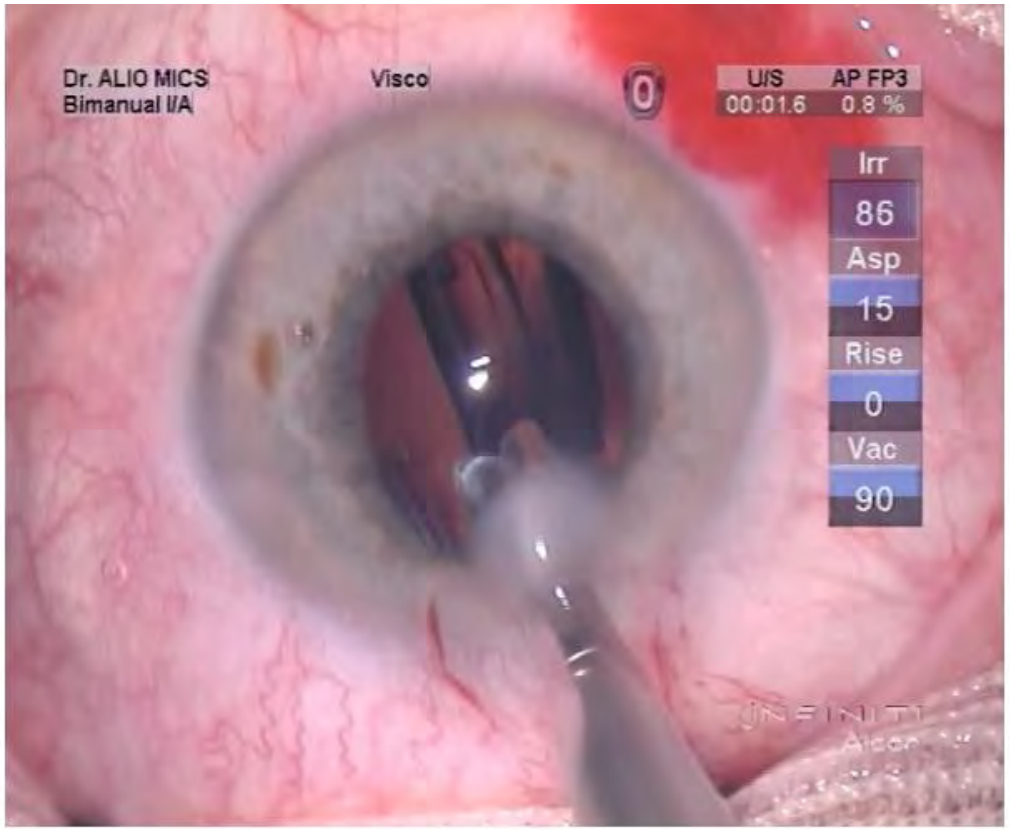
- CORTICORESPONDERS !!!



- OLDER AGE

## NON IOP related risk factors



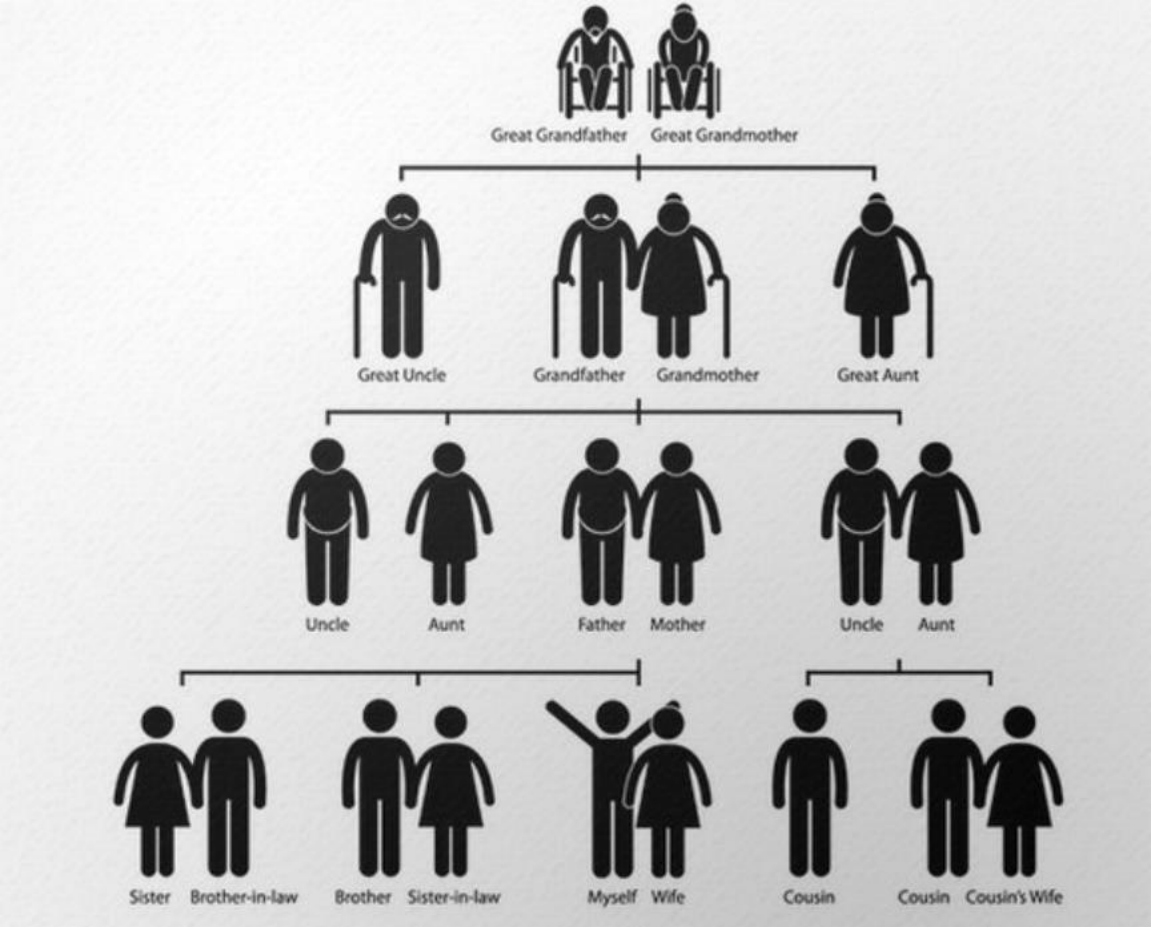

Cataract surgery may cause a spike in IOP immediately after surgery

*Source: Jorge Alio, M.D.*

**Predicting pressure spikes after cataract surgery**
**Glaucoma**
**March 2011**
**by Tony Realini, M.D.**

# FAMILY HISTORY of GLAUCOMA

**NON IOP related risk factors**



- NON WHITE ETHNICITY

**NON IOP related risk factors**

# DISC HEMORRHAGE

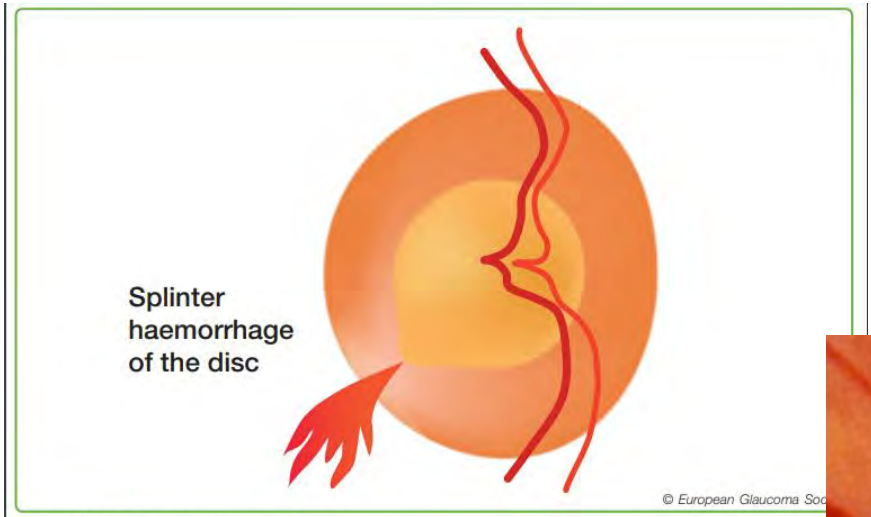
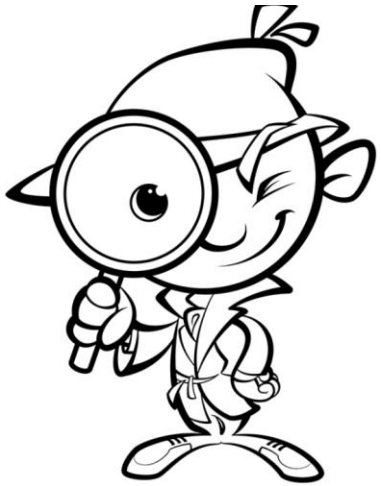


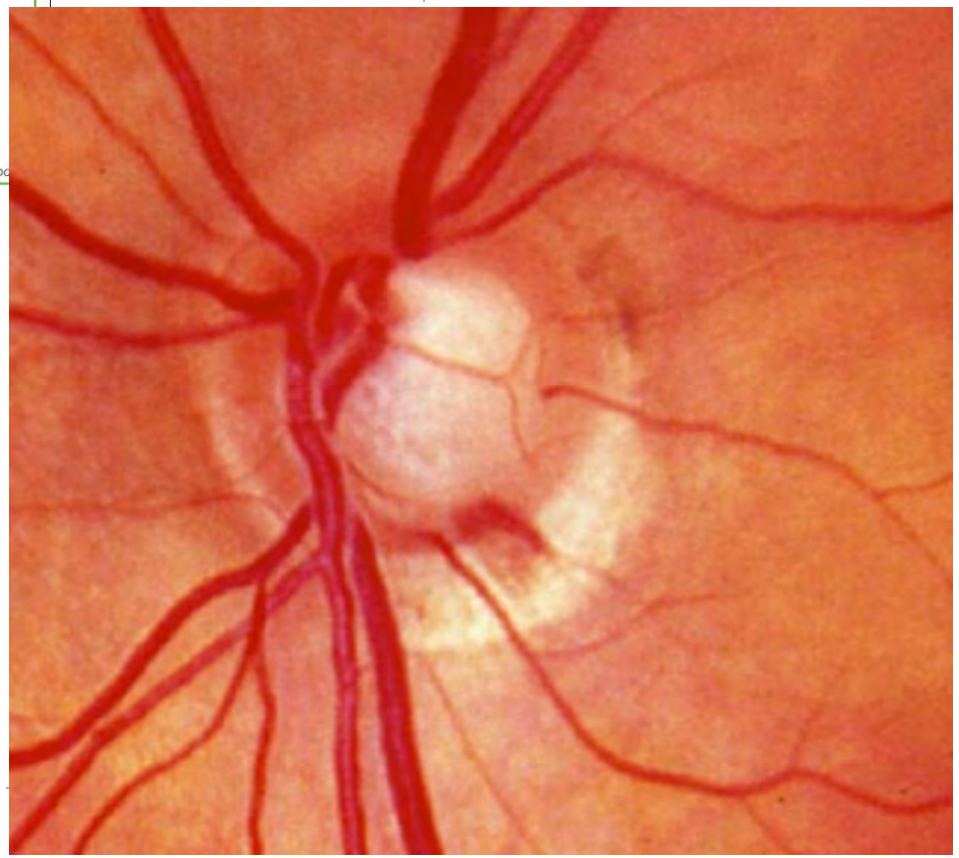

*Figure II.1.11* Optic disc haemorrhage.



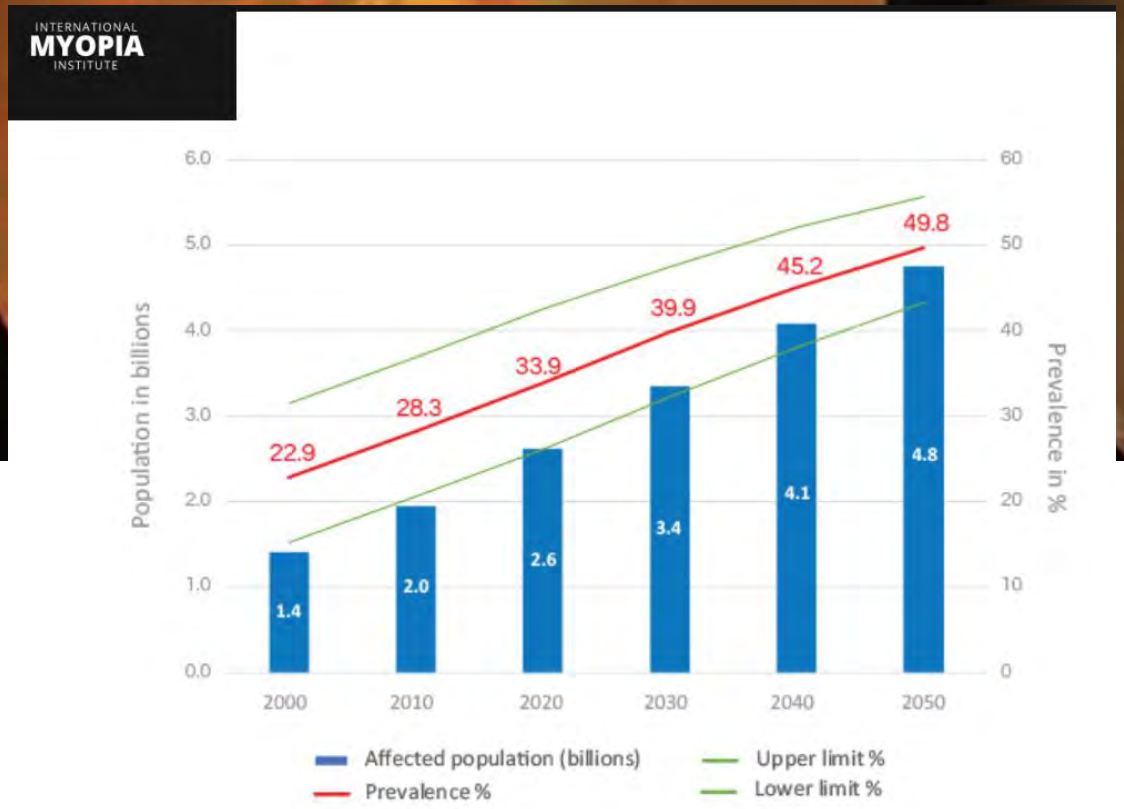
## NON IOP related risk factors

WOMEN

NTG



# MYOPIA




Review > Ophthalmology. 2011 Oct;118(10):1989-1994.e2. doi: 10.1016/j.ophtha.2011.03.012.

## Myopia as a risk factor for open-angle glaucoma: a systematic review and meta-analysis

Michael W Marcus [1], Margriet M de Vries, Francisco G Junoy Montolio, Nomdo M Jansonius

Functional loss over time guides Individualised treatment

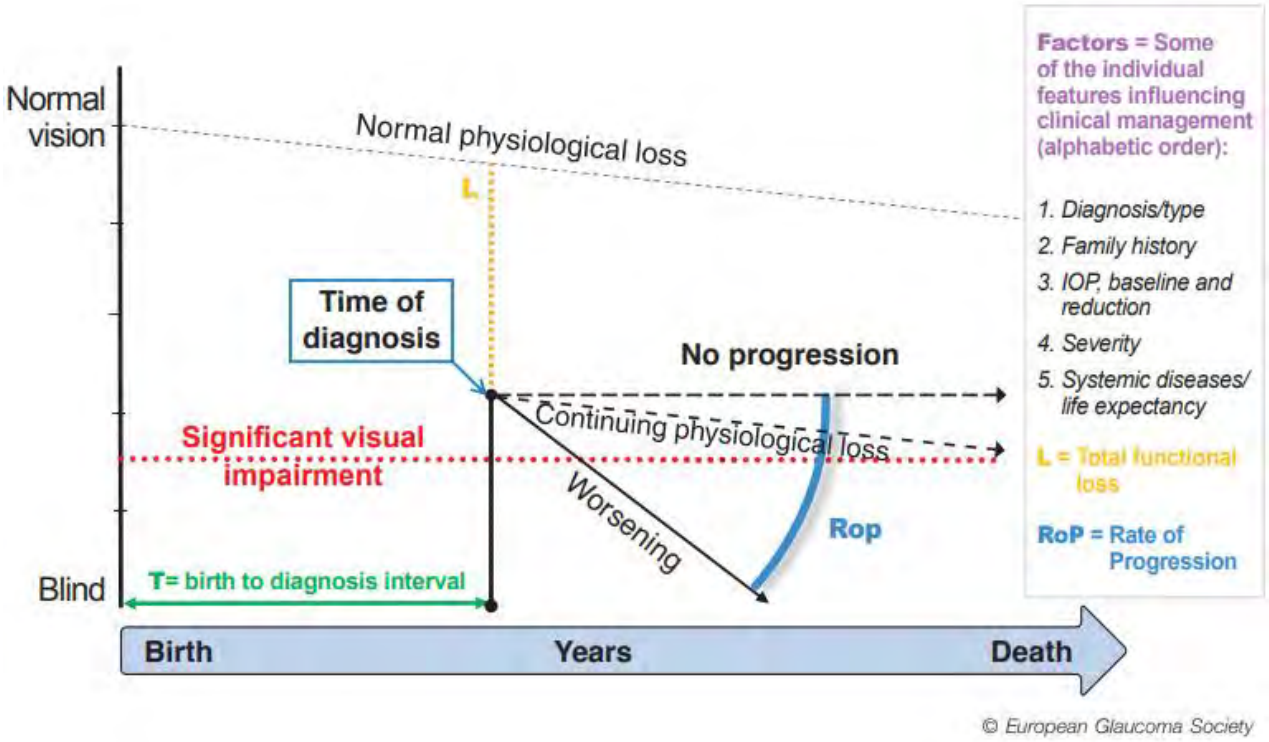



***Figure I.4.1*** *Evaluation of functional loss/time for individualised treatment*

***IOP*** *= IOP level causing damage*

***L*** *= difference of visual function between the age-matched normal and the function at the time of diagnosis*

***RoP*** *= angle representing physiological loss and disease progression*

***T*** *= time interval between birth and the time of diagnosis*

## NATURAL RATE OF PROGRESSION:

- PAOG high IOP: -1.31 dB/y
- NTG: -0.36 dB/y
- PEX: -3.13 dB/y

# IOP only modifiable risk factors

- BUT:

SEP 30, 2022

## Nature, Nurture, Neighborhood, Network, and Glaucoma

AMERICAN ACADEMY OF OPHTHALMOLOGY

Anne Louise Coleman, MD, PhD, delivered the American Glaucoma Society Subspecialty Day Lecture, “Nature, Nurture, Neighborhood, Network, and Glaucoma,” as part of Friday’s Glaucoma Subspecialty Day, discussing the non-IOP risk factors for glaucoma.

# TAKE HOME MESSAGE

## IOP risk factors

- high level of IOP

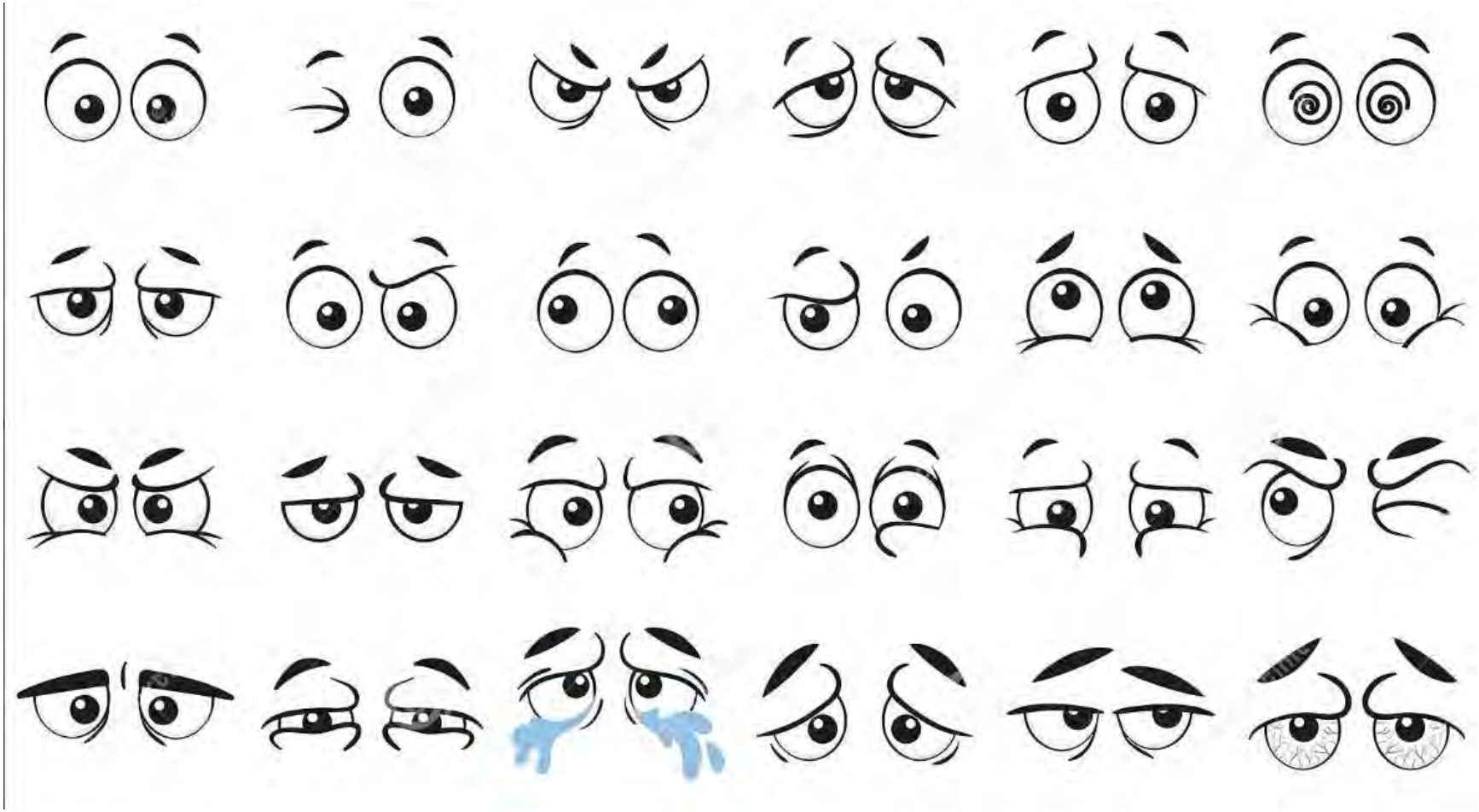
## Non IOP risk factors

- older age
- black ethnicity
- family history of glaucoma
- disc haemorrhage
- myopia
- PEX
- genetic

# BIBLIOGRAPHY


- https://eyewiki.aao.org/Primary_Open-Angle_Glaucoma
- https://eyewiki.aao.org/Steroid-Induced_Glaucomaa
- https://eyewiki.aao.org/Normal_Tension_Glaucoma
- **https://www.aao.org/eyenet/article/myopia-glaucoma-sorting-out-diagnosis**
- **Terminology and Guidelines for Glaucoma** (5th edition)
- SFO : rapports de l'AAO, 10/11/22
- eyeworld.org/2011/predicting-pressure-spikes-after-cataract-surgery/


# THANK YOU



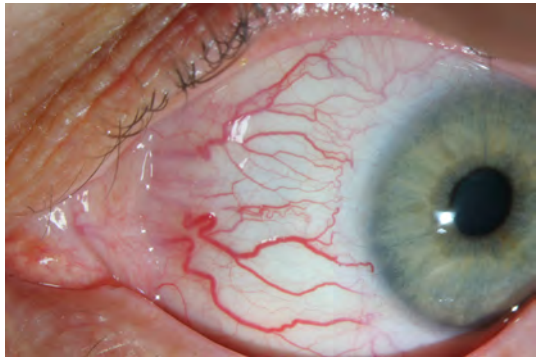
# Secondary open angle glaucoma

Dr. Philippe-Adriaan Kestelyn, MD,FEBO, FEBOS-gl

azsintlucas gent

# Secondary OAG

- heterogeneous group of diseases
- a wide variety of pathogenetic mechanisms leads to increased IOP and eventually glaucomatous damage
  - systemic disease (pseudoexfoliation, neovascular glaucoma)
  - ocular conditions (pigment dispersion syndrome)
  - inflammation (uveitic glaucoma)
  - iatrogenic (steroid-induced glaucoma)
  - trauma (trabecular meshwork damage)
  - tumour induced (uveal melanomas)
  - increased episcleral pressure
    - carotido-cavernous fistula
    - Radius-Maumenee



*Radius-Maumenee syndrome*

# Difference with primary OAG

- Since there is an underlying cause for the IOP increase

→ not only IOP reduction

but also

→ treatment of underlying condition

# Secondary OAG
# Most common entities

1. Pseudoexfoliation glaucoma
2. Pigment dispersion glaucoma
3. Uveitic glaucoma
4. Steroid-induced glaucoma

# 1.Pseudoexfoliation glaucoma

- systemic disease
- synthesis and deposition of fibrillogranular material
- strong association with lysiloxidase-like1-gen (LOXL1) on chromosome 15
- pseudoexfoliation (PEX) material deposits in:
  - eyes
  - also in skin, lungs, kidneys, heart, liver, galbladder, …
- (weak) association with cardiovascular and cerebrovascular disease
- no increased mortality

# Pseudoexfoliation glaucoma Epidemiology

- worldwide
- PEX syndrome inc. 25.9 / 100 000 / year
- PEX glaucoma inc. 9.9 / 100 000 / year

- age = risk factor
  - yearly incidence 40 – 49 yrs :0.6 / 100 000
  - yearly incidence > 79 yrs : 14 / 100 000

- starts often unilaterally
- 1/3 of unilateral cases becomes bilateral over 10 yrs follow up
- PEX = risk factor for glaucoma : 5X to 10X more likely to develop glaucoma
- risk of developing glaucoma in PEX eyes **with normal IOP** : **30% within 10 yrs**

# Pseudoexfoliation glaucoma Pathophysiology

- open angle glaucoma
- deposition of pigment and PEX material in TM: decreased outflow
- PEX associated changes in the lamina cribrosa → increased vulnerability for IOP induced glaucomatous damage?
- weakening of the zonula (lens dislocation)
- stiffening of the iris (poor pupil dilation)

# Pseudoexfoliation glaucoma
# Clinical signs / diagnosis

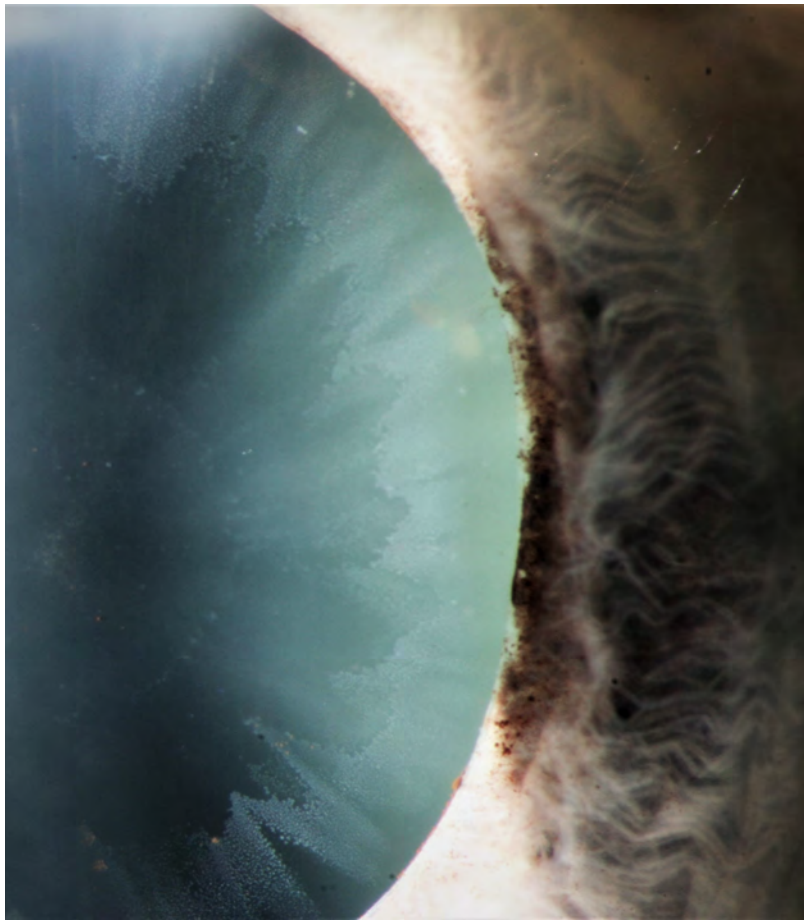
- presence of PEX material in the anterior segment
- lens :
  - dandruff-like material on the anterior capsula except in the central zone → pupillary dilation mandatory !
  - loose zonules: phacodonesis; lens subluxation
- iris :
  - PEX material on the pupil border
  - irregular collerette with moth-eaten appearance
  - pigmentary loss from the central or mid-iris evt. with positive transillumination defects
- gonioscopy :
  - dandruff-like particles and pigment in lower angle recess
  - Sampaolesi‘s line = ondulating, pigmented line on or anterior to the Schwalbe’s line (pathognomonic of PEX)

# Pseudoexfoliation glaucoma
# Clinical signs / diagnosis

presence of PEX material in the anterior segment

**LENS**

- dandruff-like material on the anterior capsula except in the central zone → pupillary dilation mandatory !
- loose zonules: phacodonesis; lens subluxation

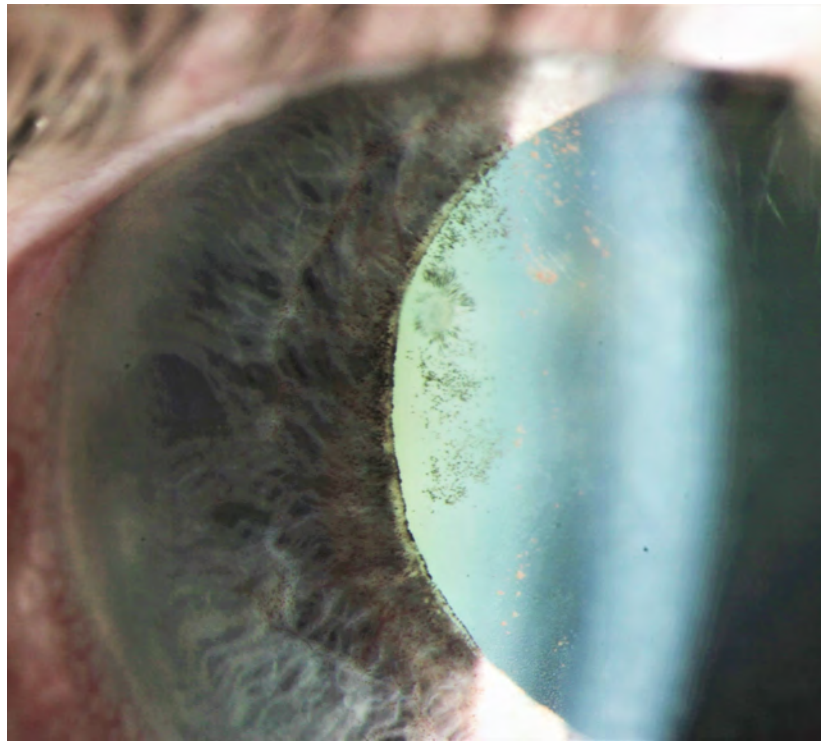


# Pseudoexfoliation glaucoma
# Clinical signs / diagnosis

presence of PEX material in the anterior segment

**IRIS**

- PEX material on the pupil border
- irregular collerette with moth-eaten appearance
- pigmentary loss from the central or mid-iris evt. with positive transillumination defects

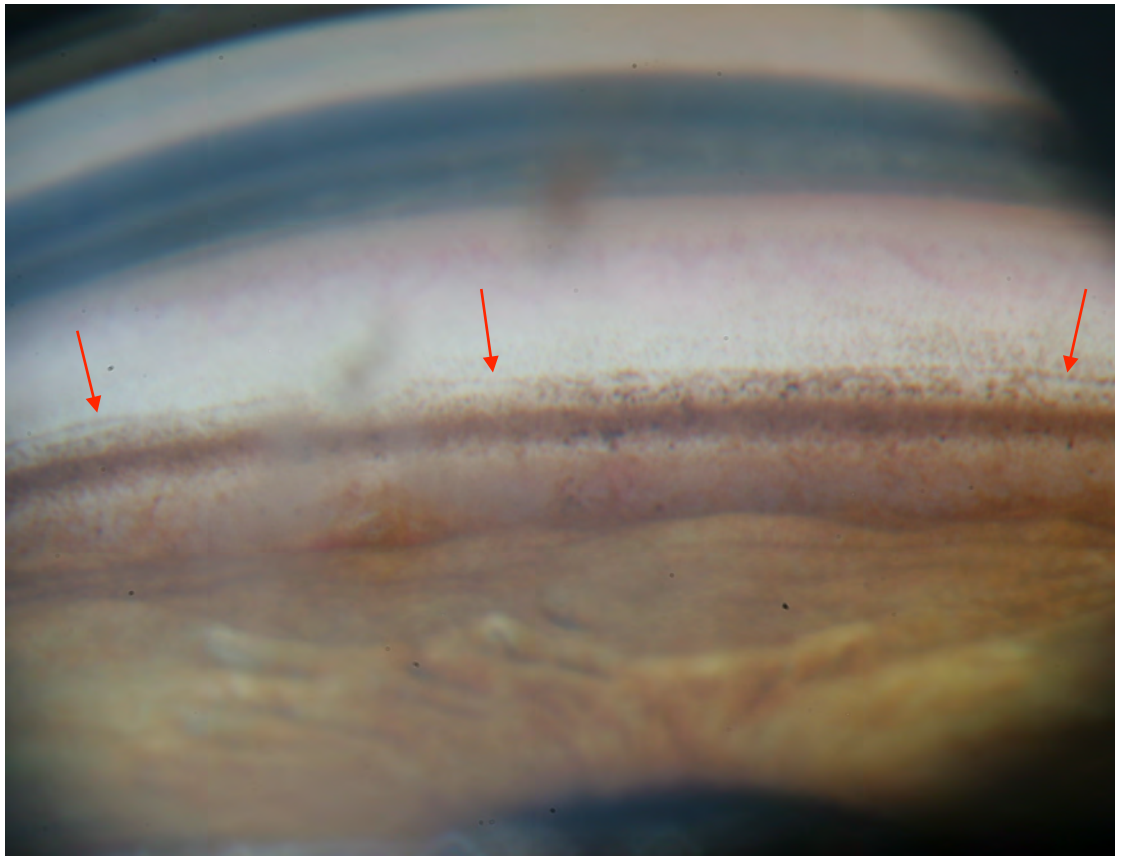


# Pseudoexfoliation glaucoma
# Clinical signs / diagnosis

presence of PEX material in the anterior segment

**GONIOSCOPY**

- dandruff-like particles and pigment in lower angle recess
- Sampaolesi‘s line = ondulating, pigmented line on or anterior to the Schwalbe’s line (pathognomonic of PEX)



# Pseudoexfoliation glaucoma Treatment

- No treatment to stop the production of PEX material
- IOP reduction cfr. primary OAG
- difference wit primary OAG
  - higher IOP values, higher IOP fluctuations
  - often more advanced VF defects at diagnosis
  - good response to LTP
  - surgery often required (trab + mito = gold standard)

# Pseudoexfoliation and cataract surgery

- PEX = risk factor for cataract formation
- PEX = increased risk of complications during cataract surgery
  - poor pupil dilation
  - fragile anterior capsula (capsular tears)
  - weakened zonula (lens subluxation; early or late IOL subluxation)

- more significant IOP drop after phacosurgery in PEX than in normal or POAG patients
  - removal of PEX material from the TM during irrigation-aspiration
  - TM aspiration = intentional removal of PEX material from the TM with a special canula

# 2.Pigment dispersion syndrome / Pigmentary glaucoma

Three entities can be described

- pigment dispersion syndrome (PDS), an ocular condition, usually bilateral, characterized by the dispersion of pigment
- pigmentary ocular hypertension (POH), PDS with elevated IOP and without glaucomatous optic neuropathy
- pigmentary glaucoma (PG), glaucomatous optic neuropathy and PDS

# Pigmentary glaucoma
# Epidemiology

- PG is a disease of young, myopic males of Causasian descent
- incidence of PDS 4.8 / 100 000 per yr
- incidence of PG 1.4 / 100 000 per yr
- risk of conversion from PDS to PG
  - after 5 yrs 5%
  - after 15 yrs 15%
- men with PDS are more prone to develop PG than women

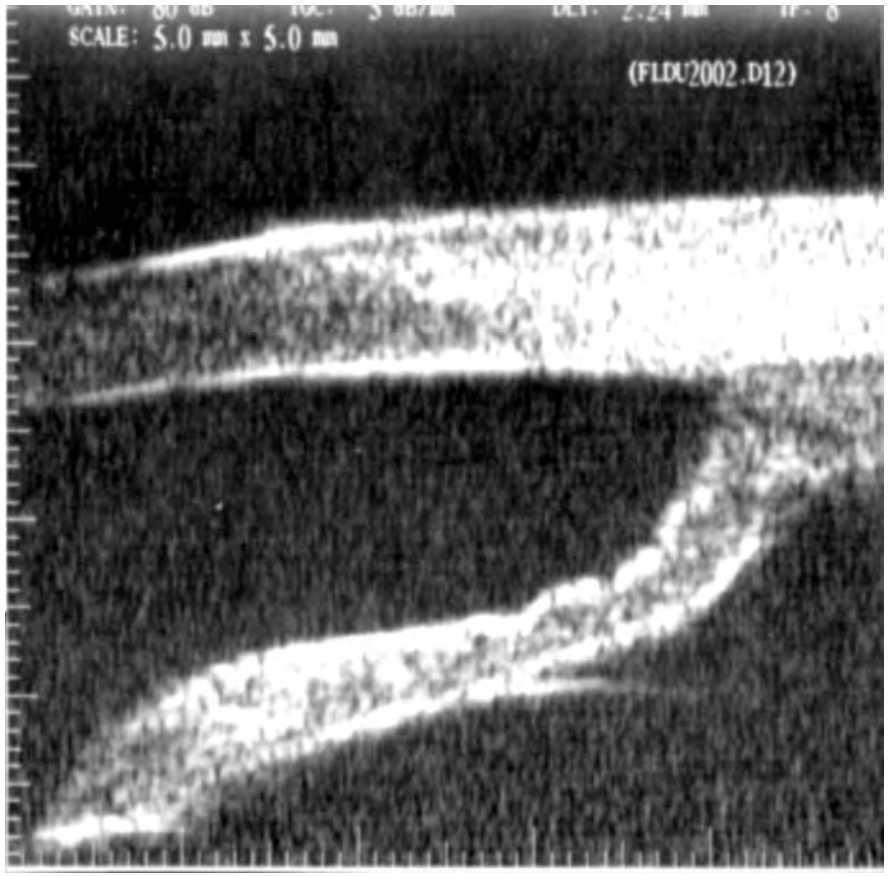
# Pigmentary glaucoma Pathophysiology

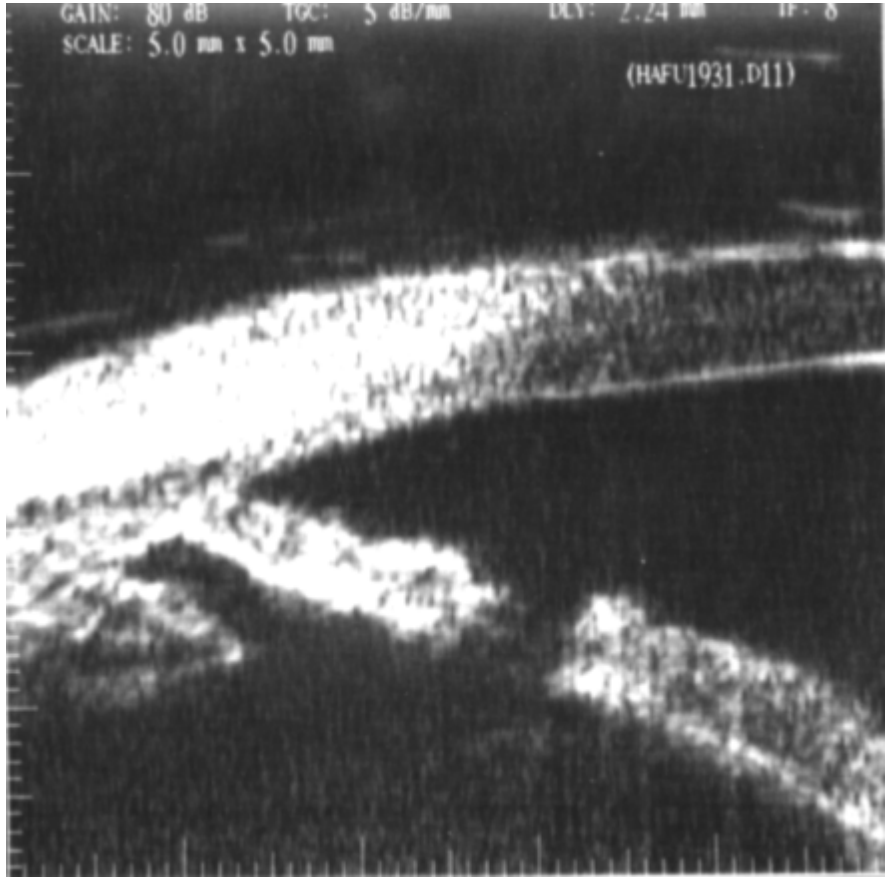
- “reverse pupillary block” is the mechanism behind PD
- the iris functions as a valve against the anterior surface of the lens and fluid is trapped in the anterior chamber while creating negative pressure in the posterior chamber

  → this pressure gradient will push the iris backward (posterior bowing) against the zonular fibers

  → during iris movement the pigmented epithelium of the iris will rub against the zonular fibers resulting in loss of melanin pigment
- accumulation of pigment granules in the TM
  - mechanically reduces outflow
  - causes cell death of the TM endothelial cells
  - induces cicatricial changes in the TM
- theory of reverse pupillary block confirmed by imaging

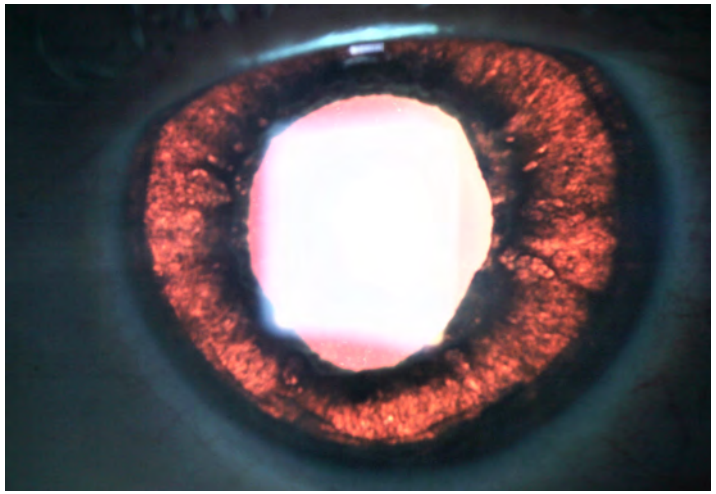
# Roberto G Carassa et al. Br J Ophthalmol 1998
# UBM in PDS before and after YAG iridotomy

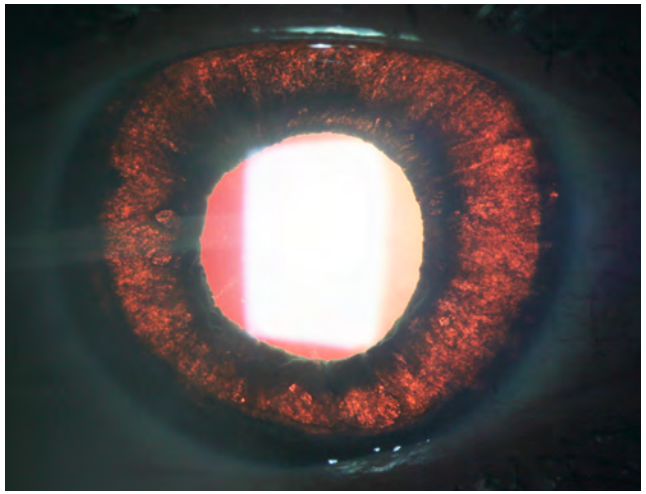


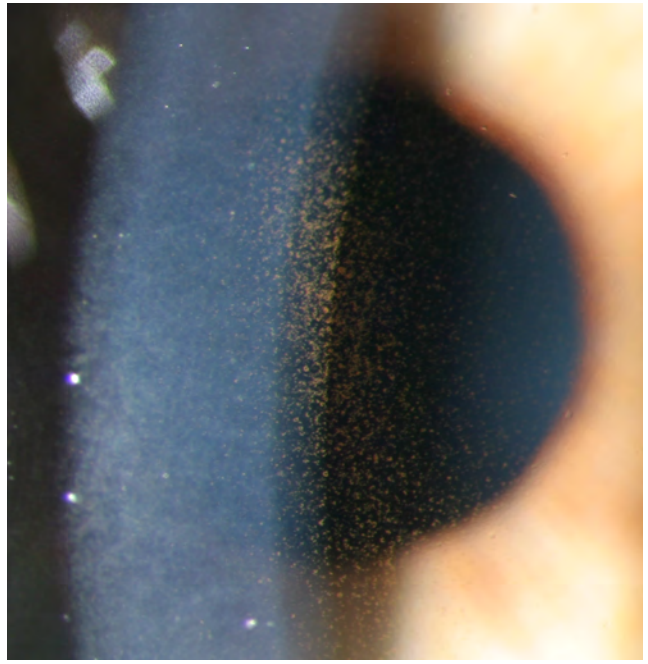



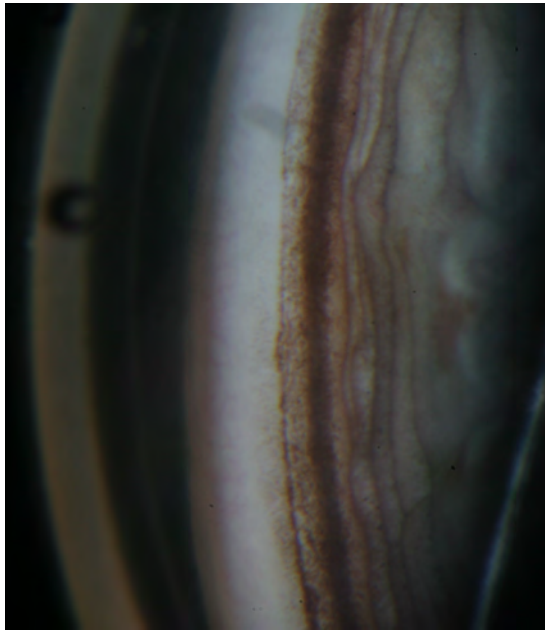
# Pigmentary glaucoma
# Clinical signs / diagnosis

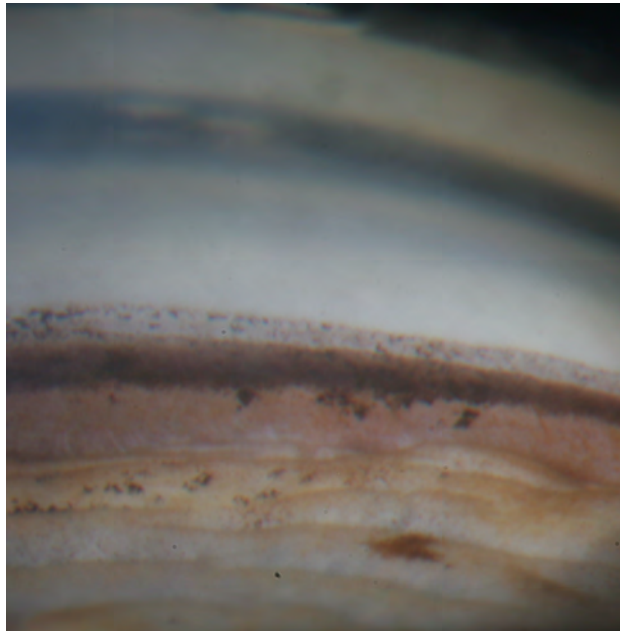
- Deep anterior chamber with concave iris base
- “Krukenberg spindle” = pigment deposits on the central corneal endothelium
    - pigment granules are phagocytized by the endothelial cells
    - absence of Krukenberg spindle does not rule out PG
- Radial transillumination defect in the mid periphery of the iris
- Gonioscopy :
    - heavy pigmentation of the TM  over 360°
    - linear pigment deposits on the posterior lens capsula at the level of the insertion of the zonular fibers (Sheie’s line)

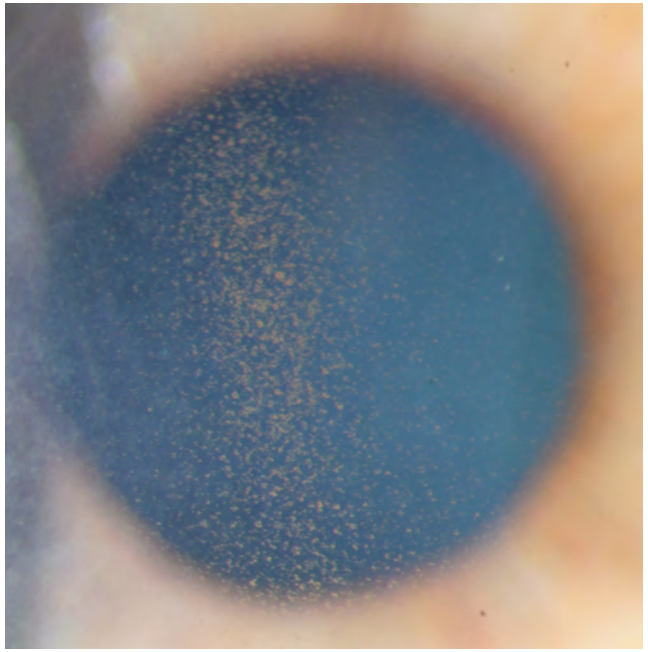












# Pigmentary dispersion
# Treatment

- strict follow up of patients with PDS or… preventive action?

→ laser iridotomy to abolish the reverse pupillary block

- no randomized studies
- but biologically very plausible intervention
- at least when performed early
- before the TM is clogged with pigment!

# Pigmentary glaucoma
# Treatment

- similar to the treatment of POAG
- LTP works well, but risk of pressure spikes and relatively short term effect
- if drops and LTP fail: trab + mito
- Cave: increased risk of hypotonous maculopathy (young, myopic patients)
  - → tight closure of the scleral flap followed by laser suture lysis
  - → deep sclerectomy + mito

# 3. Uveitic glaucoma

- Definition of *uveitic glaucoma*
  - Glaucomatous optic nerve damage in uveitis patients

    OR

  - Uveitis  patients with IOP > 30 mm Hg (SUN classification)

    → often difficult to diagnose GON damage in uveitis patients with papilloedema or atrophy

# Uveitic glaucoma
# Epidemiology

- UG in adults: 5 – 20%
- UG in children: 5 – 13.5%
- UG already present in 8.5% of uveitis patients when first diagnosed
- highest risk of UG in the following entities:
    - Fuchs uveitis syndrome
    - Posner-Schlossman syndrome
    - Herpes virus associated anterior uveitis (HS, VZV, CMV)
    - Juvenile idiopathic arthritis (JIA) most common cause of UG in children

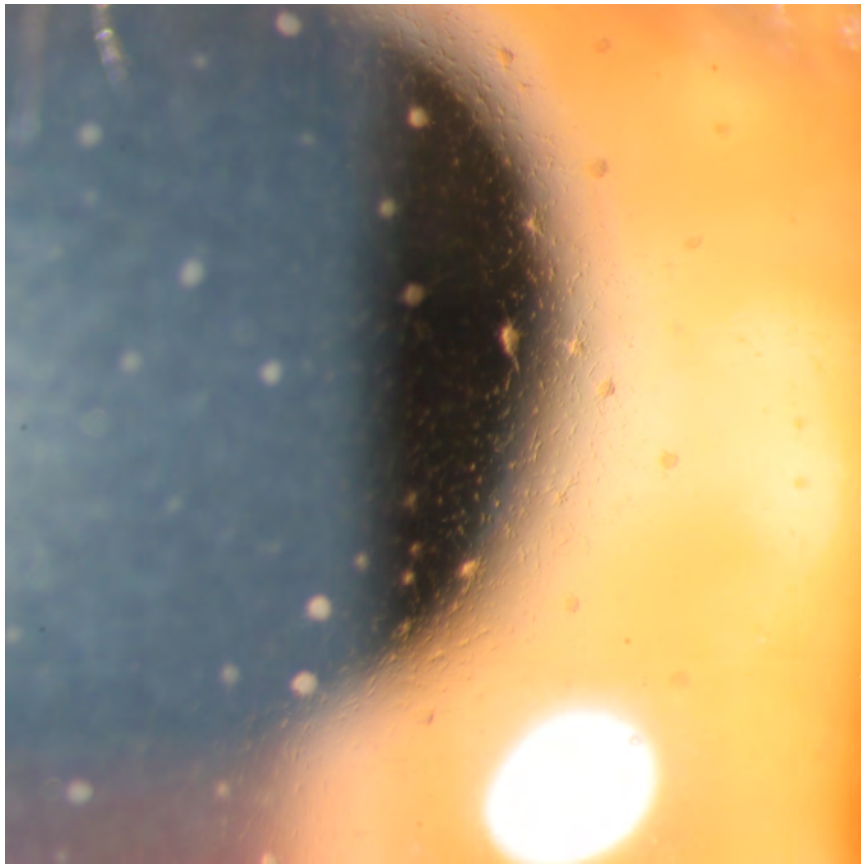
# Uveitic glaucoma
# Pathophysiology

- Mechanisms of secundary open angle glaucoma in UG
  - debris, protein and inflammmatory cells in the TM
  - viral infection of the TM cells = trabeculitis
  - cicatrical changes in the TM
  - iatrogenic: steroid glaucoma

- Mechanisms of secundary closed angle glaucoma in UG
  - angle closure (posterior synechiae and occlusio pupillae with iris bombans)
  - goniosynechiae
  - forward displacement of lens iris diaphragm (uveal effusion)

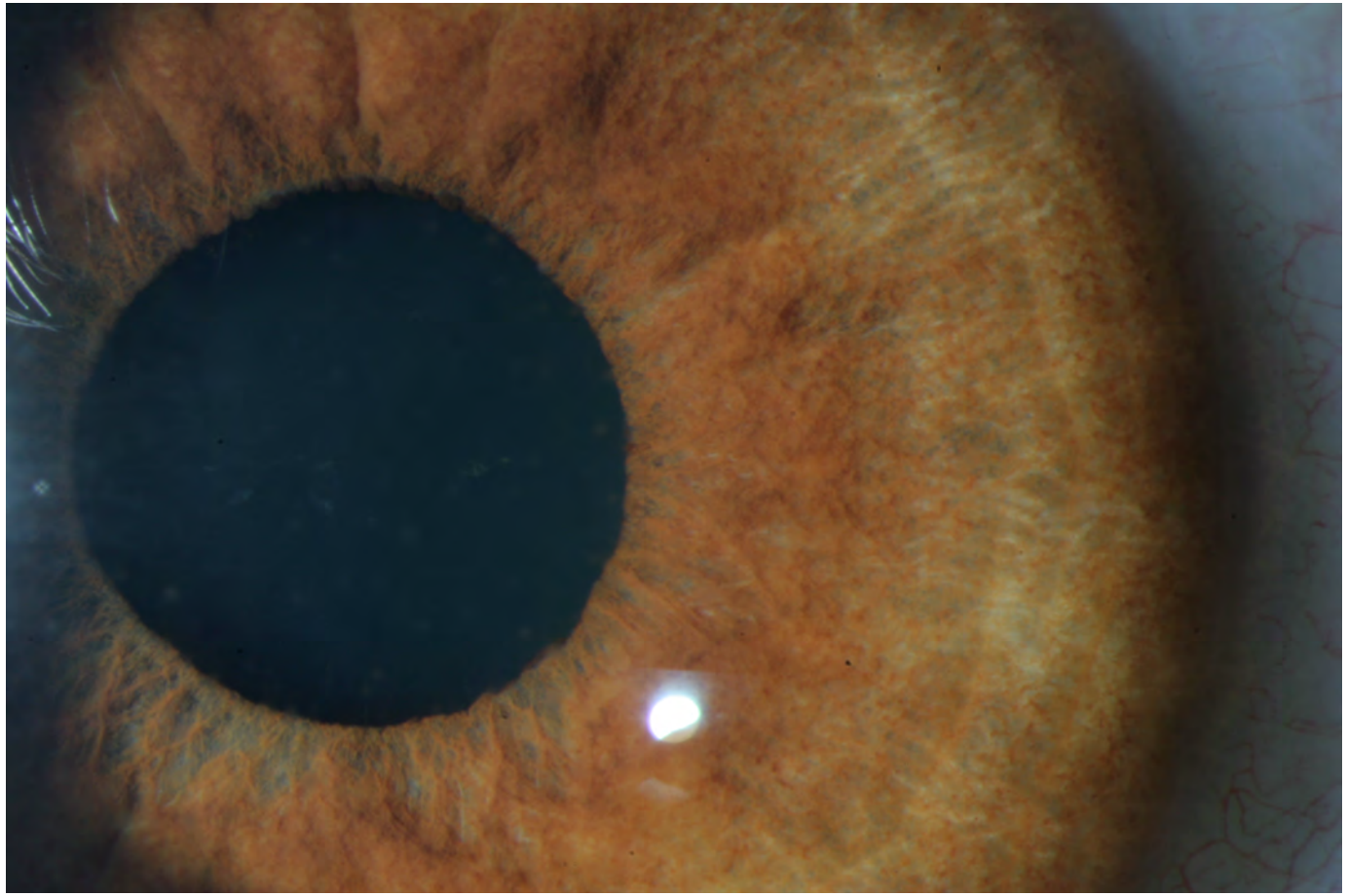
# Uveitic glaucoma
# Fuchs uveitis syndrome

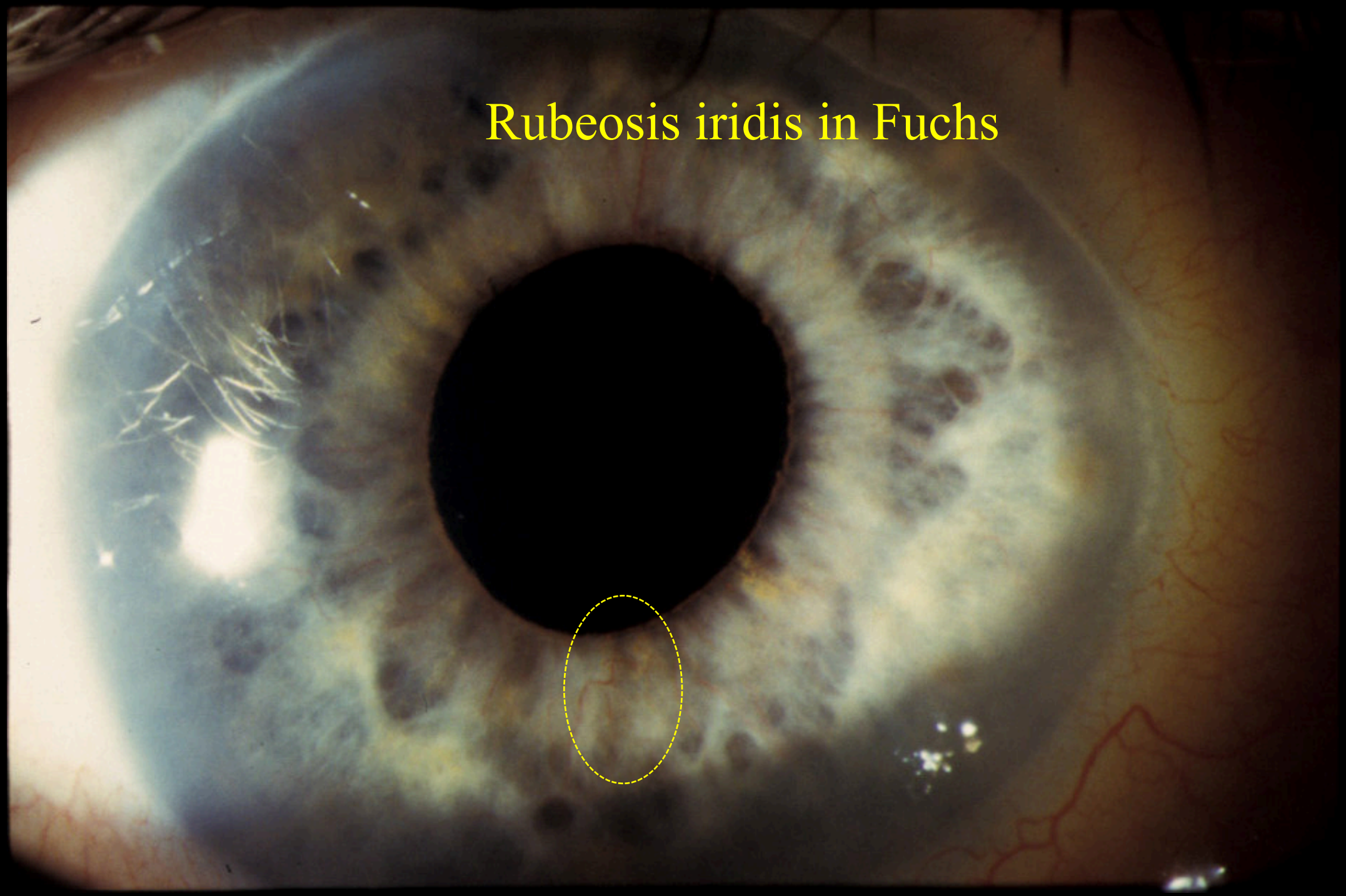
- infectious origin_ association with Rubella virus
- classic triad:
  - (irido)cyclitis, small KP
  - Vitreous floaters, cataract (80%)
  - heterochromia (1/3)
- small, stellate precipitates all over the cornea
- vitreous floaters
- no synechiae, no CMO



topical steroids are contra-indicated in FUS !!!

# loss of normal iris structure in FUS



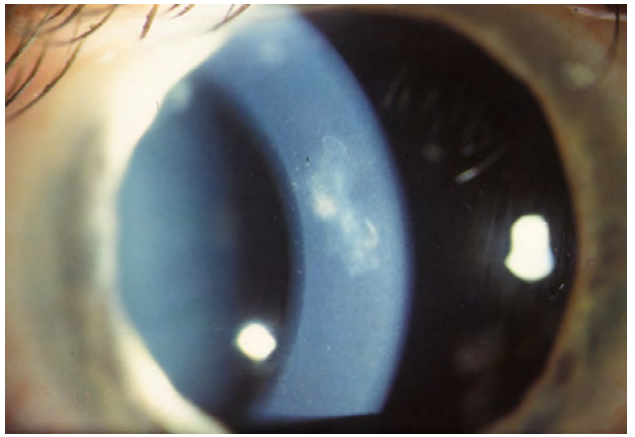

Rubeosis iridis in Fuchs

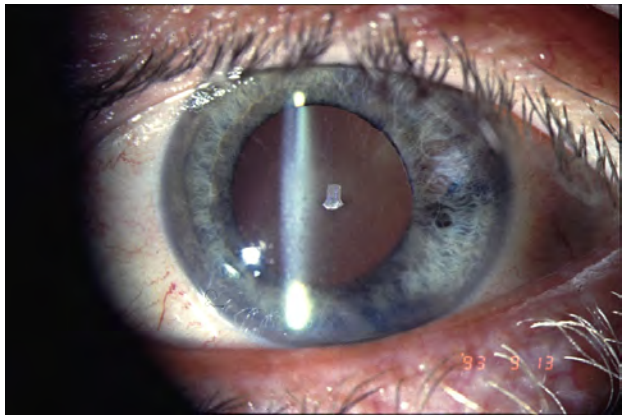
# Glaucoma in Fuchs uveitis syndrome

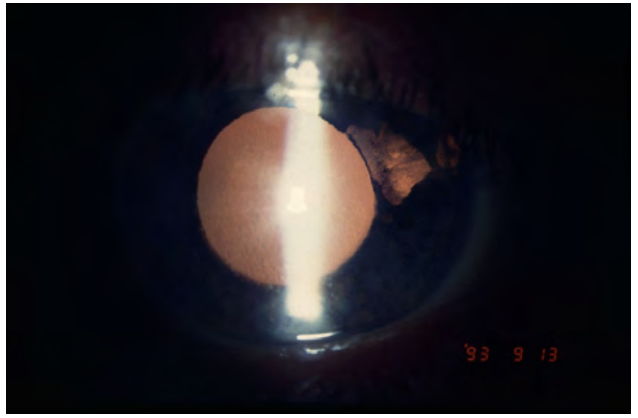
- prevalence figures for glaucoma vary from 6 to 60%
- leading cause of visual loss in FUS
- pathophysiology ? unclear…
  - trabeculitis
  - rubeosis and fine abnomal blood vessels on gonioscopy (→Amsler sign)
  - sclerosis of the TM
- 2/3 of patients fail to respond to medical therapy and need filtering surgery + MMC
- In 1/3 of FUS patients with glaucoma treatment is unable to prevent further progression of GON

# Herpes simplex virus uveitis

- not always keratouveitis
- unilateral
- elevated IOP in 28% of cases
  - inflammatory debris
  - trabeculitis
  - steroid-induced glaucoma
- iris atrophy
- chronic disease
- diagnosis:
  - history, clinical picture
  - isolation of virus (AC tap)
- long term low dose topical steroids and systemic acyclovir







# Posner-Schlossman syndrome (glaucomatocyclitic crisis)

- unilateral, recurrent attacks of nongranulomatous cyclitis
- few, fine KPs
- 20 to 50 year old patients
- elevated IOP (trabeculitis)
- unilateral blurred vision and halos
- open angle,
- self-limiting condition ?
- short term steroids/NSAIDS and antiglaucoma drugs
- etiology? HSV, CMV,…
- rare disease

# 4. Corticosteroid glaucoma Epidemiology

= GON as a result of the IOP rise induced by corticosteroid therapy

- high responders : 5% of the population > 15 mm Hg rise
- moderate responders : 1/3 of the population 6 to 15 mm

- corticosteroid induced IOP rise ~

  chemical structure, dose, frequency, route of administration, duration

  e.g. Ozurdex (dexamethasone implant) : 26.9 % of patients IOP rise > 10 mm Hg

  Iluvien (fluocinolone acetonide implant) : 7.2 % of patients IOP rise > 30 mm Hg

# Corticosteroid glaucoma Epidemiology (continued)

- topical and intravitreal administration highest risk
- but also with systemic administration, inhalations, and even skin creams applied in the vicinity of the eye
- less common with intranasal applications or local infitrations

  → monitor IOP in patients receiving corticosteroid therapy
- IOP rise occurs on average after 2 to 6 weeks of treatment, but acute and delayed reactions  may occur
- POAG patients particular prone to steroid response (> 90%)

# Corticosteroid glaucoma Pathophysiology

- increase in outflow resistance
- steroids interfere with protein synthesis in TM cells, leading to accumulation of glycosaminoglycans, elastin, fibronectin and type IV collagen
- steroids also interfere with the phagocytic properties of TM cells resulting in accumulation of debris

# Corticosteroid glaucoma
# Diagnosis

- obvious from the patient's history in most cases

- sometimes difficult differential diagnosis
  - uveitic glaucoma < -- > corticosteroid glaucoma
  - do not cut the steroids ! Increased inflammation upon steroid tapering may lead to decreased aqueous humour production by the ciliary body and IOP lowering which might by considered _ erroneously _as proof of steroid glaucoma

# Corticosteroid glaucoma
# Treatment

- medical treatment
  - beta blockers, topical and systemic carboanhydrase inhibitors = first choice
  - but, no pilocarpine !
  - in uveitis patients prostaglandines are not contra-indicated with the possible exception of herpetic disease

- switch to
  - less potent drug (fluorometholone drops)
  - non steroidal alternatives (topical / systemic NSAID's), biological,…

- if steroids are essential to control inflammation (uveitis) or rejection (corneal transplantation) do not cut on steroids, but treat the glaucoma aggressively: surgery + MMC, valves, diode if needed

# Secondary open angle glaucoma
# Final reminders

- important not the miss the differential diagnosis
  - primary versus secondary OAG

  → implications for the therapeutic approach

  → different natural history (e.g. pigmentary glaucoma more aggressive disease)

- thorough history and comprehensive eye examination mandatory
  - gonioscopy, anterior segment examination in miosis (dark) and after dilation, fundoscopy and angiography
- do not cut on steroids in uveitic glaucoma, but treat the glaucoma aggressively
- In FUS steroids are not indicated: they do not control the low grade inflammation, but they increase the risk of cataract and glaucoma

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www.belglaucoma.be

# Thank you !

# Case

Evelien Vandewalle, MD, PhD

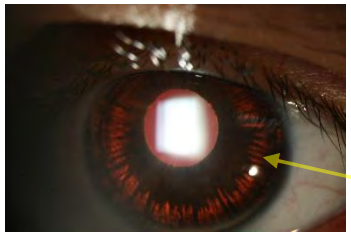
**No financial disclosure**

# Male, 56 years old

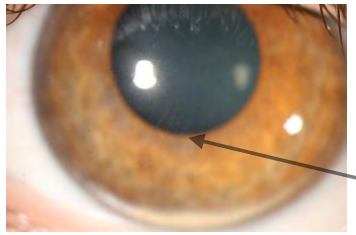
- Recently diagnosed pigment dispersion glaucoma (05/2018)
- Maximum IOP: RE 23 mmHg and LE 21 mmHg
- No family history
- Treatment: latanoprost 1x/d -> 14 mmHg

# Clinical examination, 08/2018

| | RE | LE |
|---|---|---|
| Visual Acuity | 9/10 (-5,5*-1,25 x 60°) | 12/10 (-3,5*-0,75 x 120°) |
| Reading | Snellen 2 | Snellen 1 |
| Biomicroscopy | Kruckenberg spindle<br>Iris transillumination | |



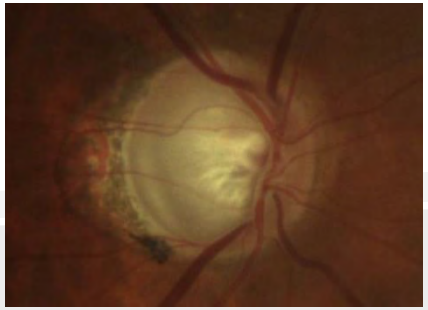
Iris transillumination

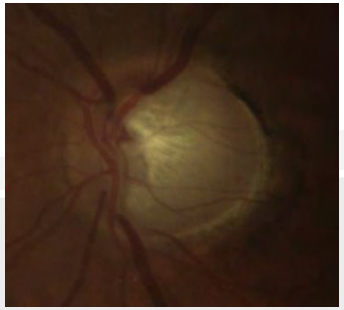


Kruckenberg spindle

# Clinical examination

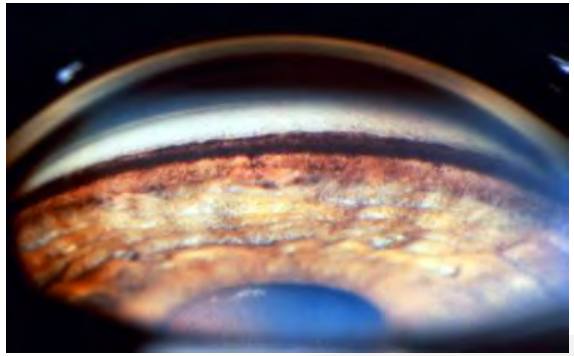
| | RE | LE |
|---|---|---|
| Visual Acuity | 9/10 (-5,5*-1,25 x 60°) | 12/10 (-3,5*-0,75 x 120°) |
| Reading | Snellen 2 | Snellen 1 |
| Biomicroscopy | Kruckenberg spindle<br>Iris transillumination | |
| Tonometry | 15 mmHg | 18 mmHg |
| Fundoscopy | c/d 0,9 | c/d 0,9 |





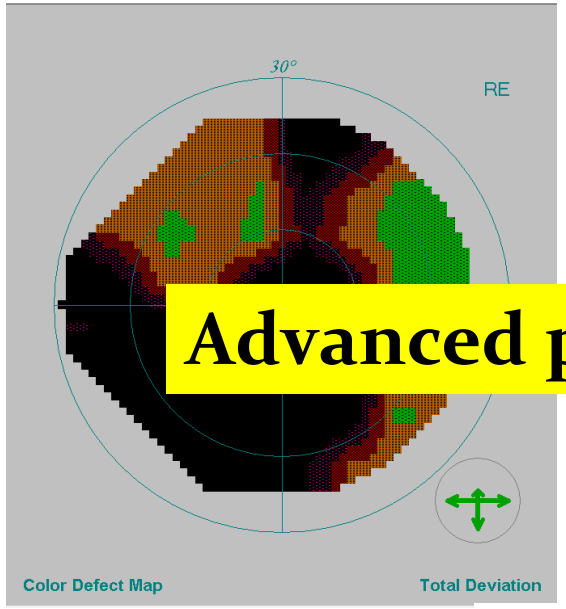
# Clinical examination

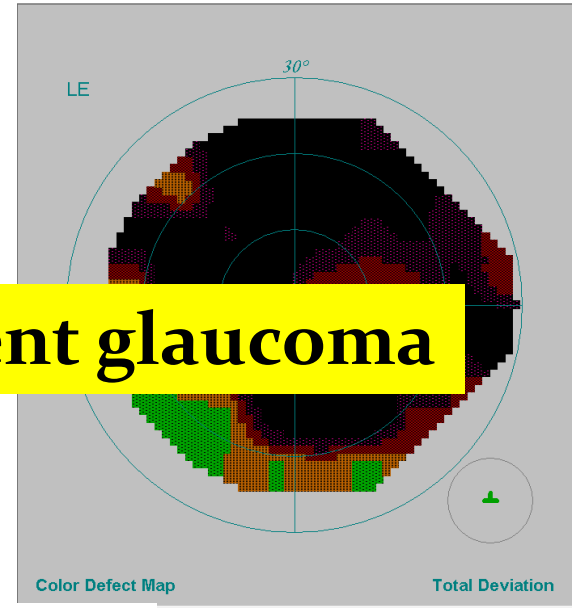
| | RE | LE |
|---|---|---|
| Pachymetry | 463 | 463 |
| Gonioscopy | Open angle, homogeneous dens pigmentation | |



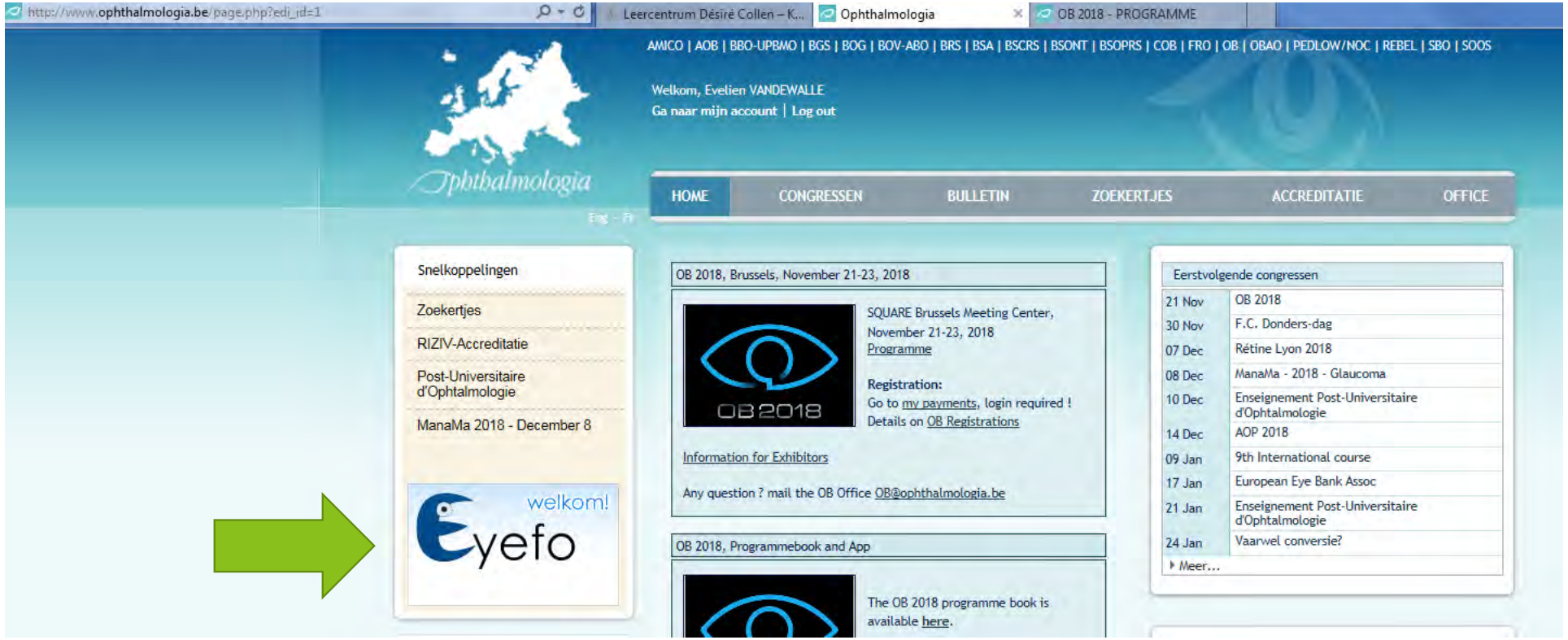
# Visual field exam

30/8/2018




**Advanced pigment glaucoma**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30 Nov F.C. Donders-dag
07 Dec Rétine Lyon 2018
08 Dec ManaMa - 2018 - Glaucoma
10 Dec Enseignement Post-Universitaire d'Ophtalmologie
14 Dec AOP 2018
09 Jan 9th International course
17 Jan European Eye Bank Assoc
21 Jan Enseignement Post-Universitaire d'Ophtalmologie
24 Jan Vaarwel conversie?
Meer...

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# Criteria for driving

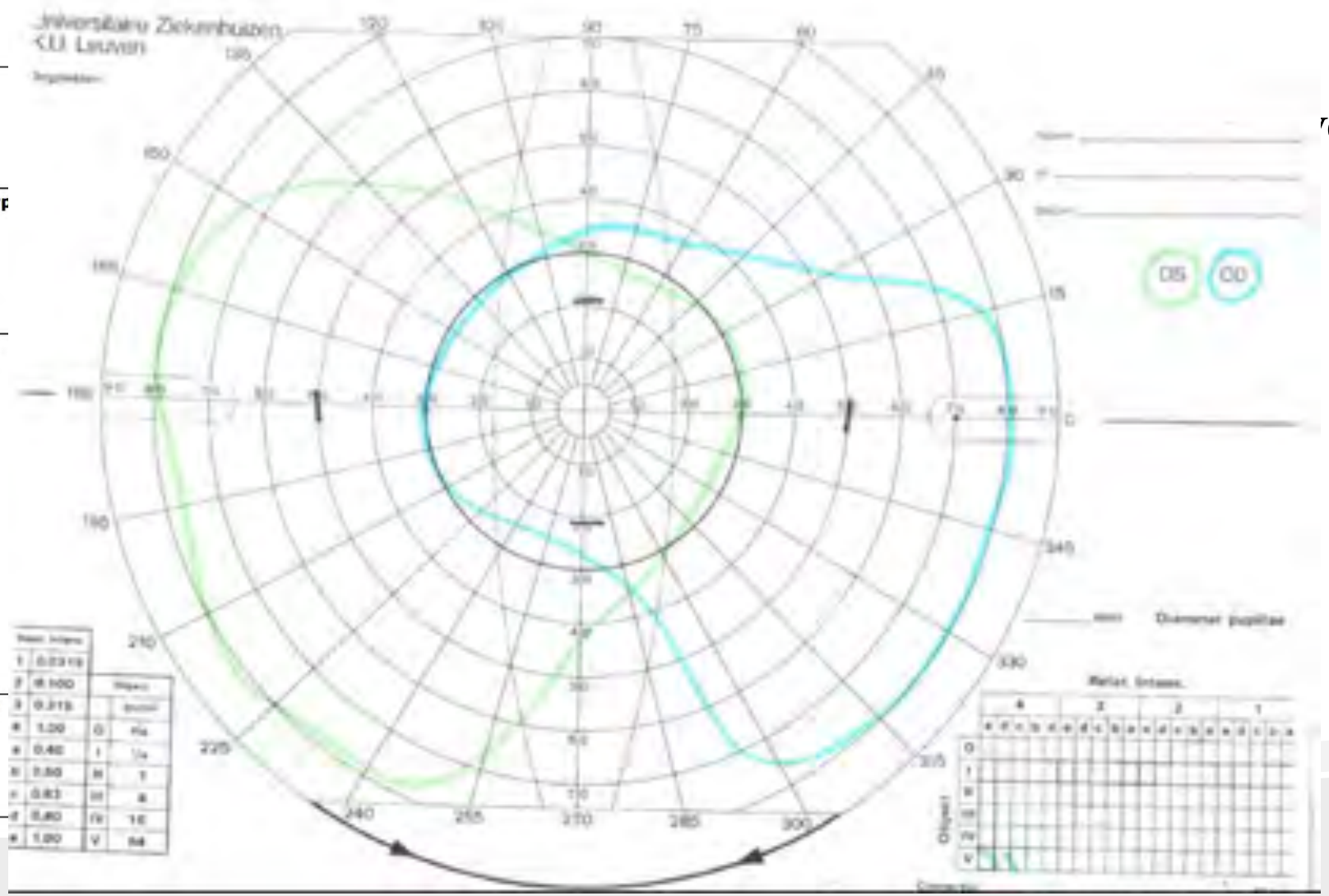
| | Groep 1: categorie A3, A, B (+E) uitgezonderd bezoldigd en hiermee gelijkgesteld vervoer | Groep 2: categorie C (+E), D (+E), B (+E) alleen bezoldigd of hiermee gelijkgesteld vervoer |
|---|---|---|
| **gezichtsscherpte**<br>1 | met optische correctie<br>binoculair ten minste 5/10<br><br>doorverwijzing naar CARA mogelijk indien visus > 3/10 met beste correctie, indien voldaan aan gezichtsveldnorm en mits gunstig advies van oogarts | met optische correctie<br>tenminste 8/10 beste oog en 1/10 minder goede oog<br><br>brilglazen niet sterker dan plus 8D |
| **gezichtsveld** | met behulp van perimeter<br>met optische correctie<br>horizontale binoculaire veld minstens 120°<br>minimaal 50° naar rechts en naar links<br>minimaal 20° naar boven en naar onder<br><br>centrale 20° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: dezelfde criteria<br><br>doorverwijzing naar CARA mogelijk indien voldaan aan gezichtsscherptenorm en mits gunstig advies van oogarts | met behulp van perimeter<br>met optische correctie<br>horizontale binoculaire veld minstens 160°<br>minimaal 70° naar rechts en naar links<br>minimaal 30° naar boven en naar onder<br><br>centrale 30° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: niet rijgeschikt |
| **schemerzicht** | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) |

Male, 56 years old

Vision RLE 12/10

# Criteria for driving

| |
|---|
| gezichtsscherp<br>1 |
| gezichtsveld<br>2 |
| schemerzicht |




ears old

# Criteria for driving

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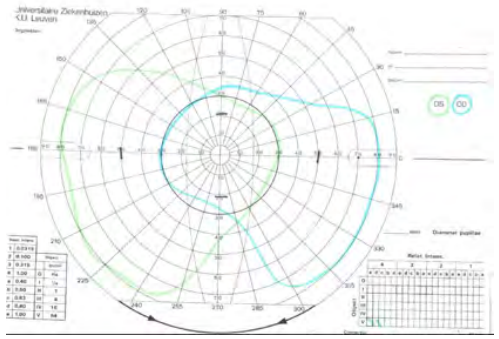
| **gezichtsveld**<br>2 | met behulp van perimeter<br>met optische correctie<br>horizontale binoculaire veld minstens 120°<br>minimaal 50° naar rechts en naar links<br>minimaal 20° naar boven en naar onder<br><br>centrale 20° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: dezelfde criteria<br><br>doorverwijzing naar CARA mogelijk indien voldaan aan gezichtsscherptenorm en mits gunstig advies van oogarts | met behulp van perimeter<br>met optische correctie<br>horizontale binoculaire veld minstens 160°<br>minimaal 70° naar rechts en naar links<br>minimaal 30° naar boven en naar onder<br><br>centrale 30° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: niet rijgeschikt |
| **schemerzicht** | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) |

Male, 56 years old

Vision RLE 12/10



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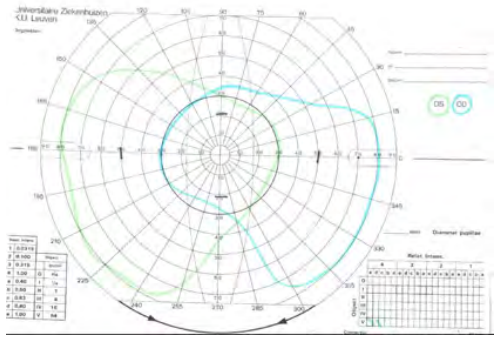
| | Groep 1: categorie A3, A, B (+E) uitgezonderd bezoldigd en hiermee gelijkgesteld vervoer | Groep 2: categorie C (+E), D (+E), B (+E) alleen bezoldigd of hiermee gelijkgesteld vervoer |
|---|---|---|
| **gezichtsscherpte**<br>1 | met optische correctie<br>binoculair ten minste 5/10<br><br>doorverwijzing naar CARA mogelijk indien visus > 3/10 met beste correctie, indien voldaan aan gezichtsveldnorm en mits gunstig advies van oogarts | met optische correctie<br>tenminste 8/10 beste oog en 1/10 minder goede oog<br><br>brilglazen niet sterker dan plus 8D |
| **gezichtsveld**<br>2<br>3 | met behulp van perimeter<br>met optische correctie<br>horizontale binoculaire veld minstens 120°<br>minimaal 50° naar rechts en naar links<br>minimaal 20° naar boven en naar onder<br><br>centrale 20° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: dezelfde criteria<br><br>doorverwijzing naar CARA mogelijk indien voldaan aan gezichtsscherptenorm en mits gunstig advies van oogarts | met behulp van perimeter<br>met optische correctie<br>horizontale binoculaire veld minstens 160°<br>minimaal 70° naar rechts en naar links<br>minimaal 30° naar boven en naar onder<br><br>centrale 30° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: niet rijgeschikt |
| **schemerzicht** | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) |

Male, 56 years old

Vision RLE 12/10

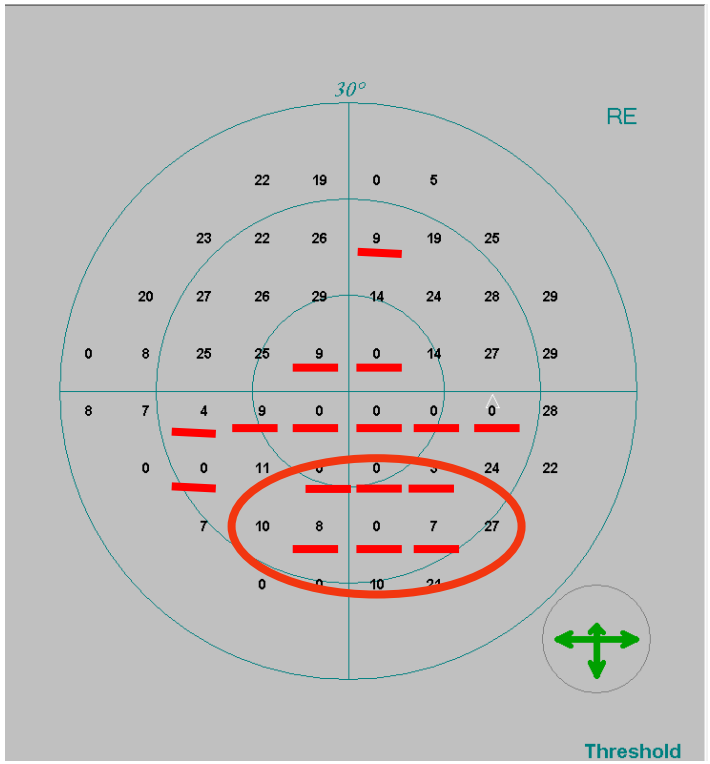


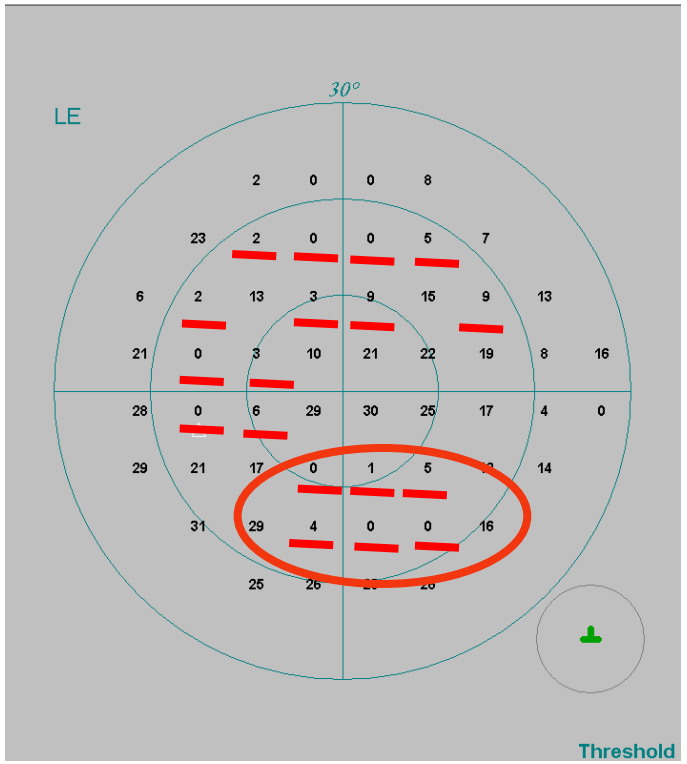
# Definition of an absolute scotoma

- The binocular visual field need to be examined with a standard automatic kinetic perimetry that allows integration of both monocular visual fields

- A binocular absolute defect within the 20° or 30° can be defined as
  1. A minimum of 3 continguous test locations
  2. with a sensitivity of < 10 dB

# Absolute scotoma present?




**Absolute scotoma within the 20°**

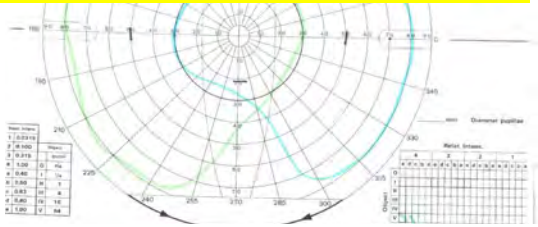
# Criteria for driving

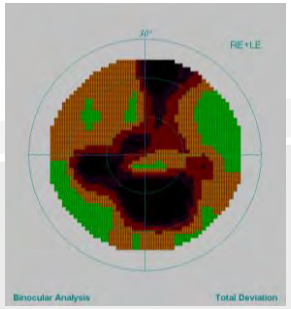
| | Groep 1: categorie A3, A, B (+E) uitgezonderd bezoldigd en hiermee gelijkgesteld vervoer | Groep 2: categorie C (+E), D (+E), B (+E) alleen bezoldigd of hiermee gelijkgesteld vervoer |
|---|---|---|
| **gezichtsscherpte**<br>1 | met optische correctie<br>binoculair ten minste 5/10<br><br>doorverwijzing naar CARA mogelijk indien visus > 3/10 met beste correctie, indien voldaan aan gezichtsveldnorm en mits gunstig advies van oogarts | met optische correctie<br>tenminste 8/10 beste oog en 1/10 minder goede oog<br><br>brilglazen niet sterker dan plus 8D |
| **gezichtsveld**<br>2<br>3 | met behulp van perimeter<br>...<br>ho<br>mi<br>mi<br><br>centrale 20° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: dezelfde criteria<br><br>doorverwijzing naar CARA mogelijk indien voldaan aan gezichtsscherptenorm en mits gunstig advies van oogarts | met behulp van perimeter<br><br>centrale 30° vrij van enig absoluut defect<br><br>in geval van één functioneel oog: niet rijgeschikt |
| **schemerzicht** | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) |

**NOT FIT TO DRIVE A CAR**

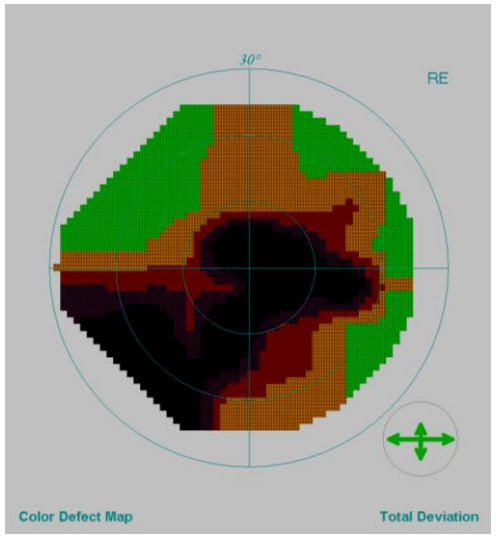
Male, 56 years old

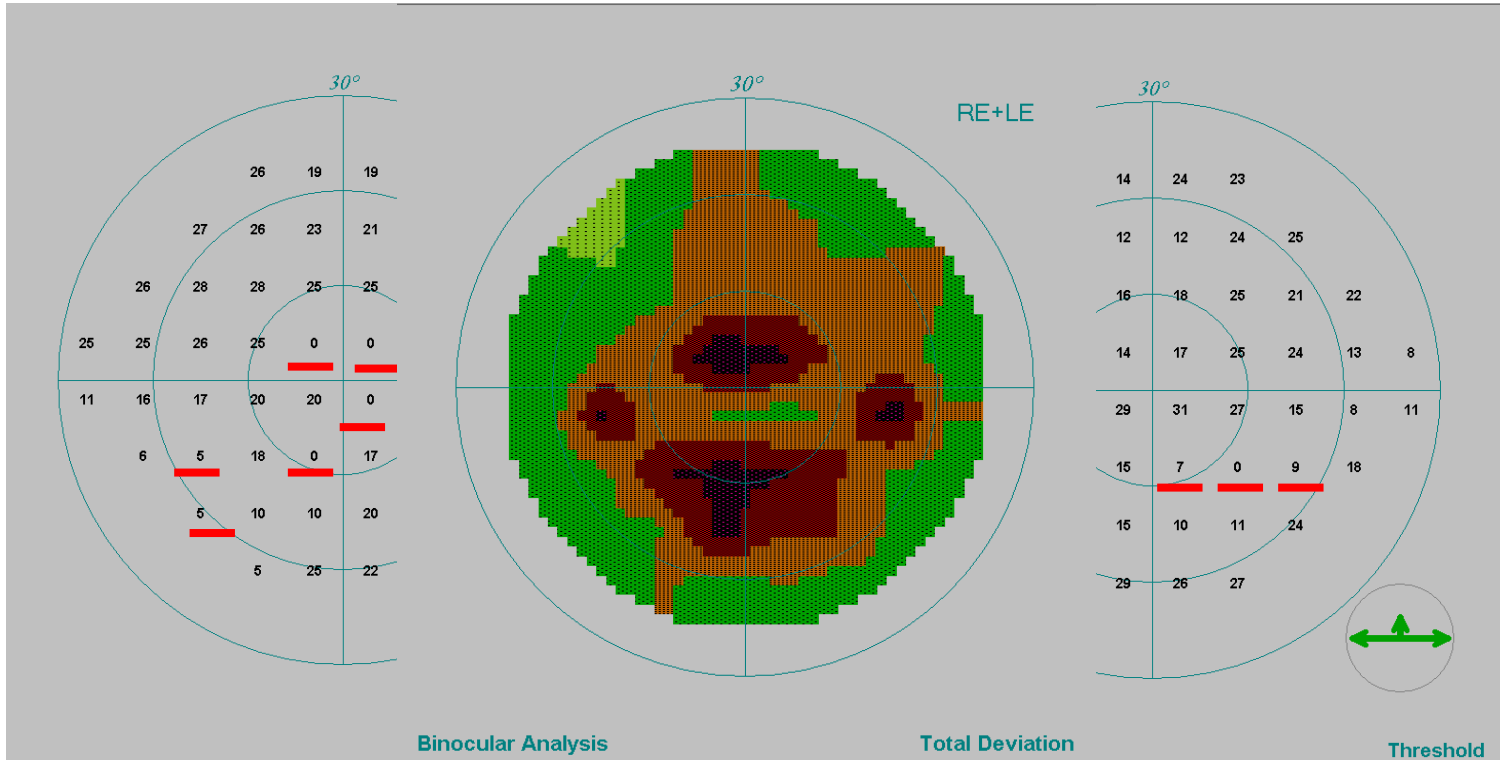
Vision RLE 12/10

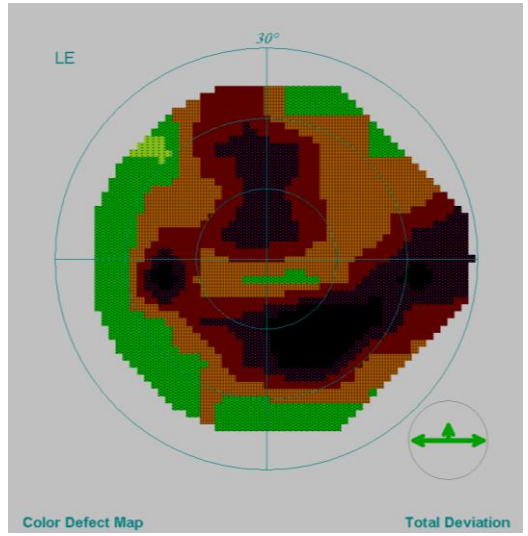




# Repeat visual field (learning curve)



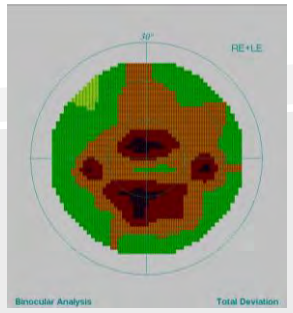

**Not an absolute scotoma**

# Criteria for driving

| | Groep 1: categorie A3, A, B (+E) uitgezonderd bezoldigd en hiermee gelijkgesteld vervoer | Groep 2: categorie C (+E), D (+E), B (+E) alleen bezoldigd of hiermee gelijkgesteld vervoer |
|---|---|---|
| **gezichtsscherpte**<br>1 | met optische correctie | met optische correctie |
| **gezichtsveld**<br>2<br>3 | doorverwijzing naar CARA mogelijk indien voldaan aan gezichtsscherptenorm en mits gunstig advies van oogarts | |
| **schemerzicht** | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) | 5' aanpassing, 1 lux belichting, 5 meter afstand<br>binoculair minstens 2/10<br>bij twijfel: Goldmann adaptometer (max 1 log afwijkend) |

**FIT TO DRIVE A CAR**
**but**
**Inform your patient**
**Follow up the visual field closely**

Male, 56 years old



# Take home message


- Check the visual field for absolute scotomas

- Inform your patient concerning the fitness to drive

- **Patiënt niet meer rijgeschikt: wat moet men doen?**

  De wet bepaalt dat de houder van een Belgisch rijbewijs dit moet inleveren bij het overheidsorgaan dat het heeft afgegeven, hetzij voor kanttekening, hetzij voor intrekking binnen vier dagen na de dag waarop de houder kennis krijgt van het lichaamsgebrek of van de kwaal (zaterdagen, zondagen en wettelijke feestdagen zijn in deze termijn niet inbegrepen).

  Afhankelijk van de verklaringen van de geneesheer, kan de geldigheid van het rijbewijs beperkt worden tot het besturen van motorvoertuigen van bepaalde categorieën of beperkt worden in de geldigheidsduur.

  Als men toch een motorvoertuig bestuurt terwijl men lijdt aan een van de lichaamsgebreken of aandoeningen, dan kan men gestraft worden met een boete van 200 EUR tot 2.000 EUR.

  De houder van een rijbewijs kan de teruggave verkrijgen als hij aan die overheid een attest voorlegt waarin bevestigd wordt dat hij opnieuw geschikt is om een motorvoertuig te besturen van de categorie waarvoor het rijbewijs geldig is.

# Plicht als oogarts

- **Uw formele wettelijke plicht als oogarts:**

  Volgens een advies van de Nat. Raad (d.d. 13.07.2013) heeft men twee opties als men vaststelt dat een patiënt niet langer rijgeschikt is:
  ofwel zelf het **specifieke attest rijgeschiktheid** (model VIII) invullen (men is hiertoe niet verplicht, maar de patiënt heeft wel de vrije keuze om dit te vragen)

- ofwel de patiënt doorverwijzen naar het CARA (Centrum voor Rijgeschiktheid en Voertuigaanpassingen). In dat laatste geval zal het CARA de patiënt verzoeken om een medische vragenlijst door de oogarts te laten invullen.

- De Orde stelt dat door het invullen van het attest model VIII en dit aan de patiënt te overhandigen (of door het doorverwijzen naar CARA) de taak als oogarts volbracht is. Volgens de Orde is het dan uitsluitend aan de patiënt om hieraan de nodige gevolgen te geven, nl. het laten aanpassen van zijn rijbewijs bij de gemeente en het inlichten van zijn autoverzekeraar.

# Informatieplicht

- **Maar ook specifieke informatieplicht**

  De patiënt heeft de plicht zelf zijn rijbewijs te moeten inleveren bij de gemeente maar de oogarts heeft de plicht om hem hierop te wijzen (informatieplicht als men vaststelt dat de patiënt niet meer rijgeschikt is). De oogarts meldt dit best aan de huisarts van de patiënt en laat tevens de patiënt een verklaring ondertekenen waarin staat dat er gewezen is op de risico's van het rijden en dat het zijn plicht is om zijn rijbewijs vrijwillig in te leveren. Weigert hij dit, dan noteert men in het dossier dat men deze informatie verstrekt heeft en dat patiënt weigerde om te tekenen.

- Een typeverklaring patiënt inlevering rijbewijs, **hier het Model**

ManaMa

Dec 3, 2022

2022 Master after Master Course organized by Collegium Ophthalmologicum Belgica

# Closed Angle Glaucoma

Evelien Vandewalle

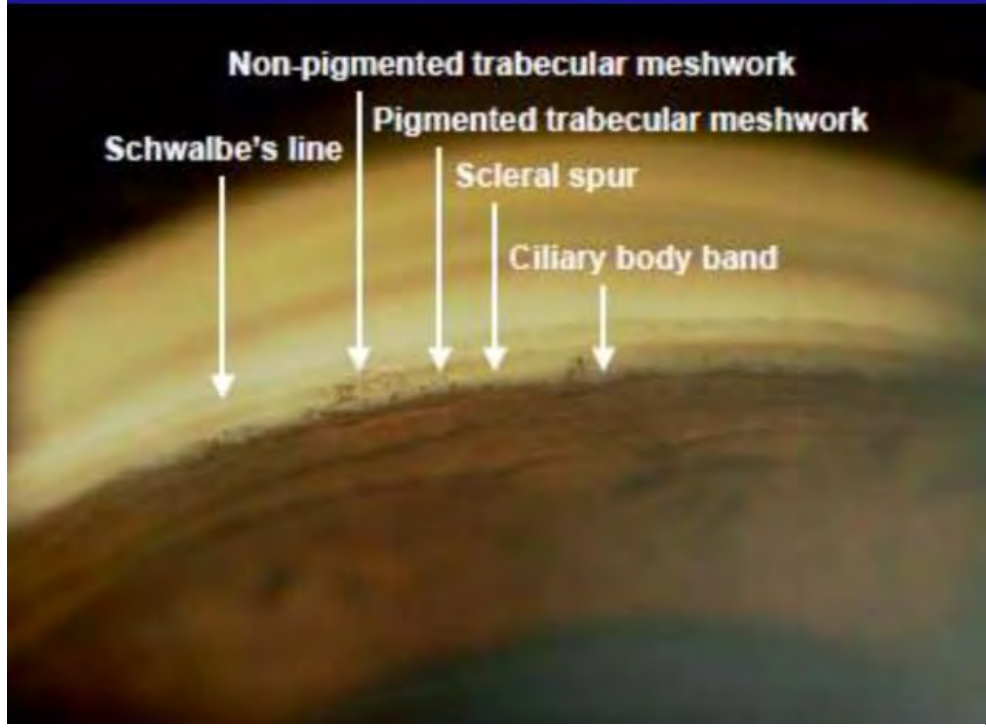
KU LEUVEN

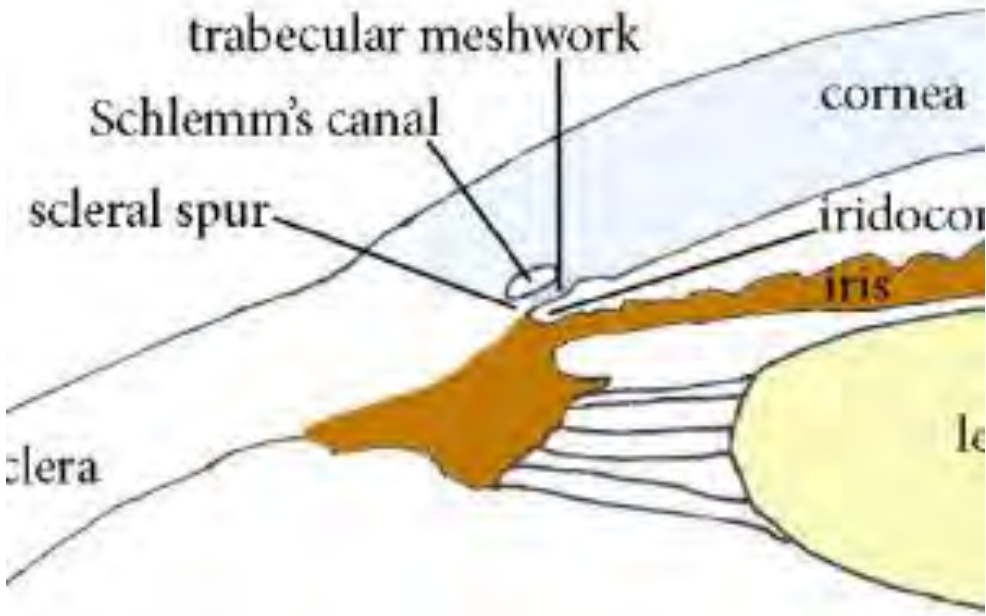
BGG

UZ LEUVEN

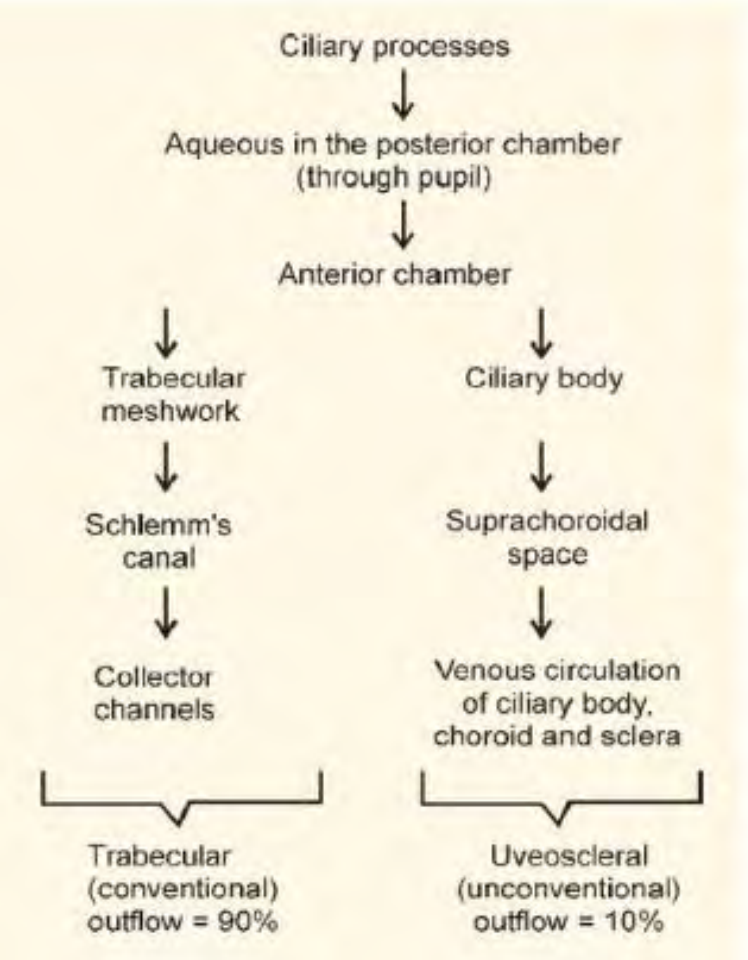
# Angle of Anterior Chamber

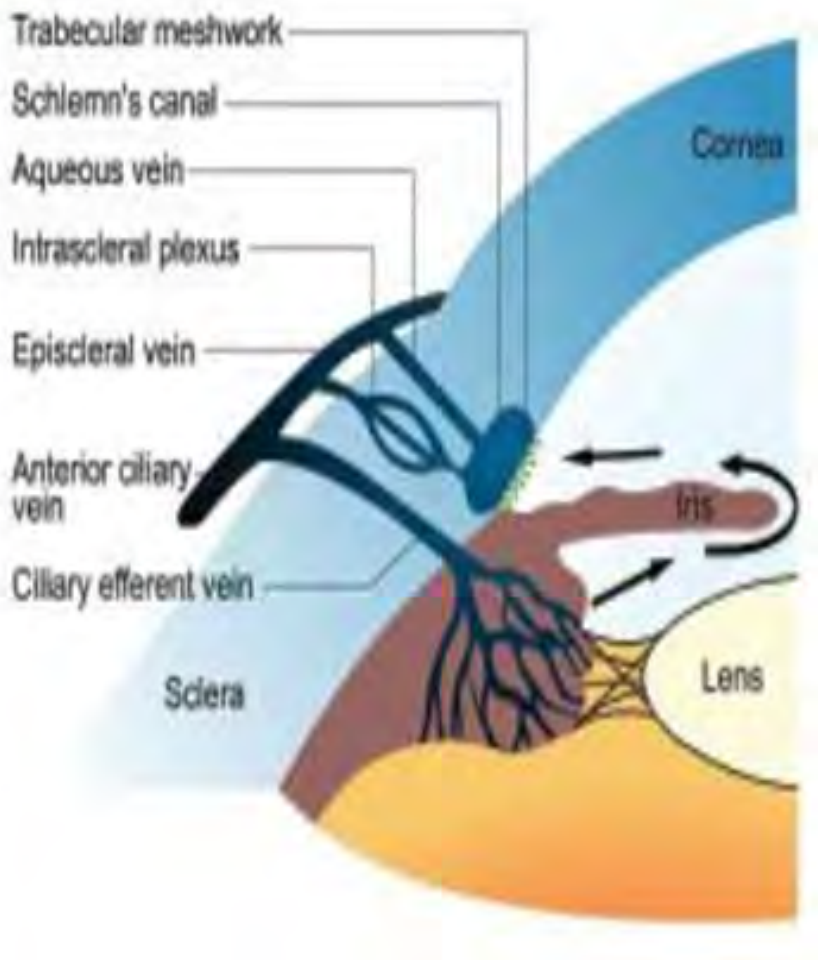
- Iris
- Ciliary body band
- Scleral spur
- Trabecular meshwork
  - Pigmented
  - Non-pigmtented
- Schwalbe’s lines



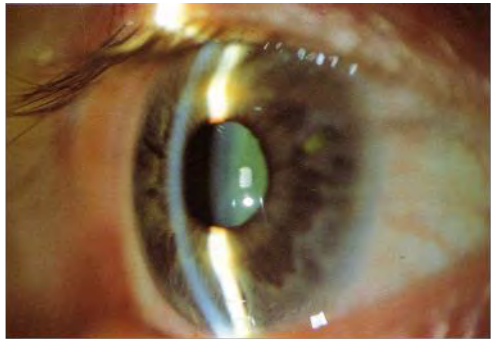
# Drainage of aqueous humor



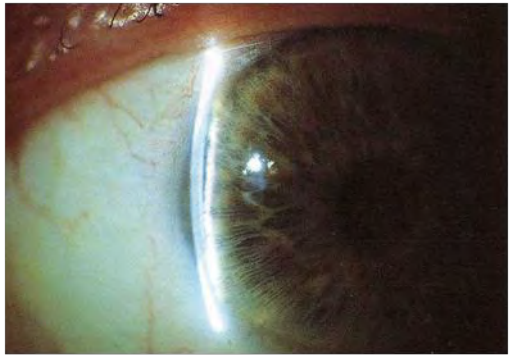



# Grading of the Angle

## Von Hercik test: biomicroscopy



1. Ondiepe voorkamer



2. Von Herick gr 1

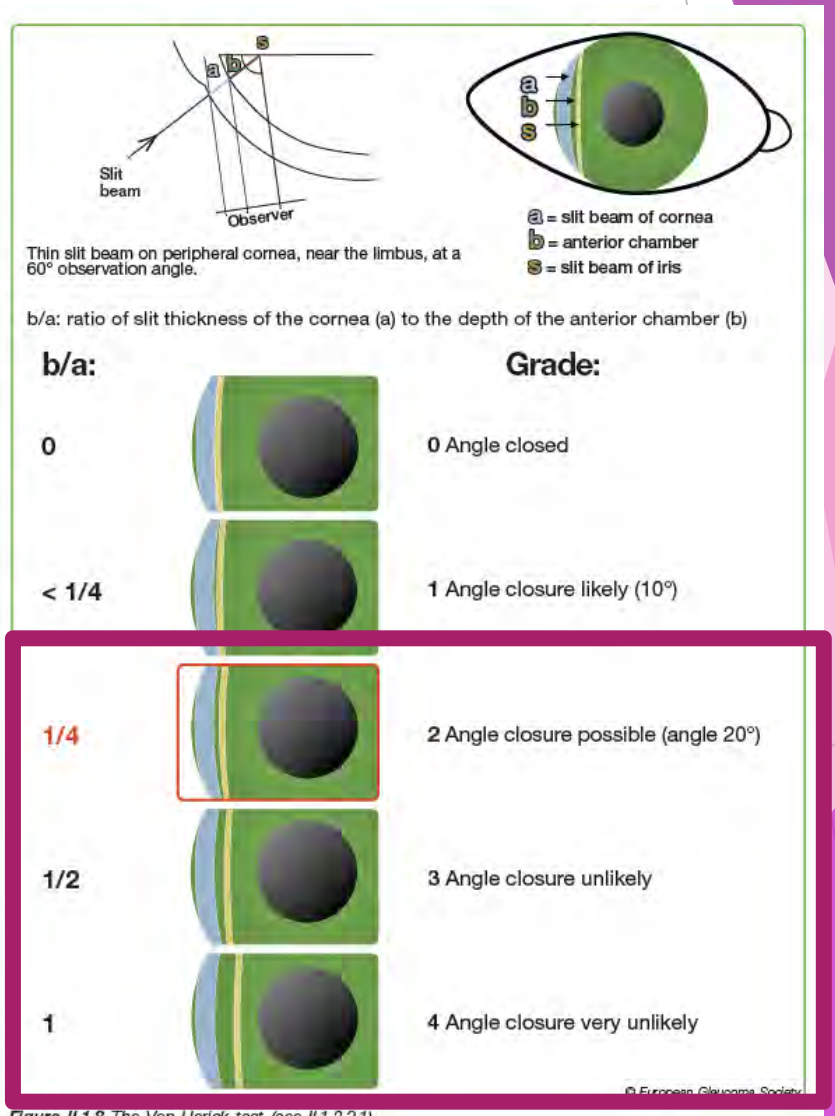



*Figure II.1.8 The Van Herick test (see II.1.2.3.1).*

# Grading of the Angle

tests

- Penlight examination

  the anterior chamber depth can be estimated with oblique penlight illumination across the surface of the iris. With the light coming from the temporal side of the eye, a relatively flat iris is illuminated on the temporal and nasal sides of the pupil, whereas an iris that is bowed forward has a shadow on the nasal side

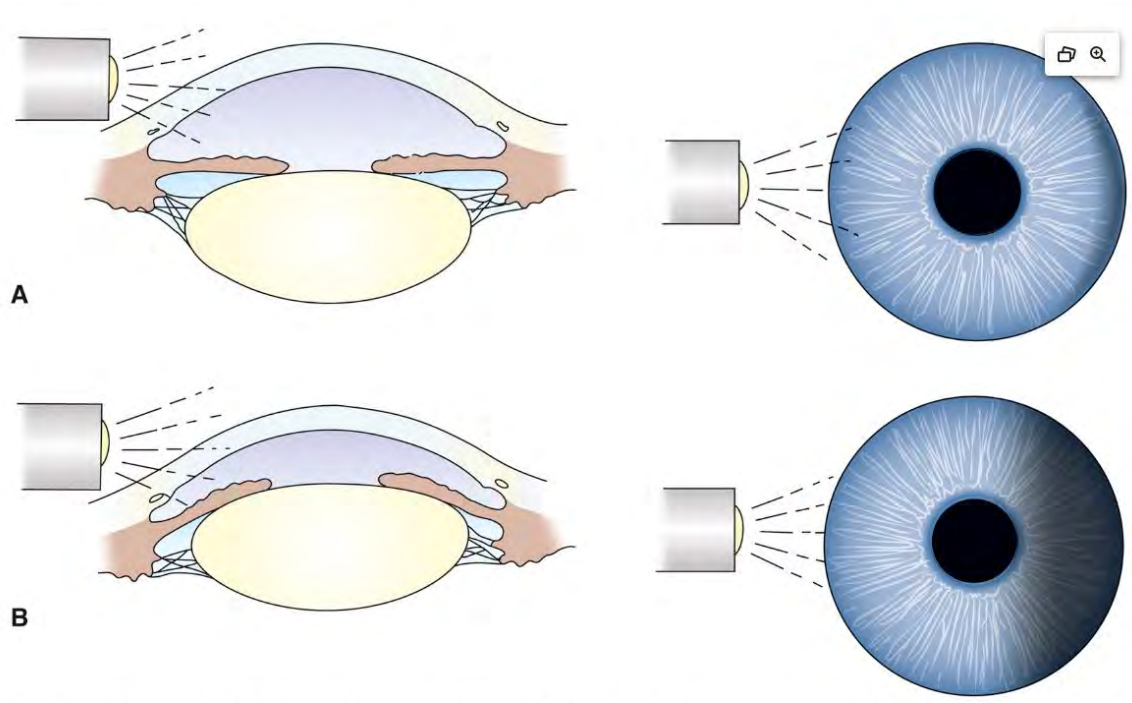
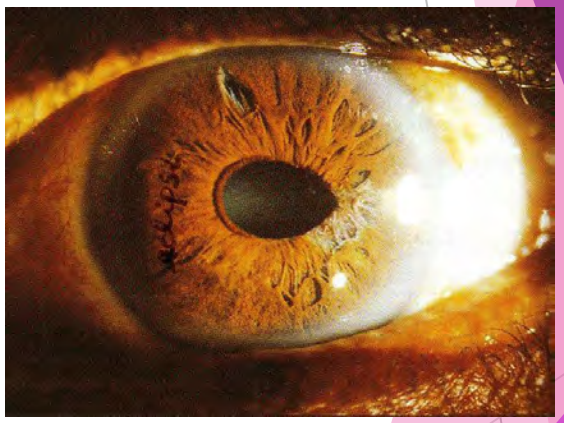



FIGURE 13.3 Penlight examination. Oblique flashlight illumination as a screening measure for estimating the anterior chamber depth. **A:** With a deep chamber, nearly the entire iris is illuminated. **B:** When the iris is bowed forward, only the proximal portion is illuminated, and a shadow is seen in the distal half.



Eclips sign

# Gonioscopic grading of Angle

- Several grading systems: Schaffer's, Spaeth's, Scheie's.

**Table 1.** Shaffer system for grading angle widths.

| Grade number | Angle width | Description | Risk of closure |
|---|---|---|---|
| 4 | 45°–35° | Wide open | Impossible |
| 3 | 35°–20° | Wide open | Impossible |
| 2 | 20° | Narrow | Possible |
| 1 | ≤ 10° | Extremely narrow | Probable |
| Slit | Slit | Narrowed to slit | Probable |
| 0 | 0° | Closed | Closed |

# Angle Closure

## Mechanisms

- **Pupillary block** mechanism (50-75%)
- Anomalies at the level of the **ciliary body** (Plateau iris)
- Anomalies at the level of the **lens** (subluxation, post-traumatic cataract)
- Anomalies **posterior to the lens** (aqueous misdirection, pushing mechanism (tumor, oil, effusion, …))

# Angle Closure

## Precipitating factors for mydriasis

- Dim illumination
- Emotional stress (due to increased sympathetic tone)
- Drugs
  - Mydriatic agents: cyclopentolate, tropicamide, atropine, homatropine,…
  - Anti-psychotica: phenothiazine, anticonvulsants, …
  - Anti-depressants: tricyclic agents, fluoxetine,
  - Anti-parkinson agents
  - Anti-spasmolytics
  - Sympathomimetic agents

# Primary Angle Closure

## Staging

- Primary angle-closure suspects
  - 2 or more quadrants closed angle, normal IOP, no PAS, no GON
- Primary angle closure
  - Angle closure resulting in PAS and/or raised IOP, nog GON
- Primary angle closure glaucoma
  - Causing GON

# Primary Angle Closure Glaucoma

## Epidemiology

- Major cause of glaucoma blindness (25%)
- Age: average age at presenation >40 yr
- Gender: F>M, 4:1
- Race: seen commonly in South-East Asian population, Chinese and Eskimos (0,1%: White European)
- Hereditary: mostly sporadic
- Refractive error: more common in hypermetropia

# Primary Angle Closure Glaucoma

## Ocular risk factors

- Shallow anterior chamber: centrally and peripherally
- Decreased anterior chamber volume
- Short axial length
- Small cornea diameter
- A thick peripheral iris
- Anterior position of the lens with respect of the position of the ciliary body
- Increased curvature of the  anterior surface and thickness of the lens

# Primary Angle Closure Glaucoma

## clinic

- Most patients are asymptomatic
- Some have symptoms during sub-acute episodes
  - Pain
  - Redness
  - Blurring of the vision
  - haloes

**Q14. What is the recommended intervention for primary angle closure disease?**

With the exclusion of eyes with cataract, following an acute attack of angle closure (AAC) or nanophthalmos.
Interventions depend on the spectrum of disease and presence of cataract.
Laser and surgical treatment is typically combined with medical treatment.

*Primary angle closure suspect (PACS):*

Comment: Not all patients with PACS need laser peripheral iridotomy (LPI). Evidence from China suggests that there is a low risk of disease progression without LPI (ZAP trial, see I.7.2.1). No studies in white European eyes.

Recommendation: LPI in high risk individuals, e.g., high hyperopia, patients requiring repeated pupil dilatation for retinal disease or with difficult access to healthcare facilities.
Level of evidence: low
Strength of recommendation: "weak"

*Primary angle closure (PAC) and primary angle closure glaucoma (PACG), for people under 50 years of age:*

Recommendation: LPI
Level of evidence: low
Strength of recommendation: "strong"

*PAC and PACG, for people over 50 years of age:*

Comment: Lens extraction is associated with better clinical and QoL outcomes (EAGLE trial, see I.7.4.1), but risk considerations need to be individualised.
Recommendation: lens extraction or LPI
Level of evidence: moderate (one good quality trial, EAGLE)
Strength of recommendation: strong

**Q16. Glaucoma surgery for PACG (after interventions for widening the anterior chamber angle have been done)?**

Interventions depend on the lens status and glaucoma severity.

*Pseudophakic with PACG:*

Recommendation: filtration surgery (trabeculectomy)
Level of evidence: very low
Strength of recommendation: strong

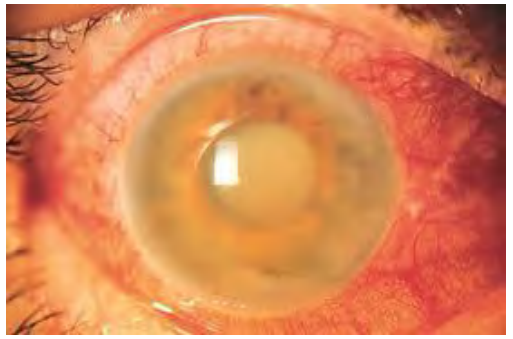
*Phakic with PACG:*

Recommendation: phacoemulsification alone or combined phacoemulsification + glaucoma surgery
Level of evidence: very low
Strength of recommendation: strong

Comment: In patients with severe glaucoma phaco-trabeculectomy may be advisable.

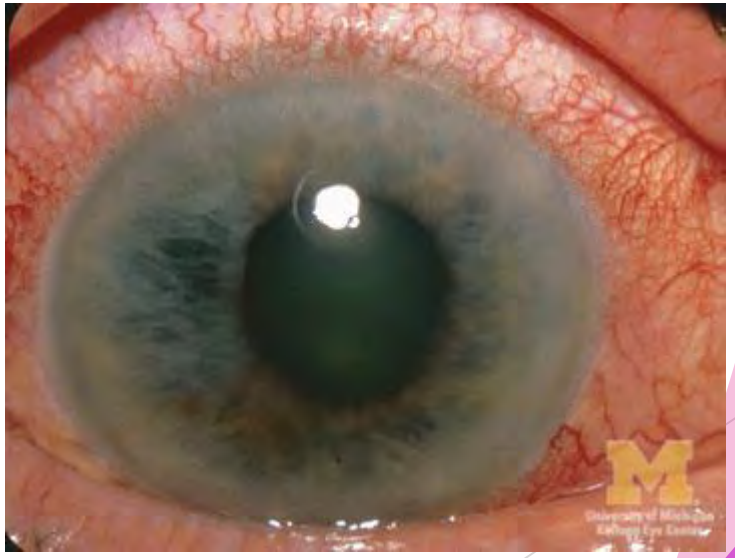
# Acute Angle Closure Glaucoma

clinic



- Prodomes
  - Halo’s around the lights
  - Intermittent headache and transient blurring of vision
  - Ocular discomfort or frontal headache

- Acute attack
  - Ocular pain, frontal headache
  - Decreased visual acuity
  - Vagal systemic symptoms: nausia, vomiting, …
  - High IOP above 40 mmHg
  - Corneal oedema
  - Shallow or flat anterior chamber
  - Venous congestion and ciliary injection
  - Pupil mid-dilated and reduced or no reactivity to light



# Acute Angle Closure Glaucoma

## Protocol acuut glaucoom

- D/ **Gonio**: hoek gesloten

➔ Pilo kuur aangedane oog: pilocarpine 2% elke 5 min gedurende eerste kwartier, erna elk kwartier gedurende eerste uur

➔ Contralaterale oog: pilocarpine 2% 3x/d tot patente YAG IT

➔ Als *heldere cornea*: YAG IT aangedane oog + contra zodra mogelijk

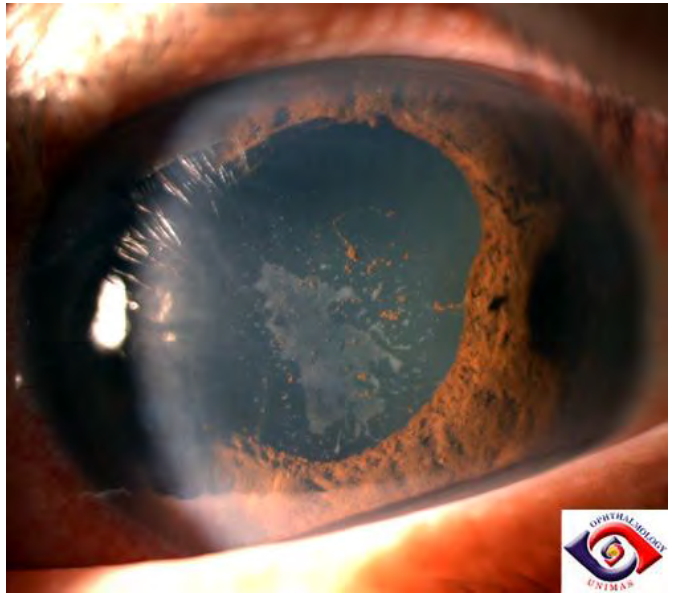
➔ Als *cornea-oedeem* YAG IT onmogelijk maakt:
- o Mannitol IV 15%
  - 500cc over 30 min indien patiënt < 70 jaar en geen comorbiditeiten
  - 200cc over 20 min indien patiënt ≥ 70 jaar en/of comorbiditeiten (CAVE hartfalen, nierproblemen, dehydratatie, actieve intracraniale bloeding/ernstig hoofdletsel)
- o Diamox 500mg IV shot
  Erna Diamox 250mg PO 4x/d (max 1g/d) (CAVE hartfalen, nierproblemen)
- o Litican 1 ampule IV i.g.v. nausea

➔ Nabehandeling:
- o Pilo 3x/d ipsi voor 2 weken, stop contra zodra patente YAG IT
- o DXM 4x/d ODS
- o Diamox 250mg 4x/d PO tot drukdaling
- o Evt start CAI/T combinatie (bv. Azarga) indien onvoldoende drukdaling

# Acute Angle Closure Glaucoma

Status post-acute angle closure attack

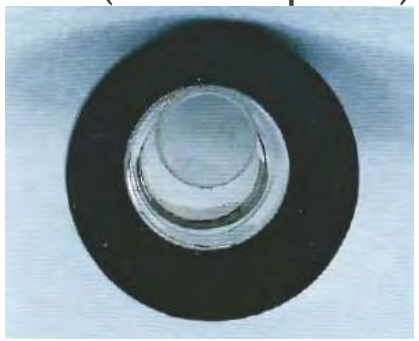
- Patchy iris atrophy
- Posterior synechiae
- Peripheral anterior synechiae
- Pupil either poorly reactive or non-reactieve
- Glaucoomflecken on the lens
- Sectoral/generalized iris atrophy
- Optic nerve cupping or/and palor

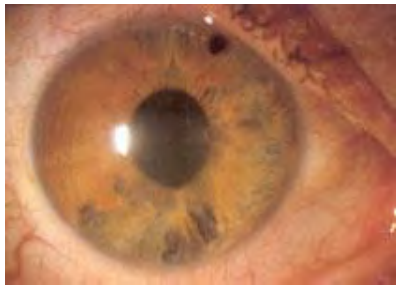


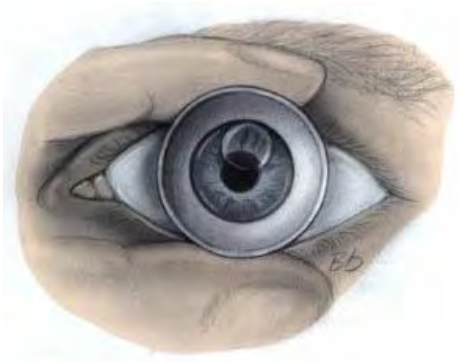
# Acute Angle Closure Glaucoma

Laser iridotomy: technique

- Contact lens
  - Abraham (+ 66 dioptres)







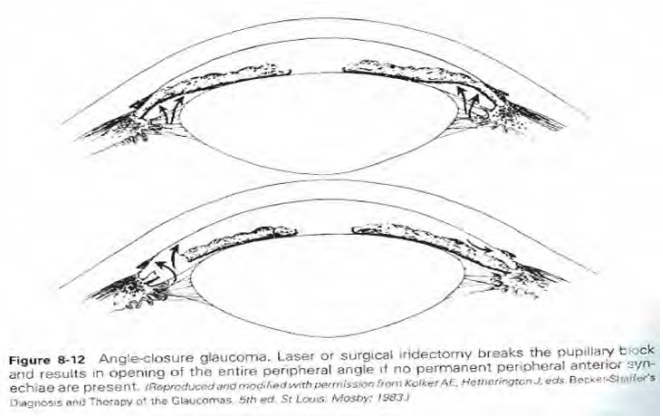
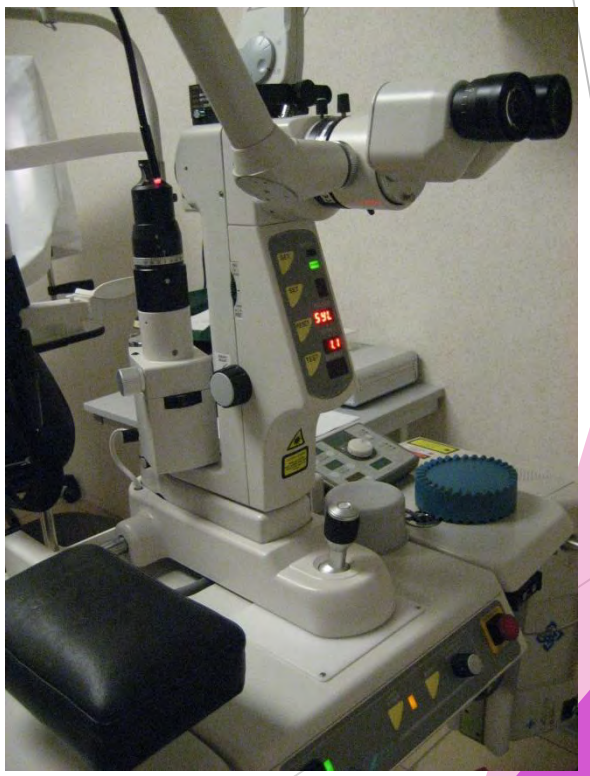
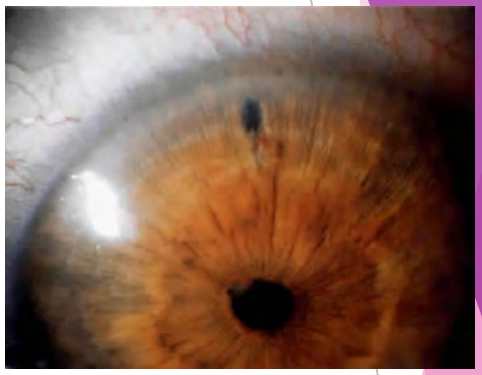


**Figure 8-12** Angle-closure glaucoma. Laser or surgical iridectomy breaks the pupillary block and results in opening of the entire peripheral angle if no permanent peripheral anterior synechiae are present. *(Reproduced and modified with permission from Kolker AE, Hetherington J, eds. Becker-Shaffer's Diagnosis and Therapy of the Glaucomas. 5th ed. St Louis: Mosby; 1983.)*



# Acute Angle Closure Glaucoma

## Laser iridotomy: technique



- 1. drop of apraclonidine 1% (Iopidine®) is instilled
- 2. drop of topical pilocarpine, pupil is ideally miosed
  - Wait 20-30 minutes
- 3. drop of anesthetic (Unicaïne®) is instilled
- 4. a special contact lens such as the Abraham iridotomy is inserted
- 5. site is selected
  - preferably in the superior iris, so that is covered by the eyelids thus preventing monocular diplopia
  - As peripheral as possible to minimize damage to the crystalline lens
  - Iris crypt is beneficial
- 6. beam is angled so that it is non-perpendicular and aimed towards the peripheral retina to avoid the remote of macular burn
- 7. laser settings Nd:YAG
  - Energy: 2.5-4 millijoules per shot
  - Thin blue iris: 1-3 millijoules
  - Brown, thick irides: need higher energy

# Acute Angle Closure Glaucoma

## Laser iridotomy: technique

- 9. laser is fired: pentration is characterized by a gush of pigment debris
- 10. NSAID (Dicloabak®) 4x for a week
- 11. Follow-up: 1-4 weeks afterwards to verify for patency

## Laser iridotomy: failures

- 1. initial failure
  - managed by re-treating the same site
  - moving to different site and increasing energy level
- 2. opening too small
  - sometimes easier to create an additional opening at different site rather than retry
  - ideal diameters is 150 – 200 µm

# Acute Angle Closure Glaucoma

## Laser iridotomy: complications

- Temporary blurring of the vision
- corneal epithelial and/ or endothelial burns
- Intraoperative bleeding, usually controlled by a gentle pressure applied to the eye with the contact lens
- Transient elevation of IOP
- Postoperative inflammation
- Posterior synechiae
- Late closure of the iridotomy
- Localised lens opacities
- Rare complications: retinal damage, cystoid macular edema, sterile hypopion, malignant glaucoma

# Acute Angle Closure Glaucoma

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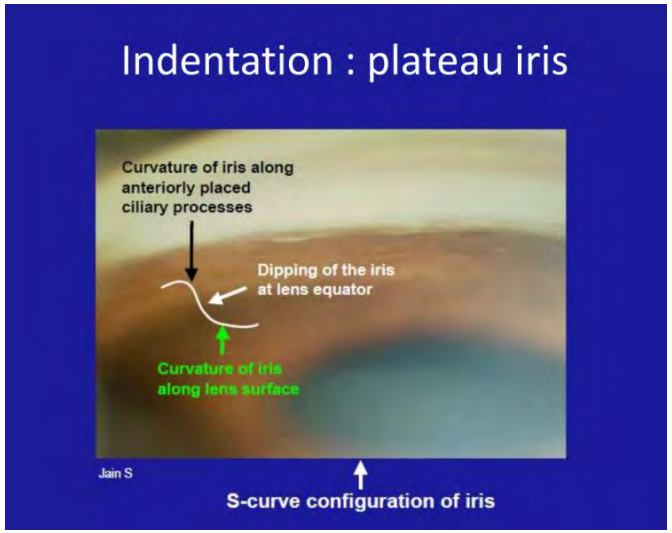
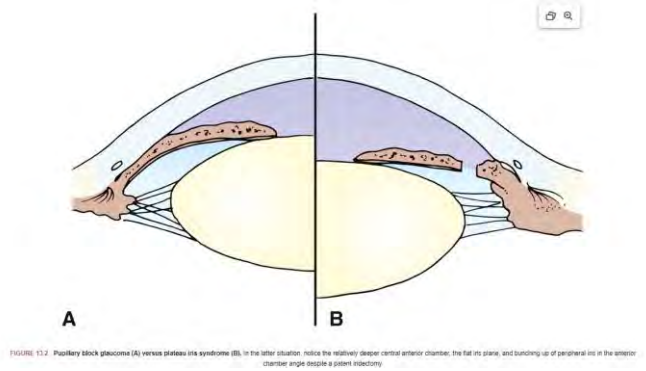



# Plateau iris

- Anterior placed ciliary processes
- Anterior chamber depth is not shallow centrally
- Iris profile is flat
- Gonioscopy: double hump sign is observed

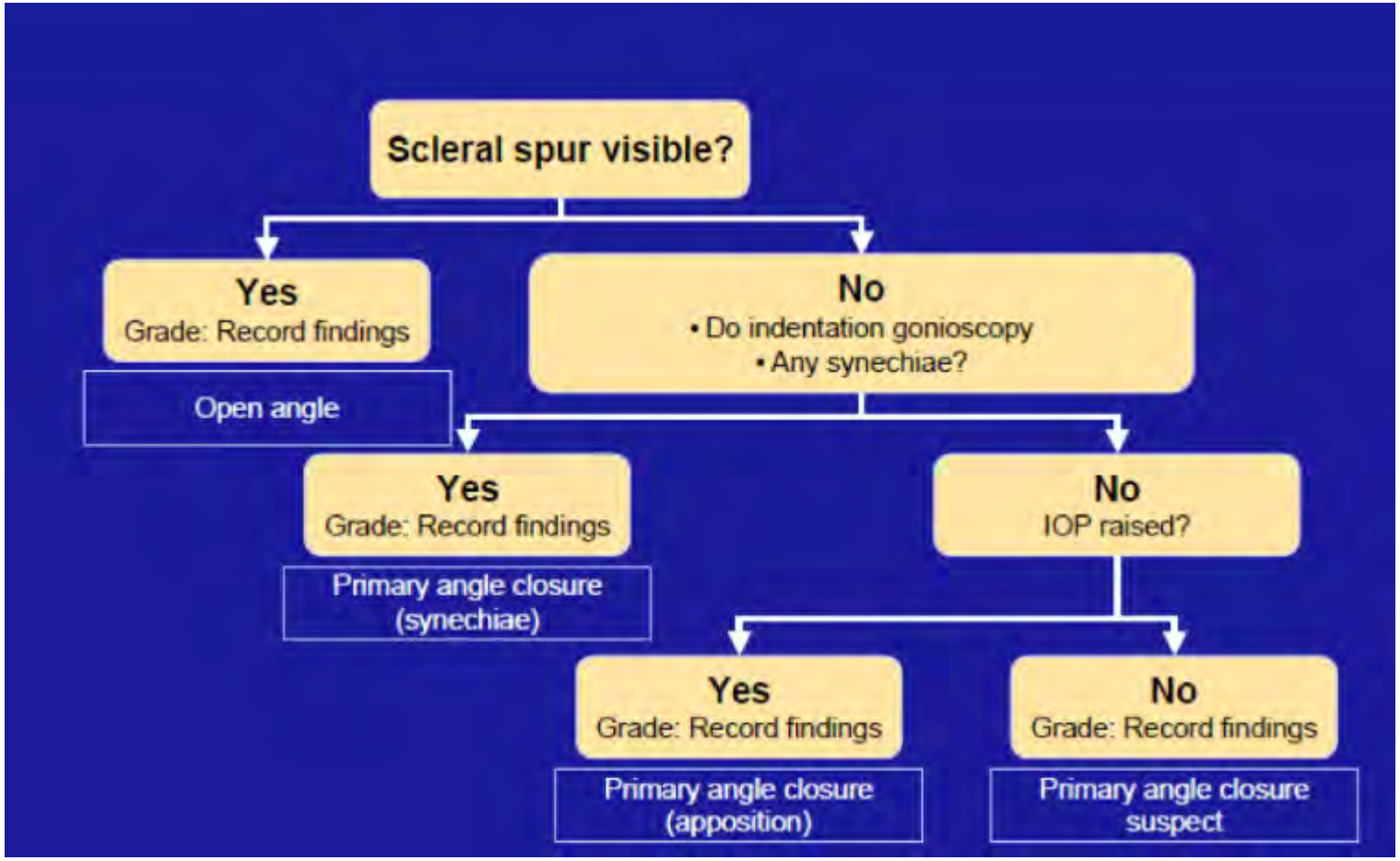
- Iris profile angulates sharply in the periphery, but no irido-trabecular contact is present

  -> **Plateau iris configuration**




- Post-laser iridotomy condition in which a patent peripheral iridotomy had removed pupillary block but gonioscopically appositional angle closure persists

  -> **Plateau iris syndrome**

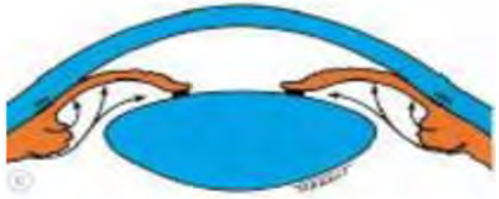

Scleral spur visible?
Yes
Grade: Record findings
Open angle
No
• Do indentation gonioscopy
• Any synechiae?
Yes
Grade: Record findings
Primary angle closure (synechiae)
No
IOP raised?
Yes
Grade: Record findings
Primary angle closure (apposition)
No
Grade: Record findings
Primary angle closure suspect

# Mechanism of Pupillary block

- Relative Pupillary block
- Normally the pressure in the post. chamber exceeds that in the anterior chamber due to physiological degree of resistance at the pupil ,since the iris rests posteriorly on the anterior lens capsule.

## Iridocorneal contact

Eventually the iris touches the posterior corneal surface, obstructing the angle and the IOP rises.

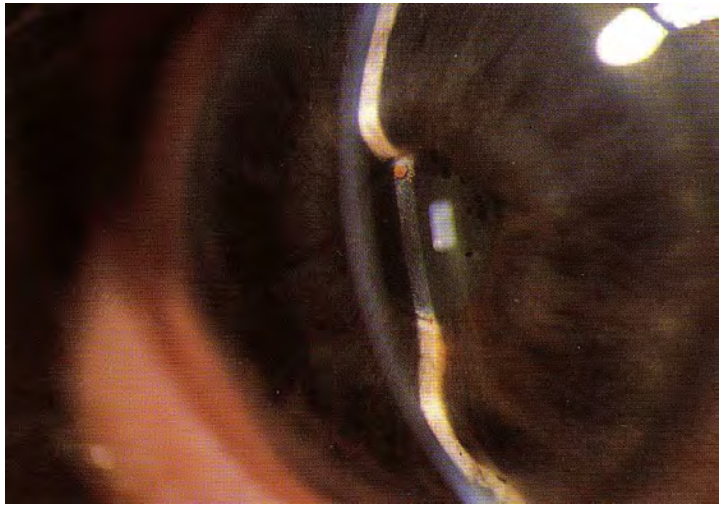


## Anterior Iris Bowing

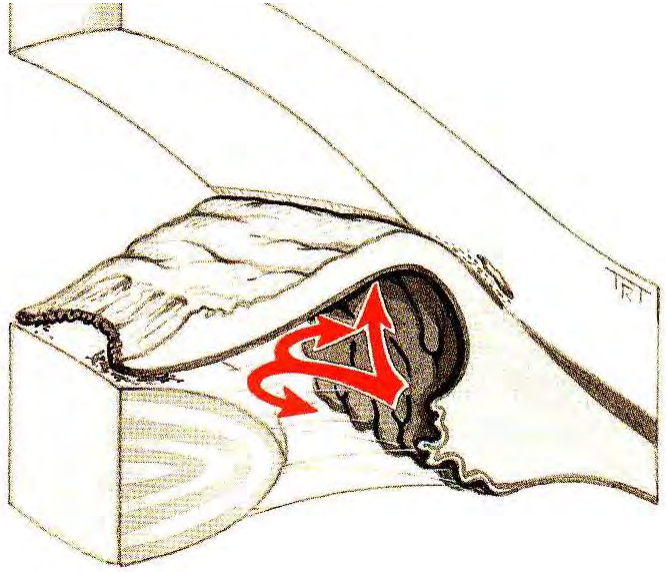
Simultaneous dilatation of the pupil renders the peripheral iris more flaccid. The pupil block causes the pressure in the Posterior Chamber to increase & peripheral iris bows anteriorly

# Seconday Angle Closure Glaucoma

Pupillary block



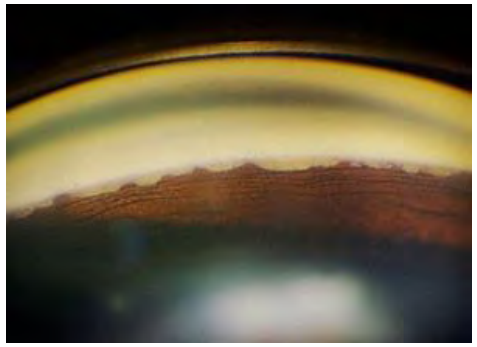
Iris bombans
pupilseclusion



iridotomy

# Seconday Angle Closure Glaucoma

Gonio synechiae



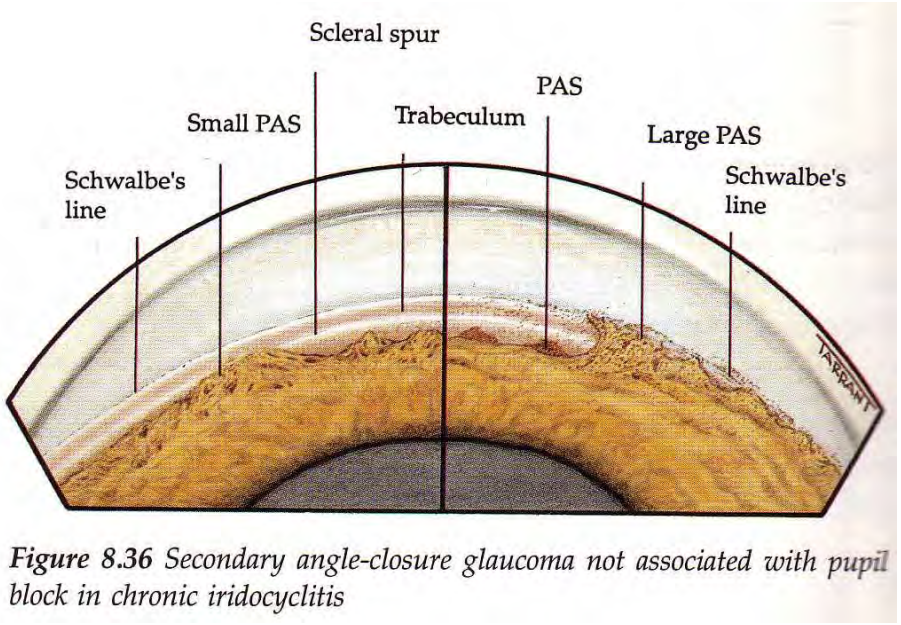
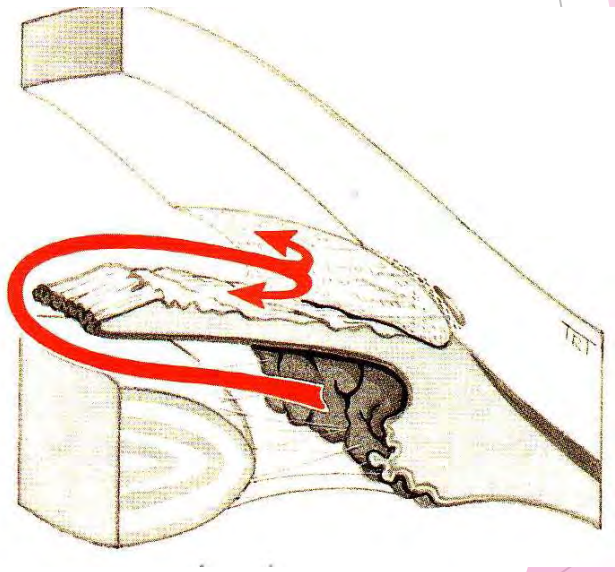



*Figure 8.36 Secondary angle-closure glaucoma not associated with pupil block in chronic iridocyclitis*



No iridotomy


Thank you

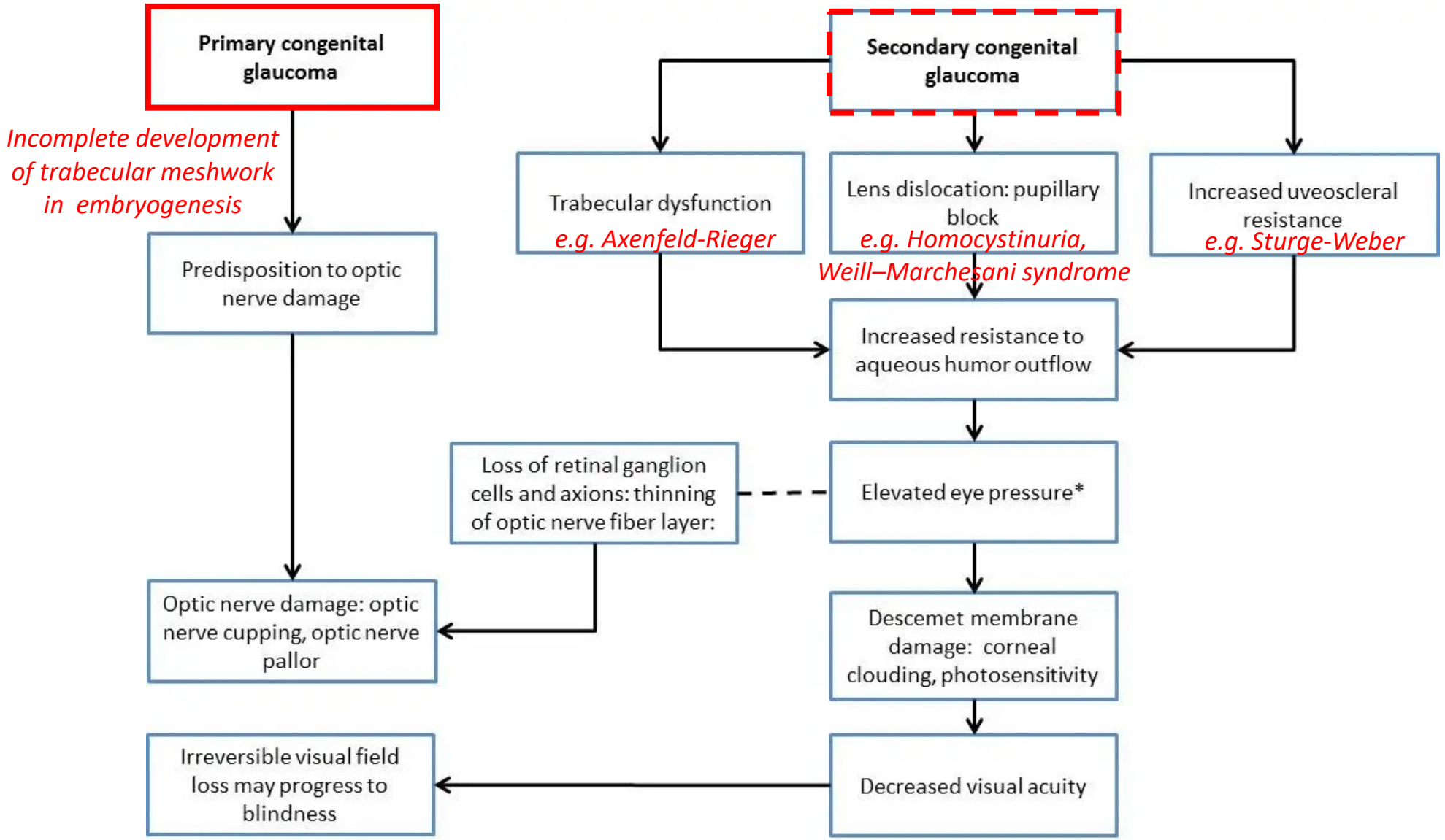
# Congenital glaucoma

Sophie Lemmens

UZ Leuven – KU Leuven

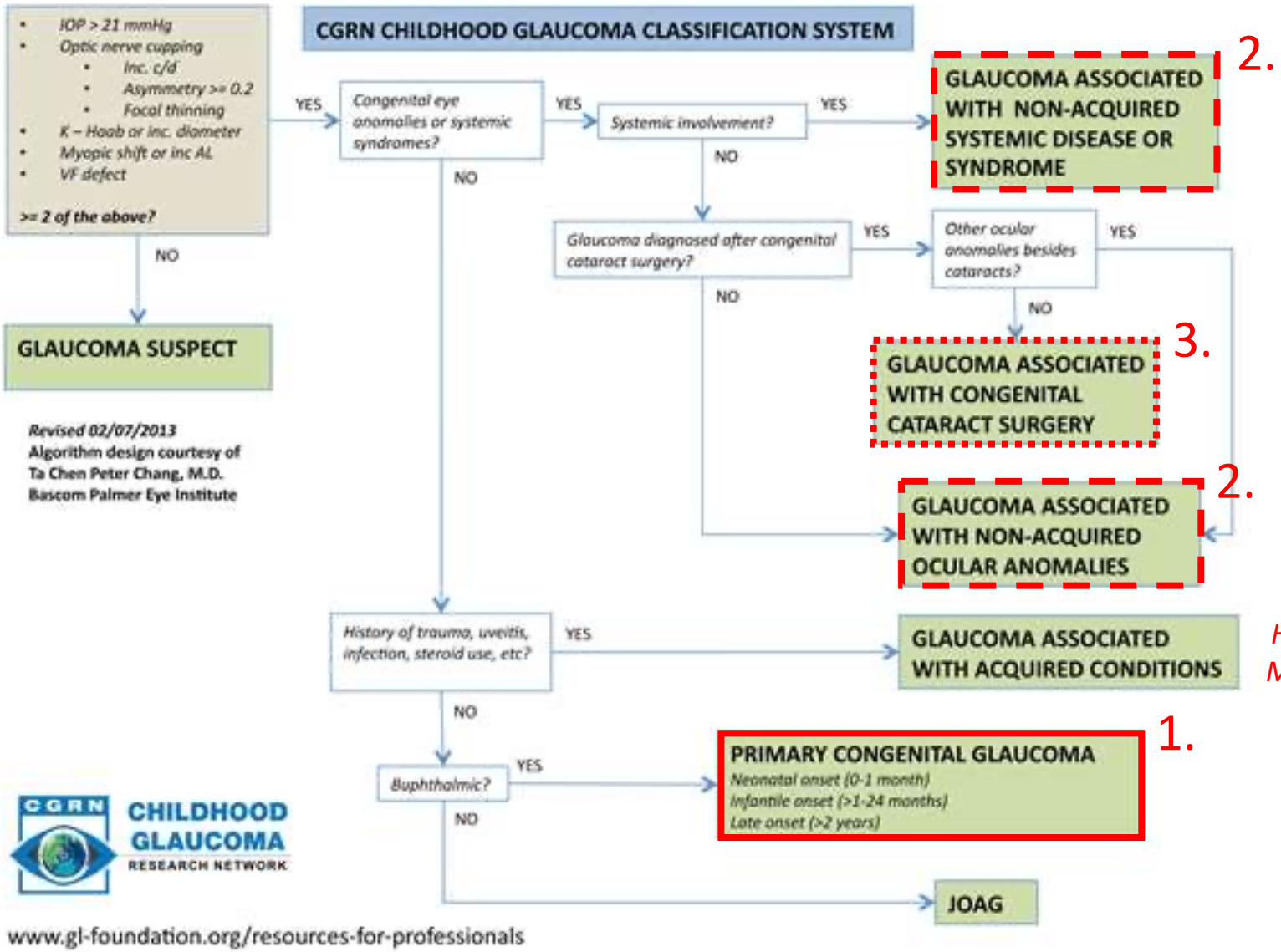
*ManaMa Glaucoma 03/12/2022 – CHU Liège*

*No financial disclosures*




* There is a relationship between nerve damage and elevated eye pressure but a physiologic cause has not been established.

# Classification of childhood glaucomas




*Congenital rubella*
*Herpes simplex iridocyclitis*
*Maternal use of topiramate*
*Fetal alcohol syndrome*
*…*

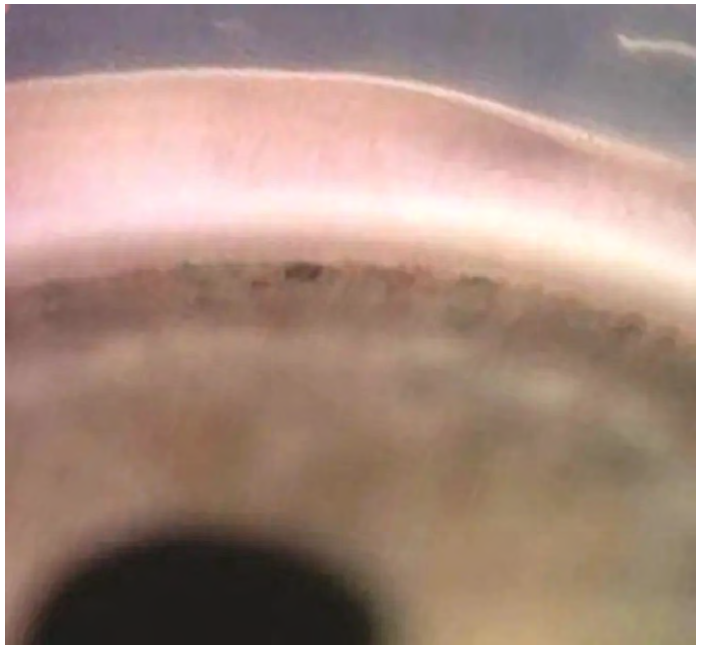
# 1. Primary congenital glaucoma

# Primary congenital glaucoma

- W/o consistent association  with other ocular or systemic anomalies
  - Newborn (0-1m) – 40%
  - Infantile (1-24m) – 50%
  - Late (>24m) – 10%
- Anteriorly inserted iris, maldeveloped angle & trabecular meshwork

## Demographics

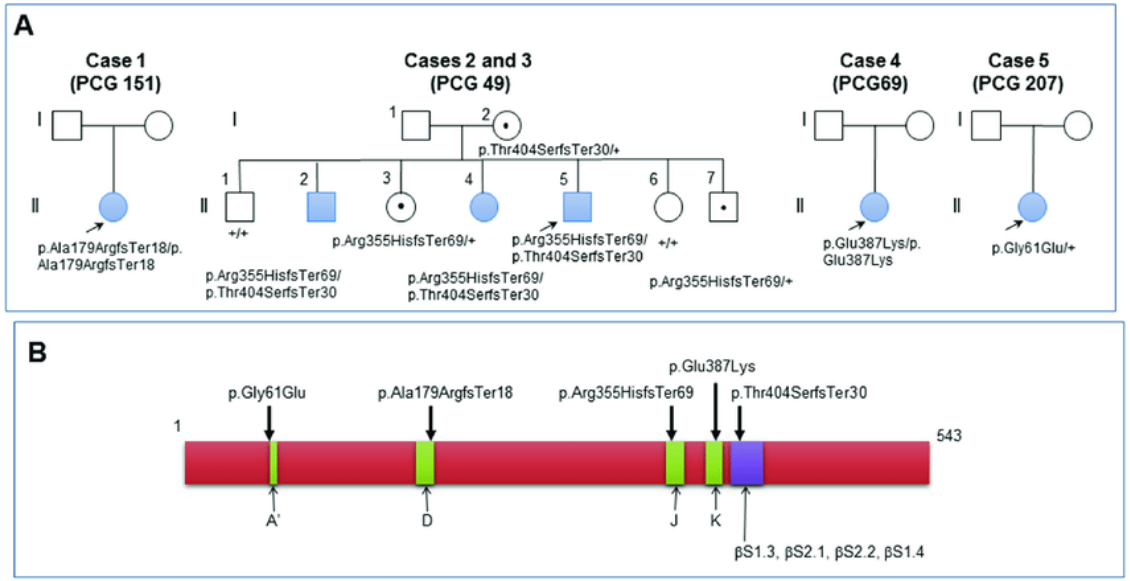
- 1/10.000 – 1/20.000 in Western countries
  - Middle-East, Roma population of Slovakia (consanguinity!)
- 75% bilateral
- M > F
- D/ in >75% in first year of life



# Primary congenital glaucoma

## Heredity

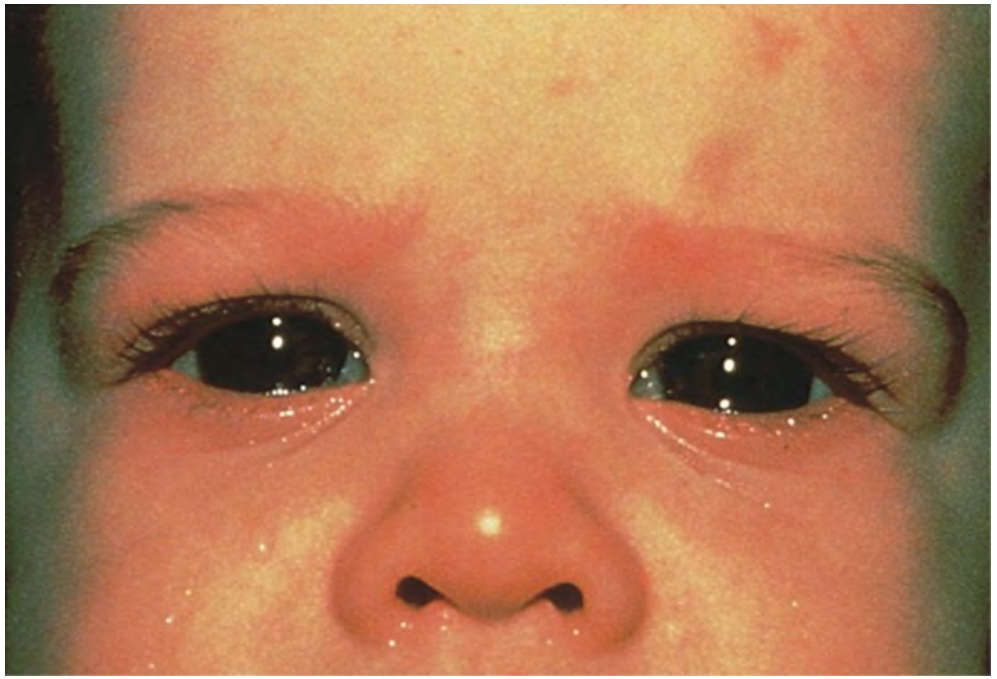
- Mostly **sporadic**
  - If familial: AR inheritance → consanguinity
  - CYP1B1, LTBP2, TEK
  - MYOC → JOAG, COAG
- Importance of screening of siblings



# Primary congenital glaucoma

## Clinical features

- History
  - Appearance of the eyes, behavior (fussy, eye rubbing)
  - Corneal opacification & enlargement
  - Classical triad
    - Epiphora
    - Photophobia
    - Blepharospasm



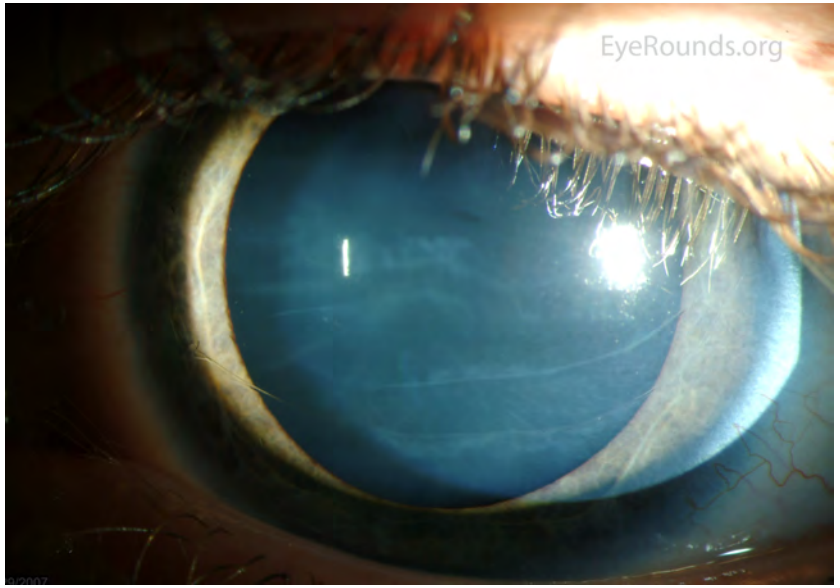
# Primary congenital glaucoma

- External examination
  - Corneal diameter & edema → Haab striae
  - Refractive error
    - Globe enlargement
      → myopic shift
      → amblyopia (asymmetry, astigmatism)
  - Tonometry = challenge
    - Usually 30-40 mmHg
    - Under anesthesia?
  - Slitlamp
    - Haab striae
      (in 25% of newborn PCG, in >60% of PCG D/ at 6m)
    - Deep AC, typically nml iris
  - Gonioscopy
    - Anterior iris insertion
    - Indistinct angle structures

**Table 13.3** Corneal Diameter in Children: Healthy and Glaucomatous Eyes[a]

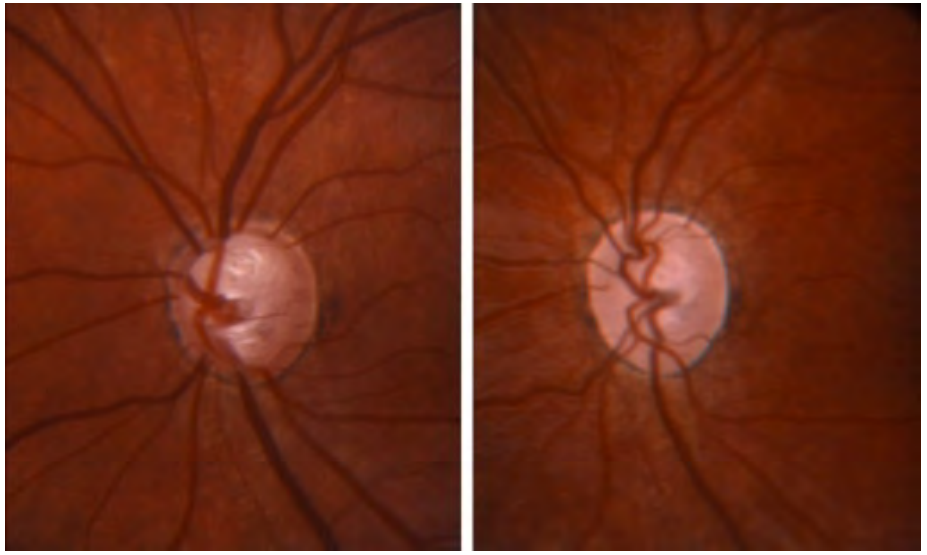
| Age | Corneal Diameter, *mm* | |
|---|---|---|
| | Normal | Suspicious for Possible Glaucoma |
| Birth–6 mo | 9.5–11.5 | >12 |
| 1–2 y | 10–12 | >12.5 |
| >2 y | <12 | >13 |

[a]Data are from Refs. 9 and 10.



# Primary congenital glaucoma

- Funduscopy
  - C/D (reversibility)
  - Asymmetry
- VF (> 8-9y)
- VA (cave amblyopia)
- Ultrasonography
  - AXL (reversibility)
- Pachymetry (rather low CCT in PCG)
- OCT

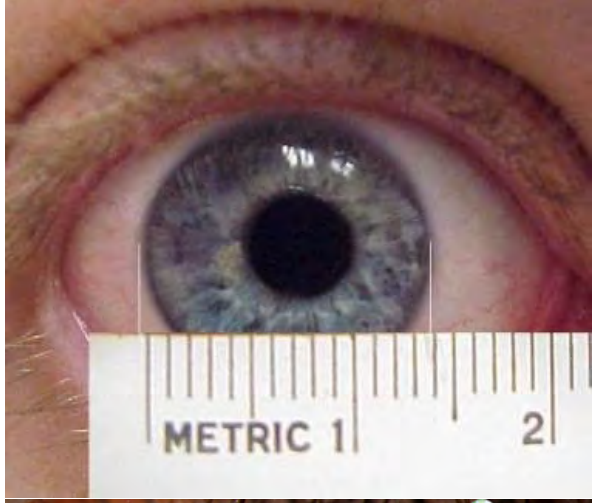


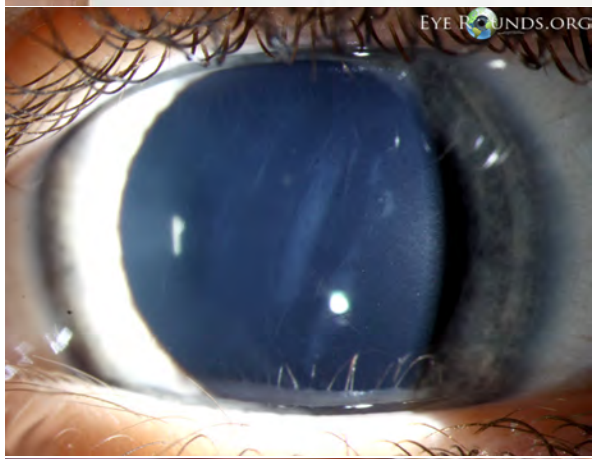
| Age group | Mean axial length (mm) | SD (mm) | *n* | 95%CI | |
|---|---|---|---|---|---|
| | | | | Lower bound | Upper bound |
| 3-6mo | 19.7643 | 0.62340 | 14 | 19.370 | 20.159 |
| 6-8mo | 20.0956 | 1.06732 | 18 | 19.748 | 20.443 |
| 9-12mo | 20.5692 | 0.90544 | 26 | 20.280 | 20.859 |
| 13-15mo | 20.7317 | 0.88479 | 24 | 20.430 | 21.033 |
| 16-18mo | 21.3114 | 0.87441 | 14 | 20.917 | 21.706 |
| 19-21mo | 21.0700 | 0.70120 | 20 | 20.740 | 21.400 |
| 22-24mo | 20.8144 | 0.56548 | 16 | 20.445 | 21.183 |
| 25-3y | 21.4499 | 0.69585 | 72 | 21.276 | 21.624 |
| 4-5y | 22.0354 | 0.67873 | 108 | 21.893 | 22.177 |
| 6-7y | 22.4156 | 0.75723 | 18 | 22.068 | 22.763 |
| Total | 21.3675 | 1.02690 | 330 | - | - |

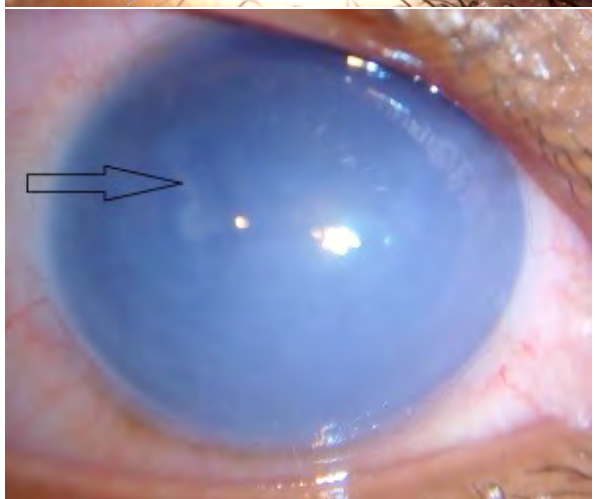
# Primary congenital glaucoma

## Differential diagnosis

- Excessive tearing
- Corneal disorders
  - Large corneas
  - Tears in Descemet membrane
  - Corneal opacification
- Other glaucomas of childhood



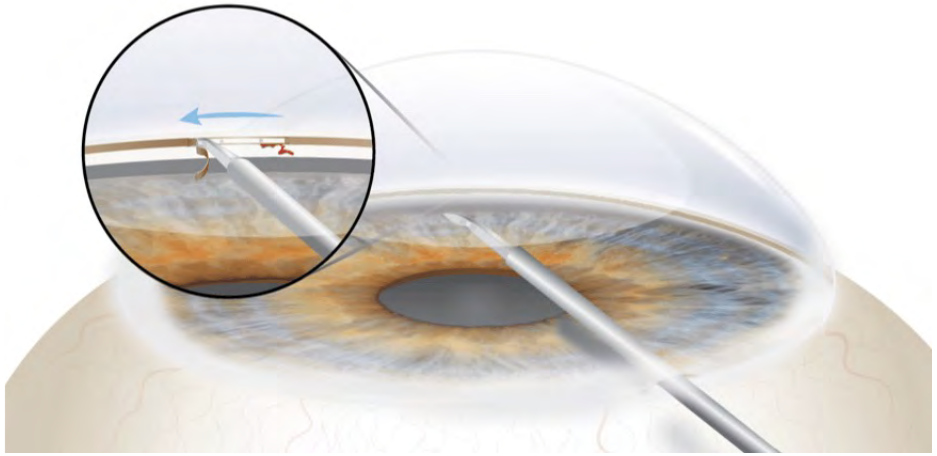





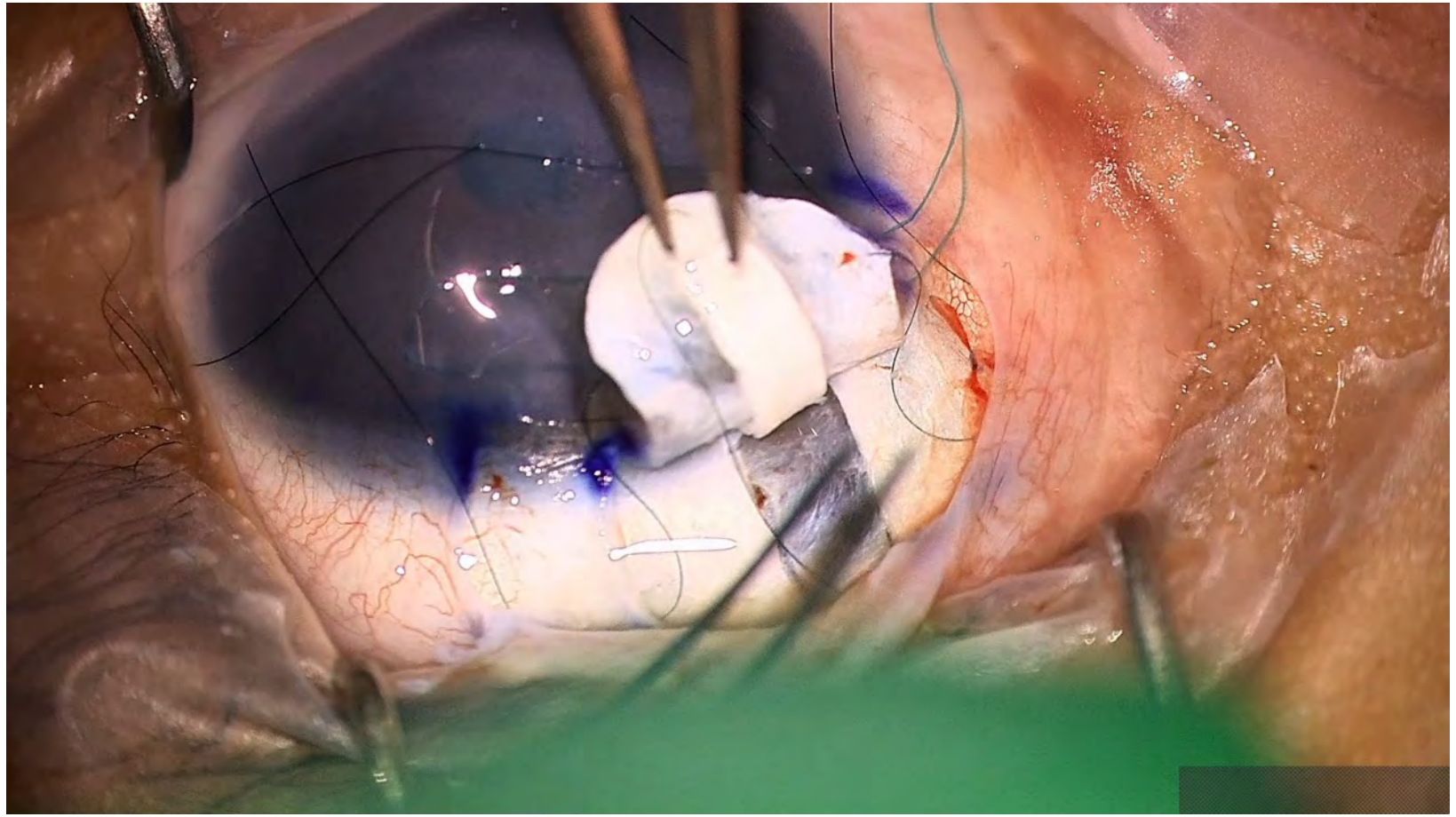
# Primary congenital glaucoma

## Management

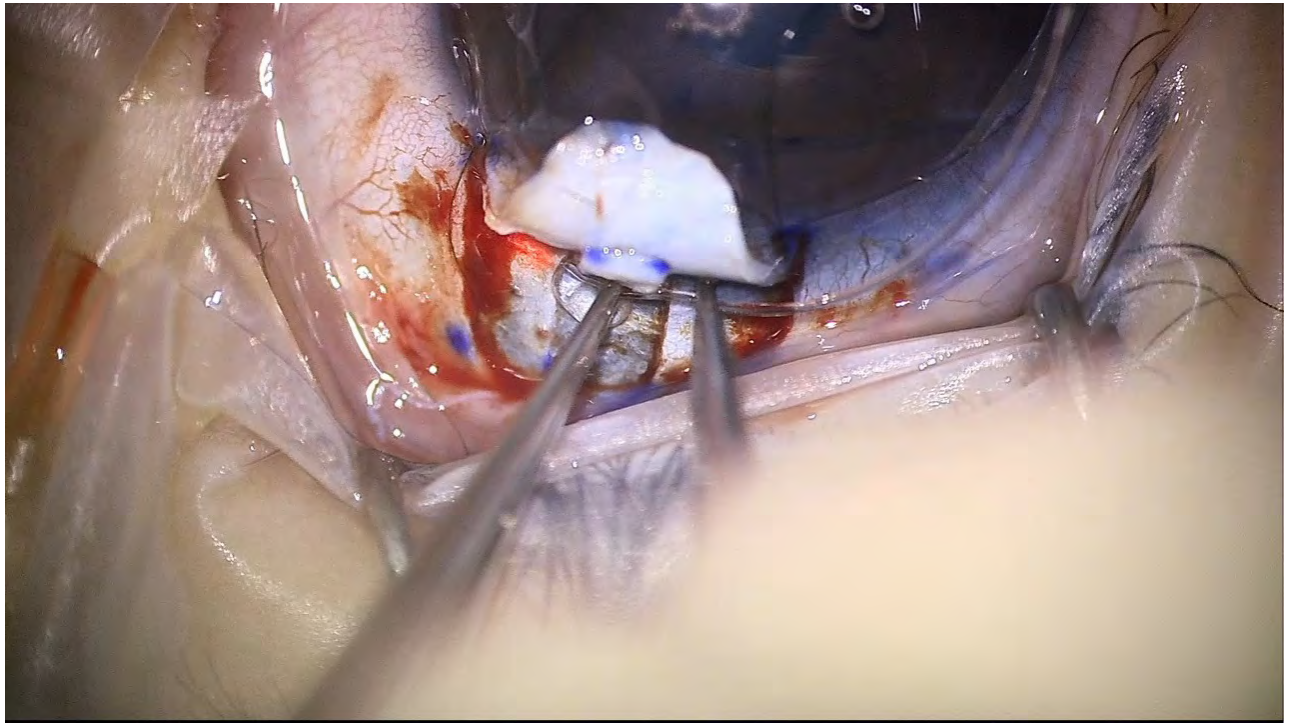
- Medical therapy ≠ definitive
- Surgical therapy
  - **Angle surgery**
    - Goniotomy = ab interno (requires clear cornea)
    - Trabeculotomy = ab externo
      - 180°
      - 360°
    - Most favorable outcome when performed at age 2-12m (infantile-onset)
  - Filtration surgery, GDD, cyclodestruction

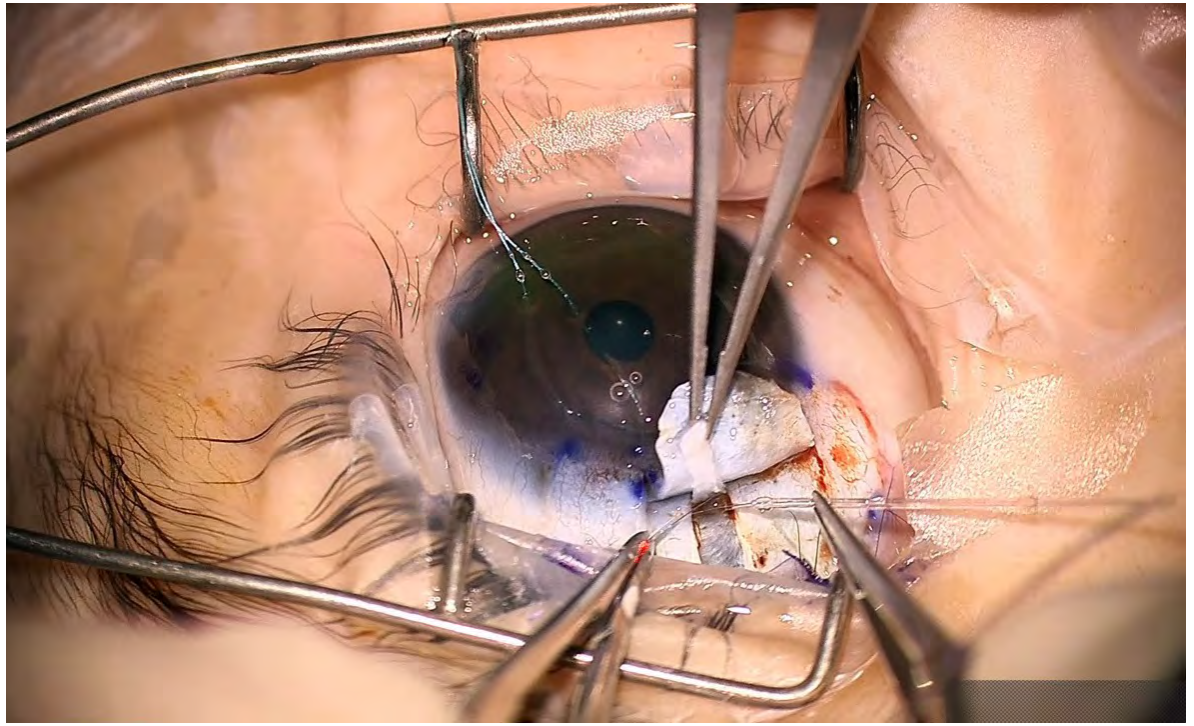


# 180° trabeculotomy, with trabectome



# 360° trabeculotomy, catheter-assisted





# Primary congenital glaucoma

- Postoperative care, prognosis, and follow-up
  - Successful glaucoma control
    - IOP reduction
    - Clearing of corneal edema
    - Reversal of optic nerve cupping
    - Reduction in myopia
  - 50%: VA < 20/50 – amblyopia!
  - IOP control achievable in > 80%
  - Many 'glaucoma years' ahead (unlike POAG population)
    - Will outlive the career of 3-4 glaucoma specialists during their lifetime
    - "For paediatric patients who may require lifelong IOP control, the first GDD is successful in 46% to 70% of patients after 5 years with medication, and the next GDD is successful in 37% to 75% of patients after 5 years after the second surgery."

      *Chen, Andrew, et al. "Valved glaucoma drainage devices in paediatric glaucoma: retrospective long-term outcomes." JAMA Ophthalmology 133.9 (2015): 1030-1035.*
  - Increased tendency to scarring - antifibrotics in filtering HK

# 2. Glaucoma associated with non-acquired systemic or ocular disorders

# Glaucoma associated with non-acquired systemic or ocular disorders

- Anterior segment dysgenesis
  - Trabecular meshwork
  - Cornea
  - Iris

+/- associated systemic abnormalities

# Glaucoma associated with non-acquired systemic or ocular disorders

**1. Axenfeld-Rieger Syndrome**

**2. Peters anomaly**

**3. Aniridia**

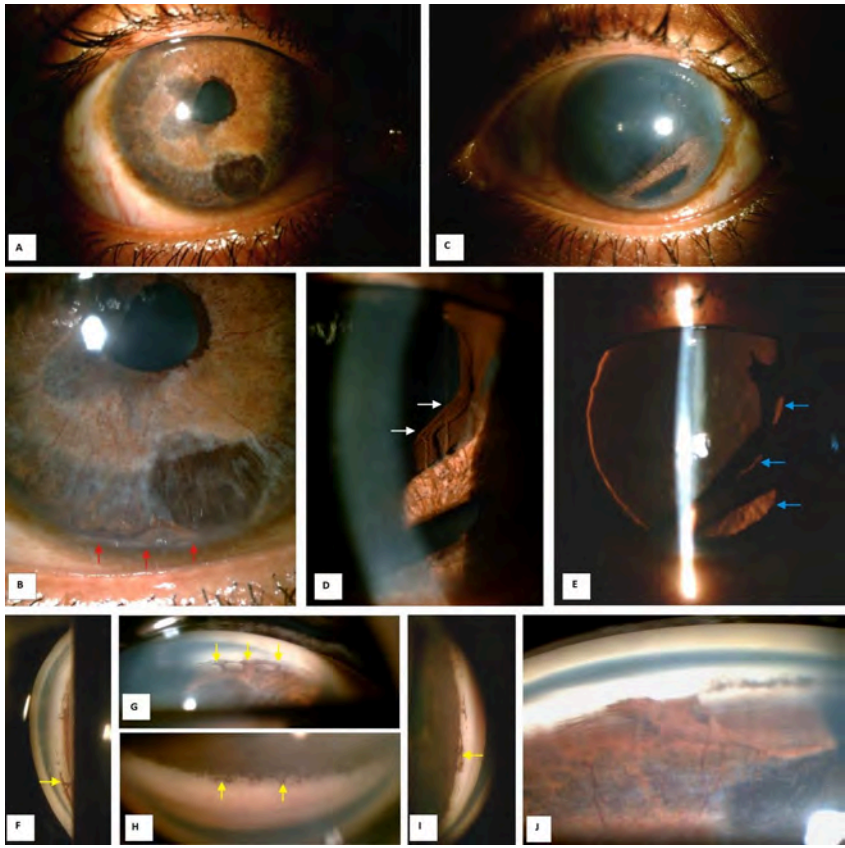
# Glaucoma associated with non-acquired systemic or ocular disorders

1. **Axenfeld-Rieger Syndrome** = spectrum

- Axenfeld anomaly
  posterior embryotoxon + peripheral iris strands

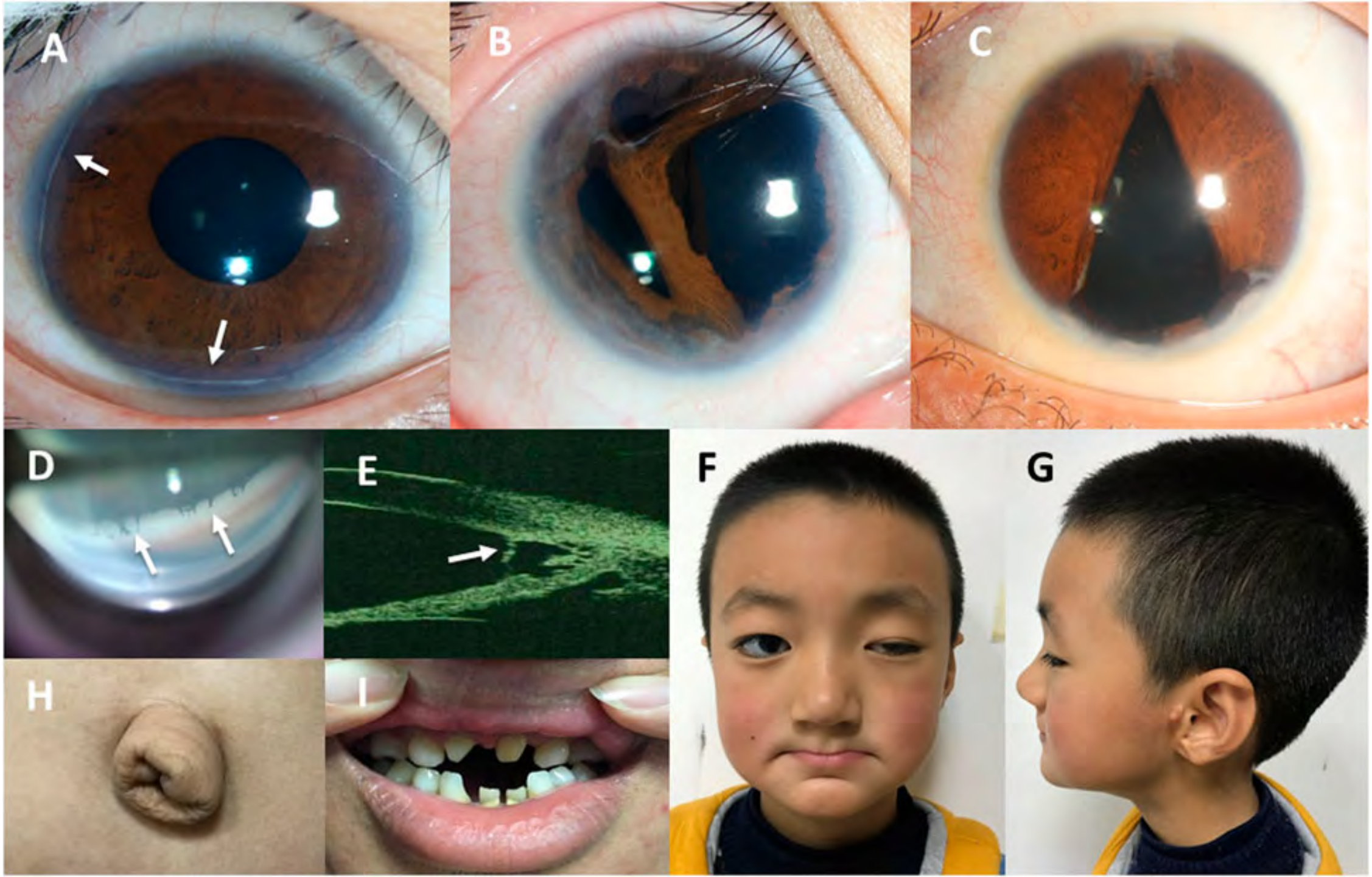
- Rieger anomaly
  + iris changes

- Rieger syndrome
  + systemic developmental defects



# Glaucoma associated with non-acquired systemic or ocular disorders

- General features
  - Bilateral involvement
  - AD pattern
- Ocular features
  - Cornea: posterior embryotoxon (10% of general population)
  - Angle: prominent Schwalbe line, peripheral iris strands, anterior/high iris insertion
  - Iris: nml, mild stromal thinning, marked atrophy (holes, corectopia, ectropion uveae)
  - Glaucoma in > 50% (most commonly in childhood or young adulthood)
- Systemic features
  - Teeth: microdontia, hypodontia, anodontia
  - Facial bones: maxillary hypoplasia
  - Hypertelorism, telecanthus, broad flat nose, micrognathia, mandibular prognathism,…
- Genetic linkage
  - PITX2, FOXC1
- Glaucoma: medical therapy → surgical therapy


A
B
C
D
E
F
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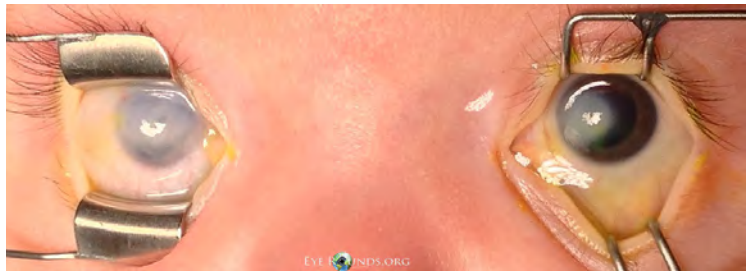
H
I

# Glaucoma associated with non-acquired systemic or ocular disorders

## 2. Peters anomaly



- General features
  - Bilateral involvement in 60%
  - Sporadic
- Ocular features
  - Cornea: central defect in DM + endothelium → stromal thinning and opacificatio
  - 3 types
  - Glaucoma in +/- 50% (frequently present at birth)
    - Mechanism: ?
  - Other associated ocular pathologies
- Peters Plus syndrome in 60%
  - Short stature, developmental delay, dysmorphic facial features, cardiac, genitourinary, and central nervous system malformations
- Genetic linkage
  - PAX6, PITX2, CYP1B1, FOXC1
- Glaucoma: usually surgical therapy required
  - Also: penetrating keratoplasty → poor outcomes

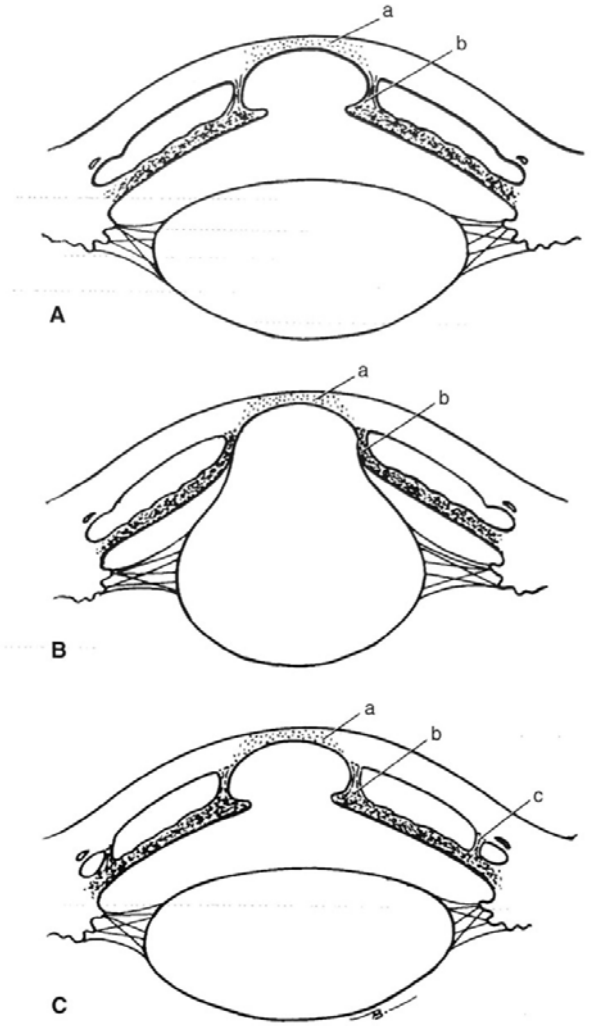
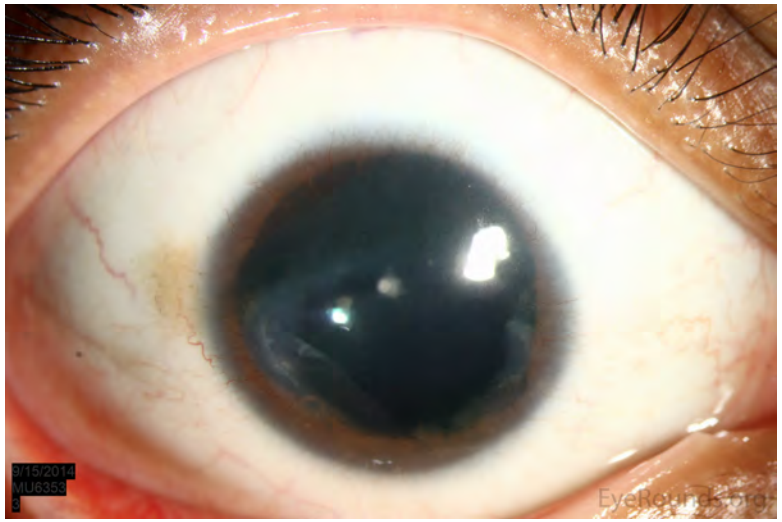



**FIGURE 15.14 Peters anomaly.** Shown are three forms described by Townsend and colleagues,[125] including, in each form, a central corneal defect (*a*) and adhesions (*b*) from a corneal defect to the central iris. **A:** Without keratolenticular contact or cataract. **B:** With keratolenticular contact or cataract. **C:** With peripheral defects of Axenfeld–Rieger syndrome (*c*).

# Glaucoma associated with non-acquired systemic or ocular disorders



## 3. Aniridia

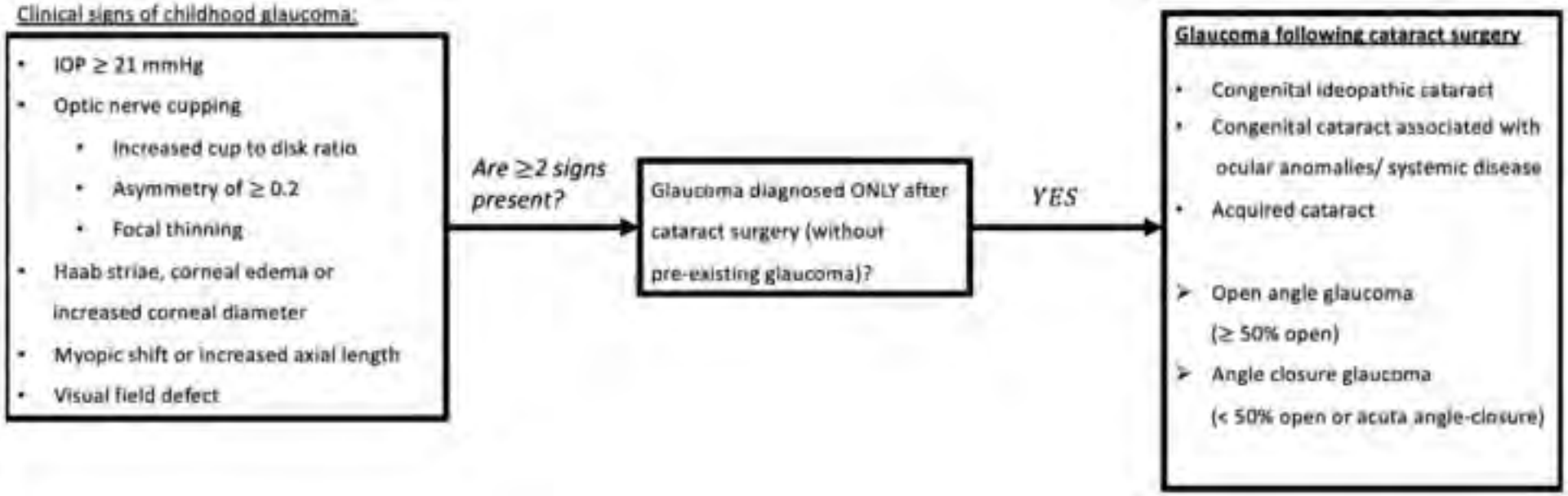
- General features
  - Bilateral
  - 2/3 AD, 1/3 sporadic
- Ocular features
  - Iris: partially absent → rudimentary stump of variable width
  - 4 phenotypes
    1. Associated with foveal hypoplasia, nystagmus, corneal pannus, glaucoma, reduced vision
    2. Predominant iris changes, nml VA
    3. Associated with Wilms tumor or other genitourinary anomalies
    4. Associated with intellectual disability
  - Glaucoma in 50-75% (most commonly in late childhood or adolescence)
    - Mechanism: progressive obstruction of the AC angle by contracture of iris stump tissue strands
- Other associated ocular and systemic pathologies
- Genetic linkage
  - PAX6 → **11p3 deletion: Wilms tumor (WT1) in 70% before the age of 3**
- Glaucoma: medical therapy → surgical therapy
  - Also: cataract surgery, penetrating keratoplasty = difficult

# Other syndromes and systemic conditions with associated glaucoma

- Chromosomal Anomalies
  - Trisomy 21: Down Syndrome
  - Trisomy 13-15: Trisomy D Syndrome
  - Trisomy 18: Edwards Syndrome
  - Turner Syndrome
- Cockayne Syndrome
- Cystinosis
- Hallermann-Streiff Syndrome
- Hepatocerebrorenal Syndrome: Zellweger Syndrome
- Kniest Dysplasia
- Lowe Syndrome
- Michel Syndrome
- Mucopolysaccharidoses
- Nail-Patella Syndrome
- Oculodentodigital Syndrome
- Präder-Willi Syndrome
- Rubinstein-Taybi Syndrome
- Stickler Syndrome and similar syndromes
- Waardenburg Syndrome
- Walker-Warburg Syndrome

# 3. Glaucoma following cataract surgery (GFCS)

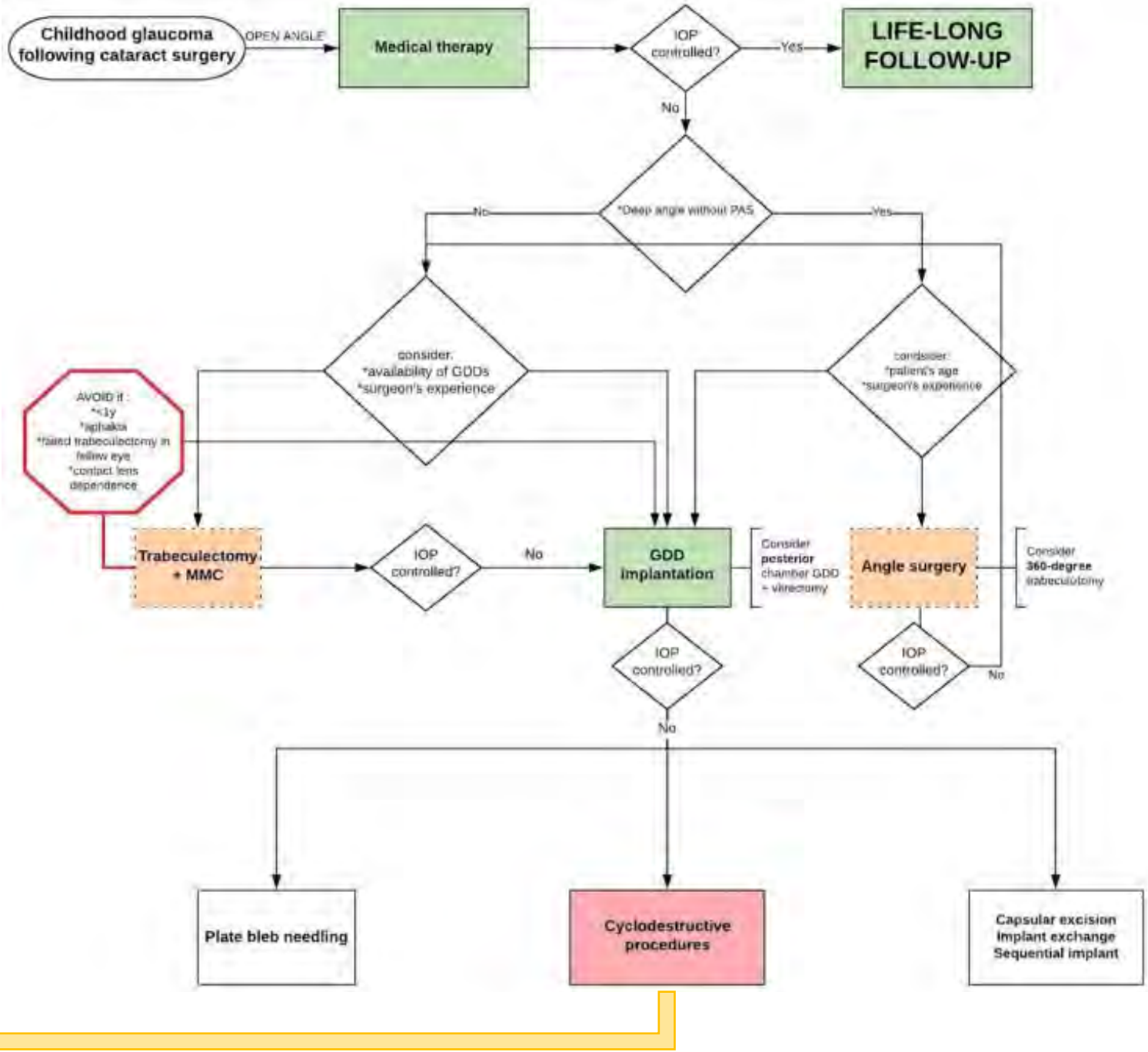
# Glaucoma following cataract surgery (GFCS)




- 3-41% after removal of congenital or developmental cataracts
- Median postsurgical onset: 5 years
- Risk factors
  - Age at time of Sx <12m
  - Microphthalmia
  - Persistant fetal vasculature
  - *Pseufophakic = aphakic*
- 75-94%: open angle
- IATS (Infant Aphakia Treatment Study): 22% after 10y of FU

*Simons AS et al. Management of Childhood Glaucoma Following Cataract Surgery. J Clin Med. 2022 Feb 17;11(4):1041.*

# Management of GFCS




**Indications according to Moorfields:**

- Advanced glaucoma with previous failed (often multiple) surgical procedures.

- Markedly elevated IOP on acute presentation, where an at least temporary IOP control was required before undertaking more definitive surgery.

- Treatment of a blind painful eye with an elevated IOP.

- Markedly elevated IOP, where the fellow eye was undergoing or had recently undergone surgery and we wished to defer surgery until the fellow eye has stabilized.

- Moderately elevated IOP with maximum medical therapy, where the risks of drainage surgery were considered high (such as where there had been severe complications in the fellow eye) or where surgery was declined by the patient or parents.

*Simons AS et al. Management of Childhood Glaucoma Following Cataract Surgery. J Clin Med. 2022 Feb 17;11(4):1041.*

# Thank you for your attention!

Sophie Lemmens

UZ Leuven – KU Leuven

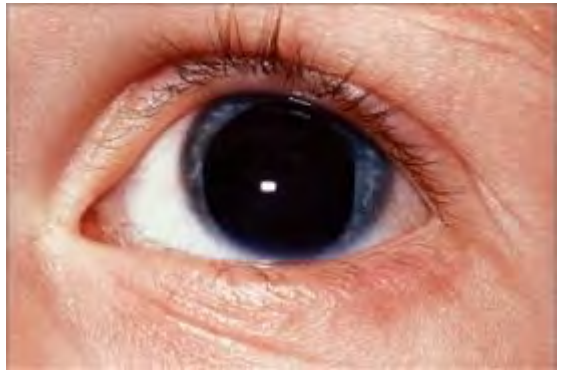
*ManaMa Glaucoma 03/12/2022 – CHU Liège*

# Case 1

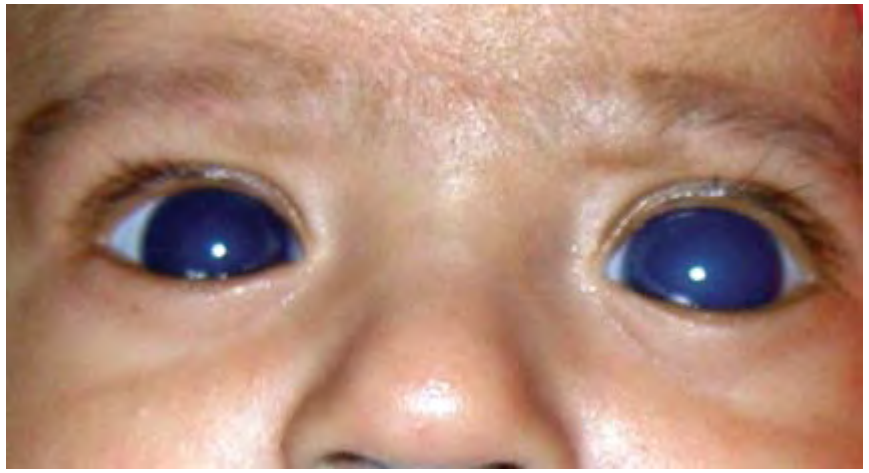
- Girl, 6m
- In good health
- Familial: brother (°2011) rare chromosome 7 abnormality (developmental delay)
- 08/07/15: first consultation @ophthalmology
  - Mother notices
    - RE  bigger, is squeezed shut, tearing +++
    - LE large pupil
  - Visual capacity seems poor, certainly in the right eye
  - Slitlamp
    - RLE: abnormally formed iris, aniridia-type
    - RE: cloudy cornea, larger than LE
    - LE: clear lens
  - IOP iCare
    - OD 37,0 mmHg
    - OS 14,0 mmHg
  - Physiologic ONH LE, no nystagmus

- Medical glaucoma treatment
  - Geltim 1x/d OD
  - Xalatan 1x/d OD
- Further investigation & surgical glaucoma treatment
  - Examination under AA + trabeculotomy OD: 14/07/15
- Paediatrics consultation
  - Echo kidney ruling out Wilms tumour: WAGR?
    - Result: negative 15/07/15, new ultrasound October
- Consult genetics
  - PAX6, FOXC1, PITX2 → Axenfeld-Rieger anomaly?
    - heterozygous mutation in PITX2 gene → diagnosis of Rieger syndrome

aniridie RLE

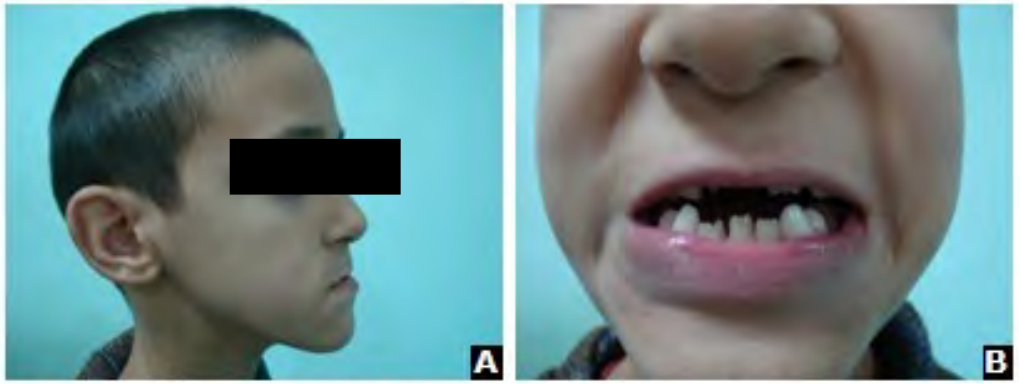


congenital glaucoma RE with buftalmia



maxillofacial anomaly

“irregular upper dental arch, hypoplasia of the maxilla and somewhat wider nasal bridge”



NO Disclosure

# Visual Field Examination: Dots, artifacts & tricky cases

Sayeh Pourjavan

Glaucoma Consultant

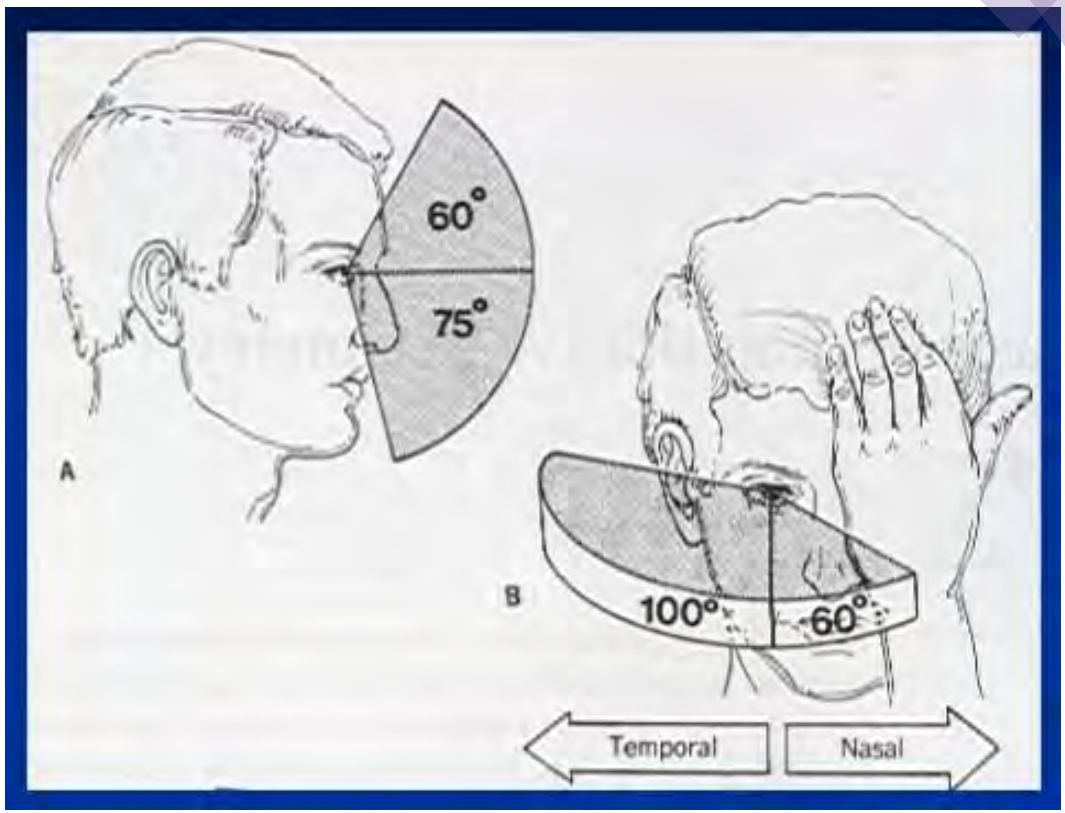
# Visual Field

- Is that portion of the external environment where the observer can detect a visual stimulus with a fixating eye.

- Different from visual acuity, the eye chart measures acuity at the centre of the VF.

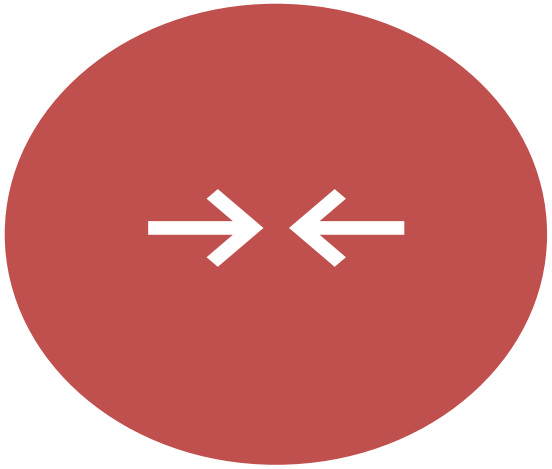
- Outside central vision the VF has poor acuity but is very sensitive to movement.

- Important for neurological & ophthalmic disease detection.

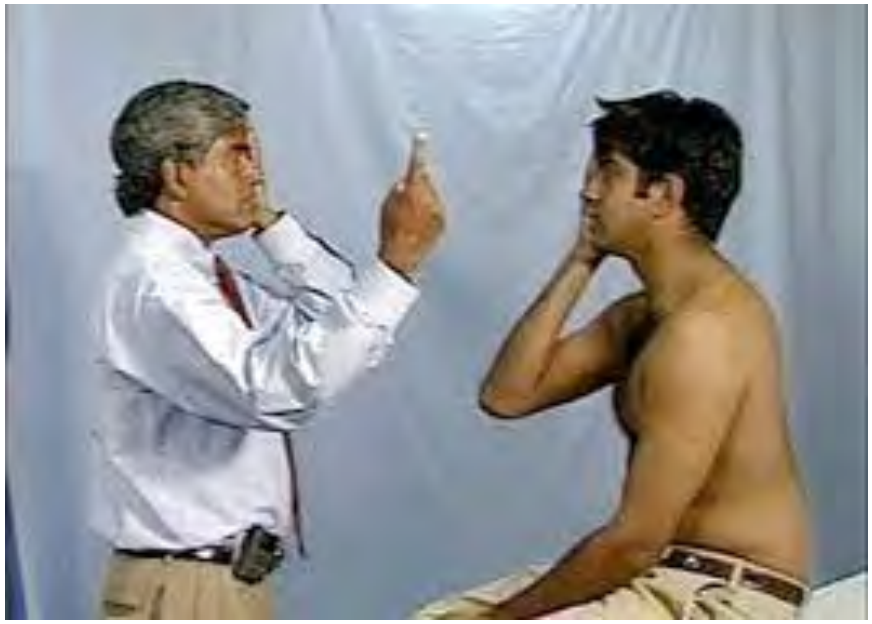


# Examination Methodology

KINETIC PERIMETRY

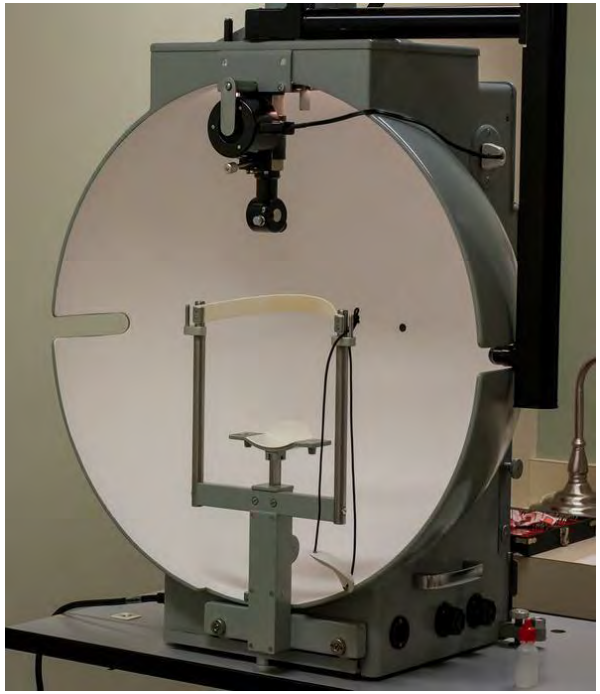


STATIC PERIMETRY



# Kinetic Visual Field testing

Confrontation with Red  Cyclo



# Methods of measuring static VF

# Automated Perimetry

Suprathreshold testing

- The brightness of the white light presented is of an intensity that should be visible and is used to screen for scotomas.
- This is a fast test strategy for screening.

Threshold testing

- The threshold measures how strong a stimulus must be before it can be detected.
- It is the intensity of the target spot that is detected by the observer above the intensity of the background illumination. White on White.
- This is used for following glaucoma progression
- This test takes 5-12 minutes to perform

# SITA

- The Swedish Interactive Thresholding Algorithm (SITA).
- It is a forecasting method, that uses Bayesian statistical properties.
- Optimizes the determination of thresholds by continuously estimating what the expected threshold is based on the patient's age and neighboring thresholds.
- By taking into account a user's results in nearby locations, stimuli that are unlikely to be seen, or extremely likely to be seen are not tested exhaustively. Instead, the stimuli that are likely near the threshold are tested.

- SITA allows for a reduction of the time necessary to acquire a visual field by up to 50%, and it decreases patient fatigue and increases reliability.

# Humphrey

- Sita Faster (2.8 min): Derived from SF
- Sita Fast (4 min): For screening, children or where the fixation is not possible (Parkinson). The difference with SS is the amount of certainty required before testing can be stopped
- Sita Standard (7 min): for follow up
  - 30-2°: a few early glaucoma patients will represent a VF outside of the 30° periphery. Also for neurological screenings. Tests 76 points.
  - 24-2°: Tests 54 points.

– 10-2°: for small central or paracentral scotoma. when only central VF is preserved. Test 68 points.

## Sitafaster 24-2C

A new SITA test that adds 10 central test points common to the 10-2 pattern to the traditional 24-2 field. The diagnostic performance of the SITA Faster 24-2C test pattern is comparable to the test locations common to the 24-2 SITA Fast and 10-2 patterns.

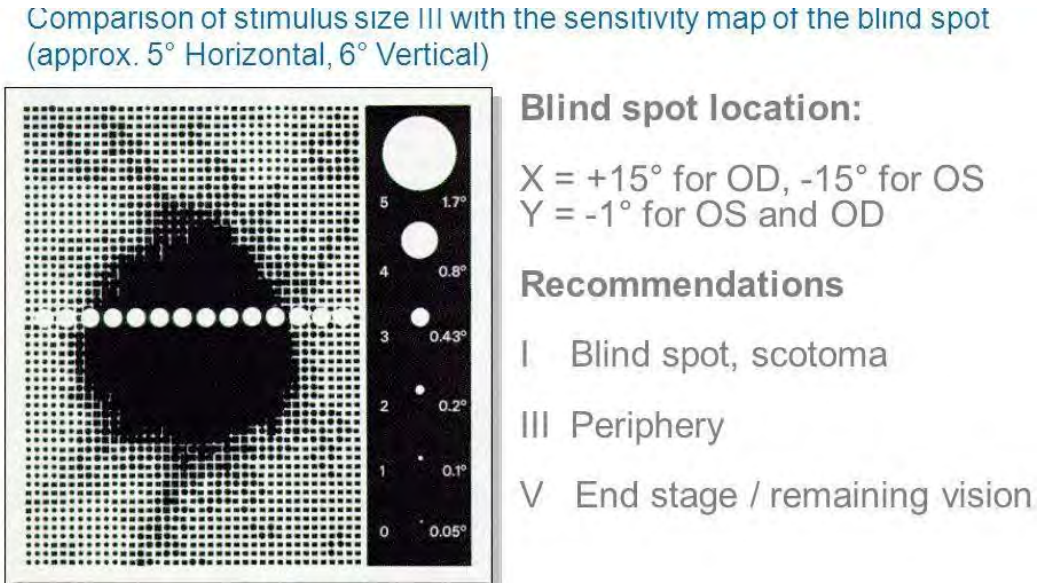
| Parameter | N | Mean ± SD of test time (sec) | Range of test time (sec) | SITA Faster 24-2 time improvement over: | SITA Faster 24-2C time improvement over: |
|---|---|---|---|---|---|
| **Normal** | | | | | |
| **SITA Faster 24-2** | 25 | 106.6 ± 9.3 | 90, 137 | - | - |
| **SITA Faster 24-2C** | 25 | 130.8 ± 10.6 | 112, 163 | 18.5%* | - |
| **SITA Fast 24-2** | 25 | 166.0 ± 16.5 | 133, 201 | 35.8%* | 21.2%* |
| **SITA Fast 10-2** | 25 | 189.0 ± 18.9 | 158, 233 | 43.6%* | 30.8%* |
| **SITA Standard 24-2** | 25 | 277.2 ± 21.8 | 232, 327 | 61.6%* | 52.8%* |
| **Glaucoma** | | | | | |
| **SITA Faster 24-2** | 25 | 134.1 ± 37.8 | 99, 245 | - | - |
| **SITA Faster 24-2C** | 25 | 162.4 ± 45.5 | 121, 296 | 17.5%* | - |
| **SITA Fast 24-2** | 25 | 198.8 ± 46.3 | 147, 344 | 32.6%* | 18.3%* |
| **SITA Fast 10-2** | 25 | 217.2 ± 61.7 | 153, 410 | 38.3%* | 25.2%* |
| **SITA Standard 24-2** | 25 | 321.0 ± 59.8 | 225, 487 | 58.2%* | 49.4%* |

*Paired t-test, $p<0.01$

# Stimulus size

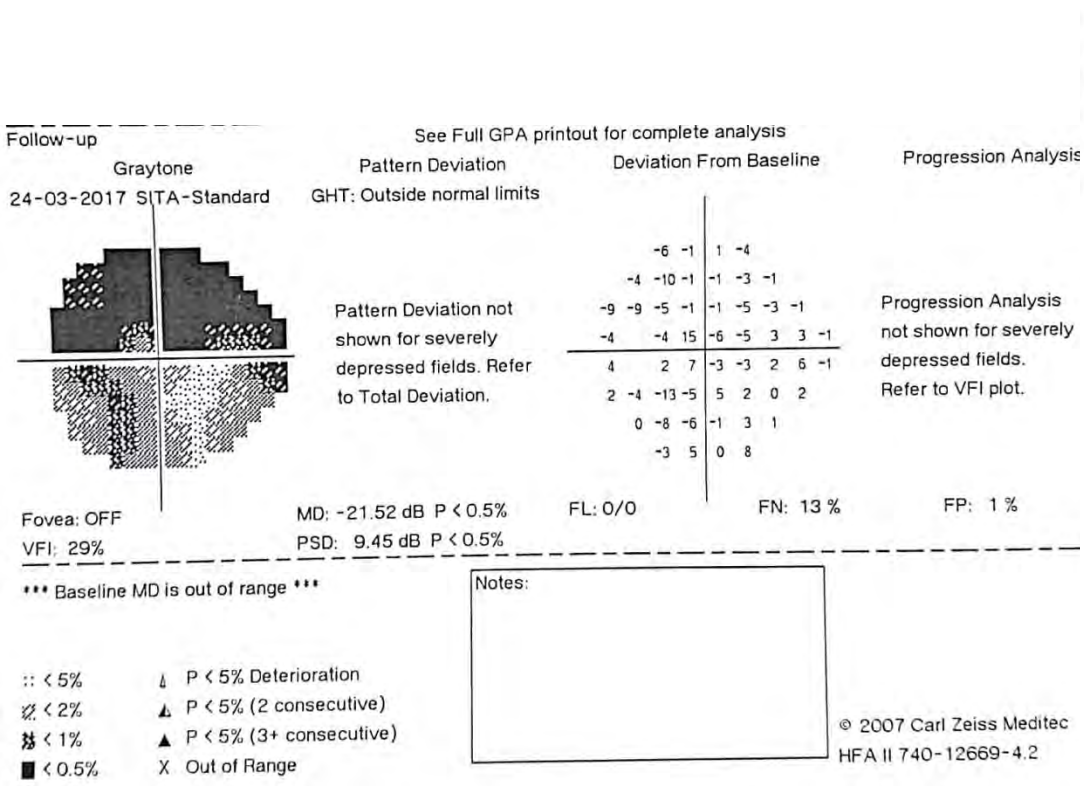
Standard size in HFA:

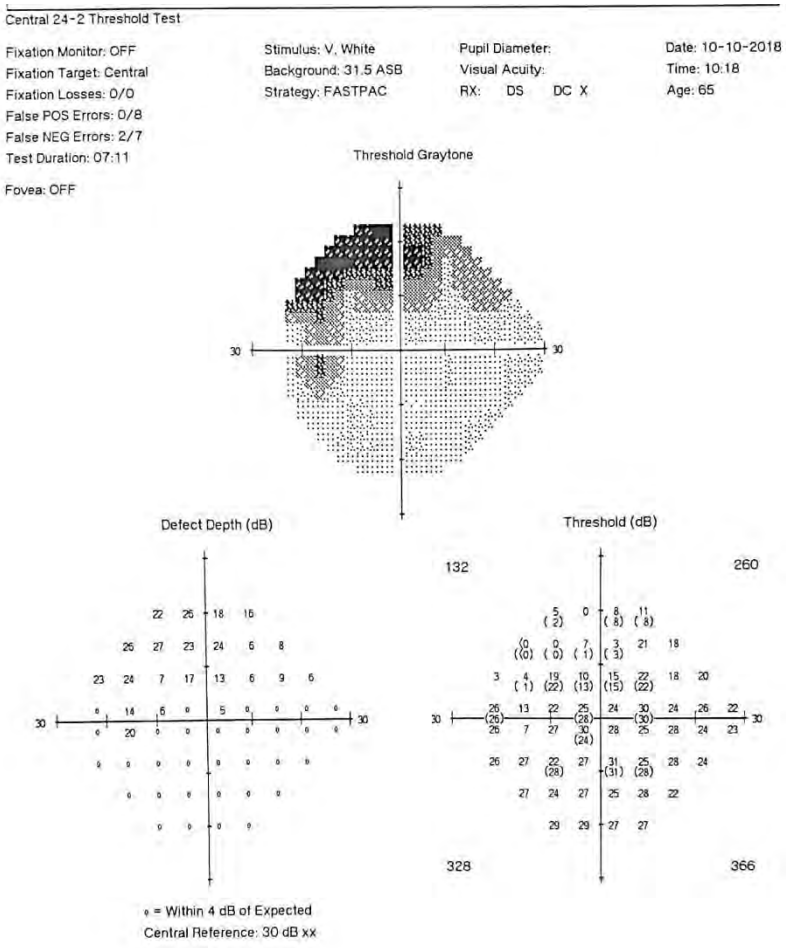
- Goldmann size III
- White stimulus
- 0.43 ° in diameter




Size V stimulus:

- 4x bigger than the standard size
- Sensibility levels are 5 to 10x higher than stimulus III
- When no longer a standard stimulus is seen, in order to be able to follow up.




# GV stim III and V example.

# Interpreting the Humphrey visual field

1. Is this the correct test?

A. Patient name

B. Date of test

C. Left or right eye?

D. Test performed

° degree of visual angle tested

° test protocol: threshold or screening

2. Can I rely on this test? 3. Is the test normal?

A. Visual sensitivity map

A. False-positive errors

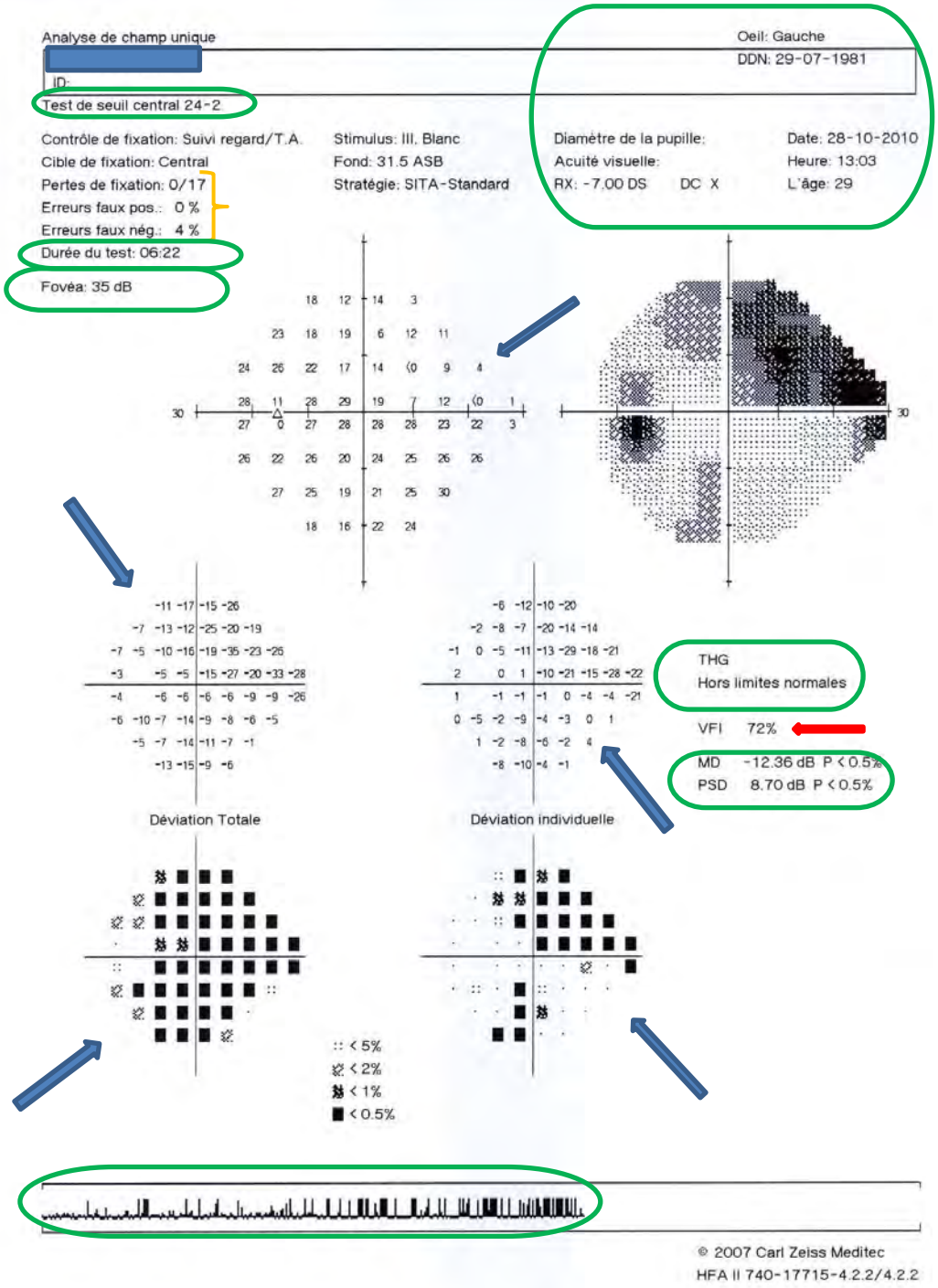
B. Total deviation map

B. False-negative errors

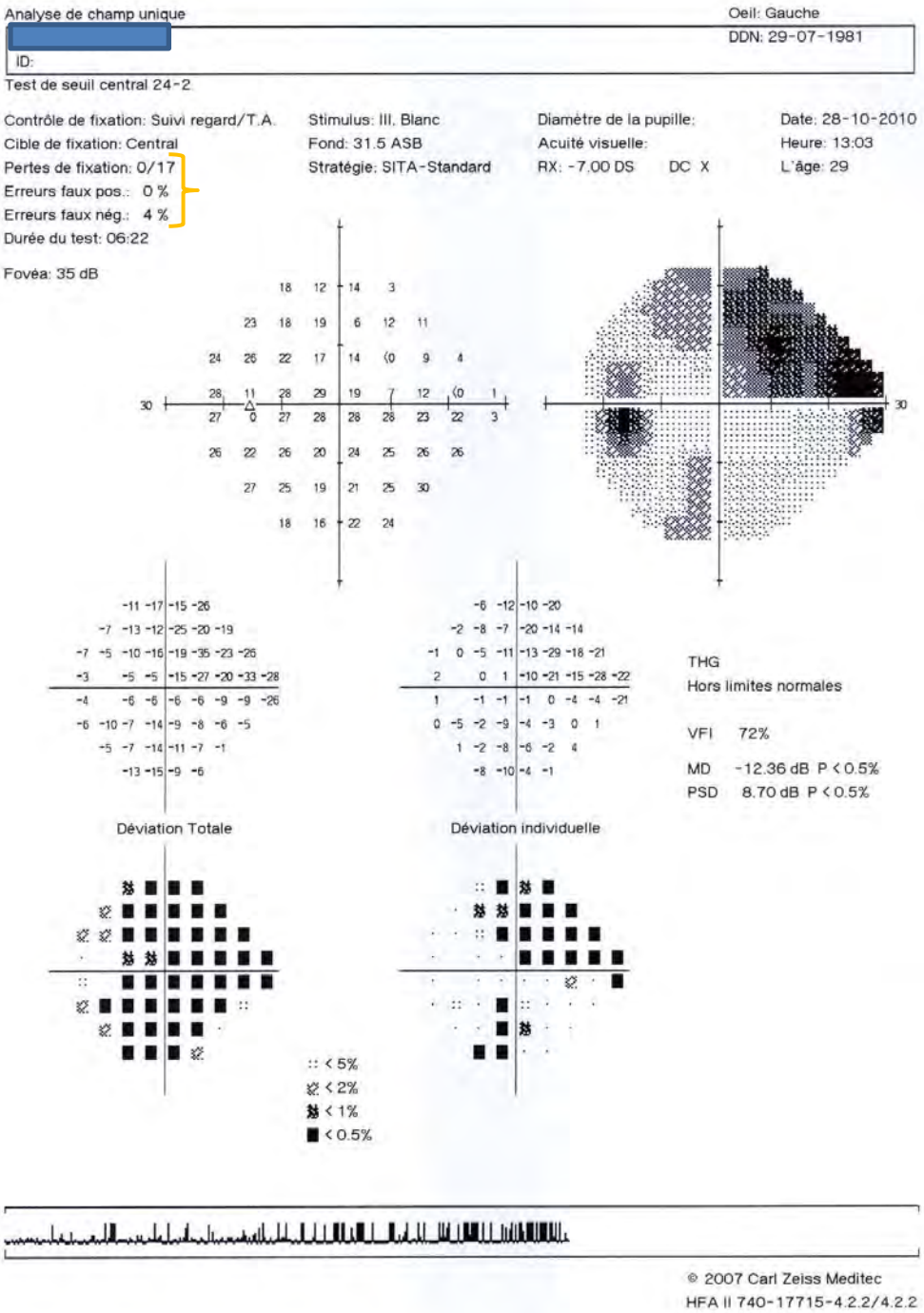
C. Pattern deviation map

C. Fixation-loss index D. GHT

D. Gaze-tracking graph




1. Test name
2. Patient data
3. Reliability indices
4. Test duration
5. Foveal threshold
6. Raw numeric sensitivities and Grey scale
7. Totale deviation numeic plot
8. Pattern deviation numeric plot
9. Total deviation probability plot
10. Patten deviation probability plot
11. Glaucoma Hemifeld test
12. Visual Field index
13. Visual Field indices
14. Gaze tracking




# Reliability indices

False + rate:

Patient presses the button even when there is no stimulus or a respons is not expect

FP>15%

Trigger happy: impossible high thresholds.

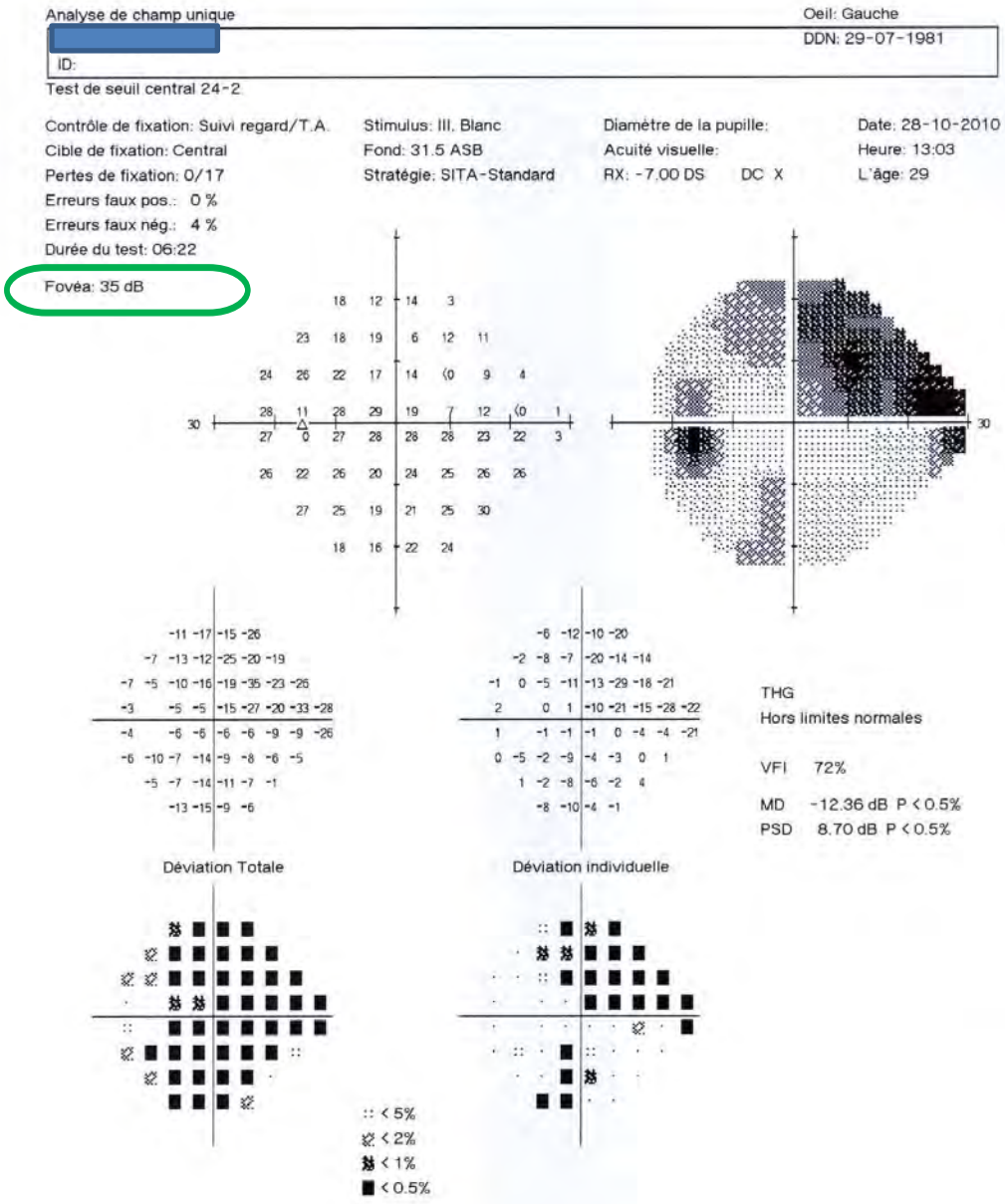
False – rate:

Patient fails to respond to a brighter stimulus on a point where he already reacted with a lower intensity.

Limited value because of the decreased reproducibility of glaucomatous VF .

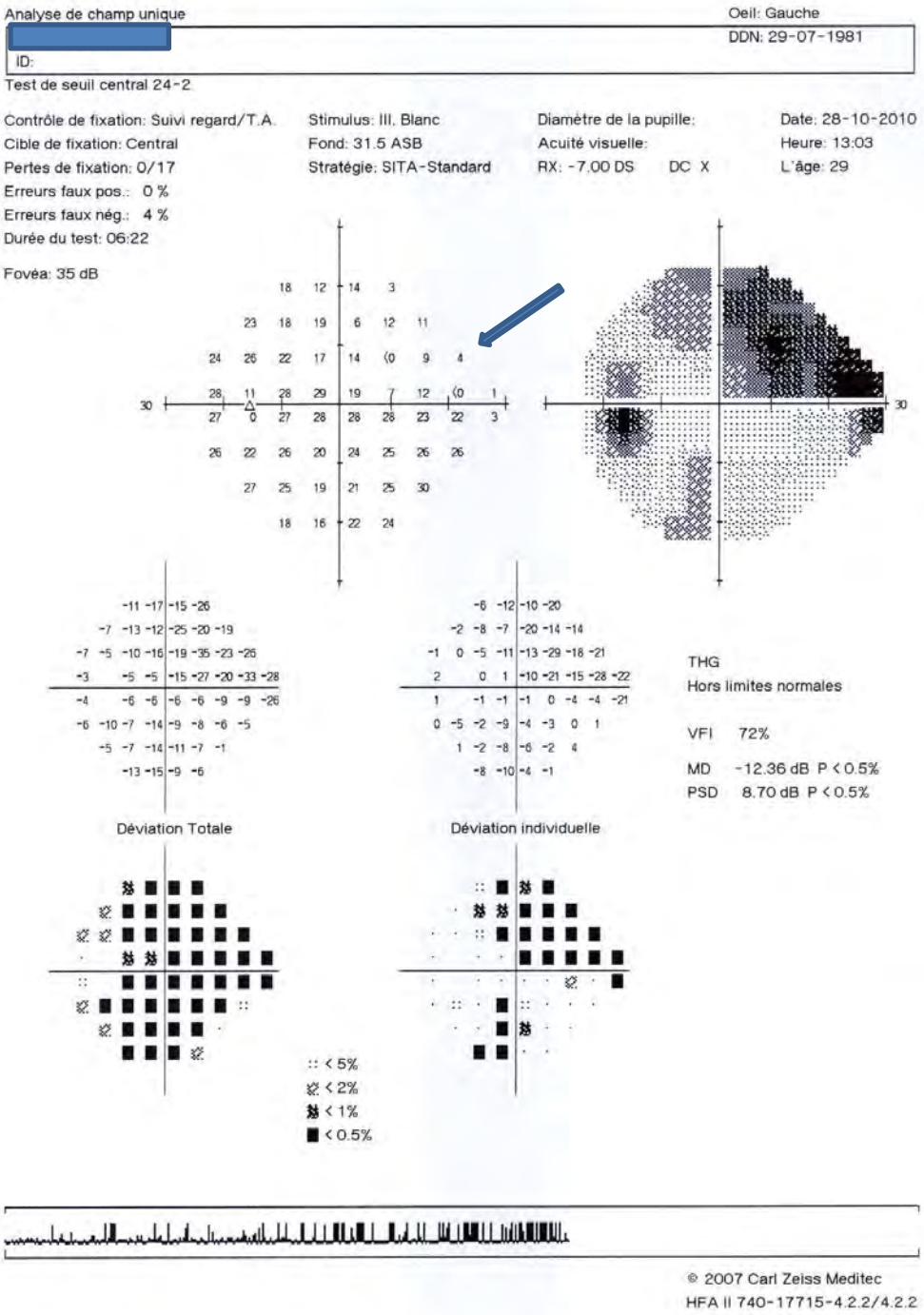
Fixation loss: Stimuli presented at the presumed blind spot.

FL>20%



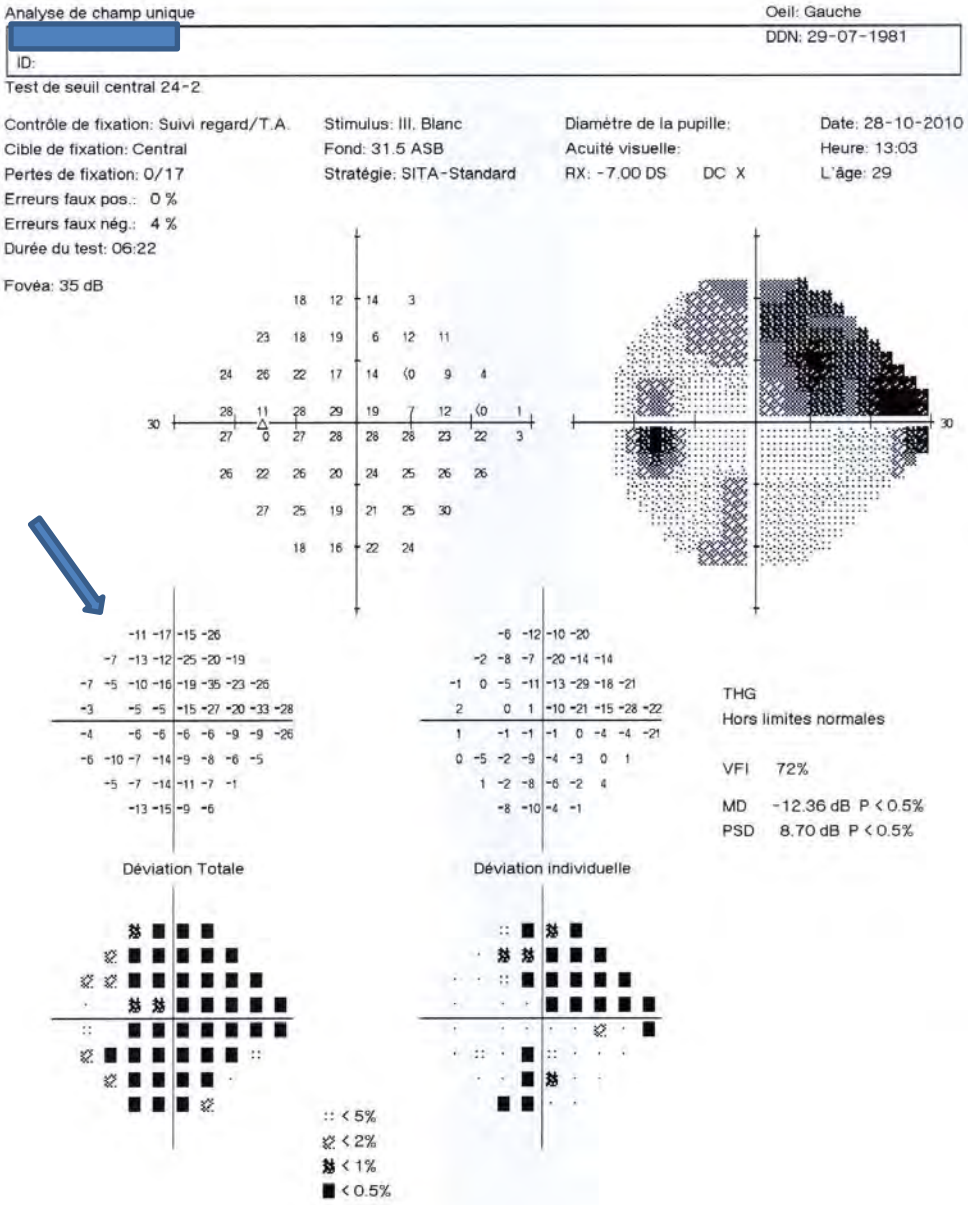

# Foveal threshold

- The min amount of luminance on a uniform background that can be detected on the center of fixation.
- This test takes 15 seconds, at the beginning of HFA.
- Test fixation is 10° lower than the fixation point for the primetry.
- It can provide valuable information when a patient with advanced glaucoma that is close to fixation complains that her vision is worse, yet Snellen acuity and the 24-2 field appear unchanged or to detect generalized depression of the sensitivity.



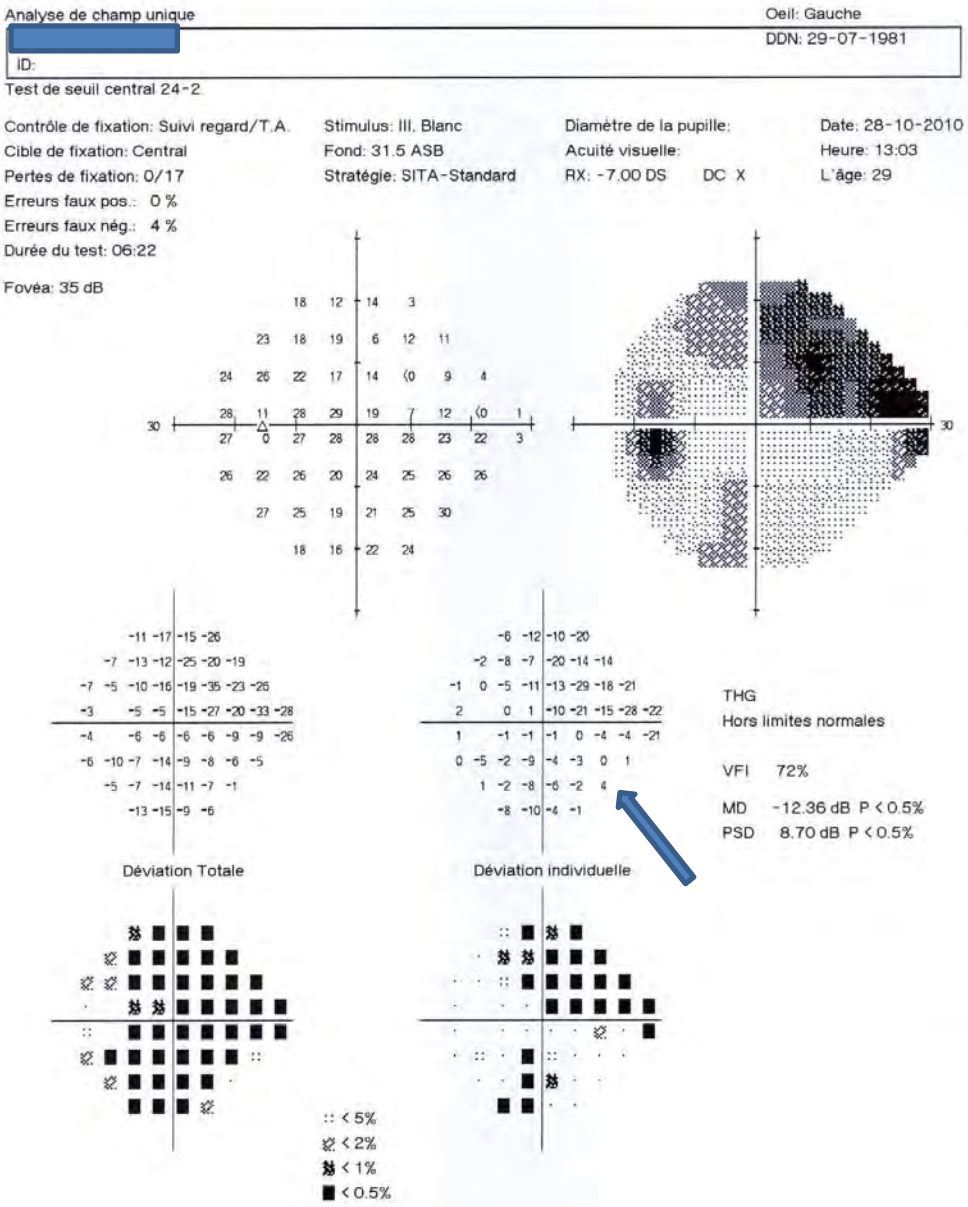

# Raw nummeric data & Greyscale

- A numerical plot gives the threshold and sensitivity for all points checked.
- Sensivities are indicated in dB.
- 0 dB indicates the max brightness the HFA produces (10,000 asb)
- 40 dB (1 asb) stimulus is slightly fainter than the foveal sensivity of a young person.
- A grey scale plot graphically demonstrates regions to visual field loss by displaying regions with decreased sensitivity in darker tones. Areas of abnormally high sensitivity are shown as white



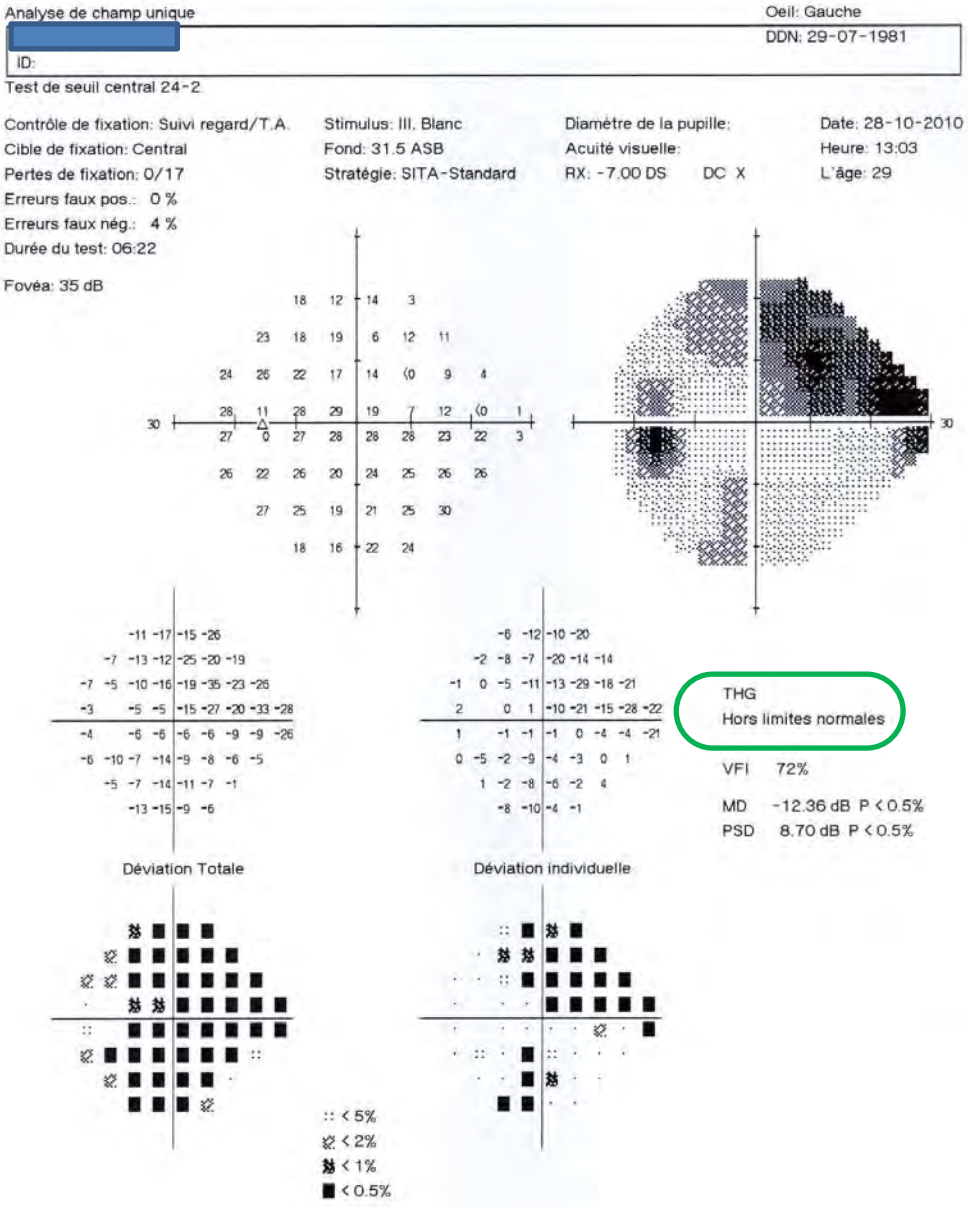

# Total deviation probability plot nr+grey scale

- Shows the deviation of the patient's result from that of age-matched controls at each test location.
- Each test location is graded as normal, or abnormal at a defined level (p value) compared to a normative population.
- The lower the p value, the greater its clinical significance and the lesser likelihood of the defect having occurred "by chance".

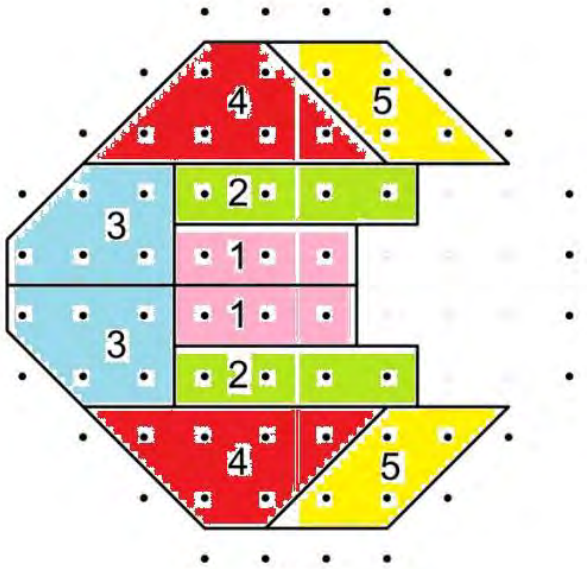



# Pattern deviation probability plot nr + grey

- Similar to total deviation plot but adjusted for any generalized depression, like cataract or miosis.
- Each test location is graded as normal or abnormal at a defined level (p value) compared to a normative population. The lower the p value, the greater its clinical significance.
- Pattern deviation plot must be carefully inspected for early detection or progression of glaucomatous VF loss.
- In advanced glaucoma (MD≥ -18) with a generalized depression the Pattern deviation plot can be normal

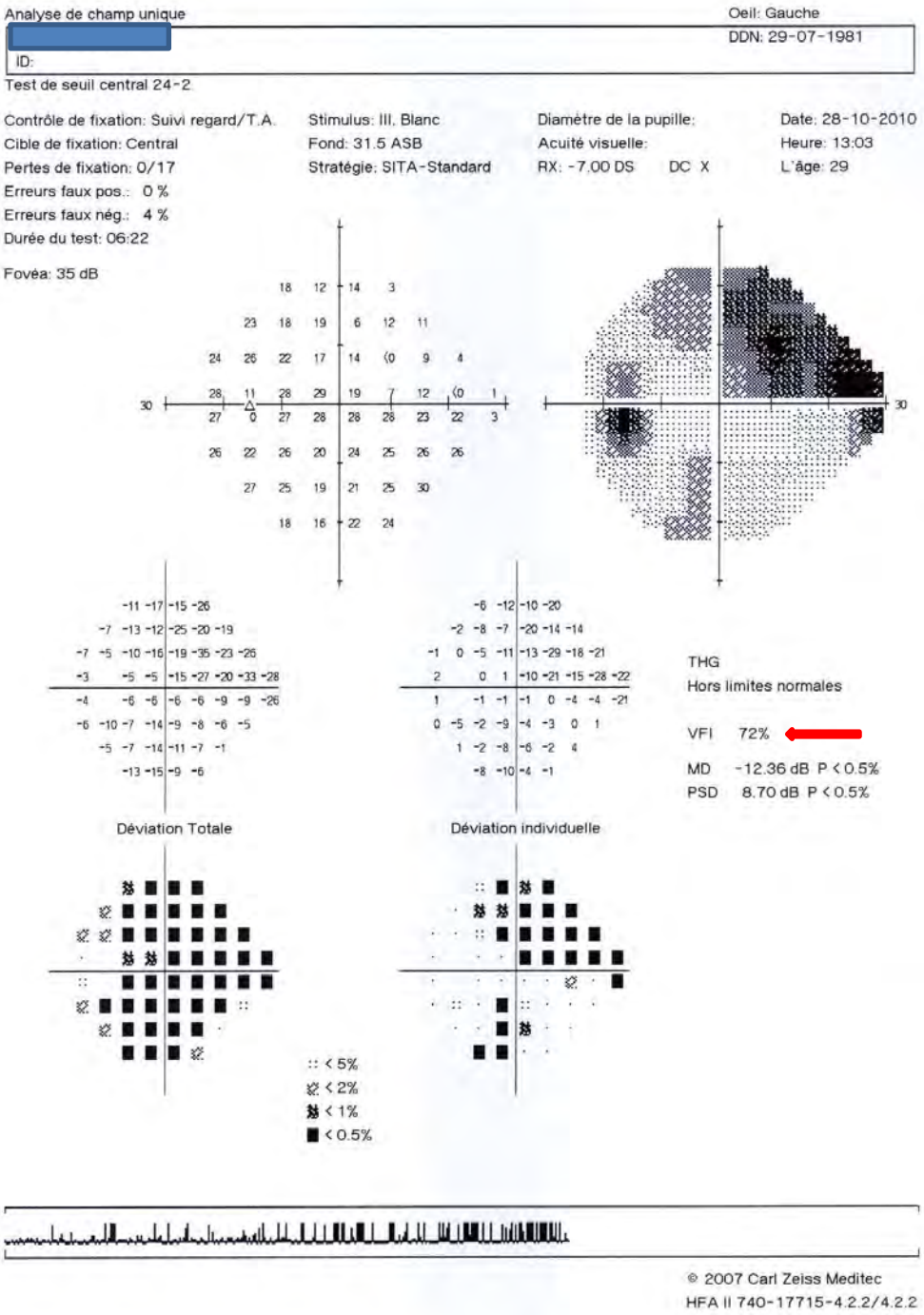



# Glaucoma Hemifield test




Five sectors of the upper hemifield are compared with their mirror image in the lower hemifield.

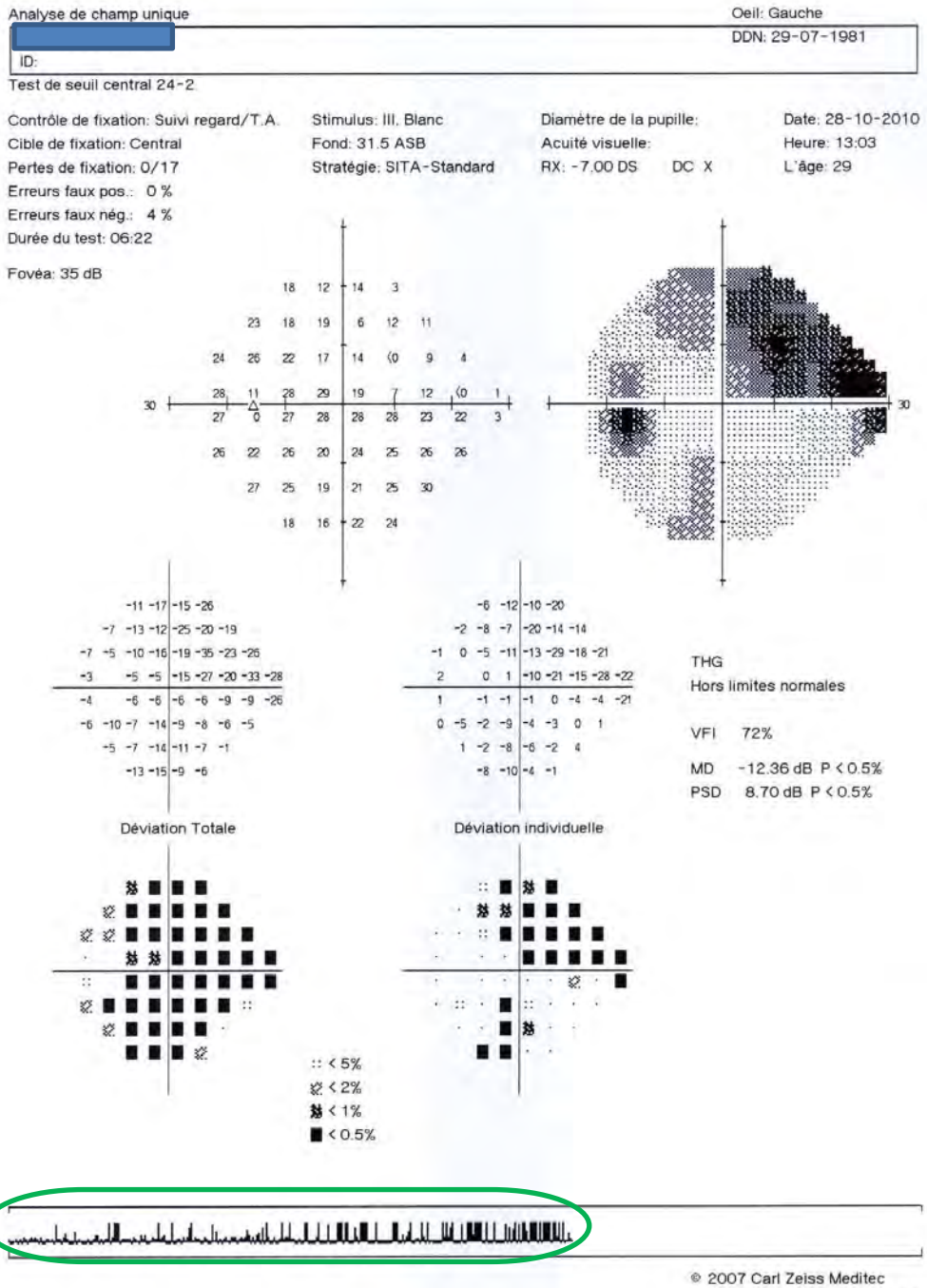
1. Normal
2. Outside Normal limits p<1%
3. Borderline p<3%
4. General depression of sensitivity 5. Abnormally high sensitivity




(Trigger happy patient)

# Visual Field index

- Represents the entire VF as a single percentage of normal.
- Is more sensitive than MD, based largely on the pattern deviation to a functional loss because it weights the defect in the center more than in the periphery.
- It is comparing the individual visual function with an age-adjusted normative database.
- A full visual field has a VFI of 100% while a perimetrically blind visual field has a VFI of 0%.




# Gaze Tracking

Measures gaze direction with a precision of 1°

Lines extending upwards indicates amount of gaze error at each stimulus

The full scale indicates an error of 10° or more

Lines downwards indicate that the instrument was unsuccessful in measuring gaze direction during that particular stimulus presentation.

From: Estimating the Usefulness of Humphrey Perimetry Gaze Tracking for Evaluating Structure–Function Relationship in Glaucoma
Invest. Ophthalmol. Vis. Sci.. 2015;56(13):7801-7805. doi:10.1167/iovs.15-17988

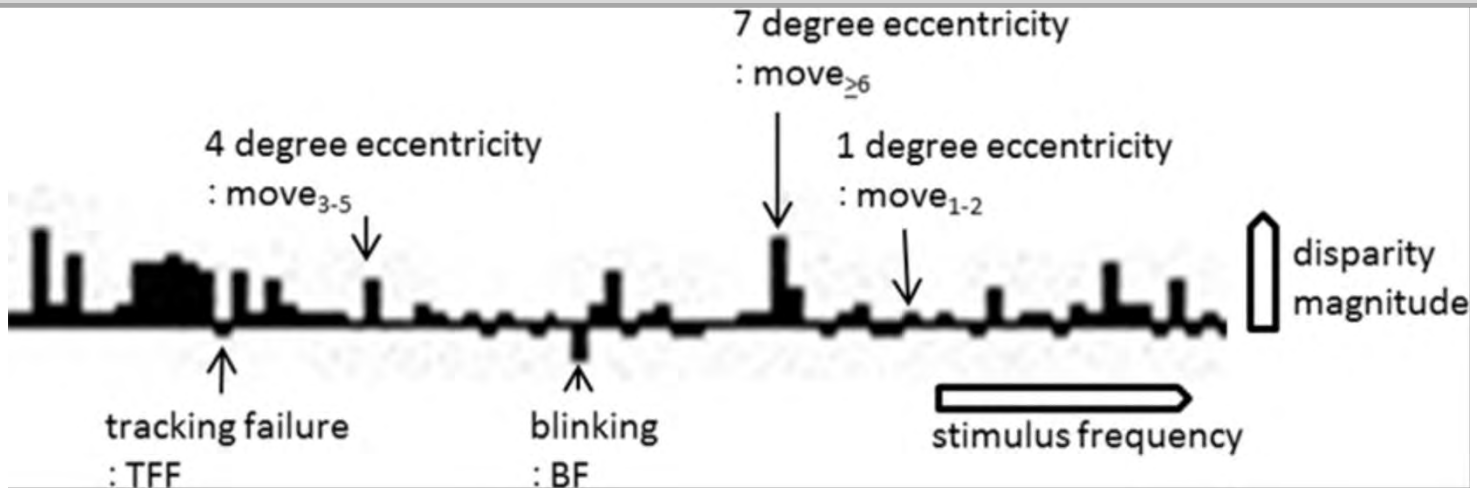
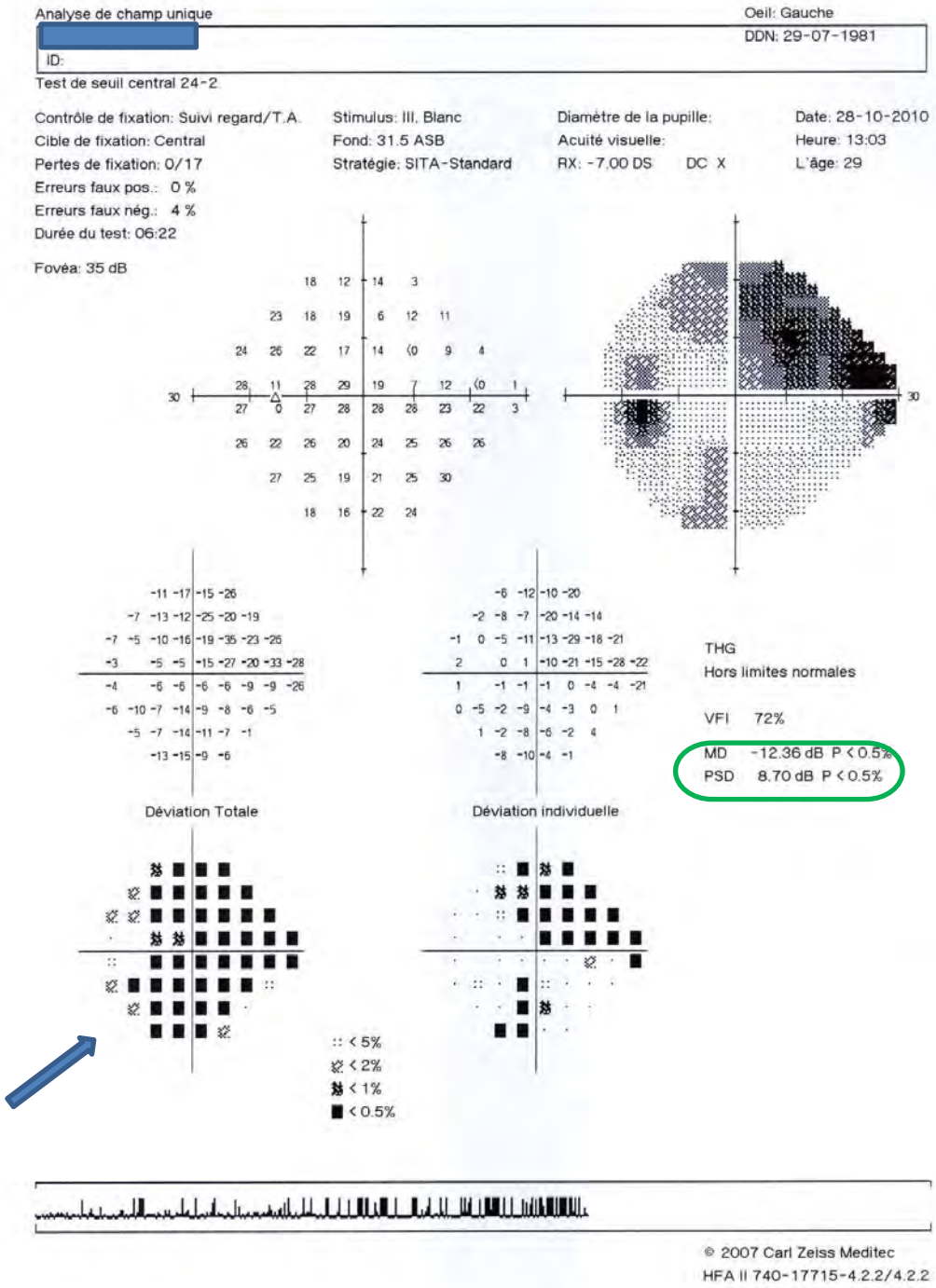



Figure Legend:

An example of a gaze tracking figure with the gaze tracking parameters. An upward bar in the chart indicates fixation disparity, and the length of the bar represents its magnitude, from 1° to a maximum of 10°. A short downward bar represents tracking failure, while a long downward bar indicates eyelid closure. GT parameters were calculated as follows: average frequency of eye movement per stimulus between 1° and 2° ($move_{1-2}$) 3° and 5° (denoted $move_{3-5}$) and equal to or more than 6° (denoted $move_{\geq 6}$), average tracking failure frequency per stimulus (TFF), and average blinking frequency per stimulus (BF).




# Global visual Field indices

## Mean Deviation

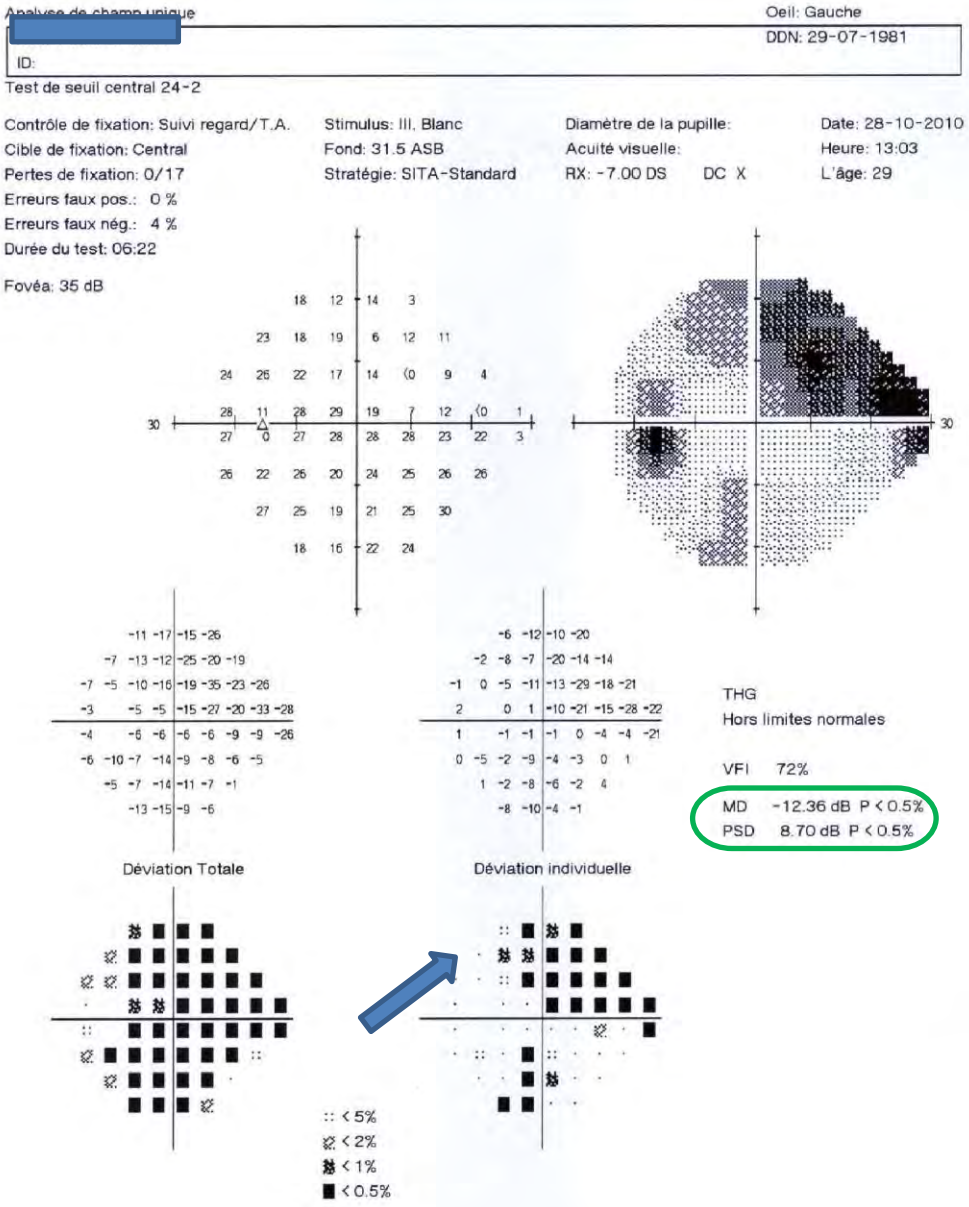
- Shows on average, the difference from age-matched normal.
- The dB deviation average is shown in the total deviation plot.
- Values for reliable tests range from +2 dB to -30 dB.
- Outdated indices, useful for scientific studies:

 Early Glaucoma MD >-6 dB

 Moderate Glaucom -6> MD >-12 dB

 Severe Glaucoma -12dB > MD

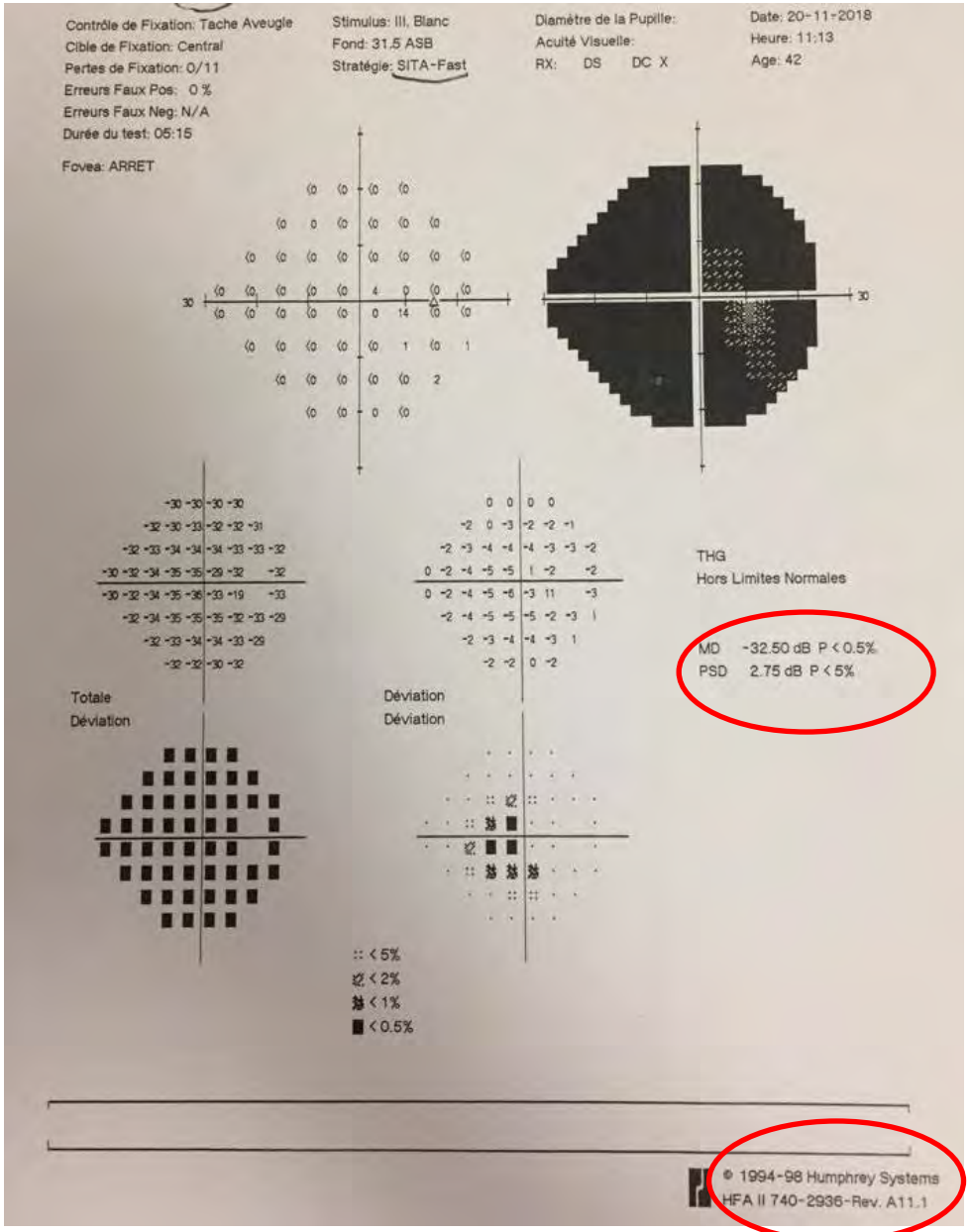
Global visual Field indices

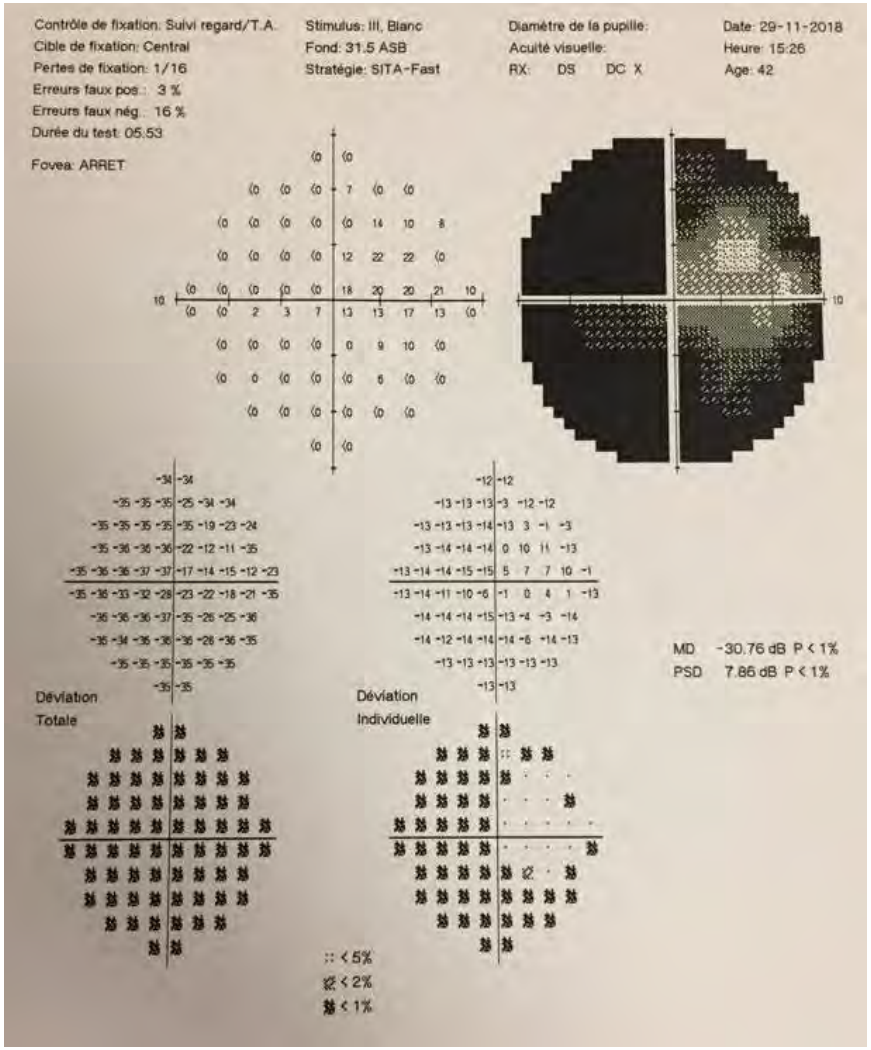



## Pattern Standard Deviation

- VF loss in glaucoma is nonuniform.
- Reflects irregularities in the field caused by localized field defects.
- Visual fields with the age-normal sensitivity at each point will have a PSD of 0, as will visual fields in which each point is uniformly depressed from the age-normal value.
- The largest PSD will be registered for focal, deep visual field defects. Near-normal and severely damaged visual fields will both have low PSD

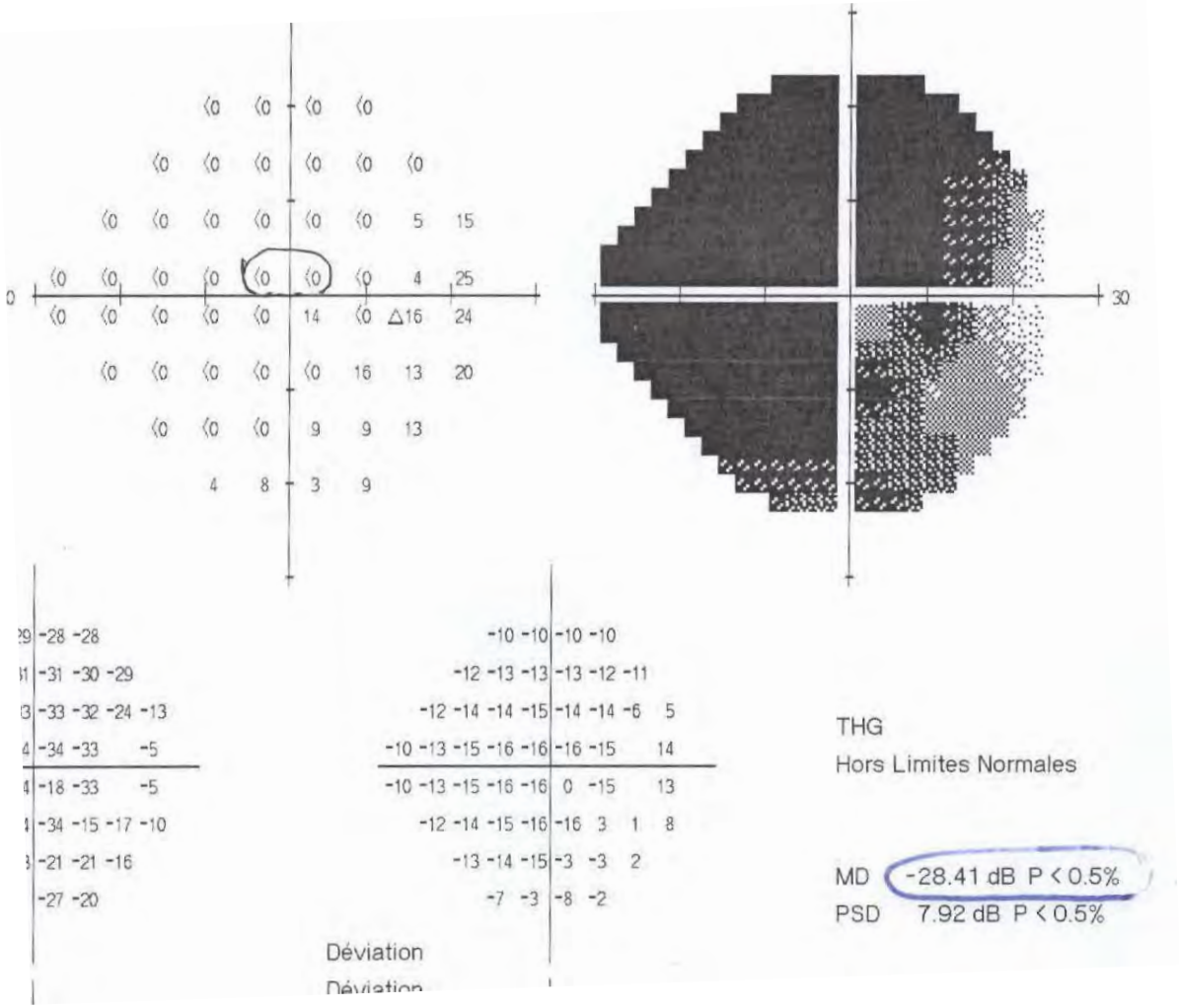
# Dilemma MD and PSD probability plot


Contrôle de Fixation: Tache Aveugle
Cible de Fixation: Central
Pertes de Fixation: 0/11
Erreurs Faux Pos: 0 %
Erreurs Faux Neg: N/A
Durée du test: 05:15
Fovea: ARRET
Stimulus: III, Blanc
Fond: 31.5 ASB
Stratégie: SITA-Fast
Diamètre de la Pupille:
Acuité Visuelle:
RX: DS DC X
Date: 20-11-2018
Heure: 11:13
Age: 42
THG
Hors Limites Normales
MD -32.50 dB P < 0.5%
PSD 2.75 dB P < 5%
Totale
Déviation
Déviation
Déviation
:: < 5%
< 2%
< 1%
< 0.5%
© 1994-98 Humphrey Systems
HFA II 740-2936-Rev. A11.1


Contrôle de fixation: Suivi regard/T.A.
Cible de fixation: Central
Pertes de fixation: 1/16
Erreurs faux pos.: 3 %
Erreurs faux nég.: 16 %
Durée du test: 05:53
Fovea: ARRET
Stimulus: III, Blanc
Fond: 31.5 ASB
Stratégie: SITA-Fast
Diamètre de la pupille:
Acuité visuelle:
RX: DS DC X
Date: 29-11-2018
Heure: 15:26
Age: 42
MD -30.76 dB P < 1%
PSD 7.86 dB P < 1%
Déviation
Totale
Déviation
Individuelle
:: < 5%
< 2%
< 1%

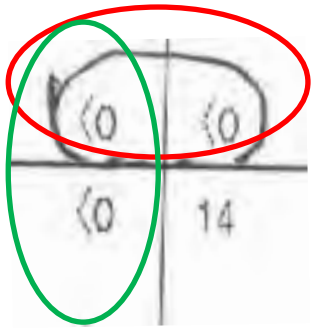
24-2

10-2




# Good to know:

# Macular




# Splitting

*Caprioli et al. 2007*

**Wipe-out syndrome**

# Common perimetric errors

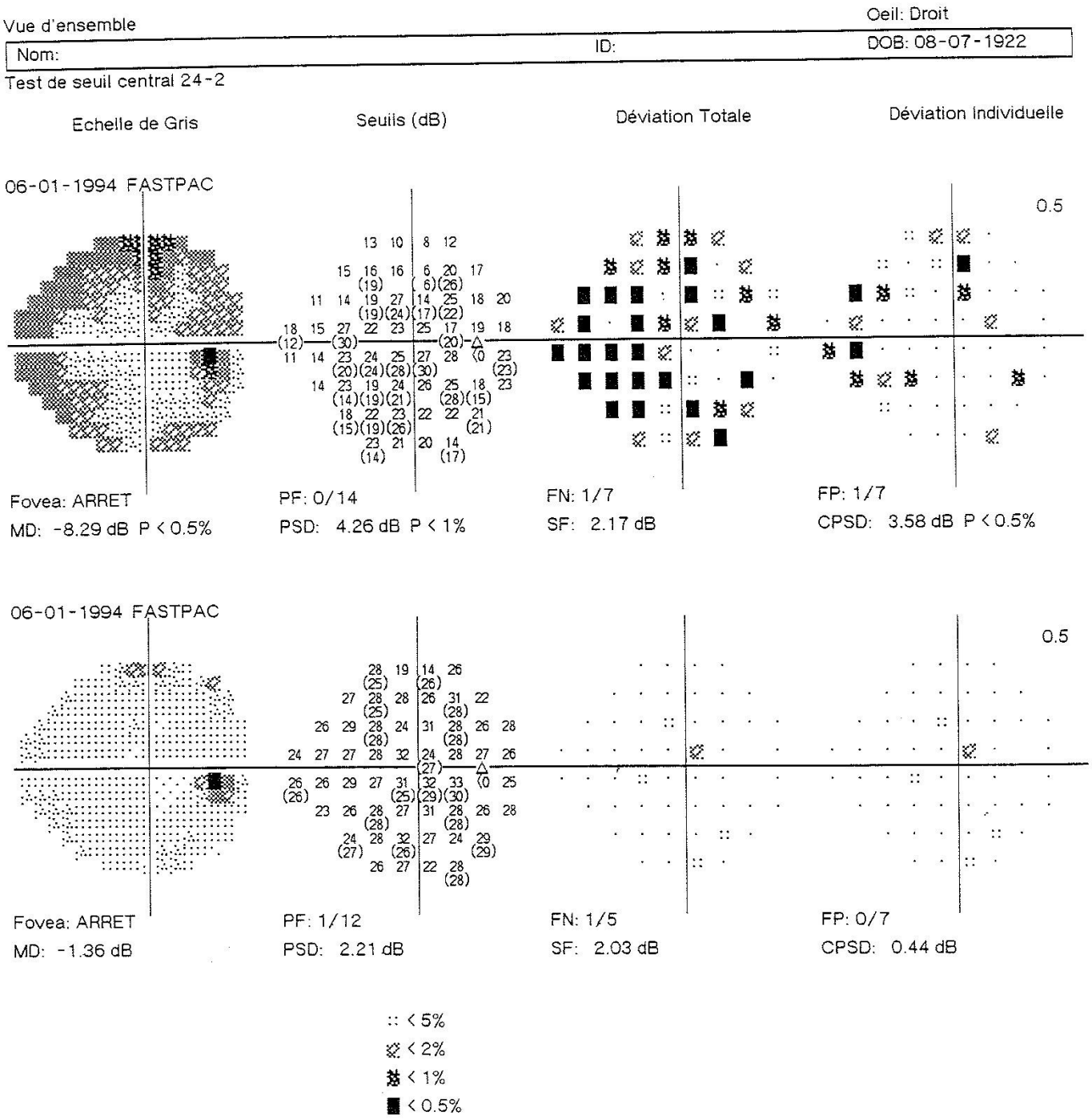
Several types of errors can lead to inaccurate results:

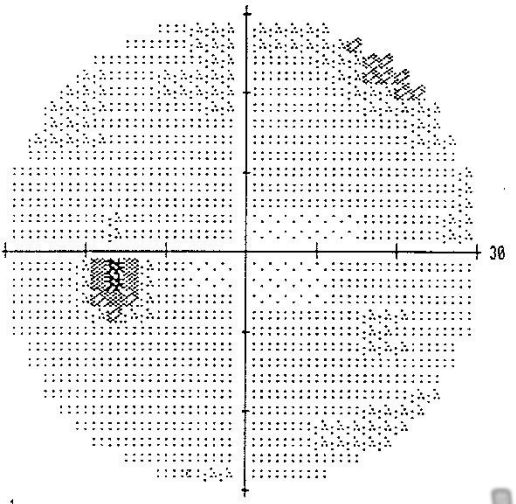
1. Incorrect patient name.
2. Incorrect patient age.
3. Inappropriate correction of refractive error.
4. Lens rim artifacts.
5. Cloverleaf fields.
6. Miotic pupils or Cataracts.

# Artifactual visual field loss

- Happy trigger
- learning effect on vF
- Glas holder
- Right-left eye
- Big nose

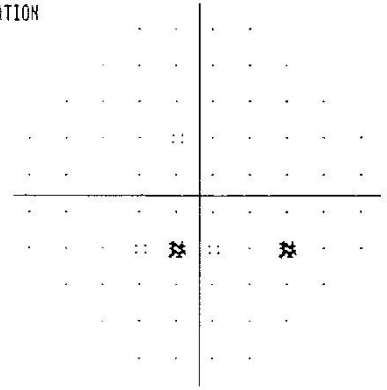
# Learning curve

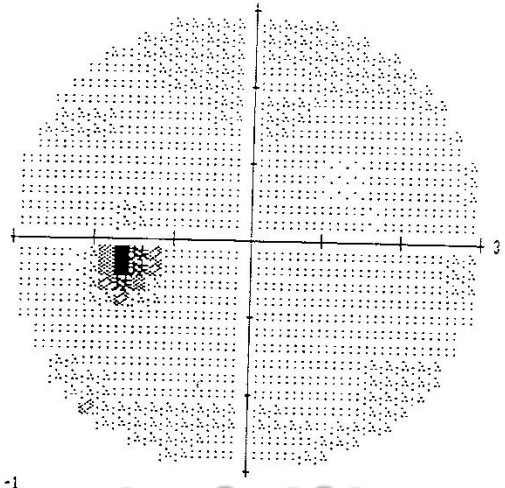




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 5 | 1 | 0 | 1 | | | |
| | | 1 | -1 | -1 | 3 | 0 | -6 | | |
| | -2 | 0 | -1 | -3 | -2 | 0 | 0 | -1 | |
| 1 | 1 | -1 | -2 | -4 | -1 | -1 | -2 | -1 | 0 |
| 0 | -2 | | -2 | -1 | 0 | 0 | 0 | -3 | -1 |
| -1 | -1 | | -2 | 1 | 0 | -1 | -3 | -3 | 0 |
| 1 | -1 | -3 | -5 | -5 | -4 | -3 | -6 | -1 | 1 |
| | 0 | -2 | -2 | -2 | -2 | -3 | -2 | 0 | |
| | | -2 | 0 | -3 | -3 | -3 | -3 | | |
| | | | 1 | -2 | -1 | 1 | | | |

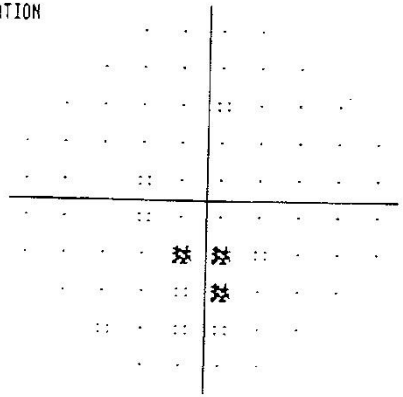
TERN
IATION

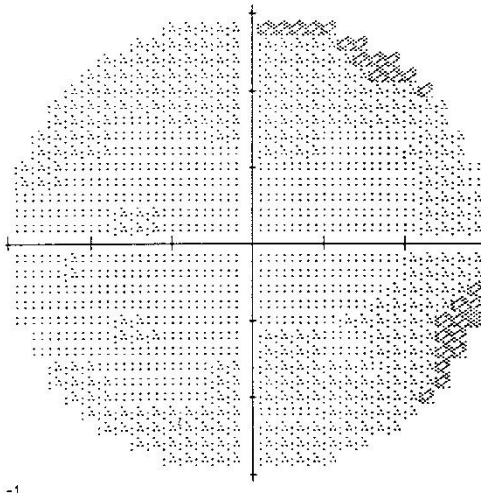




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 0 | 0 | -2 | -1 | | | |
| | | 2 | -1 | -3 | 0 | -3 | -3 | | |
| | -2 | -1 | -1 | -4 | -5 | 0 | 0 | 1 | |
| 0 | -1 | 0 | -2 | -2 | -1 | 0 | 0 | 1 | 0 |
| -1 | -2 | | -4 | -2 | -3 | -1 | 0 | -2 | 0 |
| -1 | 2 | | -4 | -3 | -3 | -3 | -3 | -3 | -3 |
| -2 | -3 | -2 | -3 | -5 | -5 | -4 | -3 | -2 | 2 |
| | -4 | 0 | -1 | -4 | -5 | -1 | -4 | -2 | |
| | | -5 | -4 | -4 | -4 | 0 | -4 | | |
| | | | -4 | 0 | -1 | -5 | | | |

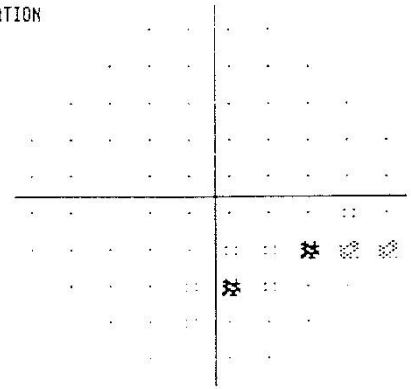
TERN
:ATION





| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 0 | 0 | -2 | -1 | | | |
| | | 0 | 0 | 0 | 0 | 0 | -5 | | |
| | 0 | 1 | -1 | -2 | -2 | -2 | -1 | 0 | |
| 0 | 0 | -1 | -1 | -2 | -3 | -1 | 0 | -1 | 2 |
| 0 | 0 | | -3 | 0 | -1 | -2 | -1 | -3 | 0 |
| 2 | -2 | | -2 | -1 | -1 | -1 | -3 | -4 | -3 |
| 1 | 1 | -3 | -3 | -2 | -4 | -4 | -6 | -6 | -10 |
| | -2 | -1 | 0 | -4 | -6 | -4 | -1 | -3 | |
| | | -2 | -3 | -4 | -1 | -2 | -2 | | |
| | | | -4 | -2 | -4 | -3 | | | |

TERN
IATION



Variability

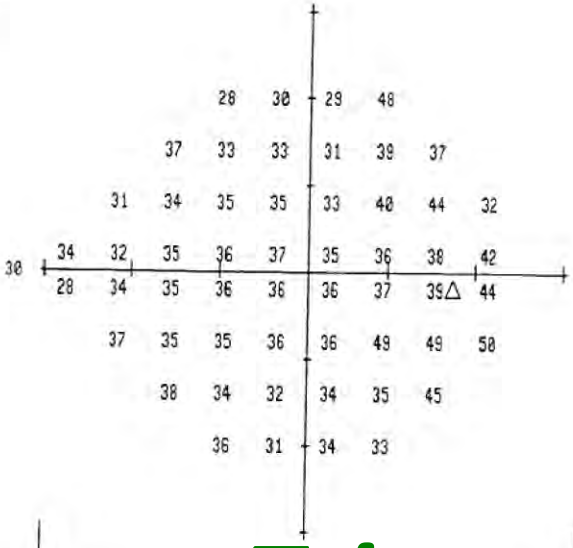
FIXATION LOSSES: 8/13
FALSE POS ERRORS: 57 %
FALSE NEG ERRORS: 26 %
TEST DURATION: 07:35

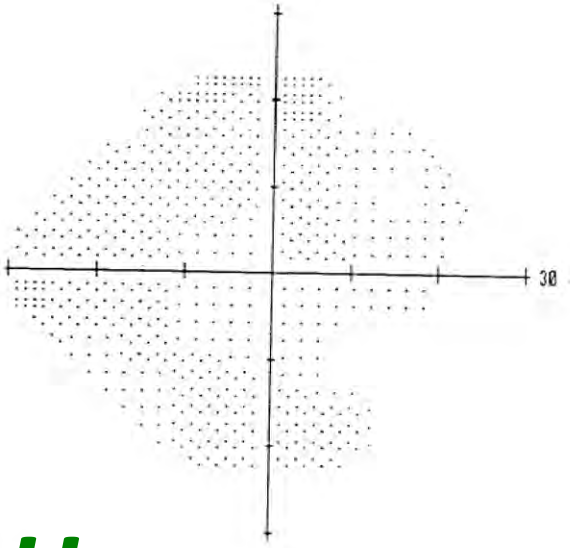
FOVEA: OFF

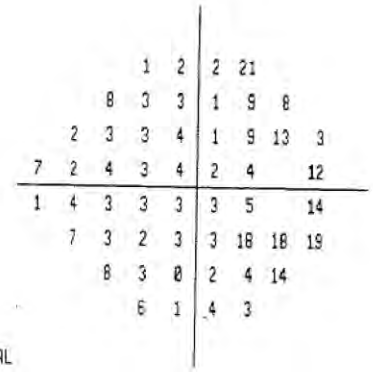
STRATEGY: SITA-STANDARD

RX: DS DC X

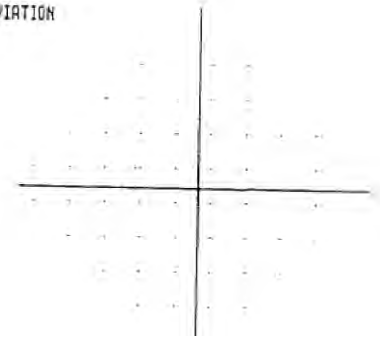
AGE: 47

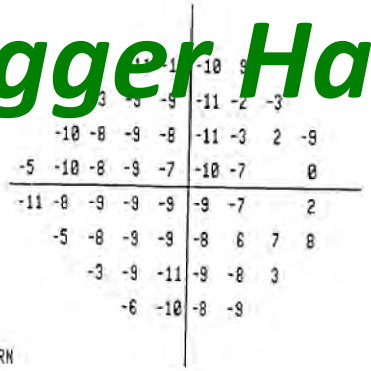


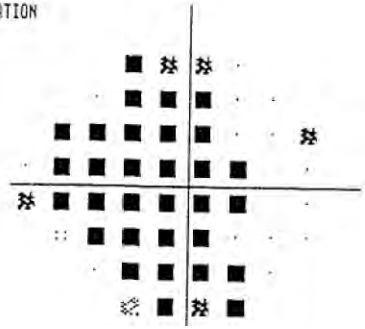




TOTAL
DEVIATION



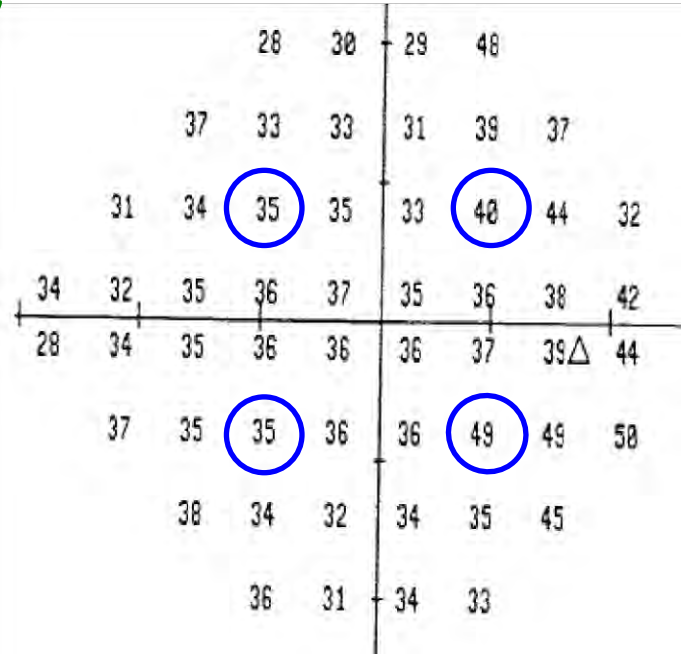



PATTERN
DEVIATION



GHT
ABNORM

MD
PSD



Analyse de Champ Unique

Oeil: Gauche

Nom: | ID: 94-1617 | DOB: 01-12-47

Test de seuil central 24-2

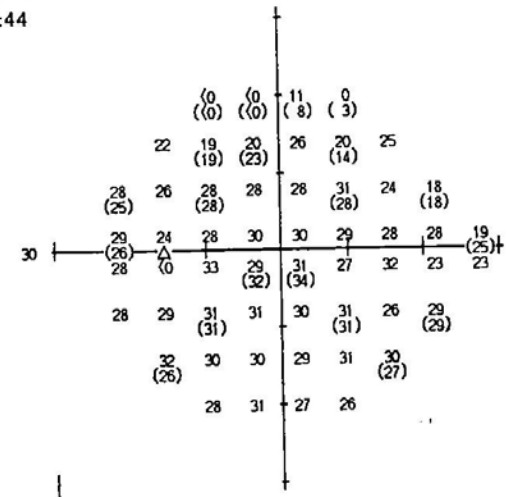
Contrôle de Fixation: Tache Aveugle
Cible de Fixation: Central
Pertes de Fixation: 1/13
Erreurs Faux Pos: 0/8
Erreurs Faux Neg: 0/7
Durée du test: 06:44

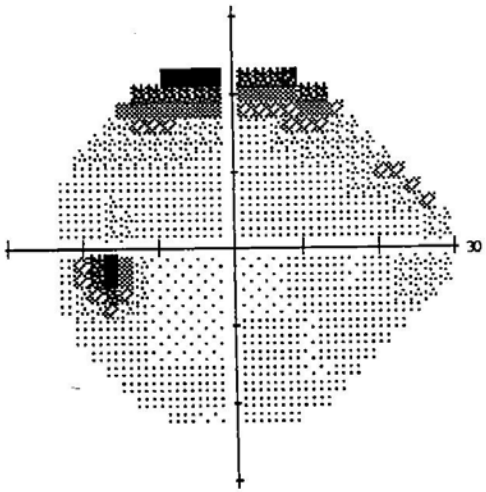
Stimulus: III, Blanc
Fond: 31.5 ASB
Stratégie: FASTPAC

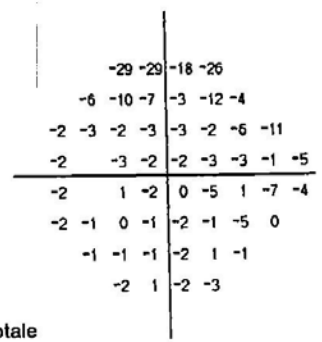
Diamètre de la Pupille:
Acuité Visuelle:
RX: +1.50 DS DC X

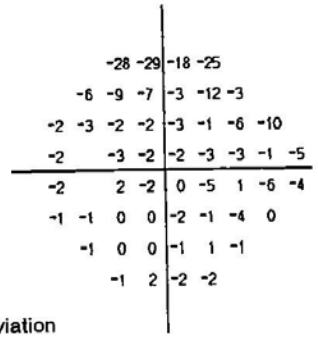
Date: 26-10-95
Heure: 14:16
Age: 47

Fovea: 36 dB



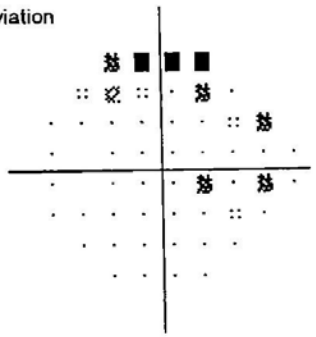




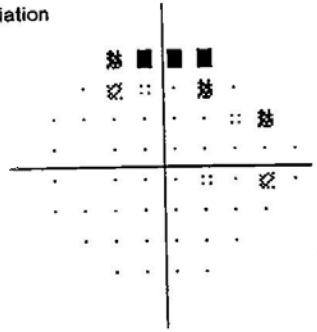


MD -3.33 dB P < 5%
PSD 5.29 dB P < 0.5%
SF 2.38 dB
CPSD 4.64 dB P < 0.5%

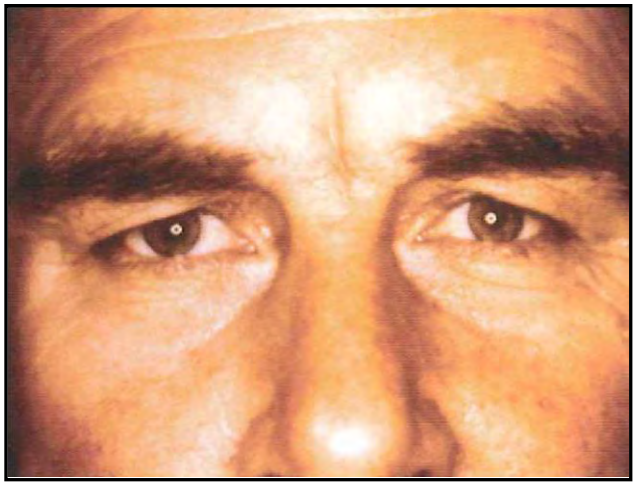
Totale Déviation



Déviation Déviation



:: P < 5%



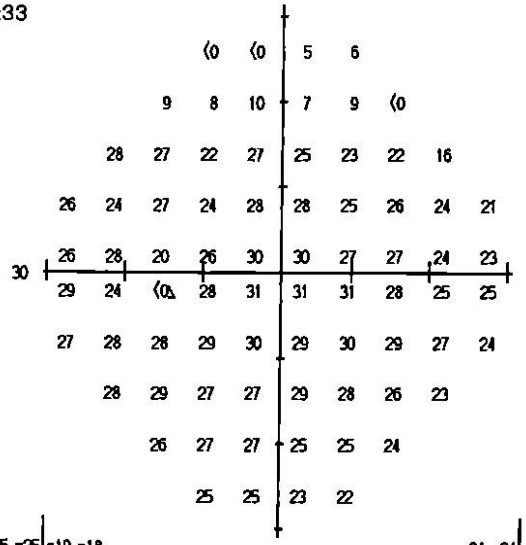
Fixation Monitor: Gaze/Blindspot
Fixation Target: Central
Fixation Losses: 3/14
False POS Errors: 10 %
False NEG Errors: 15 %
Test Duration: 06:33

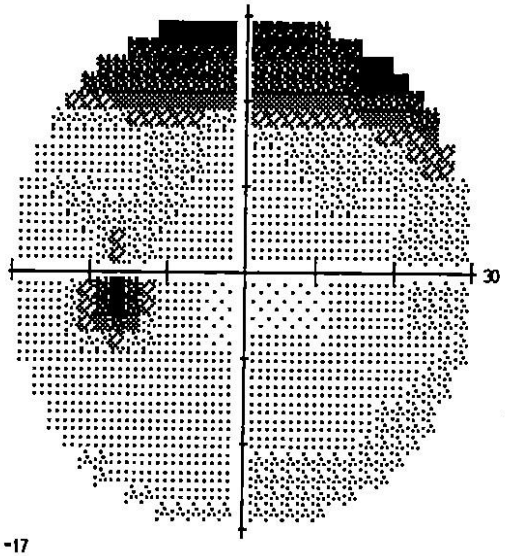
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Fast

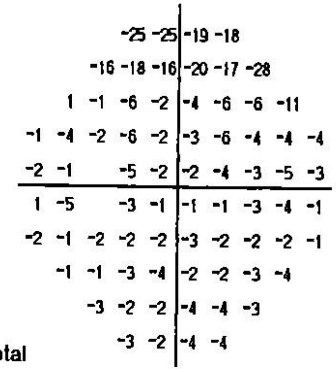
Pupil Diameter: 4.3 mm
Visual Acuity:
RX: +4.00 DS DC X

Date: 05-26-2000
Time: 10:00 AM
Age: 67

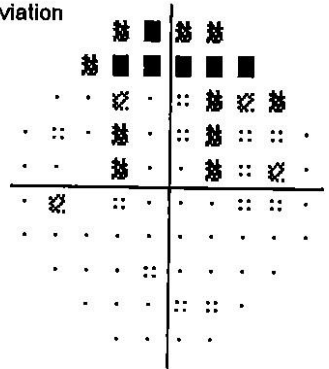
Fovea: OFF

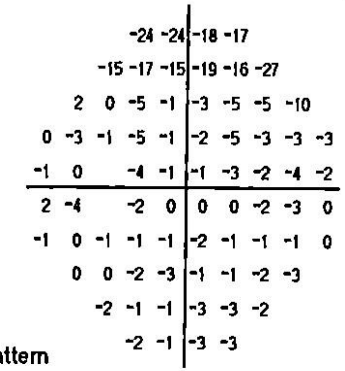


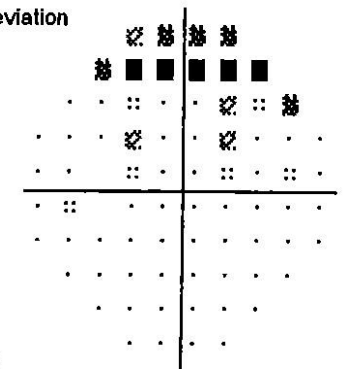



Total Deviation





Pattern Deviation



:: < 5%

GHT
Outside normal limits

MD -4.05 dB P < 1%
PSD 5.17 dB P < 0.5%

OPHTHALMOLOGY

Central 30-2 Threshold Test

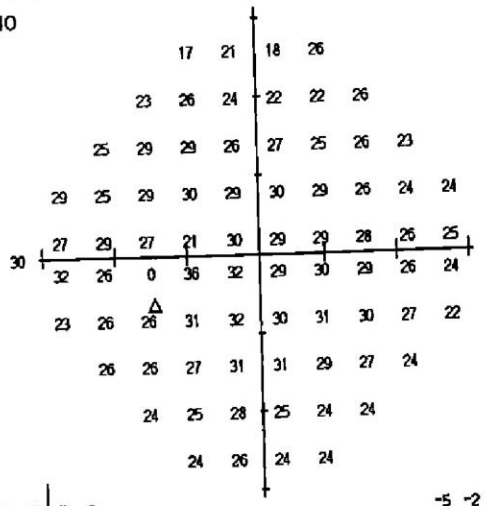
Fixation Monitor: Blindspot
Fixation Target: Central
Fixation Losses: 9/18
False POS Errors: 6 %
False NEG Errors: 6 %
Test Duration: 07:40

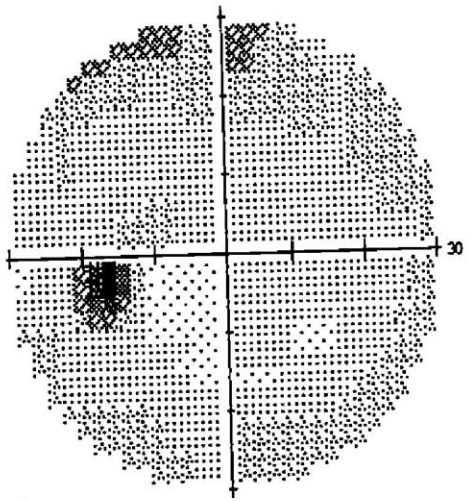
Fovea: OFF

Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard

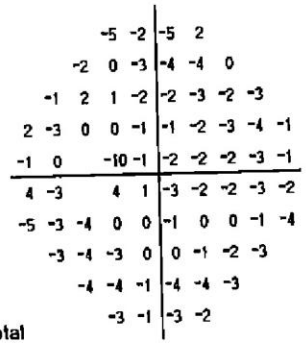
Pupil Diameter:
Visual Acuity:
RX: +4.00 DS DC X

Date: 07-03-2001
Time: 9:05 AM
Age: 68

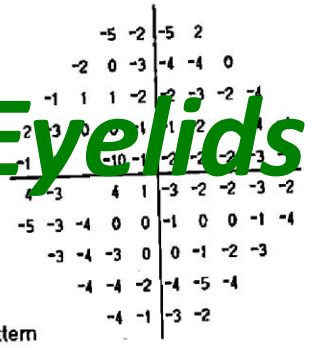




Re-test after taping the eyelid



Total Deviation



Pattern Deviation

**Eyelids**

GHT
Within normal limits

MD -1.79 dB P < 10%
PSD 2.50 dB P < 10%

:: < 5%

OPHTHALMOLOGY

# Why this shape?

**Cloverleaf**

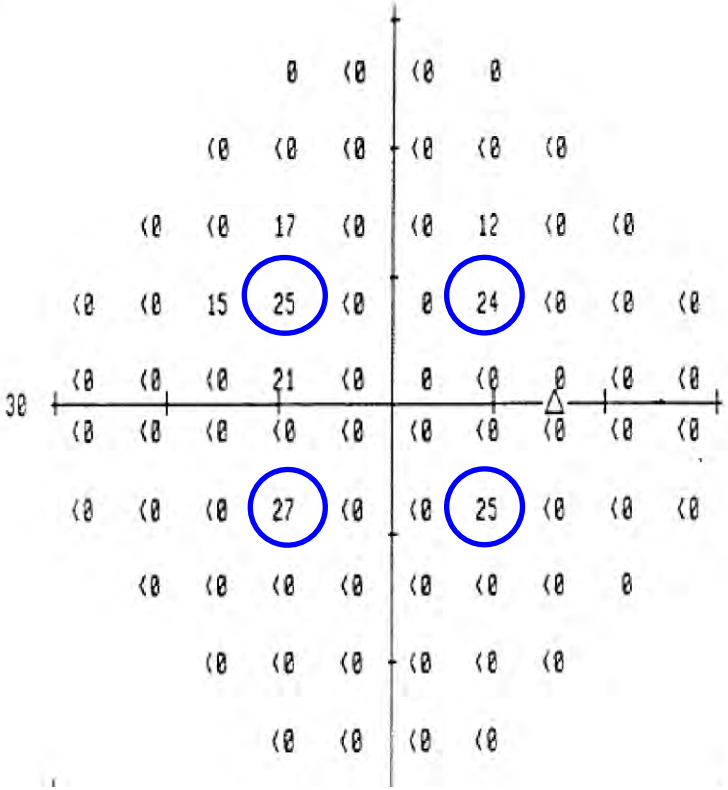
FIXATION MONITOR: BLINDSPOT
FIXATION TARGET: CENTRAL
FIXATION LOSSES: 8/21
FALSE POS ERRORS: 0 %
FALSE NEG ERRORS: 20 %
TEST DURATION: 09:14

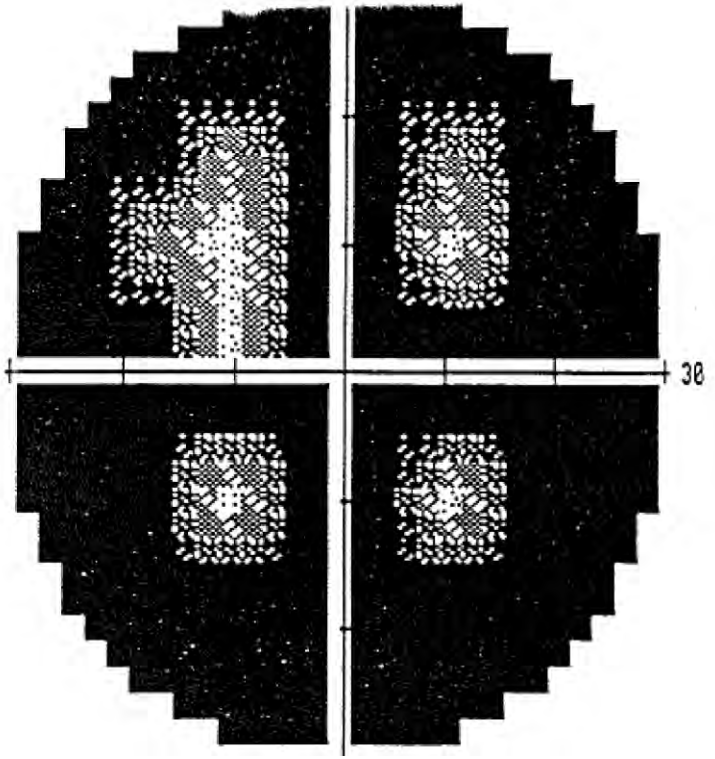
FOVEA: OFF

STIMULUS: III, WHITE
BACKGROUND: 31.5 ASB
STRATEGY: SITA-STANDARD

PUPIL DIAMETER:
VISUAL ACUITY:
RX: +2.00 DS OC X

DATE: 09-30-1996
TIME: 2:23 PM
AGE: 73



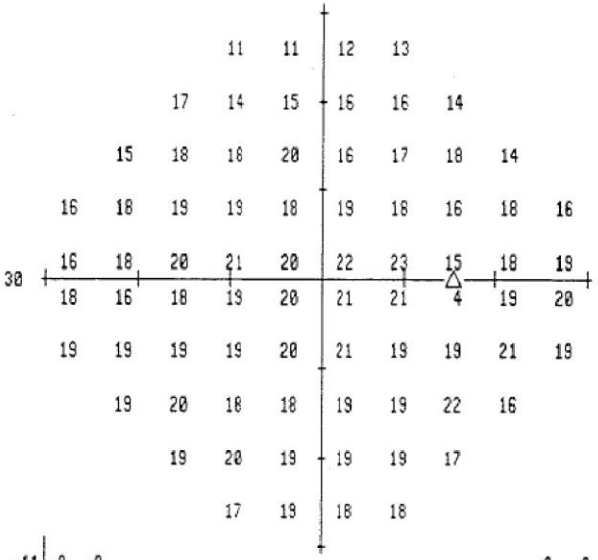
FIXATION LOSSES: 1/19
FALSE POS ERRORS: 0 %
FALSE NEG ERRORS: 0 %
TEST DURATION: 08:38

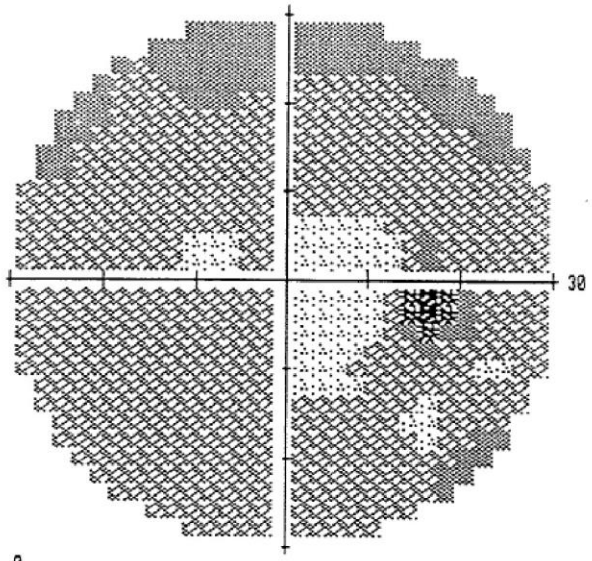
STRATEGY: SITA-STANDARD

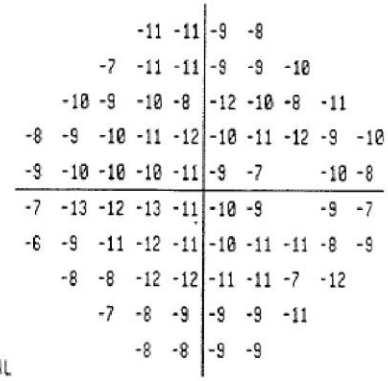
RX: +8.00 DS -2.50 DC X 105

AGE: 79

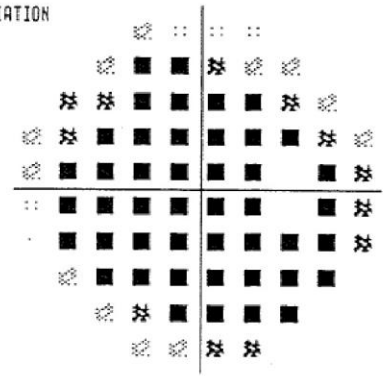
FOVEA: OFF

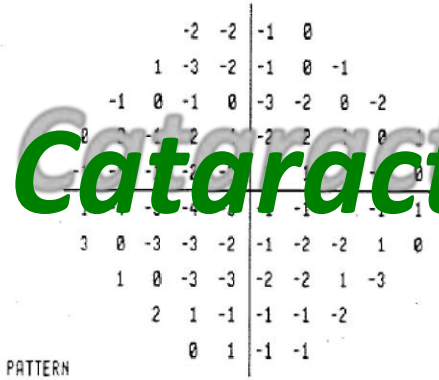


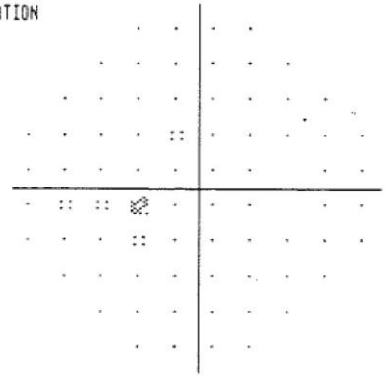




TOTAL
DEVIATION






PATTERN
DEVIATION



:: P < 5%



GHT
GENERAL REDUCTION OF SENSITIVITY

MD -9.96 DB P < 0.5%
PSD 1.77 DB

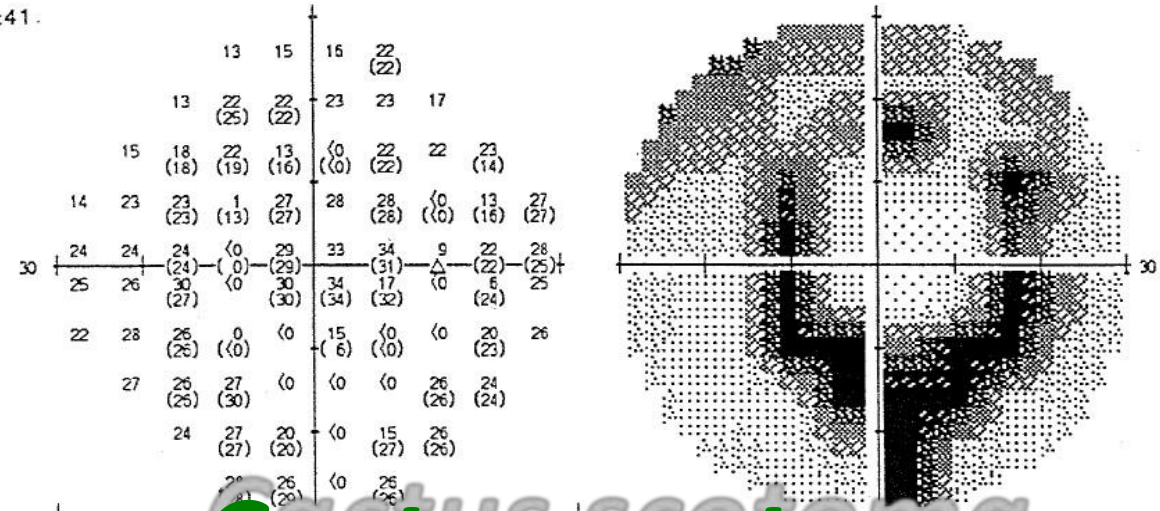
ixation Monitor: Blindspot
ixation Target: Central
ixation Losses: 0/28
alse POS Errors: 0/19
alse NEG Errors: 0/18
est Duration: 16:41

ovea: OFF

Stimulus: III, White
Background: 31.5 ASB
Strategy: FASTPAC

Pupil Diameter:
Visual Acuity:
RX: +3.50 DS DC X

Date: 20-11-97
Time: 15:13
Age: 56




Cactus scotoma

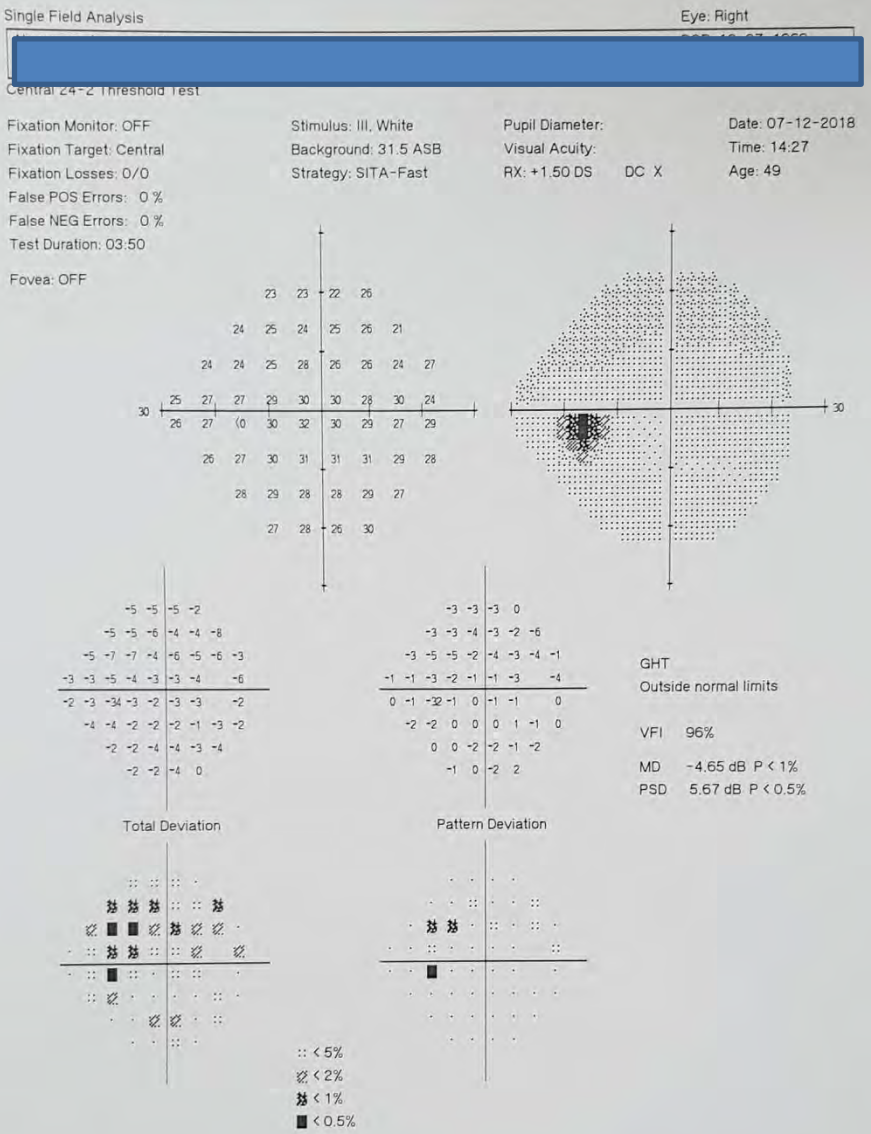
**Cactus scotoma**

Total Deviation

Pattern Deviation

MD -10.63 dB P < 0.5%
PSD 13.41 dB P < 0.5%
SF 3.02 dB P < 10%
CPSD 12.97 dB P < 0.5%

:: P < 5%


Single Field Analysis
Eye: Right
[redacted]
Central 24-2 Threshold Test
Fixation Monitor: OFF
Fixation Target: Central
Fixation Losses: 0/0
False POS Errors: 0 %
False NEG Errors: 0 %
Test Duration: 03:50
Fovea: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Fast
Pupil Diameter:
Visual Acuity:
RX: +1.50 DS
DC X
Date: 07-12-2018
Time: 14:27
Age: 49
GHT
Outside normal limits
VFI 96%
MD -4.65 dB P < 1%
PSD 5.67 dB P < 0.5%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
< 1%
< 0.5%
© 2007 Carl Zeiss Meditec
HFA II 740-12669-4.2/4.2

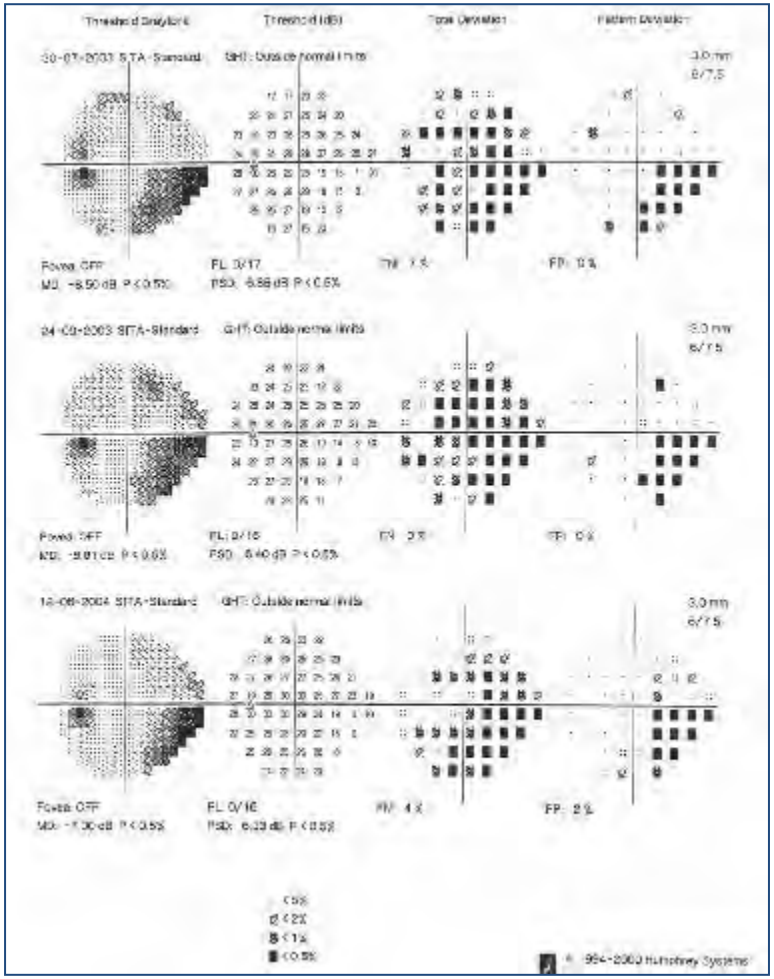
# Wrong Eye

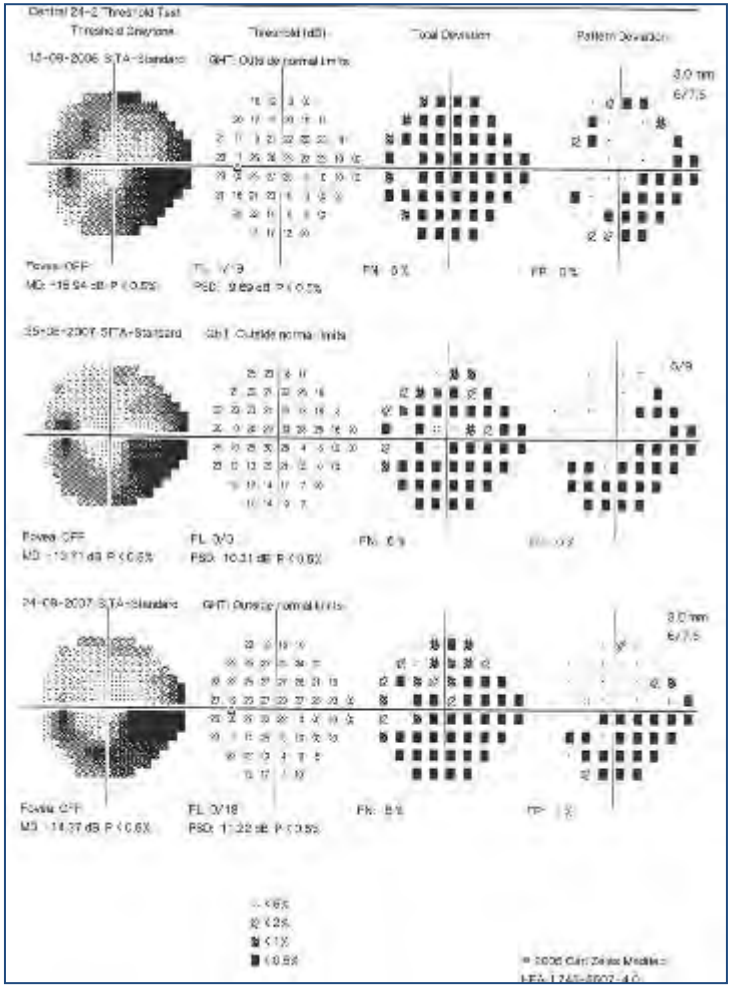
# Detecting Progression

- Sequence of threshold VF.
- Glaucoma Progression Analaysis (GPA) software.
- Peridata.

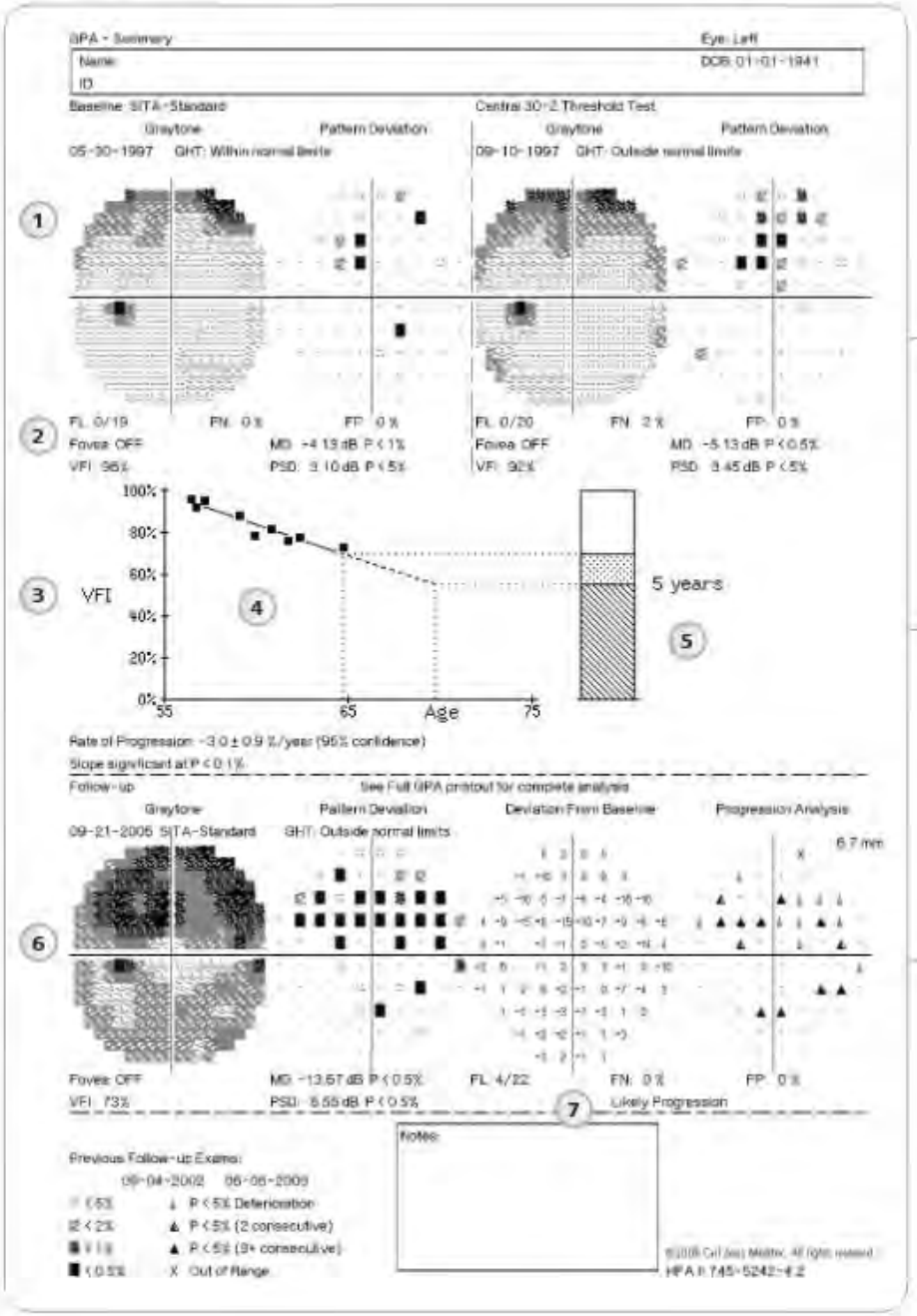
This sequence of threshold visual fields using a standard white on white static stimulus follows the progress of a glaucoma patient's left visual field over several years. After many test repetitions it is apparent that the visual field is worsening. Decisions on increasing therapy or going to surgery are made on the basis of these accumulated data.

(Refer to separate files provided to view clearer versions of the images below)



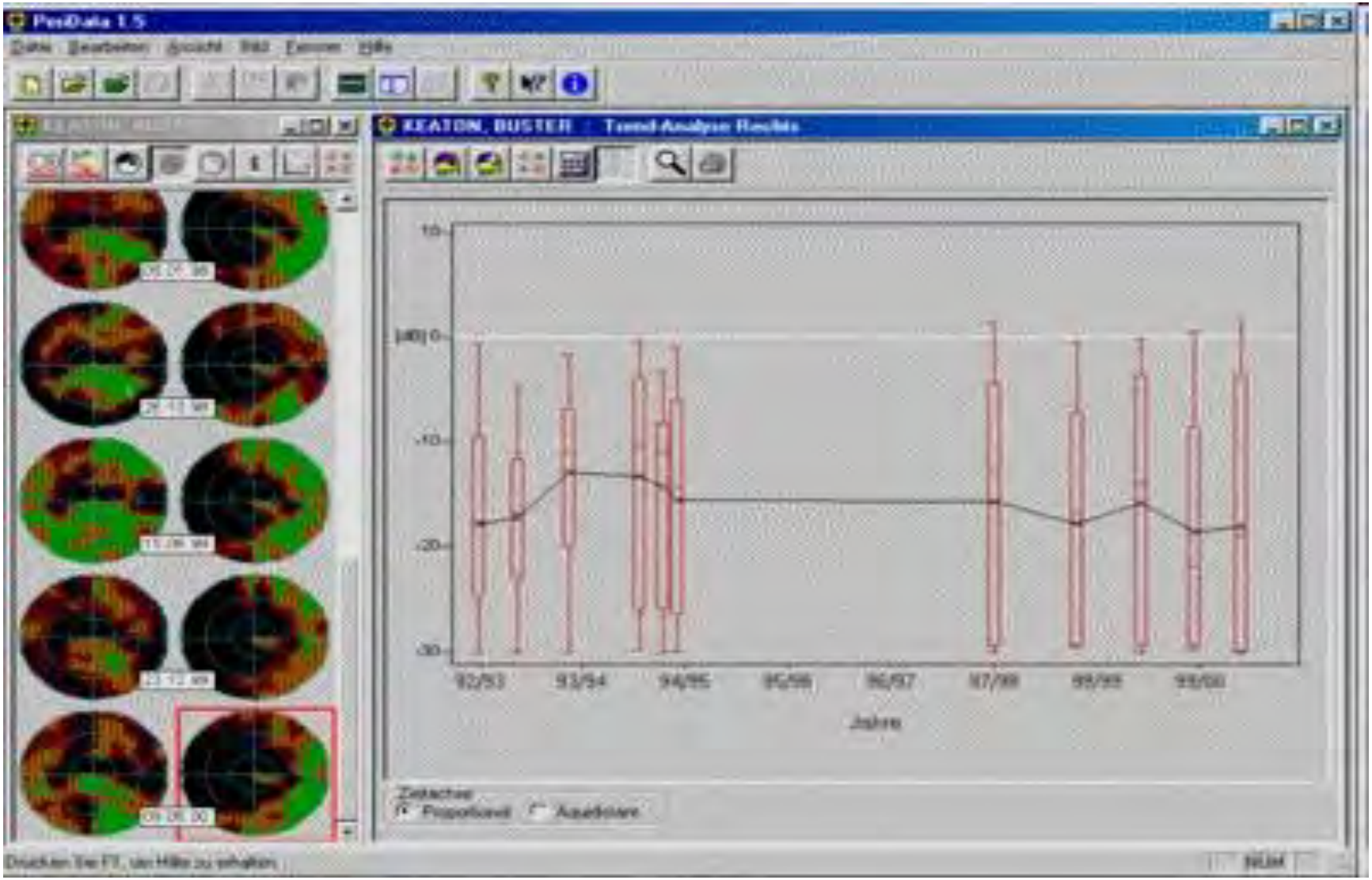


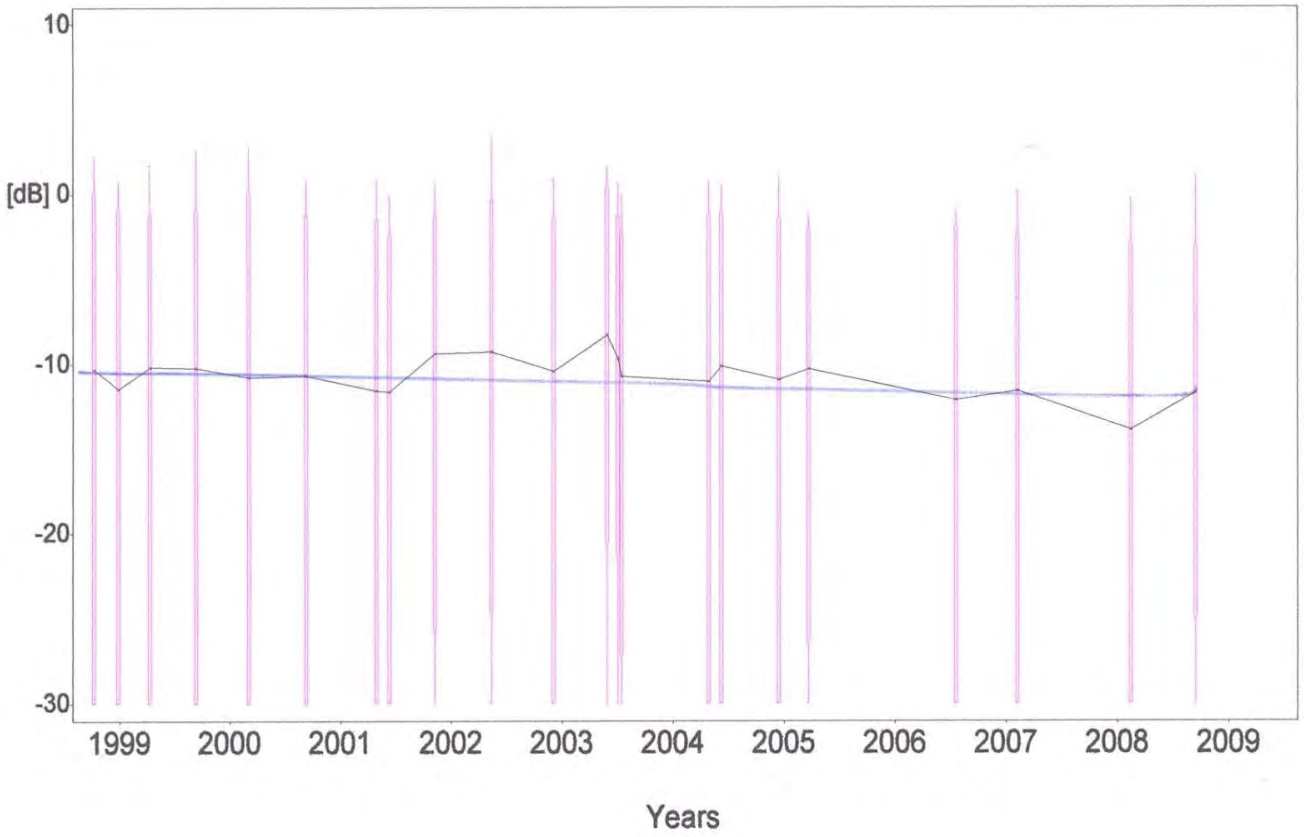
# GPA Summary Report




1. **Baseline Exams**
   Establish initial visual field status.
2. **VFI Value**
   A summary measurement of the patient's visual field status, expressed as a percent of a normal age-adjusted visual field.
3. **VFI Rate of Progression Analysis**
   Trend analysis of the patient's overall visual field history.[6]
4. **VFI Plot**
   Regression analysis of VFI values and 3 to 5 year projection.
5. **VFI Bar**
   A graphical depiction of the patient's remaining useful vision at the current VFI value along with a 3 to 5 year projection of the VFI regression line if the current trend continues.
6. **Current Visual Field Summary**
   Complete report of current visual field including VFI, MD, PSD, the Progression Analysis Plot and the GPA alert.
7. **GPA Alert**
   A message that indicates whether statistically significant deterioration was noted in consecutive tests.

# PeriData


PeriData 1.5
KEATON, BUSTER
Trend-Analyse Rechts
10
0
-10
-20
-30
92/93
93/94
94/95
95/96
96/97
97/98
98/99
99/00
Jahre
Zielachse
Proportional
Aquidistanz




MD : -1.6 p>95% (-10.0 >> -11.6)
PSD : -1.2 p>95% (11.7 >> 10.5)
CPSD : --

Indices trend

INTELLITEXT
At the average, the visual field has by 1.6 dB deteriorated. The change is highly signifikant (p>95%). The change per year was 0.2 dB. In case of a linear development, an average damage of -30dB will be reached after112.2 years.
At local consideration 56 percent of points have significantly deteriorated. 15 percent of points have significantly improved.

The power of a mathematically based analysis is limited and does not replace an evaluation by the surgeon.

# Visual Field Progression tools

1. Event- based progression tool.
   - Progressor » (Moorfields Eye Hospital, UK)
   - Peridata (GmbH, Huerth, Germany)

   - Regression analyses to measure rates of change of visual field (pointwise linear regression (PLR)).
   - To reach significance, up to six visual fields are needed

2. Trend- based progression tool.
   - GPA :Comparison of a follow-up examination to a baseline.

# Take home message

- 5 VF in the first 2 years
- Measure the rate of visual field progression.
- Use the same threshold test.
- Pay attention to VF exam quality

# Take home message

- Determine whether the visual field deficit is consistent with a glaucomatous pattern.
- Determine whether the deficit is consistent with optic nerve findings.
- Determine whether the deficit is consistent with the patient's visual function status.
- Determine whether the deficit is consistent with other testing.

# Practical OCT examination in Glaucoma



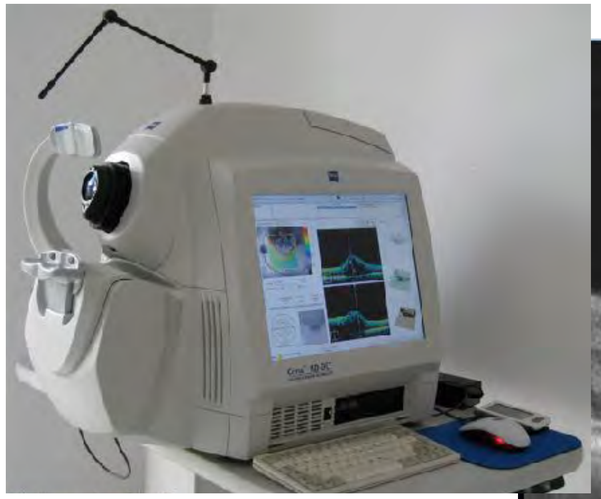
MANAMA - december 2022

Dr Dupont Géraldine

# spectral domain & swept source technologies

through the years, always quicker acquisition and higher resolution

< 5microns

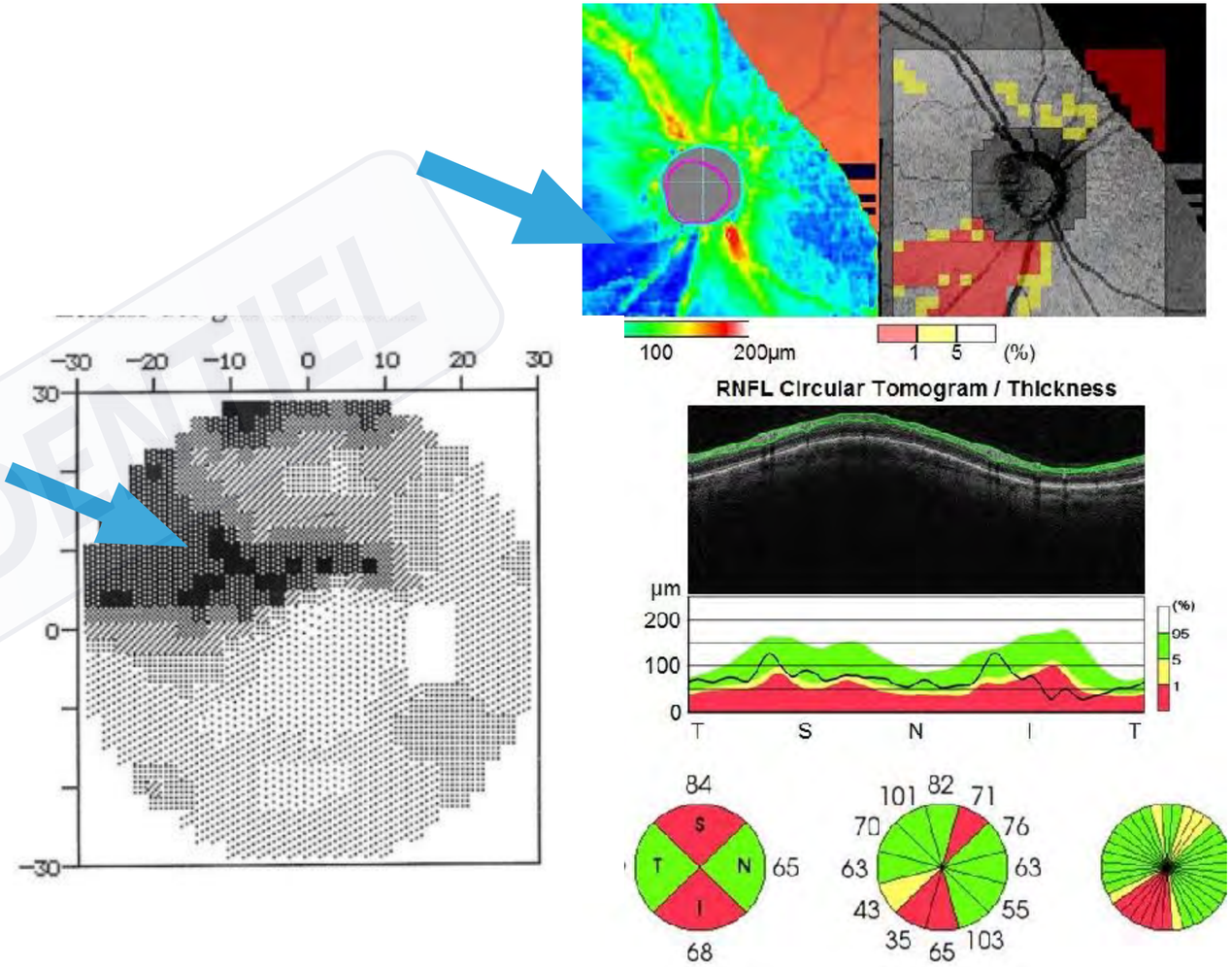


# Papillary OCT
# &
# Macular OCT

# Papillary OCT

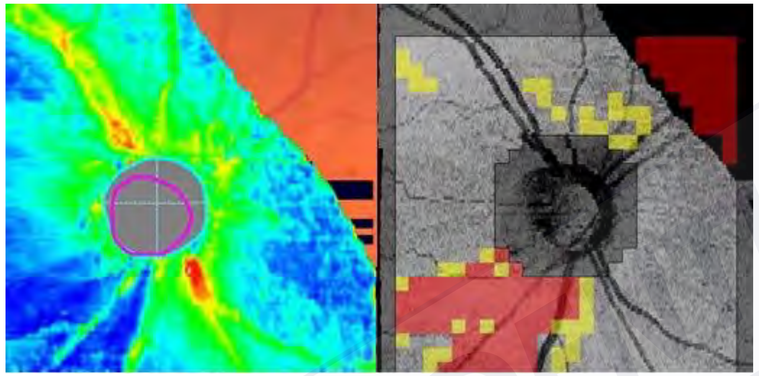
- papillary optical coherence tomography give a *structural* analysis of the nerve fibre layers around the optic disc (circle of 3,46mm diameter)

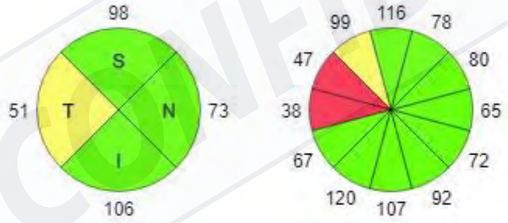
- this analysis is complementary to the *functional* analysis of the visual field



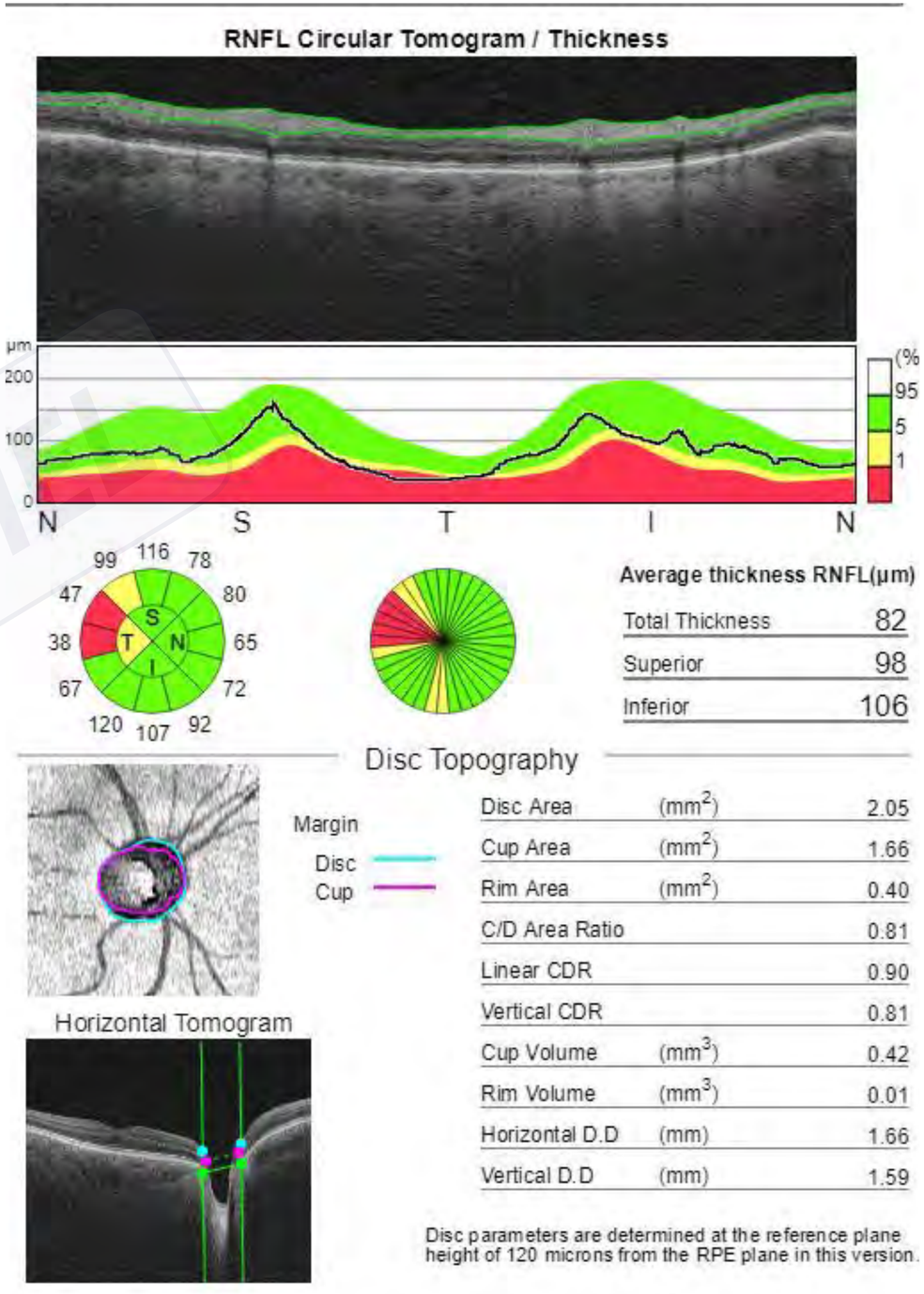
# RNFL report

- thickness map
- map of deficits
- B scan image
- double hump RNFL schema
- 4 or 12 sectors disc measurement
- disc parameters






| ⚠ | OD | OS |
|---|---|---|
| Average RNFL Thickness | 72 µm | 69 µm |
| RNFL Symmetry | 91% | |
| Rim Area | 0.91 mm² | 0.92 mm² |
| Disc Area | 2.43 mm² | 2.07 mm² |
| Average C/D Ratio | 0.78 | 0.74 |
| Vertical C/D Ratio | 0.81 | 0.75 |
| Cup Volume | 0.525 mm³ | 0.409 mm³ |



# Limits and benefits

- the papillary OCT:

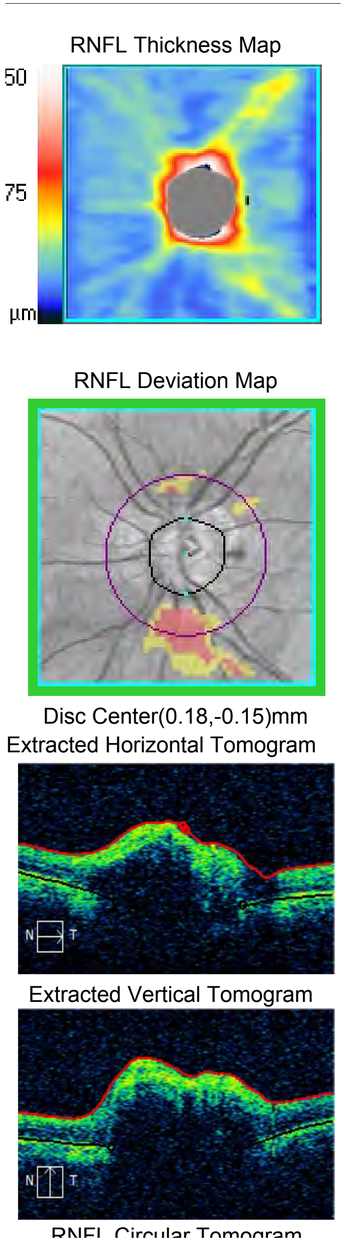
+ analyses **all** the retinal nerve fibers (RNFL) converging into the optic disc

- artefacts: blinking, bad visibility (cataract,…)

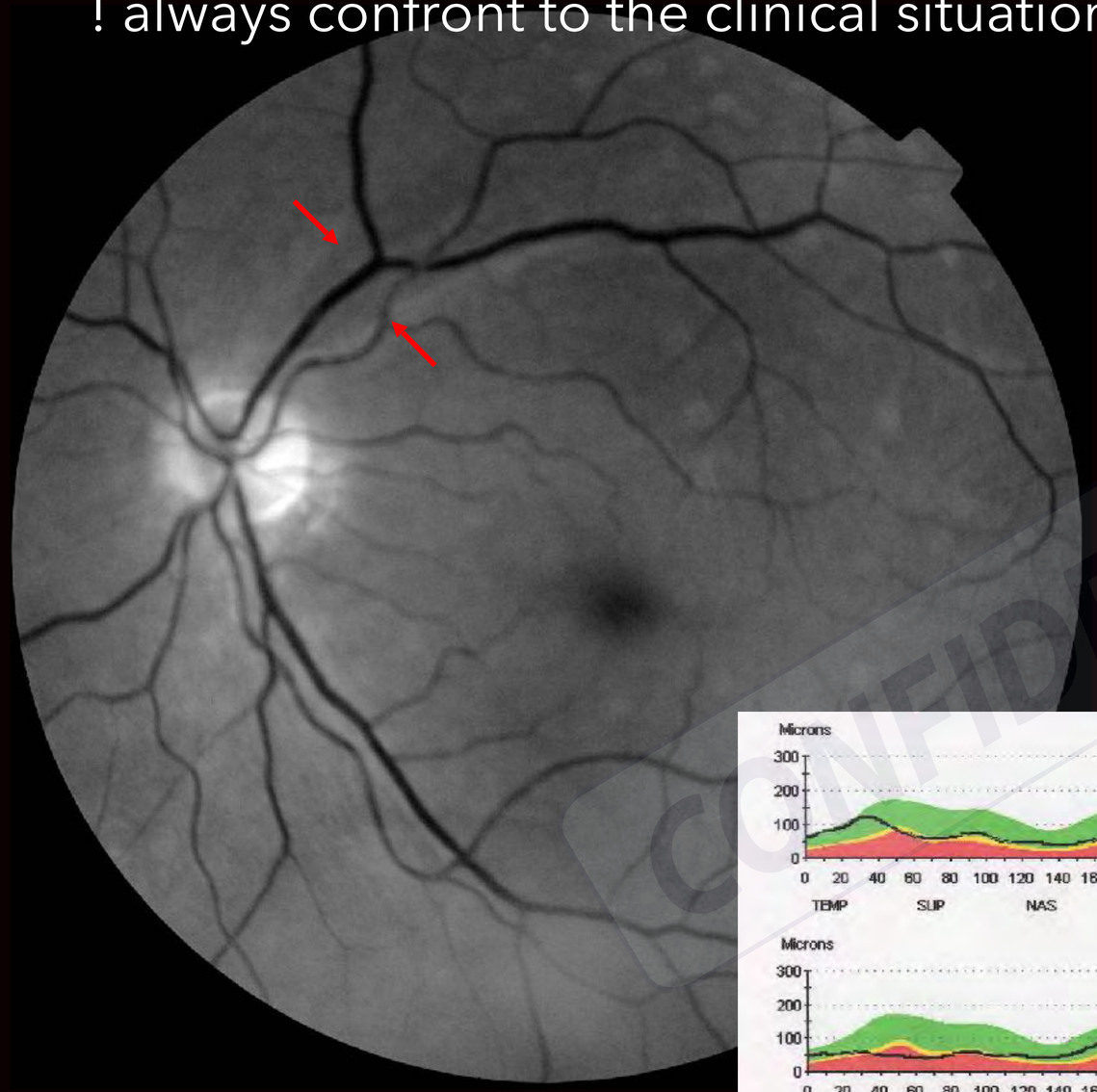
normative database

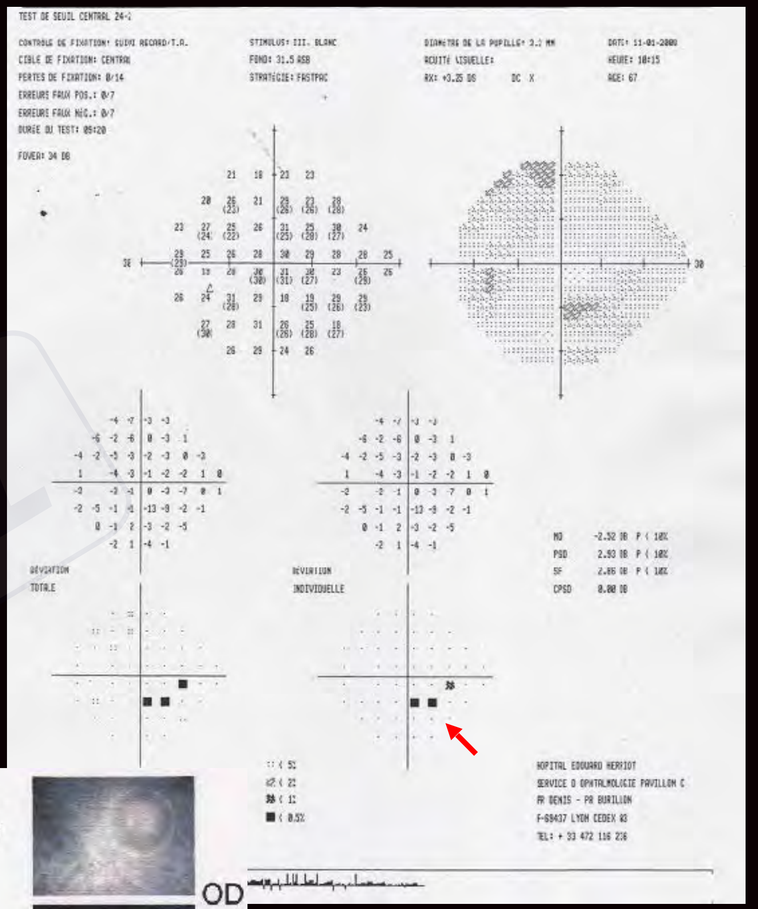
myopia, drusen…

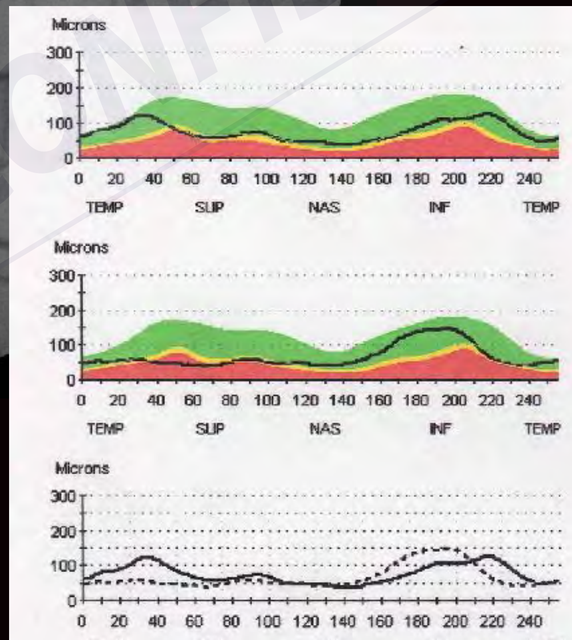
- limit of the analysis in severe glaucoma (more gial structures around the optic nerve, masking RNFL thinning)

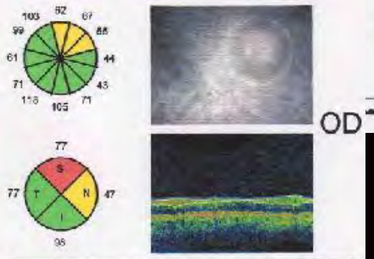


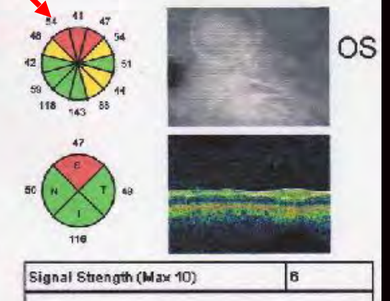
! always confront to the clinical situation





# Macular OCT

Invest Ophthalmol Vis Sci. 2010 Sep;51(9):4646-51. Epub 2010 Apr 30.

**Structure-function relationship and diagnostic value of macular ganglion cell complex measurement using Fourier-domain OCT in glaucoma.**

Kim NR, Lee ES, Seong GJ, Kim JH, An HG, Kim CY.

Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Me

J Glaucoma. 2010 Jun 23. [Epub ahead of print]

**Diagnostic Power of Optic Disc Morphology, Peripapillary Retinal Nerve Fiber Layer Thickness, and Macular Inner Retinal Layer Thickness in Glaucoma Diagnosis With Fourier-domain Optical Coherence Tomography.**

Huang JY, Pekmezci M, Mesiwala N, Kao A, Lin S.

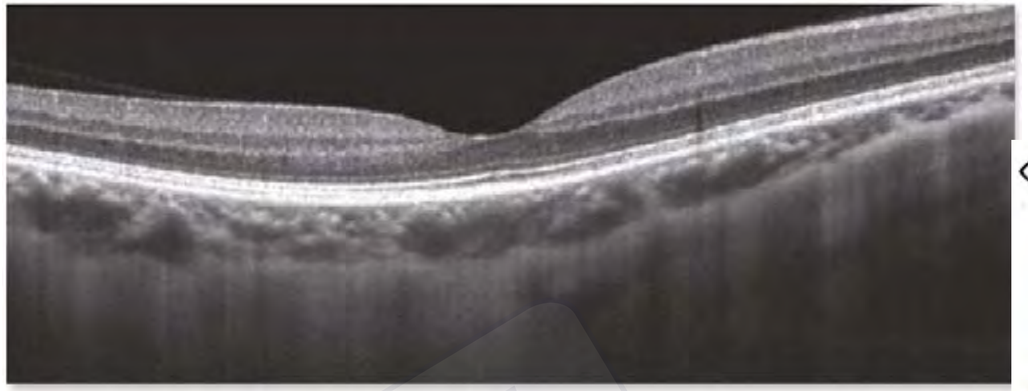
new complex, specific for glaucomatous disease: **GanglionCellComplex**

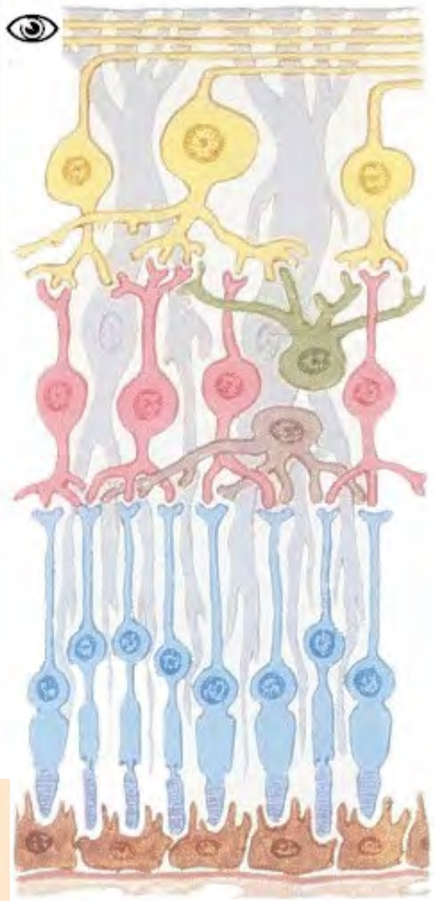
Invest Ophthalmol Vis Sci. 2010 Jul 14. [Epub ahead of print]

**Relationship between Visual Field Sensitivity and Macular Ganglion Cell Complex Thickness as Measured by Spectral Domain Optical Coherence Tomography (RTVue-100 SD OCT).**

Cho JW, Sung KR, Lee S, Yun SC, Kang SY, Choi J, Na JH, Lee Y, Kook M.

# Macular OCT



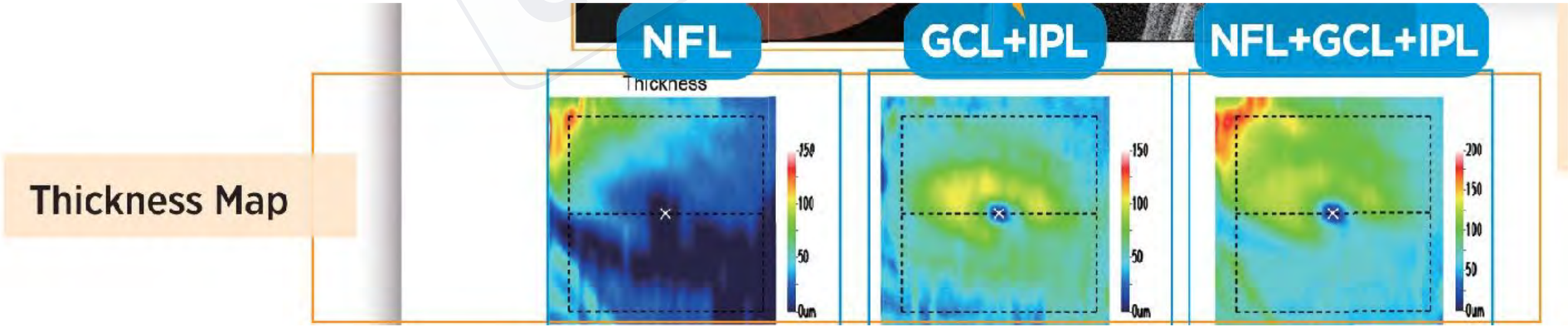


- the retinal ganglion cell complex GCC:

*2 or 3 inner retinal layers:*

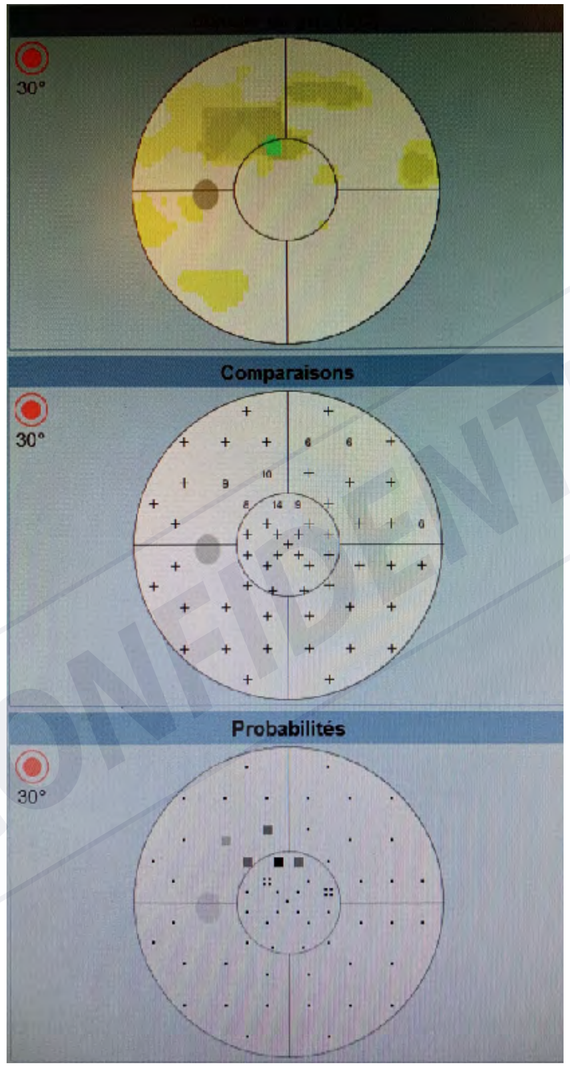
- inner plexiform layer (IPL)
- **ganglion cell** layer (GCL)
- retinal nerve fiber layer (NFL)

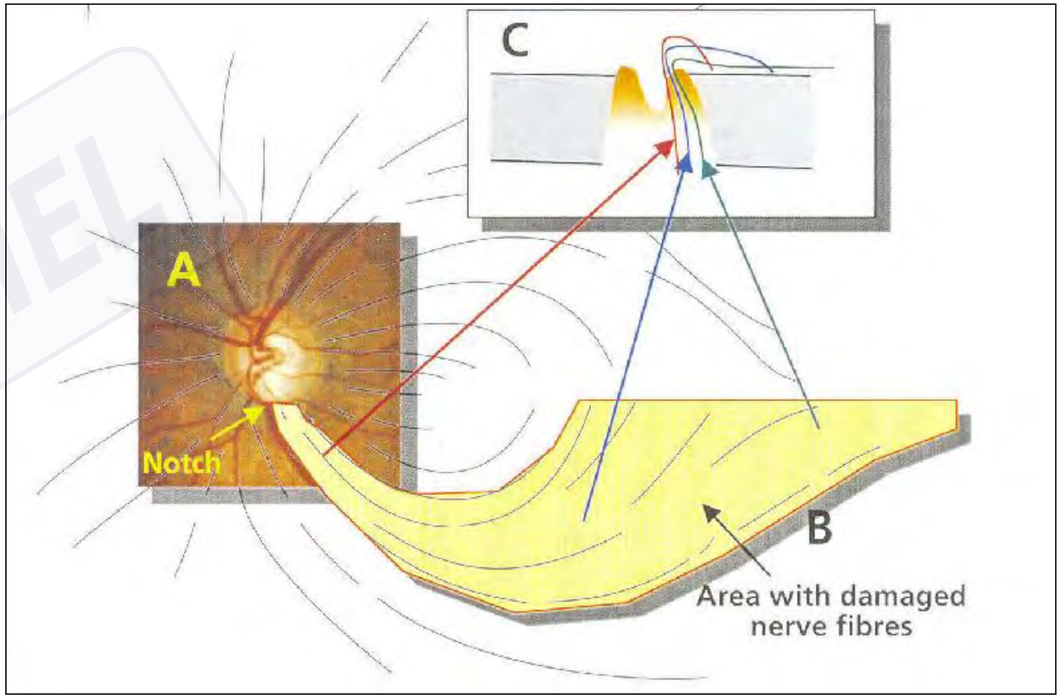
*! be aware you can't compare GCC thickness between various OCT devices*



# Macular OCT

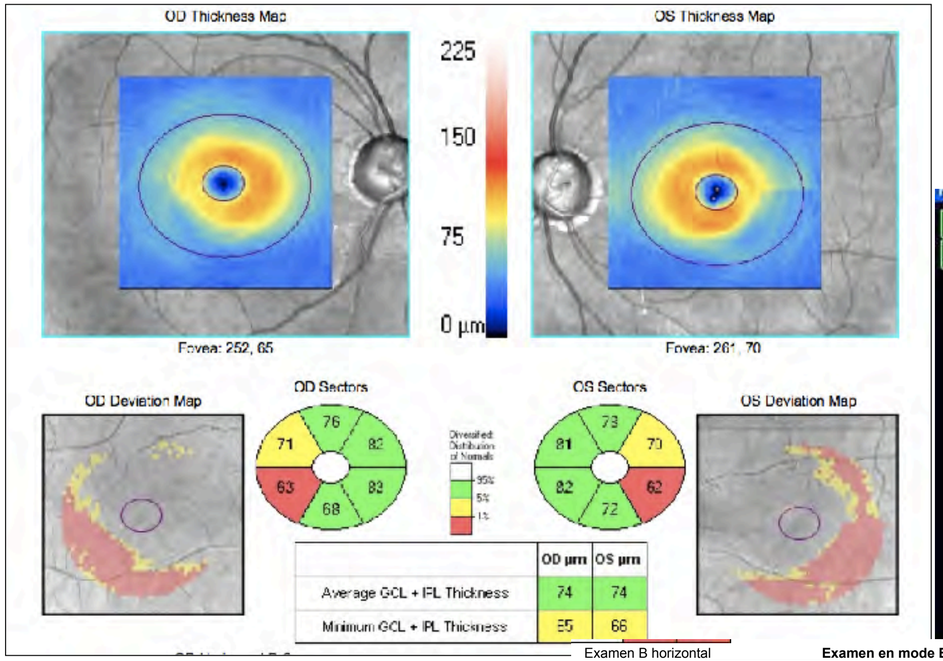
- the *structural* analysis of the GCC is also complementary to the *functional* analysis of the visual field, more precise in the central area

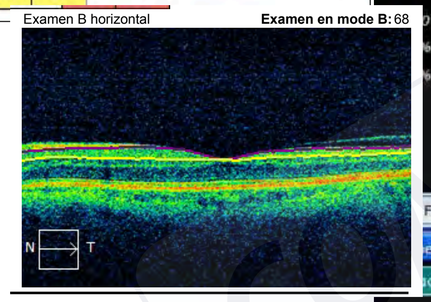


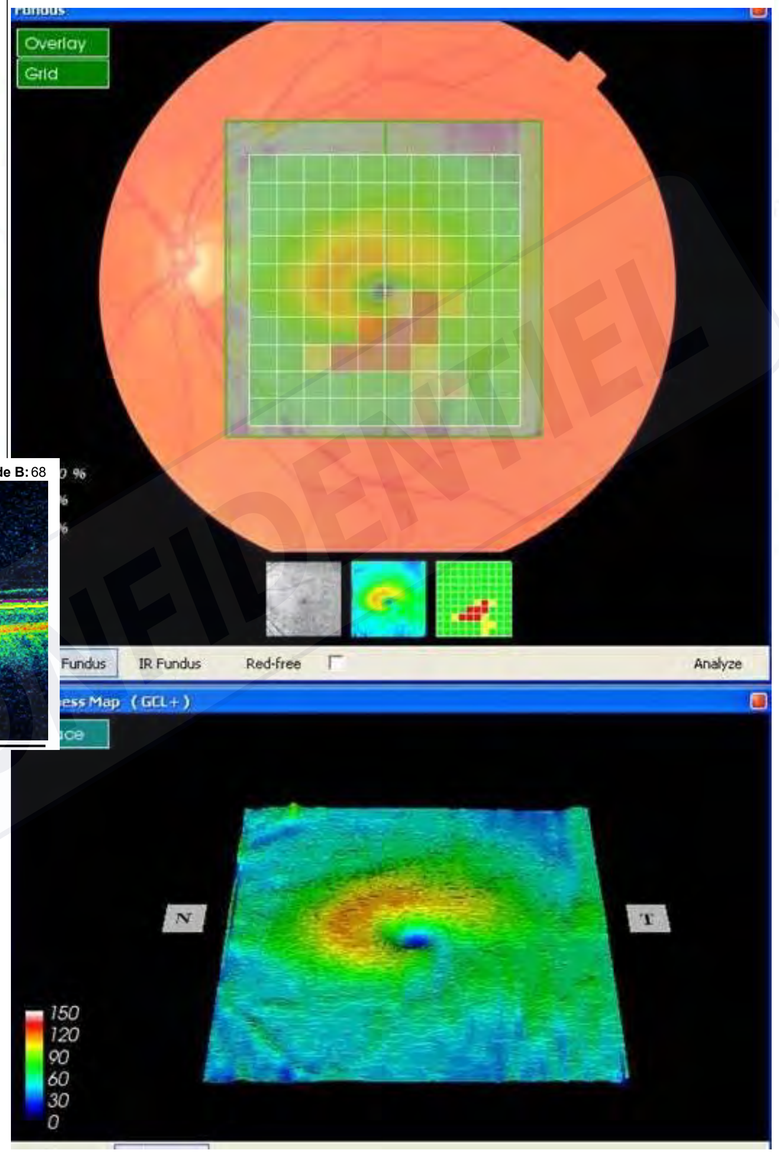



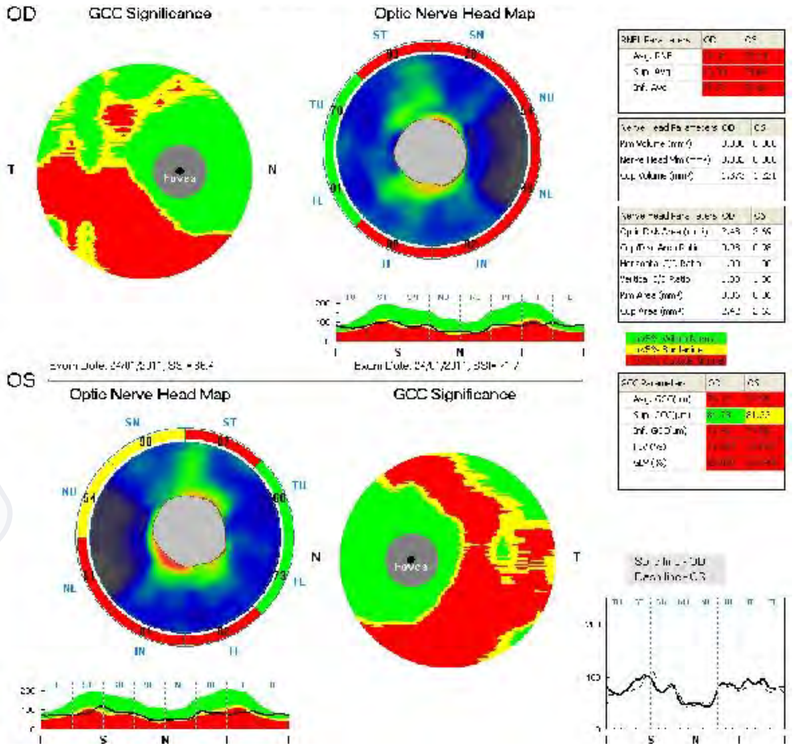

the macular area contains about 50% of the retinal ganglion cells

# GCC report



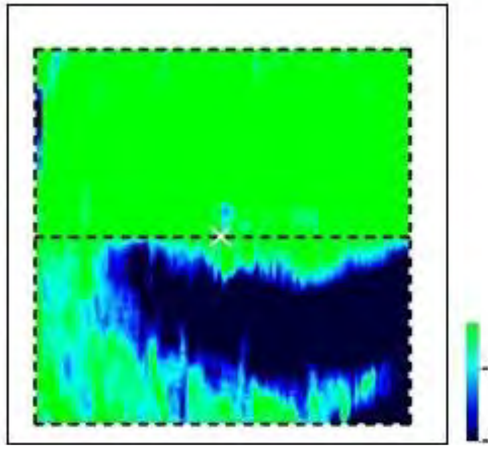



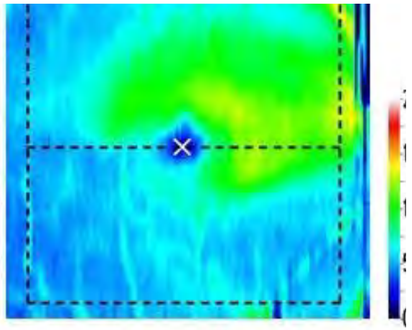



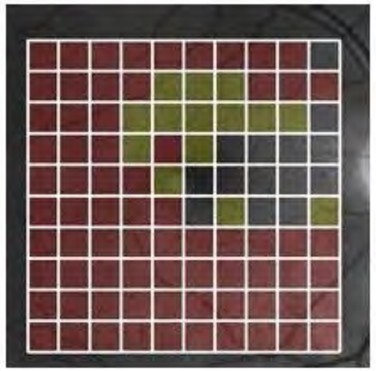




- thickness map
- deficit map
- B scan image
- thickness parameters

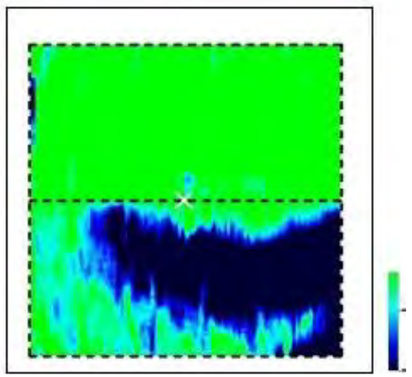
hemifield asymetry



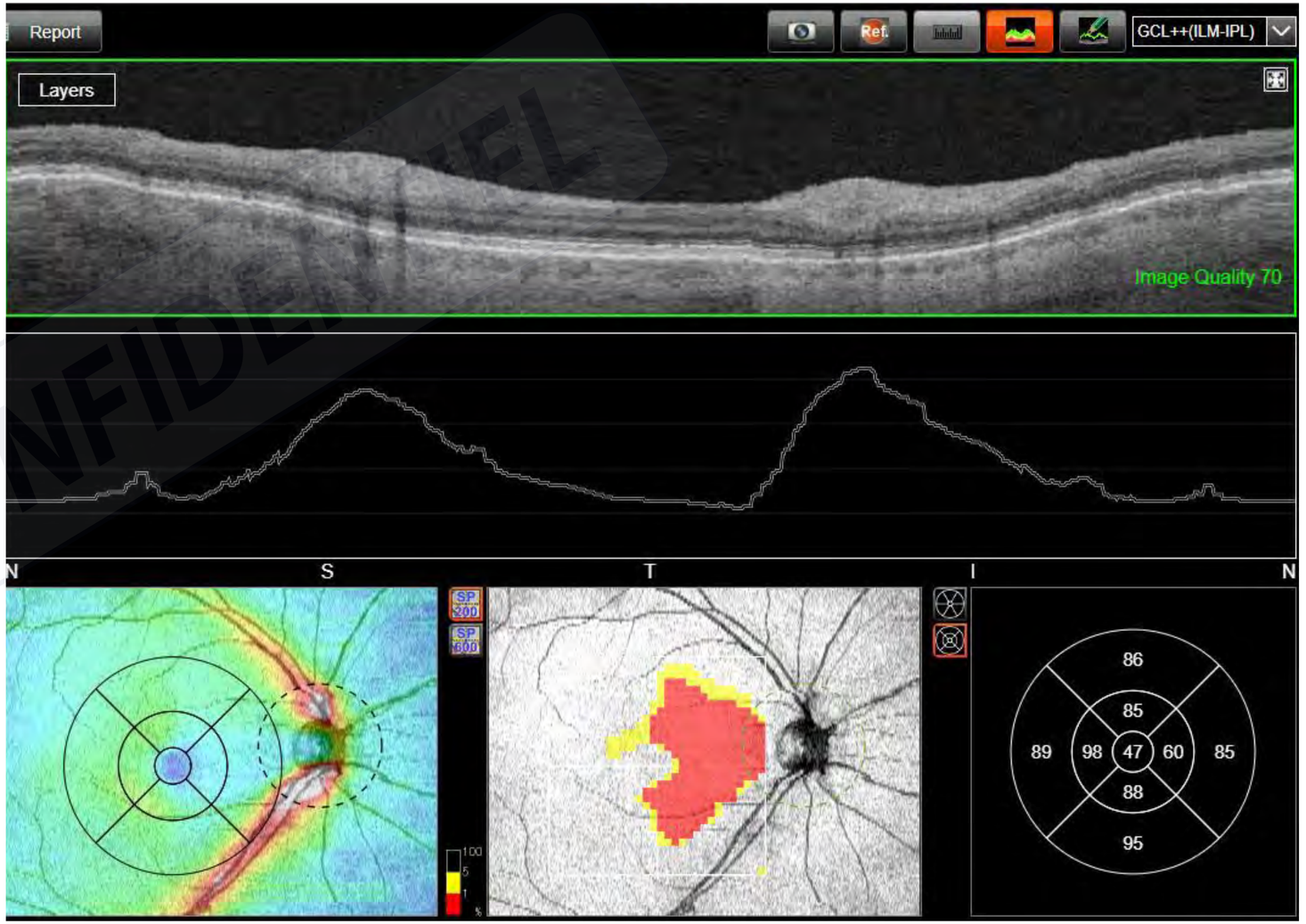




| | |
|---|---|
| Superior | 82 um |
| Inferior | 61 um |
| Total | 71 um |



# horizontal =/= vertical hemifield asymetry



# Limits and benefits

- the macular OCT:

+ analyses the ganglion cells ( >50% are located in the macular area)

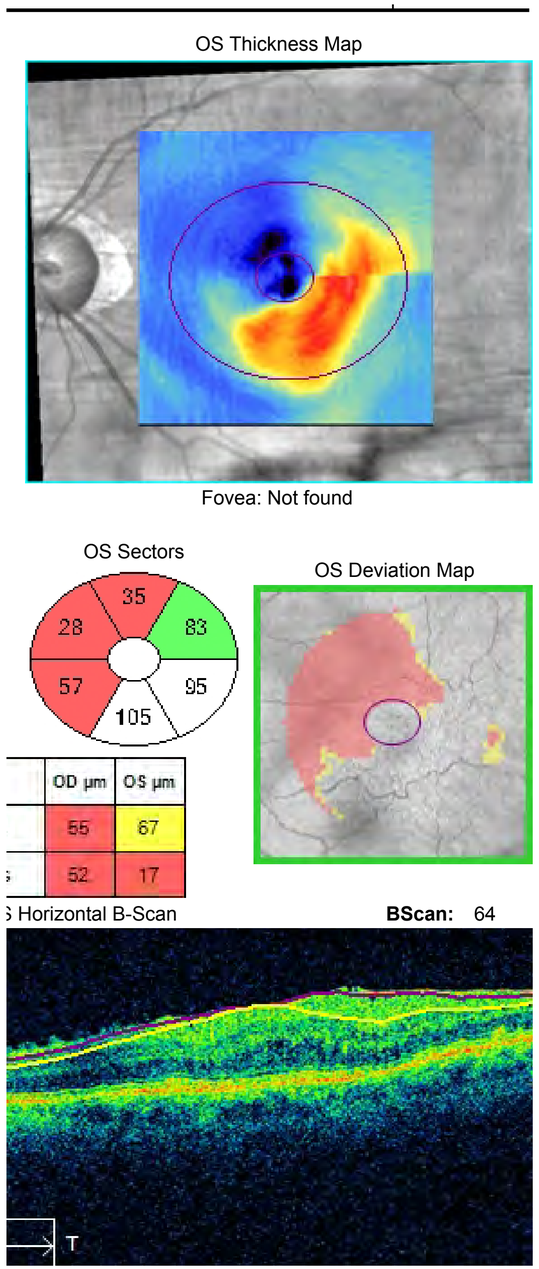
+ helps early glaucoma diagnosis

(compared to the visuel field: where the deficit appears after 20-40% ganglion cells loss)

+/- helps progression analysis in severe glaucoma (because of less gial structures)

- artefacts: blinking, bad visibility… normative database

macular edema, membrane, atrophy …

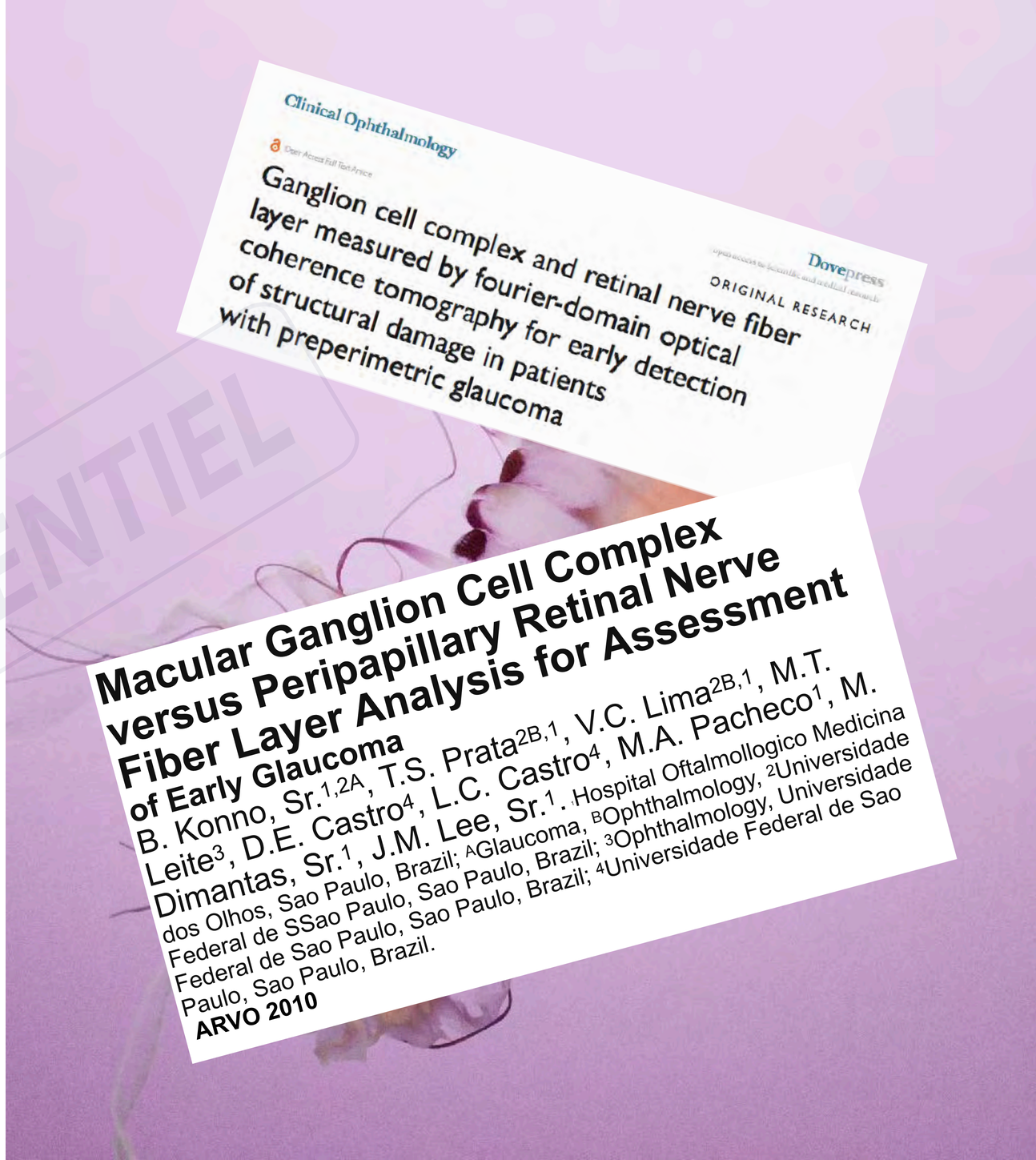


# Benefits & Limits of the OCT

- good diagnosis in *early* and pre-perimetric glaucoma
- good reproducibility to assess *progression*

… but be aware of

- out of the rules patients (children, high myopia,…)
- artefacts
- don’t forget the clinical examination



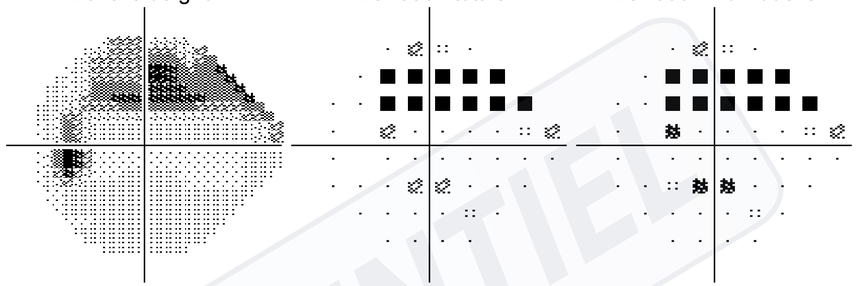
# Combined OCT analysis

# OCT & visual field combination

OU (examen simple) — Central 24-2 Test de seuil — OS

Echelle de gris | Déviation totale | Déviation individuelle

P < 5%
P < 2%
P < 1%
P < 0,5%

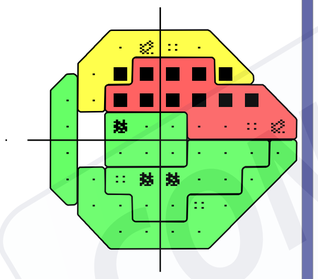


09 juil. 2020 **SITA-Fast**

FP : 0%
FN : 0%
VFI : 87%

MD24-2 : -4,87 dB P < 1%
PSD24-2 : 7,99 dB P < 0,5%
GHT : Hors limites normales

e-Fonction



té pour comparaison

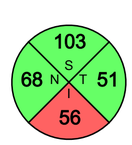
| | OS |
|---|---|
| NFL moyenne | 69µm |
| /D moyen | 0,74 |
| le l'ANR | 0,92mm² |
| /D vertical | 0,75 |
| de la cupule | 0,409mm³ |
| la papille | 2,07mm² |
| L + IPL moyenne | 63µm |
| L + IPL minimum | 43µm |

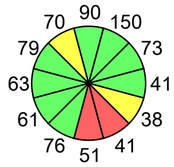
/d 95 % 5 % 1 %

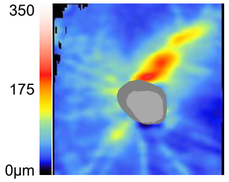
CIRRUS HD-OCT — OS

Quadrants RNFL | Heures horloge RNFL | Carte d'épaisseur RNFL

Puissance du signal : 8/10

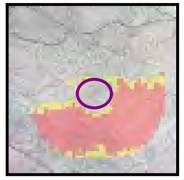


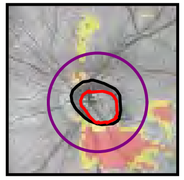




Puissance du signal : 8/10

Ganglion Cell
09 juil. 2020



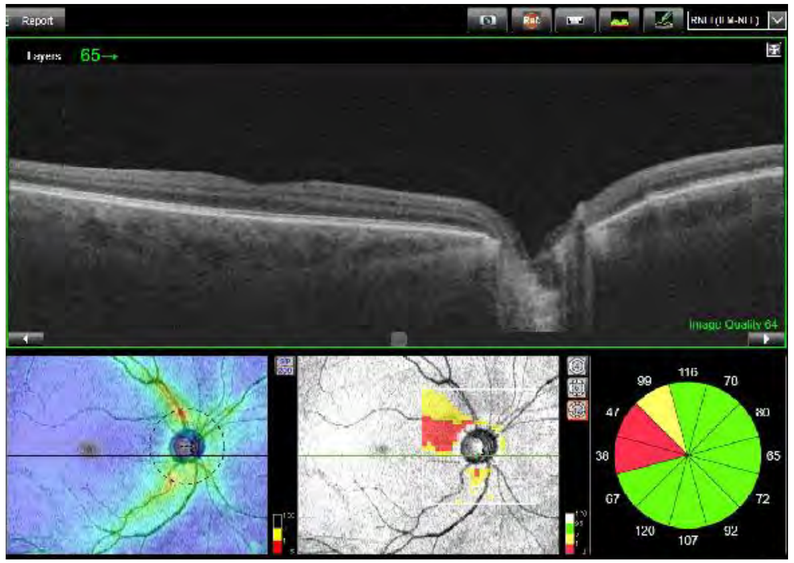
RNFL
09 juil. 2020



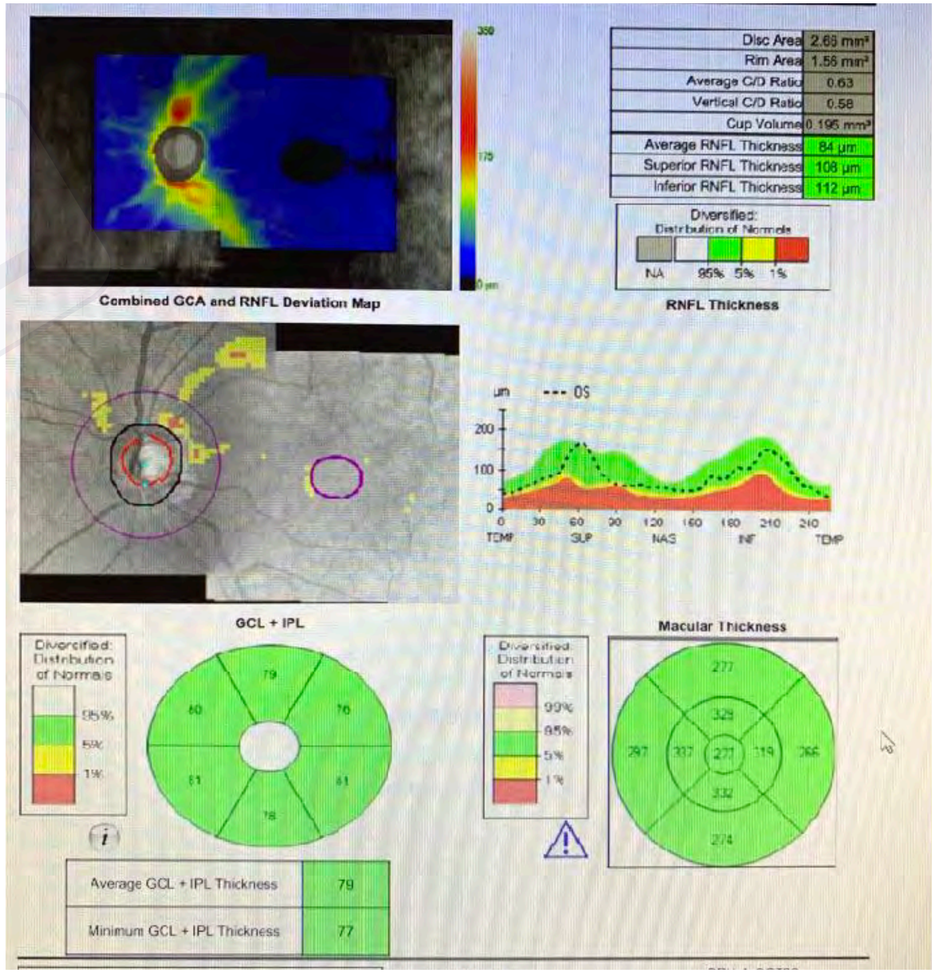
Au moins un paramètre est proche de la valeur limite de la donnée normative, ce qui peut causer une modification des couleurs en cas de répétition.

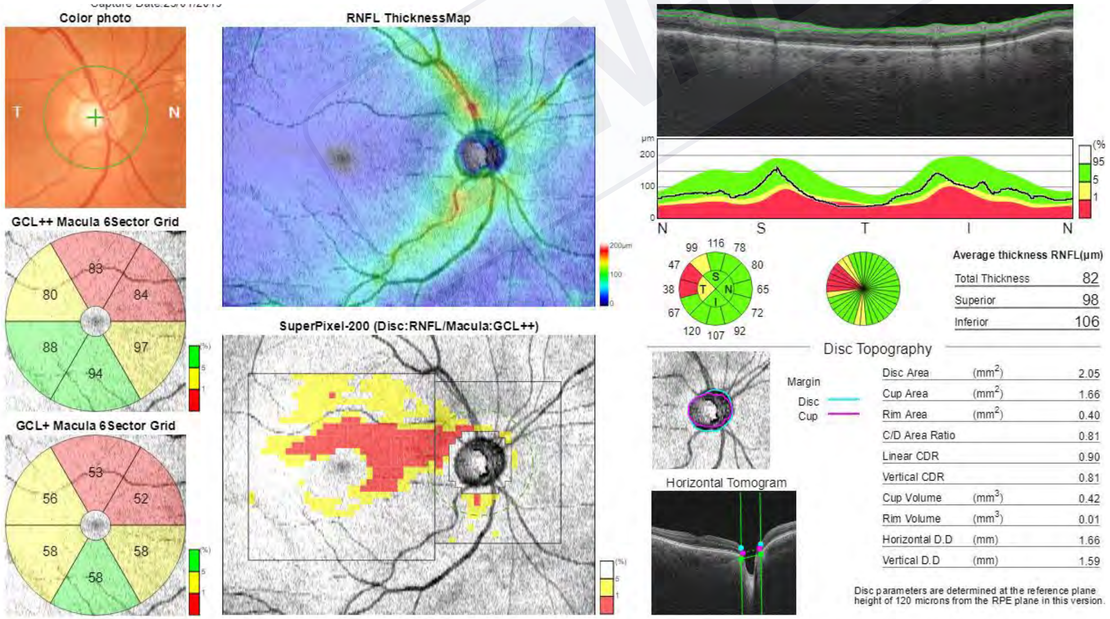
Signature

# Papillar & macular OCT combination

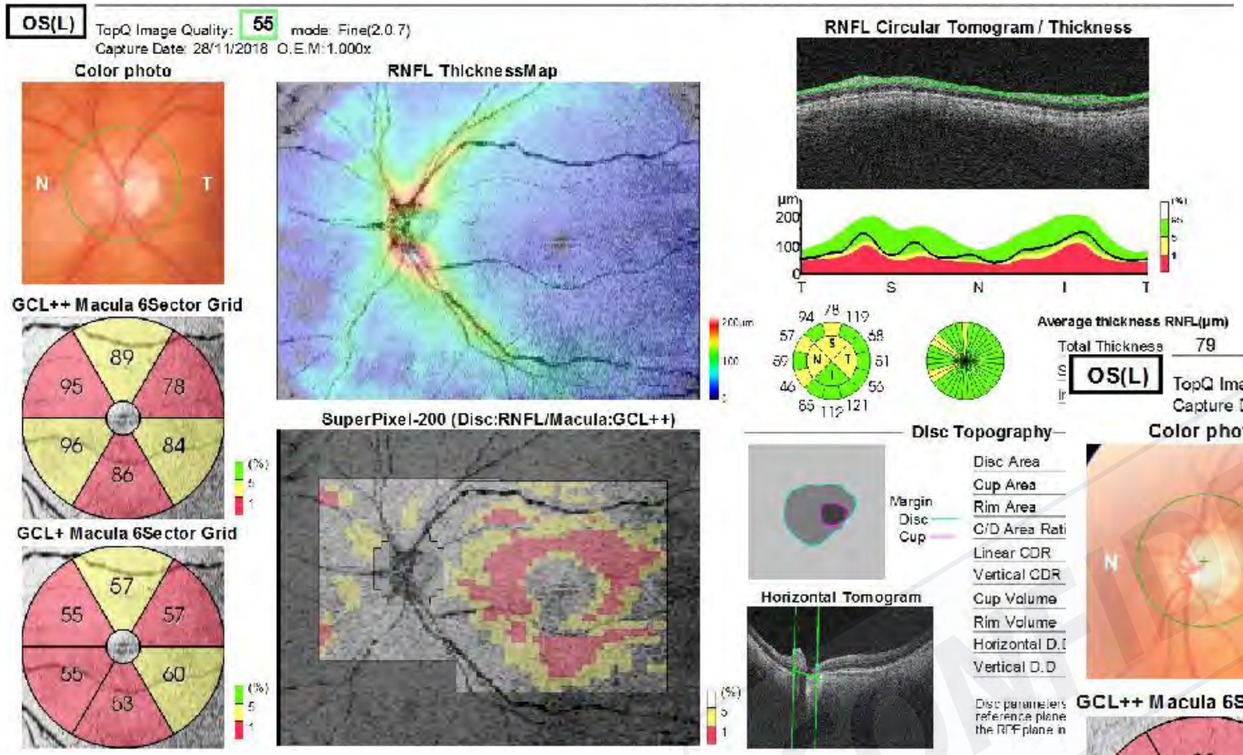


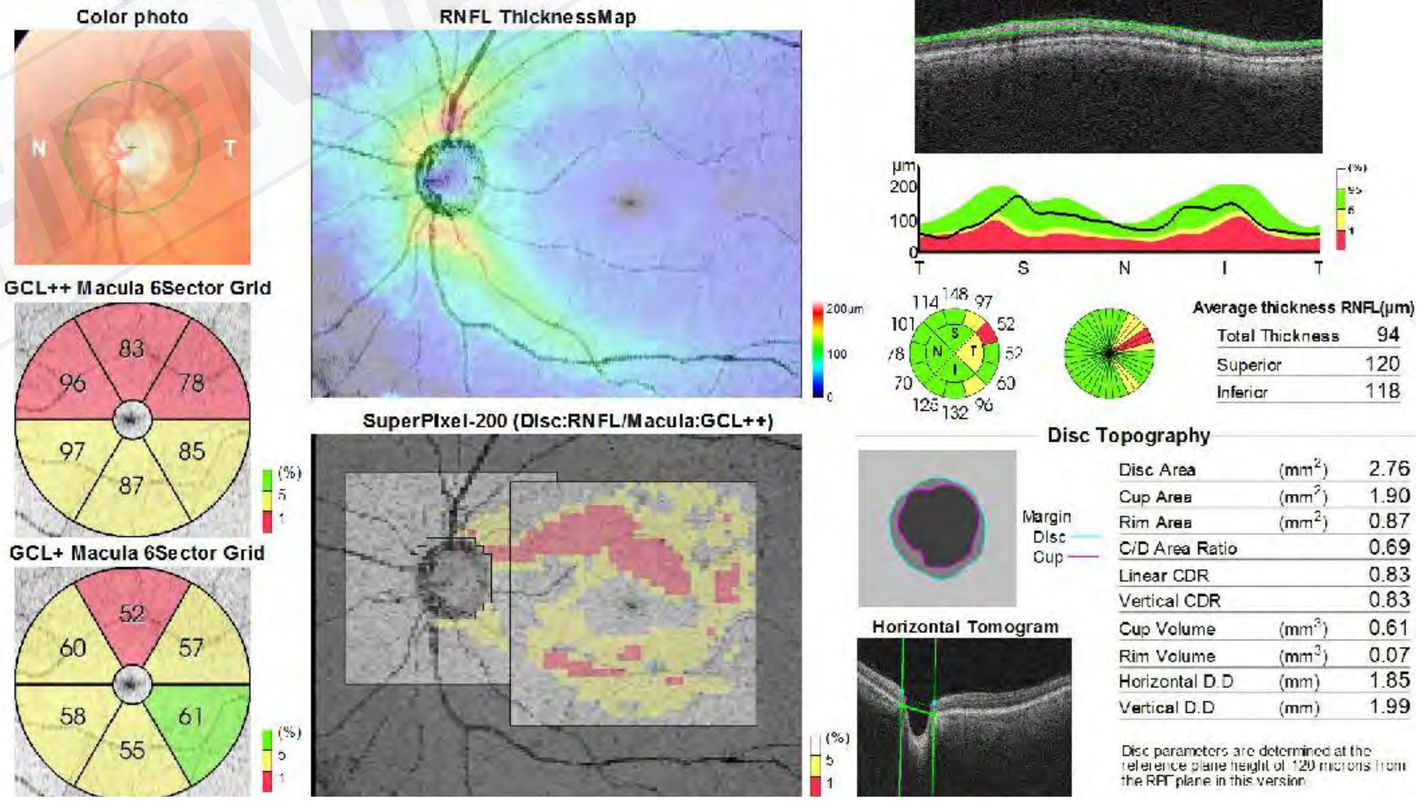

- sustaine the importance of the correlation between the suspected deficits in glaucoma diagnosis



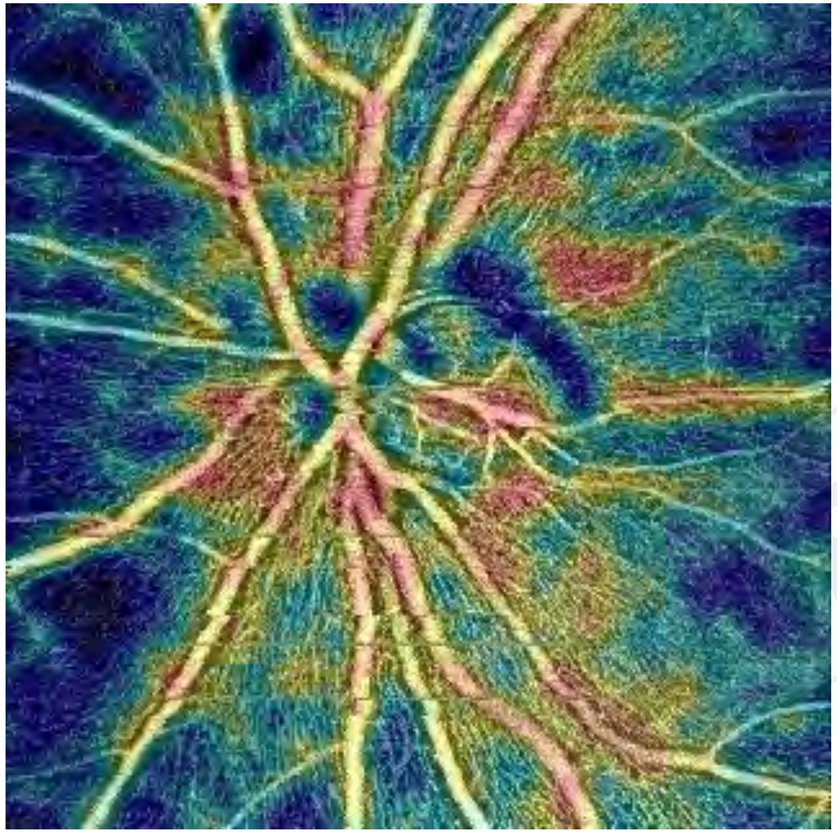



# clinical case



# Angio - OCT



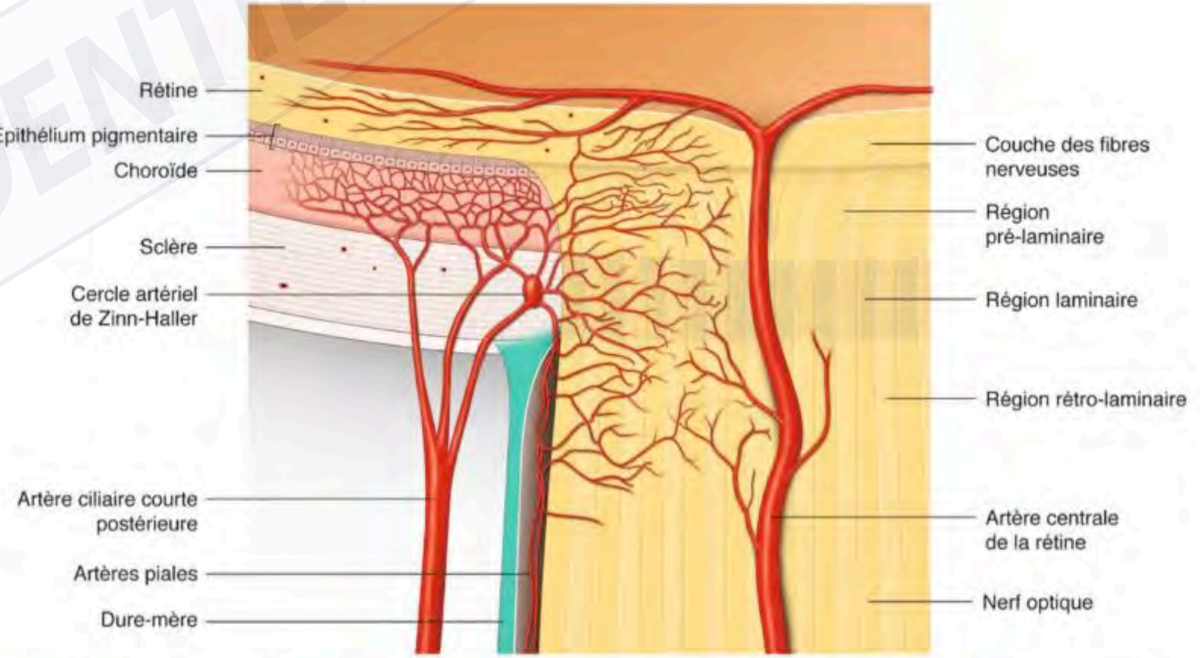
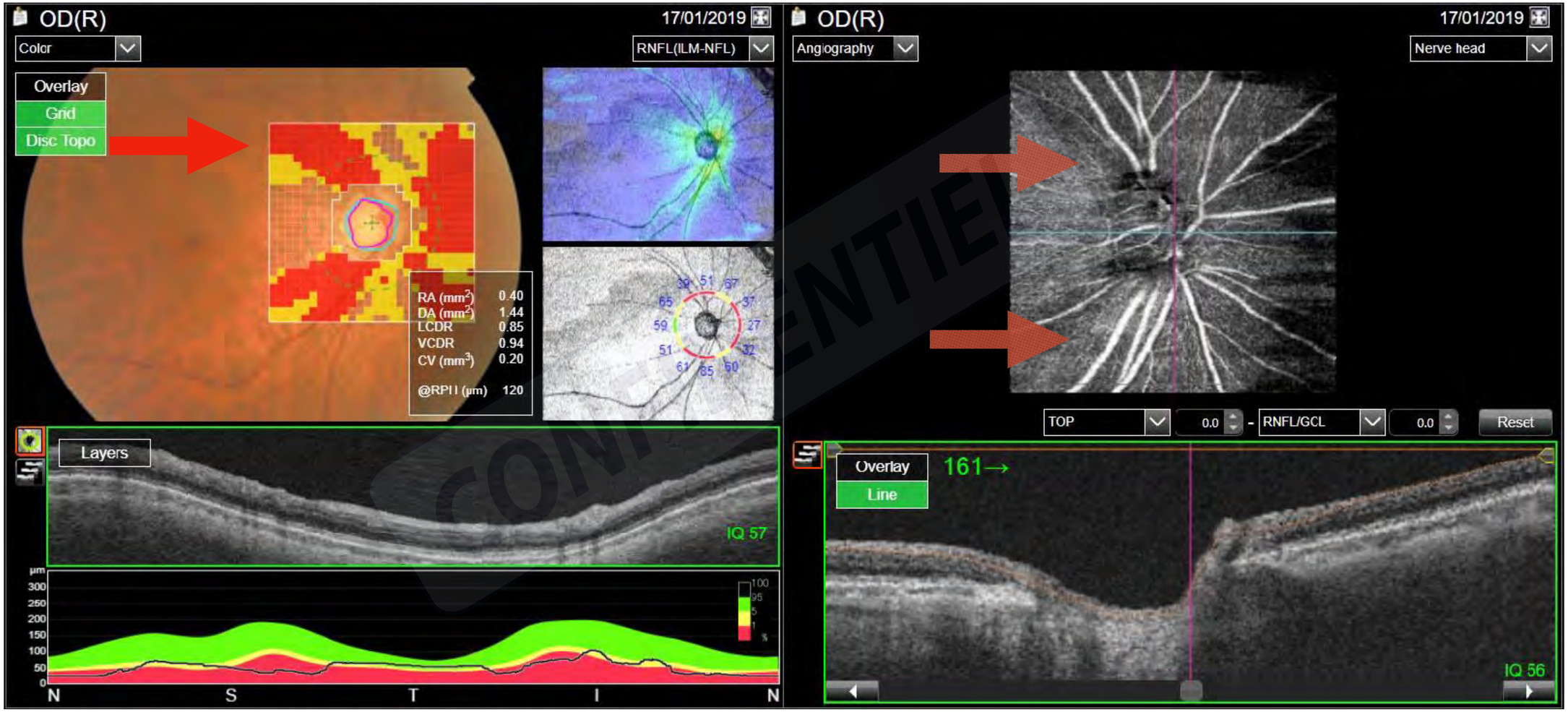



**Fig. 6-12** ***Schéma de la vascularisation artérielle de la tête du nerf optique.*** (D'après Cioffi GA, Van Buskirk EM. Vasculature of the anterior optic nerve and peripapillary choroid. Vasculature of the anterior optic nerve and peripapillary choroid. In : Ritch R, Shields BM, Krupin T (eds). The glaucomas, basic sciences. St Louis, Mosby, 1996 : 177-88.)

# Angio - OCT




- this new method of analysis could be helpful to assess progression in advanced glaucoma in the future, or even detect early glaucoma

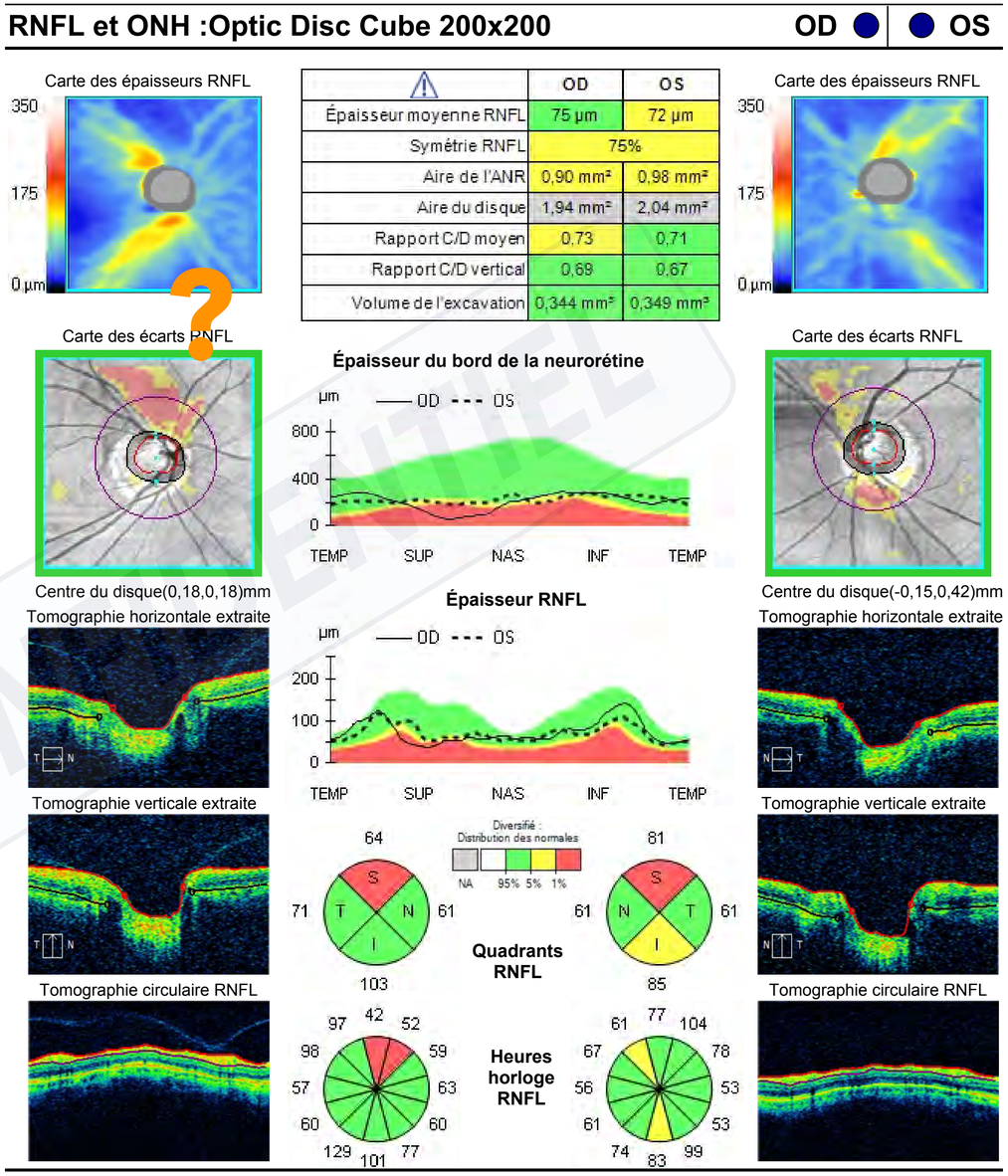
# Clinical cases



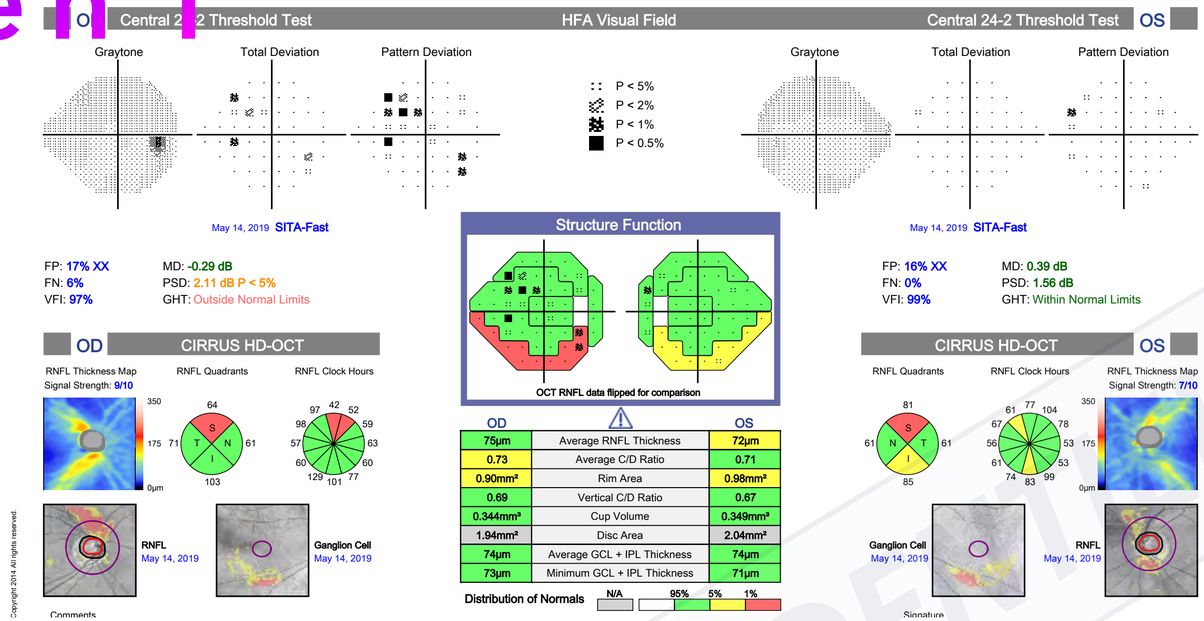
OCT helps us in
- detection -
- differential diagnosis -
- attest progression -

# Case n°1

- F 76 y
- RE: suspected superior RNFL defect

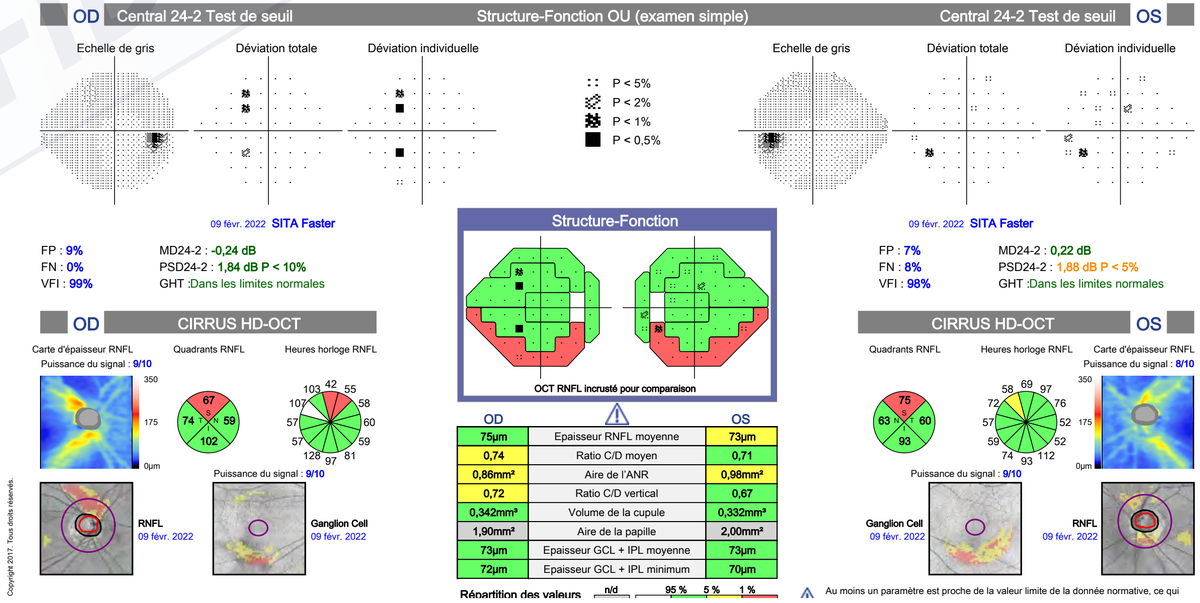


# Case n°1



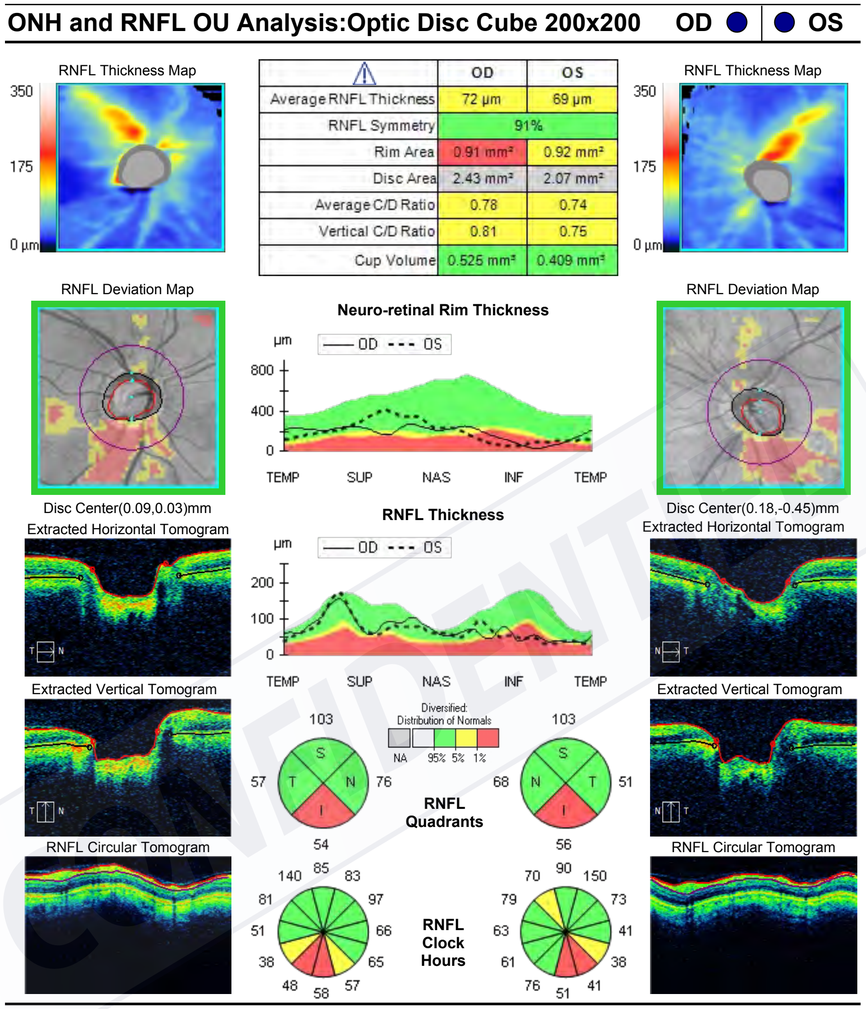

=> follow-up without treatment

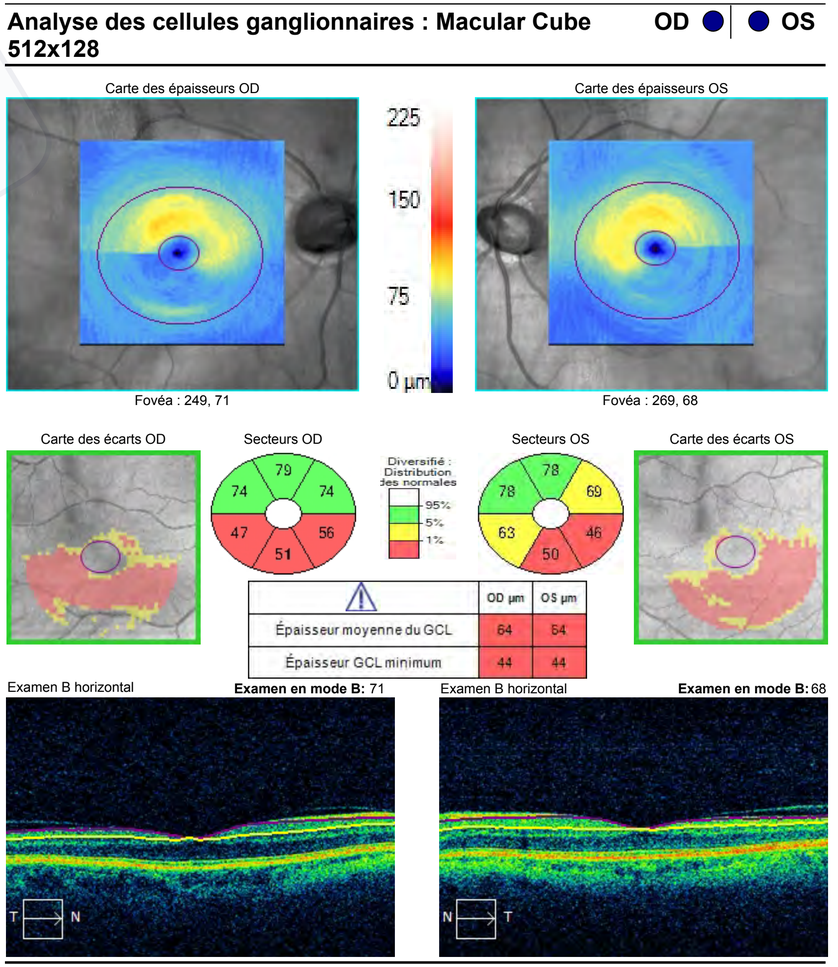
- combined analysis: no VF/OCT defect correlation
- normal IOP
- no progression within 3 years



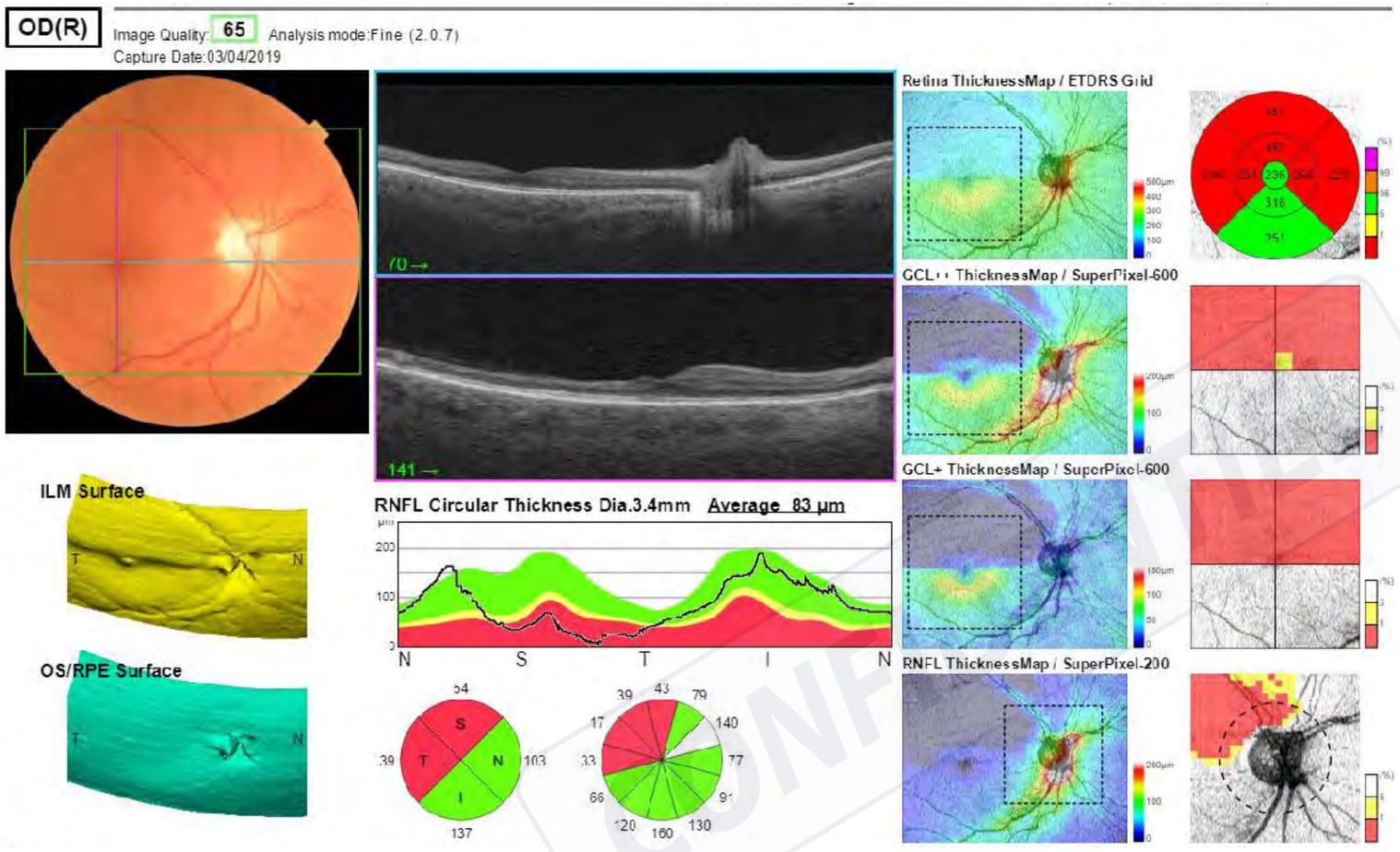
# Case n°2

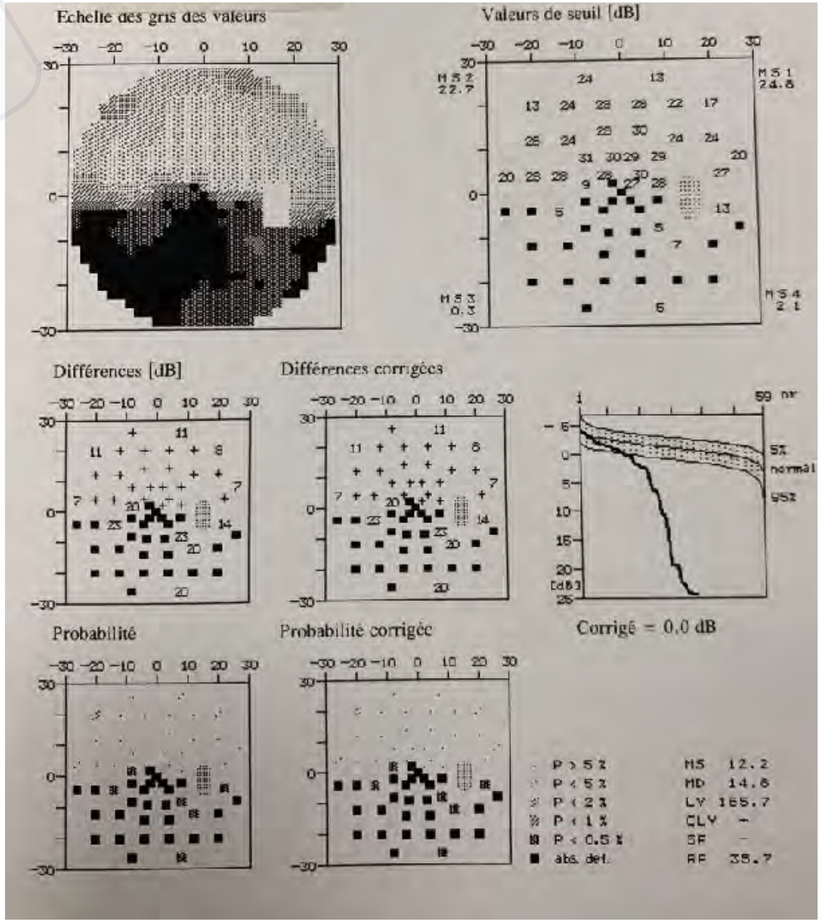
- F 65 y
- both eyes: altitudinal inferior RNFL and GCL defect




*altitudinal defect: differential diagnosis of vascular etiology*



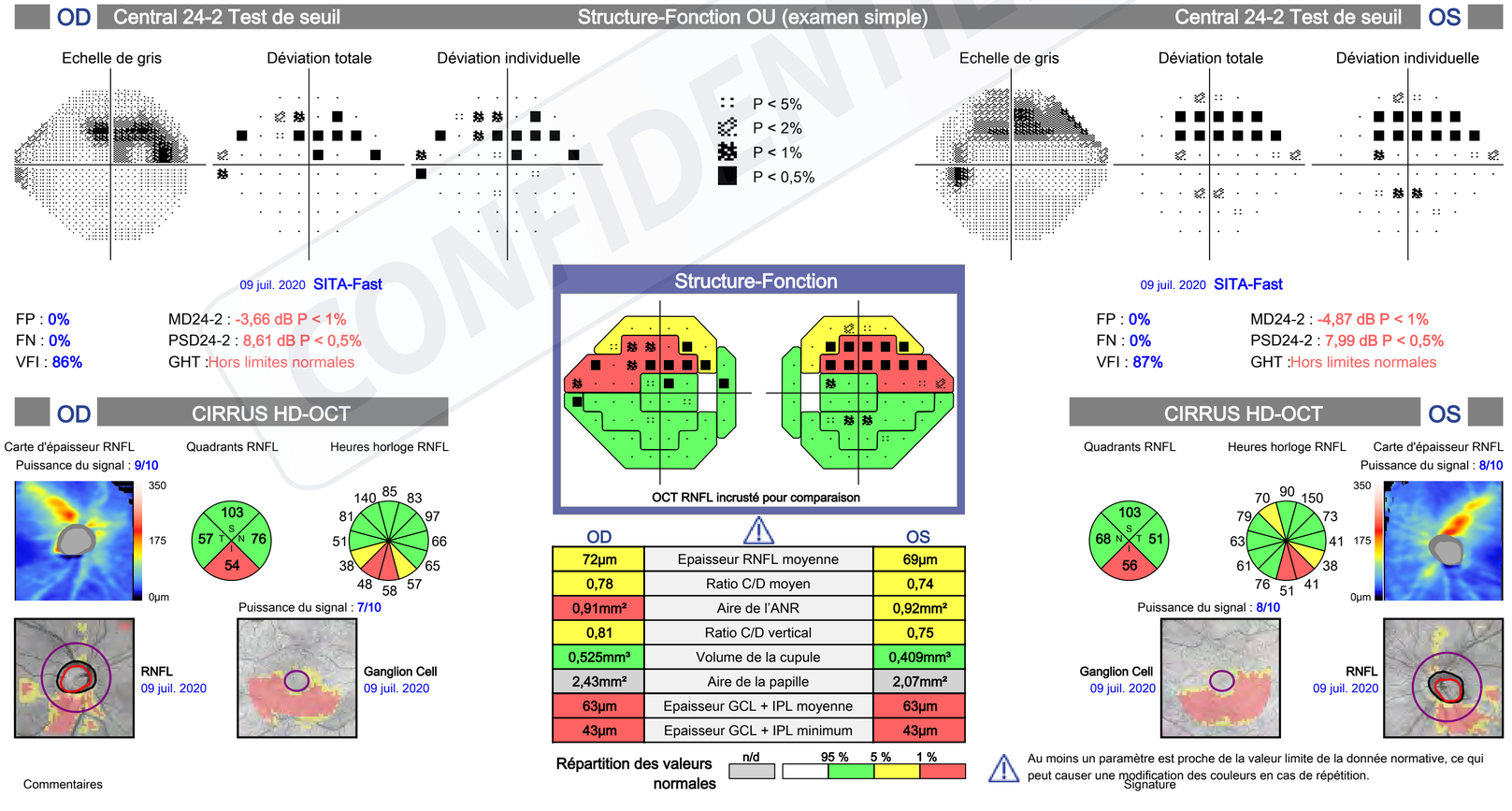

differential diagnosis of vascular etiology

=/=

# Case n°2

- superior arcuate (OU) and central VF defect (RE)
- high IOP, under topical treatment
- VF/OCT correlation

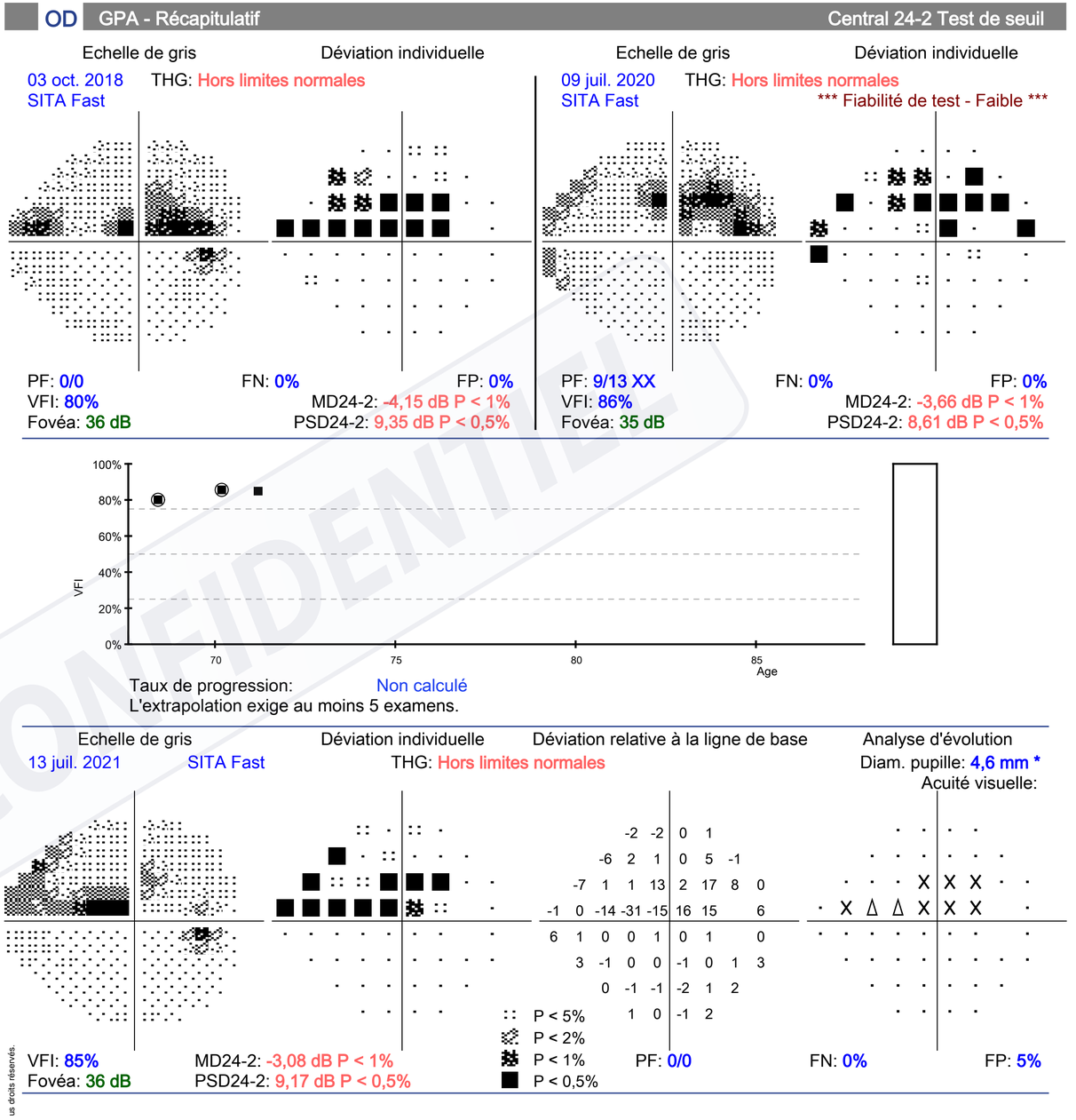
**=> treatment : surgery**



# Case n°2

**Follow-up** after surgery

- target IOP ?
- are there any signs of progression ?

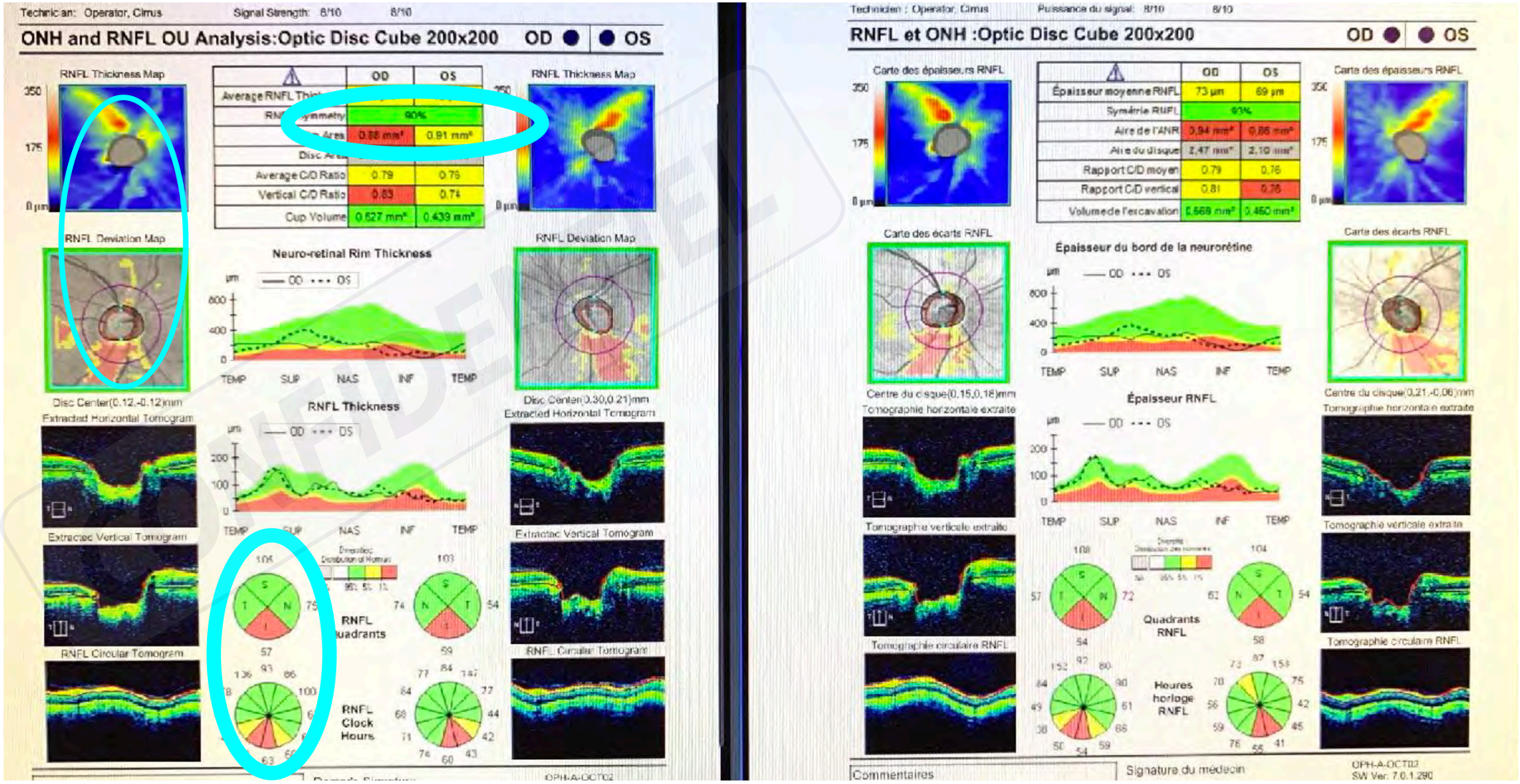


# Case n°2

Event OCT comparison
2022 - 2015

**Follow-up** after surgery

- are there any signs of progression ?



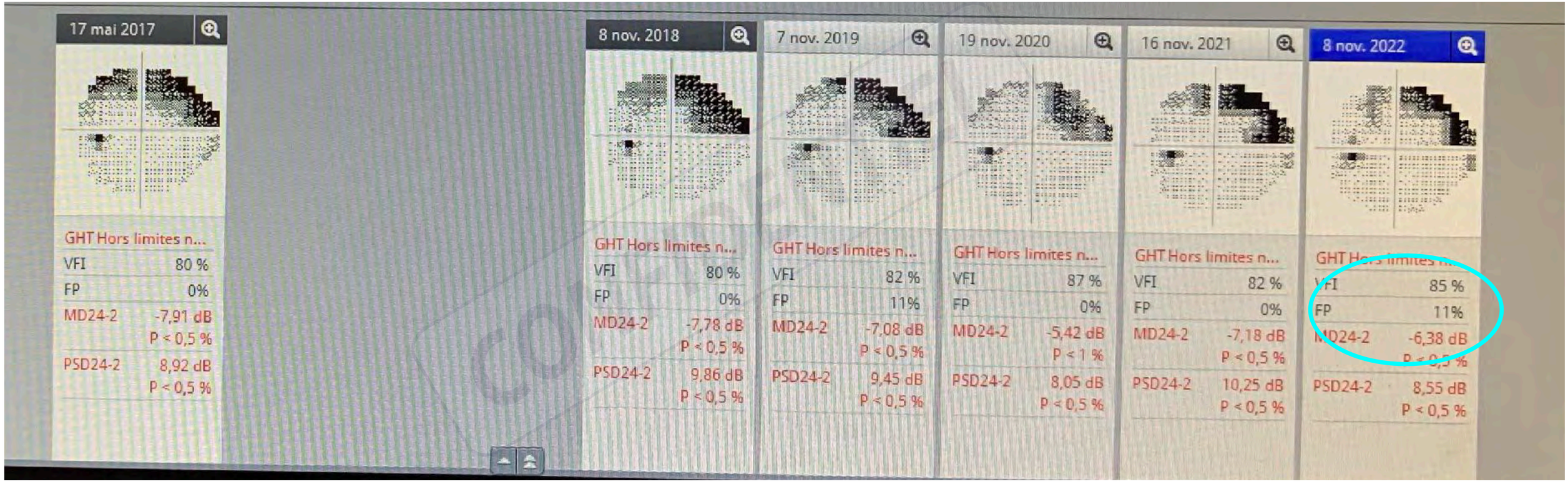
# Case n°2

- TREND analysis


=> follow-up without treatment

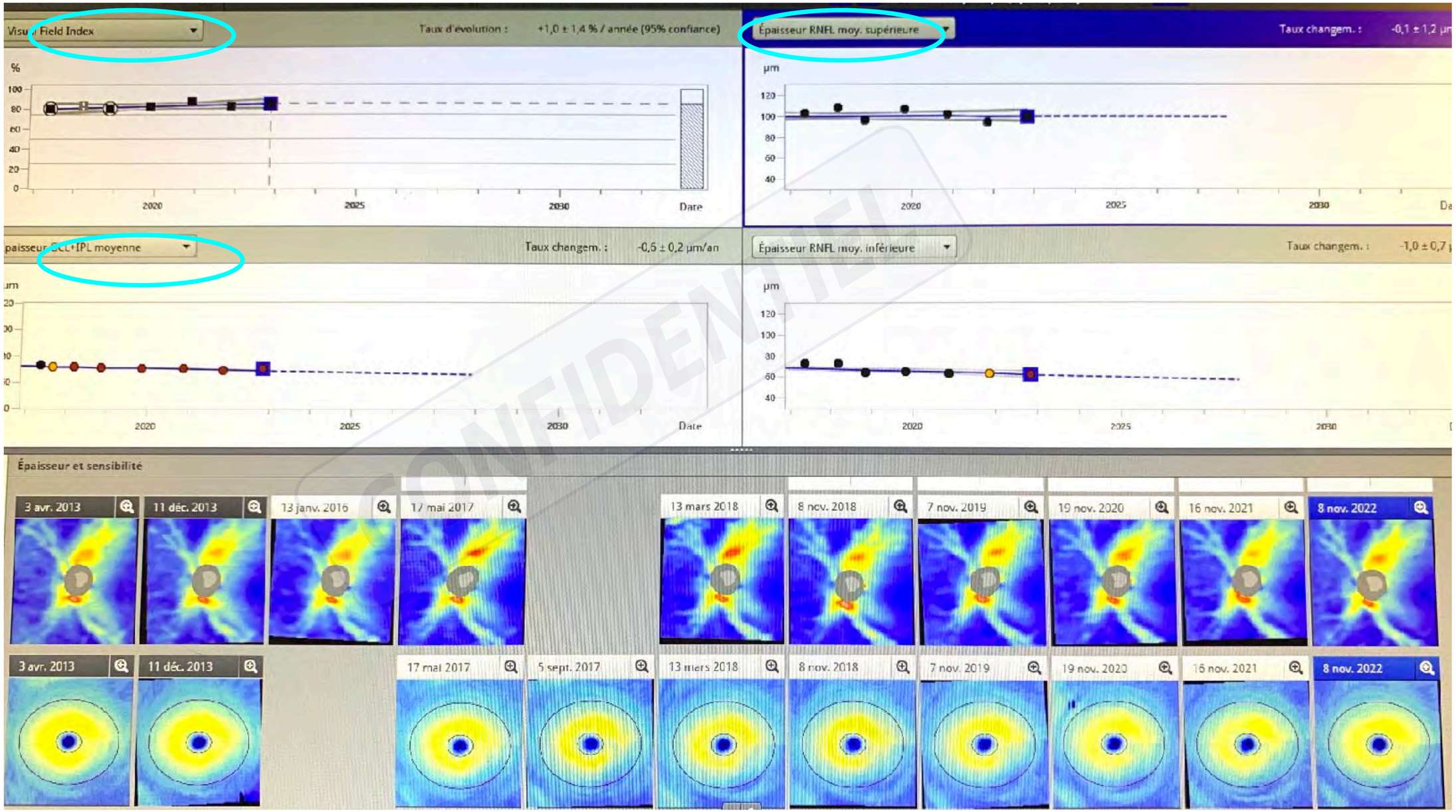
# Case n°3 looking for progression

- TREND VF grey scale+ numeral analysis



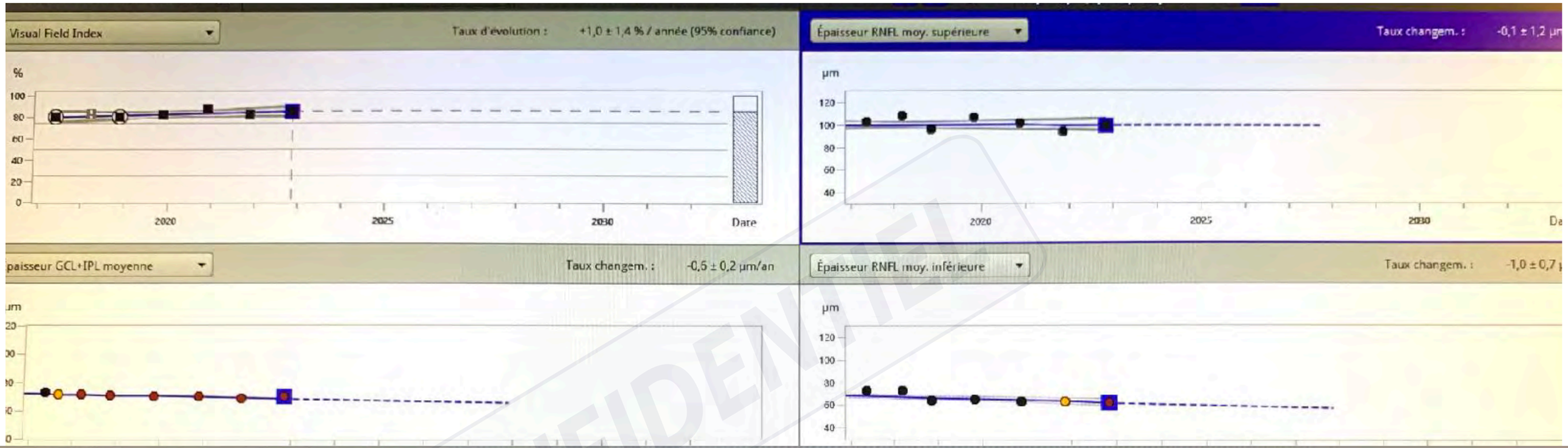
# Case n°3

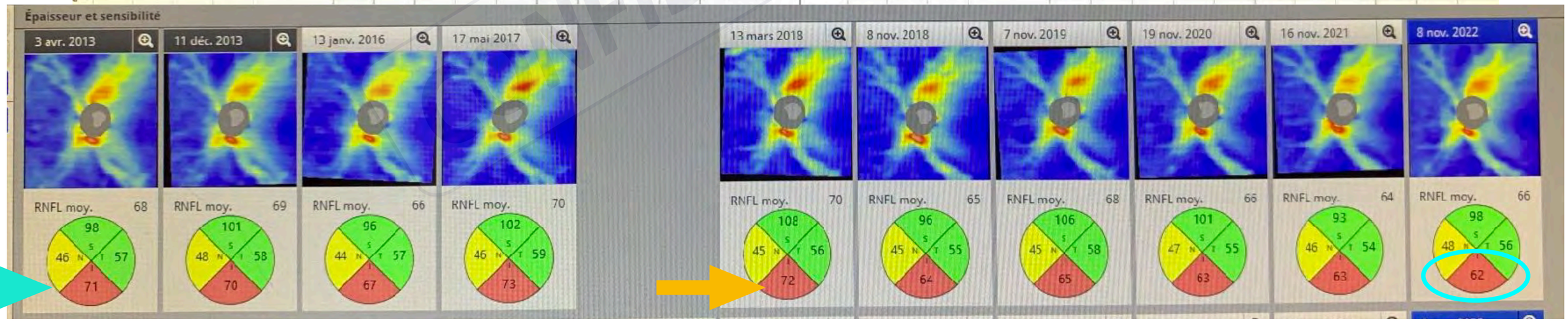
- TREND analysis: global analysis and *thickness maps*



# Case n°3

- TREND analysis: *sectors* and *thickness maps*



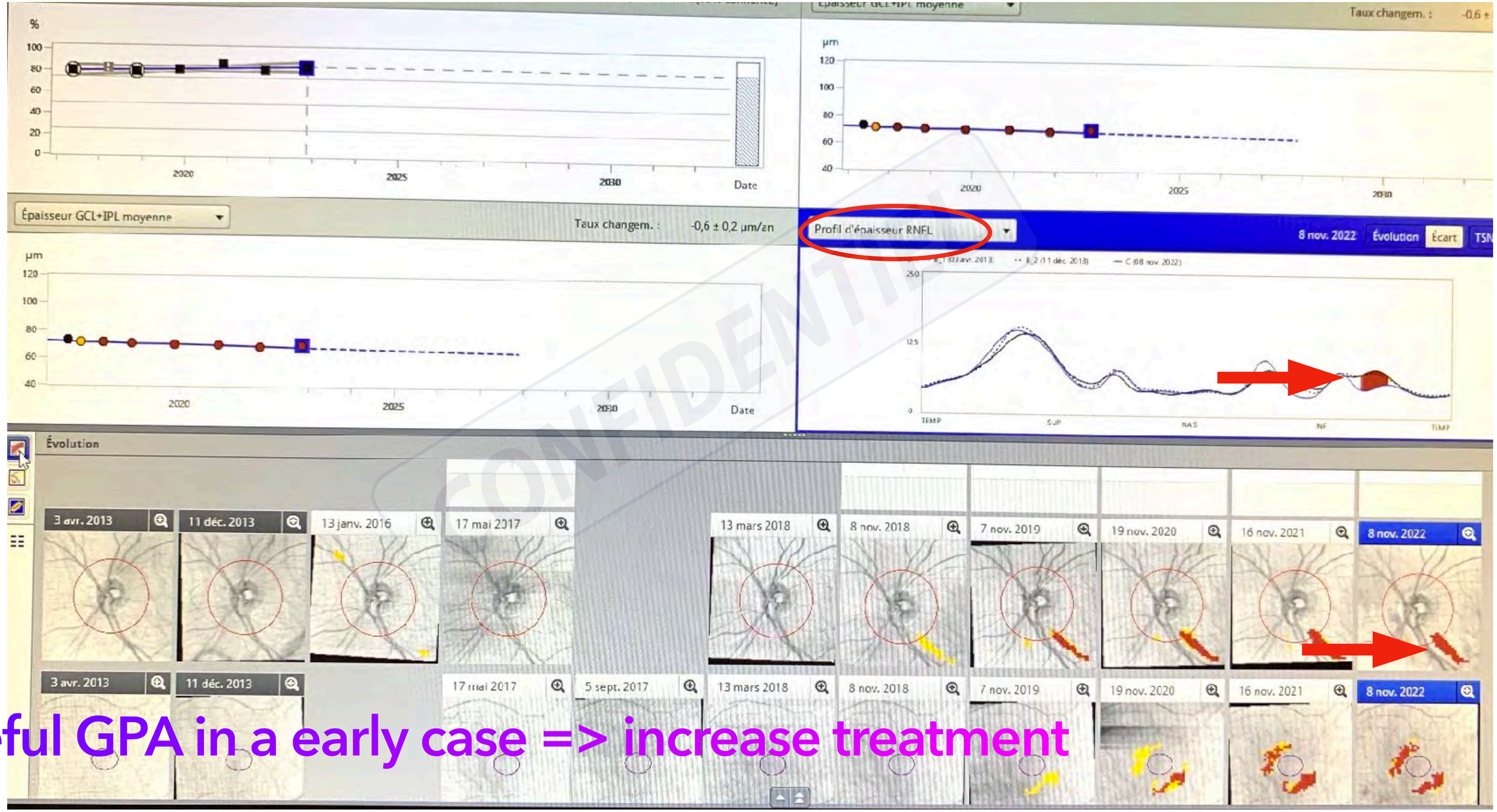




normal aging is considered as a decrease of more or less 1micron per year

=/= pathological would be >1 or 2 microns per year… but limited by the resolution of the OCT software

# Case n°3

- *thickness profile* evolution and *progression analysis*




**useful GPA in a early case => increase treatment**

# take home messages

- the structural analysis of the OCT is complementary to the functional analysis of the visual field
- it helps to the diagnosis in early and pre-perimetric glaucoma
- has good reproducibility to assess progression
- be aware of the artefacts and don’t forget to correlate the analyse to your clinical examination

# discussion



Thank you for your attention

# Genetic Testing for Glaucoma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&

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Philadelphia, PA, USA

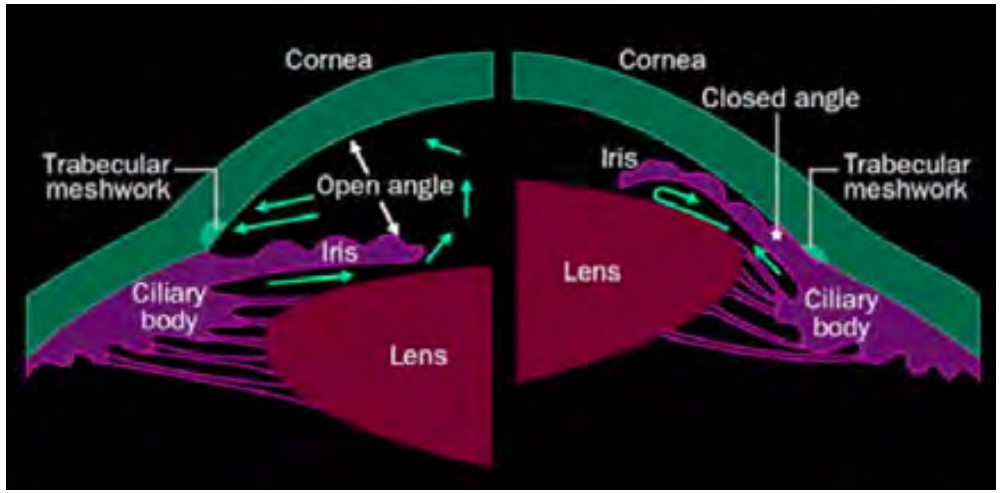
# Introduction

# Introduction
## Definitions

- Phenotype = combination of signs & symptoms due to specific condition
- Genotype = molecular basis of disease

# Introduction
# Glaucoma

- Heterogeneous group of disorders
- Characterised by progressive loss of retinal ganglion cells
- Associated with visual field loss




Adapted from JL Wiggs & LR Pasquale, Genetics of Glaucoma, Hum Mol Genet, 26, 21-27, 2017

# Introduction
# Glaucoma

- Early-onset glaucoma presents in childhood or early adulthood
- Adult-onset glaucoma presents after age 40

JL Wiggs & LR Pasquale, Genetics of Glaucoma, Hum Mol Genet, 26, 21-27, 2017

# Introduction
## Glaucoma & Genetics

- Both early-onset & adult-onset glaucoma have strong genetic component
- Genetic associations help determine relative risks
- Isolated & syndromic monogenic ocular disorders w/ glaucoma exist

# Introduction
## Genome-Wide Association Studies in Glaucoma

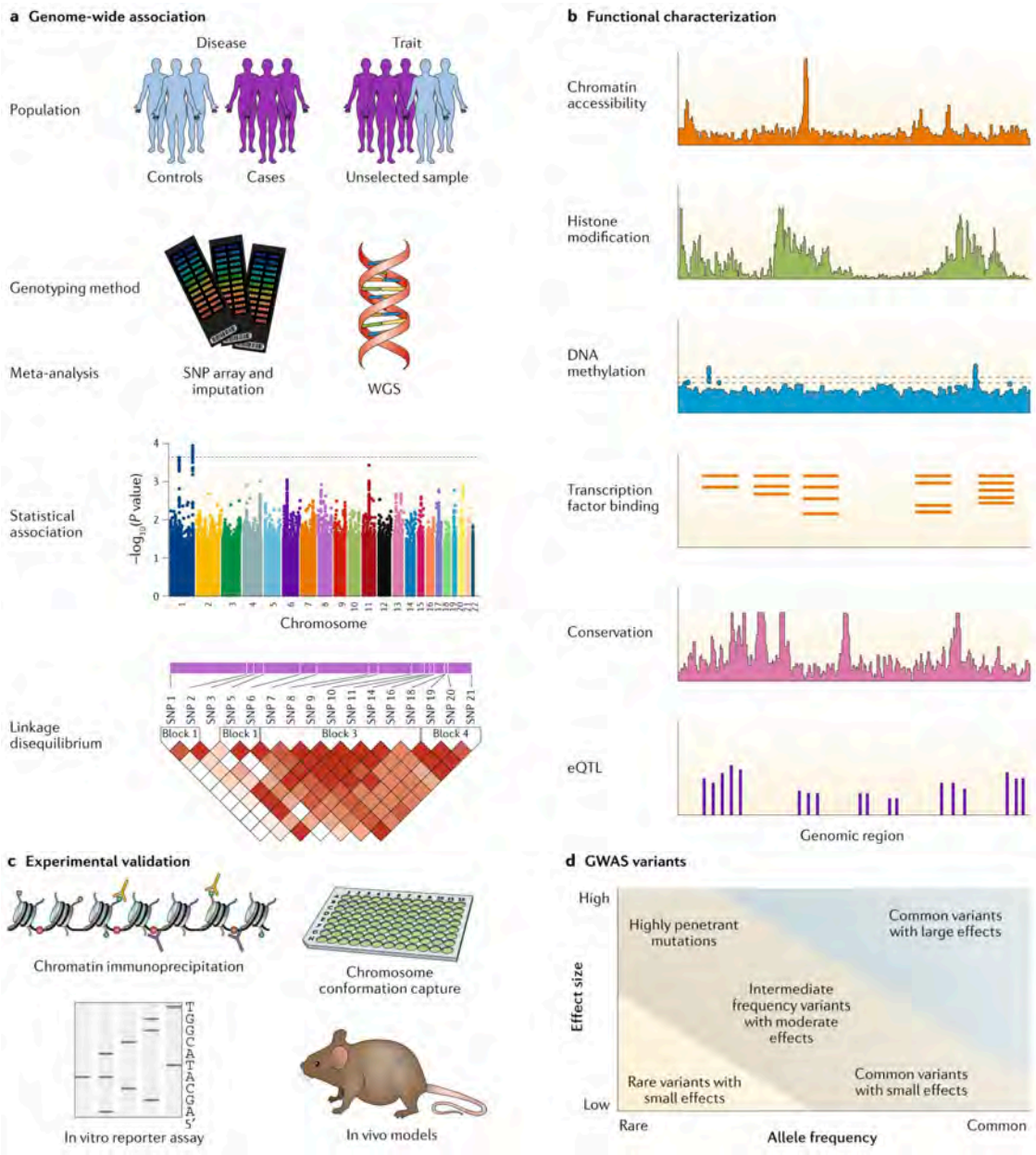
- Genetic associations are studied using Genome-Wide Association Studies (GWAS) as a practical means to study heritability of complex traits
- 1st GWAS published for ARMD in 2005 [1]
- Since 2005: more than 500000 associations between genetic variants & common diseases & traits
- Strict P values of $< 5/10^{-8}$ as consensus

[1] RJ Klein *et al.* Complement factor H polymorphism in age-related macular degeneration, *Science* **308**, 385–389, 2005

# Introduction Genome-Wide Association Studies

- Method to study genetic risk factors
- Relative risk calculated when carrying risk allele compared to wild-type allele

From V Tam *et al.*: Benefits and Limitations of genome-wide association studies, Nature Reviews Genetics, 20, 467-484, 2019

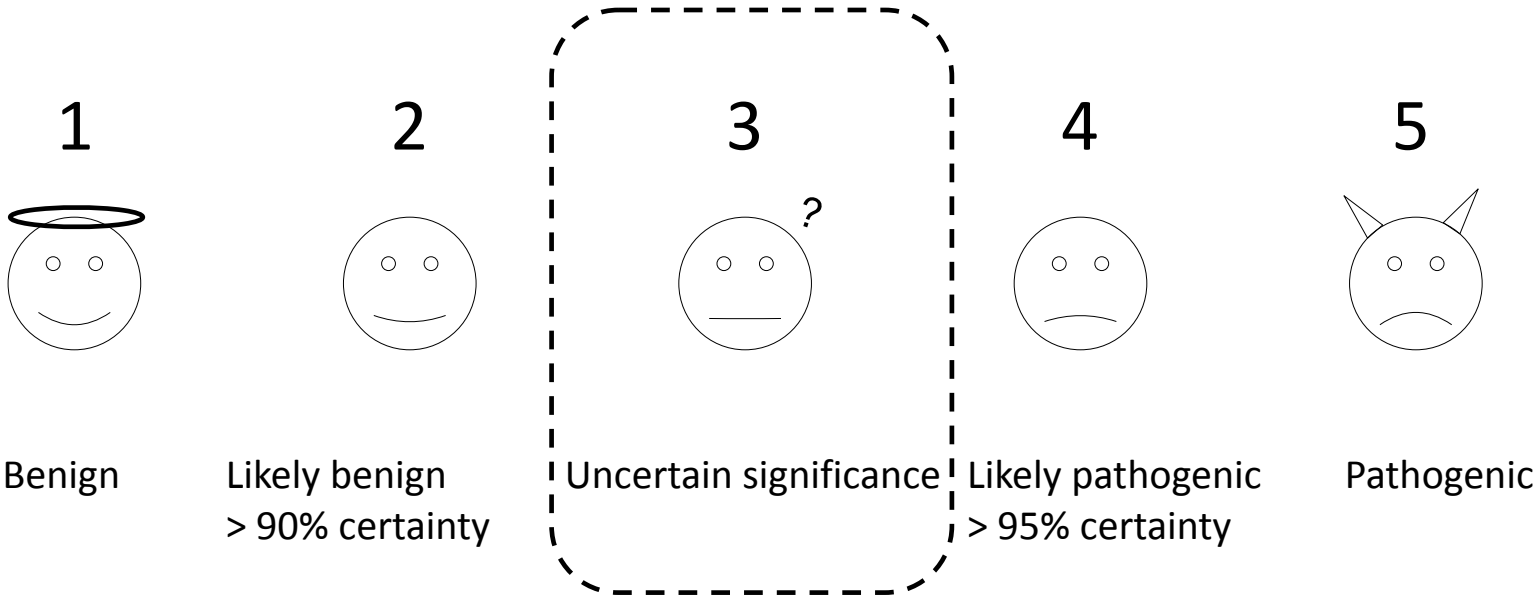


# Introduction
## Early-Onset Glaucoma & Genetics

- Some genes show
  - incomplete penetrance (= ratio of number of individuals with disease genotype who have signs and/or symptoms of disease to total number of individuals with disease genotype)
  - variable expressivity (pertains to spectrum of clinical manifestations of disease)

# Variants in Genes

## Five Classes




Adapted from Dr Caroline VAN CAUWENBERGH

# Gene Associations for Adult-onset Glaucoma

# Adult-onset Glaucoma
## Types

- Primary Open-angle Glaucoma (POAG), including Normal-tension Glaucoma (NTG)
- Pseudoexfoliation Glaucoma (PEG)
- Primary Angle-closure Glaucoma (PACG)

# Adult-onset Glaucoma

## Gene Associations for Primary Open-angle Glaucoma

| Disease | Study design[a] | # Cases/ controls | Ethnic population | Gene | Chromosomal location | Gene function |
|---|---|---|---|---|---|---|
| Primary open-angle glaucoma | Genetic Linkage Analysis | 330/471 | European-derived | *MYOC* | 1q24.3 | Extracellular matrix protein in trabecular meshwork; mutant protein aggregates intracellularly |
| | GWAS | 1263/34877 | Icelandic | *CAV1/CAV2* | 7q31 | Mechanosensation and IOP regulation; nitric oxide signalling |
| | GWAS | 615/3956 | Australian | *CDKN2B-AS* | 9p21 | Long non-coding RNA; regulates expression of *CDKN2B*, *CDKN2A* and other target genes |
| | | | | *TMCO1* | 1q24.1 | Transmembrane protein |
| | GWAS | 2170/2347 | European-derived | *SIX6* | 14q23.1 | Eye development |
| | GWAS Meta-Analysis | 1432/8102 | European and Australian | *GAS7* | 17p13.1 | Neuronal development |
| | GWAS | 1155/1992 | Australian | *ABCA1* | 9q31.1 | Cholesterol efflux pump |
| | | | | *AFAP1* | 4p16.1 | Modulates actin filament integrity |
| | | | | *GMDS* | 6p25.3 | Fructose and mannose metabolism |
| | GWAS | 1007/1009 | Chinese, Singaporean Chinese | *PMM2* | 16p13.2 | Glycosylation |
| | GWAS | 3504/9746 | Multi-ethnic (European, Asian and African descent) | *TGFBR3* | 1p22.1 | TGF-beta receptor |
| | GWAS | 1225/4117 | European | *ARHGEF12* | 11q23.3 | Rho kinase signalling |
| | GWAS | 3853/33480 | European-derived | *TXNRD2* | 22q11.21 | Thioredoxin reductase |
| | | | | *ATXN2* | 12q24.12 | Formation of p-bodies and stress granules |
| | | | | *FOXC1* | 6p25.3 | Transcription factor; early ocular and systemic organogenesis |
| | GWAS | 3071/6750 | Australian | *MYOF* | 10q23 | Endothelial cell repair after mechanical stress |
| | | | | *CYP26A1* | | Drug metabolism, lipid biosynthesis |
| | | | | *LINC02052* | 3q27.3 | long non-coding RNA |
| | | | | *CRYGS* | | Gamma crystallin; cataract formation |
| | | | | *LMX1B* | 9q33.3 | Trabecular meshwork development |

# Adult-onset Glaucoma
## Genes Associated with AD Primary Open-angle Glaucoma

- = progressive, high IOP-related optic neuropathy after 40 yrs of age
- Unobstructed iridocorneal angle
- Genes (proteins) linked in affected families identified AD genes (5% of POAG):
  - *MYOC* (myocilin) for AD POAG & AD JOAG
  - *OPTN* (optineurin)
  - *WDR336* (WD Repeat Domain 36)
  - *TBK1* (TANK Binding Kinase 1), primarily in NTG, encoding kinase in NF-kB signalling pathway

# Adult-onset Glaucoma

## Gene Associations for Primary Open-angle Glaucoma

- Majority of POAG cases are complex-inherited trait
- Multiple genes w/ small size effects
- GWAS identified 127 loci w/ SNPs associated w/ POAG risk
- Consistent across European, East Asian & African populations

# Adult-onset Glaucoma

## Gene Associations for Primary Open-angle Glaucoma

- Many of POAG-associated SNPs are in genes that function in early ocular development or are genes known for monogenic early-onset glaucoma (*SIX6*, *LMX1B*, *FOXC1*, *PITX2*, *ANGPT1*, *ANGPT2*, *RERE*, *ADAMTS18*, *MEIS2*)
- Suggestive of insufficient effect of common variants in these genes to cause disease, but additive effect of other factors may lead to late-onset POAG

# Adult-onset Glaucoma
## Gene Associations for Primary Open-angle Glaucoma

- Pathway analyses for POAG-asssociated risk identified important pathogenic mechanisms:
  - Endoplasmic reticulum stress response (*MYOC*)
  - Extracellular matrix & cell adhesion (*MYOC, FNDC3B, AFAP1, COL4A1, COL8A2, THSD7A, EXOC2, ANGPTL7*)
  - TGF beta signalling (*CDKN2B-AS, TGFBR3, SMAD6, MXRA5*)
  - TNF alpha signalling (*OPTN, TBK1*)
  - Vascular development (*ANGPT1, ANGPT2*)
  - Regulation of autophagy (*OPTN, TBK1, BCAS3*)
  - Lipid metabolism (*ABCA1, DGKG, NPC2*)
  - eNOS signalling (*CAV1/CAV2*)
  - Mitochondrial function (*TXNRD2, ME3, VPS13C*)

# Adult-onset Glaucoma
## Gene Associations for Primary Open-angle Glaucoma

- Pathway analyses for POAG-associated risk identified important pathogenic mechanisms
- At least 16 loci associated with POAG risk are targeted by existing drugs, suggesting that these drugs could potentially be repurposed for targeted, personalised POAG treatment options*

*P Gharahkhani, E Jorgenson, P Hysi *et al.*:
Genome-wide meta-analysis identifies 127 open-angle glaucoma loci with consistent effect across ancestries, Nat Commun, 12, 1258, 2021

# Adult-onset Glaucoma
## Gene Associations for Pseudoexfoliation Syndrome

- Pseudoexfoliation syndrome (XFS) is age-related systemic disorder characterised by accumulation of fibrillar material throughout body
- XFS associated w/ cardio- & cerebrovascular disease, Alzheimer-like dementia, SNHL & pelvic organ prolapse
- Nearly 50% develop pseudoexfoliation glaucoma (XFG)
- Most common secondary form of open-angle glaucoma worldwide
- XFG associated w/ higher mean IOP, more advanced VF loss at Dx & worse Tx response

# Adult-onset Glaucoma
## Gene Associations for Pseudoexfoliation Syndrome

- GWAS identified 7 loci strongly associated with XFS & XFG
- Lysyl oxidase-like 1 (*LOXL1*) gene on Chr 15 first and strongest known genetic contributor associated w/ XFG risk (OR 2.46-20.20 for 3 SNPs in initial GWAS)
  - *LOXL1* encodes enzyme that crosslinks collagen & elastin in ECM
  - Enzyme is constituent of XF material in deposits in ocular & systemic tissue
  - Functional mechanism of disease still fairly poorly understood
  - Only intronic variants associated w/ XFS & XFG (non-coding)

# Adult-onset Glaucoma
# Gene Associations for Pseudoexfoliation Syndrome

- GWAS identified 7 loci strongly associated with XFS & XFG
- Other genes than *LOXL1* with variants include
  - *CACNA1A* encoding calcium voltage-gated channel subunit alpha 1A (OR 1.16, $p = 3.36 \times 10^{-11}$)
  - *POMP* encoding proteasome maturation protein (OR 1.17, 95% CI 1.11–1.22, $p = 2.97 \times 10^{-10}$)
  - *TMEM136* encoding transmembrane protein 136 (OR 1.10, 95% CI 1.05–1.16, $p = 1.0 \times 10^{-4}$)
  - *AGPAT1* encoding 1-acylglycerol-3-phosphate O-acyltransferase 1 (OR 1.19, $p = 1.29 \times 10^{-6}$)
  - *RBMS3* encoding RNA binding motif single stranded interacting protein 3 (OR 1.15, $p = 4.9 \times 10^{-7}$)
  - *SEMA6A* encoding semaphorin 6A(OR 0.89, 95% CI 0.85–0.94, $p = 2.3 \times 10^{-5}$)

T Aung, M Ozaki M, MC Lee *et al.*: Genetic association study of exfoliation syndrome identifies a protective rare variant at *LOXL1* and five new susceptibility loci. Nat Genet, 49, 993-1004, 2017

# Adult-onset Glaucoma
# Gene Associations for Steroid-induced Glaucoma

- Steroid-induced glaucoma is form of secondary open-angle glaucoma caused by increased resistance to outflow at trabecular meshwork
- One-third of population is moderately steroid responsive (rise of IOP 6–15 mmHg from baseline w/ steroid treatment)
- 4–6% of population is highly steroid responsive (IOP increase of >15 mmHg from baseline or IOP over 31 mmHg after steroid exposure)
- Studies have found an increased risk of steroid-induced glaucoma among 1st degree relatives of affected individuals, and in those with personal or family history of POAG

  —> genetic factors may contribute to steroid response
- No genetic associations yet known

W Chan, JL Wiggs, L Sobrin: The genetic influence on corticosteroid-induced ocular hypertension: a field positioned for discovery, Am J Ophthalmol,202, 1-5, 2019

# Adult-onset Glaucoma
## Gene Associations for Primary Angle-closure Glaucoma

- Primary angle-closure glaucoma (PACG) is diagnosed based on presence of occludable anterior chamber angle, trabecular meshwork obstruction by peripheral iris & evidence of glaucomatous optic neuropathy
- Most common underlying aetiology = pupillary block
- Estimates: 30 million PACG patients worldwide by 2040
- PACG carries 3-fold higher risk of severe, bilateral visual impairment than POAG
- Risk factors: hypermetropia, advanced age & female gender
- Higher prevalence in certain ethnic groups & 1st degree relatives suggests genetic influence

# Adult-onset Glaucoma
## Gene Associations for Primary Angle-closure Glaucoma

- GWAS have identified 8 loci strongly associated w/ higher risk of PACG:
  - *PLEKHA7* encoding pleckstrin homology domain–containing protein 7 (OR = 1.22, $p = 5.33 \times 10^{-12}$), which plays a critical role in maintenance & stability of adherens junctions; expressed in PACG relevant ocular tissues & in tissues that maintain blood-aqueous barrier. *PLEKHA7* gene expression is downregulated in lens epithelial cells & iris tissue samples from PACG patients
  - *COL11A1* encoding collagen type 11 alpha-1 chain (OR = 1.20, $p = 9.22 \times 10^{-10}$); variants in this gene may impact axial length

# Adult-onset Glaucoma
## Gene Associations for Primary Angle-closure Glaucoma

- GWAS have identified 8 loci strongly associated w/ higher risk of PACG:
  - SNP located between *PCMTD1* (protein-L-isoaspartate o-methyltransferase domain containing 1) & *ST18* (ST18 C2H2C-type zinc finger transcription factor) (OR = 1.50, $p = 3.29 \times 10^{-9}$)
  - *EPDR1* encoding ependymin-related 1 (OR = 1.24, $p = 5.94 \times 10^{-15}$), also involved in cell-adhesion
  - *CHAT* encoding choline o-acetyltransferase (OR = 1.22, $p = 2.85 \times 10^{-16}$), which synthesises acetylcholine, which causes pupillary constriction
  - *GLIS3* encoding GLIS family zinc finger 3 (OR = 1.18, $p = 1.43 \times 10^{-14}$)
  - *FERMT2* encoding FERM domain-containing kindlin 2 (OR = 1.14, $p = 3.43 \times 10^{-11}$), also involved in cell-adhesion
  - SNP located between *DPM2* (dolichyl-phosphate mannosyltransferase-2) & *FAM102A* (early oestrogen-induced gene 1) (OR = 1.15, $p = 8.32 \times 10^{-12}$)

# Gene Associations for Early-onset Glaucoma

# Early-onset Glaucoma
## Primary Congenital Glaucoma

- PCG presents in infancy w/ buphthalmos, Haab striae, elevated IOP & optic nerve cupping
- Cause: developmental abnormalities of AS & aqueous outflow pathway
- Most cases sporadic, 10-40% familial (most AR, some AD)
- Five distinct loci associated with PCG: GLC3A (chromosome 2p22-p21), GLC3B (1p36.2-p36.1), GLC3C (14q24.3), GLC3D (14q24.2-q24.3, but not overlapping with GLC3C), & GLC3E (9p21)
- Causal gene at GLC3A locus is *CYP1B1* (first gene identified; AR PCG)
- CYP1B1 belongs to cytochrome P450 family of enzymes involved in metabolism of medications, vitamins, steroids, fatty acids & other chemicals

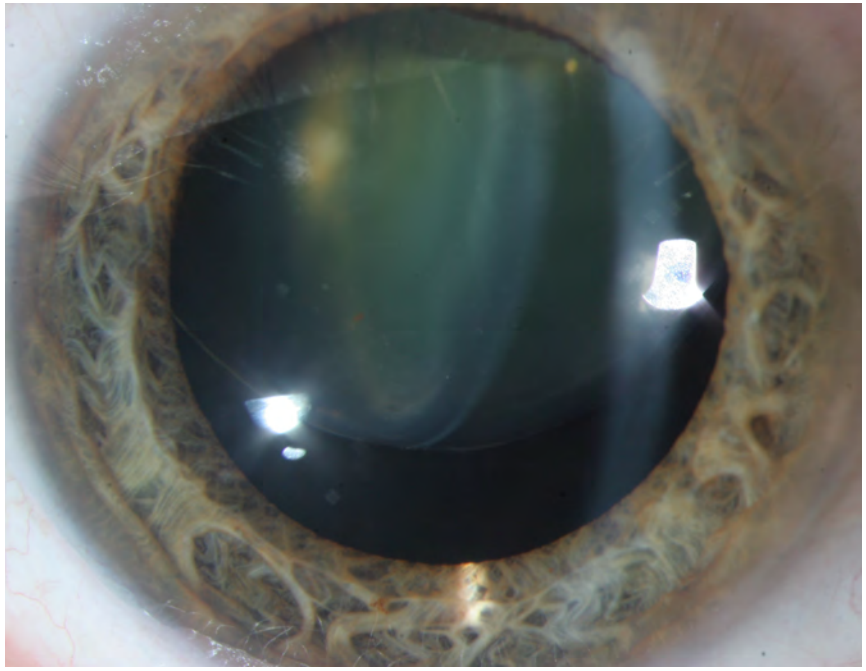
# Early-onset Glaucoma
## Primary Congenital Glaucoma

- Causal gene at GLC3D locus is *LTBP2* (Latent Transforming Growth Factor Beta Binding Protein 2; AR PCG)
- LTBP2 belongs to latent TGF-β binding protein family, which are multi-domain extracecullar matrix proteins that play roles in cell adhesion, elastic fibre assembly & microfibril structure; gene is expressed in anterior segment, particularly in ciliary processes
- Biallelic mutations in *LTBP2* also cause Ectopia Lentis et Pupillae

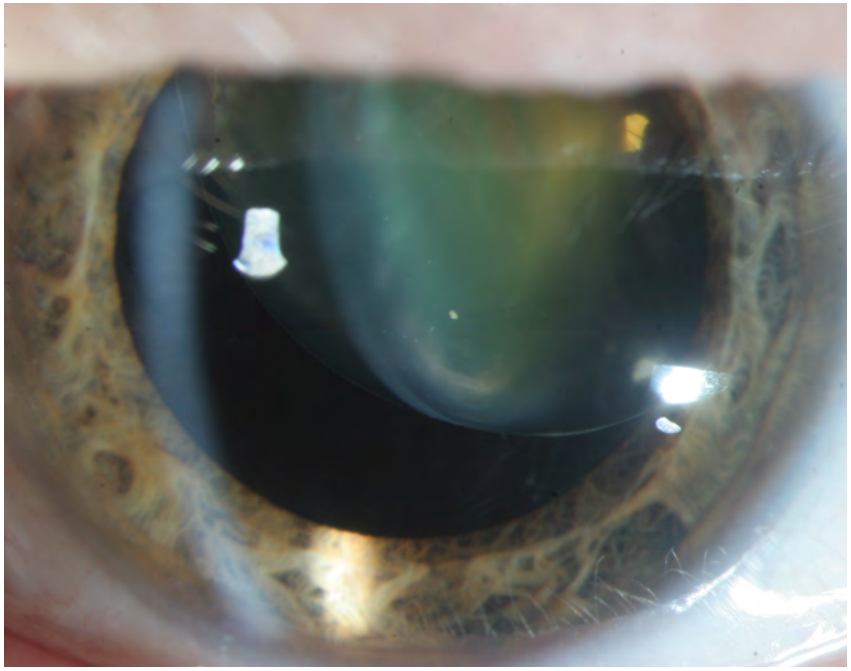
# Ectopia Lentis et Pupillae + Glaucoma

*LTBP2+*

RE



LE

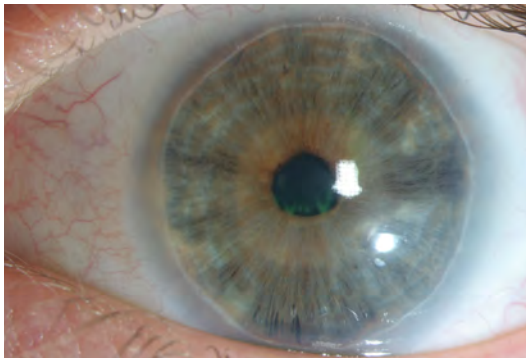


- M, 66 yrs
- Bilateral lens subluxation
- HoZ for c.4964A>G (p.(Tyr1655Cys) in exon 34 of *LTBP2*

# Early-onset Glaucoma
## Primary Congenital Glaucoma

- Other PCG genes include
  - *TEK* (Tunica Interna Endothelial Cell Kinase; AD PCG) on GLC3E locus
  - *ANGPT1* (Angiopoetin 1; AD PCG) on GLC3E locus
  - HeZ mutations in one of these genes cause hypomorphic Schlemm canal & TM in mouse model; same pathway

# Early-onset Glaucoma
# Axenfeld-Rieger Syndrome

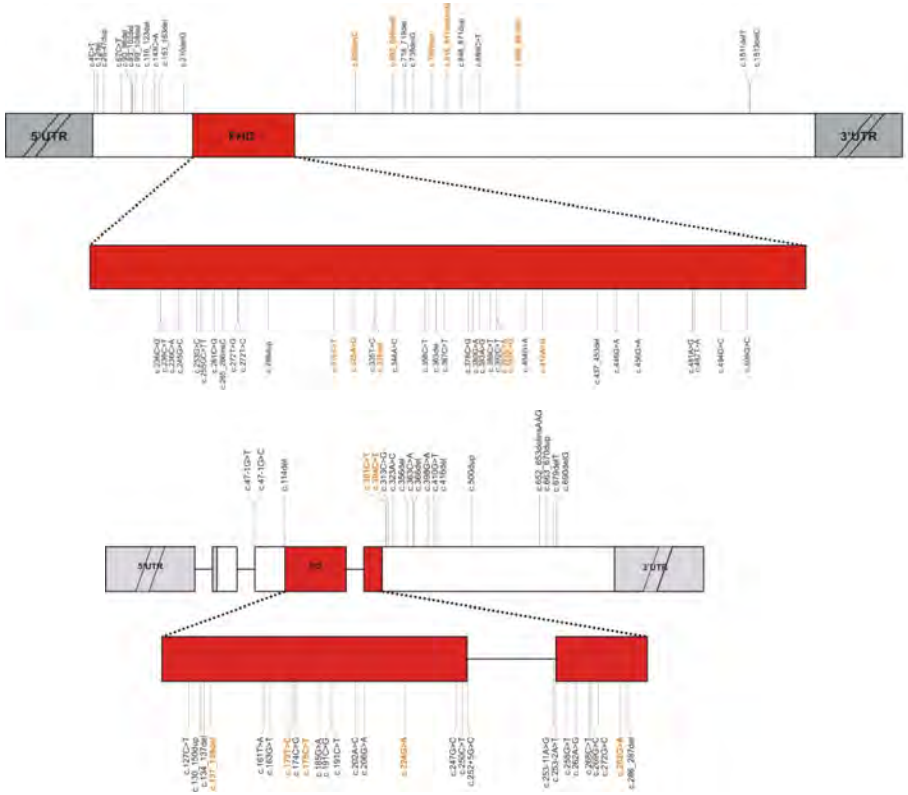


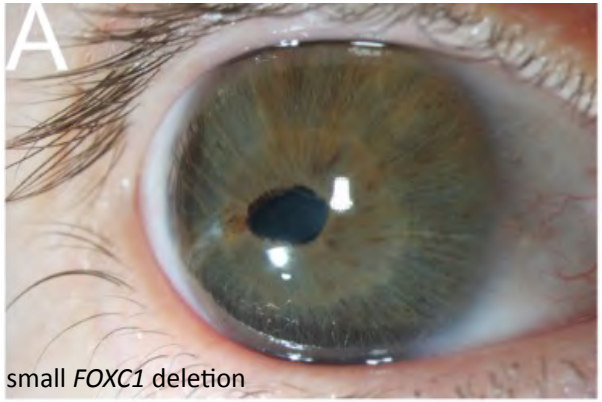
M, , *FOXC1* HeZ c.316C>T (p.Gln106X)

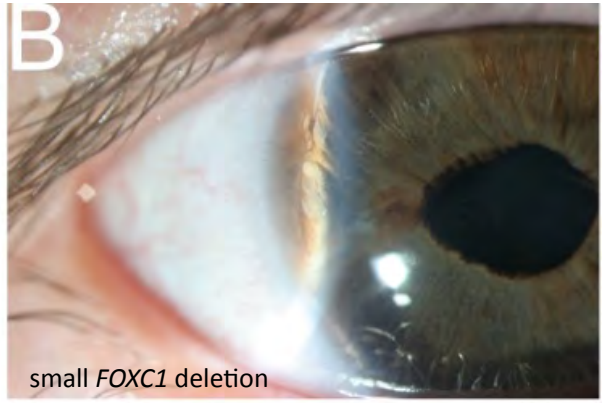
- Characterised by anterior segment dysgenesis (posterior embryotoxon & iris abnormalities) + systemic abnormalities (facial dysmorphism, dental abnormalities, redundant periumbilical skin, cardiac defects)
- Up to 50% develop glaucoma in infancy or early adulthood
- Genes are *PITX2* (pituitary homeobox 2 on Chr 4q25) & *FOXC1* (forkhead box C1 on Chr6p25), encoding transcription factors activating genes for early systemic & anterior segment development

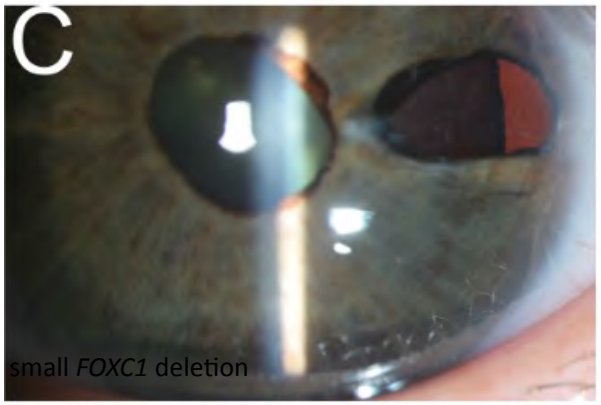
# Early-onset Glaucoma
# Axenfeld-Rieger Syndrome

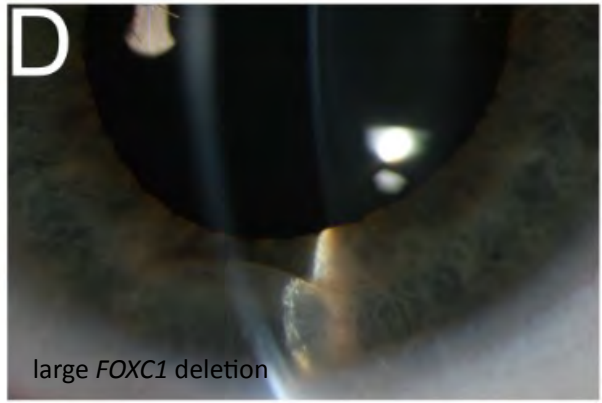
B D'haene, F Meire, I Claerhout, …, P Kestelyn, BP Leroy, E De Baere: Expanding the spectrum of *FOXC1* and *PITX2* mutations and copy number changes in patients with anterior segment malformations, IOVS, 52,324-333, 2011

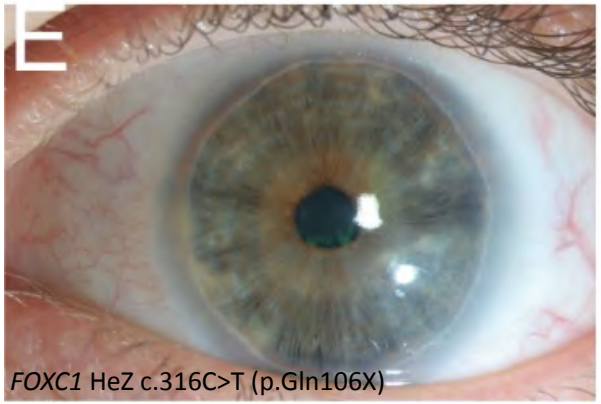


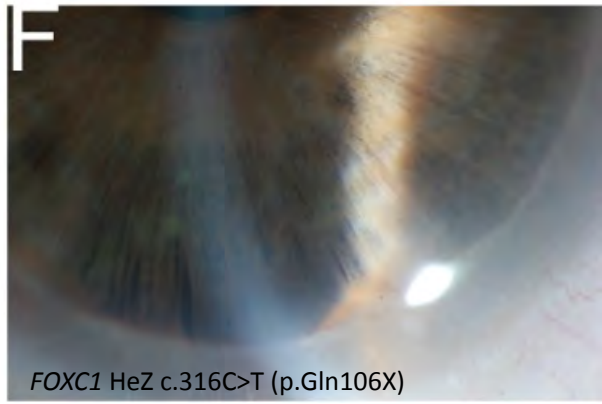



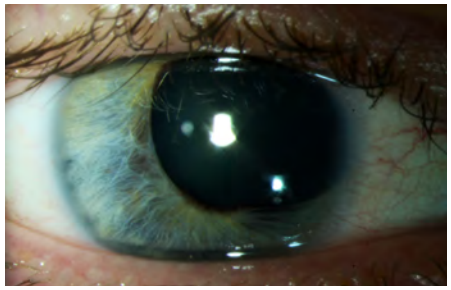



# Early-onset Glaucoma
## Aniridia

- Known eye abnormalities due to *PAX6* mutations:
  - Complete or partial absence of iris w/ photophobia
  - Foveal hypoplasia leading to nystagmus
  - Optic nerve hypoplasia
  - Corneal stem cell failure w/ keratopathy (78-90%)
  - Abnormal AS angle structures w/ glaucoma (50-70%)
  - Cataract (frequently anterior polar)
  - Microphthalmia & chorioretinal colobomata
  - Peters anomaly (corneal clouding & iridolenticulocorneal adhesions)

# Aniridia

RE



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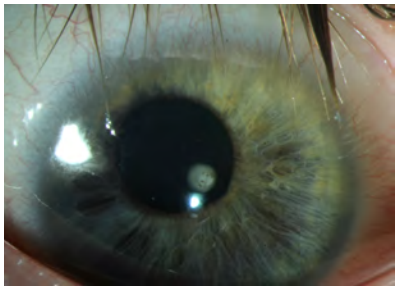


## Case

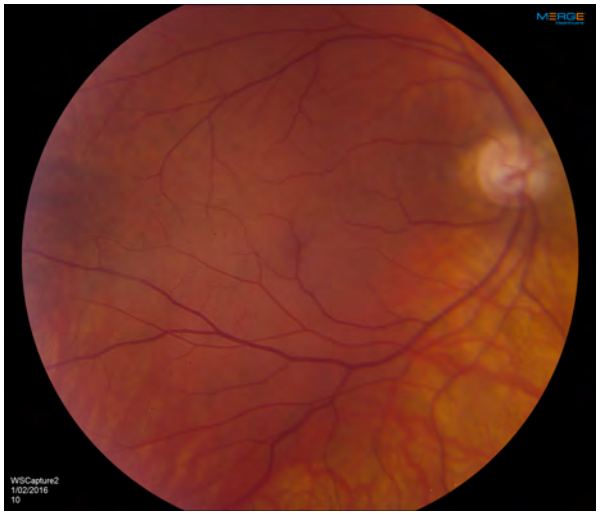
M, 33 yrs, aniridia

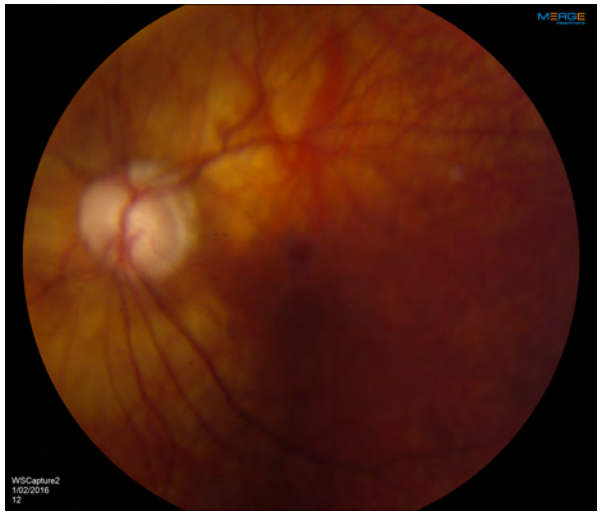
*PAX6* c.10+1G>T p.Arg254X

BCVA

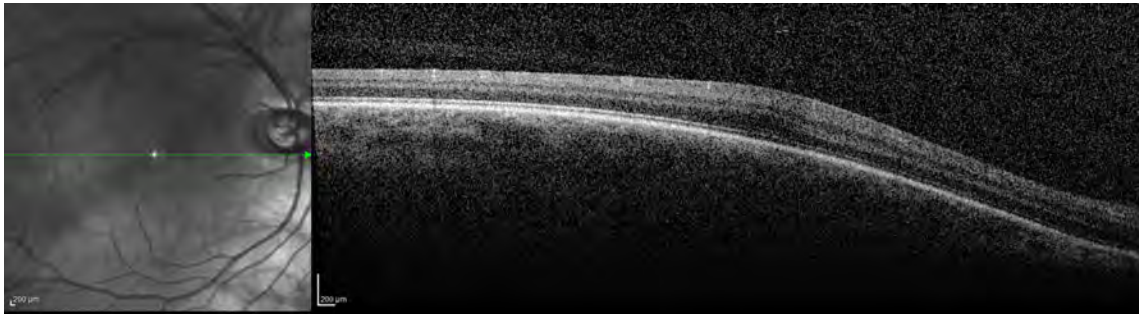
BE 6/60

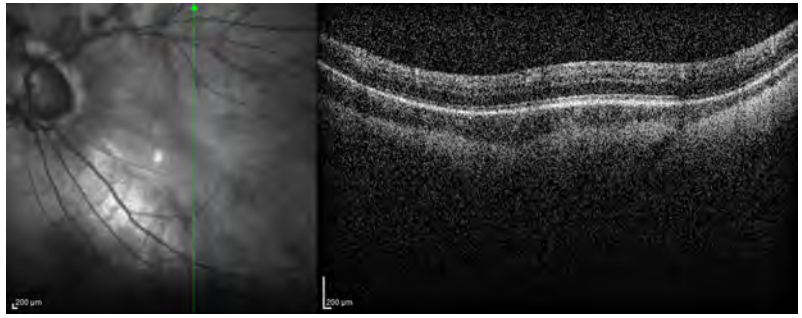
Nystagmus





OCT





# Aniridia

## Case

M, 19 yrs, aniridia

*PAX6* c.760C>T p.Arg254X

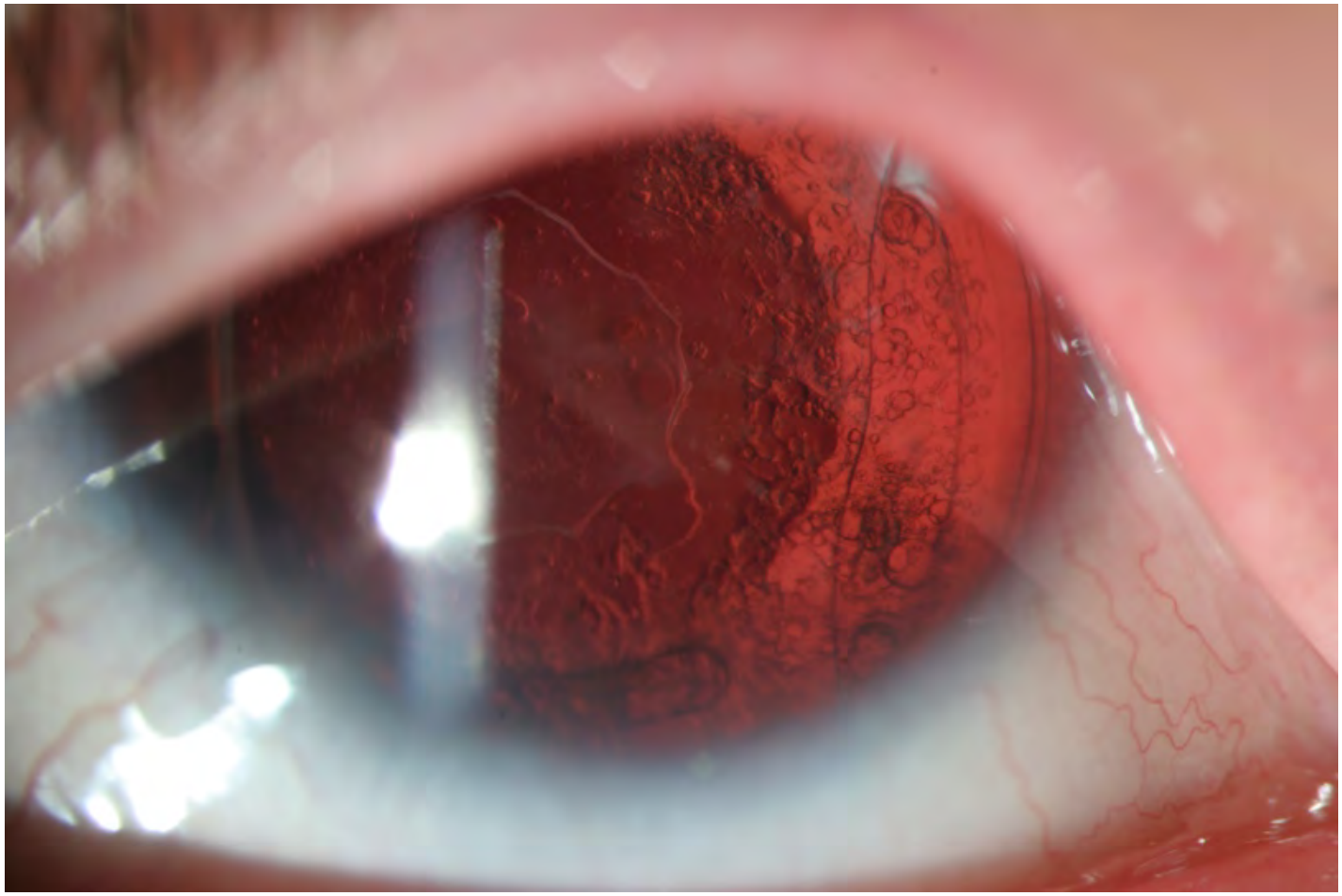
BCVA

BE 6/60

Nystagmus

RE

pseudophakia



# Case

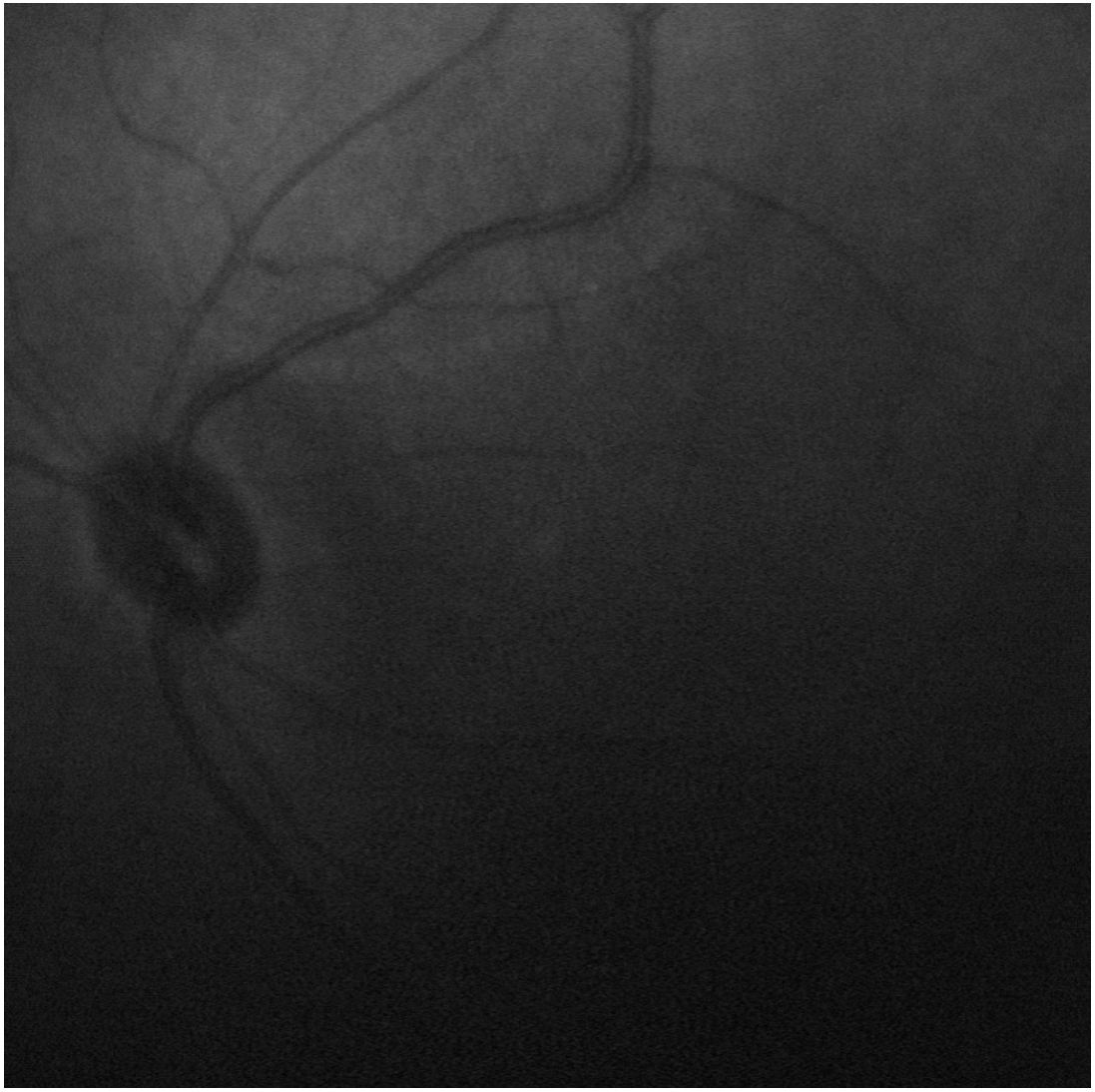
M, 19 yrs, aniridia
*PAX6* c.760C>T p.Arg254X

BCVA
BE 6/60

Nystagmus

IR Movie RE

# Aniridia



# Aniridia
## Symptoms & Signs

- Known non-ocular abnormalities due to *PAX6* mutations:
  - Brain development abnormalities (absent anterior and/or posterior commissure, absence/hypoplasia of pineal gland, pyramidal syndrome, cerebellar syndrome, absent corpus callosum)
  - Cognition & functional disorders (low IQ, poor control of affectivity, epilepsy)
  - Anosmia/hyposmia
  - Auditory interhemispheric processing problems
  - Endocrine conditions (pancreatic, pituitary dysfunctions)

# Aniridia
# Genetics

- Heterozygous mutations cause haploinsufficiency of *Paired box 6* gene (*PAX6*) on Chr 11p13 (potentially also dominant negative for mutations in exons 13 & 14)
- Familial (2/3) or sporadic (1/3)
- Autosomal dominant when familial
- Due to deletion in sporadic cases:
  - Sometimes including adjacent *WT1* gene
  - Wilms tumour-Aniridia-Genitourinary abnormalities-mental Retardation (WAGR) syndrome (contiguous gene syndrome)

# Aniridia
## Genetics

- *PAX6* expression in eye:
  - Developing iris, lens, ciliary body, corneal epithelium & retina
  - After completion of eye development, expression remains in neural retina, lens epithelium & cornea
- In combination w/ additional TFs, level & spatial distribution of *PAX6* expression in developing eye important to establish eye axes:
  - PAX2-PAX6 is critical in defining optic stalk/optic cup boundary
  - PAX6-cVAX & TBX5 expression mediates dorsoventral patterning of eye

# Aniridia
# Genetics

- *PAX6* expression in eye:
  - Known dose-dependent effect of *PAX6* gene product & range of eye abnormalities seems to correlate w/ level of *PAX6* activity
  - Predicted premature truncations are by far most common *PAX6* mutations in multiple populations (>70% w/ >50% in frame PTC)
  - Missense mutations lead to atypical or milder aniridia phenotypes (underreported or misdiagnosed?)

# Early-onset Glaucoma
# Juvenile Open-angle Glaucoma

- Early form of open-angle glaucoma
- Presents between ages 3 & 40
- JOAG typically has higher IOP, more rapidly progressive, less response to Rx
- JOAG is AD trait, due to HeZ mutations in *MYOC* encoding myocilin, on GLA1A locus on Chr 1q21-31 (previously known as *TIGR*)
- Between 8 & 63% of JOAG cases caused by *MYOC* mutations (3-4% adult-onset POAG cases)
- *MYOC* mutations have variable phenotypes: Pro370Leu, Tyr437Ile, Ile477Asn are all associated with early onset disease, whereas Gln368X associated with late onset disease & overall milder phenotype; compared to more common Gln368X, Thr377Met is associated with younger age of onset, higher peak IOP & increased likelihood of undergoing incisional glaucoma surgery

JH Fingert, EM Stone, VC Sheffield, WL Alward: Myocilin glaucoma, Surv Ophthalmol, 47, 547-561, 2002
DA Mackey, DL Healey, JH Fingert, *et al.*: Glaucoma phenotype in pedigrees with the myocilin Thr377Met mutation, Arch Ophthalmol, 121, 1172-1180, 2003

# Early-onset Glaucoma
# Pigmentary Glaucoma

- Pigment Dispersion Syndrome (PDS) is characterised by bilateral pigment deposition on posterior central cornea (Krukenberg spindle), midperipheral iris transillumination defects & dense trabecular meshwork pigmentation
- Between 35-50% of individuals with PDS will develop pigmentary glaucoma due to outflow obstruction
- Typically starts during 3rd or 4th decade of Life, although childhood pigmentary glaucoma has been described
- Between 26 & 48% of PG patients have positive family Hx
- *PMEL* gene (Premelanosome Protein) encodes melanosome component involved in melanin synthesis, storage & transport

SK Dorairaj, A Robin, W Shihadeh, S Greenberg, JM Liebmann, R Ritch: Phenotypic variability of pigment dispersion syndrome in children, Arch Ophthalmol, 125, 136-138, 2007
AA Lahola-Chomiak, T Footz, K Nguyen-Phuoc, *et al.:* Non-synonymous variants in premelanosome protein (PMEL) cause ocular pigment dispersion and pigmentary glaucoma. Hum Mol Genet, 28, 1298–1311, 2019

# Diagnostic Options & Therapeutic Opportunities in Glaucoma Genetics

# Genetics of Glaucoma
## Diagnostic Options

- Mendelian, early-onset forms of glaucoma:
  - Testing w/ gene panel at Molecular Lab CMG Ghent (Prof E De Baere)
  - Screening of relatives allows identification of at-risk individuals —> treatment or follow-up

Referral to ocular genetics
specialist essential

# Genetics of Glaucoma
# Glaucoma Gene Panel CMGG

| glaucoma panel | | |
|---|---|---|
| **versie** | v2 (31 genen) | Centrum voor Medische Genetica Gent |

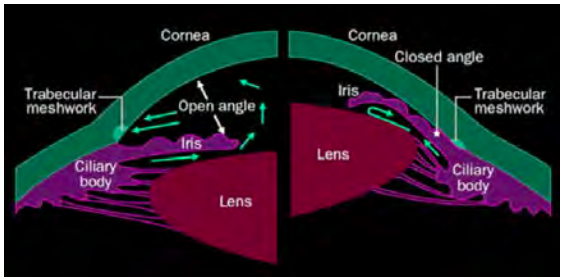
| Gene | OMIM gene ID | Associated phenotype, OMIM phenotype ID, phenotype mapping key and inheritance pattern |
|---|---|---|
| *ADAMTS10* | 608990 | Weill-Marchesani syndrome 1, recessive, 277600 (3), Autosomal recessive |
| *ADAMTS17* | 607511 | Weill-Marchesani 4 syndrome, recessive, 613195 (3), Autosomal recessive |
| *ASB1* | 605758 | No OMIM phenotype |
| *B3GLCT* | 610308 | Peters-plus syndrome, 261540 (3), Autosomal recessive |
| *BEST1* | 607854 | Macular dystrophy, vitelliform, 2, 153700 (3), Autosomal dominant; ?Microcornea, rod-cone dystrophy, cataract, and posterior staphyloma 2, 193220 (3), Autosomal dominant; Retinitis pigmentosa-50, 613194 (3); Retinitis pigmentosa, concentric, 613194 (3); Vitreoretinochoroidopathy, 193220 (3), Autosomal dominant; Bestrophinopathy, autosomal recessive, 611809 (3) |
| *COL18A1* | 120328 | Knobloch syndrome, type 1, 267750 (3), Autosomal recessive; Glaucoma, primary closed-angle, 618880 (3), Autosomal dominant |
| *COL4A1* | 120130 | ?Retinal arteries, tortuosity of, 180000 (3), Autosomal dominant; {Hemorrhage, intracerebral, susceptibility to}, 614519 (3); Angiopathy, hereditary, with nephropathy, aneurysms, and muscle cramps, 611773 (3), Autosomal dominant; Microangiopathy and leukoencephalopathy, pontine, autosomal dominant, 618564 (3), Autosomal dominant; Brain small vessel disease with or without ocular anomalies, 175780 (3), Autosomal dominant |
| *CPAMD8* | 608841 | Anterior segment dysgenesis 8, 617319 (3), Autosomal recessive |
| *CREBBP* | 600140 | Menke-Hennekam syndrome 1, 618332 (3), Autosomal dominant; Rubinstein-Taybi syndrome 1, 180849 (3), Autosomal dominant |
| *CYP1B1* | 601771 | Glaucoma 3A, primary open angle, congenital, juvenile, or adult onset, 231300 (3), Autosomal recessive; Anterior segment dysgenesis 6, multiple subtypes, 617315 (3), Autosomal recessive |
| *DDX58* | 609631 | Singleton-Merten syndrome 2, 616298 (3), Autosomal dominant |
| *FBN1* | 134797 | Geleophysic dysplasia 2, 614185 (3), Autosomal dominant; Weill-Marchesani syndrome 2, dominant, 608328 (3), Autosomal dominant; Ectopia lentis, familial, 129600 (3), Autosomal dominant; MASS syndrome, 604308 (3), Autosomal dominant; Marfan lipodystrophy syndrome, 616914 (3), Autosomal dominant; Acromicric dysplasia, 102370 (3), Autosomal dominant; Marfan syndrome, 154700 (3), Autosomal dominant; Stiff skin syndrome, 184900 (3), Autosomal dominant |
| *FOXC1* | 601090 | Axenfeld-Rieger syndrome, type 3, 602482 (3), Autosomal dominant; Anterior segment dysgenesis 3, multiple subtypes, 601631 (3), Autosomal dominant |
| *FOXD3* | 611539 | {Autoimmune disease, susceptibility to, 1}, 607836 (3), Autosomal dominant |
| *FOXE3* | 601094 | Anterior segment dysgenesis 2, multiple subtypes, 610256 (3), Autosomal recessive; {Aortic aneurysm, familial thoracic 11, susceptibility to}, 617349 (3), Autosomal dominant; Cataract 34, multiple types, 612968 (3) |
| *GJA1* | 121014 | Erythrokeratodermia variabilis et progressiva 3, 617525 (3), Autosomal dominant; Craniometaphyseal dysplasia, autosomal recessive, 218400 (3), Autosomal recessive; Oculodentodigital dysplasia, 164200 (3), Autosomal dominant; Hypoplastic left heart syndrome 1, 241550 (3), Autosomal recessive; Palmoplantar keratoderma with congenital alopecia, 104100 (3), Autosomal dominant; Syndactyly, type III, 186100 (3), Autosomal dominant; Oculodentodigital dysplasia, autosomal recessive, 257850 (3), Autosomal recessive; Atrioventricular septal defect 3, 600309 (3), Autosomal dominant |
| *IFIH1* | 606951 | Aicardi-Goutieres syndrome 7, 615846 (3), Autosomal dominant; Singleton-Merten syndrome 1, 182250 (3), Autosomal dominant |
| *LMX1B* | 602575 | Focal segmental glomerulosclerosis 10, 256020 (3), Autosomal dominant; Nail-patella syndrome, 161200 (3), Autosomal dominant |
| *LTBP2* | 602091 | Glaucoma 3, primary congenital, D, 613086 (3); Microspherophakia and/or megalocornea, with ectopia lentis and with or without secondary glaucoma, 251750 (3), Autosomal recessive; ?Weill-Marchesani syndrome 3, recessive, 614819 (3), Autosomal recessive |
| *MYOC* | 601652 | Glaucoma 1A, primary open angle, 137750 (3), Autosomal dominant |
| *NTF4* | 162662 | Glaucoma 1, open angle, 1O, 613100 (3) |
| *OCRL* | 300535 | Dent disease 2, 300555 (3), X-linked recessive; Lowe syndrome, 309000 (3), X-linked recessive |
| *OPTN* | 602432 | Glaucoma 1, open angle, E, 137760 (3), Autosomal dominant; Amyotrophic lateral sclerosis 12 with or without frontotemporal dementia, 613435 (3); {Glaucoma, normal tension, susceptibility to}, 606657 (3) |
| *PAX6* | 607108 | Optic nerve hypoplasia, 165550 (3), Autosomal dominant; Cataract with late-onset corneal dystrophy, 106210 (3), Autosomal dominant; ?Coloboma, ocular, 120200 (3), Autosomal dominant; ?Coloboma of optic nerve, 120430 (3), Autosomal dominant; Aniridia, 106210 (3), Autosomal dominant; Anterior segment dysgenesis 5, multiple subtypes, 604229 (3), Autosomal dominant; ?Morning glory disc anomaly, 120430 (3), Autosomal dominant; Foveal hypoplasia 1, 136520 (3), Autosomal dominant; Keratitis, 148190 (3), Autosomal dominant |
| *PITX2* | 601542 | Ring dermoid of cornea, 180550 (3), Autosomal dominant; Axenfeld-Rieger syndrome, type 1, 180500 (3), Autosomal dominant; Anterior segment dysgenesis 4, 137600 (3), Autosomal dominant |
| *PITX3* | 602669 | Cataract 11, multiple types, 610623 (3), Autosomal recessive, Autosomal dominant; Anterior segment dysgenesis 1, multiple subtypes, 107250 (3), Autosomal dominant; Cataract 11, syndromic, autosomal recessive, 610623 (3), Autosomal recessive, Autosomal dominant |
| *SBF2* | 607697 | Charcot-Marie-Tooth disease, type 4B2, 604563 (3), Autosomal recessive |
| *SH3PXD2B* | 613293 | Frank-ter Haar syndrome, 249420 (3), Autosomal recessive |
| *TBK1* | 604834 | {Encephalopathy, acute, infection-induced (herpes-specific), susceptibility to, 8}, 617900 (3), Autosomal dominant; Frontotemporal dementia and/or amyotrophic lateral sclerosis 4, 616439 (3), Autosomal dominant |
| *TEK* | 600221 | Venous malformations, multiple cutaneous and mucosal, 600195 (3), Autosomal dominant; Glaucoma 3, primary congenital, E, 617272 (3), Autosomal dominant |
| *WDR36* | 609669 | Glaucoma 1, open angle, G, 609887 (3) |

Gene symbols used are according to the HGNC guidelines. For some genes a previously HGNC-approved symbol is in brackets.
Each Phenotype is followed by its MIM number, phenotype mapping key and inheritance pattern.
OMIM release used for OMIM disease identifiers and descriptions: July 26, 2021

Possible phenotype mapping keys
(1) the disorder is placed on the map based on its association with a gene, but the underlying defect is not known
(2) the disorder has been placed on the map by linkage; no mutation has been found
(3) the molecular basis for the disorder is known; a mutation has been found in the gene
(4) a contiguous gene deletion or duplication syndrome, multiple genes are deleted or duplicated causing the phenotype

Brackets, "[ ]", indicate "nondiseases," mainly genetic variations that lead to apparently abnormal laboratory test values (e.g., dysalbuminemic euthyroidal hyperthyroxinemia).
Braces, "{ }", indicate mutations that contribute to susceptibility to multifactorial disorders (e.g., diabetes, asthma) or to susceptibility to infection (e.g., malaria).
A question mark, "?", before the phenotype name indicates that the relationship between the phenotype and gene is provisional. More details about this relationship are provided in the comment field of the map and in the gene and phenotype OMIM entries.

# Genetics of Glaucoma Diagnostic Options




Adapted from JL Wiggs & LR Pasquale, Genetics of Glaucoma, Hum Mol Genet, 26, 21-27, 2017

- Multifactorial glaucoma:
  - Polygenic Risk Score (PRS) calculations evaluate cumulative effect of multiple SNPs in different genes on disease risk
  - E.g. in study by XR Gao *et al.* an IOP-based PRS was applied to the UK Biobank dataset (n = 435678 participants); compared to bottom quintile, individuals in top quintile were found to have 6.34 times higher likelihood of having POAG (95% CI 4.82–8.33, $p = 2.1 \times 10^{-57}$) (1)
  - Study by C Liu *et al.* a PRS was constructed using eight disease associated SNPs in 844 PACG patients of Chinese ethnicity from Singapore; compared to individuals in lowest quartile, those in highest quartile of weighted PRS were more likely to have severe disease on visual field testing (OR = 3.11, 95% CI 1.95–4.96, $p < 0.001$) (2)

1/ Gao XR, Huang H, Kim H. Polygenic risk score is associated with intraocular pressure and improves glaucoma prediction in the UK biobank cohort. Transl Vis Sci Technol, 8, 10, 2019
2/ Liu C, Nongpiur ME, Cheng CY, *et al.* Evaluation of primary angle-closure glaucoma susceptibility loci for estimating angle closure disease severity. Ophthalmology, 128, 403-409, 2021

# Genetics of Glaucoma
# Therapeutic Opportunities

- Mendelian, early-onset forms of glaucoma:
  - A Jain *et al.*: CRISPR/Cas9 based gene editing for *MYOC* tested in human trabecular meshwork cell culture & in vivo mouse models: knockdown expression of mutant *MYOC* led to reduced misfolded protein load & ER stress in human trabecular meshwork cells, preventing glaucoma in mice (1)
  - CRISPR/Cas9 editing of a *PAX6* mutation was recently shown to rescue eye phenotype in a mouse model of aniridia (2)
- Multifactorial glaucoma:
  - Future Rx may focus on pathway (e.g. mitochondrial or lipid pathway genes) to generate individualised Rx

1/ A Jain, G Zode, RB Kasetti, *et al.* CRISPR-Cas9-based treatment of myocilin-associated glaucoma, Proc Natl Acad Sci USA, 114, 11199-11204, 2017
2/ SZ Mirjalili Mohanna, JW Hickmott, SL Lam, *et al.* Germline CRISPR/Cas9-mediated gene editing prevents vision loss in a novel mouse model of Aniridia. Mol Ther Methods Clin Dev., 17, 478-490, 2020

# Hereditary Optic Neuropathies
## Isolated & Syndromic OA

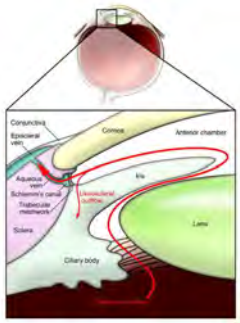
- Isolated AROA or ADOA: *ACO2* (AR syndromic phenotype also described: infantile cerebellar-retinal degeneration)
- Isolated mt-LHON: acute-onset, consecutive, bilateral loss of vision 3 primary mutations account for > 90% of patients (m.11778G>A in mt NADH dehydrogenase subunit IV (>70%) (*ND4*); m.14484T>C in mt NADH dehydrogenase subunit VI (14%) (*ND6*); m.3460G>A in mt NADH dehydrogenase subunit I (13%) (*ND1*))
- Isolated AR-LHON: w/ similar phenotype as mt-LHON, including male predominance *DNAJC30*
- ADOA Plus: ADOA, SNHL, ptosis, ophthalmoplegia, myopathy: c.1334G>A (p.R445H) mutation in *OPA1* on chr 3q29
- Arts syndrome or ADOA w/ rod-cone dystrophy: *SSBP1*
- Behr S: AR early-onset OA, spasticity, spinocerebellar ataxia, peripheral neuropathy GI dysmotility, intellectional disability: biallelic mutations in *OPA1* on chr 3q29
- DIDMOAD or Wolfram syndrome: AR progressive optic atrophy, juvenile DM, diabetes insipidus, SNHL
  - *WFS1* encodes Wolframin on 4p16, often associated w/ mtDNA deletions (WS1)
  - *CISD2* on 4q22-24 (WS2)
- Wolfram-like S: AD optic atrophy, SNHL: *WFS1*
- Syndromic ADOA: ADOA, cataract, SNHL, peripheral neuropathy, ataxia, areflexia: *OPA3*
- Costeff S or AR 3-methylglutaconic aciduria type 3: *OPA3*
- Syndromic AD & AR OA w/ mild intellectual disability, SCA 28 & spastic ataxia 5 (HeZ or bi-allelic mutations): *AFG3L2*

# Genetics of Glaucoma
## Conclusions

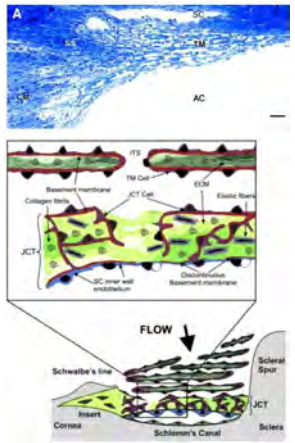
- Monogenic early-onset forms of glaucoma can be confirmed using specific gene panel
- Multifactorial glaucoma has a genetic component w/ PRS enabling tailored Rx in future
- Never forget that monogenic optic neuropathy can present as Low Tension Glaucoma

# Laser treatment in glaucoma: selective laser trabeculoplasty

## Trabecular meshwork



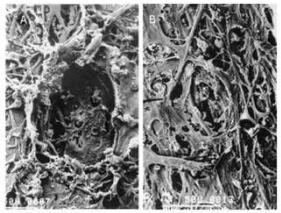

Fan, B.J. and J.L. Wiggs, Glaucoma: genes, phenotypes, and new directions for therapy. J Clin Invest, 2010. 120(9): p. 3064–72.




Tamm, E.R., 2009. The trabecular meshwork outflow pathways: structural and functional aspects. Exp Eye Res 88, 648–655.
Acott, T.S., Kelley, M.J., 2008. Extracellular matrix in the trabecular meshwork. Exp Eye Res 86, 543-561.

## Mechanism of action of SLT

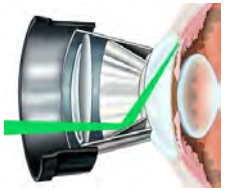
- selective targeting of pigmented trabecular meshwork endothelial cells with a very short laser pulse duration
- Q-switched, frequency doubled Nd:YAG laser: 0.6–1.0 mJ per pulse
- recruitment of macrophages > remodelling of extracellular matrix > an increase in aqueous outflow



Ekici, Feyzahan & Waisbourd, Michael & Katz, L.. (2016). Current and Future of Laser Therapy in the Management of Glaucoma. The Open Ophthalmology Journal. 10. 56-67. 10.2174/1874364101610010056.

## Aspects of the procedure: how to?

- 400 µm spot size
- 3 nanosecond duration
- across the pigmented trabecular meshwork
- between 50 and 100 laser burns
- between 180 and 360 degrees of the trabecular meshwork respectively
- 0.6–1.4 mJ
- titrated for bubble formation
- optimum power being approximately 0.1 mJ lower than that required to produce bubbles



Acott, T.S., Kelley, M.J., 2008. Extracellular matrix in the trabecular meshwork. Exp Eye Res 86, 543-561.

Selective Laser Trabeculoplasty (SLT) Compilation. Chris Teng, MD - YouTube

## Pre and Post laser treatment

**Topical IOP-lowering medications**

- preoperatively or immediately post-laser to prevent IOP spikes
- lower risk of the IOP increasing by 10 mm Hg or more within the first 2 h compared with those receiving no medication or placebo
- no advantage to medication being administered before or after laser and no difference in effectiveness between different alpha2-agonists.

Zhang L, Weizer JS, Musch DC. Perioperative medications for preventing temporarily increased intraocular pressure after laser trabeculoplasty. Cochrane Database Syst Rev. 2017;2:Cd010746.

**Topical anti-inflammatory drops**

- SLT works via a biological pathway
- topical indomethacin 0.1% or dexamethasone 0.1% TDS for 1 week vs control (no treatment) post SLT: No statistically significant difference in anterior chamber reaction, conjunctival redness, reported pain, or IOP lowering

De Keyser M, De Belder M, De Groot V. Randomized prospective study of the use of anti-inflammatory drops after selective laser trabeculoplasty. J Glaucoma. 2017;26:e22–e29.

## What to expect? Clinical efficacy.

Average IOP reduction

- 21.8-29.4% at 6 months
- 16.9–30% at 12 months
- 7.7–27.8% at 2 years

IOP-lowering effect of SLT diminishes with time

IOP reduction >20% from baseline IOP

- 66.7 to 75% eyes at 6 months
- 58 to 94% at 12 months
- 40 to 85% at 2 years

Leahy KE, White AJ. Selective laser trabeculoplasty: current perspectives. Clin Ophthalmol. 2015;9:833–841.

## Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT

**Functional: visual field**

proportion of eyes undergoing moderate or fast total deviation progression:

- medical therapy group: 26.2%
- SLT group: 16.9% (P < 0.001)

**Extension study: 6 years**

- disease progression at 6 years: drops: 26.8% vs SLT: 19.6% (p=0.006)
- trabeculectomy required: drops: 32 eyes vs SLT: 13 eyes (p<0.001)

## SLT in glaucoma subtypes

**Normal tension glaucoma**

- Reduce diurnal (especially night) fluctuations
- Stabilising a worsening visual field (Tojo et al., 2014)

**Pigmentary glaucoma**

- Substantial response to SLT (85% being medication free at one year) (Ayala et al., 2014)
- Significant IOP spikes of over 6 mmHg (Koucheki et al., 2012)

**Pseudoexfoliative glaucoma**

- High tension glaucoma with greater IOP spikes (Shazly et al. 2010)
- Responds good to SLT, with a larger proportion of success (Kara et al., 2013)

**Steroid induced glaucoma**

- Up to 50% reduction in IOP at 12 months post SLT (Maleki et al., 2016)
- Rubin et al., 2008: might prevent IOP spikes after subtenon injections of triamcinolone

# Adverse effects?

**LiGHT study**

- 34% of patients reported adverse effects: transient and self-limiting
  - ocular discomfort
  - Headache
  - blurred vision
- Six eyes (of 6 patients) experienced immediate post-laser IOP spike (over 5 mmHg from pre-treatment IOP) at 60 minutes, but only 1 of these eyes required medical treatment
- No IOP spikes (over 5 mmHg from baseline IOP) were detected at the 2-week safety check post-SLT.

**Other literature**

- Incidence of IOP spike varied from 0% to 62%
- After prophylactic or empirical anti-glaucoma medications: 0%–28.8%.[42]
- Rare: bilateral anterior uveitis
- corneal haze post-procedure: transient corneal oedema and one corneal decompensation
- Cystoid macula oedema has been reported in two patients
- Two cases: hyphaema
- Peripheral anterior synechiae: 3%

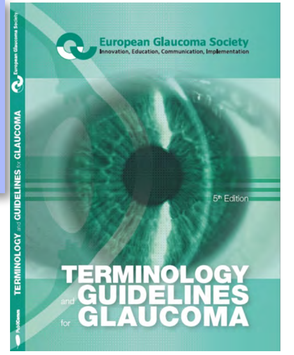
# Surgical treatment: who needs it?



Prof Nathalie Collignon

ManaMa, 3rd December 2022

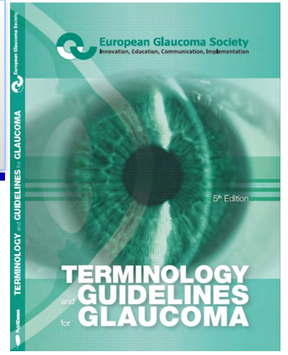
# Take home messages (2)




## Don’t delay surgery

1. In cases where other forms of therapy have failed
2. In cases where a target pressure cannot be reached
3. In cases where other forms of therapy are not suitable (where compliance or side effects are a problem)
4. In cases which have such advanced glaucoma and high IOP at presentation

# Glaucoma management : EGS guidelines 5th edition




**First Choice Drug monotherapy**

**consider laser trabeculoplasty**

**Effective on IOP**

**Non-Effective on IOP**

**Target IOP reached**

**Target IOP not reached***

**Continue**

**Add 2nd drug**
**Consider laser trabeculoplasty**

**change monotherapy**

**consider laser trabeculoplasty**

**Effective**

**Non-Effective**

**Target IOP maintained**

**Target IOP reached**

**Target IOP not reached**

**Substitue the 2nd drug**

**Other therapic options e.g. Laser, Surgery etc**

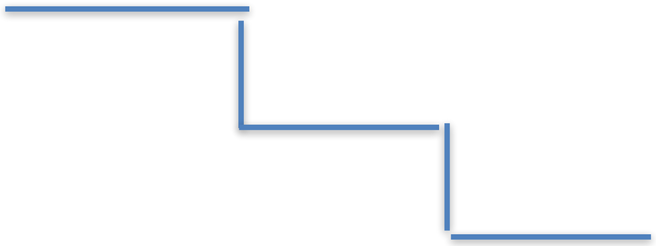
**Periodically Verify Endpoints**
- **Quality of life**
- **Visual Field**
- **Optic disc**
- **IOP**

Preservation of visual function AND of the individual needs for the expected lifetime of the patient

# Is it time to change the treatment paradigm ?

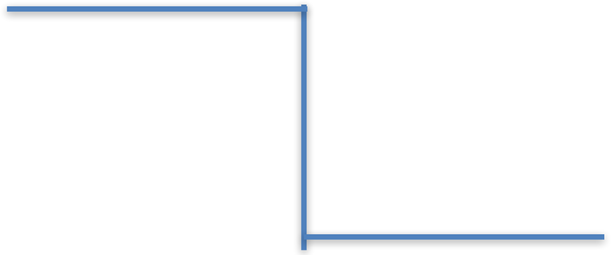
## Traditional

- Step wise initial approach
- Modest IOP targets
- Watch and Wait
- Escalate therapy if IOP target or progression



## New approach

- More aggressive from the start
- Aim lower earlier
- Get down and stay protected
- Balance compliance and risks with more agressive therapy
- Interventional approach



# Is it time to change the treatment paradigm ?

## Avoid the effect of the snowball

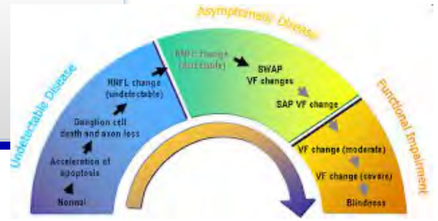

MIGS surgery versus  medication - laser

Risk/Benefit

Trabeculectomy versus  Tube

Risk/Benefit

# Indications:
# Which Glaucoma Surgery at which stage of the disease?




- Accordding to the EGS (1), « the GS are currently performed in selected glaucoma patients according to the Risks Benefits Ratio»


Depending:

the target pressure

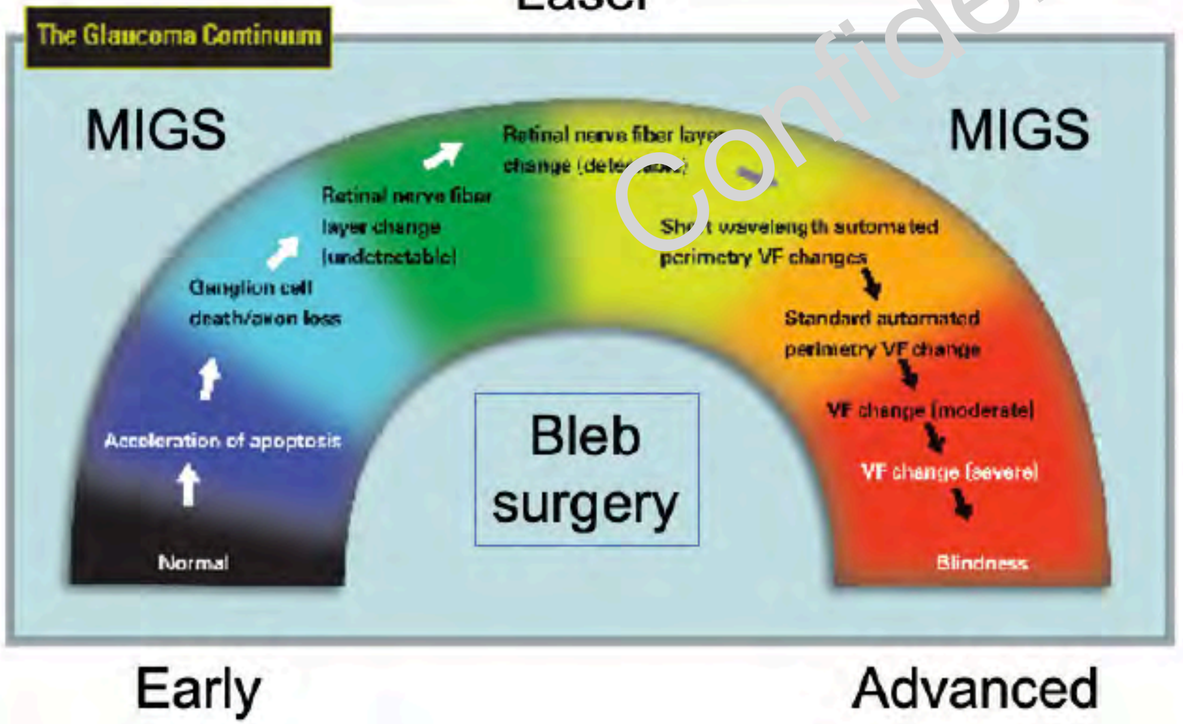
the severity of the disease

life expectancy

## Glaucoma Continuum

SUBCONJ
MIGS

Laser



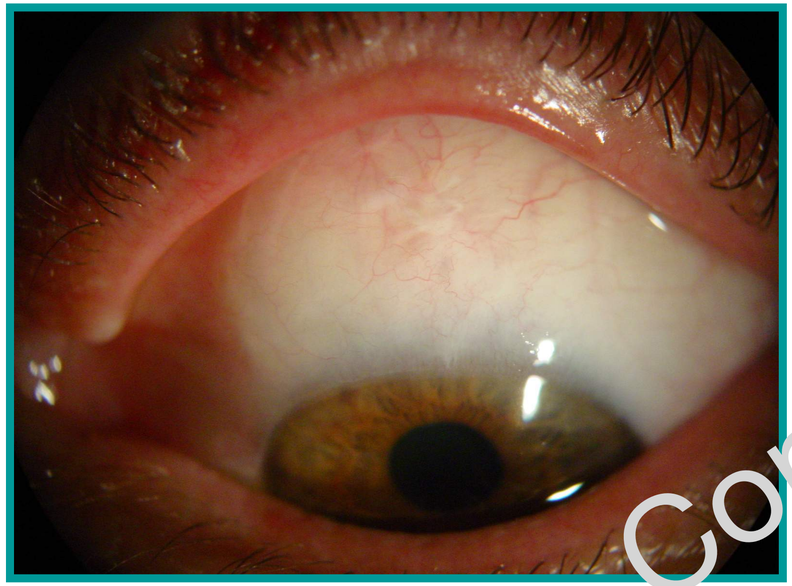

Drops/
laser

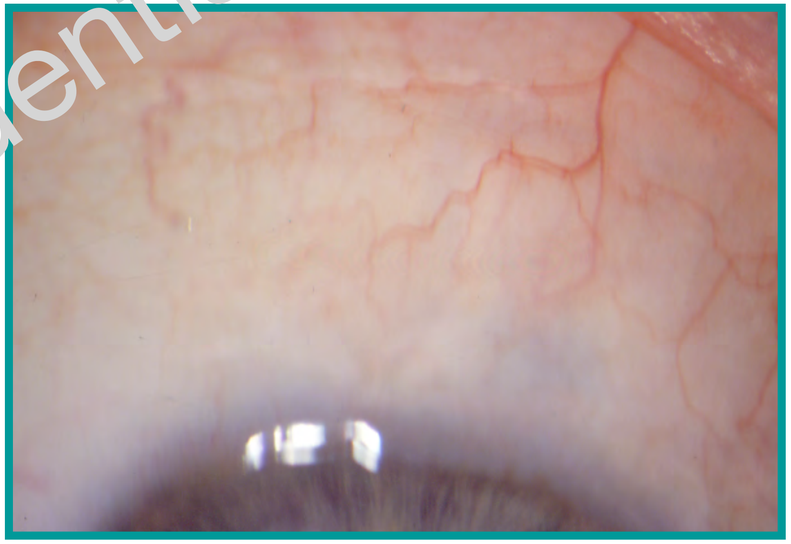
Bleb
surgery

Early

Advanced

# Glaucoma surgery: 21st century goal







Long term FU

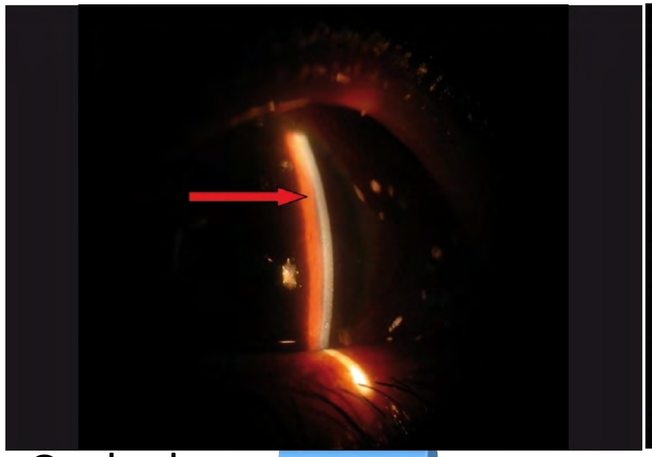
IOP= 12 mmHg

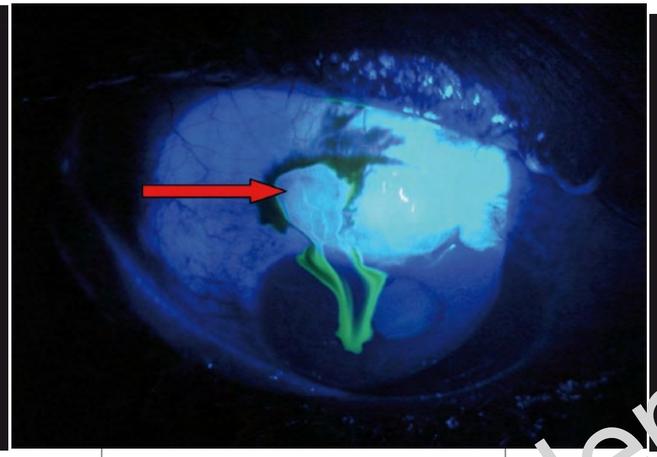
Diffuse non cystic bleb

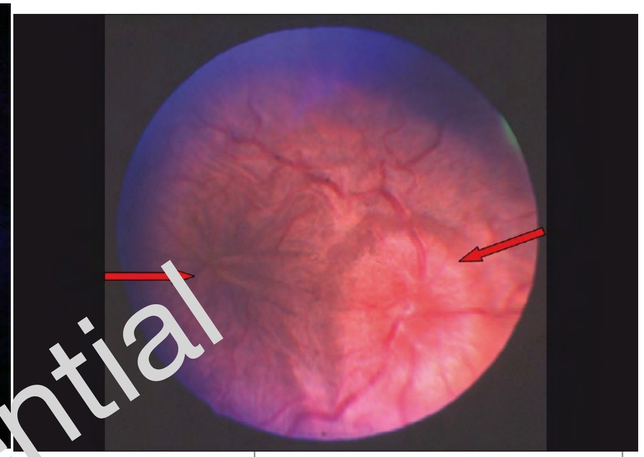
No progression

No medication

# Indications:Relative complication Rates by subspecialty

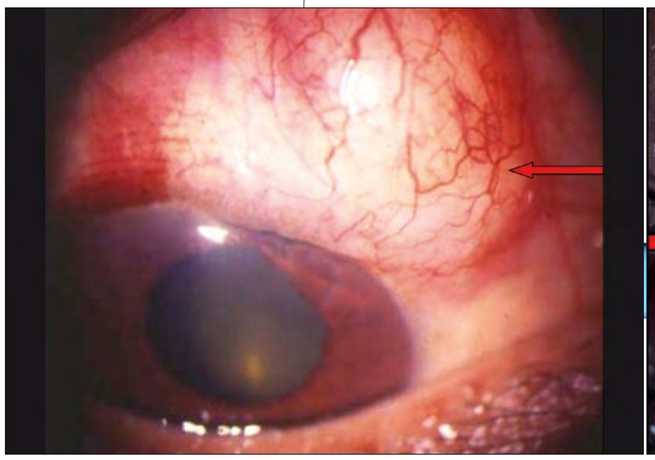


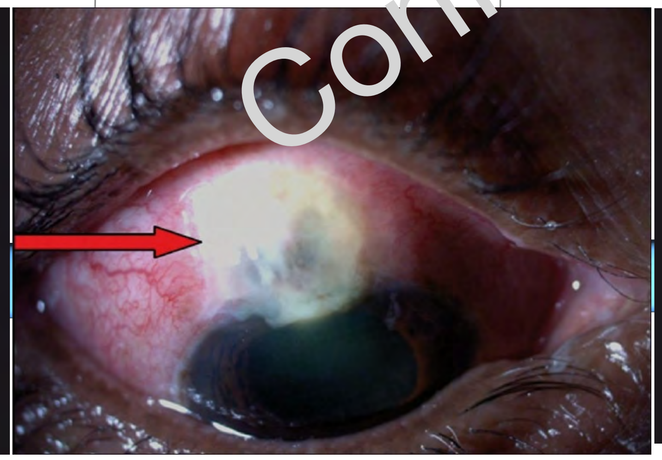


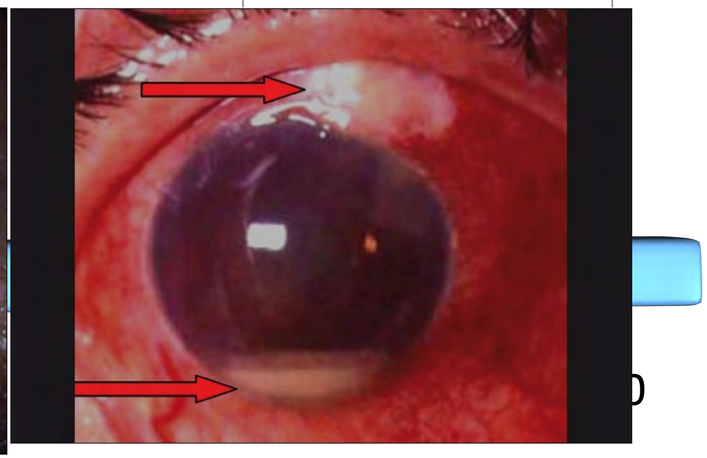


Oculoplasty

Glaucoma surgery :
Deserving love







Complications % at 3 years

Source: Marketscape

# Glaucoma Surgery: Pro and Con

| Aqueous outflow | | | Aqueous inflow |
|---|---|---|---|
| **Subconjunctival** | **Schlemm** | **Suprachoroidal** | **Cyclodestruction** |
| **Ab Externo** | **Ab Externo** | **Ab Externo** | **Ab Externo** |
| Trabeculectomy | Canaloplasty | Gold Shunt | Cryotherapy |
| Aqueous shunts/tube | Canal expanders | Starflow | Diode |
| Deep sclerectomy | | Aquashunt | Ultra Sound UC3 |
| Microshunt | | | |
| **Ab Interno** | **Ab Interno** | **Ab Interno** | **Ab Interno** |
| Xen 45 | Trabectome- OMNI | Cypass | Endolaser |
| | iStent | iStent supra | |
| | Hydrus | Starflow minijet | |

# 50 years old : Red eye and foreign body sensation in RE

2010: OHT treated
Baseline IOP 25 mmHg

Risks Factors:
Family history+
Myopia
Long lifetime


First treated with xalatan

IOP control at 18 mmHg

Switch to another PGS

Combined drops 2 times a day

IOP uncontrolled at 25 mmHg

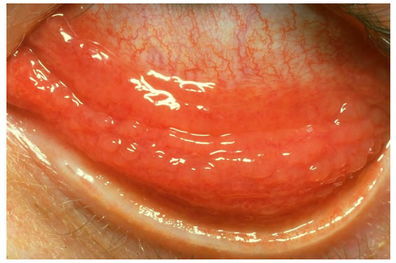
GGH
Migraine
Low AP

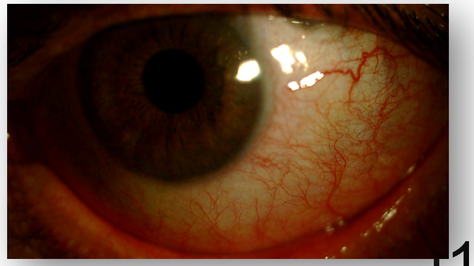
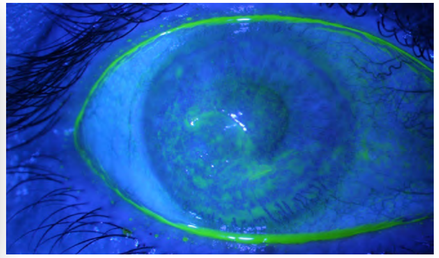
Bisoprolol 2.5 mg

# 50 years old : Red eye and foreign body sensation in RE


| | Right eye | Left eye |
|---|---|---|
| *VA far* | *9/10* | *9/10* |
| *VA near* | *Sn2* | *Sn2* |
| *Biomicroscopy* | SPK, BUT, Conj Hyperhemia | SPK, BUT, Conj Hyperhemia |
| *Goldmann IOP* | *24 (Tritherapy)* | *18 (Tritherapy)* |
| *Pachymetry* | *594 µm* | *590 µm* |
| *Fundus* | *C/D 0.55* | *C/D 0.4* |
| *Visual field* | *Inferior arcuate defect* | *normal* |





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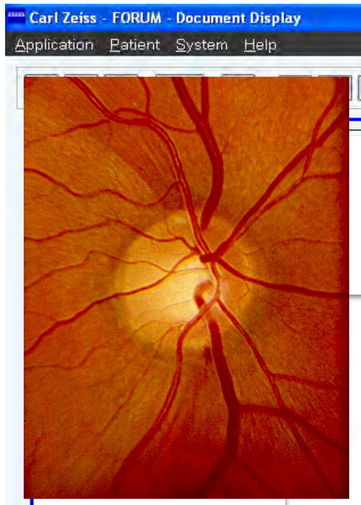


Target IOP= 16 mmHg



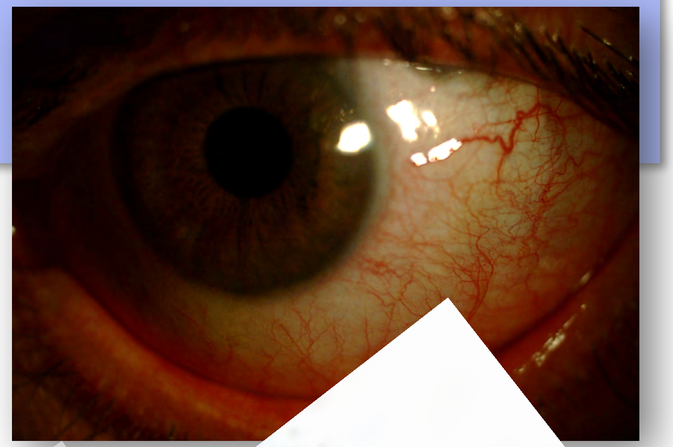





Target IOP= 18 mmHg

# Gonioscopic exam

- Does the angle opened or closed ?
- Does the angle appositional or not?

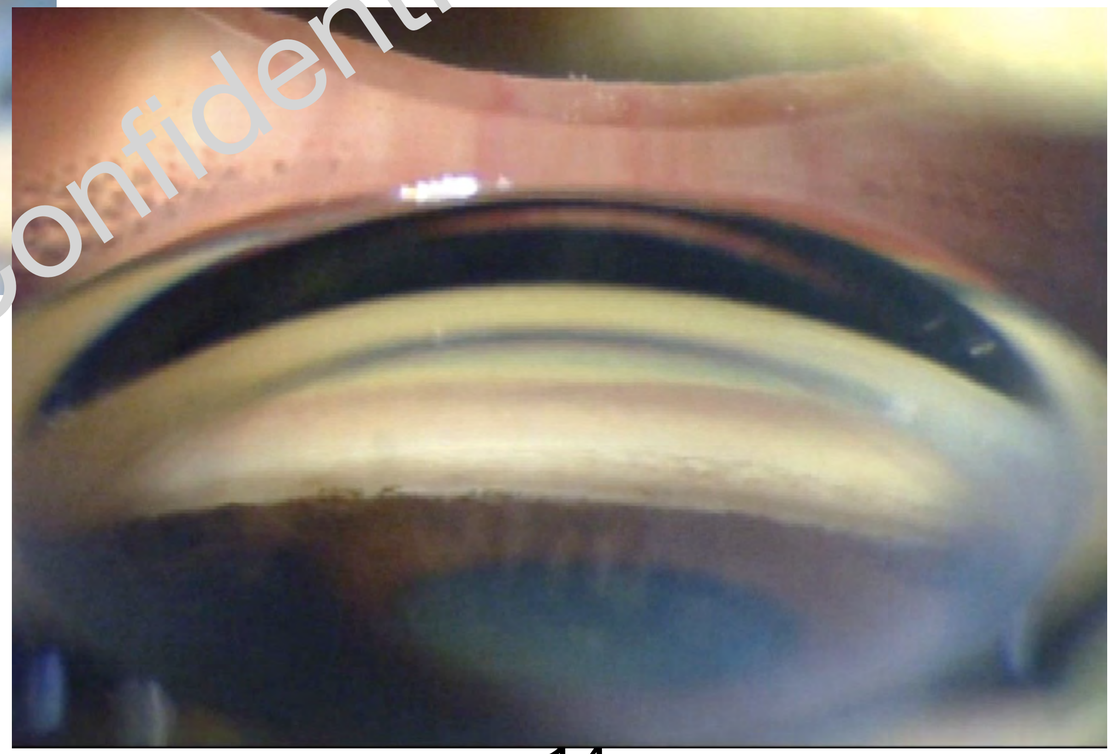


*Gonioscopy*

*and*

*Dynamic gonioscopy*

# 50 years old : Red eye and foreign body sensation in RE



# Angle closure classification

Acute angle closure= iridotrabecular (ITC) apposition- rapid severe rise in IOP

Intermittent angle closure : self limiting of ITC

Creeping angle closure:slowly progressive ITC toward AS and OHT

Chronic angle closure: irreversible ITC adhesion, asymptomatic significant raised IOP

# Angle Closure Glaucoma in case of early closed angle glaucoma

- Medical treatment
- Laser treatment : Laser Yag IP + Laser Argon iridoplasty
- Surgical treatment
  - Cataract surgery
  - Gonioscopy control
    - if angle open , MIGS in order to reduce drops
    - if not, Trabeculectomy +MMc

Target IOP= 16 mmHg

Long life expectancy

Mild glaucoma

# Angle Closure Glaucoma in case of advanced closed angle glaucoma

- Medical treatment
- Laser treatment : Laser Yag IP + Laser Argon iridoplasty
- Surgical treatment
  - Cataract surgery
  - Trabeculectomy +MMc

Target IOP= 10-12 mmHg

Long life expectancy

Advanced glaucoma

# Per-operative recommendations

## *Low risk patients*

Nothing or intraoperative 5-FU 50 mg/ml

1. No risk factors
2. Topical Medications (Beta-blockers/pilocarpine)
3. Afro-Caribbean (Elderdy)
4. Youth<40 with no other risk factors

## *Intermediate risk patients*

Intraoperative 5-FU 50 mg/ml or
MMC 0.2 mg/ml

1. Topical medications (adrenaline)
2. Previous Cataract surgery
3. Several low risk factors
4. Combined glaucoma filtration surgery / cataract extraction
5. Previous conjunctival surgery



## *High risk patients*

Intraoperative MMC 0.2-0.4 mg/ml

1. Neovascular glaucoma
2. Chronic persistent uveitis
3. Previous failed trabeculectomy /tubes
4. Chronic conjunctival inflammation
5. Multiple risk factors
6. Aphakic glaucoma

# 80 years old : Blurred vision at the right eye

2010: OAG
Baseline IOP 25 mmHg

Risks Factors:
Family history+
Myopia
Long lifetime


First treated with xalatan

IOP control at 18 mmHg

Switch to another PGS

Combined drops 4times a day

IOP uncontrolled at 25 mmHg

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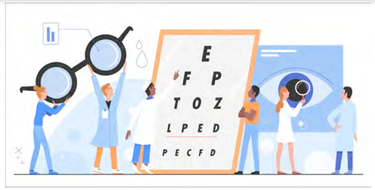
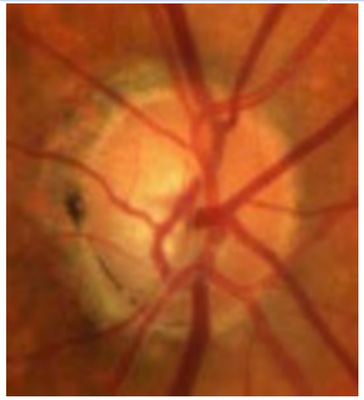
Migraine
Low AP

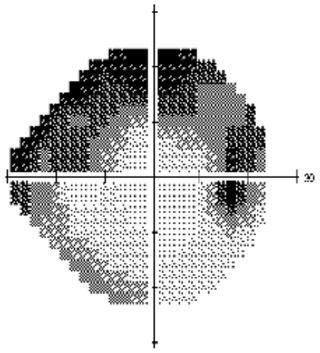
Bisoprolol 2.5 mg

# 80 years old : Blurred vision at the right eye

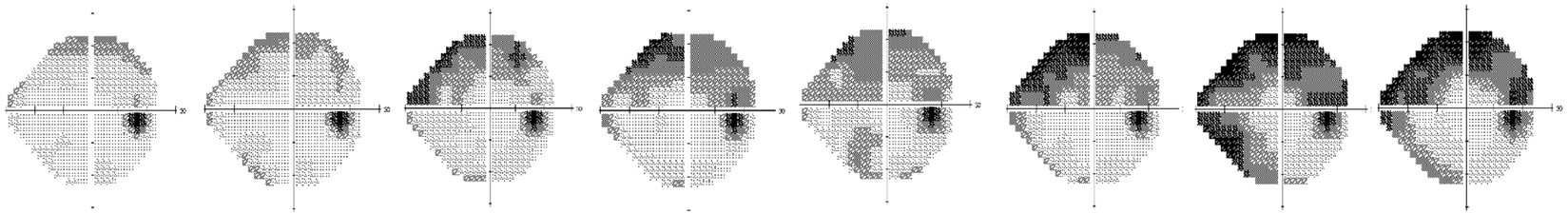



| | Right eye | Left eye |
|---|---|---|
| *VA far* | *7/10* | *2/10* |
| *VA near* | *Sn2* | *Sn2* |
| *Biomicroscopy* | cataract ++ | Cataract + |
| *Goldmann IOP* | *24 (Tritherapy)* | *18 (Tritherapy)* |
| *Pachymetry* | *594 µm* | *590 µm* |
| *Fundus* | *C/D 0.85 , inferior notch* | *C/D 0.4* |
| *Visual field* | *superior arcuate defect* | *normal* |

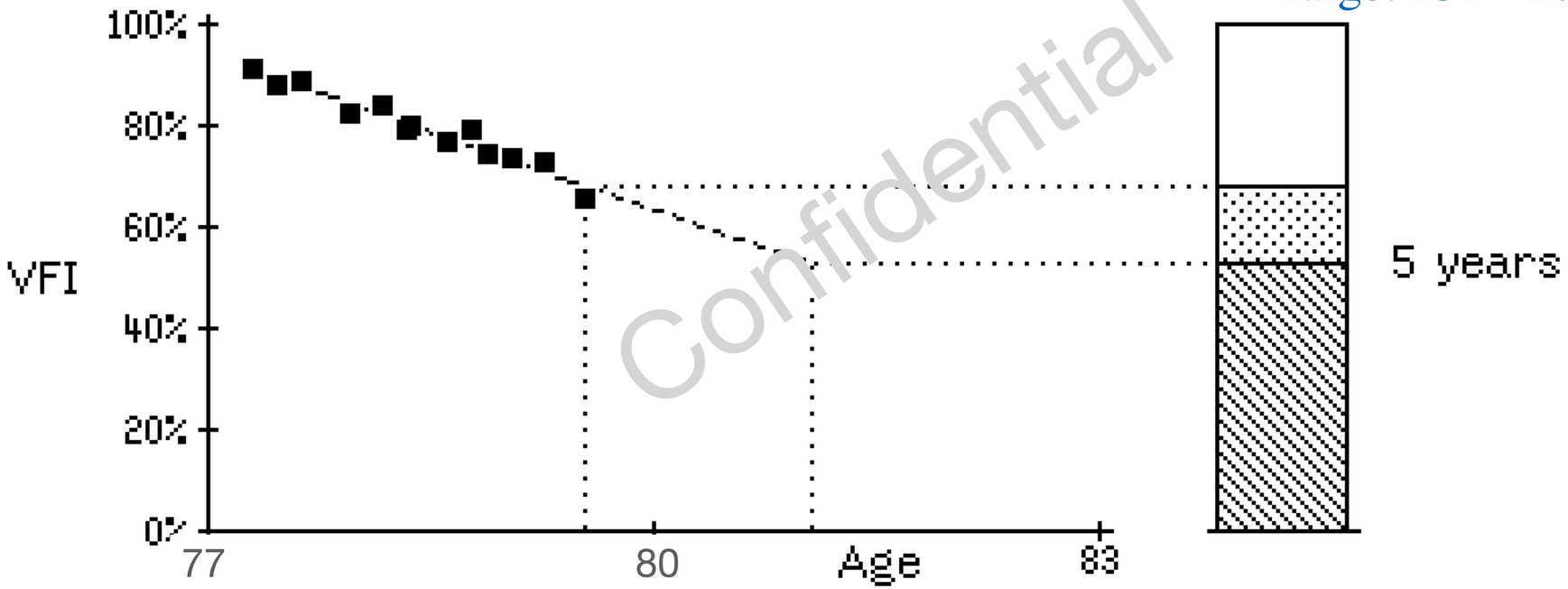




# 80 years old : Blurred vision at the right eye



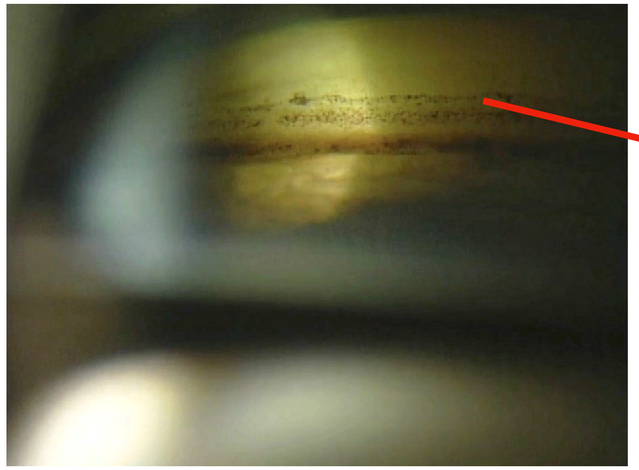
Target IOP= 10-12 mmHg






- **Rate of progression: -3.0 ± 0.5%/year (95% CI)**
- **Slope is significant at p < 0.1%**

# 80 years old : Blurred vision at the right eye



Sampaolesii line



Target IOP= 12 mmHg

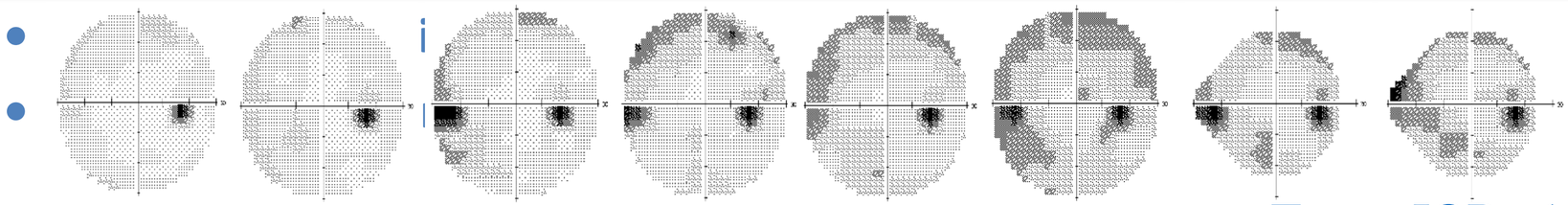
Short life expectancy

Advanced and rapid progressive glaucoma

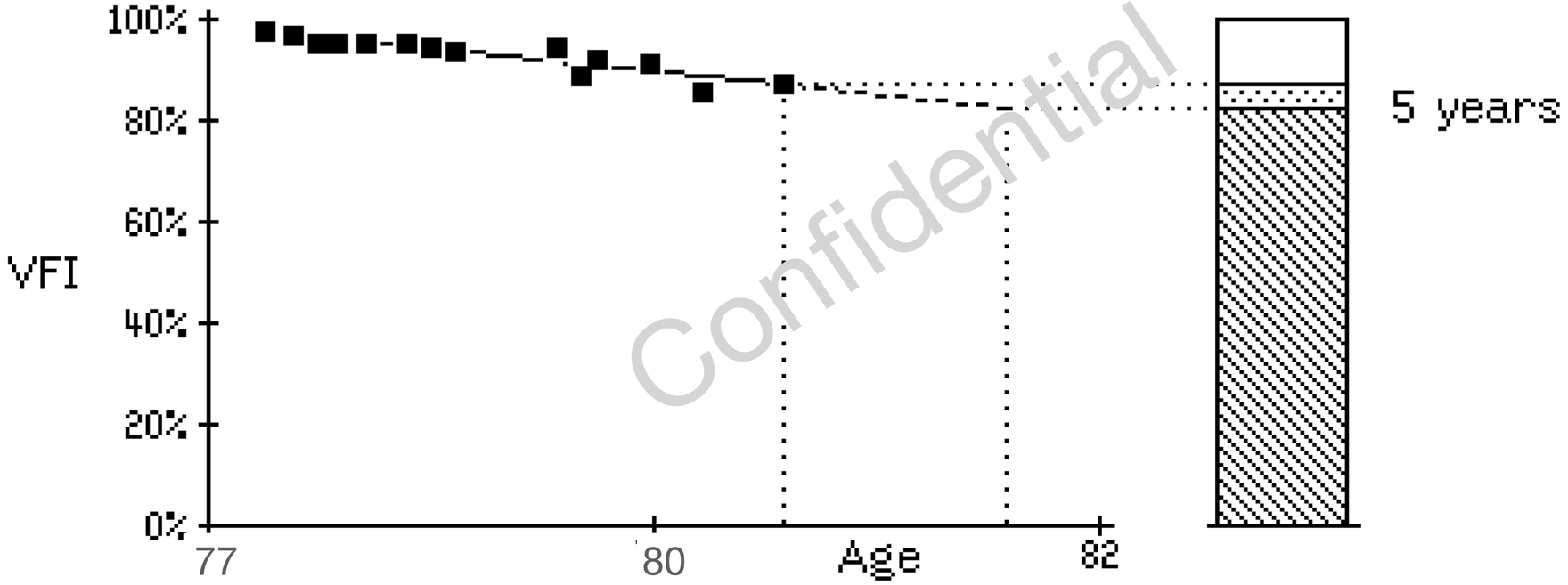
| | |
|---|---|
| Complains | Cataract |
| Disease | Glaucoma |

Combined Surgery

# 80 years old : Blurred vision at the right eye



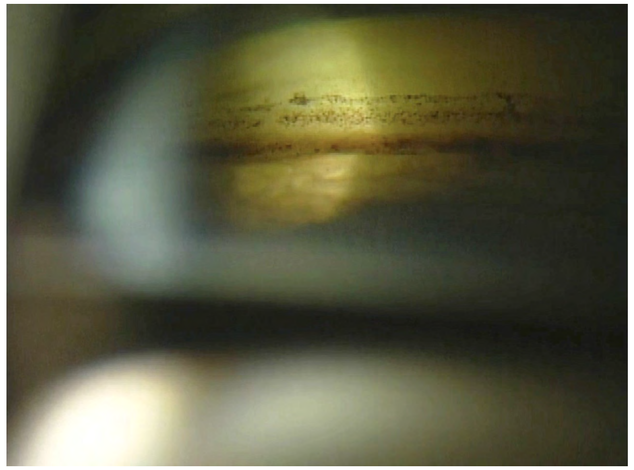
Target IOP= 16 mmHg






- **Rate of progression: -1.0 ± 0.5%/year (95% CI)**
- **Slope is significant at p < 0.1%**

# 80 years old : Blured vision at the right eye






Target IOP= 16 mmHg

Short life expectancy

Moderate and slow progressive glaucoma

| Complains | Cataract |
|---|---|
| Disease | Glaucoma |
| Treatment | 4 drops |

Cataract +/- MIGS

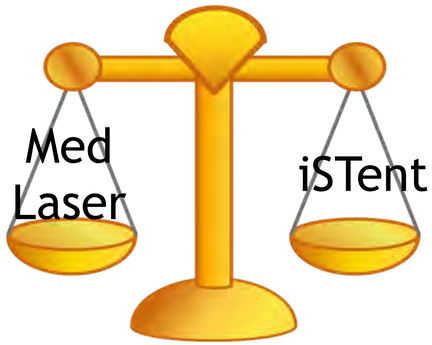
6 months

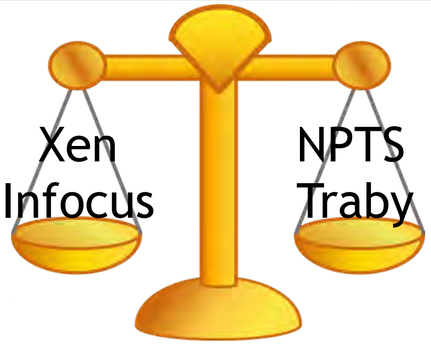
Glaucoma

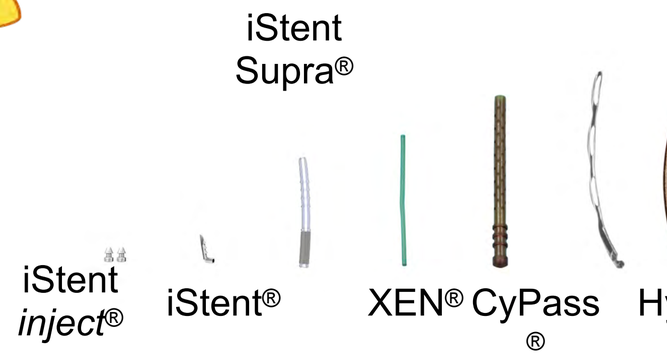
# MIGS : Pro and Con

| Internal MIGS | | | | | MIGS Plus |
|---|---|---|---|---|---|
| Schlemm's Canal | | | | Suprachoroidal | Subconjunctival |
| Stenting | Dilation | Cutting | Ablation | | |
| iStent<br>iStent inject<br>Hydrus | Visco360<br>ABiC (Ab-interno Canaloplasty) | Goniotomy<br>GATT (Gonioscopic -Assisted Transluminal Trabeculotomy)<br>Trab360<br>Kahook Dual Blade | Trabectome | Cypass<br>iStent Supra | Xen<br>InnFocus* |





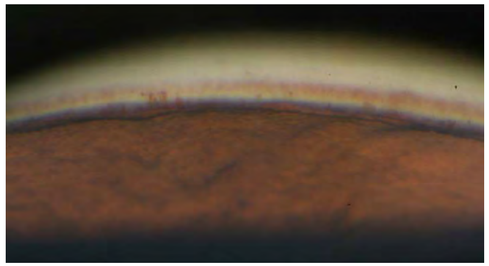


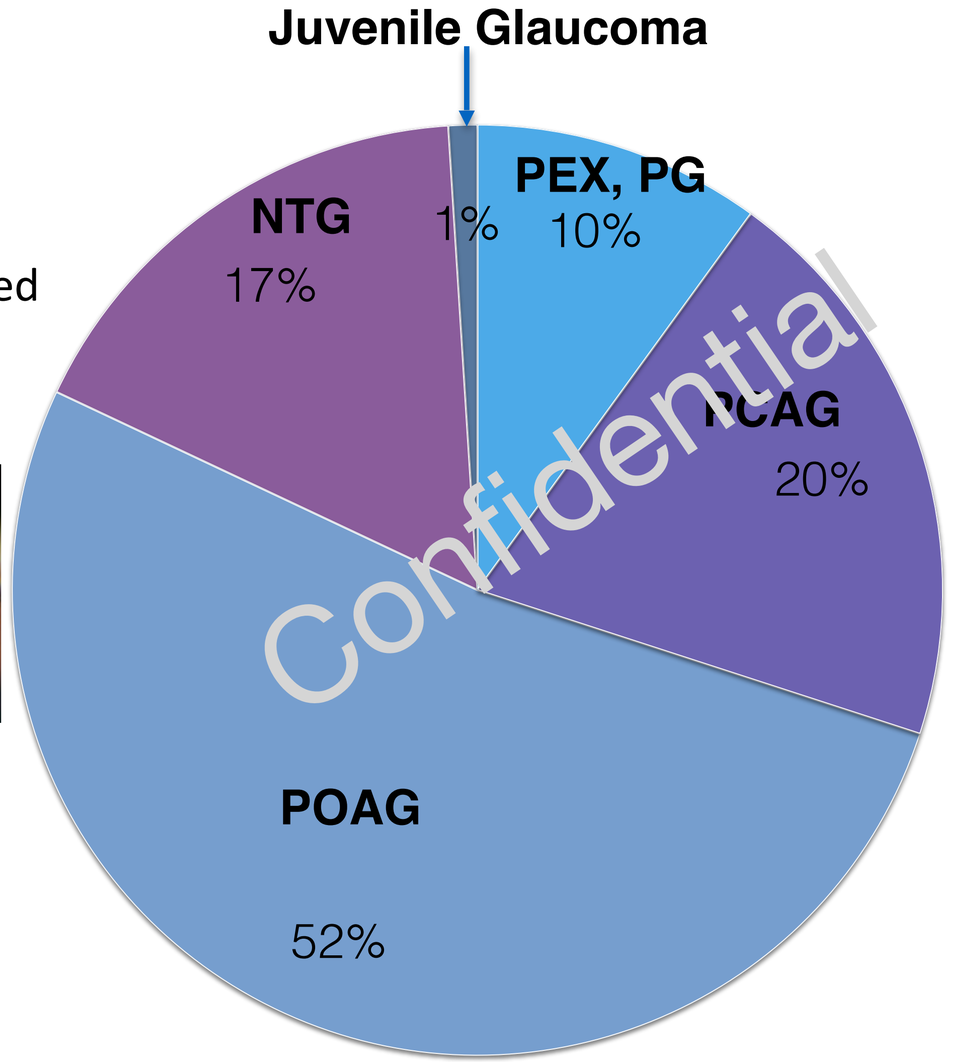
Microshunt

# Indications: Glaucoma prevalence in Europa

MIGS

Only if the angle is opened








Trabeculectomy / Tube

All kind of angles

(1) Ansari E. – An Update on Implants for Minimally Invasive Glaucoma Surgery (MIGS). *Ophthalmol Ther*, 2017,
(2) Lavia C, Dallorto L, Maule M, Ceccarelli M, Fea AM. – Minimally-invasive glaucoma surgeries (MIGS) for open angle glaucoma: A systematic review and meta-analysis. *PLoS One*, 2017, **12**, e0183142

# Results : Are MIGS a reliable technique over years?

RESEARCH ARTICLE

## Minimally-invasive glaucoma surgeries (MIGS) for open angle glaucoma: A systematic review and meta-analysis

**Carlo Lavia[1☯], Laura Dallorto[1☯], Milena Maule[2], Manuela Ceccarelli[3], Antonio Maria Fea[1]***

**Table 2** Summary of efficacy and safety data

| | Phaco/iStent [8] | Phaco/ Hydrus [13] | Phaco/ CyPass [17] | Phaco/XEN45 [22] | InnFocus [3] |
|---|---|---|---|---|---|
| Pre-op IOP | 18.6 | 26.3 | 24.4 | 16 | 23.8 |
| Post-op IOP | 17.0 | 16.9 | 17.0 | 12 | 10.7 |
| % IOP drop; % medication reduction | 8.0%; 87% (versus 5.5%; 73% in controls) | 50%; 73% (versus 28%; 38% in controls) | 30.3%; 85.7% (versus 22%; 53.9% in controls) | 25%; 84.2% | 55%; 69.2% |
| AEs | | 12% focal peripheral anterior synechiae | | Transcient choroidal detachment = 2, tube extrusion = 1, trabeculectomy = 2 | Transcient hypotony = 13%, transcient choroidal effusion = 8.7% |

### Conclusions

Although MIGS seem efficient in the reduction of the IOP and glaucoma medication and show good safety profile, this evidence is mainly derived from non-comparative studies and further, good quality RCTs are warranted.

**Clinical & Experimental Ophthalmology**

Broadway and Clark, J Clin Exp Ophthalmol 2014, 5:6
http://dx.doi.org/10.4172/2155-9570.1000371

Research Article | Open Access

## The Norwich Trabeculectomy Study: Long-term Outcomes of Modern Trabeculectomy with Respect to Risk Factors for Filtration Failure

**David C Broadway[1-3*] and Allan Clark[2]**

100 papers
92 definitions of success
36 to 98% of complete success at 5 years

**Conclusions:** In a large cohort of mainly Caucasian patients, appropriately augmented, 'modern', 'safe-technique' trabeculectomy was highly successful and, together with 'modern' post-operative management, appeared to annul the effect of most 'traditional' risk factors for failure such as previous surgery, long-term exposure to topical medication, relative youth and secondary glaucoma.



(1) Schlenker MB, Gulamhusein H, Conrad-Hengerer I, Somers A, Lenzhofer M, Stalmans I, et al. - Efficacy, Safety, and Risk Factors for Failure of Standalone Ab Interno Gelatin Microstent Implantation versus Standalone Trabeculectomy. *Ophthalmology*, 2017, **124**, 1579-1588

(1) Stalmans I, Gillis A, Lafaut AS, Zeyen T. - Safe trabeculectomy technique: long term outcome. *Br J Ophthalmol*, 2006, **90**, 44-47.

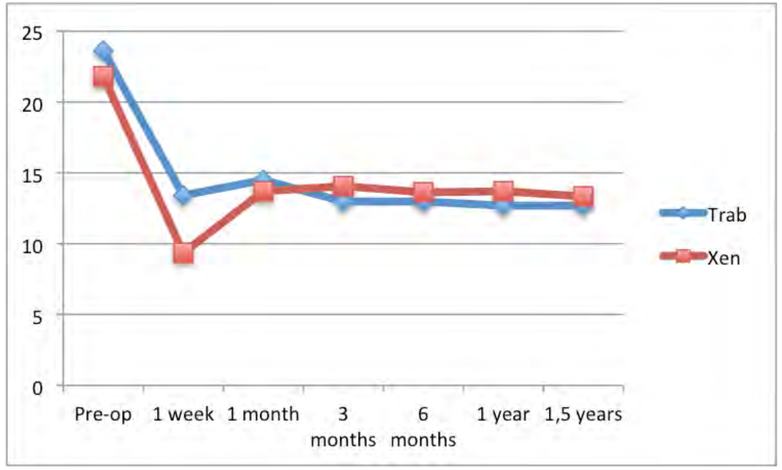
# Retrospective interventional cohort study

Prof N Collignon , Dr G Dupont

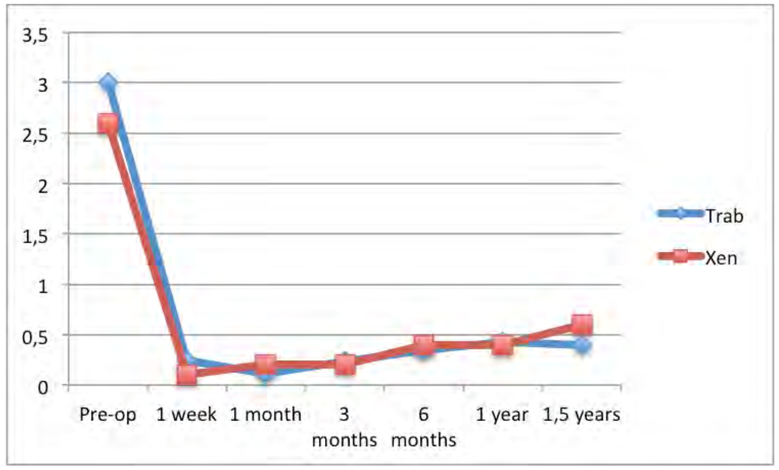
| | **Xen N= 61 eyes** | **Trabeculectomy N=80** |
|---|---|---|
| FU (months) | 18 | 18 |
| MD | <8 dB | > 10 dB |
| POAG (%) | 73 | 1[illegible] |
| PG (%) | 7.9 | 28 |
| PEX (%) | 3.2 | 9 |
| Juvenile Glaucoma (%) | 7.9 | 4 |
| PCAG (%) | 0 | 37 |
| Revision (%) | 43 | 32 |



IOP reduction




Reduction of medications



# Filtration surgery ab-interno vs ab-externo

## Retrospective interventional cohort study

AMERICAN ACADEMY™ OF OPHTHALMOLOGY

CrossMark

# Efficacy, Safety, and Risk Factors for Failure of Standalone Ab Interno Gelatin Microstent Implantation versus Standalone Trabeculectomy



*Matthew B. Schlenker, MSc, MD,[1] Husayn Gulamhusein, BHSc,[2] Ina Conrad-Hengerer, MD, PhD,[3] Alix Somers, MD,[4] Markus Lenzhofer, MD,[5] Ingeborg Stalmans, MD, PhD,[4] Herbert Reitsamer, MD,[5] Fritz H. Hengerer, MD, PhD,[6,7] Iqbal Ike K. Ahmed, MD[1]*

***Conclusions:*** There was no detectable difference in risk of failure and safety profiles between standalone ab interno microstent with MMC and trabeculectomy with MMC. *Ophthalmology 2017;124:1579-1588 © 2017 by the American Academy of Ophthalmology*

(1) Lavia C, Dallorto L, Maule M, Ceccarelli M, Fea AM. – Minimally-invasive glaucoma surgeries (MIGS) for open angle glaucoma: A systematic review and meta-analysis. *PLoS One*, 2017, **12**, e0183142

(2) An Update on Implants for Minimally Invasive Glaucoma Surgery (MIGS). *Ophthalmol Ther*, 2017

(3) Schlenker MB, Gulamhusein H, Conrad-Hengerer I, Somers A, Lenzhofer M, Stalmans I, et al. – Efficacy, Safety, and Risk Factors for Failure of Standalone Ab Interno Gelatin Microstent Implantation versus Standalone Trabeculectomy. *Ophthalmology*, 2017, **124**, 1579-1588

# Filtration surgery ab-interno vs ab-externo

AMERICAN ACADEMY OF OPHTHALMOLOGY

CrossMark

## Efficacy, Safety, and Risk Factors for Failure of Standalone Ab Interno Gelatin Microstent Implantation versus Standalone Trabeculectomy

*Matthew B. Schlenker, MSc, MD,[1] Husayn Gulamhusein, BHSc,[2] Ina Conrad-Hengerer, MD, PhD,[3] Alix Somers, MD,[4] Markus Lenzhofer, MD,[5] Ingeborg Stalmans, MD, PhD,[4] Herbert Reitsamer, MD,[5] Fritz H. Hengerer, MD, PhD,[6,7] Iqbal Ike K. Ahmed, MD[1]*

Bleb leakage is avoidable in Traby groups

><

Serious Complications  in Xen groups

Bleb revision

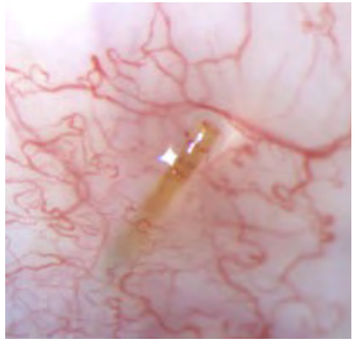
43% in Xen group ><30% in the traby group

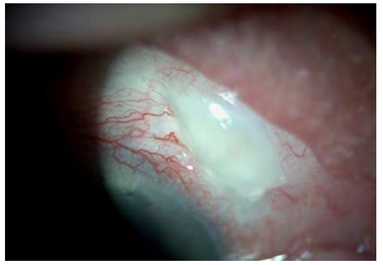
## Retrospective interventional cohort study

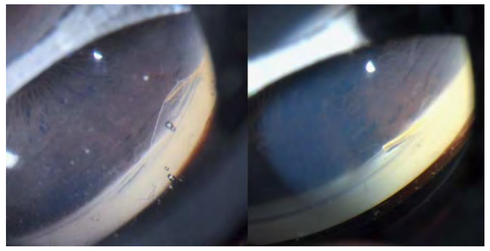
Table 4. Postoperative Complications in Microstent and Trabeculectomy Eyes

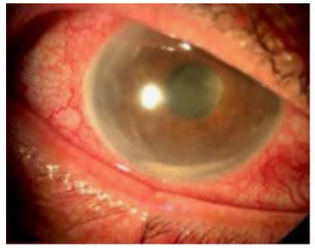
| Complication (>1 Month) | Microstent | Trabeculectomy |
|---|---|---|
| No. | 185 | 169 |
| Leak/dehiscence | 3 | 12 |
| Hyphema | 2 | 2 |
| Vitreous hemorrhage | 2 | 1 |
| Choroidals or choroidal folds | 1 | 2 |
| Hypotony maculopathy | 2 | 1 |
| Uveitis | 2 | 1 |
| Corneal decompensation | 0 | 1 |
| Macular edema | 0 | 3 |
| Diplopia | 0 | 0 |
| Iris incarceration | — | 2 |
| Blocked microstent | 1 | — |
| Exposed microstent | 1 | — |
| Microstent–iris touch | 2 | — |
| Shallow anterior chamber | 0 | 2 |
| Dellen | 2 | 0 |
| Serious complication (anytime) | | |
| Retinal detachment | 0 | 0 |
| Angle closure | 0 | 0 |
| Suprachoroidal hemorrhage | 0 | 0 |
| Malignant glaucoma | 4 | 2 |
| Blebitis | 0 | 1 |
| Endophthalmitis | 0 | 0 |
| No light perception | 0 | 0 |
| Total | 22 | 30 |

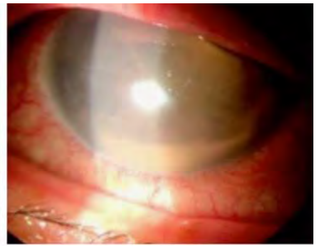












# 45 years old : Stiffness in the right eye

2010: OAG
Baseline IOP 25 mmHg

Risks Factors:
Family history+
Myopia
Long lifetime


First treated with xalatan

IOP control at 18 mmHg

Switch to another PG-S

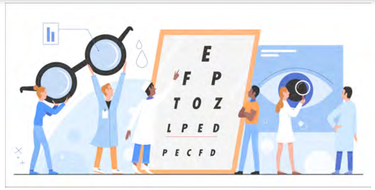
Combined drops 4times a day

IOP uncontrolled at 35 mmHg

GGH
Migraine
Low AP

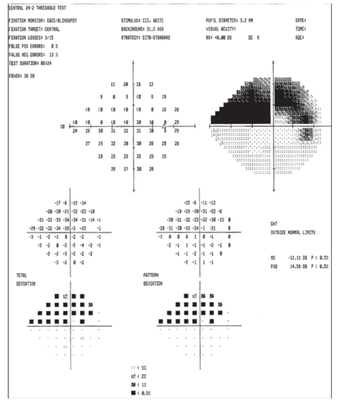
Bisoprolol 2.5 mg

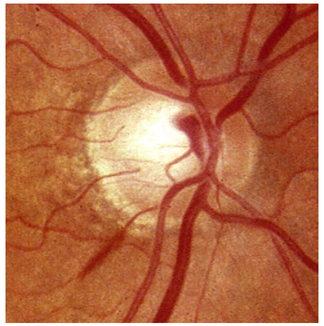
# 45 years old : Stiffness in the right eye



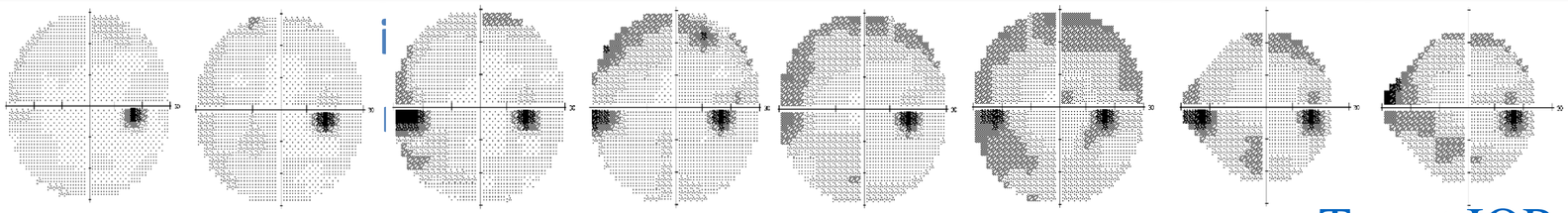

| | Right eye | Left eye |
|---|---|---|
| *VA far* | *9/10 -4D* | *10/10 -4D* |
| *VA near* | *Sn2* | *Sn2* |
| *Biomicroscopy* | Normal | normal |
| *Goldmann IOP* | *35 (Tetratherapy)* | *18 (Tritherapy)* |
| *Pachymetry* | *594 µm* | *590 µm* |
| *Fundus* | *C/D 0.75 inferior notched , hemorraghe* | *C/D 0.4* |
| *Visual field* | *superior arcuate defect* | *normal* |



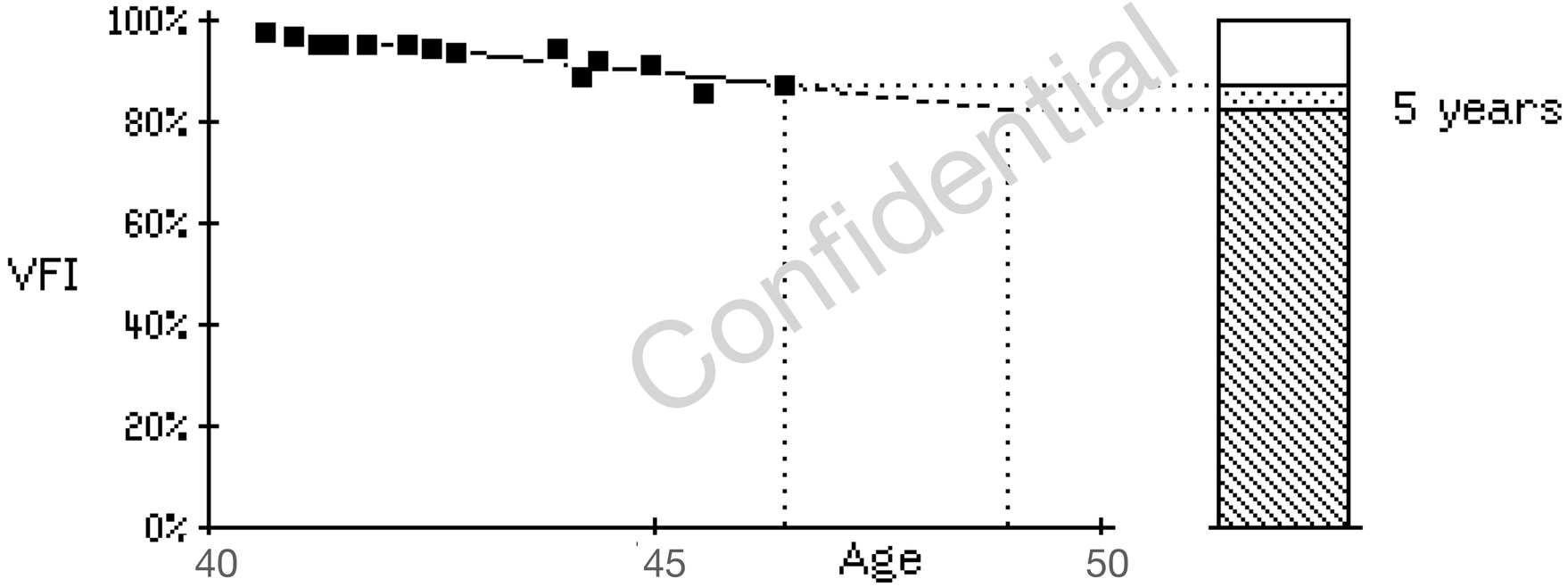




# 45 years old : Stiffness in the right eye



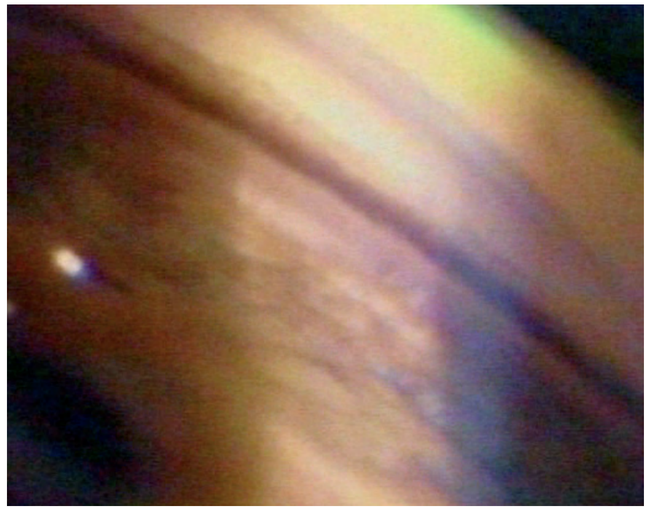
Target IOP= 14 mmHg






- **Rate of progression: -1.0 ± 0.5%/year (95% CI)**
- **Slope is significant at p < 0.1%**

# 45 years old : Stiffness in the right eye





Target IOP= 14 mmHg

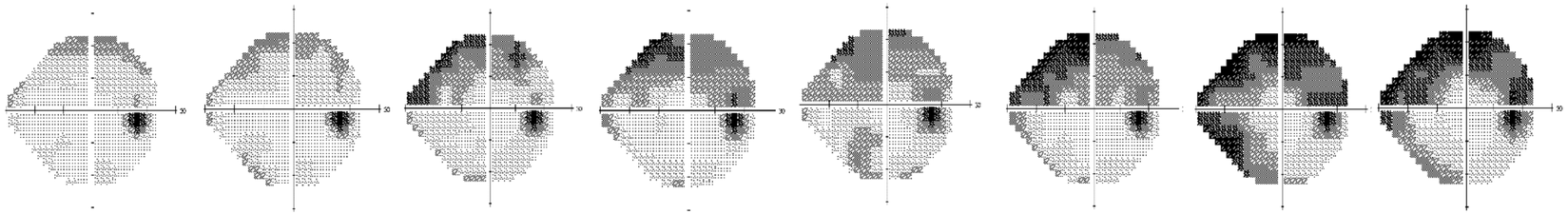
Long life expectancy

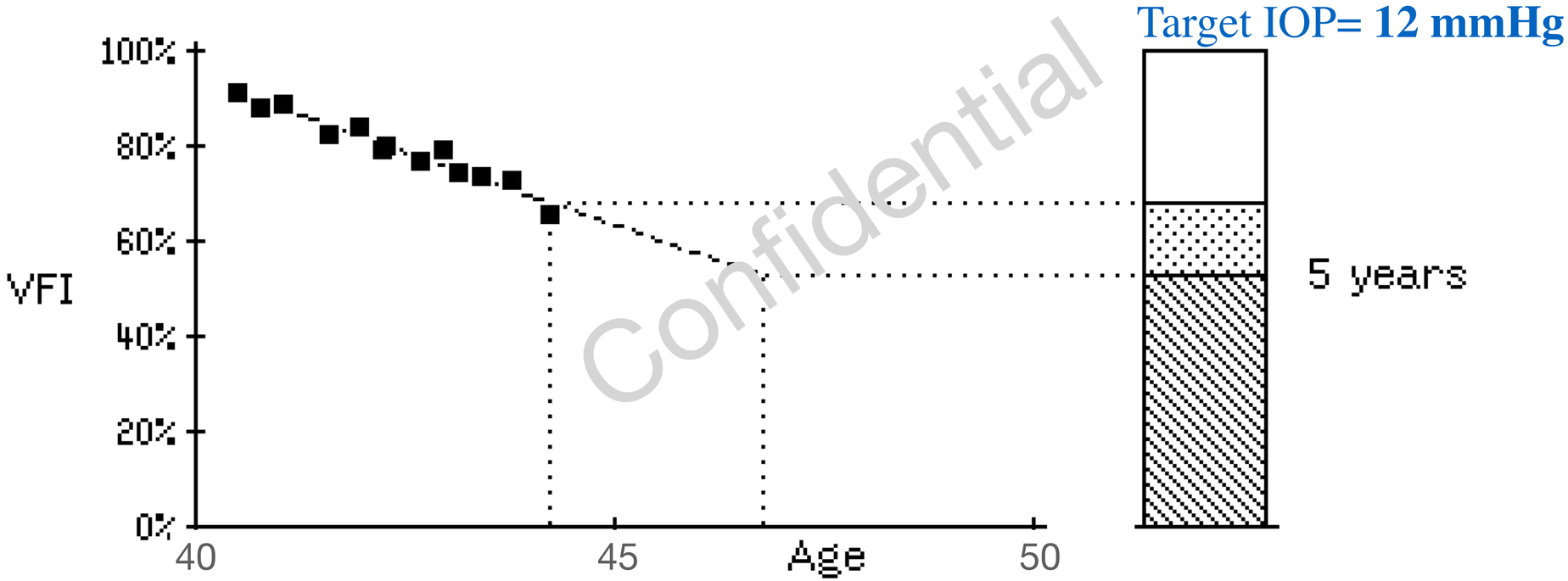
Advanced and slow progressive glaucoma

| Complains | OHT |
|---|---|
| Disease | Glaucoma |
| Treatment | 4 drops |

MIGS plus
Canaloplasty

# 45 years old : Stiffness in the right eye

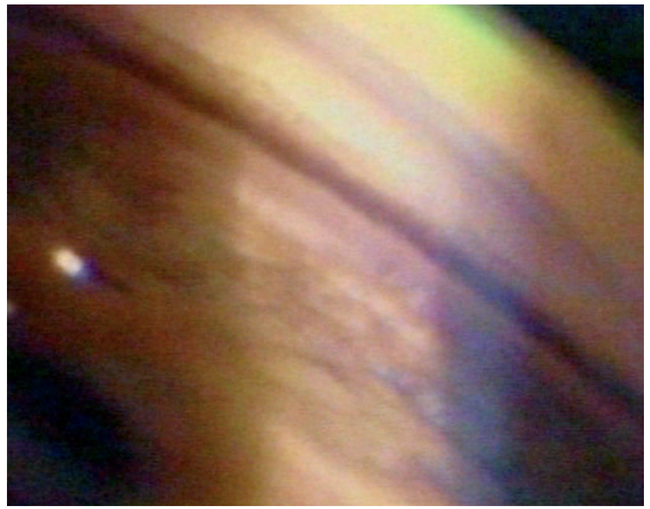







- **Rate of progression: -3.0 ± 0.5%/year (95% CI)**
- **Slope is significant at p < 0.1%**

# 45 years old : Stiffness in the right eye






Target IOP= 12 mmHg

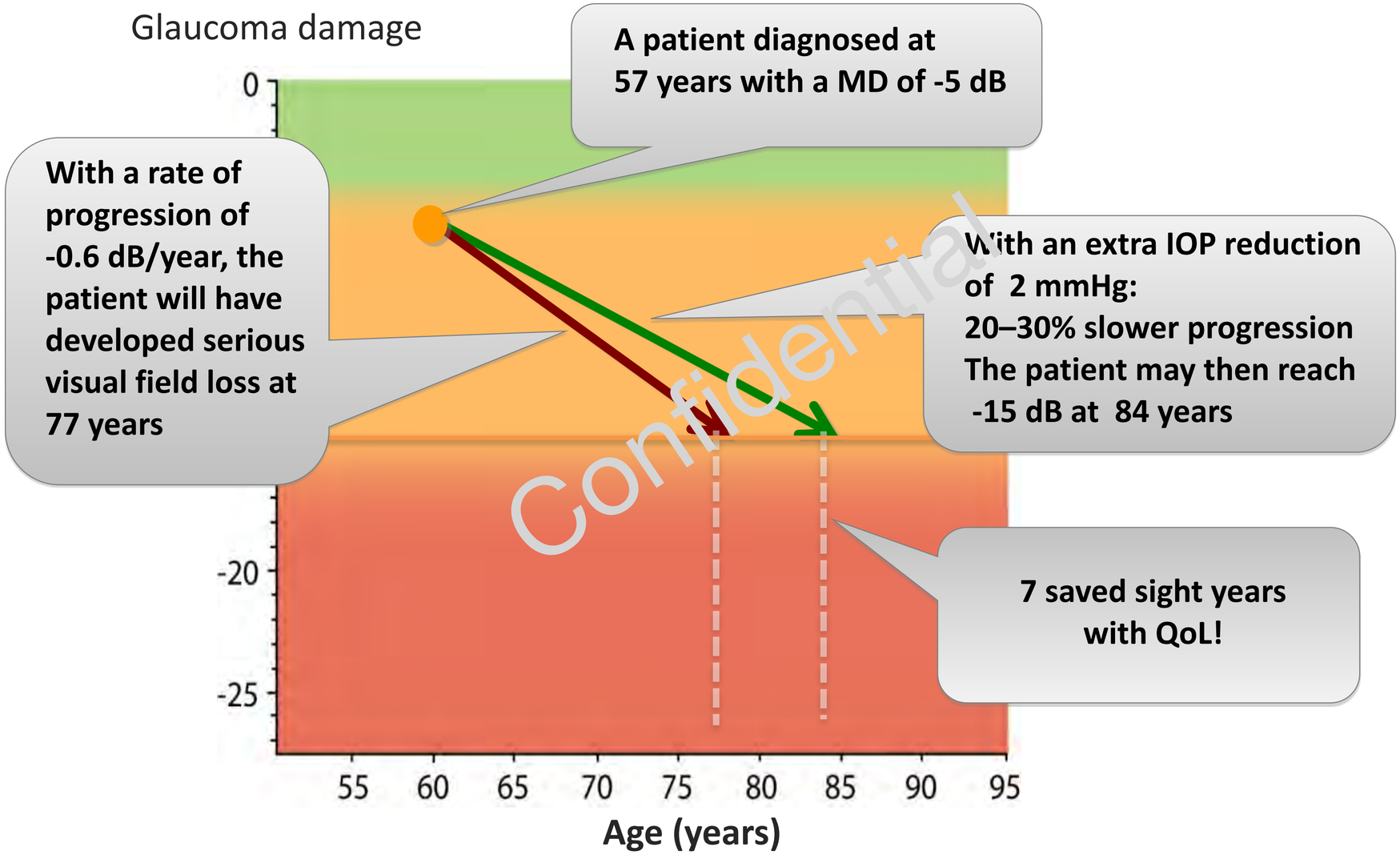
Long life expectancy

Advanced and rapid progressive glaucoma

| Complains | OHT |
|---|---|
| Disease | Glaucoma |
| Treatment | 4 drops |

Trabeculectomy
Deep sclerectomy
Preserflo

# By Changing the Visual Field Rate of progression, a patient's QoL can be preserved for longer








Heijl et al. Acta Ophthalmol 2013;91:406–12.

# 58 years old : Loss of vision in RE

2010: OAG
Baseline IOP 25 mmHg

Risks Factors:
Family history+
Myopia
Left retinal detachment
Long lifetime


First treated with xalatan

IOP control at 18 mmHg

Switch to another PGS

Combined drops 4 times a day

IOP uncontrolled at 35 mmHg

02//2017: Trabeculectomy RE

05//2017: Revision + 5 FU (2x)

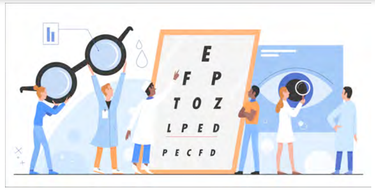
back to Duotrav 1x /J

2022 : IOP raised up to 23 mmHg

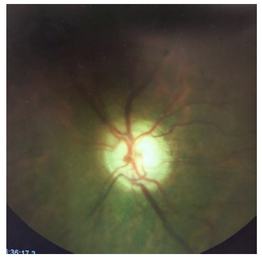
GGH
Migraine
Low AP

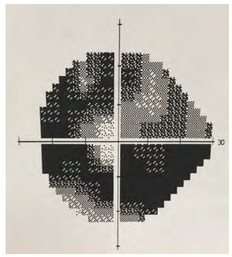
Bisoprolol 2.5 mg

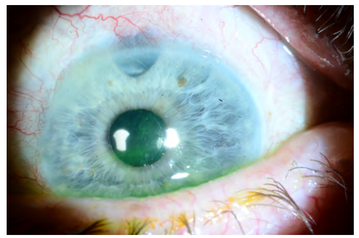
# 58 years old : Loss of vision in LE




| | Right eye | Left eye |
|---|---|---|
| *VA far* | *10/10* | *8/10* |
| *VA near* | *Sn2* | *Sn2* |
| *Biomicroscopy* | Cataract+ | Cataract+ bleb |
| *Goldmann IOP* | *18 (combitherapy)* | *23 (Tritherapy)* |
| *Pachymetry* | *500 µm* | *500 µm* |
| *Fundus* | *C/D 0.7* | *C/D 0.95, pale* |
| *Visual field* | *inferior arcuate defect* | *Tunnel visual field defect* |







# 58 years old : Loss of vision in LE

Target IOP= 12 mmHg

Long life expectancy

End stage glaucoma



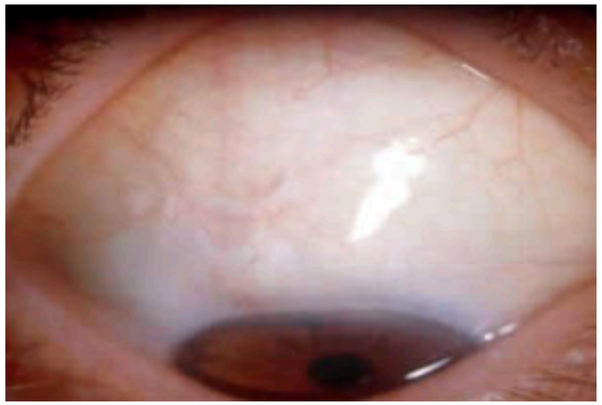
| Complains | OHT |
|---|---|
| Disease | Glaucoma |
| Medical history | Glaucoma surgery |
| Treatment | 5 meds |

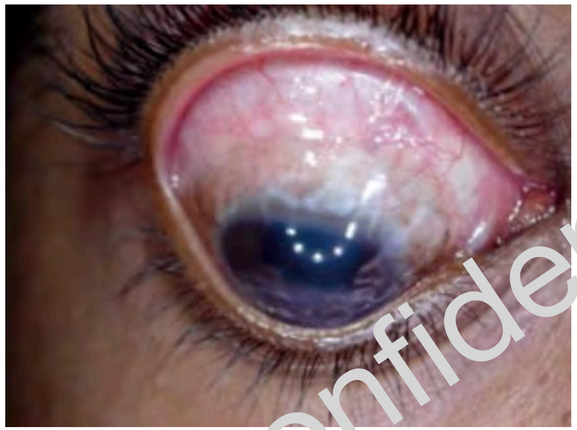
Paul Tube in pars plana

# Indications: Glaucoma Drainage Device

**“Recent trials…potential role as primary surgical procedure in selected cases.”**

**MMT GLAUCOMA PATIENTS**





**POOR ANTERIOR SURFACE**

**Mobility of conjunctiva**

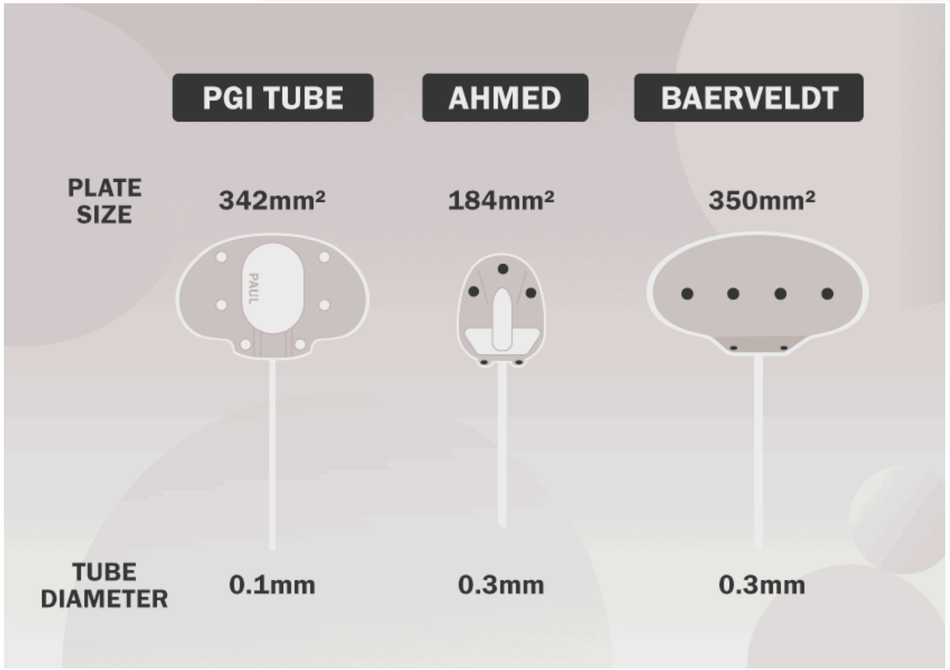


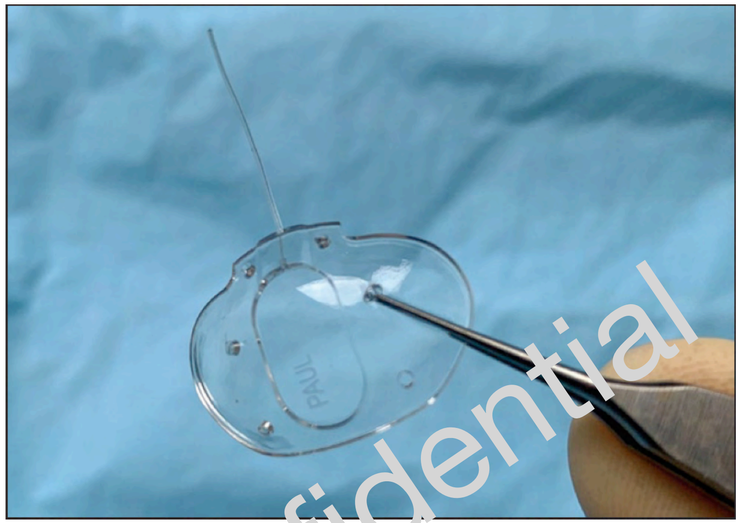
**≥ 3 drops**





# Glaucoma Drainage Device: New generation



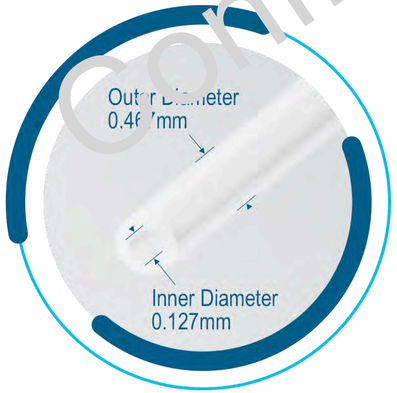
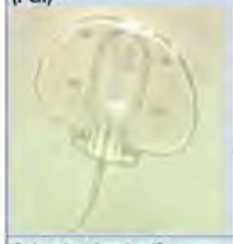






**Table I: Types of GDIs**

| | |
|---|---|
| **Valved GDI** | |
| **Ahmed Glaucoma Valve (AGV)**[3,4,7]  | • Introduced in 1993<br>• Available in four different designs<br>• Two models consist of a flexible silicone endplate<br>• Two models consist of a rigid polypropylene plate<br>• Endplate consists of a valved system which restricts aqueous outflow at an IOP below 8–10 mmHg<br>• Silicone tube connected to a silicone sheet valve |
| **Krupin slit valve**[4,7]  | • Introduced in 1976<br>• Silicone endplate with a surface area of 184 mm²<br>• Distal portion of the tube contains horizontal and vertical silicone slits<br>• Slits open at an IOP above 11 mmHg and close at an IOP below 9 mmHg<br>• Allows for unidirectional flow of aqueous |
| **Others: Joseph, Optimed** | |
| **Non-valved GDI** | |
| **Molteno**[4,7]  | • Introduced in 1969, with numerous modifications made to the initial design<br>• Seven models available<br>• Two of the models are double plate implants which consists of two separate polypropylene endplates connected by a 10 mm silicone tube – requires placement in two conjunctival quadrants (total surface area of 265 mm²)<br>• Single plate model is the most recent model and is available in 135 mm², 175 mm² and 230 mm²<br>• Consists of primary and secondary drainage areas within the plate thus allowing for a 'biological' valve which may prevent postoperative hypotony and long-term IOP control |
| **Baerveldt glaucoma implant (BGI)**[4,7]   | • Introduced in 1993<br>• Consists of a silicone tube connected to a barium-impregnated silicone endplate<br>• Three models available with surface areas of 250 mm², 350 mm² and 500 mm²<br>• There is a 350 mm² plate connected to a smaller, angled (Hoffman Elbow) by a 7 mm silicone tube; this angulation allows for insertion into the pars plana |
| **Paul Glaucoma Implant (PGI)**[8,9]  | • Introduced in 2017<br>• Novel aqueous shunt<br>• Made from medical grade silicone with a 342 mm² endplate<br>• The tube has a smaller internal and external diameter compared to other GDIs (127 µm and 467 µm respectively)<br>• A ripcord 6.0/7.0 polypropylene intraluminal stent allows for less IOP variability in the early postoperative period and helps prevent hypotony |
| **Schocket implant**[3] | • Silastic tube which inserts into the anterior chamber while the other end is tucked beneath a retinal encircling band |
| **Ex-Press**[3] | • Single piece stainless steel translimbal implant |

# Indications: Glaucoma Drainage Device

**MMT GLAUCOMA**

**POOR ANTERIOR SURFACE**

**EXTENSIVE CONJUNCTIVAL SCAR**

**CORNEA GRAFT SECONDARY GLAUCOMA**

**UVEITIC GLAUCOMA**

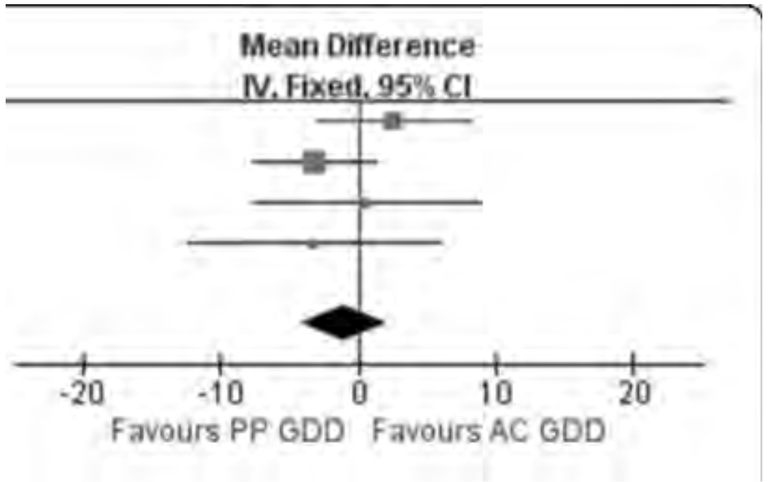
**NEOVASCULAR GLAUCOMA**

**SILICONE ADVANCED GLAUCOMA**

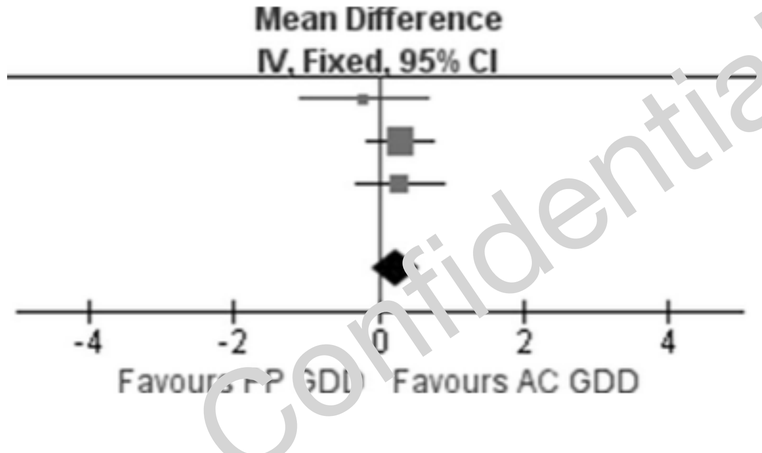
# Back to science:
# Comparison of Pars Plana to Anterior Chamber GDDI : A meta analysis

Wang and Li BMC Ophthalmology (2018) 18:212

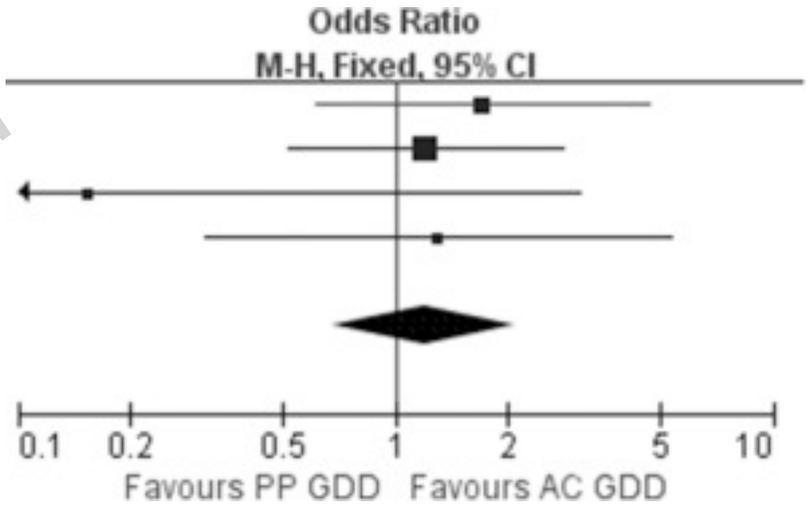
4 retrospective study involving 275 eyes




Reduction of IOP between
PP GDD group and AC GDD group




Reduction of glaucoma medications between
PP GDD group and AC GDD group




Incidence of overall complications between
PP GDD group and AC GDD group

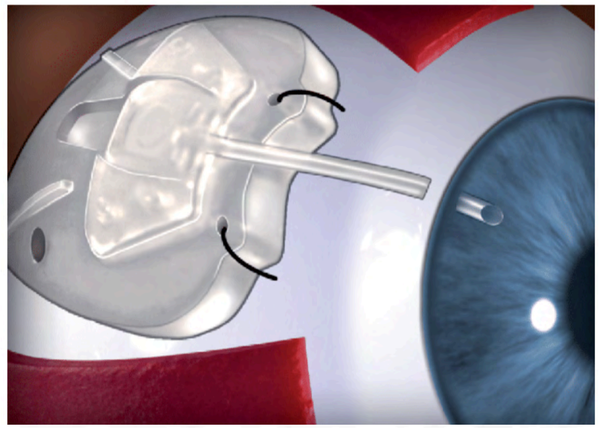


**Conclusions:** Both PP GDD and AC GDD procedures had similar efficacy of reduction in the IOP and number of medications. They are also both comparable on the safety with similar incidence of corneal failure and overall complications. → Higher

# Back to science:
# The effect of tube location on Endothelial corneal cells in patients with tube or valve

**Ophthalmology. 2021 February ; 128(2): 218–226.**

- **RTC**
- **106 eyes > 101 pseudophakic patients with AGV placed in the AC**
- **105 eyes > 94 pseudophakic patients with AGV placed into the ciliary sulcus**
- **Sulcus versus anterior chamber**



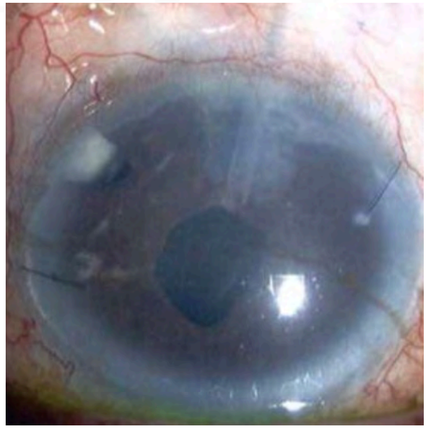
**Conclusions**—Compared to anterior segment placement, ciliary sulcus tube implantation may be a preferred surgery approach to reduce endothelial cell loss in pseudophakic patients.



FDA unlikely to approve GDD use if endothelial cell count assessment was mandatory

Comparison of monthly change in each of the central corneal endothelial measurements between treatment groups

| Measurements | Mean monthly change (SD) | | |
|---|---|---|---|
| | acAGV (N=106 eyes) | sAGV (N=105 eyes) | P value [b] |
| ECD, cells/mm$^2$ | −29.3 (29.7) | −15.3 (20.7) | <0.0001 |
| %ECD change [a] | −1.37 (1.43) | −0.72 (0.91) | <0.0001 |
| CV | 0.08 (0.58) | 0.36 (1.63) | 0.28 |



# Back to science BVA study: Baerveldt VS Ahmed valve

Postoperative Complications in the Ahmed Baerveldt Comparison Study During Five Years of Follow-up

DONALD L. BUDENZ, WILLIAM J. FEUER, KEITH BARTON, JOYCE SCHIFFMAN, VITAL P. COSTA, DAVID G. GODFREY, AND YVONNE M. BUYS, ON BEHALF OF THE AHMED BAERVELDT COMPARISON STUDY GROUP

Late complications :

- 39% Ahmed group
- 50% Baerveldt group

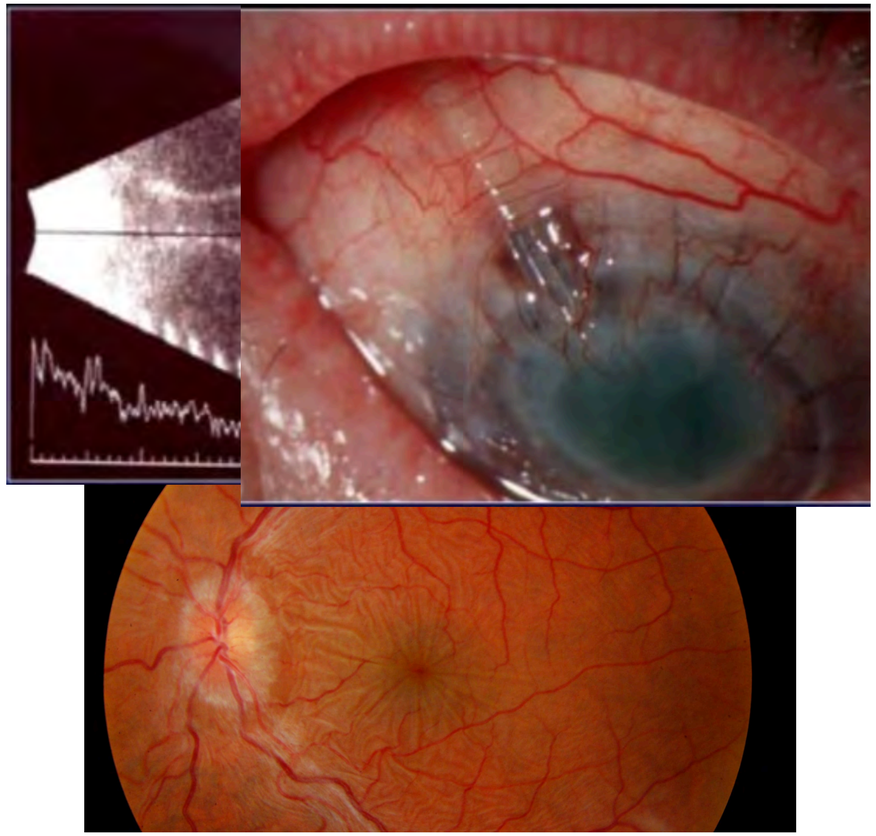


**TABLE 2.** Five-Year Incidence of Late Complications in the Ahmed Baerveldt Comparison Study

| Complication | Year 5 N, Cumulative Proportion (SE) | | Log-Rank *P* Value | Risk Ratio[a] | 95% CI |
|---|---|---|---|---|---|
| | Ahmed | Baerveldt | | | |
| Tube occlusion | 1, 0.8% (0.8%) | 6, 5.7% (2.3%) | .037 | 6.93 | 0.83, 57.5 |
| Choroidal effusion | 0, 0.0% NA | 2, 1.8% (1.2%) | [illegible] | NA | NA |
| Endophthalmitis | 0, 0.0% NA | 2, 2.2% (1.6%) | .16 | NA | NA |
| Cystoid macular edema | 6, 6.2% (2.5%) | 7, 7.2% (2.7%) | .81 | 1.14 | 0.38, 3.40 |
| Shallow anterior chamber | 2, 2.2% (1.5%) | 3, 3.7% (2.1%) | .64 | 1.53 | 0.26, 9.16 |
| Hypotony maculopathy | 0, 0.0% NA | 1, 0.8% (0.8%) | .30 | NA | NA |
| Diplopia | 16, 12.7% (3.0%) | 14, 11.8% (3.0%) | .81 | 0.92 | 0.45, 1.88 |
| Corneal edema-all | 18, 20.1% (4.4%) | 18, 20.4% (4.3%) | .71 | 1.13 | 0.59, 2.18 |
| Corneal edema-likely attributable to implant | 9, 11.9% (3.8%) | 9, 11.7% (3.7%) | .82 | 1.10 | 0.49, 2.44 |
| Tube-corneal touch | 4, 3.5% (1.7%) | 4, 3.7% (1.8%) | .91 | 1.08 | 0.27, 4.34 |
| Corneal graft rejection | 8, 7.1 (2.4%) | 8, 7.0% (2.4%) | .96 | 0.98[b] | 0.37, 2.62 |
| Band keratopathy | 1, 1.2% (1.2%) | 2, 2.0% (1.4%) | .57 | 1.99 | 0.18, 21.9 |
| Corneal neovascularization | 0, 0.0% NA | 1, 1.0% (1.0%) | .33 | NA | NA |
| Tube erosion | 3, 2.9% (1.7%) | 1, 1.0% (1.0%) | .33 | 0.34 | 0.04, 3.31 |
| Encysted bleb | 1, 0.9% (0.9%) | 0, 0.0% NA | .32 | NA | NA |
| Recurrent or persistent iritis | 7, 6.2% (2.3%) | 6 5.5% (2.2%) | [illegible] | 0.89 | 0.30, 2.63 |
| Phthisis bulbi | 1, 0.8% NA | 6, 5.7% (2.3%) | .037 | 6.93 | 0.83, 57.5 |
| Hyphema | 2, 1.5% (1.1%) | 2, 1.6% (1.1%) | .97 | 1.04 | 0.15, 7.40 |
| Vitreous hemorrhage | 3, 2.7% (1.5%) | 3, 2.5% (1.4%) | .96 | 1.04 | 0.21, 5.17 |
| Pupillary membrane | 1, 0.8% (0.8%) | 0, 0.0% NA | .33 | NA | NA |
| Epiretinal membrane | 0, 0.0% NA | 1, 0.8% (0.8) | .31 | NA | NA |
| Retinal detachment | 2, 1.6% (1.1%) | 2, 1.7% (1.2%) | .98 | 1.02 | 0.14, 7.25 |
| Corneal blood staining | 0, 0.0% NA | 2, 1.6% (1.1%) | .15 | NA | NA |

CI = confidence interval; GDI = glaucoma drainage implant; NA = not applicable; PKP = penetrating keratoplasty; SE = standard error.

[a]Ahmed is the reference group.

[b]Adjusted for previous PKP prior to enrollment and implantation of study GDI, which was itself highly significantly related to corneal graft failure ($P < .001$).

# Take home message (1)

- Trabeculectomy remains the gold standard surgical procedure for all narrow or closed angle glaucoma
- Blebless glaucoma surgery (MIGS) could be proposed and performed in an early stage of glaucoma
- Potential advantages of the pars plana Tube are :
  - posterior flow,
  - **no MMC use,**
  - no Tube extrusion,
  - less corneal decompensation .




SLT IStent Xen Microshunt NPTS/Traby/Tube

# Take home messages (2)

## Don’t delay surgery

1. In cases where other forms of therapy have failed
2. In cases where a target pressure cannot be reached
3. In cases where other forms of therapy are not suitable (where compliance or side effects are a problem)
4. In cases which have such advanced glaucoma and high IOP at presentation

# Post-operative management in Glaucoma

MANAMA - december 2022

Prof Collignon Nathalie & Dr Dupont Géraldine

# Management of « normal » post-operative cases

# Bleb versus No Bleb surgeries

**<u>Without bleb: … almost nothing to do</u>**

the result depend on the position and efficacy of the devices

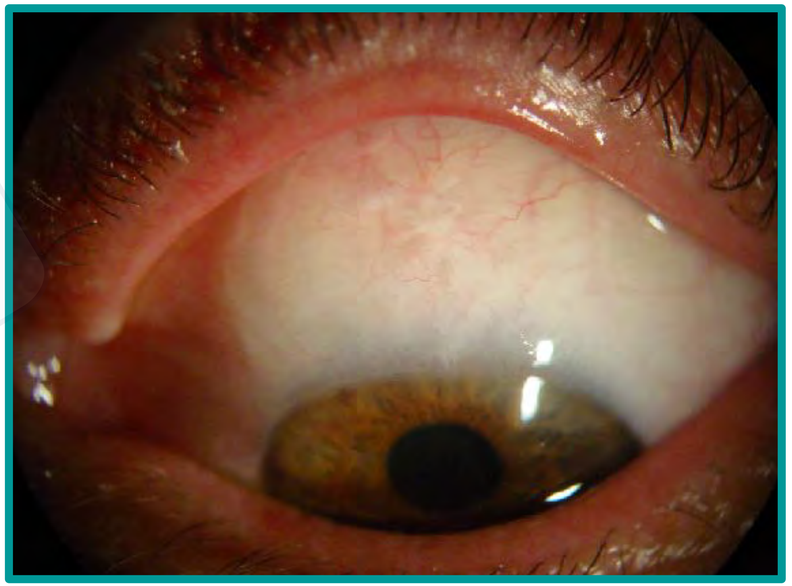
**<u>With bleb: … the challenge is</u>**

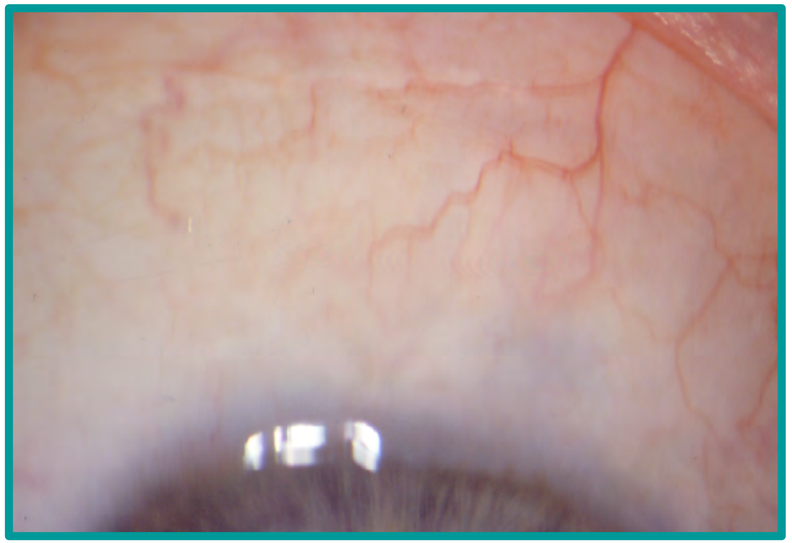
**<u>a lasting filtering bleb with a good eye pressure</u>**

the bleb formation depends on the conjonctival wound healing

…if you want to perform glaucoma surgery,

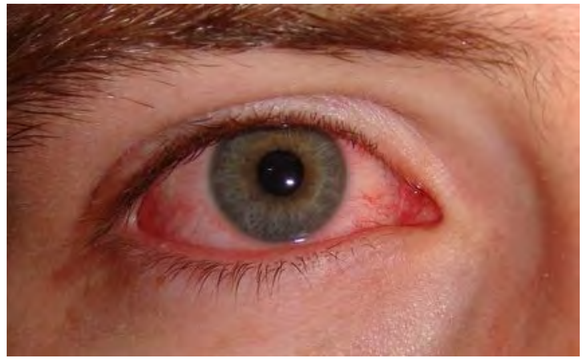
you are willing to « marry » your patient for at least 3 months…

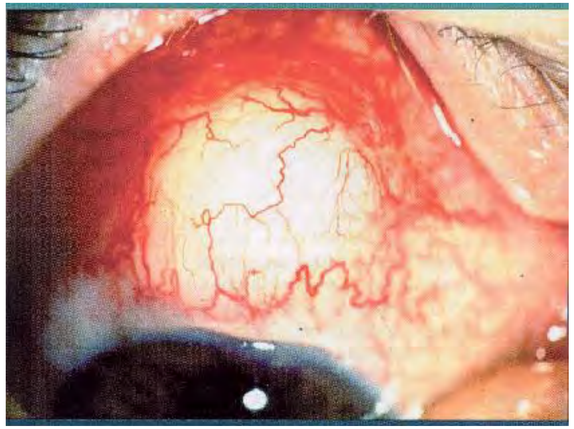




# Risk factors of fibrosis

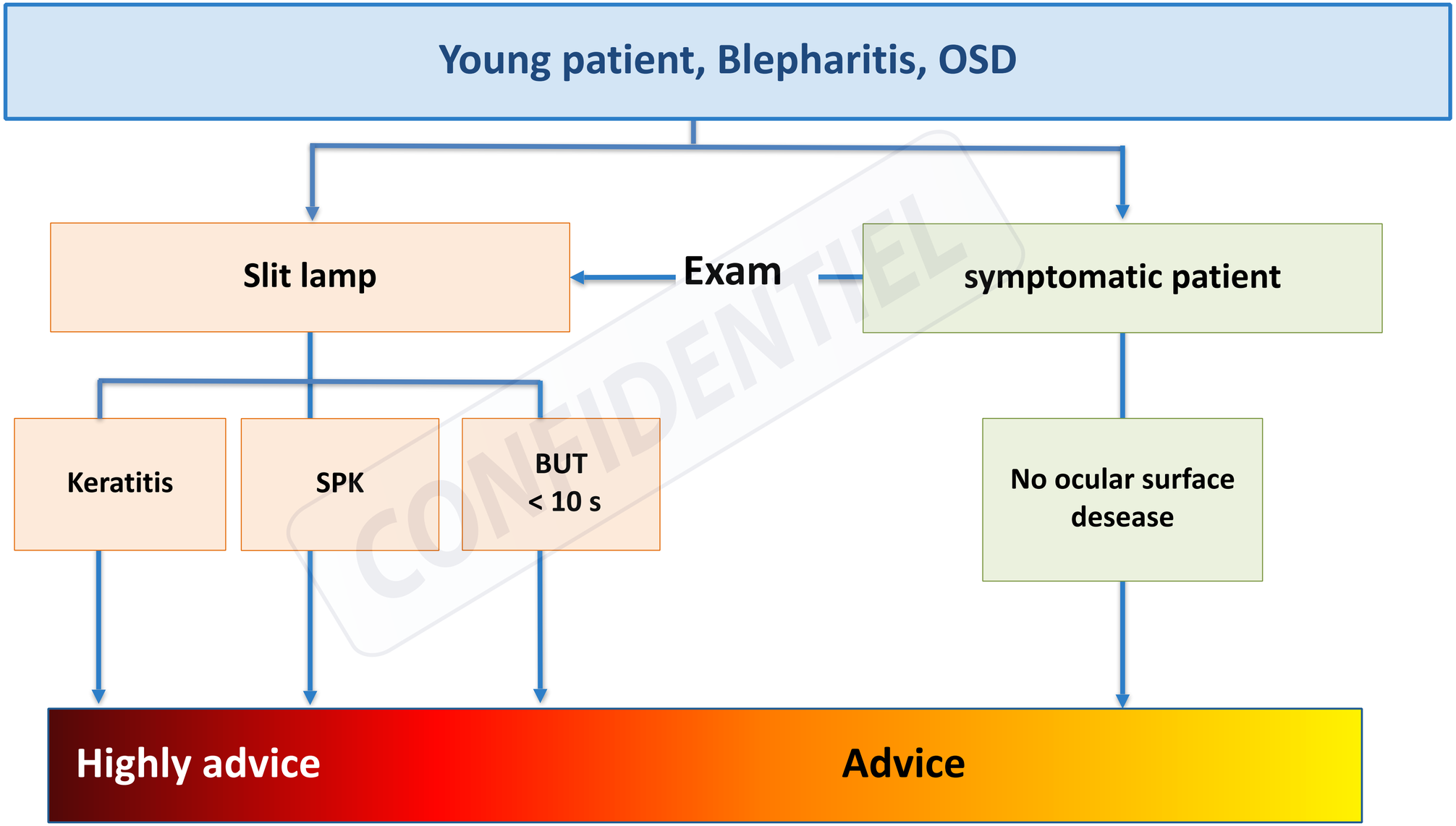
- young population: child and young adults
- ethnic origin: afro-amercian patients
- previous ocular surgeries
- failed contralateral glaucoma surgery
- conservative ocular drops
- secondary glaucoma: inflammatory, neovascular, traumatic, …





ocular surface disease = high risk of bleb scarring

# With or without preservative

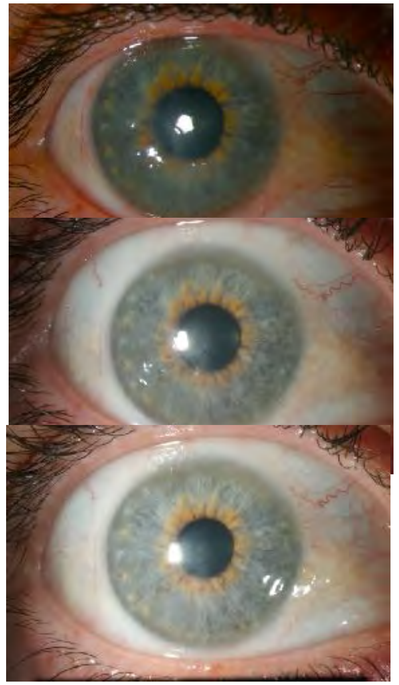





EGS Guidelines edition 5th

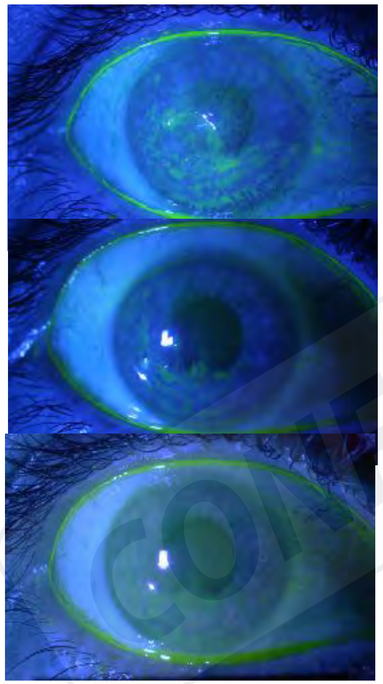
# Risk factors of fibrosis

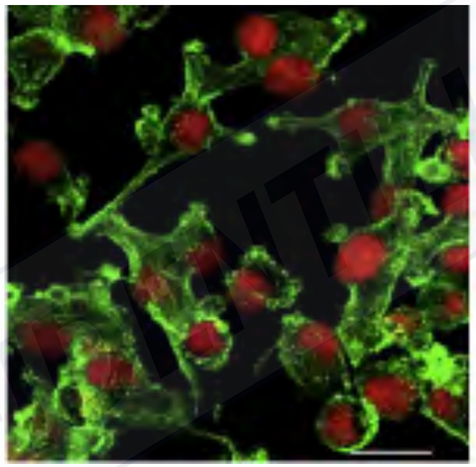
- action of preserved drops on the conjunctiva and the trabecular meshwork

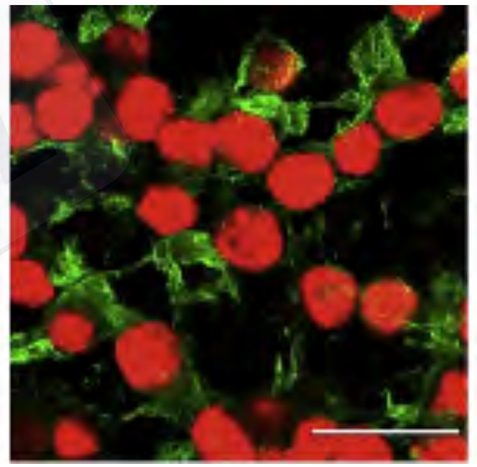


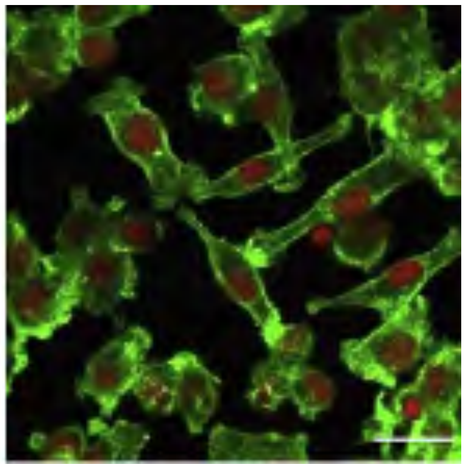
BAK

ABAK









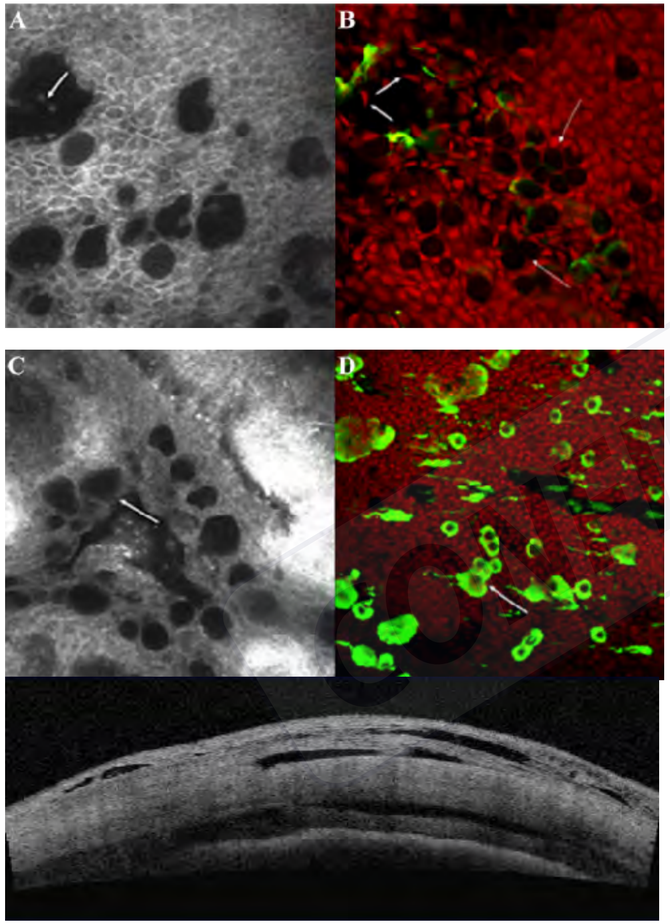
0.01% BAK

Unpreserved drops

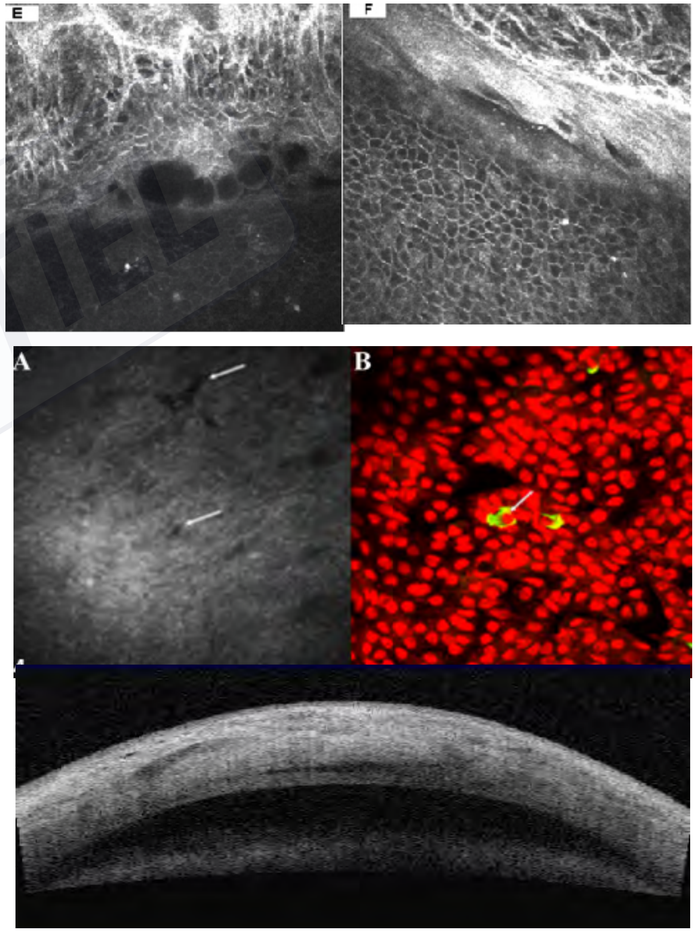
Oxydative stress
Apoptosis- Apo 2.7
Trabecular senescence

switch to unpreserved drops and prepare the ocular surface with NSAI

# Filtreting bleb




# Fibrotic bleb






Labbé A et al. J Fr Ophthalmol 2004
Labbé A et al. Ophthalmology 2005
Amar N et al. Ophthalmology 2007

# How to prevent fibrosis?

## per-operative recommendations

- Low risk patients ..... Nothing or intraoperative 5-FU 50 mg/ml
- Intermediate risk patients ..... Intraoperative 5-FU 50 mg/ml or MMC 0.2 mg/ml for 2'

topical medications

previous cataract surgery

several low risk factors

combined glaucoma filtration and cataract surgery

pervious conjunctival surgery

- High risk patients ..... Intraoperative MMC 0.2 to 0.4mg/ml for 3'

Neovascular glaucoma

Chronic persistent uveitis

Previous failed trabeculectomy /tubes

Chronic conjunctival inflammation

Multiple risk factors

Aphakic glaucoma

# How to prevent fibrosis?

## per- and post-operative use of drugs

- 5-FU (50mg/ml)

- prevent RNA replication and decreased fibroblasts proliferation (producing type I collagen)

- acts only on cell division

- 1 week lasting action

- MMC (0,2 to 0,4mg/ml)

- interfere with the DNA synthesis and  inhibit the mitotic process of the fibroblasts and vascular cells

- risks: corneo conjunctival and intraocular toxicity (ischemic blebs, cataract,…)

- 1 month lasting action

# Phases of wound healing

**Surgery**

**Blood and TGFβ can reverse MMC**

Inflammation (DAYS)

- Release of plasma proteins
- Release of growth factors

Proliferation (WEEKS)

- Cells migrations (macrophages)
- Cells proliferations (fibroblasts)
- Wound contraction

Remondeling (MONTHS)

- Collagen synthesis

**Pre-operative NSAI**
**Per-operative technics**

**Atropine**
**Corticosteroids**
**NSAI??**

**Antimetabolites**
**β radiation**
**Tabio (anti-TGFβ)**
**VEGF antibody**
**(Bevacizumab-Avastin)**

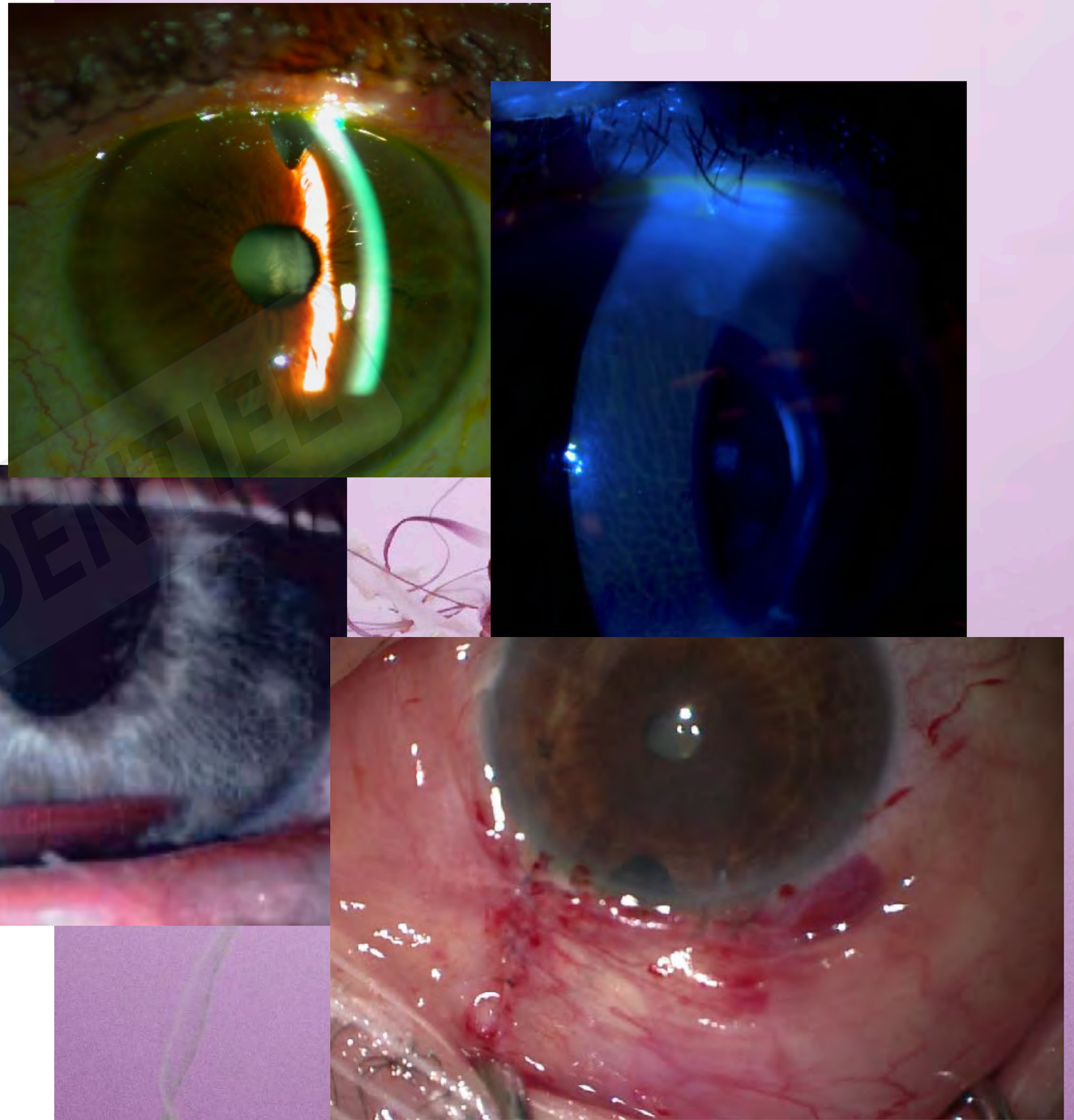
**MMPs inhibitors,Etoposide**
**D-penicillamine**

# Post-operative examination

# Post-operative examination
# Day 1 - Week 1

from the surface to the depth

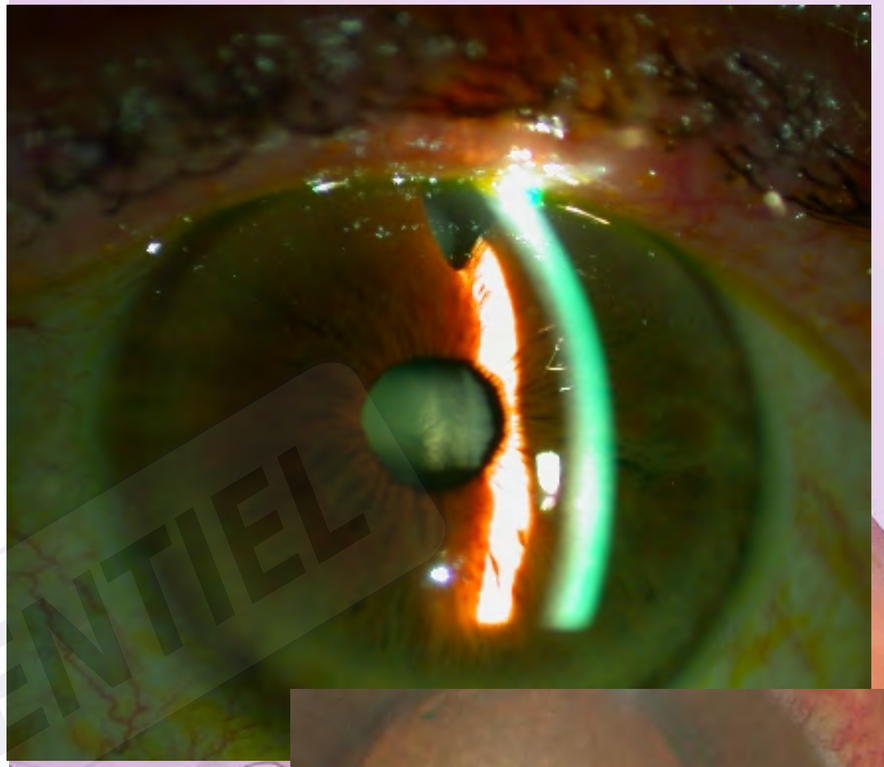
- cornea
- conjunctiva
- anterior chamber, iris and lens
- intraocular pressure
- fundus

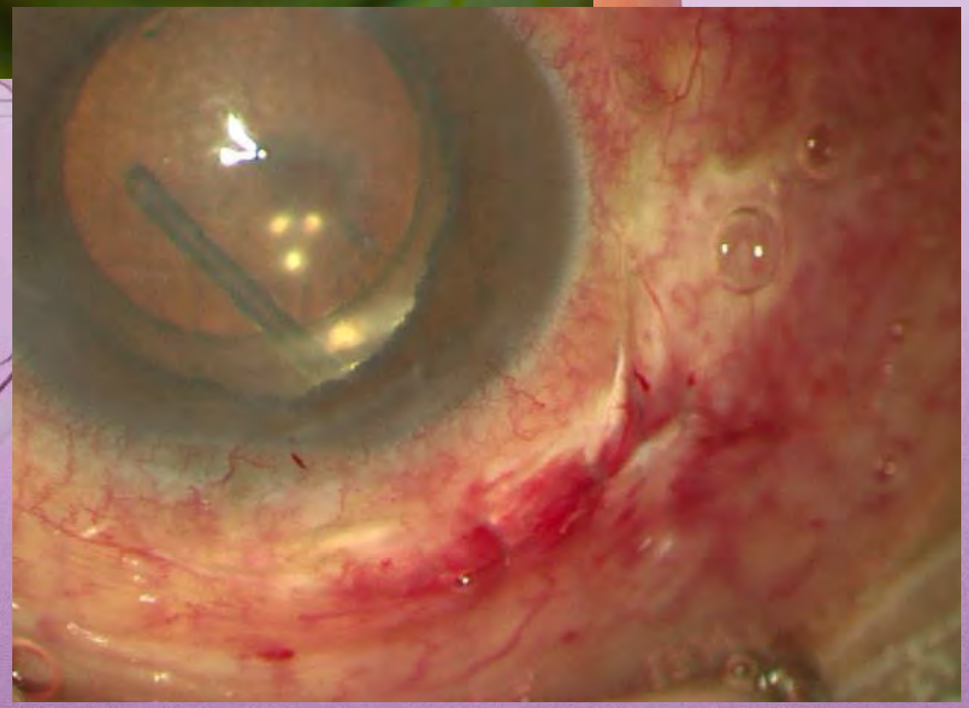


# Post-operative treatment

- antibiotic drops / ointment
- corticosteroids
- +/- NSAI

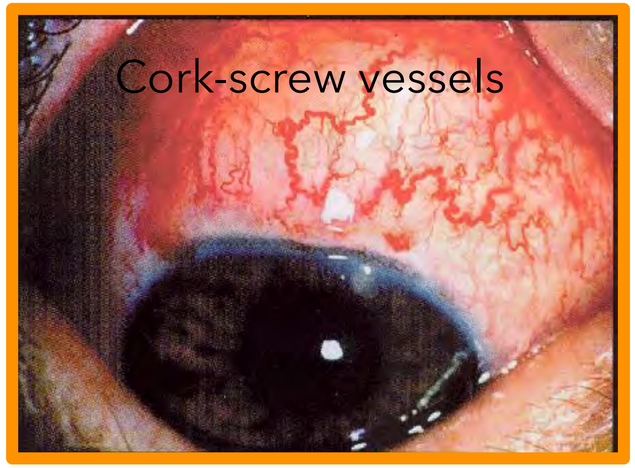
- mydriatics
- +/- hypotensive drops



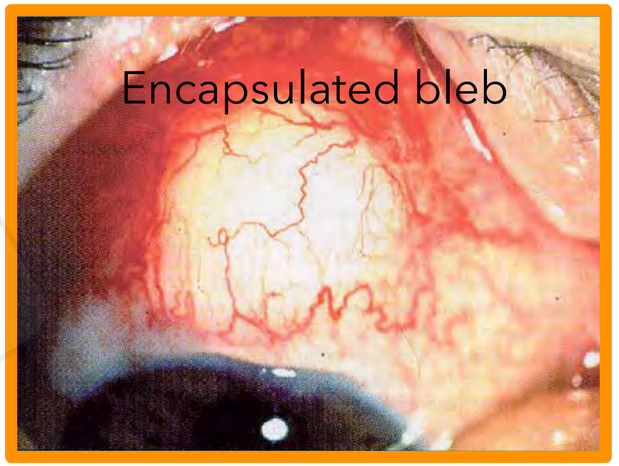


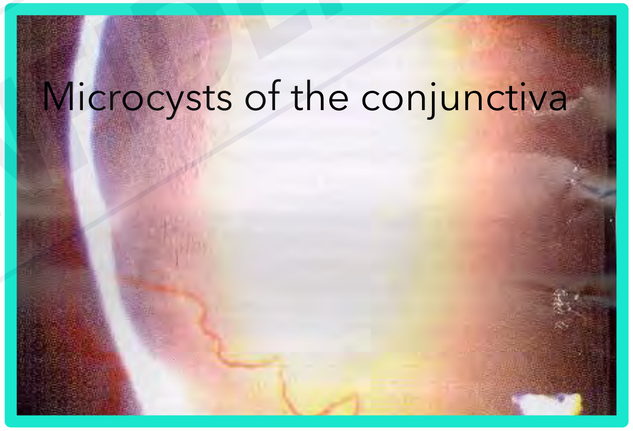
# Post-operative examination: Bleb classification and follow-up

# Filtrering Bleb classification




**< 3 months**



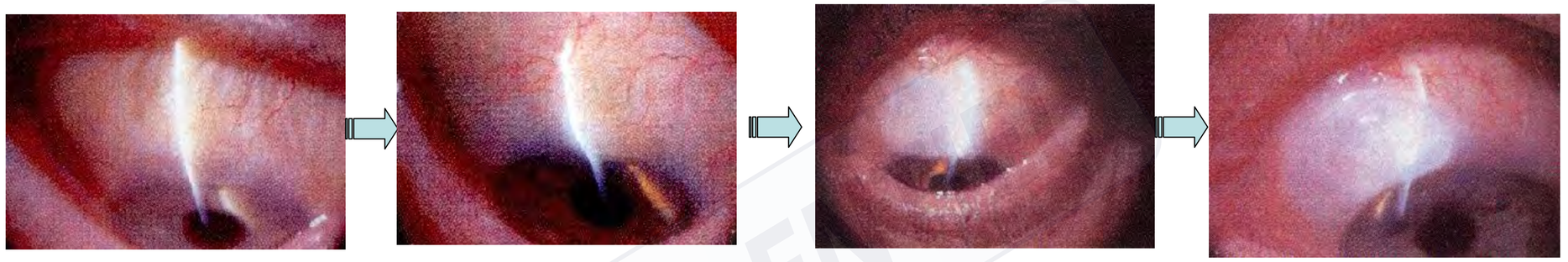

Favourable sign:
Transconjunctival flow



*Kronfeld PC. Trans Pac Coast OtoOphthalmol Soc Ann Mett 1949;33: 23-40 Picht G, Grehn F.Curr Opin Ophthalmol 2001;12:143-148*

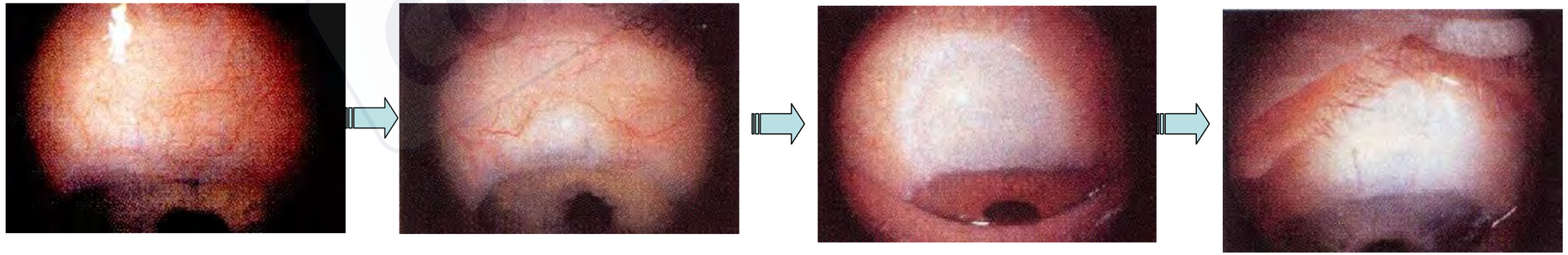
# Filtrering Bleb classification

## Bleb Height H0-H3



Narrow beam from the scleral surface to the bleb

## Horizontal extent E0-E3



< 1 o'clock

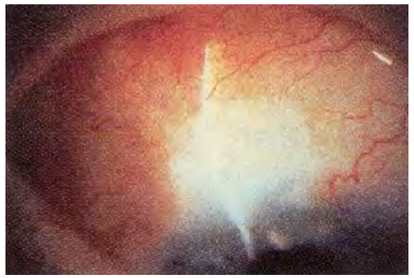
> 4 o'clock

Indiana Bleb Appearance Grading Scale= IBAGS

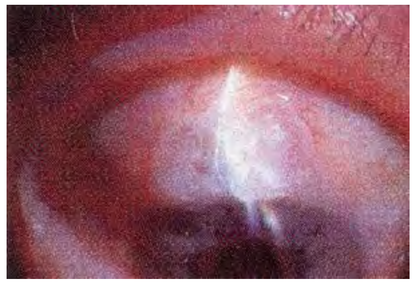
*Cantor LB et al. J Glaucoma 2003;12:266-271*

# Filtrering Bleb classification

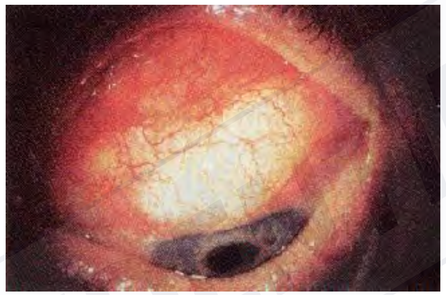
## Vascularity V0-V4



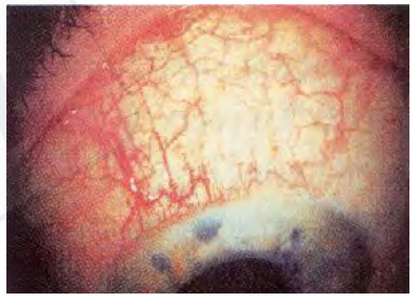
Avascular white



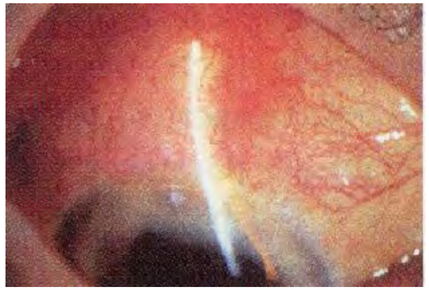
Avascular cystic



Mild Vascularity



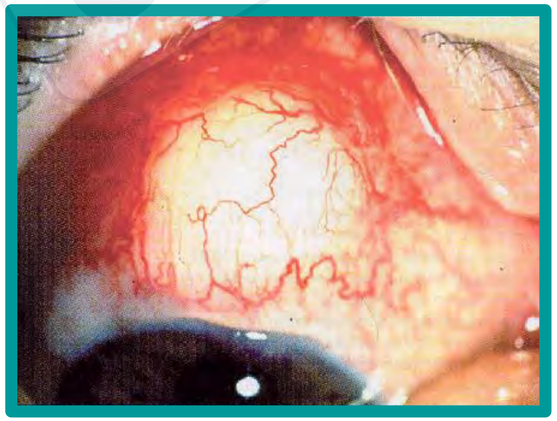
Moderate Vascularity



Extensive Vascularity

For example:

an encapsulated bleb falls within IBAGS score range of
H2-H3, E1-E2, V3-V4

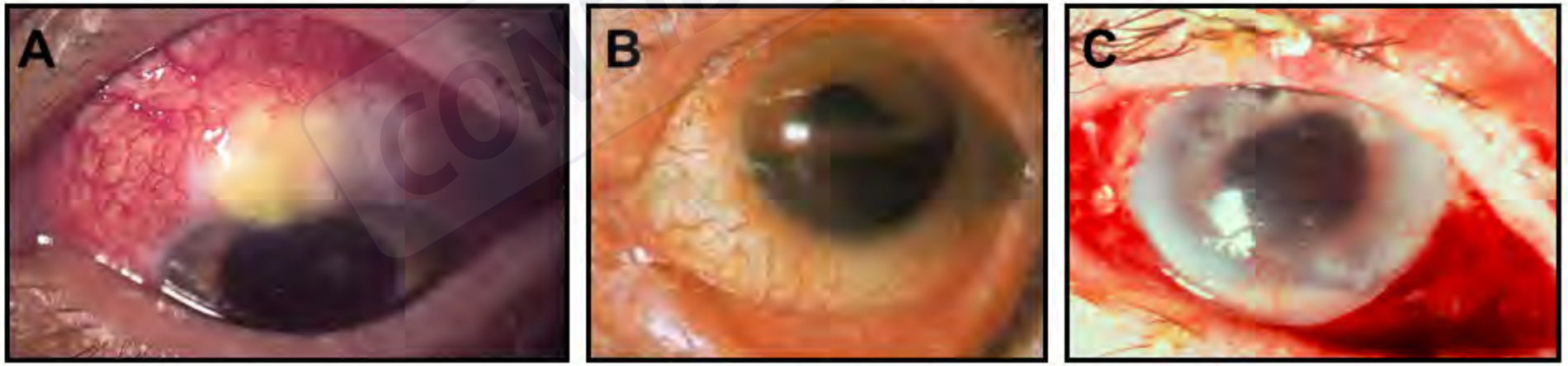


*Cantor LB et al. J Glaucoma 2003;12:266-271*

# Management of « complicated » post-operative cases

# Complications of Traditional Filtering Surgery

- Infection
- Hypotony
- Flat anterior chamber
- Hyphema
- Cataract
- Transient IOP elevation
- CME
- Hypotonic maculopathy
- Choroidal effusion
- Suprachoroidal hemorrhage
- Persistent uveitis
- Dellen formation
- Loss of vision
- Bleb leak
- Late bleb failure
- Blebitis/endophthalmitis
- Dysesthesia






Jampel HD, et al. *Ophthalmology*. 2012;119:712-722; Gedde SJ, et al. *Am J Ophthalmol*. 2012;153:804-814.e1.

A,B: Images from Rakesh Ahuja, MD/Wikimedia Commons/Public Domain. C: Image courtesy of Joan W. Miller, MD, and Mehran Afshari, MD, Massachusetts Eye and Ear Infirmary, Boston, Mass.

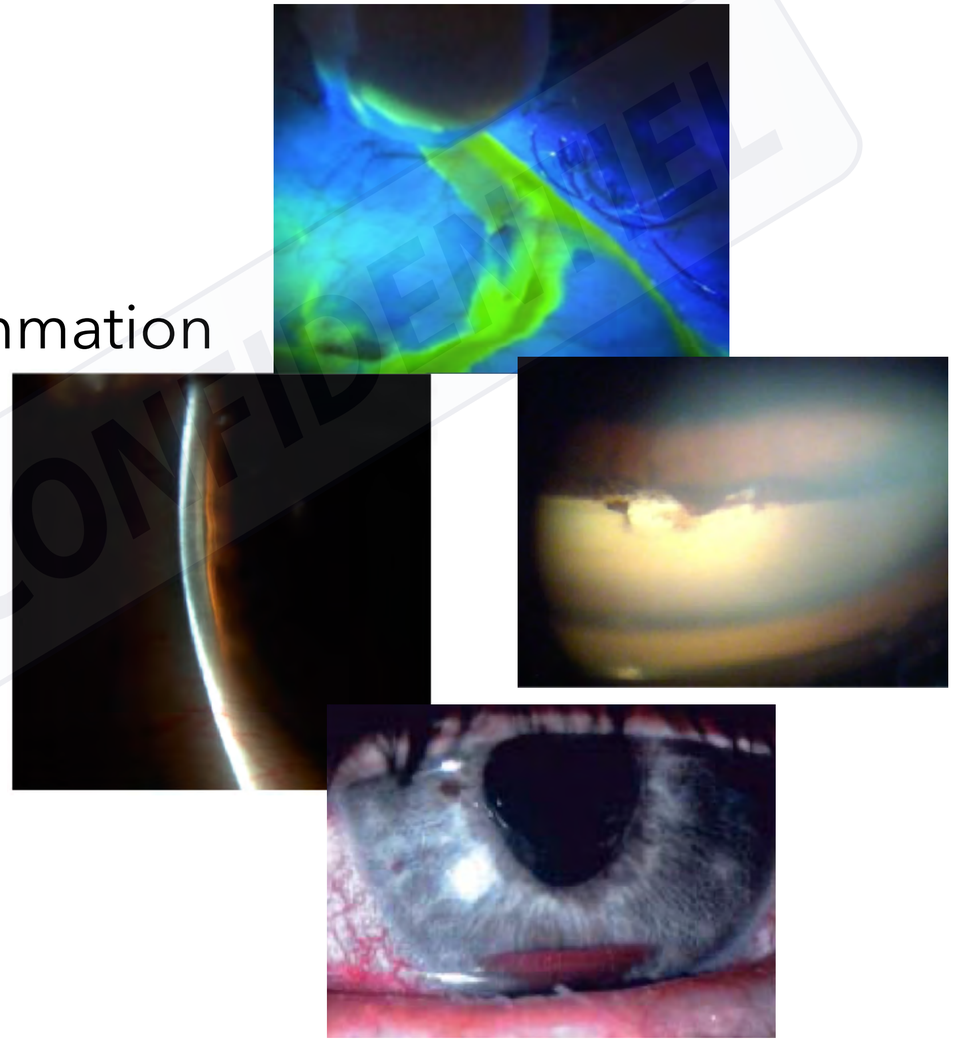
# Early post-operative complications

# Post-operative complications

## Cornea and anterior chamber

### Early problems

- erosion or keratitis
- from conjunctival inflammation
  ..to bleb failure



- flat anterior chamber
- inflammation
- hyphema

### What to check ?

- sutures / Seidel ?
- conjunctival bleb

- pupil form
- iridectomy
- gonioscopy

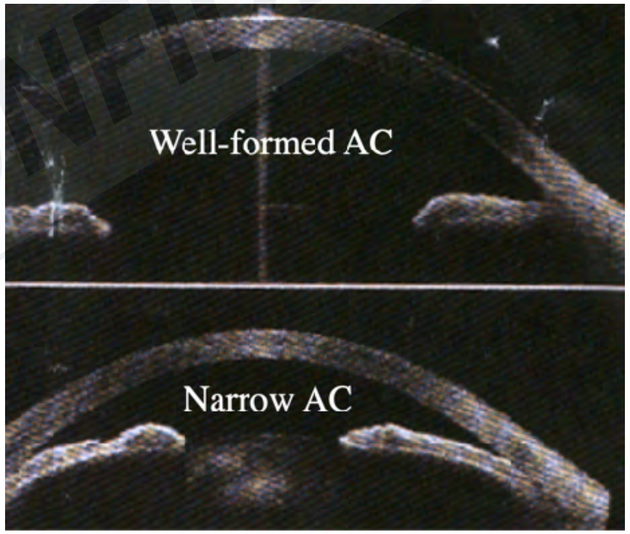
# Post-operative complications

Intraocular pressure

## Hypotony

- well formed AC
- narrow AC

**check the anterior chamber**




## Hypertony

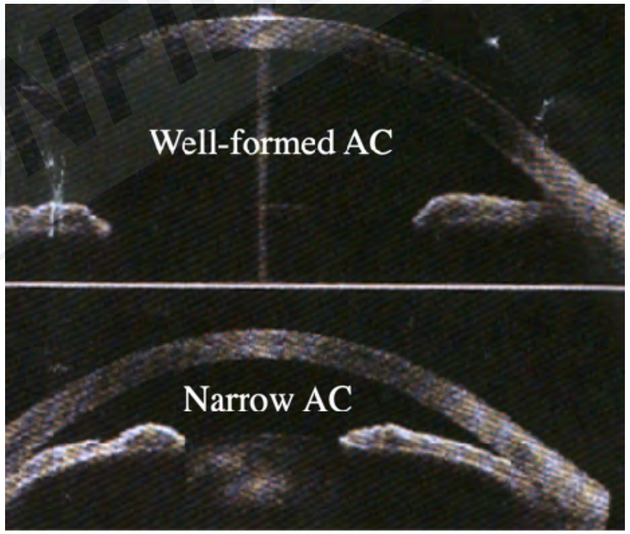
- well formed AC
- narrow AC

# Post-operative complications

Intraocular pressure

## Hypotony

- **well formed AC**
- narrow AC



# Post-operative complications

ocular **hypotony**

**with well formed AC**



<u>Overfiltration</u> : high bleb

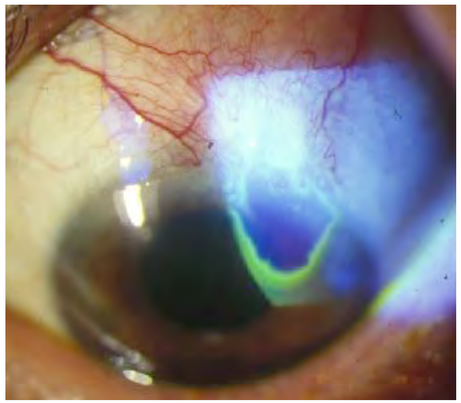
- rest +/- adjust steroids

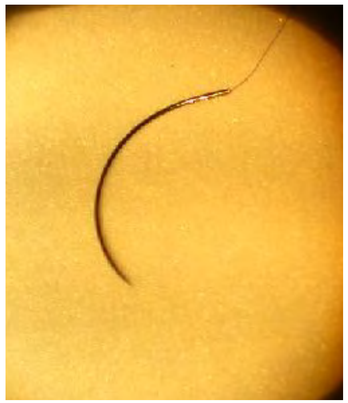
<u>Positive Seidel sign</u>

- ointment
- Diamox +/- mydriatic drops

<u>Leakage or conjunctival retraction :</u>

- don’t delay the suture of the conjunctiva
- bleb formation is crucial



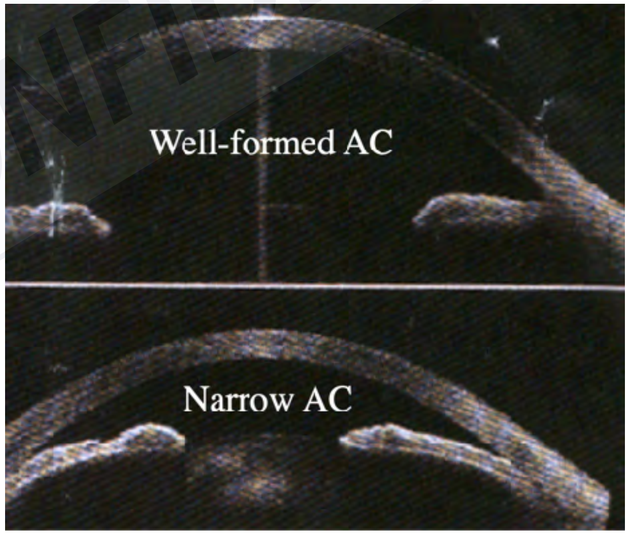


# Post-operative complications

Intraocular pressure

## Hypotony

- well formed AC
- **narrow AC**



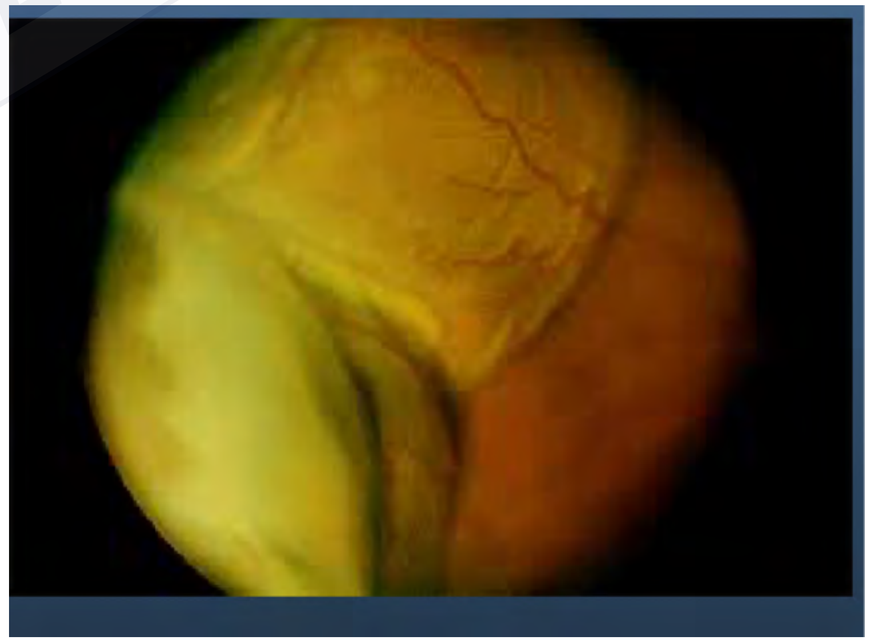
# Post-operative complications

## ocular **hypotony**

### with narrow AC

- the first treatment is the same: mydriatic drops, rest, ointment, Diamox, contact lens, bleb resuture, +/- steroids

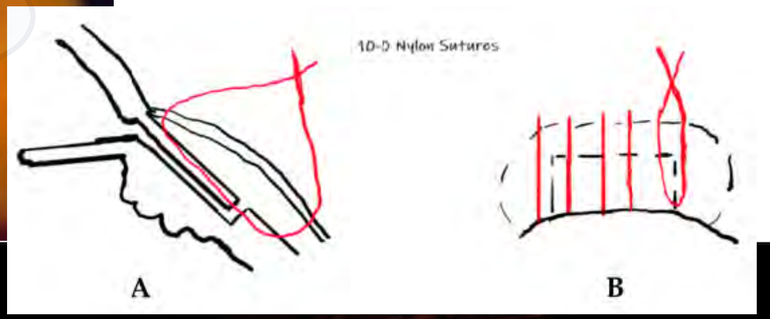
- but **check the fundus**…!

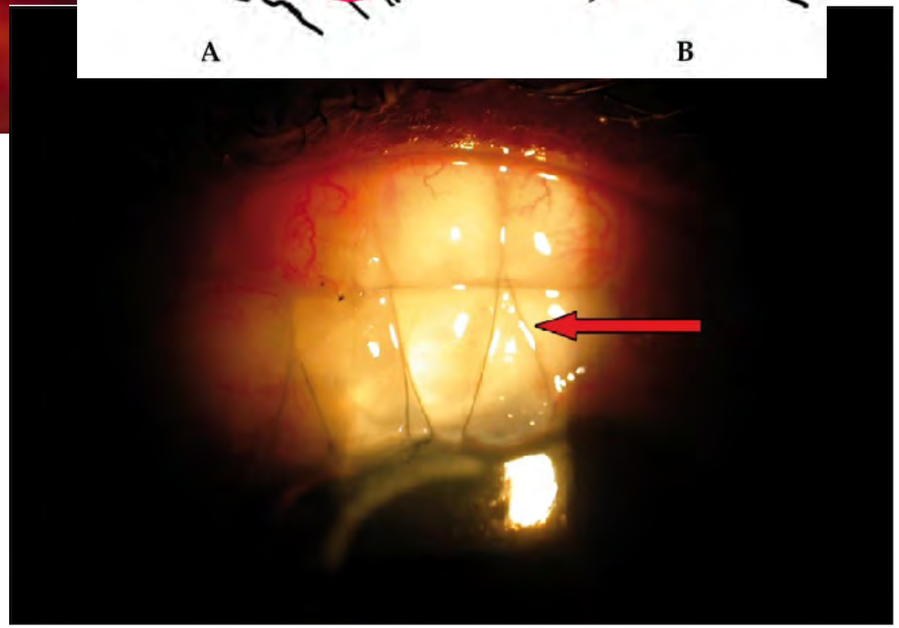


# Post-operative complications

## ocular **hypotony**

### with narrow AC



Choroidal detachment

- wait (relative rest, no Valsalva)
- atropine, increase steroids
- viscoelastic in AC
- flap revision : compressive  or scleral sutures

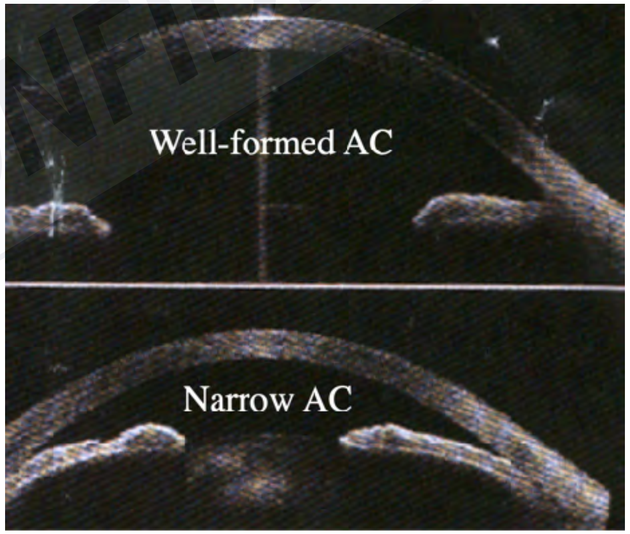
Choroidal hematoma

- Drain (not too early , not too late)
- in association with the vitreo-retinal surgeon

# Post-operative complications

Intraocular pressure






## Hypertony

- **well formed AC**
- narrow AC

# Post-operative complications

## ocular **hypertony**

### with well formed AC

| bleb | anterior chamber | gonioscopy | ***cause*** |
|---|---|---|---|
| - | + | + | *scarring* |
| + | + | + | *cystic bleb* |
| _ | + | _ | *intraocular* |
| _ | _ | +/_ | *malignant glaucoma pupillary bloc, choroidal hemmorage* |

Comment prévenir et traiter les échecs de la chirurgie du glaucome ? A. Brion
JFO-12-2001-24-10-0181-5512-101019-ART17

### Where is the problem?

- outer resistance

tight scleral suture

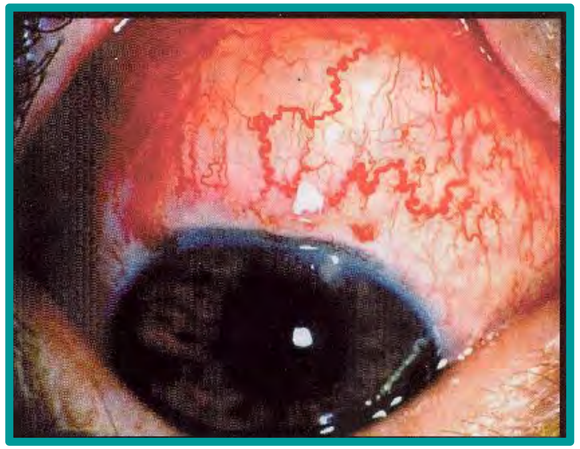
encasulated bleb

or

rarely steroid response

# Post-operative complications

## ocular **hypertony**



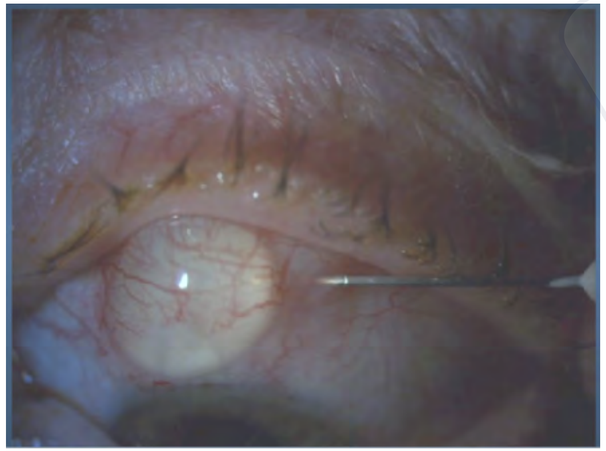
How to treat ?

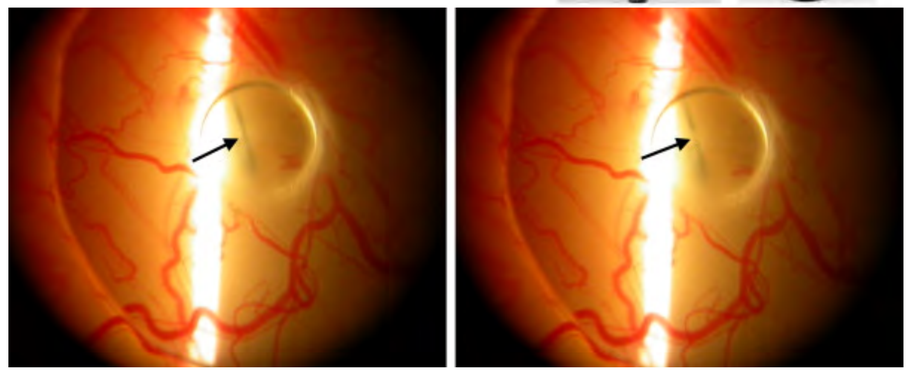
increase steroids

eye or bleb massage

suturolysis

needling (at slit lamp)



Blumenthal lens

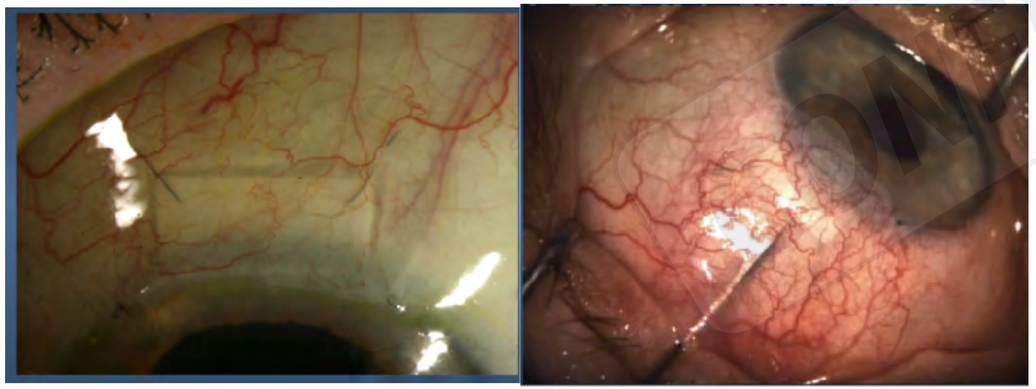
532 nM Argon laser , 0.1 s time,

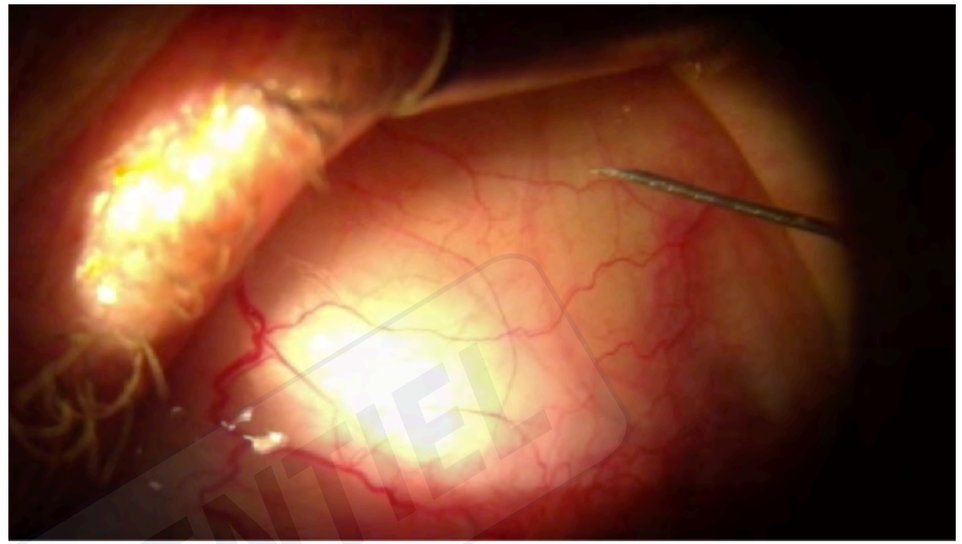
250- 500 mW energy, 100 microns spot size

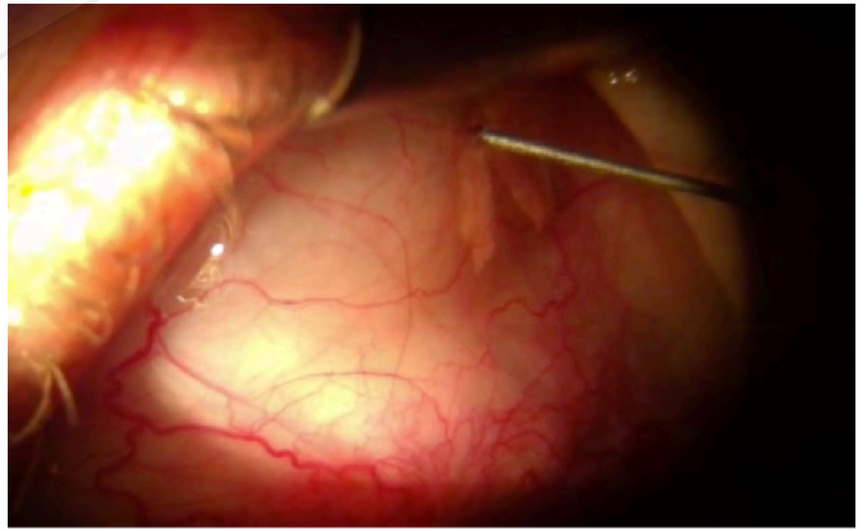
# How to treat ?

needling in OR

cyst resection









Suivi des chirurgies filtrantes en consultation - 19/03/15 jfo.2014.07.002
J.-R. Fenolland, J.-P. Renard, C. Baudouin, P. Hamard

# Filtrering Bleb classification

| Favorable Bleb development | Unfavorable Bleb development | | Intensified Postoperative Care |
|---|---|---|---|
| Microcysts of the conjunctiva | Increased vascularization | → | Increased topical steroid administation |
| Paucity of the vessels | Cork Screw vessels | → | Increased topical steroid administation or Avastin |
| Diffuse bleb | Encapsulation of the bleb | → | Needling or revision plus 5-FU and Avastin |
| Moderate elevation of the bleb | High-Domed appearance | → | Repeated 5-FU and Avastin injection |



*Marquardt D, et al.Graefe's Arch Clin Exp Ophthalmol 2004;242:106-113*

# Post-operative complications

## ocular **hypertony**

with well formed AC

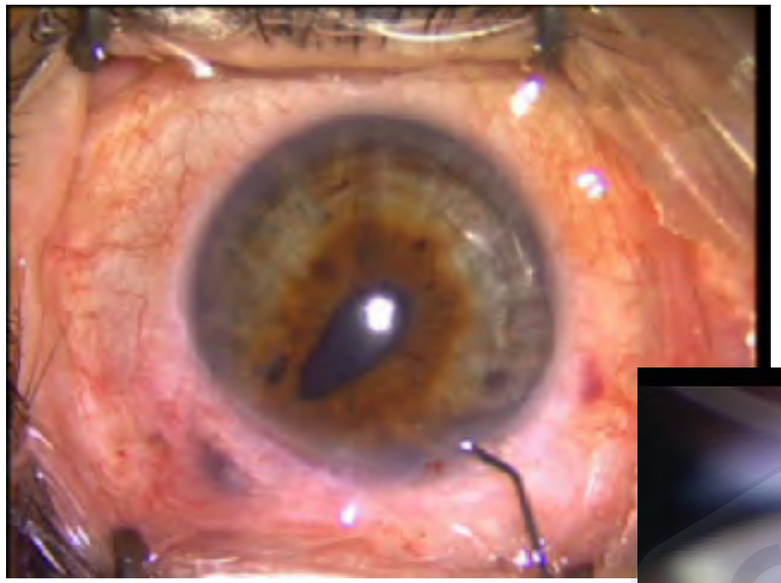
Where is the problem?

| bleb | anterior chamber | gonioscopy | ***cause*** |
|---|---|---|---|
| - | + | + | *scarring* |
| + | + | + | *cystic bleb* |
| _ | + | _ | *intraocular* |
| _ | _ | +/_ | *malignant glaucoma pupillary bloc, choroidal hemmorage* |

- inner dysfunction

# Post-operative complications

## ocular **hypertony**





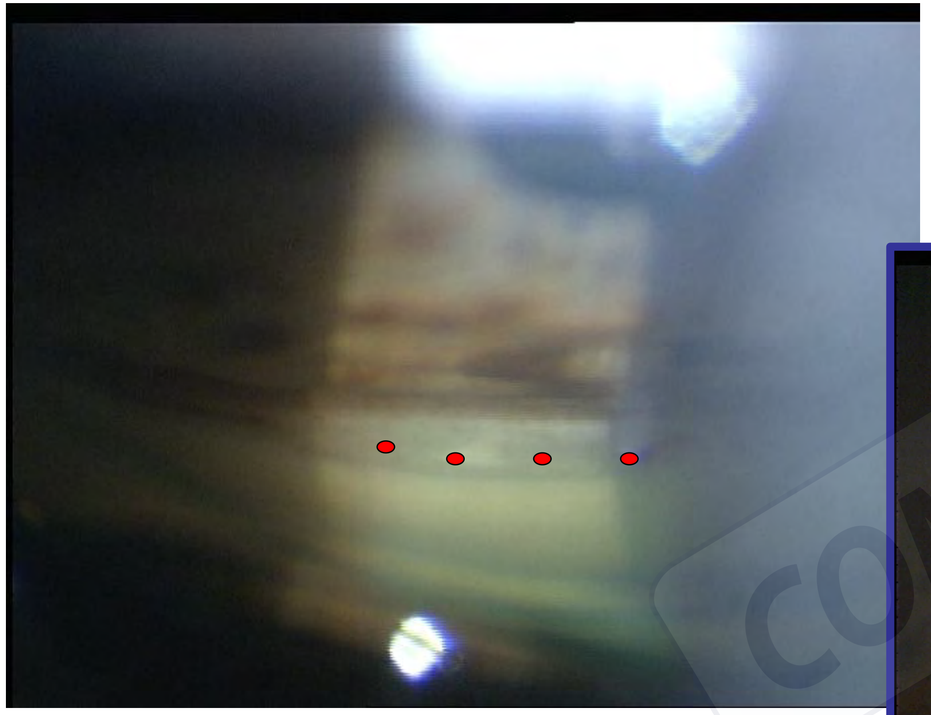
### How to treat ?

reopen the pathway for the aqueous humor :

Argon laser iris retraction + pilocarpine

# Post-operative complications

## ocular **hypertony**



How to treat ?

goniopuncture

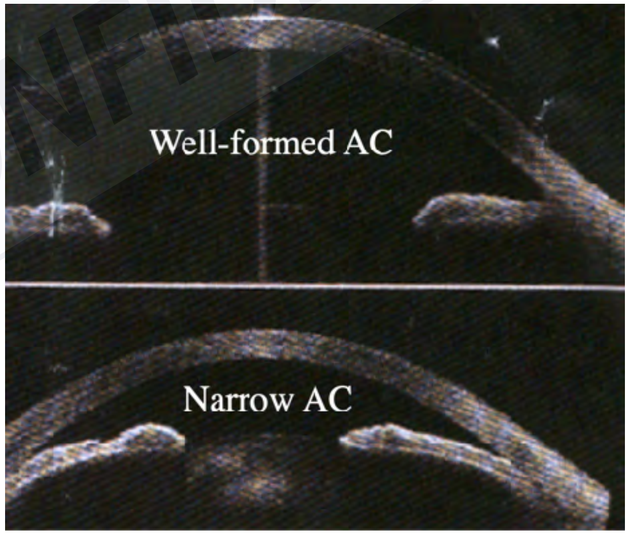


Mermoud A, Karlen ME, Schnyder CC, Sickenberg M, Chiou AG, Hediguer, Sanchez
Nd:Yag goniopuncture after deep sclerectomy with collagen implant. Ophthalmic Surg Lasers. 1999 Feb;30(2):120-5.

# Post-operative complications

Intraocular pressure






## Hypertony

- well formed AC
- **narrow AC**

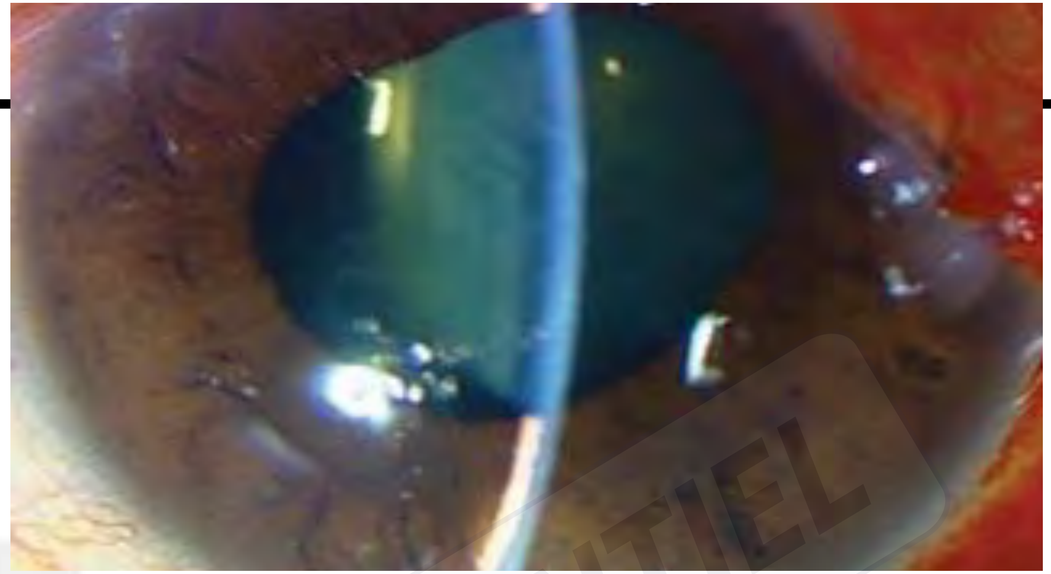
# Post-operative complications

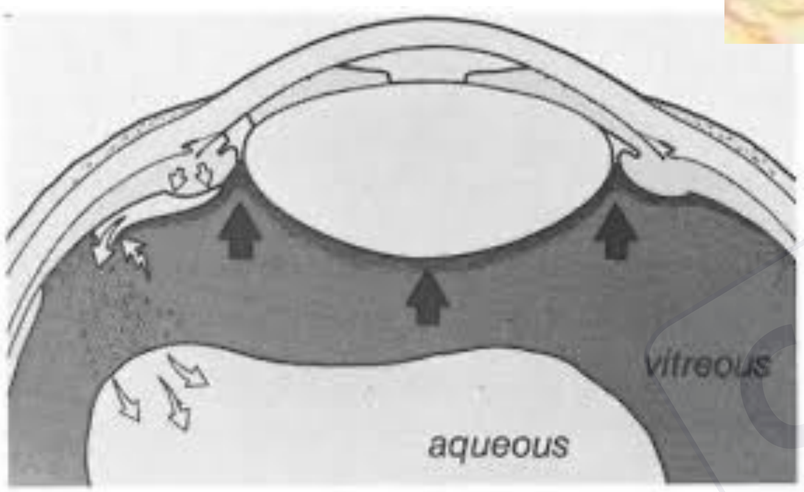
with narrow AC

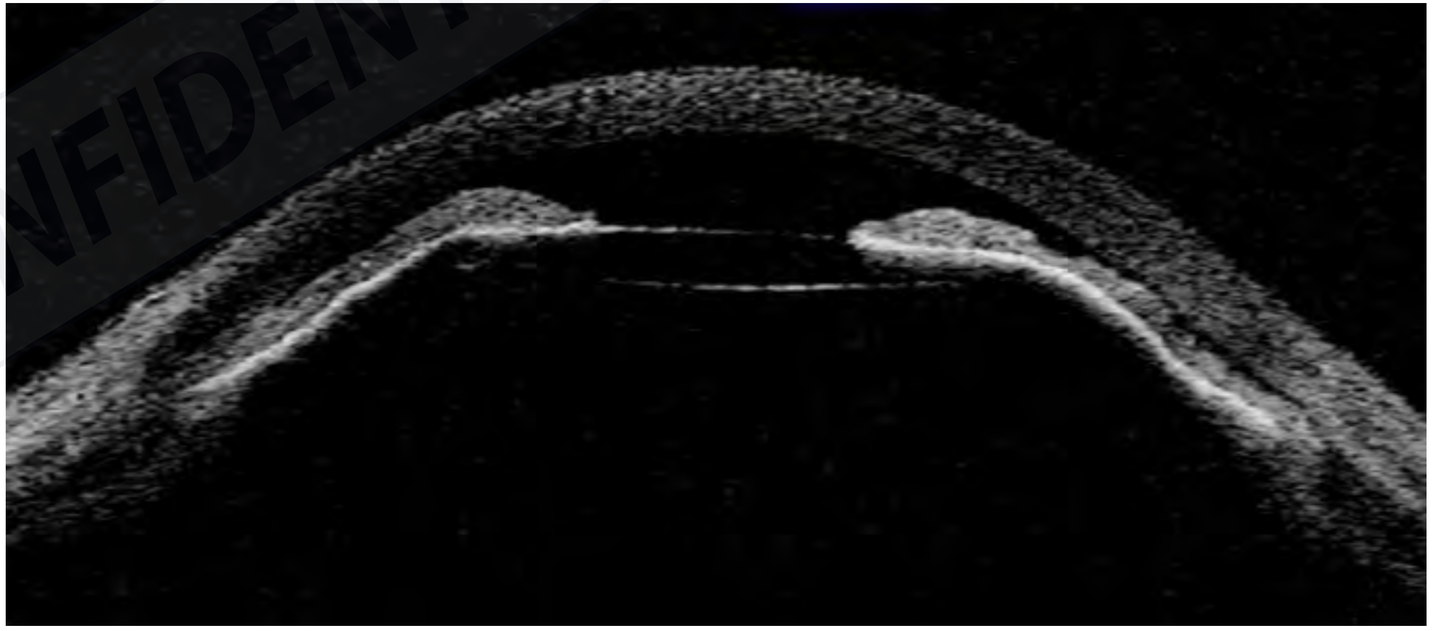
Where is the problem?

| bleb | anterior chamber | gonioscopy | ***cause*** |
|---|---|---|---|
| - | + | + | *scarring* |
| + | + | + | *cystic bleb* |
| – | + | – | *intraocular* |
| - | - | +/- | *malignant glaucoma pupillary bloc, choroidal hemmorage* |

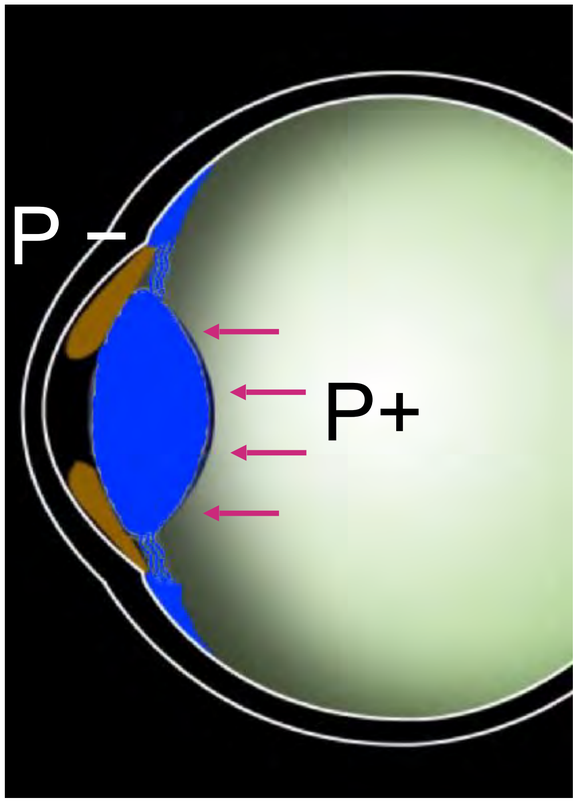
**Malignant glaucoma**



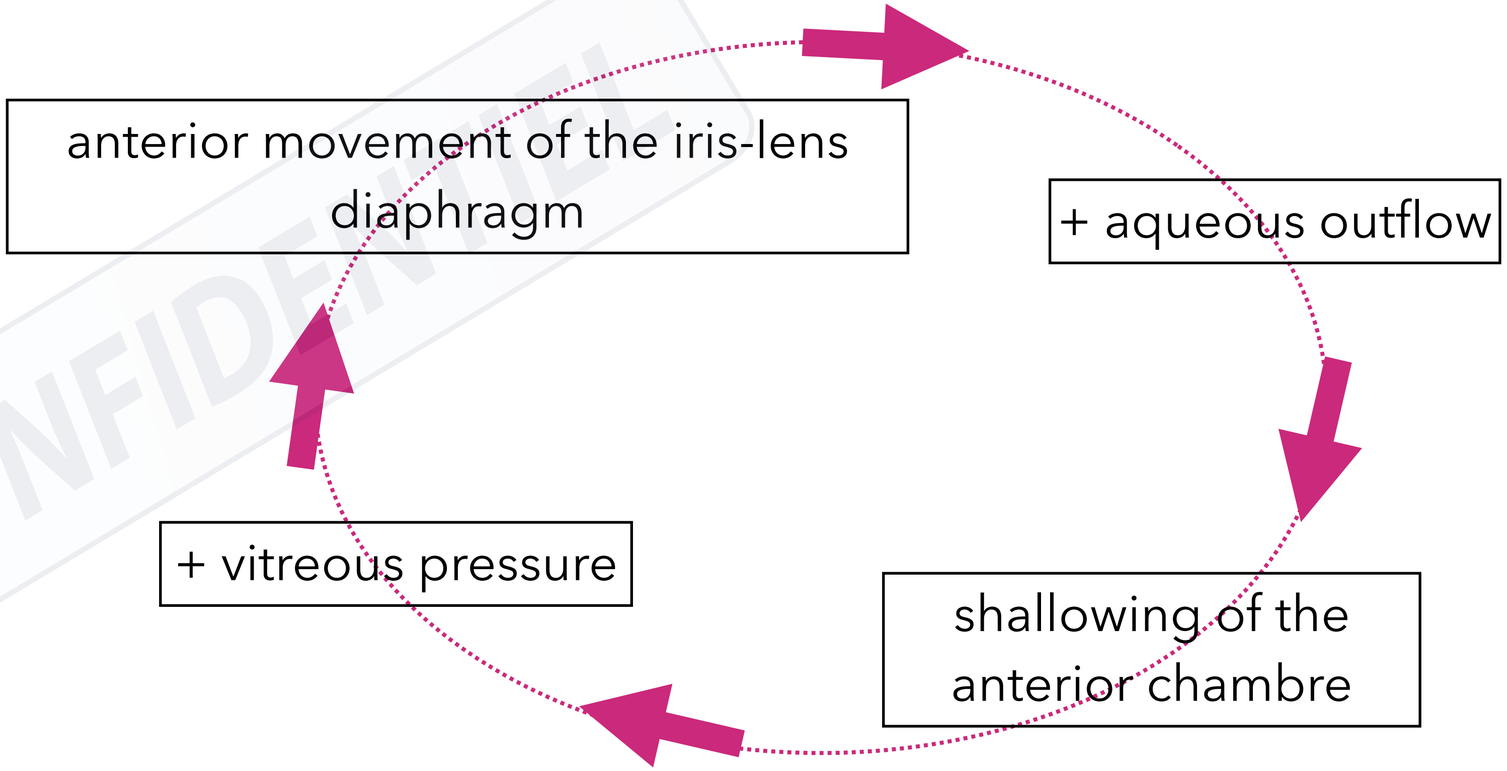


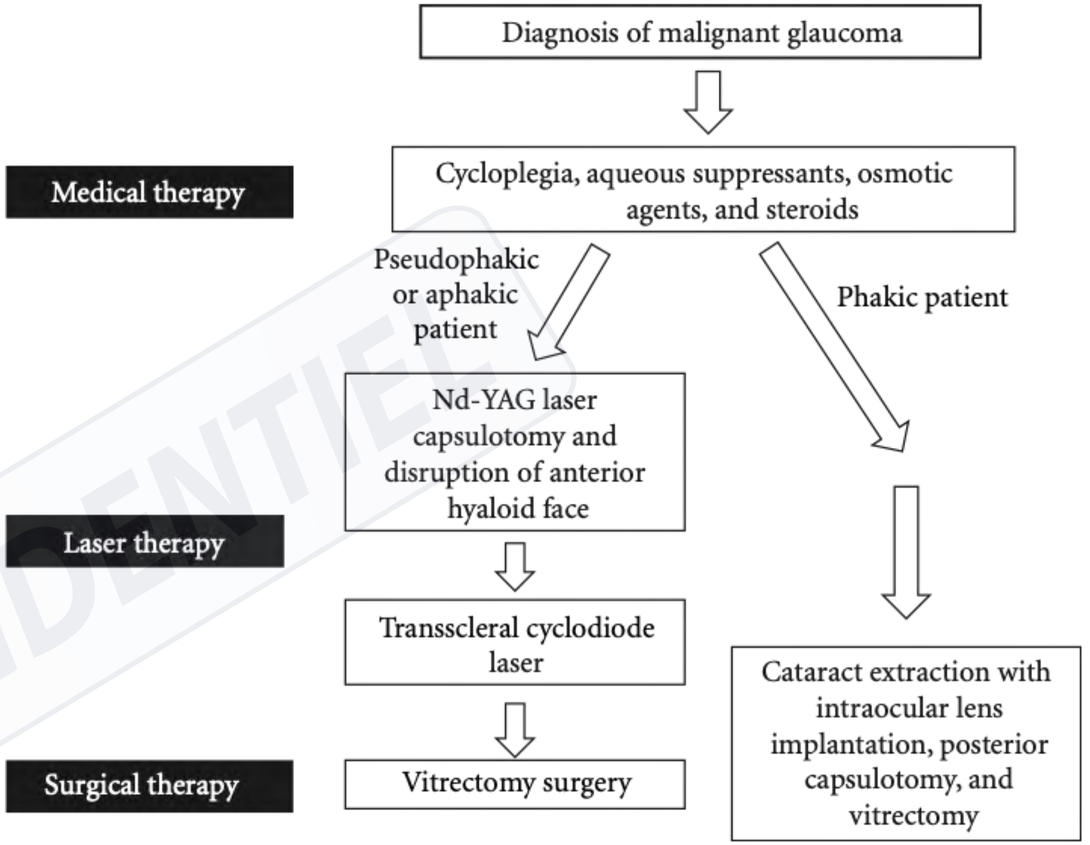
# PHYSIOPATHOGENESIS




Vicious circle:



# TREATMENTS





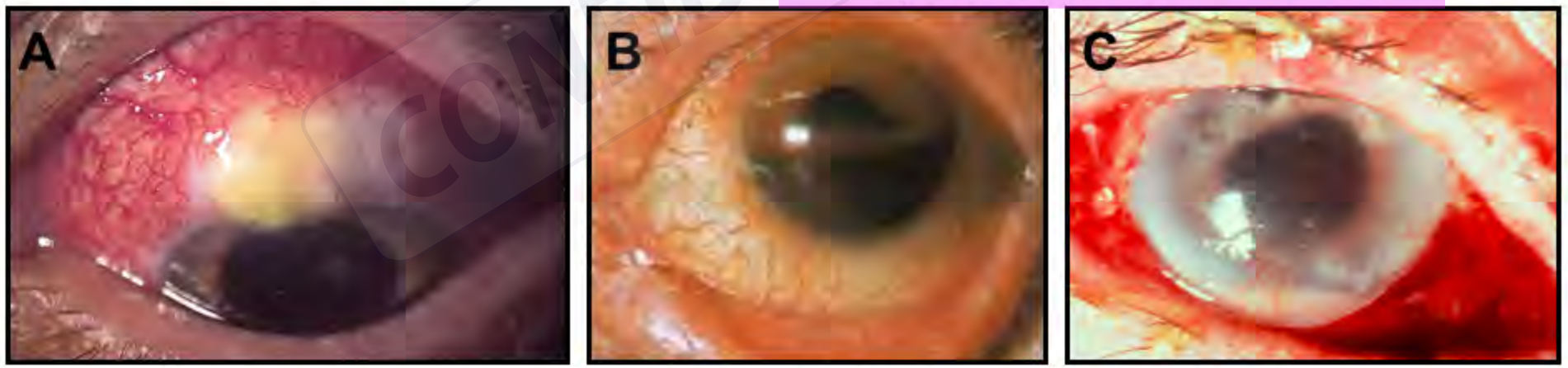

But, most of the time, medical treatment is insufficient..

It is necessary to break the resistance between AC and Vitreous cavity, by performing vitrectomy (+/- IOL) and posterior « hyaloido-zonulo-iridectomy »

# Intermediate or late post-operative complications

# Complications of Traditional Filtering Surgery

- Infection
- Hypotony
- Flat anterior chamber
- Hyphema
- Cataract
- Transient IOP elevation
- CME
- Hypotonic maculopathy
- Choroidal effusion
- Suprachoroidal hemorrhage
- Persistent uveitis
- Dellen formation
- Loss of vision
- Bleb leak
- Late bleb failure
- Blebitis/endophthalmitis
- Dysesthesia





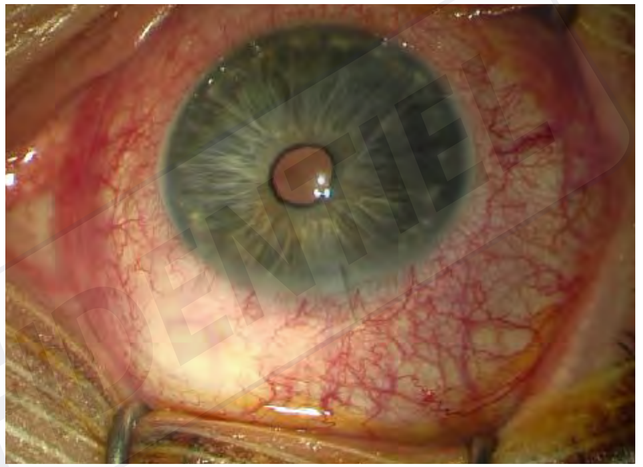

Jampel HD, et al. *Ophthalmology*. 2012;119:712-722; Gedde SJ, et al. *Am J Ophthalmol*. 2012;153:804-814.e1.

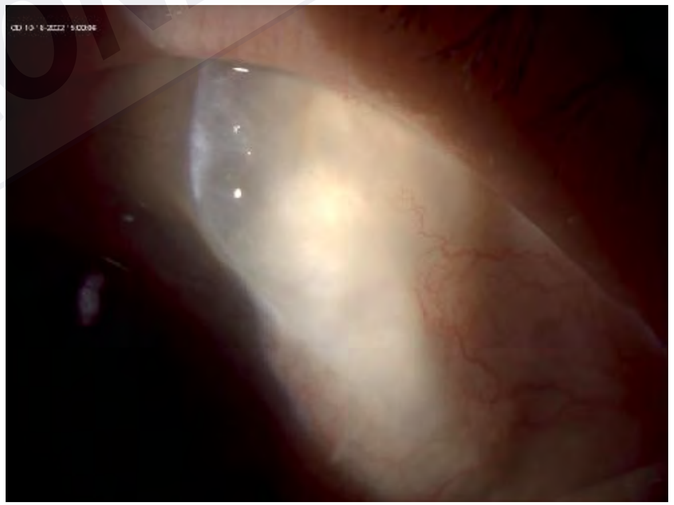
A,B: Images from Rakesh Ahuja, MD/Wikimedia Commons/Public Domain. C: Image courtesy of Joan W. Miller, MD, and Mehran Afshari, MD, Massachusetts Eye and Ear Infirmary, Boston, Mass.

# Post-operative Follow-up

## Later problems

- ocular surface disease
- bleb weakness
- loss of filtration / hypertension





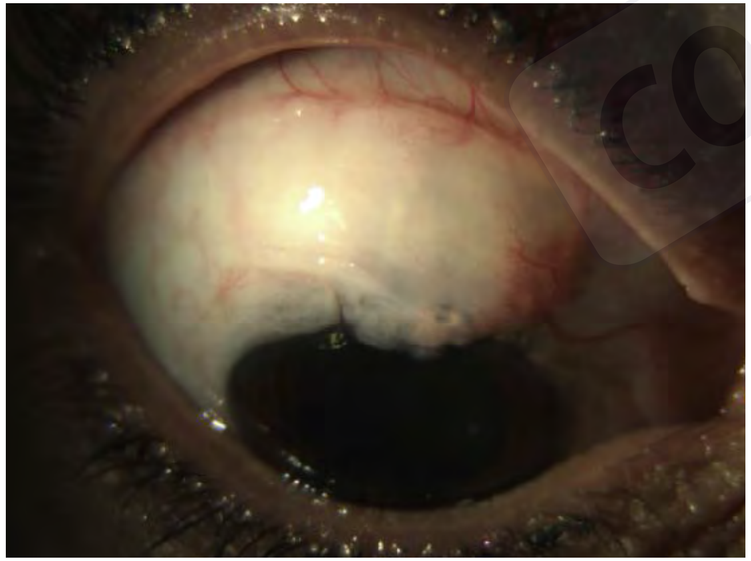
## What to check ?

- conjunctiva
- anterior chamber
- gonioscopy
- fundus

# Post-operative Follow-up

## What to check ?

- avascular ischemic bleb
- risk of blebitis



## How to treat ?

- surgical sanction:

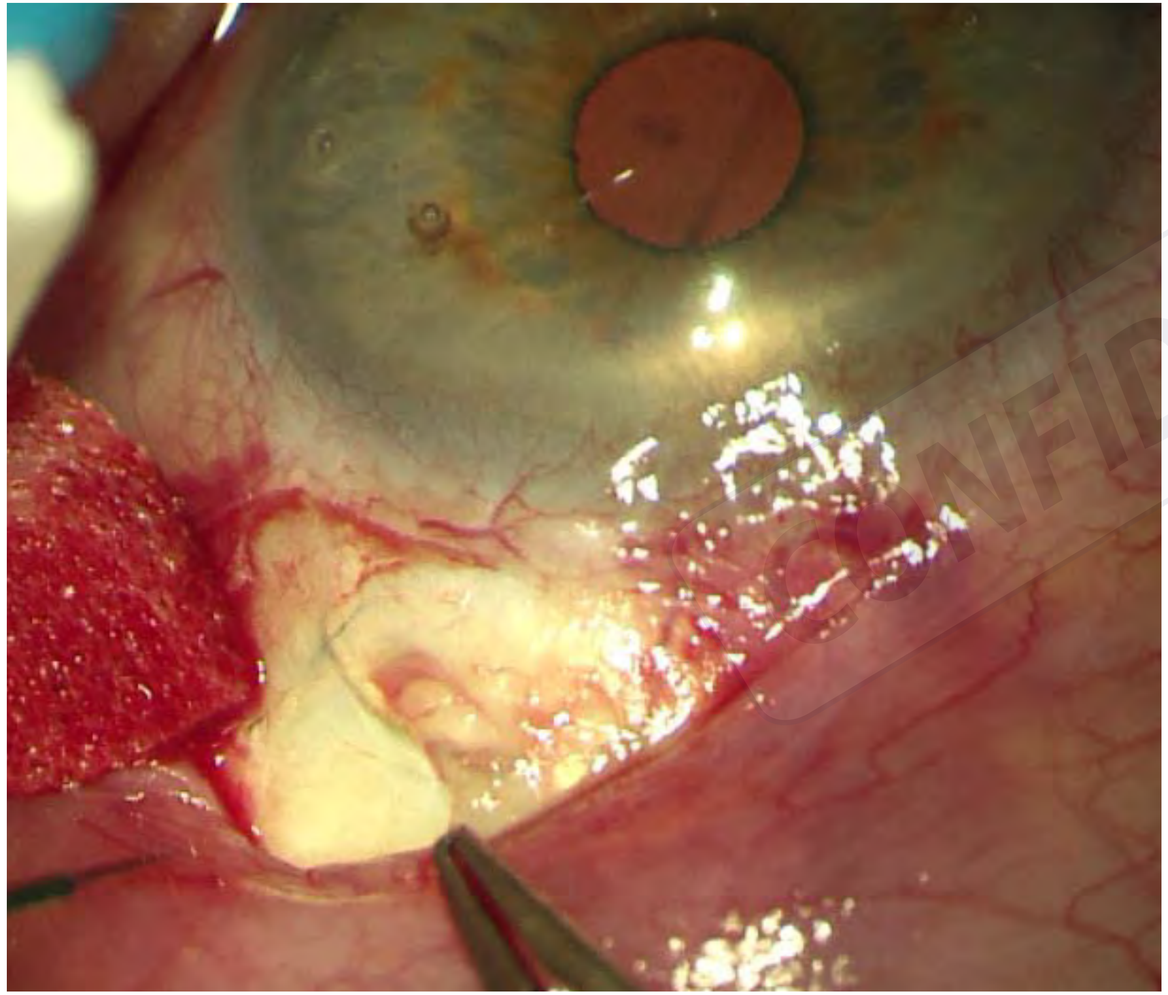
cyst resection, revision

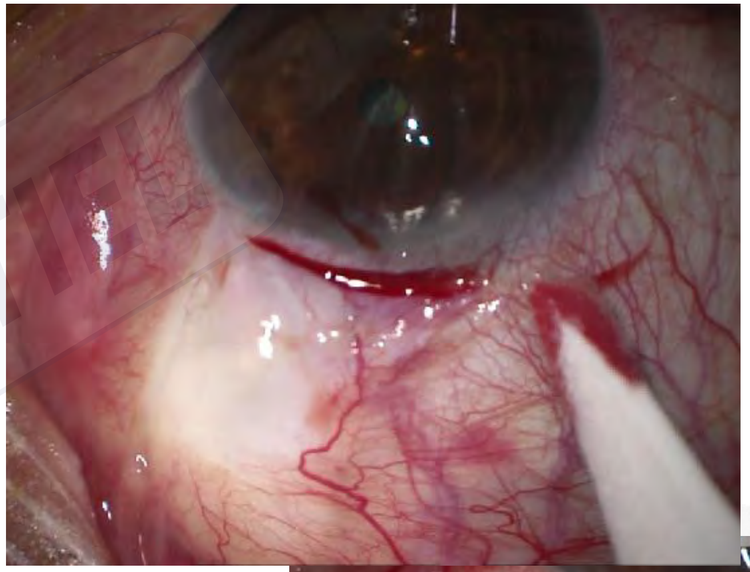
or

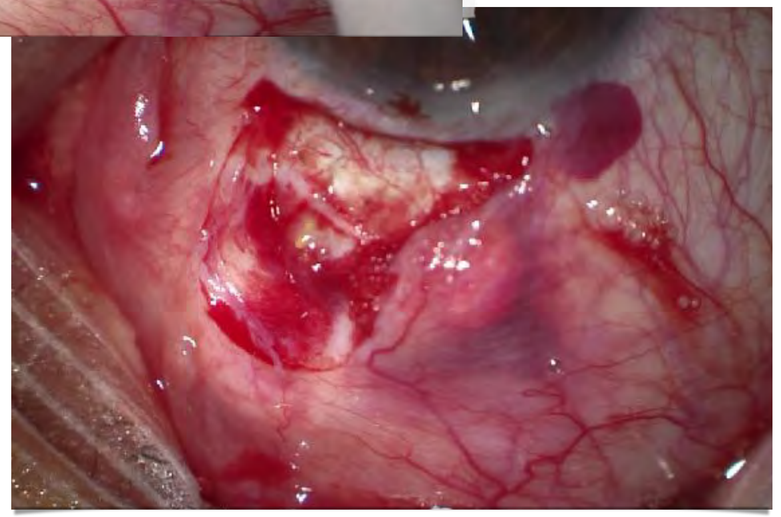
bleb reconstruction, conjunctival flap

# Post-operative Follow-up

revision for fibrosis & ischemic bleb resection







# Take home messages

- the follow-up is crucial to optimize the results of each filtration surgery
- act as soon as possible to prevent fibrosis (preservative free drops)
- adapt your treatment to each single patient and clinical situation
- be aware of the late complications, even many years after surgery

# discussion



Thank you for your attention

CHU de Liège

LIÈGE université