Interventional Glaucoma - A Paradigm Shift?

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OVERVIEW

- WHAT IS INTERVENTIONAL GLAUCOMA?
  - “A proactive approach that utilises early, minimally invasive procedures like lasers and MIGS, to lower eye pressure and reduce optic nerve damage, shifting from the traditional method of waiting to use stronger medications or late-stage surgery. This paradigm aims to decrease reliance on daily eye drops, improve patient adherence, and preserve vision by intervening sooner in the disease process”

OVERVIEW

- Term derived from interventional cardiology
- Traditional glaucoma disease management
  - Initiate drug therapy, add drug classes until treatment targets achieved
  - If unstable and/or rapid progression on MMT, refer for surgical intervention
- Works well for majority of patients
- Avoids unnecessary surgical cost
- Avoids healthcare societal costs, funds can be utilised elsewhere

OVERVIEW

- All drug therapies limited by
  - compliance (10% of glaucoma blindness)
  - side effects
  - allergy
  - pharmacokinetics and pharmacodynamics
- Could early surgical intervention results in better outcomes?
- But, better outcomes for whom?
  - all glaucoma patients?
  - only those who are unstable and rapidly progressing?
  - ophthalmologists?
- Is there evidence? What does it show?

GLAUCOMA INTERVENTIONS

- Laser Peripheral Iridotomy (LPI)
- Selective Laser Trabeculoplasty (SLT)
- Minimally Invasive Glaucoma Surgery (MIGS)
  - trabecular bypass (iStent, Hydrus)
  - [suprachoroidal] (CyPass, iStent Supra)
  - subconjunctival space (Xen)
- [Drug delivery devices]
  - bimatoprost pellets, liposomal latanoprost

1. LASER PERIPHERAL IRIDOTOMY

- All anterior chambers shallow with age
- Can lead to development of narrow angle glaucoma
- Compounds management of open angle glaucoma
  - mixed mechanism
- LPI potential intervention
  - laser now v. angle closure attack later

LASER PERIPHERAL IRIDOTOMY

- Classification:
  - PACS: no TM seen in 2 or more quadrants without indentation
  - PAC: no TM seen in 2 or more quadrants with indentation
  - PACG: PAC with structural and/or functional losses
- ZAP Trial (Zhongshan Angle Closure Prevention Trial)
  - n = 889, PACS in both eyes
  - LPI in one eye, fellow eye acts as control
  - 6 year follow-up, 14 year update
- DFE every year (phenylephrine and tropicamide)
- ZAP Trial aim: how many progressed to PAC?
- Progression defined as
  - IOP >24 mmHg
  - 1 clock hour of PAS
  - A-PAC attack

LASER PERIPHERAL IRIDOTOMY

- ZAP Trial outcomes
- Conversion to PAC: Laser 19 (2%) Control 36 (4%)
- A-PAC attacks: Laser 1 Control 5 (not s/significant)
- A-PAC induced by dilation: Laser 1 Control 2 (not s/significant)
- ZAP Trial Conclusions
  - PAC and PACG are rare events in high risk Asian population with existing PACS
  - LPI did reduce conversion to PAC, but virtually none developed A-PAC or PACG
- ZAP Trial Recommendations
  - No community benefit in LPI intervention
  - Warn of the signs of A-PAC, attend for immediate treatment
  - Possible LPI for those living in remote areas, FOH of angle closure
  - Pupil dilation is *very safe* in PACS: 1 A-PAC attack per 1600 dilations

2. SELECTIVE LASER TRABECULOPLASTY

- Glaucoma primarily occurs due to reduced aqueous outflow
  - not increased aqueous production
- SLT improves TM outflow, “unblocks the drain”
  - tightens trabecular beams
  - clears extra-cellular GAG
  - clears debris via phagocytosis
  - release of pro-inflammatory mediators
- SLT effect similar to PGA drug class
  - IOP lowering efficacy 7-36%
  - Efficacy strongly affected by starting IOP

- Wong MO et al. *Systematic review and meta-analysis on the efficacy of selective laser trabeculoplasty in open-angle glaucoma*. Surv Ophthalmol. 2015 Jan-Feb; 60(1):36-50.

SELECTIVE LASER TRABECULOPLASTY

- Side effects and Complications:
- IOP spike in 5-30% of patients
  - sometimes permanent, requiring trabeculectomy surgery
- Chronic macular edema
- Corneal edema
- PAS formation
- Most require retreatment
  - typically 1 to 3 years

Complication	SLT
IOP Spike	4.5%
PAS Formation	1.1%
ALT treatment within 1 year	3.4%
SLT treatment within 1 year	6.7%
Trabeculectomy within 1 year	9.0%

SELECTIVE LASER TRABECULOPLASTY

- *"Laser in glaucoma and OHT study (LiGHT)"* Gazzard et al, *Lancet* 2019; 393: 1505–16
- n=718, SLT compared to latanoprost in treatment-naive patients
- patients with OHT and early glaucoma only (no NTG, no moderate or severe glaucoma)
- Target IOP set depending on glaucoma severity
- Excluded all co-morbidities
- IOP reduction -7.9 mmHg
- Target IOP achieved: SLT 93% Eye drops 91%
- Trabeculectomy required: SLT Zero Eye drops 11 patients *protocol issue
- CONCLUSION: "Selective laser trabeculoplasty should be offered as a first-line treatment for open angle glaucoma and ocular hypertension, supporting a change in clinical practice."

* SLT/more SLT/drops/more drops/surgery
* Drops/more drops/surgery

SELECTIVE LASER TRABECULOPLASTY

- CONTRARY STUDIES
- *Glaucoma Initial Treatment Study (GITS)"* Ang GS, et al. *Br J Ophthalmol.* 2020 Jun;104(6):813-821.
- n= 145
- Early and moderate POAG, PXF glaucoma (no OHT or NTG cases)
- randomised to SLT v Topical
- Target IOP 25% reduction
- "At month 24, the rate of successful IOP reduction was 18.6% higher in the medication compared with SLT group"

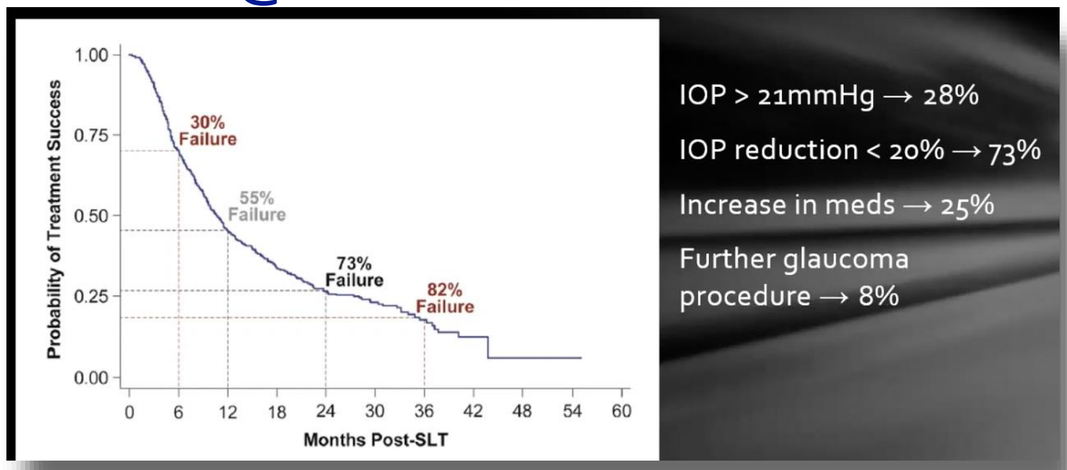
Conclusion: Overall, we did not find evidence that SLT was superior to medication in improving glaucoma-specific QoL. While we found superior IOP reduction in the medication arm, eyelid erythema and conjunctival hyperaemia were more prevalent in these patients compared with the SLT group.

SELECTIVE LASER TRABECULOPLASTY

- *"Peripheral anterior synechiae after selective laser trabeculoplasty among Chinese patients"* Chan JC, et al. Graefes Arch Clin Exp Ophthalmol. May 2022.
- n=509 eyes, Hong Kong Chinese
- All phakic
- 14% developed PAS average 5 years after initial SLT

SELECTIVE LASER TRABECULOPLASTY

- *"Real-World Outcomes of Selective Laser Trabeculoplasty in the United Kingdom"* Khawaja AP, et al. Ophthalmology. June 2020; 127(6):748-757.
- n=831 from 5 major UK eye hospitals, retrospective chart review
- majority OHT/POAG (7% NTG). 37% primary therapy, 63% adjunct therapy
- Drops/laser and target IOP set by clinician, not study protocol
- IOP reduction at 12-18 months: -4.2 mmHg; at 24-36 months: -3.4 mmHg
- Additional glaucoma surgery required in 8% of patients @ 36 months
- SLT treatment failure: 82% at 36 months



SELECTIVE LASER TRABECULOPLASTY

- Comparing “LiGHT” Study and “RealWorld” outcomes
  - Treatment success at 36 months: LiGHT 74%, RealWorld 18%
- Why doesn’t SLT perform as well in clinical practise?
- LiGHT recruited and treated candidates based on protocols
  - lots of OHT, but excluded moderate/advanced glaucoma and NTG
  - excluded ocular co-morbidities
  - excluded secondary risk factors e.g. PXF
  - excluded prior topical treatment
- i.e. not real world clinical glaucoma patients

SELECTIVE LASER TRABECULOPLASTY

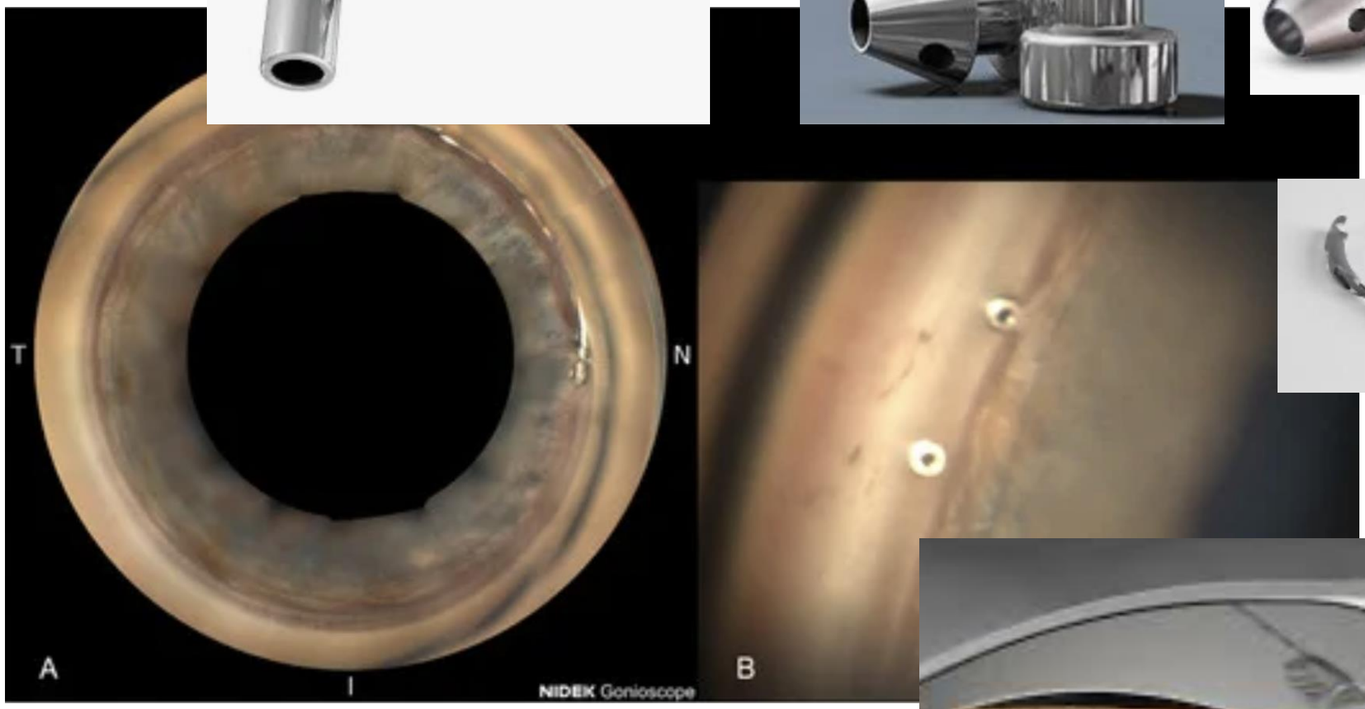
- In real life…SLT lowers IOP 3 to 4 mmHg for about 1-3 years
  - Painless, non-invasive, aids compliance, reduces drop intolerance, prevents allergy
- BUT… SLT not suitable as a primary glaucoma intervention in many patients
- More serious risks compared to topical therapy: permanent IOP spikes, endothelial damage, PAS
- Poor to no efficacy in normal tension glaucoma (majority of glaucomas)
- Unlikely to reach target IOP with SLT alone in real world situations
- Treatment should be *individualised*, not generalised
- SLT makes better sense as adjunct therapy
  - poorly compliant patients
  - simplifying treatment plan
  - drug or preservative allergy
  - medical contraindications

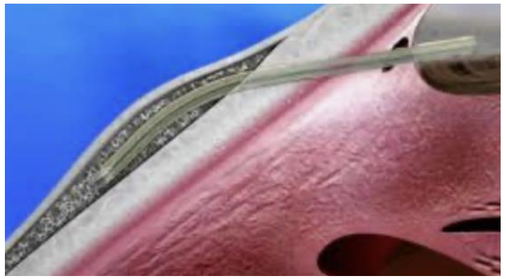
3. MINIMALLY INVASIVE GLAUCOMA SURGERY

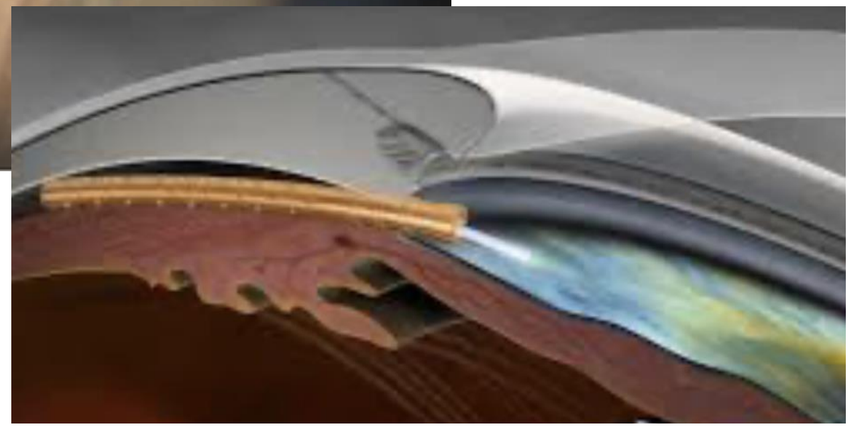
- Intraocular devices or implants
- *ab interno*
- Designed to improve aqueous outflow
- Initial approval only in conjunction with cataract extraction
  - more effective than cataract surgery alone
  - Recent approval for use after previous cataract surgery
- Not approved in phakic eyes
  - induces cataract formation
- Efficacy 25-44% IOP reduction, non-inferior to drops

MINIMALLY INVASIVE GLAUCOMA SURGERY

- 3 designs
  - trabecular bypass
  - supachroidal space
  - subconjunctival space

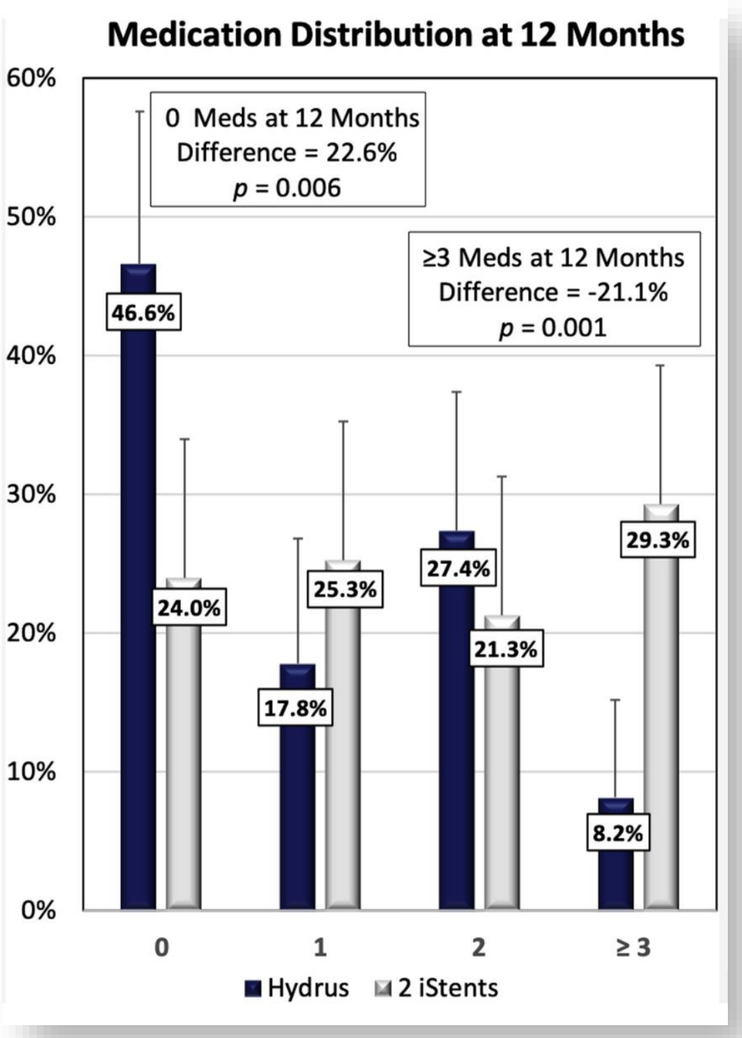






MINIMALLY INVASIVE GLAUCOMA SURGERY

- Strong safety profile, complications similar to cataract surgery
- Adverse events
  - transient inflammation
  - transient IOP spikes
  - transient corneal edema
  - initial hyphaema
  - lumen obstruction (YAG laser)
- No increased corneal endothelial cell loss @ 5 years
- Comparison: Hydrus v. iStent Inject

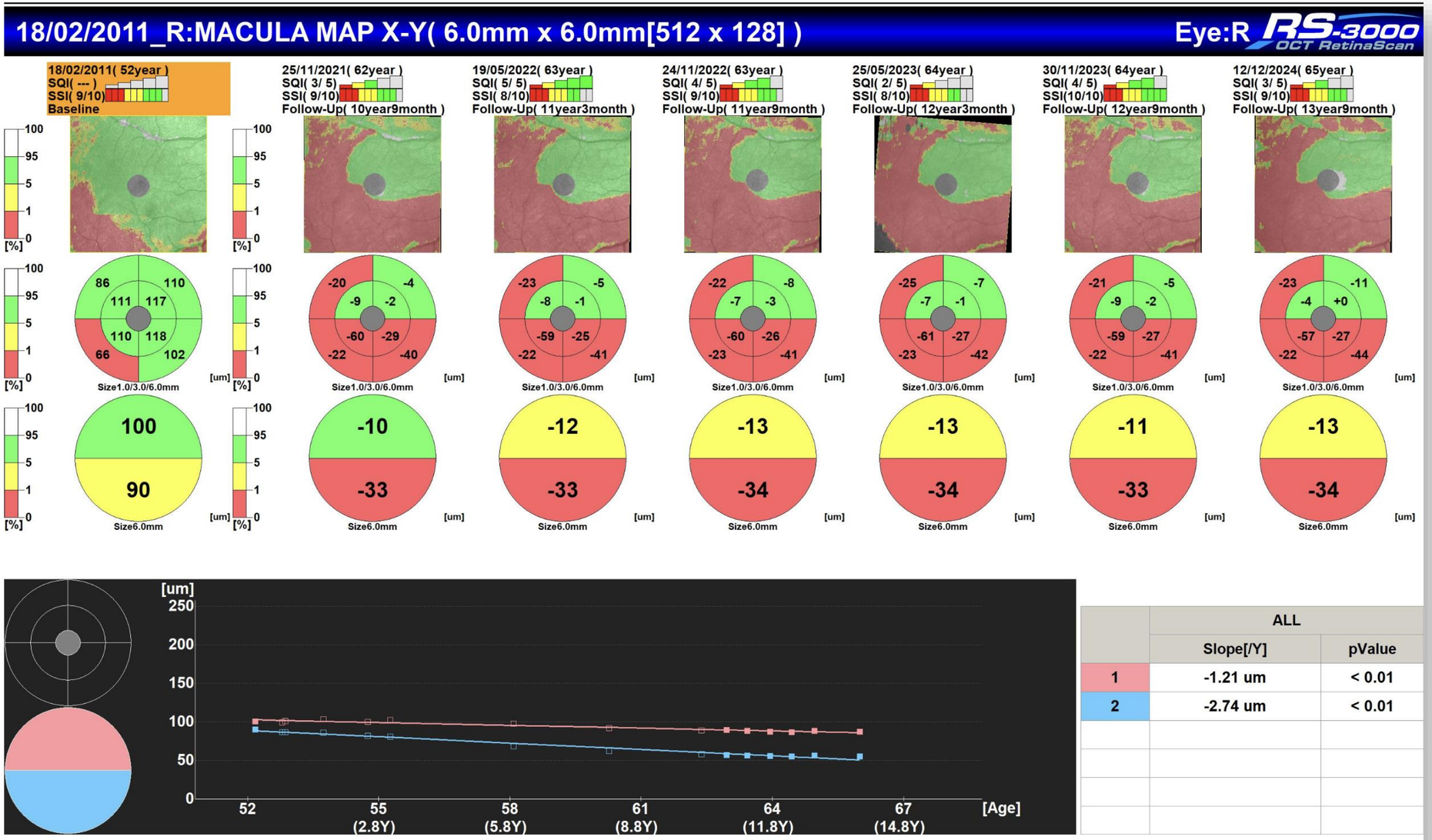


MINIMALLY INVASIVE GLAUCOMA SURGERY

- Real life MIGS experience
- Tricky to insert accurately
  - paralax error
- IOP reduction varies
- Progression rates however often improve
- MIGS results in better diurnal pressures
  - i.e. continuous IOP control v. the rollercoaster of pharmacodynamics

MIGS Case 1

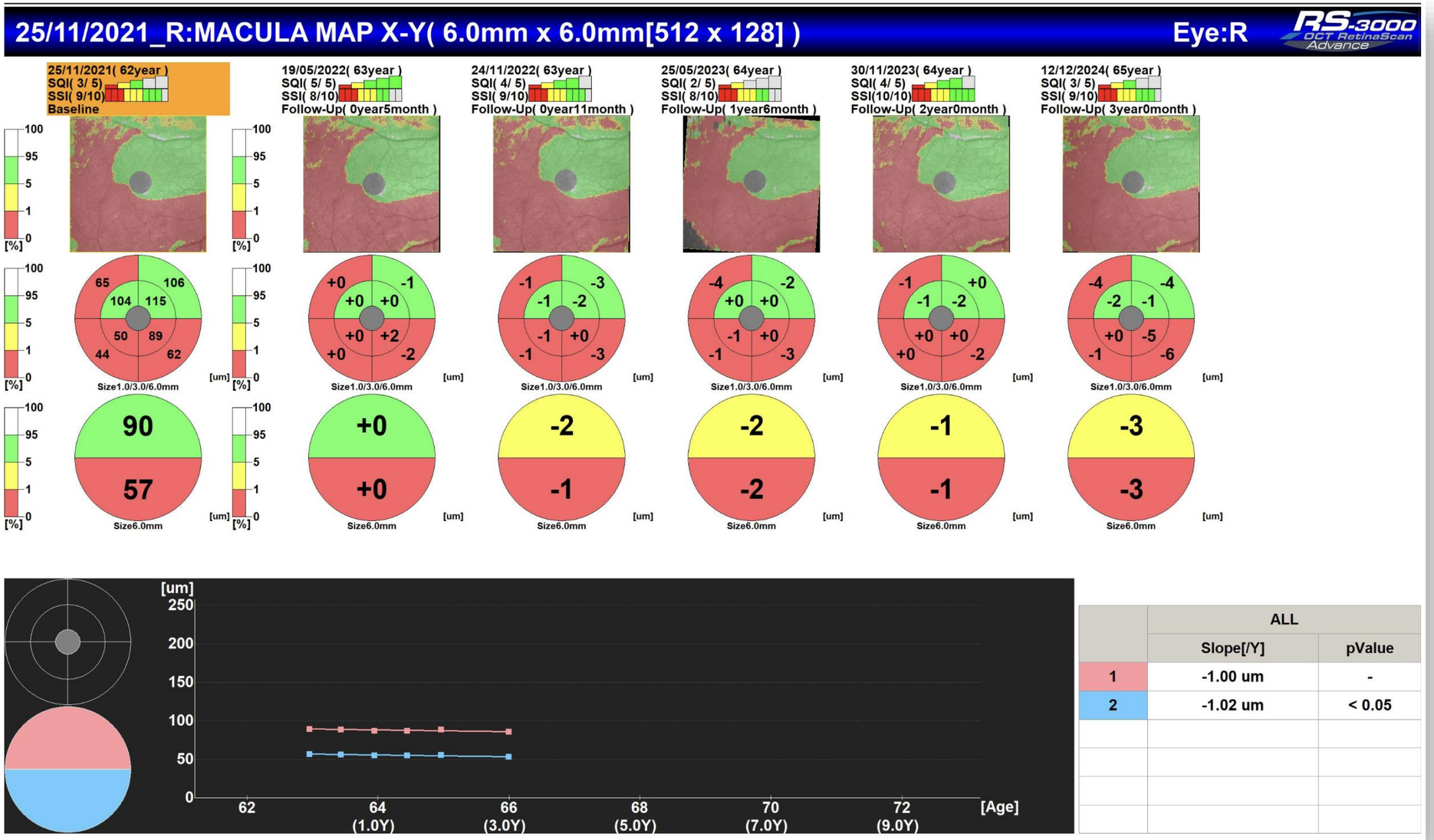
R progression rate since baseline (2011-2024)



	ALL	
	Slope[/Y]	pValue
1	-1.21 um	< 0.01
2	-2.74 um	< 0.01

MIGS Case 1

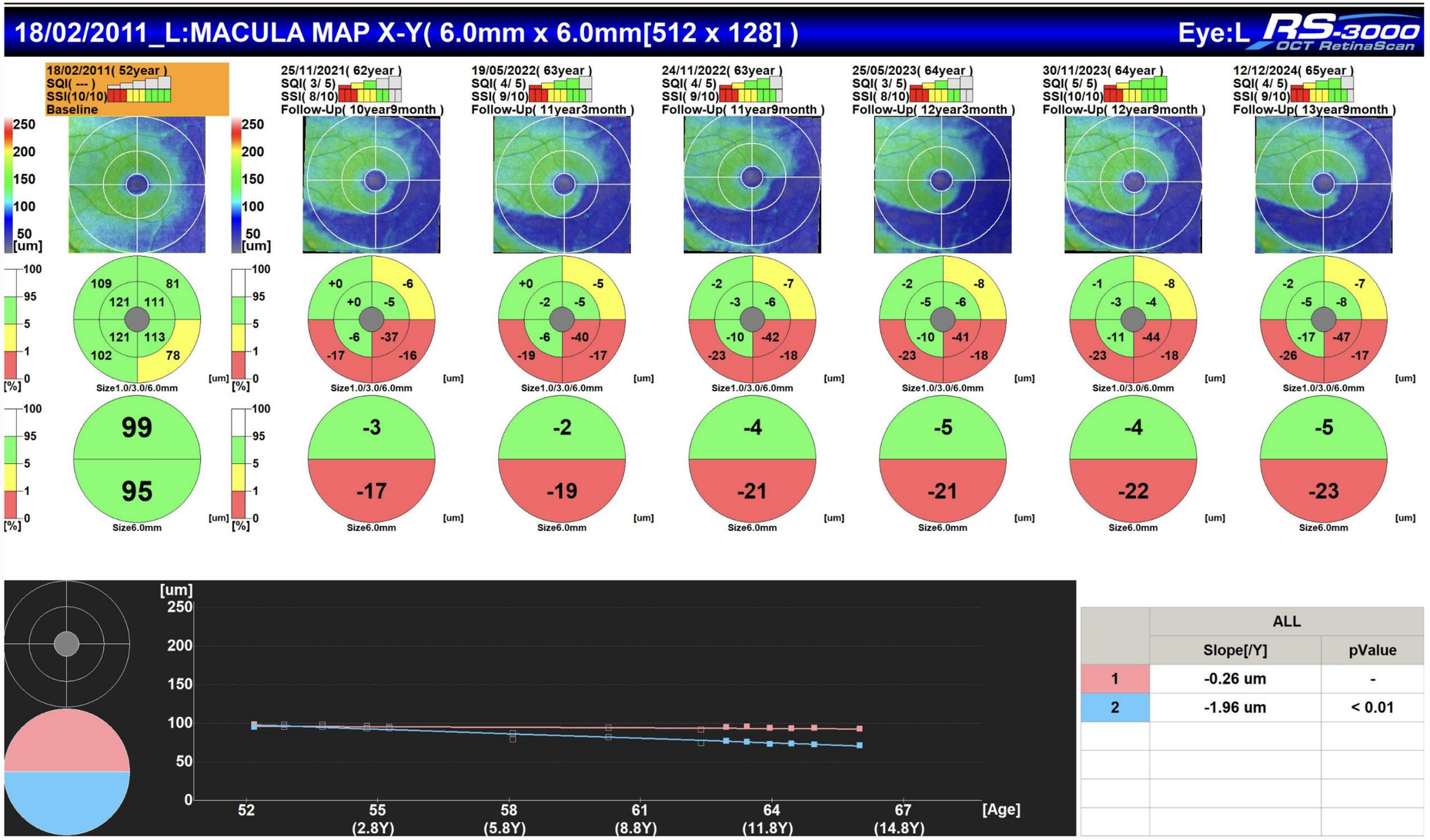
R progression rate since iStent Inject (2021-2024)



	ALL	
	Slope[/Y]	pValue
1	-1.00 um	-
2	-1.02 um	< 0.05

MIGS Case 1

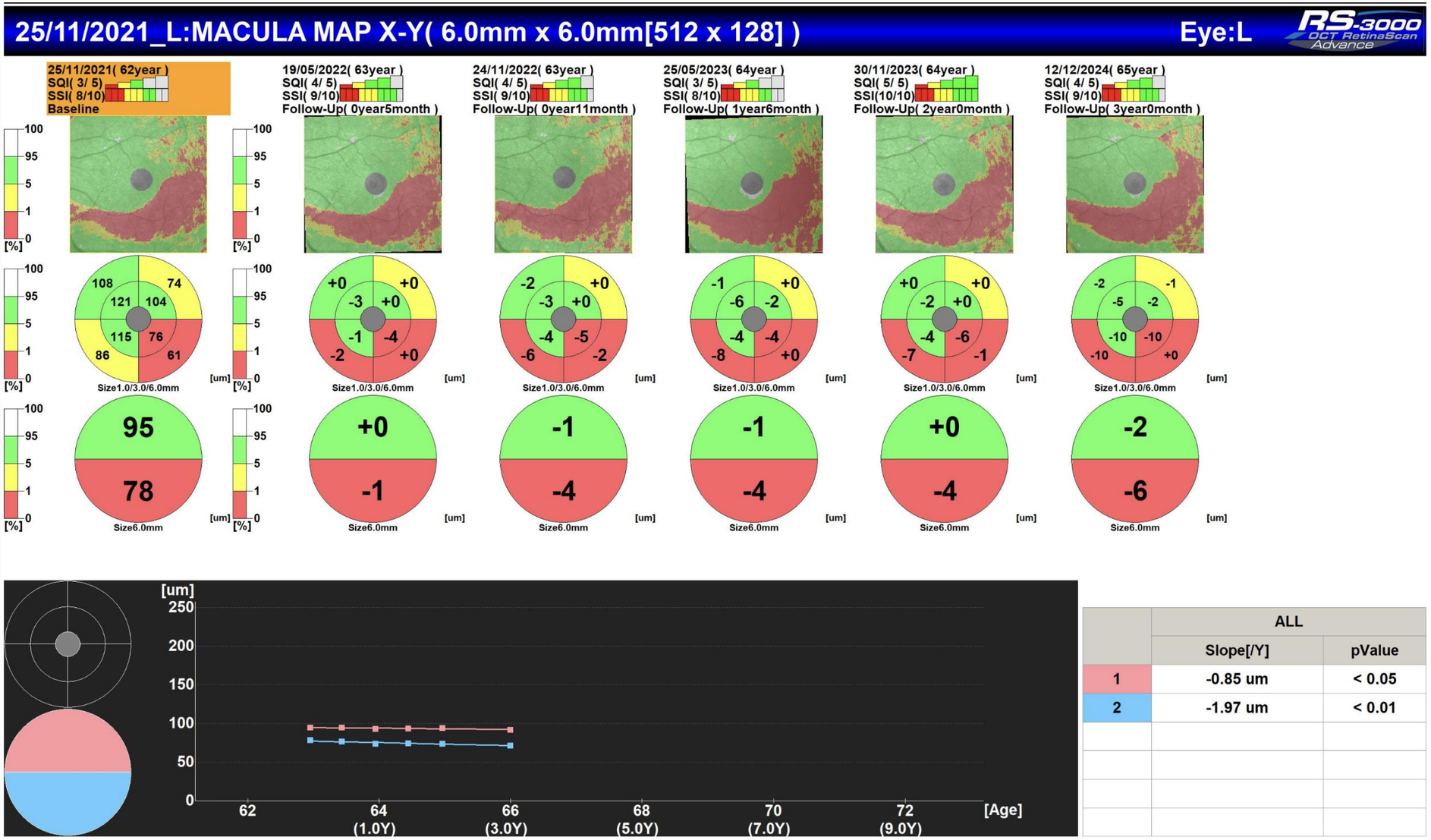
L progression rate since baseline (2011-2024)



	ALL	
	Slope[/Y]	pValue
1	-0.26 um	-
2	-1.96 um	< 0.01

MIGS Case 1

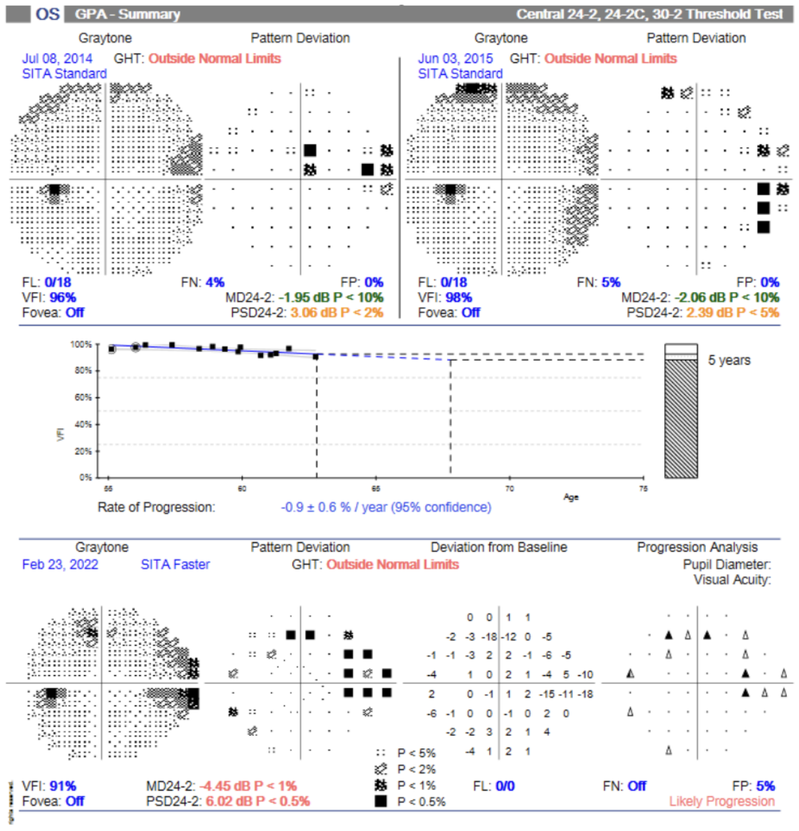
L progression rate after cataract surgery (2021-2024)

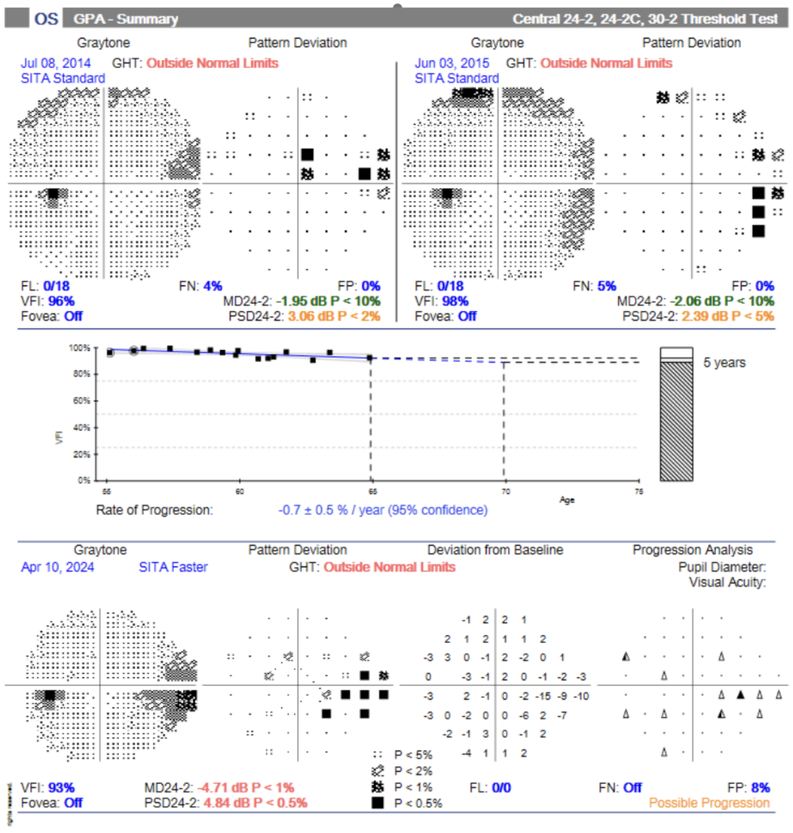


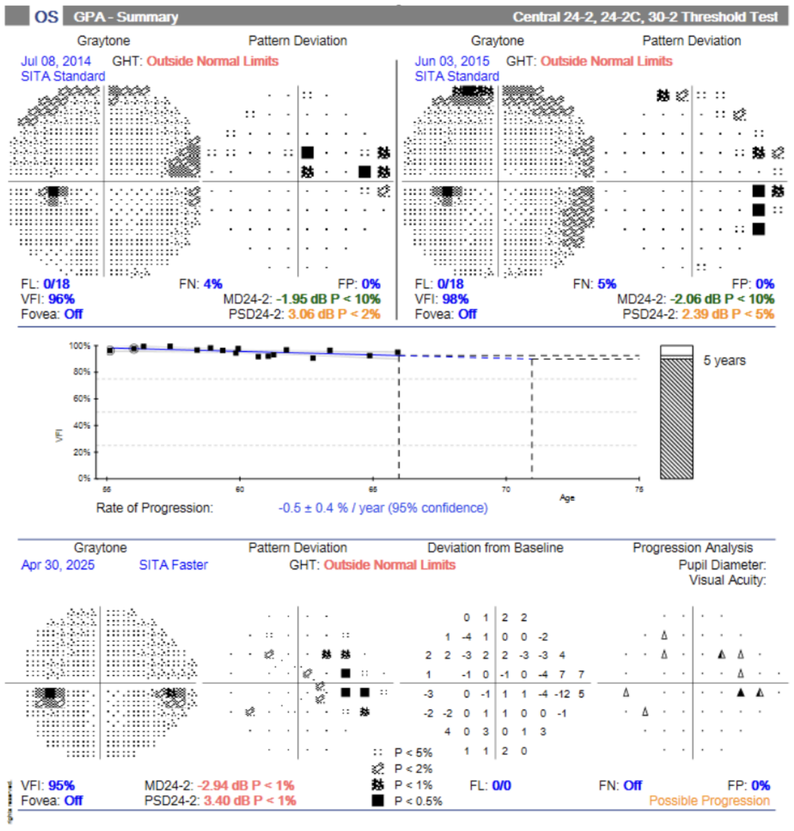
	ALL	
	Slope[/Y]	pValue
1	-0.85 um	< 0.05
2	-1.97 um	< 0.01

MIGS Case 2

R progression ratec(2014-2025)
iStent Inject in 2022.







CONCLUSION

- Interventional Glaucoma
  - PRO's: compliance, side effects, diurnal control, better stability, long term cost?
  - CON's: unnecessary procedures, bad outcomes, long term cost?
- Real life scenario
  - early disease in older age: no surgical intervention required
  - good clinicians can detect rapid progressors in 2-3 years
  - prior to major ganglion cell loss
    - refer for intervention e.g. MIGS
- Individualised therapy v. population-wide strategies

THANK YOU !

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