Treatment of primary angle closure: What do the trials tell us?

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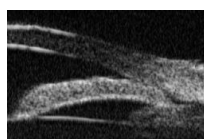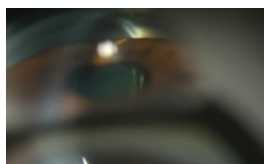Moorfields Eye Hospital, London

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Angle closure: Definitions

Standardised definitions of disease (ISGEO 2002)

ITC (PACS)
Iridotrabecular contact

PAC
Primary angle closure

PACG
Primary angle closure glaucoma

ISGEO Diagnostic classification of glaucoma for prevalence surveys
Foster et al. BJO 2002
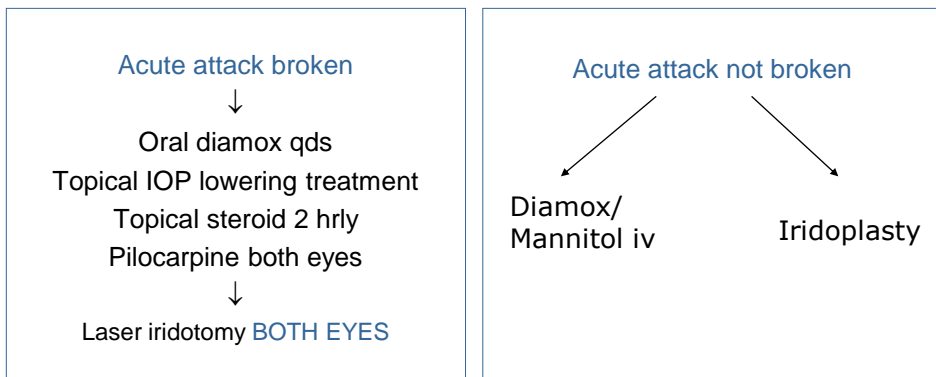
Angle closure: Management

Stages
- Acute angle closure
- Primary angle closure
- Primary angle closure glaucoma
- Asymptomatic narrow angles (ITC)

Treatment options
- Laser iridotomy
- Surgical iridectomy
- Iridoplasty
- Lens extraction
- Trabeculectomy
- Drops

Acute angle closure - Management

Acute attack broken
↓
Oral diamox qds
Topical IOP lowering treatment
Topical steroid 2 hrly
Pilocarpine both eyes
↓
Laser iridotomy BOTH EYES

Acute attack not broken

Diamox/ Mannitol iv   Iridoplasty
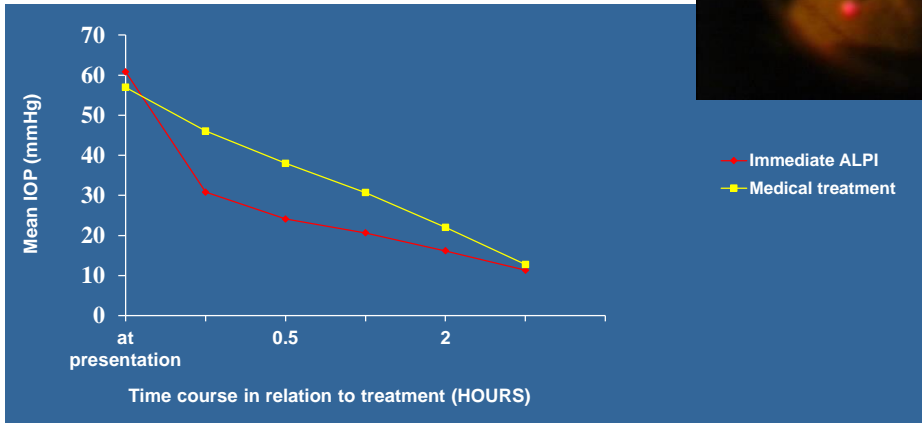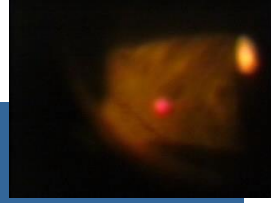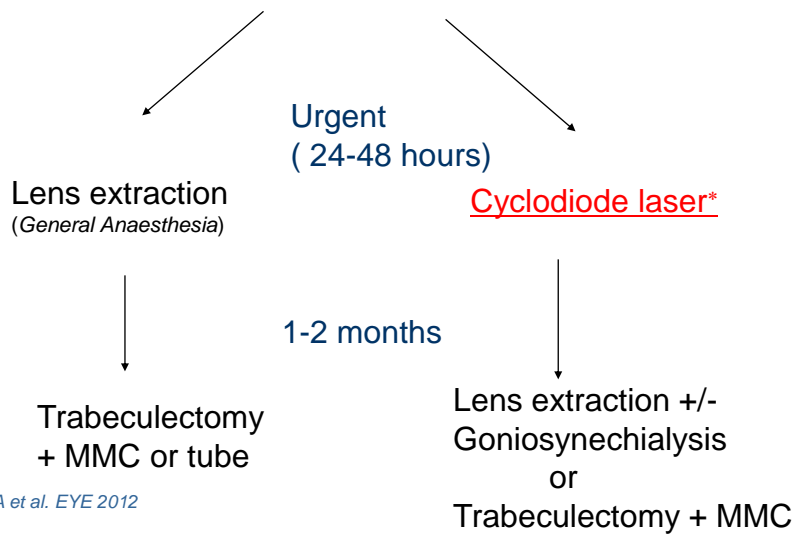
WGA consensus statement:
"Laser iridotomy should be performed as soon as feasible in the affected eye(s), and should also be performed as soon as possible in the contralateral eye"

RCT of iridoplasty vs medical treatment for APAC

Mean IOP (mmHg) vs Time course in relation to treatment (HOURS)

- Immediate ALPI
- Medical treatment

Lam DS et al Ophthalmology 2002

Refractory acute angle closure

Urgent
(24-48 hours)

Lens extraction
(*General Anaesthesia*)

Cyclodiode laser*

1-2 months

Trabeculectomy
+ MMC or tube

Manna A et al. EYE 2012

Lens extraction +/-
Goniosynechialysis
or
Trabeculectomy + MMC

Asymptomatic narrow angles
(Iridotrabecular contact)

Treatment options:

1. Observe
2. Laser iridotomy
3. Cataract extraction: only when symptomatic ↓ VA

Laser peripheral iridotomy

Evidence supporting iridotomy?

Good evidence that protects eyes against acute angle closure

*   Fellow eye data: Caucasian eyes
    50% untreated $\rightarrow$ APAC
    2% iridectomy $\rightarrow$ APAC

Fellow eye data: Asian eyes
    No APAC in 71 fellow eyes treated with PI at 4 years

Lowe RF, Snow JT
Ang L, 2000

Laser peripheral iridotomy for the prevention of angle closure: a single-centre, randomised controlled trial

Mingguang He, Yuzhen Jiang, Shengsong Huang, Dolly S Chang, Beatriz Munoz, Tin Aung, Paul J Foster*, David S Friedman*

*   Guangzhou, China
*   Randomised controlled trial
*   Subjects 50-70 years old
*   Asymptomatic narrow angle (ITC in 2 or more quadrants)
*   Identified through community screening
*   Randomised one eye to laser iridotomy and fellow eye control

Primary outcome:
*   Incident primary angle closure disease: elevated IOP, PAS or AAC
*   Follow up 6 years

Lancet 2019; 393: 1609-18

Results

		No endpoint	Endpoint	Total
		Laser peripheral iridotomy		
		No endpoint	Endpoint	Total
	No endpoint	844	9	853
Control	Endpoint	26	10	36
	Total	870	19	889

Figure 2: Pair-wise analyses of primary endpoint (intention-to-treat analysis) at 72 months
p=0·0041 with McNemar's test.

4.19 per 1000 eye-years (PI)
7.97 per 1000 eye-years (control)

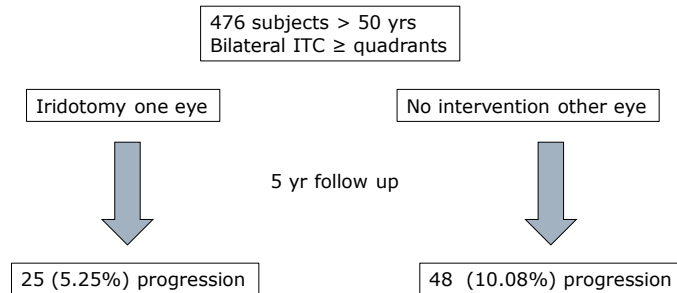Hazard ratio = 0.53 (95% CI: 0.3-0.92, p =0.024)
No sight –threatening events

Baseline Findings associated with endpoint

	Eyes that did reach endpoint, n= 55, 3%	Eyes that did not reach endpoint, n=1723, 97%	Hazard ratio (95% CI)	p value
Univariate model				
Randomly assigned to laser peripheral iridotomy	34·5%	50·5%	0·53 (0·30-0·92)	0·024
Multivariate models				
Age, years (per 1 year older)	60·91 (5·76)	59·25 (4·97)	1·07 (1·01-1·13)	0·015
Female (vs male)	81·8%	82·9%	1·11 (0·55-2·24)	0·765
Randomly assigned to laser peripheral iridotomy (vs control)	34·5%	50·5%	0·52 (0·30-0·91)	0·023
Baseline intraocular pressure, mm Hg (per 1 mm Hg increase)	15·76 (3·02)	15·06 (2·83)	1·09 (0·99-1·19)	0·075
Total angle width*, score (per 1 score higher)	4·80 (2·37)	5·36 (2·38)	0·91 (0·82-1·02)	0·098
Limbal anterior chamber depth†, % (per 10% higher)	18·64 (8·41)	22·28 (7·57)	0·49 (0·34-0·71)	<0·001
Central anterior chamber depth‡, mm (per 1 mm deeper)	2·47 (0·24)	2·55 (0·22)	0·21 (0·06-0·72)	0·013
Lens thickness‡, mm (per 1 mm thicker)	4·95 (0·37)	4·87 (0·32)	1·57 (0·65-3·79)	0·318
Dark room prone provocative test, mm Hg (per 1 mm Hg increase)	3·76 (3·39)	4·27 (2·97)	0·94 (0·86-1·03)	0·199

All values are mean (SD) unless stated otherwise. Multivariable Cox proportional hazards models include laser peripheral iridotomy, age, gender, baseline intraocular pressure, and variables of interest. *Total angle width was calculated by the sum of Shafer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle). †Limbal anterior chamber depth was evaluated by modified van Herick grading. ‡Central anterior chamber depth and lens thickness were measured by ultrasound A-scan.

Table 3: Baseline ocular biometrics and gonioscopic factors associated with endpoint at 72 months

Singapore Asymptomatic narrow angles laser iridotomy study (ANA-LIS)

476 subjects > 50 yrs
Bilateral ITC ≥ quadrants

Iridotomy one eye

No intervention other eye

5 yr follow up

25 (5.25%) progression

48 (10.08%) progression

Progression = PAS, ↑iop, acute attack, symptomatic angle closure, PACG
2 AAC in observation group, one in PI group

NNT to prevent progression = 20.7

Baskaran M, Sasikumar R, Wong HT et al. ARVO 2016

Impact on clinical practice

- Incidence of angle closure disease in individuals with asymptomatic narrow angles is <u>very low</u>
- Benefit of prophylactic iridotomy is limited
- Laser iridotomy for all narrow angle patients is NOT indicated

- Assess risk factors and discuss with patient:
- Diabetics/ frequent mydriatic exam
- Angle width and mechanism
- Family history of AAC
- Other medications eg anti anxiety medication
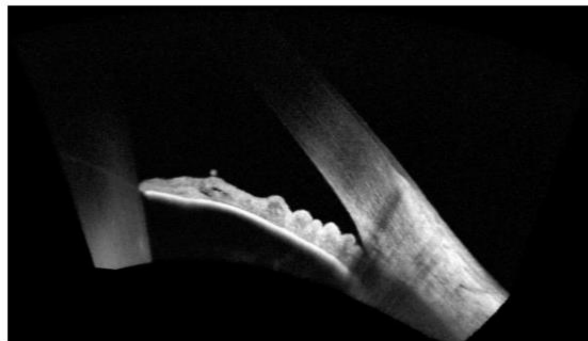- Clinical judgement

Example: 53 yr old man

- Left amblyopia, 270 ° ITC both eyes
- Mother Acute angle closure
- Offer PI
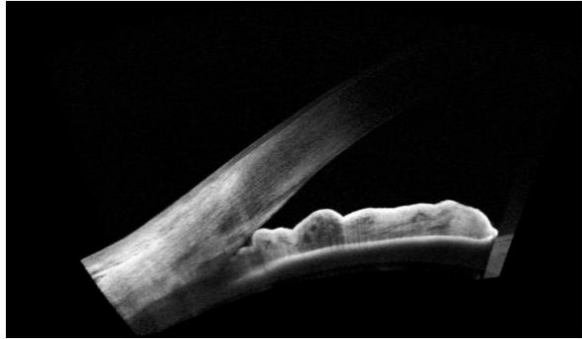
Example: 64 yr old woman

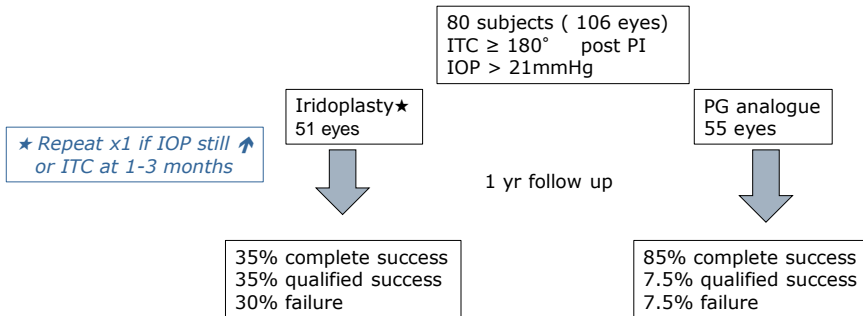- ITC one quadrant
- Early cataract
- Watch

PAC and PACG

Treatment options:

1. Laser iridotomy
2. Laser iridoplasty
3. Eye drops
4. Lens extraction

Argon laser peripheral iridoplasty

ALPI for PAC (G) : RCT

80 subjects (106 eyes)
ITC ≥ 180°   post PI
IOP > 21mmHg

Iridoplasty★
51 eyes

★ *Repeat x1 if IOP still ↑
or ITC at 1-3 months*

PG analogue
55 eyes

1 yr follow up

35% complete success
35% qualified success
30% failure

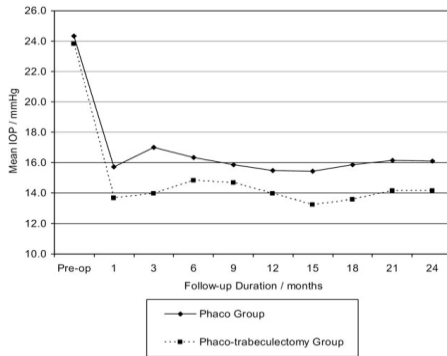85% complete success
7.5% qualified success
7.5% failure

Change in IOP at 12 months: ALPI: -4.9mmHg (3.5-6.3)
Meds: -6.1mmHg (5.1-7.1) (p<0.001)

Narayanaswamy A, Baskaran M, Perera S et al. Ophthalmology 2016

Lens extraction

Phaco vs Phaco trab trial
Tham CC et al, Ophthalmol 2009

Key: 'Pre-op' = Pre-operative / before surgery.

Medically uncontrolled PACG

Phaco
27 eyes

Phaco + Trab
24 eyes

• IOP lower in Phaco + trab
• ↓ meds required for phaco + trab
• 4 (14.8%) in phaco arm → trab

Complication rate: phaco only = 8.1%
phaco + trab = 26.2% (p = 0.007)

The Effectiveness of Early Lens Extraction for Primary Angle Closure Glaucoma

Design: pragmatic RCT

PAC with IOP>30 mmHg or PACG

Phaco

Laser iridotomy

If both eyes eligible both received the same intervention
Index eye: the one with more advanced disease

Follow-up = 3 years

Azuaro-Blanco A, Burr J, Ramsay C et al. Lancet. Oct 2016

eagle

Inclusion criteria

- PACG with IOP $\geq$ 21 mmHg or PAC with IOP $\geq$ 30 mmHg
- At least 180 degrees of angle closure
- Newly diagnosed (up to 6 months)
- Age $\geq$ 50 years
- Phakic in affected eye (no cataract)

Exclusion criteria

- Previous acute angle closure
- Severe glaucoma (C/D ratio $\geq$ 0.9 or MD $\geq$ 15 dB)
- Symptomatic cataract
- Axial length $\leq$ 19 mm (nanophthalmos)
- Previous surgery (IOL, laser iridotomy)
- Increased surgical risk

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eagle
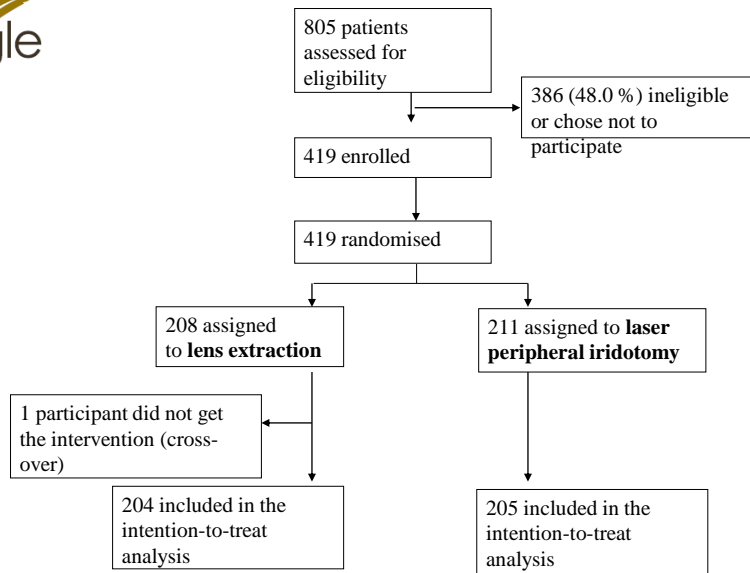
Primary outcome

- Patient-centred: Health status (EQ-5D)
- Clinical: IOP
- Cost-effectiveness

Completed recruitment (n=419)

Asia – 7 sites

UK – 23 sites

Australia – 1 site
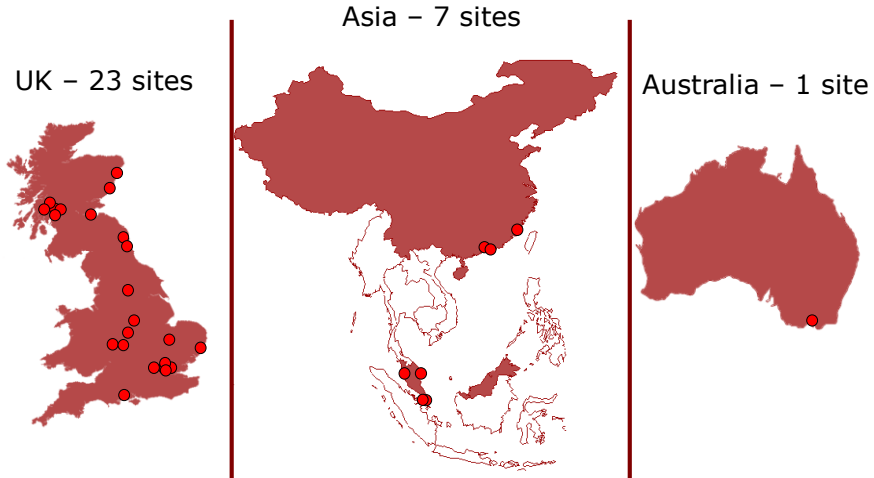
Baseline characteristics (n=419)

- **Race:**   Chinese = 121 (29%)

- **Age:** 67.0 (+/- 9.8) years

- **EQ-5D:** 0.871 (+/- 0.18)

- **Diagnosis:** PAC= 157 (37%), PACG = 261 (62%)

- **IOP:** 28.9 (+/- 9.7) mmHg

- **Humphrey MD:** -4.2 (+/-6.0) dB

EAGLE study profile

805 patients assessed for eligibility

386 (48.0 %) ineligible or chose not to participate

419 enrolled

419 randomised

208 assigned to **lens extraction**

211 assigned to **laser peripheral iridotomy**

1 participant did not get the intervention (cross-over)

204 included in the intention-to-treat analysis

205 included in the intention-to-treat analysis

Primary outcome: EQ-5D

EQ-5D score	Lens extraction		Laser PI		
	N	mean (SD)	N	mean (SD)	
Baseline	204	0·87 (0·19)	204	0·88 (0·18)	
36 months	176	**0·87** (0·21)	175	**0·84** (0·23)	p=0·005

eagle Primary clinical outcome: IOP

	Lens extraction		Laser PI		
IOP (mmHg)	N	mean (SD)	N	mean (SD)	
Baseline IOP	208	29·5(8·2)	211	30·3(8·1)	
36 months IOP*	182	**16·6** (3·5)	184	**17·9** (4·1)	p = 0·004

*Includes patients who had glaucoma surgery during the 3-year follow-up

eagle Medications at 36 months

Number of medications	Lens Extraction	Laser PI
0 medications, N (%)	**126 (60·6%)**	**45 (21·3%)**
1 medications, N (%)	33 (15·9%)	67 (31·8%)
2 medications, N (%)	15 (7·2%)	46 (21·8%)
3 medications, N (%)	3 (1·4%)	19 (9·0%)
4 medications, N (%)	1 (0·5%)	4 (1·9%)
Mean ± SD	**0·4 ± 0·8**	**1·3 ± 1·0**

eagle Intra-operative* complications

	Lens extraction N=208	Laser PI N=211
Posterior capsule rupture	2 (1·0%)	
Iris prolapse	2 (1·0%)	
Vitreous loss	1 (0·5%)	
Broken haptic	1 (0·5%)	
Bleeding or haemorrhage		16 (7·6%)
*Pre-operative attack angle closure	1 (0·5%)	

eagle Post-operative complications

	Lens extraction (N=208)	Laser PI (N=211)	
Flat anterior chamber	2 (1·0%)	1 (0·5%)	
Retinal detachment or tear		1 (0·5%)	
Malignant glaucoma	1 (0·5%)	2 (1·0%)	
Corneal decompensation	1 (0·5%)		
Macular Oedema	5 (2·4%)	3 (1·4%)	
IOP spike	2 (1·0%)	5 (2·4%)	
Post-operative inflammation	5 (2·4%)	1 (0·5%)	
Central retinal vein occlusion		1 (0·5%)	
Dysphotopsia		1 (0·5%)	
Posterior vitreous detachment		1 (0·5%)	
Macular hole	1 (0·5%)		

Conclusion

- Initial lens extraction for PACG and PAC with high IOP (>30mmHg) is associated with better clinical and patient-reported outcomes than laser PI
- Initial lens extraction for PACG and PAC with high IOP is likely to be cost-effective
- Lens extraction has a risk of PC rupture and other complications: individualised decision making!
- (EAGLE does not support that we must do lens extraction in all, it is an option)
- EAGLE results not applicable to ITC (Asymptomatic narrow angles only)
- Note IOP cut off of >30mmHg for PAC patients – if IOP <30 discuss with patient

The effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma: a randomized controlled trial (EAGLE). The Lancet, *2016*

Summary - Indications for iridotomy

- Acute angle closure – affected and fellow eye
- ITC – particularly high risk patients:
    - Diabetic
    - Family History
    - Travel frequently
- PAC with IOP <30mmHg (not fulfilling EAGLE criteria)
- PAC > 30mmHg and patient does not want surgery

Indications for lens/ cataract surgery

- Symptomatic cataract
- PACG with IOP > 21mmHg RE
- PAC with IOP >30mmHg
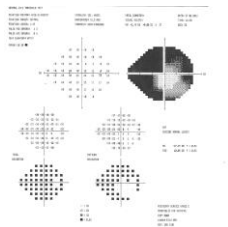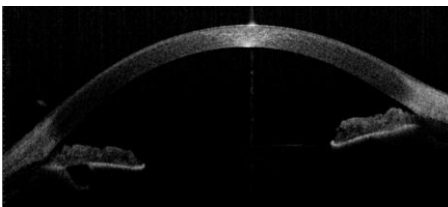- Refractory or recurrent acute or subacute angle closure

Is there a role for trabeculectomy in PACG?

32 yr old woman, blurred vision, PACG

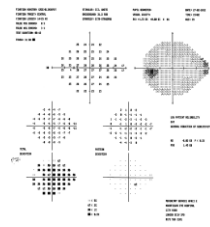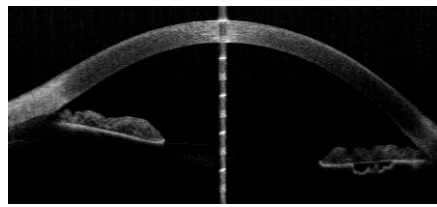

Anterior segment OCT images

Right   Left

Summary - Advanced PACG, non- pupil block

- Age → Young (34)
- Lens status → Clear
- PAS - extent, onset → extensive, onset unknown
- Glaucomatous optic neuropathy → Advanced
- Chronicity of disease → Chronic
- Refractive error → None
- Biometry → AL 23.4 mm
- Mechanism of angle closure → Plateau/ iris cysts
- Patient - circumstances and wishes → foreign service

Tips for trabeculectomy in angle closure

- Counsel patient re complications/ aqueous misdirection
- GA anaesthesia if small eye /high IOP
- Anterior chamber maintainer
- 3 - 4 tight releasable sutures
- No flow on table
- AC deep and formed at end of surgery
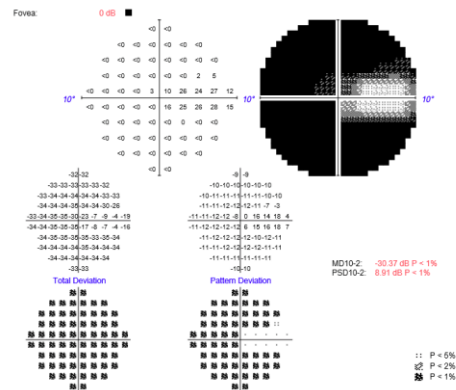- Atropine at end of surgery

Challenging case - 74 yr old man

- 2nd opinion
- West African
- Advanced PACG
- Left phaco ➔ CMO
- Patient delayed intervention RE

- Maximum drops + Diamox
- + 5.0 D hypermetrope

- 6/60 ph 6/24 RE
- HM LE
- 360° PAS
- IOP 24mmHg RE, 54 mmHg LE
- Cataract
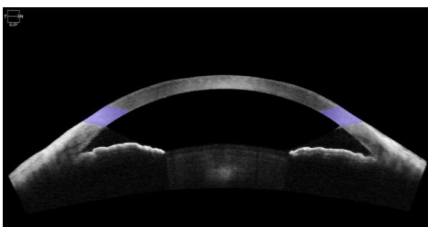
WHICH OP ??

10-2 VF Right eye

Thankyou